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INVITED SPEAKERS

ACADEMY OF AUTOIMMUNITY - AUTOIMMUNITY UP-TO-DATE

17-05-2024 12:15 - 17:15

IS001 / #896

Autoimmunity vs Autoinflammation: Same or Different?

Zoltan Szekanecz
Department of Rheumatology, University of Debrecen, Faculty of Medicine, Debrecen, Hungary

Most rheumatic and musculoskeletal diseases (RMDs) can be placed along a spectrum of disorders, with autoinflammatory diseases (including monogenic systemic autoinflammatory diseases) and autoimmune diseases (such as systemic lupus erythematosus and antiphospholipid syndrome) representing the two ends of this spectrum. However, although most autoinflammatory diseases are characterized by the activation of innate immunity and inflammasomes and classical autoimmunity typically involves adaptive immune responses, there is some overlap in the features of autoimmunity and autoinflammation in RMDs. Indeed, some 'mixed- pattern' diseases such as spondyloarthritis and some forms of rheumatoid arthritis can also be delineated. A better understanding of the pathogenic pathways of autoinflammation and autoimmunity in RMDs, as well as the preferential cytokine patterns observed in these diseases, could help us to design targeted treatment strategies.

IS002 / #897

Regulatory T Cells and Autoimmunity

Mitesh Dwivedi
C. G. Bhakta Institute of Biotechnology, Uka Tarsadia University, Bardoli, India

Regulatory T cells (Tregs) are critical for the maintenance of immune cell homeostasis. Treg cells maintain order in the immune system by enforcing a dominant negative regulation. Treg cells can target both innate and acquired immunity by modulating various immune cells including neutrophils, monocytes, antigen-presenting cells, B cells, and T cells. Treg cells have become the emerging field of interest as their altered numbers and dysfunction can lead to devastating human diseases including various autoimmune diseases. Here we shall discuss the different types of Treg cells, their distinct immunosuppressive mechanisms, role of Treg cell markers and implications of Treg cells in inducing autoimmunity.

IS003 / #900

Primary Biliary Cholangitis (PBC)-A Classical Autoimmune Disease

Ehud Zigmond
Liver Diseases Center, Sheba Medical Center, Ramat Gan, Israel

Primary biliary cholangitis (PBC) is a prototypic autoimmune liver disease characterized by female predominance, destructive lymphocytic cholangitis and specific anti-mitochondrial antibodies (AMAs) and T cells targeted at well-defined mitochondrial autoantigens- primarily the E2 subunit of the pyruvate dehydrogenase complex E2 (PDC-E2). The etiology of PBC is unclear, and involves a combination of environmental, infectious, genetic, epigenetic, metabolic and immunological factors. There is a debate in the hepatologists community weather the break of immunological tolerance initiating the disease is caused due to primary dysfunction of the biliary epithelium or due to a hyper activity of the immune system directed against the biliary epithelium that serve as an innocent bystander. Interestingly, immunosuppression, including corticosteroids has limited therapeutic effect in PBC while drugs that presumably affect bile metabolism like Ursodexoycholic acid, FXR agonists and PPAR agonists proved to be beneficial. Interestingly, new evidences suggest that an immune modulatory mechanism of these medications may be responsible for the favorable effect on disease activity. The importance of the innate immune system in the pathogenesis of PBC is largely unknown. Intriguingly, many genes revealed by genome-wide association studies (GWAS) to be associated with PBC are expressed specifically by innate immune cells. Several of these genes including IL12A, IL12RB2, STAT4, IRF5, CD80, IL7R and SPIB are known to be important for the differentiation and function of macrophages and dendritic cells. Our lab has recently explored the role of macrophages and specific type of dendritic cells in a pre-clinical model of PBC and revealed a crucial role for these cells in disease development. These results may pave the road for the development of new immune-based and cell specific therapeutic modalities for PBC patients not responding to current therapies.

IS004 / #901

Thyroid Autoimmunity in Other Autoimmune Diseases

Poupak Fallahi[1], Giusy Elia[2], Francesca Ragusa[2], Valeria Mazzi[2], Eugenia Balestri[2], Chiara Botrini[2], Licia Rugani[2], Emilio Barozzi[2], Armando Patrizio[3], Yehuda Shoenfeld[4], Alessandro Antonelli[2], Silvia Martina Ferrari[5]
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[2]Department of Surgical, Medical, Molecular Pathology and Critical Area, University of Pisa, Pisa, Italy
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Thyroid autoimmunity (TA) and thyroid dysfunctions have been shown in patients with other organ specific and systemic autoimmune diseases (SAD). Autoimmune thyroid diseases are organ-specific autoimmune disorders whose main clinical presentations are Hashimoto's thyroiditis

(HT), or Graves' disease (GD). Most of the studies present in the literature show a high prevalence, and incidence, of new cases of hypothyroidism and TA in patients with systemic lupus erythematosus (SLE), systemic sclerosis (SS), Sjögren syndrome, rheumatoid arthritis and mixed cryoglobulinemia (MC), overall in the female gender. A limited number of cases of Graves' disease have been also reported in SAD patients, in agreement with the higher prevalence of TA. It has been also demonstrated that a Th1 predominance is associated with TA in SAD patients. Furthermore, a higher prevalence of papillary thyroid cancer has been recently reported in SLE, in SS and in MC patients, particularly in the presence of TA. Data from literature strongly suggest that female SAD patients, with a high risk of TA (a normal but at the higher limit thyroid-stimulating hormone value, positive antithyroid peroxidase antibodies, a hypoechoic pattern, and small thyroid), should undergo periodic thyroid function follow-up and thyroid ultrasonography, and appropriate treatments when needed. On the whole, a careful thyroid monitoring would be opportune during the follow-up of these patients.

IS005 / #903

Comorbidities in Autoimmune Diseases- State of The Art. Lessons Learnt from Big Data Analyses

Howard Amital
Department of Internal Medicine B & Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Ramat Gan, Israel

While it is believed that the Holy Grail of clinical studies are randomized controlled prospective studies, they also carry drawbacks. Many of these studies do not represent the entire population due to biases caused by stringent inclusion and exclusion criteria. In contrast "real life" databases analysis of medical insurances provide a more reliable representation of all strata of society. Such studies also help us to understand the impact of logistical issues such as drug adherence, anthropometric data such as weight, height, or sex on various clinical outcomes. Analysis of large databases also confers an interesting opportunity to follow the effects of various exposures on an immense number of subjects throughout a considerable amount of time. In this presentation I will also mention the significance of drug adherence patterns on clinical outcomes and of serological characteristics on the emergence of different aspects of autoimmune disorders.

IS006 / #904

Ivig as Panacea in Autoimmune Diseases

Maria Giovanna Danieli[1,2]
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[2]Sos Immunologia Delle Malattie Rare E Dei Trapianti, AOU delle Marche, Ancona, Italy

Intravenous immunoglobulin (IVIg) is a polyclonal medical preparation of human IgG derived from the blood of human donors and used in the first instance for the treatment of humoral immunodeficiencies. It is a safe therapy, well tolerated by the patient. IVIg also appears to have a powerful immunomodulatory effect. For this reason, it is used for treating inflammatory and autoimmune diseases with excellent results. The mechanisms of action are different: modulation of the function of Fc receptors, regulation of the activity of T and B lymphocytes, inhibition of complement, and neutralization of pathogenic antibodies. Treatment with immunoglobulins also has positive effects on remyelination mechanisms, and this would explain the effectiveness of the treatment of demyelinating pathologies. Today, there are many pathological conditions in which IVIg determines a clinical benefit and for which it is indicated. Could IVIg be the panacea for all ills? In this literature review, we search for the applications known so far, analyze the mechanisms of action involved, and evaluate the state of the art and possible future applications.

IS007 / #942

Skin Autoimmune Diseases

Abdul Razzaque Ahmed
Department of Dermatology, Tufts University School of Medicine, Boston, United States of America

Autoimmune Diseases of the Skin This session will address two issues. First section will describe autoimmune diseases that primarily involve the skin. These will be divided into bullous and non-bullous diseases. The second section will discuss cutaneous manifestations of system autoimmune diseases. Autoimmune bullous disease are a distant group because any of them are potentially fatal, have distinct histology, immunopathology and serological features. These are primarily intraepidermal which include the pemphigus group. The subepidermal include several clinical entities including the pemphigoid diseases, epidermolysis bullosa acquisita, Dermatitis herpetiformis and others. Other autoimmune diseases with only cutaneous manifestations may include morphea (scleroderma), discoid lupus erythematosus, Henoch-Schönlein purpura, and others. Cutaneous manifestation may occur in patients with rheumatoid arthritis, systemic lupus erythematosus, scleroderma, dermatomycosis, immune thrombocytopenia, ulcerative colitis, and Sjogren syndrome.

IS008 / #944

Prediction in Autoimmunity

Luis Eduardo Andrade
Division of Internal Medicine / Rheumatology, Universidade Federal de São Paulo, São Paulo, Brazil

Systemic and organ-specific autoimmune diseases cause considerable morbidity and mortality in all ethnic groups, age strata, and geographic areas, with increasing incidence along the last decades. Despite demographic and clinical peculiarities, autoimmune diseases share some fundamental elements. First, there is considerable heterogeneity among patients across the spectrum of clinical severity. Second, there are periods of disease activity intercalated with periods of disease remission. Third, there are disease-specific immunogenetic associations of variable strength across the different autoimmune diseases. Fourth, there are autoantibodies that vary in frequency and disease specificity in each autoimmune disease. Fifth, the autoantibodies precede the clinical onset of the diseases by months or years. At the individual level there is a considerable degree of uncertainty on several aspects of autoimmunity, such as the probability of development of an autoimmune disease, the severity and phenotypic features of the disease, the disease activity state, and the probability of response to a given therapeutic approach. Although the absolute prediction of outcome of these variables in the individual patient is currently not possible, there are several elements that can contribute to narrow down the probabilities, allowing for an educated guess aiming to the best management of the patient. In the investigation of a supposedly autoimmune individual, the family history an important clues, as first-degree relatives of autoimmune patients have increased prevalence of autoimmune diseases. The patient's own clinical history may also help as some autoimmune diseases tend to aggregate in the same patient, e.g., type 1 diabetes mellitus (DM1) and celiac disease (CeD). Individuals with some forms of primary immunodeficiency (e.g., chronic granulomatous disease, selective IgA deficiency or deficiency of early components of the complement classic pathway) are more susceptible to the development of

systemic lupus erythematosus (SLE) and other autoimmune diseases. Immunogenetics can also be of help as some alleles are strongly associated with some autoimmune diseases with clinical application in some cases, such as the presence of the HLA-B27 allele favoring the diagnosis of ankylosing spondylitis and the absence of HLA-DQ2/HLADQ-8 or HLA-B29 in the exclusion of celiac disease and birdshot uveitis, respectively. Autoantibodies are also useful in the investigation of individuals suspected of autoimmune diseases because several of the disease-specific autoantibodies are detected already at the early stages of disease. Therefore, when considering an individual with ill-defined clinical features potentially related to an autoimmune disease, a comprehensive clinical and familial history, autoantibody determination, and immunogenetic analysis can contribute to assessing the odds of actual disease or the development of full-blown disease in the future. Another source of uncertainty in autoimmunity is the degree of severity and the spectrum of phenotypic features of the disease in a given individual. Immunogenetic and autoantibody associations can be helpful in estimating these two variables. For example, rheumatoid arthritis (RA) has a wide spectrum of severity from mild and non-erosive synovitis at one end of the spectrum to rapidly erosive and destructive polyarthritis at the other end of the spectrum. In addition, some patients show only arthritis whereas some others show extensive extra-articular manifestations including interstitial pneumonitis, pleuritis, pericarditis, and systemic vasculitis. The presence of shared-epitope HLA-DRB1 alleles (especially in double dose) and high titer autoantibodies to IgG-Fc (rheumatoid arthritis) and citrullinated peptides (ACPA) is strongly associated with severe disease with extra-articular involvement. In patients presenting with autoimmune myositis, over a dozen autoantibodies help in the assessment of the probabilities of development of different clinical manifestations (e.g., skin lesions, interstitial lung disease, muscle necrosis, and soft tissue calcinosis) as well of an underlying malignant disease. An analogous situation applies to systemic sclerosis. Several autoimmune diseases are characterized by temporal fluctuation in the degree of disease activity. Prompt therapy at the earliest stages of disease reactivation contributes to the therapeutic success and minimization of target organ accrual damage. Prediction of impending disease activity would be helpful in allowing the implementation of early therapy. In this regard, some autoantibodies may be helpful, as their serum levels tend to correlate with disease activity. Classically, the serum level of anti-dsDNA and anti-nucleosome antibodies tend to increase early in the reactivation of proliferative lupus nephritis and tend to decrease or disappear as the nephritic process wanes. Other examples of such phenomenon include anti-PLA2R antibodies and primary membranous glomerulonephritis, anti-PR3 and granulomatosis with polyangiitis, anti-aquaporin 4 antibodies and neuromyelitis optica, and anti-basal glomerular membrane antibodies and Goodpasture disease. In contrast, several other autoantibodies show no consistent correlation with disease activity and are not used for monitoring impending disease activity. Finally, autoimmune patients are known to present heterogeneous therapeutic response to any given pharmacologic approach. As a result, clinicians often apply a try and error approach seeking for the optimal choice for a given patient. The identification of guiding parameters for the a priori selection of the pharmacologic therapy would be of great value. Preliminary evidence is already available for such a model in some diseases. For example, SLE patients presenting high type I IFN signature are more prone to respond to JAK inhibitors and RA patients presenting high titer rheumatoid factor and ACPA are more prone to respond to rituximab. The ability to predict several relevant aspects in autoimmune diseases is of utmost importance and object of intense research for several decades. There is consistent evidence for the prediction ability of several fragmentary parameters, which help decreasing the uncertainty in different aspects of autoimmunity. In parallel with continuing efforts to the discovery of novel such parameters, the next step is the development of multiparameter algorithms integrating immunogenetics, autoantibodies, and cytokines, aiming towards a more assertive prediction degree. Big data analysis coupled to machine learning should be instrumental to this endeavor.

PLENARY 01

18-05-2024 08:00 - 09:30

IS009 / #920

Uveitis in Autoimmune Diseases- Why The Uvea is so Prevalently Involved

Vicktoria (Vicky) Vishnevskia-Dai
The Goldschleger Eye Institute, Sheba Medical Center,- Tel-Aviv University, Faculty of Medicine, Qiriyat Ono, Israel

Uveitis is a group of ocular inflammatory diseases affecting the uvea. It is one of the leading causes of preventable vision loss in the western world and its diagnosis is still challenging. The uvea, builds the middle layer of the globe and is consists of the iris, ciliary body, and choroid. The uvea is particularly susceptible to inflammation in autoimmune diseases due to several factors: The uvea is highly vascularized, allowing access to the immune cells and antibodies that are involved in autoimmune responses. Although the eye is generally considered an immune-privileged site, the uvea has specific characteristics that can trigger immune responses. It is hypothesis that presence of certain antigens in the uvea may attract immune cells antibodies and cytokines contribute to inflammation. Moreover, mechanisms like molecular mimicry or antigenic similarity may exist between components of the uvea and components of the immune system. This similarity can lead to the immune system mistakenly attacking the uvea when it is targeting a perceived threat elsewhere in the body. In addition, there is evidence to suggest that genetic factors play a role in the development of uveitis in autoimmune diseases. And finally environmental factors, such as infections or other external stimuli, may contribute to the development of autoimmune responses in the uvea. Common autoimmune conditions associated with uveitis include rheumatoid arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, systemic lupus erythematosus and others. Management of uveitis in the context of autoimmune diseases often involves treating the underlying autoimmune condition and addressing the inflammation in the eye with medications such as corticosteroids and immunomodulatory medications. Early detection and prompt definitive treatment are crucial to prevent complications and preserve vision.

IS010 / #49

What's Still Unresolved in Hughes Syndrome / Anti Phospholipid Syndrome

Graham Hughes
London Lupus Centre, London Bridge Hospital, London, United Kingdom

Hughes Syndrome (the antiphospholipid syndrome) is now 40 years old and recognised worldwide.

However, many aspects remain poorly defined – the detailed thrombotic pathway and the precise treatment options, to give 2 examples.

This presentation focusses on some of the clinical features of the disease and its importance in various specialties, such as cardiology, orthopaedics and neurology.

IS011 / #50

Genetic Predisposition to Autoimmunity and Autoinflammation

Bodo Grimbacher, Michele Proietti, Máté Krausz
Institute for Immunodeficiency, University Hospital Freiburg, Freiburg, Germany

CTLA-4 insufficiency is a monogenetic condition caused by heterozygous mutations in *CTLA4* that is characterized by immune dysregulation, including autoimmune enteropathy. The disease presents with a reduced (~70%) penetrance, so we hypothesized that affected and unaffected *CTLA4* mutation carriers have distinct intestinal microbiome signatures compared to each other and to healthy controls, and that the microbiome may identify patients with disease-related organ involvements. We collected stool samples and clinical data from healthy donors (HDs, n=178), affected (n=33) and unaffected CTLA-4 patients (n=8) and performed 16S rRNA sequencing. We also compared samples from patients with and without a history of specific organ involvement (enteropathy, splenomegaly, lymphadenopathy, GLILD). Affected patients had a significantly decreased alpha-diversity (Shannon), compared to unaffected carriers and HDs. Moreover, CTLA-4 patients with a history of specific organ involvement had decreased alpha-diversity (not significant). Additionally, we identified significantly different taxa in affected and unaffected CTLA-4 mutation carriers. We found that the Proteobacteria were significantly enriched in affected patients, compared to unaffected carriers and controls. Furthermore, we could identify various taxa that are the main drivers of the differences between affected and unaffected mutation carriers. In affected individuals Veillonella, Escherichia, and Haemophilus were enriched, in unaffected individuals Ruminococcaceae, Tenericutes, and Lachnospiraceae were expanded. Some of these taxa are known to be correlated with inflammatory bowel disease. Here we show, that affected *CTLA4* mutation carriers have distinct intestinal microbiome structures, and that the microbiome may be a relevant disease modifier. Our results could serve as a basis for further interventional studies.

PLENARY 01 (CONT.): CHALLENGE THE EXPERT

18-05-2024 09:30 - 10:00

IS012 / #51

CT vs. MRI. Who Needs CT When There is MRI? Is There a Future for CT Imaging?

Iris Eshed
Sheba Medical Center, Ramat Gan, Israel

Both CT and MRI exhibit distinct strengths and weaknesses, and comprehending their nuances is crucial for optimizing diagnostic approaches in modern medicine. On one hand, MRI, renowned for its unparalleled soft tissue contrast and absence of ionizing radiation, poses challenges related to examination duration, patient discomfort, and non-compatibility with certain body implants—disadvantages that, despite technological advancements, remain unresolved. On the other hand, CT imaging, known for its rapid acquisition of detailed cross-sectional images, has traditionally been associated with high radiation exposure. However, with the introduction of advanced CT units, contemporary technology has significantly reduced radiation doses. These advancements often rival or even surpass those associated with conventional X-ray procedures. This presentation aims to provide insights into the evolving roles of CT and MRI, acknowledging their respective strengths and weaknesses. Additionally, it contemplates the future trajectory of CT imaging within the context of emerging technological advancements and enhanced radiation safety measures.

IS013 / #52

Diffuse Idiopathic Skeletal Hyperostosis, Is It an Inflammatory Disease?

Iris Eshed
Sheba Medical Center, Ramat Gan, Israel

Diffuse Idiopathic Skeletal Hyperostosis (DISH), traditionally viewed as non-inflammatory, is reconsidered in this review. While DISH is characterized by entheseal new bone formation in the axial skeleton, recent evidence suggests potential inflammatory aspects, challenging the notion of a purely metabolic etiology. Shared features with spondyloarthritis (SpA), including enthesitis and new bone formation, raise questions about the inflammatory nature of DISH. Imaging studies reveal similarities between DISH and SpA, suggesting a potential overlap in inflammatory processes. Genetic factors, such as familial occurrences and specific gene associations, hint at a genetic basis for DISH. Increased visceral fat in DISH and SpA may contribute to low adiponectin levels, promoting inflammation and new bone formation. Angiogenesis emerges as a common link between DISH and chronic conditions, influencing inflammatory processes and bone remodeling. In conclusion, DISH's pathogenesis remains unclear, with metabolic and possibly inflammatory aspects requiring further exploration. The distinction between these pathways is crucial for future therapeutic interventions.

IS014 / #924

Is There a Difference between SAPHO (Sacroiliitis, Acne Pustulosis, Hyperostosis, Osteits) and CRMO (Chronic Relapsing Multifocal Osteomyelitis)?

Iris Eshed
Sheba Medical Center, Ramat Gan, Israel

This presentation delves into the nuanced distinctions between Chronic Recurrent Multifocal Osteomyelitis (CRMO) and SAPHO syndrome (Sacroiliitis, Acne, Pustulosis, Hyperostosis, Osteitis), underscoring the pivotal role of advanced imaging techniques in achieving precise diagnoses. CRMO, characterized by recurrent non-infectious inflammation affecting multiple bones, contrasts with SAPHO, which combines osteoarticular inflammation with dermatological manifestations. Radiological findings highlight the significance of MRI in identifying multifocal lesions in CRMO and spotlight imaging modalities revealing hyperostosis and osteitis, especially in the sternoclavicular region, for SAPHO. Additionally, age plays a crucial role, as CRMO often manifests in the pediatric population, while SAPHO is more prevalent in adults. It is imperative to distinguish between these conditions, considering both clinical and imaging aspects, as treatment strategies significantly differ. This presentation underscores the indispensable role of cutting-edge imaging in delineating the distinctive features of CRMO and SAPHO syndrome, enabling clinicians to enhance diagnostic precision and tailor therapeutic strategies for optimal patient outcomes.

PARALLEL SESSION 01: APS - WHAT'S NEW IN ANTIPHOSPHOLIPID SYNDROME?

18-05-2024 10:30 - 12:00

IS015 / #54

New Classification Criteria for The Antiphospholipid Syndrome

Ricard Cervera
Autoimmune Diseases, Hospital Clínic, Barcelona, Spain

Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterised by arterial,

venous, or microvascular thrombosis, pregnancy morbidity, or nonthrombotic manifestations in patients with persistent antiphospholipid antibodies (aPL). Classification of APS, for the identification of homogeneous research cohorts, was based on the Sapporo criteria published in 1999 and revised in 2006. The revised Sapporo criteria for APS require clinical features (thrombosis or pregnancy morbidity) and laboratory tests (for lupus anticoagulant (LAC), IgG/IgM anticardiolipin antibodies (aCL), and/or IgG/IgM anti–β2-glycoprotein I antibodies [anti-β2GPI]) with at least 2 aPL tests performed at least 12 weeks apart. Since the introduction of the Sapporo criteria, advancements in our understanding of APS include better characterisation of aPL-associated nonthrombotic clinical manifestations, identification of the role of traditional thrombosis risk factors in aPL-positive individuals, and risk stratification by aPL profile. Given the limitations of the previous criteria, an international effort, jointly supported by the American College of Rheumatology (ACR) and EULAR, was recently performed with the goal of using rigorous methodology to develop a new APS classification system based on a more modern disease understanding, allowing for the weighting of individual criterion, and demonstrating excellent operating characteristics with the highest possible specificity.

IS016 / #933

Do The Last Classification Criteria Change Our Routine Approach to Anti Phospholipid Syndrome?

Pier Luigi Meroni[1], Claudia Grossi[1], Maria Borghi[2]

[1]Immunorheumatology Research Laboratory, IRCCS Istituto Auxologico Italiano, Cusano Milanino, Milan, Italy
[2]Clin Sci And Community Health, University of Milan, Milan, Italy

There are three tests commonly used to detect anti-phospholipid antibodies (aPL): Lupus Anticoagulant (LAC), which is a functional coagulation test, and anti-cardiolipi (aCL) and anti-β2-glycoprotein-I (β2GPI), which are solid phase techniques. These tests are used both for classification and diagnosis purposes, and the results can help predict the risk of clinical manifestations of the disease. The new ACR/EULAR APS classification criteria require at least one positive aPL test within three years after an aPL-associated clinical criterion, followed by weighted criteria clustered into six clinical and two laboratory domains (LAC, and aCL and/or anti-β2GPI IgG/M detected by ELISA). Patients who accumulate at least three points from clinical and laboratory domains are diagnosed with APS. The solid phase assays (SpA) for aPL detection were originally represented by RIA and then by ELISA and FEIA. Despite the effort to standardize both ELISA and FEIA, the harmonization of the aPL SpA is still incomplete. Recently, the Luminex and chemiluminescence (CLIA) techniques offered better feasibility and reproducibility but displayed different results because of increased sensitivity. The new techniques' main issue is interpreting the clinical meaning of aPL levels close to the cutoff established for ELISA and FEIA. This is important since the new ACR/EULAR APS classification criteria include medium/high aPL levels according to the values detectable by ELISA. Due to the increasing use of new techniques, there is a need for correct clinical interpretation of the results based on the comparison between different methods. β2GPI-dependent aPL is widely accepted as the clue antibodies in APS. The new classification criteria require combined positivity for aCL and anti-β2GPI assays. The Committee on Harmonization of Autoimmune Testing of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), in collaboration with the Joint Research Institute of the European Commission, developed a certified reference material (CRM) with an assigned property value (anti-β2GPI IgG antibodies concentration in a matrix material). The CRM is commutable and can serve as a quality control of anti-β2GPI IgG measurements and/or for the calibration of immunoassays.

IS017 / #56

Time to Treat to Target in Aps

Savino Sciascia

University Center of Excellence on Nephrological, Rheumatological and Rare Diseases (ERK-net, ERN-Reconnect and RITA-ERN Member) including Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the, Torino, Italy

This review will examine the novel therapeutic targets that are presently being investigated for the development of safer and more tailored therapeutics for clinical symptoms mediated by antiphospholipid antibodies (aPL). Potential novel therapy strategies that could be considered include monoclonal antibodies targeting CD20, anti-BAFF and anti-CD38. Current research is investigating methods to disrupt cell activation mediated by aPL, targeting specific components of the complement system, and exploring the novel approach of employing customized peptides to prevent the pathogenic subset of aPL. Antiphospholipid syndrome (APS) is an autoimmune disorder that is distinguished by the presence of thrombosis and pregnancy complications in individuals who consistently test positive for antiphospholipid antibodies (aPL). The existing treatment choices are limited to the administration of vitamin K antagonists for long-term anticoagulation. The future exhibits considerable potential with the discovery of new prospective targets, a significant portion of which are presently undergoing examination. The primary task at hand will involve formulating prospective randomized controlled clinical trials in order to get the requisite evidence that will substantiate the incorporation of these medicines into clinical practice.

IS018 / #57

Implementation of The New ACR/EULAR Classification Criteria for Antiphospholipid Syndrome in Clinical Practice

Saša Čučnik[1,2]

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Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by arterial, venous, or microvascular thrombosis, pregnancy morbidity, or nonthrombotic manifestations in patients with persistent antiphospholipid antibodies (aPL). The aPL included in the 2023 ACR/EULAR classification laboratory criteria for APS are lupus anticoagulant (LA), anticardiolipin (aCL) IgG/IgM, and anti-β2-glycoprotein I (anti-β2GPI) IgG/IgM antibodies. The new classification criteria included two levels of aCL/anti-β2GPI positivity (moderate and high), and the levels for moderate and high positivity were applied to ELISA tests but not to other automated platforms. The aim was to present the main obstacles we encountered in implementing the 2023 ACR/EULAR classification criteria for APS, focusing on aPL testing by solid-phase-based assays (aCL and anti-β2GPI). First, according to the criteria, the thresholds for moderate (40-79 units) and high (>80units) aCL and anti-β2GPI antibodies should be based on a standardized ELISA and not on other assays. The aPL test results are inconsistent between different detection methods, including ELISAs, partly due to the lack of standardization and to analytical problems (choice of solid phase and coating, type and source of antigen, ...). Traditionally, ELISA has been used because of its relative time and cost efficiency. In recent years, new automated detection systems such as the chemiluminescent immunoassay (CLIA) have been introduced and are

increasingly used routinely worldwide. These assays are as standardized as ELISA. Second, the correlation of numerical values between the moderate and high thresholds of ELISA and automated platforms varies considerably. It is well known and has been presented above that ELISA results are also not comparable due to the lack of standardization. Third, if there are no options other than using an automated platform, one of the recommendations is to identify and validate the moderate and high thresholds of the platform in correlation with ELISA. Accordingly, we decided to establish and validate our own thresholds for CLIA on the BIO-FLASH (Werfen, Inova Diagnostics) analyzer, which was introduced into our laboratory work as a replacement for in-house ELISA due to the IVDR. We established moderate and high thresholds comparable to those of our in-house ELISAs, which have been used for more than two decades. We have used ROC analysis of CLIA results to calculate thresholds in chemiluminescence units (CU) that provide the same diagnostic specificity and sensitivity as the thresholds of the in-house ELISA. In conclusion, standardization of aPL tests is still needed, because only standardization of the different assays could improve the consistency of aPL test results and make the classification criteria useful for laboratories and clinicians worldwide. Until then, there will always be inconsistencies in aPL test results.

PARALLEL SESSION 02: COVID-19, POST COVID SYNDROME AND AUTOIMMUNITY

18-05-2024 10:30 - 12:00

IS019 / #60

Myositis in The COVID-19 Era- Mere Coincidence

Dennis Mcgonagle
The University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom

Background: We noted new onset myositis in Yorkshire in 2021. Anti-MDA5 (Melanoma differentiation-associated protein-5) positive dermatomyositis (MDA5$^+$-DM) is characterised by rapidly progressive interstitial lung disease (ILD) and high mortality. MDA5 senses single-stranded RNA and is a key pattern recognition receptor for the SARS-CoV-2 virus. We investigated MDA5+ disease spanning the years 2018-2022.

Methods: We evaluated MDA5 autoimmunity, as determined using a 15 muscle-specific autoantibodies (MSAs) panel, between January 2018-December 2022 in Yorkshire, UK. MDA5-positivity was correlated with clinical features and outcome, and regional SARS-CoV-2 positivity and vaccination rates. Gene expression patterns in COVID-19 were compared with autoimmune lung disease and idiopathic pulmonary fibrosis (IPF) to gain clues into the genesis of the observed MDA5$^+$-DM outbreak.

Results: Sixty new anti-MDA5+, but not other MSAs surged between 2020-2022, increasing from 0.4% in 2019 to 2.1% (2020), 4.8% (2021) and 1.7% (2022). Few (8/60) had a prior history of confirmed COVID-19, peak rates overlapped with regional SARS-COV-2 community positivity rates in 2021, and 58% (35/60) had received anti-SARS-CoV-2 RNA vaccines. 25/60 cases developed ILD which rapidly progression with death in 8 cases. Among the 35/60 non-ILD cases, 14 had myositis, 17 Raynaud phenomena and 10 had dermatomyositis spectrum rashes. Transcriptomic studies showed strong *IFIH1* (gene encoding for MDA5) induction in COVID-19 and autoimmune-ILD, but not IPF, and *IFIH1* strongly correlated with an IL-15-centric type-1 interferon response and an activated CD8+ T cell signature that is an immunologic hallmark of progressive ILD in the setting of systemic autoimmune rheumatic diseases. The *IFIH1* rs1990760TT variant blunted such response.

Conclusions: A distinct pattern of MDA5-autoimmunity cases surged contemporaneously with circulation of the SARS-COV-2 virus during COVID-19. Bioinformatic insights suggest a shared immunopathology with known autoimmune lung disease mechanisms.

IS020 / #61

COVID-19, Post COVID Syndrome, "ME/CFS" Vaccines and Autoimmune Adverse Effects

Carmen Scheibenbogen
Institute for Medical Immunology, Charité, Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt Universität zu Berlin, Berlin, Germany

Post Covid Syndrome and ME/CFS: autoimmune effects and autoantibody-targeting therapies Carmen Scheibenbogen, Institut für Med. Immunologie, Charité, Berlin, Germany After a mild-to-moderate SARS-CoV-2 infection, approximately 5% of patients develop long-lasting symptoms that can be attributed to different conditions and symptom complexes, referred to as Post-COVID-19 Condition or Syndrome (PCS). ME/CFS is one of the most disabling post-infectious syndromes, affecting an estimated 17 million people worldwide already before the COVID 19 pandemic, and an estimated doubling during the pandemic. Studies reveal several potential pathomechanisms of PCS and ME/CFS, including inflammation, autoantibodies, circulatory disturbances, and viral persistence. Autoimmunity is postulated to play a major role in the pathophysiological mechanisms of ME/CFS. The ß2-adrenergic receptor antibody (ADRB2 AAB) was the best discriminator of PCS, and both fatigue and vasomotor symptoms were strongly associated with the levels of ADRB2 AABs in PCS-ME/CFS patients. These results align with previous findings in post-infectious ME/CFS patients, which described associations of clinical symptoms and structural central nervous system alterations with levels of AABs against receptors of the autonomic nervous system. There is first evidence that treatments targeting AABs including B cell depletion and immunoadsorption have efficacy in ME/CFS. There are three ongoing placebo-controlled trials of AAB depletion by immunoadsorption in PCS and ME/CFS. Results from observational trials provide first evidence for efficacy of immunoadsorption in patients with postinfectious including post-COVID-19 ME/CFS.

IS021 / #217

Severity of Neurological Long-COVID Symptoms Correlates with Increased Level of Autoantibodies Targeting Vasoregulatory and Autonomic Nervous System Receptors – Single Center Experience

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The Long-COVID syndrome constitutes a plethora of persisting symptoms with neurological disorders being the most disabling ones. The pathogenesis of Long-COVID is currently under heavy scrutiny and existing data on the role of auto-immune reaction to G-protein coupled receptors (GPCR) are conflicting. This monocentric, cross-sectional study included patients who suffered a mild to moderate SARS-CoV-2 infection up to 12 months prior to enrollment

with (n = 72) or without (n = 58) Long-COVID diagnosis according to the German S1 guideline or with no known history of SARS-CoV-2 infection (n = 70). While autoantibodies towards the vasoregulation associated Adrenergic Receptor (ADR) B1 and B2 and the CNS and vasoregulation associated muscarinic acetylcholine receptor (CHR) M3 and M4 were measured by ELISA, neurological disorders were quantified by internationally standardized questionnaires. The prevalence and concentrations of evaluated autoantibodes were significantly higher in Long-COVID compared to the 2 other groups ($P = 2.1*10^{-9}$) with a significantly higher number of patients with simultaneous detection of more than one autoantibody in Long-COVID group ($P = .0419$). Importantly, the overall inflammatory state was low in all 3 groups. ARB1 and ARB2 correlated negatively CERAD Trail Marking A and B ($R <= -0.26$, $P <= .043$), while CHRM3 correlated positively with Chadler Fatigue Scale ($R = 0.37$, $P = .0087$).Concentrations of autoantibodies correlates to intensity of neurological disorders including psychomotor speed, visual search, attention, and fatigue.

IS022 / #259

New Onset Autoimmune Diseases After The Sputnik Vaccine

Olga Vera-Lastra[1], Gabriela Mora[2], Abihai Lucas Hernández[3], Alberto Ordinola Navarro[4], Emanuel Rodriguez Chavez[5], Ana Peralta Amaro[1], Gabriela Medina[6], Maria Pilar Cruz Dominguez[7], Luis Jara Quezada[8], Yehuda Shoenfeld[9]

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The vertiginous advance for identifying the genomic sequence of SARS-CoV-2 allowed the development of a vaccine including mRNA-based vaccines, inactivated viruses, protein subunits, and adenoviral vaccines such as Sputnik. This study aims to report on autoimmune disease manifestations that occurred following COVID-19 Sputnik vaccination. A retrospective study was conducted on patients with new-onset autoimmune diseases induced by a post-COVID-19 vaccine between March 2021 and December 2022, in two referral hospitals in Mexico City and Argentina. The study evaluated patients who received the Sputnik vaccine and developed recent-onset autoimmune diseases.Twenty-eight patients developed recent-onset autoimmune diseases after Sputnik vaccine. The median age was 56.9 ± 21.7 years, with 14 females and 14 males. The autoimmune diseases observed were neurological in 13 patients (46%), hematological autoimmune manifestations occurred in 12 patients (42%), with thrombotic disease observed in 10 patients (28%), and autoimmune hemolytic anemia in two patients (7.1%). Rheumatological disorders were present in two patients (7.1%), and endocrine disorders in one patient (3.5%). Although the COVID-19 Sputnik vaccine is generally safe, it can lead to adverse effects. Thrombosis and Guillain-Barre were the most frequent manifestations observed in our group of patients.

IS023 / #62

Ivig as A Treatment Option for The Post-COVID-19 Condition. Personal Experience

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Background and aims: COVID-19 infection revealed at least 10% of patients, who report such post-sequelae symptoms as chronic fatigue, arthralgia, myalgia, burning pain in limbs, brain fog, and dysautonomia. The aim of this study was to evaluate the impact of intravenous immunoglobulin therapy on the manifestations of post-COVID syndrome.

Methods: 36 patients (18 women, 18 men), an average age 35.4 (30.4;37.6) years with verified COVID-19 according to the WHO definition have been examined. Patients received a standardized intravenous immunoglobulin preparation at a dosage recommended by the manufacturer for alleviating the viral infections complications - 5 grams intravenously three times with a 72-hour interval. The condition was assessed before and 30 days after the treatmnets with validated scales- COMPASS-31, DN-4, HADS, MFI-20. The obtained results were statistically processed, *P* value was counted as significant if < 0.05.

Results: Dysautonomia, manifested primarily as cardiovascular dysregulation, became less pronounced in patients. Scores on the COMPASS-31 scale decreased from 31.8 (29.4; 34.5) to 25.6 (23.2; 28.4), $P = .056$. In the orthostatic domain- from 15.4 (12.4;17.7) to 13.2 (11.3;16.4), $P = .034$. Neuropathic pain scores on the DN4 scale decreased from 6.4 (4.3;7.9) to 5.5 (4.9;6.3) points, $P = .070$. Anxiety, depression (HADS), and asthenia scores (MFI-20) did not show statistically significant differences.

Conclusion: Intravenous immunoglobulin therapy, having a beneficial effect on regulating immune and inflammatory processes, as well as correcting small fiber neuropathy and vasculitis, has a significant positive effect in the post-COVID patients even at low doses. Such therapy allows a reduction in the analgesic medications and an improvement in the quality of life during the post-COVID period. The research is funded by RSF grant № 22-15-00113 от 13.05.2022, https://rscf.ru/project/22-15-00113.

PARALLEL SESSION 03: CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL AND NOVEL THERAPIES IN AUTOIMMUNE DISEASES-SESSION DEDICATED IN MEMORY OF PROF. ALAN WIIK

18-05-2024 10:30 - 12:00

IS024 / #65

Use of Chimeric Antigen Receptors CART_T In Sytemic Lupus

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Université Paris Cité, IRSL, Rech, Paris, France

Systemic Lupus (SLE) is a rare, heterogeneous, potentially life threatening auto-immune disease. In addition to the kidney, major organ (lung, heart or brain) involvement are predictors of poor outcome, with still a 10 year mortality around 10-15% in a subset of patients, when resistant to 1er or 2nd line conventional treatment and despite the use of new biological therapies or monoclonal antibody (mAb).

Chimeric Antigen Receptors (CAR) are chimeric molecules, allowing to redirect the specificity of engineered cells against target antigens, while simultaneously boosting their activation.

Following breakthrough results observed in the treatment of hematological malignancies, conventional CAR-T cell therapy approach has recently been applied for refractory SLE patients. Compared to the use of mAb, antiCD19 CAR-T cells allow to confer new antigen-specificities and to restore the immune tolerance, by achieving deeper depletion of autoreactive B cells, including at the site of inflamed tissues and lymphoid organs (ie. lymph node and spleen) while they simultaneously boost cell activation. All clinical data reported so far showed that autologous CD19-CART effectively deplete B cells and plasmablasts in SLE patients, without major toxicities and only mild cytokine-release syndrome. It also allowed to obtain impressive short and longer term resolution of nephritis and other severe disease-related symptoms in these patients. These clinical effects persisted after B cell reconstitution and were associated with normalization of serum double-stranded DNA antibodies and complement levels. Overall, these initial experiences suggest a rapid response of SLE to CAR-T cell therapy, although extended follow up is needed to determine long-term efficacy. Available current literature evidence on the use of CART in SLE will be presented as well as expert-based consensus, recommendations for indications, contraindication, clinical management, and immune monitoring protocols.

IS025 / #66

Cell Therapy Approaches for Autoimmune Diseases

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Cell therapy is based on the transfer of viable cells into a patient aiming to destroy pathologic cells, replace damaged tissues, or modulate the function of a biological system. The mainstream of cell therapy research addresses regenerative medicine and cancer, however, a considerable bulk of studies focus on chronic inflammatory and autoimmune diseases. The most promising forms of cell therapy in autoimmune diseases are mesenchymal stromal cell (MSC) transplantation and the infusion of chimeric antigen receptor (CAR) T cells. Autoantibodies play a prominent role in the pathogenesis of several autoimmune diseases. Conventional immunosuppressive anti-proliferative drugs and B cell-targeted therapy have only partial effectivity on these diseases because they cannot affect long-lived plasma cells (LLPC), which are protected in specific niches and are not affected by the traditional anti-proliferative treatment. CAR T cells targeting the surface B-cell molecules CD19 or BCMA (B cell maturation antigen) enter the intimacy of tissues and successfully deplete most antibody-secreting cells, including LLPC. Patients with systemic lupus erythematosus (SLE) treated with CAR T cells have entered complete disease remission for several months, indicating that, although promising, this therapeutic approach requires successive procedures. In response to these preliminary positive results, several ongoing randomized controlled trials are using CD19 or BCMA-targeted CAR T cells in SLE and other autoimmune diseases, such as ANCA-associated vasculitis, anti-phospholipid syndrome, pemphigus vulgaris, myasthenia gravis, systemic sclerosis, Sjögren's syndrome, dermatomyositis, and neuromyelitis optica. As an adverse side effect, CAR T cell therapy also affects B cells and LLPC producing protective antibodies, with the consequent possibility of inducing secondary immunodeficiency. Therefore, the next step is the development of chimeric autoantibody receptor (CAAR) T cells, which express the autoantigen of interest on their surfaces and exert cytotoxic effector functions selectively against antigen-specific B cells or LLPC that bind to the autoantigen. Thus, CAAR T cell therapy should affect exclusively the harmful autoreactive B cell lineage, preserving the protective B cells. Importantly, the CAR and CAAR T cell therapy potential is mostly notable in autoimmune diseases in which the respective autoantibodies play a prominent pathogenic role, such as myasthenia gravis (anti-acetylcholine receptor, anti-muscle specific kinase MUSK) and pemphigus (anti-desmoglein 1 and anti-desmoglein 3), for example. An alternative cell therapy approach is the use of chimeric immunomodulatory cells derived from mesenchymal stromal cells, dendritic cells, and T regulatory cells (Treg). Since the mere expansion and infusion of natural immunomodulatory cells have achieved modest results, current efforts focus on the engineering of immunomodulatory cells so that they recognize an antigen that is prevalent in the affected tissues in each disease. This strategy would allow the concentration of the engineered immunomodulatory cells in the areas where they are most useful. Preliminary studies have provided promising results with CAR Treg cells specific for carcinoembryonic antigen (CEA), myelin oligodendrocyte glycoprotein (MOG), and insulin in animal models for ulcerative colitis, multiple sclerosis, and type 1 diabetes mellitus, respectively. Practical issues related to safety and costs need to be addressed regarding CAR T cell therapy. Stable CAR or CAAR T cells engineered by viral vectors (lentivirus and gammaretrovirus) have long persistence and potentially can cause deleterious genotoxic and immunosuppressive effects. In contrast, mRNA-based CAR and CAAR T cells are transient, providing a therapy amenable to control and reversion. A preliminary trial has shown promising results with anti-BCMA mRNA-CAR T cells in patients with myasthenia gravis. Up to now, the availability of CAR T and CAAR T cell therapy is restricted due to the extremely high cost, warranting efforts to develop cost-effective protocols. Although the CAR T cell therapy model is gaining wide acceptance as a promising therapeutic alternative for severe and refractory cases of several autoimmune diseases, there are challenges to overcome before it becomes a standard treatment for autoimmune diseases. The extremely high cost must be brought down by optimization of the production, introduction of automation, and use of allogeneic off-the-shelf CAR/CAAR T cells. The efficacy/safety balance needs to be established for each disease and existing comorbidities, with special attention to the choice between stable and transient chimeras, the dose of cells infused, and the periodicity of infusion of mRNA-based CAR/CAAR T cells. Another important class of cell-based therapy uses the immunomodulatory potential of stromal cells, including those derived from hematopoietic stem cells and mesenchymal stromal cells (MSC), utilizing cells derived from the bone marrow (BM-SCT), umbilical cord (UC-SCT), and adipose tissue (AD-SCT). MSCs are capable of regulating both innate and adaptive immune responses through cell–cell contact and the production of paracrine mediators. The MSC immunomodulatory mechanisms include suppression of T-cell activity, inhibition of B cells, activation of Treg, inhibition of NK cells, induction of macrophage M2 immunomodulatory phenotype, and induction of tolerogenic dendritic cell (DCreg). MSC therapy has been successful in animal models of collagen-induced arthritis, lupus nephritis, and autoimmune encephalomyelitis (EAE). Several pilot clinical trials and phase II clinical trials by different groups have demonstrated promising results of MSC therapy in patients with rheumatoid arthritis, SLE, SSc, amyotrophic lateral sclerosis, and multiple sclerosis. MSC therapy was approved for the treatment of graft versus host disease in 2015 in Japan. A randomized, double-blind, parallel-group, placebo-controlled phase III clinical trial showed the long-term efficacy of allogeneic adipose MSC in treating complex perianal fistula in patients with Crohn's disease, which has been recently approved by the European Medicines Agency. An open-label phase III trial demonstrated the

long-term benefit of BM-derived MSC in 55 children with steroid-refractory acute GvHD. The mechanism of action of MSC is still a matter of debate. The infused cells are short-lived and tend to concentrate in the lungs, not necessarily reaching the tissues of interest. MSC-derived exosomes and microvesicles can deliver cytokines, microRNA, and other molecules with immunomodulatory potential and have been successfully tested in different in vitro and in vivo models. On the other hand, accumulating evidence suggests that host cells, especially monocytes, interact with MSCs and their products, undergoing differentiation into immunomodulatory phenotypes. Potential adverse effects of SCT can be related to allergic reactions to animal proteins present in the cell medium, infection, embolization, and ectopic tissue formation or malignant transformation. A concern is that MSC can be recruited by an underlying tumor microenvironment and differentiated into cancer-associated fibroblasts (CAF), which might enrich the milieu with M2 macrophages and favor tumor growth. On the other hand, senescent MSC could counteract by inducing bystander senescence of tumor cells. These phenomena await further characterization to convey an appropriate assessment of the potential interaction of SCT and cancer modulation. A recent meta-analysis including 62 randomized clinical trials and 3546 participants investigated adverse events related to SCT, indicating a low frequency of fever, local inflammatory reactions, sleepiness, fatigue, constipation, nausea, vomiting, blurred vision, and thromboembolism. An important consideration is the source of the MSC, i.e., autologous versus allogeneic. Allogeneic MSCs have the advantages of immediate availability (off-the-shelf), better quality (control of age and general health of the donor), and higher quantities. On the other hand, allogeneic MSCs can be recognized and rejected by the host immune system, whereas autologous MSCs are tolerated as self by the immune system. In conclusion, cell therapy has emerged as a feasible therapeutic alternative for patients with severe and refractory autoimmune diseases. However, the definite establishment of this therapeutic approach depends on filling in some traditional requirements. One important step will be the development of open-label multi-center clinical trials evaluating the long-term efficacy and safety of CAR/CAAR T cell therapy and MSC transplantation. In addition, practical feasibility issues need to be addressed, including the cost, safety, reproducibility, and worldwide availability of cell-based therapy in autoimmune diseases.

IS026 / #67

Novel Therapy Cannabis in Autoimmunity

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Cannabis plants have played a significant role in human history for thousands of years, being utilized for various cultural rituals and medical purposes throughout centuries. To date, approximately 500 different cannabinoids have been identified. However, in medical practice, cannabis plants are typically categorized based on the concentrations of two primary compounds: tetrahydrocannabinol (THC) and cannabidiol (CBD). It is widely recognized that consuming multiple cannabinoids through methods such as smoking, inhalation, or sublingual administration can provide beneficial analgesic and immunomodulatory effects. Moreover, research suggests that cannabis interacts with primarily two cannabinoid receptors in humans: the CB1 receptor, predominantly located in the central nervous system, and the CB2 receptor, found in various organs and tissues, including lymphoid cells. Consequently, there is belief in the medical community that cannabis may exert immunomodulatory or immune suppressant effects through these receptors. In this presentation, I will explore the potential impact of cannabis on different autoimmune rheumatic conditions, highlighting its potential therapeutic benefits in managing various rheumatic disorders.

IS027 / #45

How Therapeutic Peptides Work in Autoimmune Diseases: P140 Peptide Corrects Failures in Secondary Lymphoid Organs with An Impact on Remote Tissues

Laura Talamini, Dylan Mastrippolito, Philippe Georgel, Sylviane Muller
Neuroimmunology and Peptide Therapeutics, UMR7242 CNRS Biotechnologie et Signalisation Cellulaire, Strasbourg, France

Among therapeutic peptides, the phosphopeptide P140, also known as Lupuzor, shows significant promise in treating autoimmune and inflammatory diseases. P140/Lupuzor is currently evaluated in phase III-clinical trials worldwide for systemic lupus erythematosus. Notably, P140 has also demonstrated positive outcomes in diverse animal models mimicking Sjögren's syndrome, chronic inflammatory demyelinating polyneuropathy, inflammatory bowel disease, gout, asthma and periodontitis. The intriguing question arises: how can a single peptide effectively corrects such a diverse range of inflammatory diseases?Through biochemical and cellular analyses we explored whether P140 might exert an abscopal effect of P140 – a phenomenon described in oncology- that would imply a direct primary effect, for example targeting a cell receptor in a lymphoid structure, and then a secondary effect at a distance, which influences an inflamed organ. P140 targets key elements of endo-lysosomal autophagy, a pathway often dysregulated in the forementioned model of acute and chronic inflammation. The experimental results of our investigation will be presented. Our study's findings shed light on this phenomenon in autoimmunity. Globally, they underline the importance of considering the possible abscopal effect of small molecules and peptides as a crucial component of therapeutic mechanism.

IS028 / #159

Predicting Treatment Response According to RNA Gene Expression in Systemic Sclerosis, from Bench to Bedside

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Systemic sclerosis (SSc) is a rare and chronic autoimmune disease characterized by a pathogenic triad of immune dysregulation, vasculopathy, and progressive fibrosis. Clinical tools commonly used to assess patients, including the modified Rodnan skin score, difference between limited or diffuse forms of skin involvement, presence of lung, heart or kidney involvement, or of various autoantibodies, are important prognostic factors, but still fail to reflect the large heterogeneity of the disease. SSc treatment options are diverse, ranging from conventional drugs to autologous hematopoietic stem cell transplantation, and predicting response is challenging. Genome-wide technologies, such as high throughput microarray

analyses and RNA sequencing, allow accurate, unbiased, and broad assessment of alterations in expression levels of multiple genes. In recent years, many studies have shown robust changes in the gene expression profiles of SSc patients compared to healthy controls, mainly in skin tissues and peripheral blood cells. The objective analysis of molecular patterns in SSc is a powerful tool that can further classify SSc patients with similar clinical phenotypes and help predict response to therapy. In this review, we describe the journey from the first discovery of differentially expressed genes to the identification of enriched pathways and intrinsic subsets identified in SSc, using machine learning algorithms. Finally, we discuss the use of these new tools to predict the efficacy of various treatments, including stem cell transplantation. We suggest that the use of RNA gene expression-based classifications according to molecular subsets may bring us one step closer to precision medicine in Systemic Sclerosis.

PARALLEL SESSION 04: LUPUS - 2025

18-05-2024 14:00 - 15:30

IS029 / #73

Belimumab vs. Anifrolumab in SLE: Which Drug in Which Patient?

Andrea Doria
Rheumatology Unit, Department of Medicine Dimed, University of Padova, Padova, Italy

Two Biologics have been approved for SLE and are currently in our therapeutic armamentarium: they are Belimumab, which is B lymphocyte stimulator (BLyS) inhibitor, and Anifrolumab, which is a type 1 Interferons (IFNs) inhibitor. BLyS and type 1 INFs are both overexpressed in SLE and are correlated with disease activity. However, their biological effects are different. BLyS mediates its biological effects via the BAFF receptor (BAFF-R) expressed on transitional 1 B cells in the bone marrow, blood, and spleen and on follicular B cells and marginal zone B cells in the spleen. BLyS has a specific role in the induction and maintenance of adaptive immune responses and, thus, anti-BLyS monoclonal antibody (MoA) modulates systemic SLE activity and prevent flares. Type 1 INFs mediate their biologic effects via IFN receptor (IFNAR) which is expressed not only on immune cells but also on nearly all cells of the body and, thus, Type 1 IFNs via IFNAR are involved in innate and adaptive immune response and might elicit organ specific effects. Anti-IFNRA MoA inhibits all type 1 IFNs modulating disease activity and exerting organ specific effects. For example, Type 1 IFNs via IFNAR can induce the transcription of pro-inflammatory genes and the production of pro-inflammatory cytokines in different organ tissues. Phase 3 randomized controlled trials (RCTs), BLISS 52 and BLISS 76 for belimumab and TULIP 1 and TULIP 2 for anifrolumab are substantially similar in study design and inclusion and exclusion criteria. BLISS 52, BLISS-76 and TULIP 2 met the primary end points which was SRI-4 in BLISS trials and BICLA in TULIP 2. Among the secondary end points, only Anifrolumab in TULIP-2 was able to significantly reduce the daily dosage of glucocorticoids (GCs) and only Belimumab in BLISS-52 and BLIS-76 was able to reduce the flare rate. Predictors of response to Belimumab were SLEDAI>=10, positive anti-dsDNA, low C3 and/or C4 and GCs intake, all variables indicative of high disease activity and among clinical SLEDAI domains, mucocutaneous and musculoskeletal manifestations. Belimumab was recently approved also for lupus nephritis based on the success of a phase 3 RCT. Predictors of response to Anifrolumab were high IFN signature, serological abnormalities at baseline, and among clinical SLEDAI domains, mucocutaneous, musculoskeletal and hematological features. Based on these observations, we can tentatively state that Belimumab is more indicated in patients with active mucocutaneous, articular, and renal manifestations, active serology, relapsing-remitting patter of disease activity. Anifrolumab is more indicated in patients with active mucocutaneous, articular, and haematological manifestations; chronic active disease (persistent inflammation), and high IFN signature.

IS030 / #70

Flares in SLE: How to Predict and Measure in Daily Clinical Practice?

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The treatment target in patients with Systemic lupus erythematosus (SLE) is remission or at least low disease activity (LDA), that is attained in a growing proportion of patients. Importantly, the natural history of SLE is characterised by a remitting-relapsing course, with new flares of disease activity making sustained remission a less achievable target. To optimize the management and outcomes of patients, SLE disease activity should be assessed at each clinical visit using validated instruments. This is paramount for an accurate and early identification of flares to guide the physicians' decisions to increment treatment. In addition, flares in patients in remission/LDA cause the loss of the treatment target and are associated with higher damage accrual. Therefore, stratification of the risk of flares by assessing their predictors is of utmost importance to maximize prevention of flares and optimize the management of patients with SLE. Flare predictors can guide the physicians' decisions to individualize the frequency of clinical visits, drug tapering and withdrawal schemes. However, until recently, there was no single validated instrument with the measurement properties to enable at the same time the assessment of the treatment targets, grading of SLE disease activity, identification of flares and their severity categories, and clinically meaningful improvement. Several instruments were validated to identify remission, such as the DORIS and Doria criteria, LDA (including the LLDAS), others to identify flares, including the SELENA Flare Index (SFI) and the revised SFI (R-SFI), while the SLEDAI can grade global disease activity, and the BILAG can assess flares and improvement in individual organ systems. These instruments present limitations of accuracy, sensitivity to change and/or are not feasible to apply in the clinical setting. The SLE Disease Activity Score (SLE-DAS) was recently developed and validated to measure all these aspects of disease activity, while being highly sensitive to change, and easy to apply in the daily clinical practice with its online calculator (http://sle-das.eu/). It provides an accurate, sensitive and feasible instrument to identify flares and categorize them as mild, moderate or severe flares. In this presentation, the performance of the different instruments to identify SLE flares is discussed. Predictors that can be assessed in the clinical practice and their use to prevent SLE flares and optimize the management of patients are also discussed.

IS031 / #71

Immune Complex Analyses in Systemic Lupus Erythematosus

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Published autoimmune serology research almost universally only concern free autoantibodies in body fluids, mostly in serum. In a number of autoimmune diseases, like rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), disease-associated autoantibodies are known to form immune complexes (IC) in the circulation and/or in the target organs; in

joints of RA patients and in e.g. in kidneys and skin of SLE patients. We regard "serum" as functionally constituting two separate compartments: free monomeric autoantibodies, and autoantibodies bound in immune complexes (IC), and hypothesise that the autoantibody fraction bound in IC is pathologically more relevant in a number of IC-associated autoimmune diseases. Following this hypothesis, it is logical to aim to evaluate autoantibody levels in the IC fraction in serum. But techniques to quantitate and to study the functional role of autoantibodies in IC is an unmet need, which our group explores. We have developed a technique to quantitate autoantibodies in the IC fraction in sera and other body fluids. The technique is based on magnetic beads with covalently coupled bioactive C1q. When the beads are mixed with body fluids, IgG/IgM-containing IC attach. Subsequently we elute and dissolve the bound IC, whereafter autoantibody content is measured in the eluates and results compared to serum levels and related to clinical phenotypes e.g. disease activity and treatment responses. In the presentation I will present our work using this technique to study the amount, qualities and roles of IC-bound autoantibodies, mainly anti-dsDNA autoantibodies, in belimumab-treated SLE, in a lupus nephritis cohort, and in a large population-based lupus cohort.

IS032 / #46

Defective Lysosomes and Lysosomal Autophagy in Lupus

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Lysosomes are organelles that contribute to the degradation of intracellular constituents through autophagy and of extracellular components through endocytosis, phagocytosis and macropinocytosis. They have roles in secretory mechanisms, generation of extracellular vesicles, certain cell death pathways as well as in inflammation, antigen presentation and maintenance of long-lived immune cells. Lysosome dysfunction and alterations in lysosomal autophagy processes have been identified in a wide variety of diseases, including autoimmune diseases. Biochemical and cellular analyses were performed to analyse lysosomal deffects in the context of both murine and human lupus.We showed that peripheral T lymphocytes from both lupus-prone mouse models and patients suffering from lupus exhibit high levels of autophagic vacuoles compared to normal mice and healthy subjects, respectively. These results were validated using morphological studies by electron microscopy and by detecting lipidated LC3 protein by western immunoblots. In addition, chaperone-mediated autophagy (CMA) is hyperactivated in B cells from MRL/lpr mice. The autophagy modulator peptide P140 was able to moderate abnormally-regulated autophagy flux and CMA activity and decrease the overexpression of CMA markers.Targeting lysosomes with specific autophagy regulatory drugs may represent an attractive therapeutic strategy in a variety of autoimmune/inflammatory diseases.

IS033 / #48

The Digital Patient Pathway in Autoimmune Diseases

Laurent Arnaud
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The past decade has seen tremendous development in digital health, including in innovative new Technologies such as Electronic Health Records, telemedicine, virtual visits, wearable technology and sophisticated analytical tools such as artificial intelligence (AI) and machine learning for the deep-integration of BIG DATA. In the field of rare connective tissue diseases (rCTDs), these opportunities include increased access to scarce and remote expertise, improved patient monitoring, increased participation and therapeutic adherence, better patient outcomes and patient empowerment. In this review, we discuss opportunities and key-barriers to improve application of digital health technologies in the field of autoimmune diseases. We also describe what could be the fully digital pathway of rCTD patients. Smart technologies can be used to provide real-world evidence about the natural history of rCTDs, to determine real-life drug utilization, advanced efficacy and safety data for rare diseases and highlight significant unmet needs. Yet, digitalization remains one of the most challenging issues faced by rCTD patients, their physicians and healthcare systems. Digital health technologies offer enormous potential to improve autoimmune rCTD care but this potential has so far been largely unrealized due to those significant obstacles. The need for robust assessments of the efficacy, affordability and scalability of AI in the context of digital health is crucial to improve the care of patients with rare autoimmune diseases.

PARALLEL SESSION 05: PREGNANCY AND AUTOIMMUNITY

18-05-2024 14:00 - 15:30

IS034 / #76

The Joints in The Pregnant Lady

Iris Eshed
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Pregnancy induces profound physiological changes in the human musculoskeletal system, particularly impacting the sacroiliac joints (SIJ). This presentation delves into a comprehensive exploration of the influence of pregnancy on the SIJ, employing advanced MRI techniques. Insights from MR imaging of the sacroiliac joints in pregnant and peripartum females contribute to our understanding of crucial differential diagnoses related to axial spondyloarthritis. The increasing utilization of MRI reveals a shift in the diagnostic landscape, highlighting the necessity for nuanced evaluation and awareness of non-specific findings in pregnant women. The presentation examines the prevalence, evolution, and topography of sacroiliac joint MRI lesions, providing guidance for clinicians in differentiating postpartum strain-related conditions from axial spondyloarthritis-related sacroiliitis. An understanding of these nuances is vital for healthcare providers, particularly rheumatologists and radiologists, enabling them to address peripartum and postpartum MRI lesions and interpret their significance effectively.

IS035 / #75

Gender Medicine in Autoimmunity: From Bench to Bedside and More

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Gender medicine studies the influence of sex (biological differences) and gender (cultural, relationship and social rules) on health and disease. Autoimmune diseases affect women and men with different epidemiology, clinical manifestations and response to treatment. In order to reach an accurate and personalized management of each patient, sex and gender analysis should be included at any stage of research, from preclinical studies (considering animal models of both sexes, sex of cells in culture etc) to clinical trials that should include subjects of different gender, and to clinical guidelines that take into

account sex and gender differences in the clinical expression and response to treatment of autoimmune diseases. In addition, sex and gender analysis should be included in the final report of the result following the SAGER guidelines, which are growingly requested by peer-reviewed scientific journals. Finally, an analysis of the access to healthcare should not be overlooked, in order to design gender-inclusive pathways that allow gender equality in healthcare.

IS036 / #74

Thyroid, Autoimmune Diseases, Recurrent Spontaneous Abortion and Rafs

Caterina De Carolis
Gynecology and Obstetrics, Past Head S. Giovanni and S. Giacomo Hospital, Rome, Italy

Recurrent spontaneous abortion (RSA) and RAFS are heterogeneous conditions that have been frequently explained with an immunological pathomechanism. A deeper insight into apparently unexplained infertility and RSA shows increasing evidences supporting both alloimmune and autoimmune mechanisms, in which not only antiphospholipid antibodies but also natural killer (NK) cells and other autoantibodies seem to play a relevant role. Implantation is an event depending on at least several steps. At every step, there is a continuous embryo–uterus interaction, and evidence reports that pregnancy failure (PF) in women with autoimmune diseases consists mainly of preterm delivery (PD) and intrauterine growth restriction (IUGR). Pregnancy is a stress test for the thyroid, resulting in hypothyroidism in women with limited thyroidal reserve or iodine deficiency, and postpartum thyroiditis in women with underlying Hashimoto's disease who were euthyroid prior to conception. So in my presentation I'll focus on the interplay between thyroid and autoimmune diseases, and on their prevalence in RSA and RAFS.

PARALLEL SESSION 06: SYSTEMIC SCLEROSIS, PSORIASIS AND SPONDYLOARTHRITIS

18-05-2024 14:00 - 15:30

IS037 / #78

Systemic Sclerosis: From Pathophysiology to Novel Therapeutic Approaches

Katja Lakota
Departmet of Rheumatology, UMC Ljubljana, Ljubljana, Slovenia

Systemic sclerosis (SSc) is a chronic multisystem autoimmune disease with a heterogeneous presentation and poor prognosis. Marked immune system activation and vasculopathy are key profibrotic stimuli triggering SSc pathology. Therefore, general immunosuppression represents a traditional treatment approach with limited efficacy and numerous side effects. Recently, tocilizumab and rituximab demonstrated to be effective and have been added to armor of treatment options in Ssc-ILD. For the treatment of vascular complications in SSc, such as pulmonary arterial hypertension, few vasoactive therapies such as endothelin receptor antagonists and phosphodiesterase type 5 are successfully combined. However, antifibrotic therapy was lacking until the introduction of nintedanib, a tyrosine kinase inhibitor that has been shown to be effective in SSc-ILD but less so in skin fibrosis. Thus other novel strategies to treat fibrosis in SSc patients are urgently needed. One of these strategies includes direct targeting of extracellular matrix (e.g., enzymes for hydroxylation or crosslinking of collagen) or affecting altered mechanical properties of the extracellular matrix, with reducing matrix stiffness or affecting mechanotransduction. The latter is achieved by targeting focal adhesion kinase or integrins, which are essential for the activation of latent TGFβ in addition to the activation of intracellular transcriptional factors YAP and MRTFA. Another promising novel therapeutic strategy is also to target cellular senescence. Senescent phenotypes have been observed to be involved in SSc pathology, including immunosenescence, senescence of endothelial and smooth muscle cells involved in vasculopathy and senescence of fibroblasts that produce increased amounts of extracellular matrix and plethora of cytokines, chemokines, and growth factors, that drive fibrosis. As senescent cells are less sensitive to cytotoxic and proapoptotic signals they accumulate in tissues. Recent pilot studies in SSc and other fibrotic diseases have shown that some patients clinically improved with the use of senolytics. However, because of the complex pathology of SSc and the inability of any specific substance to treat all stages of disease, personalized decision making will be of key importance when new therapies become available.

IS038 / #251

Connective Tissue Diseases Associated Pah

Luc Mouthon
Department of Internal Medicine, Cochin Hospital and Université Paris Cité, Paris, France

Pulmonary arterial hypertension (PAH), corresponding to group 1 of pulmonary hypertension classification, is a rare disease with a major prognostic impact on morbidity and mortality. PAH can be either primary in idiopathic and heritable forms or secondary, such as related to connective tissue diseases (CTD-PAH). Within CTD-PAH, the leading cause of PAH is systemic sclerosis (SSc) in Western countries, whereas systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD) are predominantly associated with PAH in Asia. The European Society of Cardiology (ESC) and European Respiratory Society (ERS) 2022 guidelines 6th World Symposium of pulmonary hypertension 2018 proposed to redefine the pulmonary hypertension from mean pulmonary artery pressure ≥ 25 mmHg to > 20 mmHg, and incorporating a revised cut-off level for pulmonary vascular resistance and a definition of exercise PH. PAH is the leading cause of morbimortality in patients with the course of SSc and MCTD. The screening of these patients at risk of developing PAH is important, but different depending on the underlying CTD. The early detection may improve survival in patients with SSc-related PAH. Therapeutic advances in the field of PAH have improved outcomes of for patients with CTD-PAH, Therapeutic advances in the field of PAH have improved outcomes of patients with CTD-PAH, with certain therapeutic specificities, such as the use of immunosuppressants in combination with specific PAH treatments excluding the SSc.

IS039 / #181

Complete Resolution of Gastric Antral Vascular Ectasia in Systemic Sclerosis After Autologous Stem Cell Transplantation - A Case Series with Long Term Results

Doron Rimar, Gleb Slobodin, Shiri Keret
Rheumatology Unit, Bnai- Zion Medical Center, Technion Institute of Technology, Haifa, Israel

Background: Gastric antral vascular ectasia (GAVE) is a known vascular gastrointestinal (GI) complication of systemic sclerosis (SSc), characterized by a distinctive endoscopic appearance of a "watermelon stomach". In patients screened for autologous hemopoietic stem cell transplantation (AHSCT) in the "Scleroderma: Cyclophosphamide or Transplantation" (SCOT) trial, the reported prevalence was up to 22%, and even higher, 45%, specifically in patients with RNA polymerase III antibodies. GAVE carries significant morbidity due to frequent and recurrent GI bleeding, requiring blood transfu-

sions and repeated endoscopic interventions with Argon plasma coagulation (APC). There is no well-established specific therapy for GAVE in the literature. AHSCT is grade A therapy for early diffuse progressive SSc, the population at risk for GAVE. During the conditioning period, thrombocytopenia may result in bleeding from active GAVE. In the SCOT trial, patients with active GAVE were excluded from the study. The data regarding the safety and efficacy of AHSCT in SSC patients with GAVE is scarce.

Objectives: To evaluate the safety and efficacy of AHSCT in SSc patients with GAVE.

Methods: We selected from our cohort of twenty adult dcSSc patients who underwent AHSCT, patients who had GAVE according to gastroscopy prior to AHSCT. We recorded the number of APC procedures before AHSCT, The complications during AHSCT: the nadir thrombocytopenia level, the need for blood transfusions and treatment-related mortality at 100 days. We report endoscopic and clinical results 12 months following AHSCT.

Results: Five dcSSc patients (mean age 49.2 ± 9.0 years, 4 [80%] females, 4 patients [80%] with RNA polymerase III antibodies and one [20%] with SCL-70 antibodies) were diagnosed endoscopically and histologically with GAVE 1-4 months prior to AHSCT. Two of them needed APC. The mean Hb level at baseline was 9.6±2.5 g/dl. At the AHSCT, three patients received conditioning with Cyclophosphamide 200mg/kg and 7.5 mg/Kg ATG, and two patients received "cardiac-safe" conditioning with rituximab 1000 mg, cyclophosphamide 60 mg/kg and fludarabine 120 mg/m^2. The mean nadir thrombocyte level was 41.2 × 10^9/L (±39.1 × 10^9/L). The mean duration of thrombocytopenia below 50× 10^9/L was 4.6±4.8 days. The mean number of blood transfusions during hospitalization for AHSCT was 4.4 ±4.0 units. Only one GI bleeding episode (melena) was noted in one patient during the transplantation. Treatment-related mortality was 0%. At the repeated upper gastrointestinal endoscopy following AHSCT (mean time after AHSCT 7.8 ± 4.4 months, range 4-12 months), all five patients (100%) had a complete resolution of the endoscopic as well as the histological findings of GAVE. The Hb level at the time of the second gastroscopy increased from baseline by 1.7 ± 1.8 g/dl, range 0-4.1 g/dl).

Conclusion: We describe the complete resolution of GAVE 12 months after AHSCT in five consecutive patients without treatment-related mortality.

PARALLEL SESSION 07: MECHANISMS IN AUTOIMMUNITY PART 1 - SESSION DEDICATED IN MEMORY OF PROF. NOEL ROSE

18-05-2024 15:45 - 16:45

IS040 / #26

Triggering of Autoimmunity by Mechanical Stress

George Wick
Institute of Pathophysiology, Medical University Innsbruck, Innsbruck, Austria

Mechanosensation is a fundamental process through which living organisms perceive and respond to their environment. It serves the recognition of a wide range of physical cues, such as pressure, touch, tension and stretch and shear stress. Mechanosensation convert mechanical stress into biochemical signals, a phenomenon that occurs in all tissues of the body. However, the effects of mechanical stress during immune reactions have so far not been elucidated in greater detail. In this presentation, the consequences of mechanical stress on immune reactivity will first be briefly discussed. Then, more room will be allotted to the expression/modification of (auto)antigens upon exertion of mechanical stress to cells of different organs/systems. A special focus will be attached to the induction of the expression of stress proteins (notably heat shock protein 60 – HSP60) and their role in triggering humoral and cellular autoimmunity. Finally, atherosclerosis, rheumatoid arthritis, glaucoma and fibrotic side effects of silicone mammary implants will be described as examples for autoimmunity against HSP60 induced by mechanical stress. Mechanical stress can either induce the development of autoimmune diseases by itself, e.g., via direct induction of an autoimmune reaction against the stress protein HSP60, or exert indirect effects by rendering target cells / molecules more sensitive to other environmental autoimmunity - triggering factors.

IS041 / #82

Galectins in Autoimmune Diseases Friends or Foes?

Katia Mangano, Paolo Fagone, Gian Marco Leone, Ferdinando Nicoletti
University of Catania, Catania, Italy

The Galectin family comprises a set of glycan-binding proteins expressed in various tissues, including immune and non-immune cells. These molecules play vital roles as regulators in both innate and adaptive immune responses and are involved in a wide array of cellular and pathophysiological functions, including cell division, adhesion, motility, and invasion. Recent research indicates that galectins, and most notably galectin-1 (Gal-1) and galectin-3 (Gal-3), play a role in the initiation and progression of autoimmune conditions, such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), type 1 diabetes (T1D), and systemic sclerosis (SSc). Through interactions involving proteins and glycans, or between proteins, these endogenous lectins have the potential to shape the onset, progression, and resolution of these processes, suggesting their importance in disease monitoring and potential treatment strategies. A deeper comprehension of the molecular basis of galectin-ligand interactions, particularly their interaction with specific glycans, the biochemical nature of their receptors, and the underlying signaling mechanisms, may pave the way for rational therapeutic approaches to address a wide spectrum of pathological conditions.

IS042 / #83

Vitamin D in Autoimmunity

Ifigenia Kostoglou-Athanassiou
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Vitamin D is a secosteroid hormone which is synthesized within the human skin from cholesterol. The hormone is involved in the regulation of calcium metabolism and deeply affects bone metabolism. It has become apparent that it is also involved in the regulation of the immune system and its deficiency may be related to the development of autoimmune diseases. Research at all levels, cellular, animal and human has shown that vitamin D is a hormone, a nutrient and an immunoregulator. Vitamin D deficiency may be involved in the pathogenesis of rheumatoid arthritis, and it is inversely related to disease activity. Vitamin D deficiency may also be involved in the pathophysiology of systemic lupus erythematosus and is inversely related to disease activity and kidney involvement. Vitamin D deficiency has also been described in ankylosing spondylitis, psoriatic arthritis, Sjogren's syndrome and systemic sclerosis. It has been shown that vitamin D deficiency may be involved in the pathogenesis and pathophysiology of multiple sclerosis. Inflammatory bowel disease is characterized by severe vitamin D deficiency, where its role in the pathogenesis of the disease has been explicitly proved. Vitamin D deficiency may also be related to the pathogenesis of Hashimoto's thyroiditis. Vitamin D has been administered to

patients with RA and SLE to mitigate the autoimmune process and combat pain. Vitamin D has also been administered to patients with diabetes mellitus type 1 with conflicting results. It has thus been shown that vitamin D is a steroid hormone involved in the regulation of the immune system. Vitamin D deficiency may be involved in the pathogenesis of autoimmune diseases and may be used therapeutically to treat patients with autoimmune diseases to mitigate the autoimmune process and treat pain.

IS043 / #176

The Use of Advanced Infrared Spectroscopy for Diagnosis of Rheumatic Disorders (Fibromyalgia and Rheumatoid Arthritis)

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Introduction: Infrared spectroscopy (IR) is a technique that can be used to analyze the chemical composition (biomarkers) of blood samples by measuring the absorption or transmission of infrared radiation. This technique has shown potential in the diagnosis and management of autoimmune diseases (AIDS).

Aim of the study: Our aim was to directly unveil the unique spectra of the blood samples obtained from patients with fibromyalgia (FM), rheumatoid arthritis (RA), and healthy subjects.

Material and methods: We have evaluated blood samples from patients with RA (no=34), FM (no=24), and healthy persons (no=16) using Bruker Vertex 80V instrument for the measurement of the IR spectra with various accessories Bruker's microplate extension HTS-XT, Bruker's Bio-ATR cell, and ATR-Diamond measurement accessories.

Results: Using Bruker Vertex 80V instrument (1^{st} derivative to absorbance spectra 2830 – 3000 cm^{-1}) we were able to obtain unique IR spectra patterns that discriminate patients with FM; RA and healthy subjects

Conclusion: The FTIR spectroscopy of plasma from patients with fibromyalgia and different control subjects pointed to the possibility of using this tool for diagnosis and follow-up of patients with autoimmune disorders.

PARALLEL SESSION 08: VASCULITIS - UPDATE

18-05-2024 15:45 - 16:45

IS044 / #84

Innate Immunity in Anca-Associated Vasculitis

Jan Damoiseaux
Maastricht University Medical Center, Maastricht, Netherlands

Although it is evident from animal studies that the adaptive immune system plays a crucial role in ANCA-associated vasculitis (AAV), inflammation is crucial in the generation of the adaptive immune response. Moreover, innate immunity participates in the effector functions of the adaptive immune response. Neutrophils are primed, for instance by infection, and may cause tissue necrosis due to NETosis. In this process histones are citrullinated and the extruded DNA-fragments bind myeloperoxidase, all together creating a highly inflammatory micro-environment. Based on staining for citrullinated histone 3 and myeloperoxidase, NETosis can be visualized in the glomeruli of patients with active AAV. In addition, serum of AAV patients induces NETosis in neutrophils of healthy donors. This is most apparent during active disease and even might predict flares. Although ANCA are known to further activate primed neutrophils, it is not proven if ANCA are responsible for the serum-factor induced NETosis. Activation of neutrophils also activates the alternative complement pathway, generating C5a and causing a positive feedback loop because C5a attracts and activates neutrophils. The activated neutrophils may, subsequently damage the endothelial cells resulting in activation of the intrinsic coagulation pathway and increased prevalence of thrombotic events in AAV patients. The combination of inflammation, complement activation and coagulation, therefore, may be considered as a Bermuda triangle of the innate immune system in AAV. Interestingly, similar interactions have been observed in patients with severe COVID-19 infection.

IS045 / #85

CNS Vasculitis - Update

Gisele Zandman-Goddard[1,2], Ron Dabby[3], Alexander Puzhevsky[4], Milena Tocut[1,2]
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CNS vasculitis is classified as primary (PCNSV) (Type I and II) or secondary (SCNSV) (type III or IV). The classification refers to vasculitis restricted to the CNS (Type I), associated with a systemic vasculitis (Type II), associated with an autoimmune disease (Type III), or associated with non-autoimmune systemic diseases (Type IV) including infections, drugs, and malignancies. Other classifications, based on the size of the vessels involved, by MRI findings, and by histopathology based on brain biopsy. The major updates points to advancements in radiographic modalities including MRI, high resolution contrast enhanced MRI, MRA, and digital subtraction angiography (DSA). Utilization of these methods support the differentiation between primary and secondary CNS vasculitis, but also between CNS vasculitis and its mimickers. New mimickers include reversible cerebral vasoconstriction syndrome (RCVS) which is the most common, cerebral amyloid angiopathy-Ab-elated angiitis (ABRA), cerebral amyloid angiopathy- related inflammation (CAA-RI), and intravascular lymphoma (IVL). Cerebrospinal fluid analysis and serologic tests have not yielded more specific results than in the past. MRI-guided biopsy is more specific than a blind biopsy. The most common treatment is high dose glucocorticoids and cyclophosphamide. Intravenous immunoglobulin (IVIG) therapy was beneficial for SLE patients with diffuse neuropsychiatric manifestations. Rituximab is a possible option although only utilized in a few cases. In addition, mycophenolate mofetil and azathioprine are used for maintenance therapy. We present an update of the medical literature on this topic.

IS046 / #238

Adult Iga Vasculitis

Alojzija Hocevar
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IgA vasculitis (IgAV) is a small-vessel, immune-complex mediated vasculitis characterized by dominant deposition of IgA in affected vessels (mostly postcapillary venules). Two disease forms can be distinguished – a systemic form and a skin-limited form. IgAV represents the most frequent vasculitis in children, however also in adults the disease is not uncommon. Prospective studies investigating IgAV in adults are rare. In adults IgAV is more frequent in males. In addition to genetic factors, also environmental triggers have been implicated in adult IgAV (e.g. infections, medications, vaccines, cancer). Systemic IgAV typically presents with a tetrad of signs of skin, joint, gastroin-

testinal, and renal involvement. Other organs are less frequently involved. In comparison to children, adults have more severe acute disease (frequently necrotic purpura, potentially severe gastrointestinal involvement, acute kidney injury related to IgAV nephritis), as well as worse long-term prognosis, the latter being mostly related to the progression of chronic kidney disease. Studies that evaluated predictors of severity of acute disease reported mixed results, however age, gender, extension of skin lesions, smoking status, certain laboratory results (among others neutrophile to lymphocyte ratio, serum IgA level) seem important as risk factors. Relapses affect around 20% of adults. Furthermore, the mortality of adult patients is increased compared to general population and is partly related to the IgAV and partly to the burden of comorbidities. Presently the treatment of adult IgAV has not been standardized, however patients frequently need a systemic immunomodulatory treatment.The management of adult IgAV patients is challenging.

IS047 / #87

Polymyalgia Rheumatica (PMR) or Late Onset PMR-Like RA - A Diagnostic Conundrum

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Rheumatoid arthritis (RA) is one of the most prevalent rheumatic diseases in the elderly and affects up to 2% of the population > 60 years of age. While the majority of elderly patients with RA have signs and symptoms of a classic RA, seen in all ages, polymyalgia (PMR)-like late-onset RA is also common and may be the first manifestation of the disease in up to 25% of older individuals. The keys to the diagnosis of this subtype of RA are often hidden at the first encounter, while the high level of suspicion and focused quest are frequently the decisive factors, leading to the right judgment. Concomitant synovitis of peripheral joints, such as wrists, ankles, or knees is an essential clinical feature in favor of RA but sometimes requires a thorough physical examination to be disclosed. Elevated CRP and ESR are seen in both PMR and PMR-like RA, but a positive test for ACPAs, although not very sensitive in this setting, can be diagnostic for late-onset RA. Sometimes, less than expected in genuine PMR clinical and laboratory improvement under treatment with glucocorticoids can lead to the reevaluation of the whole clinical picture and the alternative diagnosis of RA. A single clinic experience with 66 new patients with late-onset RA, presenting within 2 years, demonstrated that 50% of the cohort had overlapping features of classic onset and PMR-like onset RA, with involvement of both peripheral and axial joints at the beginning of the disease. The other 50% of the cohort were evenly distributed between the classic RA presentation with only peripheral joint involvement and PMR-like disease. The three subgroups of patients did not differ significantly regarding their age, gender distribution, disease duration before the diagnosis, utilization of glucocorticosteroids, synthetic or biological DMARDs. Serum levels of C-reactive protein were numerically higher and RF/ACPA positivity was seen less in the group of PMR-like RA, however, the differences did not reach statistical significance. PMR-like late-onset RA is a frequently seen disease pattern, typically with acute onset, involvement of shoulders/hips, very high levels of C-reactive protein and frequently negative RF/ACPA, anemia, and sometimes low-grade fever. Its differentiation from genuine PMR can be difficult or even impossible on the first encounter, and a high level of suspicion is needed for an accurate timely diagnosis.

IS048 / #88

Predictors of Remission and Flare in Patients with Polymyalgia Rheumatica

Carlo Perricone
Department of Medicine and Surgery, Rheumatology, University of Perugia, Perugia, Italy

To date, several predictive factors of remission and fare in patients with polymyalgia rheumatica (PMR) have been proposed but evidence is limited. In a retrospective study we evaluated clinical charts of PMR patients up to 24 months and we analyzed the diferences between patients who achieved remission within 6 months of diagnosis, those who achieved remission at 24 months, and patients who did not. Among 137 patients, 57 (41.6%) achieved remission at 6 months and complete remission at 24 months was achieved by 104 patients (75.9%). The erythrocyte sedimentation rate at baseline was higher in patients who did not achieve remission than in patients who achieved it (P =.012). Female patients were less likely to achieve complete remission (45/68, 66.2% vs. 59/69, 85.5%, P =.01) compared to males. Fifty-four patients (39.4%) experienced at least one fare. Patients who did not achieve sustained complete remission sufered a fare more often (22/39 vs. 32/98, P =.01) and earlier than patients who did (10.33±7.89 months vs. 13.64±6.97 months, P =.011). Multivariate analysis confrmed that female sex (RR=3.2, 95% CI 1.3–7.9) and higher baseline prednisone dosage (RR=1.1, 95% CI 1.007–1.109) were negative independent predictors of complete remission at 24 months. A signifcant percentage of patients with PMR requires prolonged steroid treatment and may experience fares at 24 months of follow-up. Female sex and higher baseline prednisone dosage are negative independent predictors of complete remission at 24 months.

IS049 / #886

Pathways Deregulated in Giant Cell Arteritis by Gene Expression Profiling in Temporal Artery Biopsies

Stefania Croci[1], Ilaria Ferrigno[1,2], Martina Bonacini[1], Alessandro Rossi[1], Francesco Muratore[3,4], Luigi Boiardi[4], Alberto Cavazza[5], Alessandra Bisagni[5], Luca Cimino[3,6], Angelo Ghidini[7], Giuseppe Malchiodi[8], Alessandro Zerbini[1], Carlo Salvarani[3,4]
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Background: Giant Cell Arteritis (GCA) is a systemic inflammatory disease that affects large and medium-sized. Temporal artery biopsies (TABs) are routinely performed for diagnosis, giving the invaluable opportunity to analyze inflamed tissues. Different histological patterns of inflammation can be found in TABs: transmural inflammation (TMI) is the most frequent pattern (78% of the positive TABs), while inflammation limited to adventitia (ILA) can be found in 7% of the positive TABs. Knowledge on disease pathogenesis is growing, but high-throughput assays in TABs are still scarce. GCA patients are actually treated with glucocorticoids, irrespective of clinical presentations and inflammation patterns. It is necessary to increase the knowledge on the molecular features of GCA to implement precision medicine.

Objectives: We aimed to identify differentially expressed genes (DEGs) in TAB from patients with GCA *versus* controls and to increase the knowledge on TMI and ILA histological patterns in GCA.

Methods: A retrospective cohort of patients subjected to TABs at AUSL-IRCCS at Reggio Emilia (Italy) was included: 42 patients had GCA with TMI; 7 patients had GCA with ILA; 7 patients had normal TABs and received a different diagnosis. All the patients with TMI and normal TABs were naïve from therapy while 4/7 patients with ILA were receiving glucocorticoids at the time of TABs. RNA was extracted from formalin-fixed paraffin-embedded TABs. The expression of 770 genes was profiled with the NanoString nCounter PanCancer Immune Profiling Panel. Data were analyzed with nSolver software 4.0. Background thresholding using the negative control probes was applied, then data were normalized over the positive control probes and housekeeper genes. DEGs with fold changes > 2.0 and Benjamini-Yekutieli adjusted *P*-values <.05 were considered significant.

Results: Unsupervised clustering based on the expression of the 770 genes revealed two groups of samples: the first group contained all the normal TABs plus TABs with ILA, while the second group contained 41/42 TABs with TMI. In particular, the subset of TNF superfamily genes allowed to cluster TABs with TMI from ILA and normal TABs. TABs with TMI showed 31 down- and 256 up-regulated genes compared to normal TABs; 26 down- and 187 up-regulated genes compared to TABs with ILA. TABs with ILA revealed a gene expression profile similar to normal TABs: 38 genes reached fold changes > 2.0, but *P*-values did not maintain statistical significance after correction for multiple testing. These genes were also up-regulated in TABs with TMI. Functional annotation clustering of the up-regulated DEGs with DAVID highlighted the following pathways as enriched: Toll Like Receptor TLR2, TLR6:TLR2, TLR1:TLR2, TLR7/8, TLR9 cascade, MyD88 cascade, chemokine signaling, PD-1 signaling, cellular response to IL-1β and TNFα.

Conclusions: TABs with TMI had a distinct transcriptome compared to TABs with ILA. Genes deregulated in ILA were also deregulated in TMI, suggesting that ILA might represent early stages of the disease. Gene profiling allowed to deepen the knowledge on GCA pathogenesis.

Acknowledgements: Azienda Unità Sanitaria Locale (AUSL)-IRCCS, Reggio Emilia, Italy: "Bando per la valorizzazione della Ricerca Istituzionale 2019" and Foundation for Research in Rheumatology (FOREUM).

PANEL DISCUSSION 01: HIPPOCRATES VERSUS CHATGPT

18-05-2024 17:15 - 18:30

IS050 / #887

Hemophagocytic Lymphohistiocytosis: Artificial Intelligence and Its Role in Aiding Diagnosis

António Lamas
Unidade de Imunologia Clínica - Centro Hospitalar Universitário de Santo António Porto [European Reference Network (ERN) for Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases (RITA) Center], Porto, Portugal

***Background and Aims*:** Hemophagocytic lymphohistiocytosis (HLH) is a rare hyperinflammatory syndrome with unspecific features often overlapping more common conditions. Prompt diagnosis is essential to improve outcomes. Large language models (LLM), including ChatGPT-4, could assist diagnosis/decision making. We present two cases of HLH with overlapping features but opposing outcomes, differing in time-to-diagnosis, to reflect on the potential role of LLM.

Methods: Retrospective patient review. Natural language interrogation of ChatGPT3.5/4 for probable diagnoses.

Results: Patient 1 (77-year-old female) and patient 2 (71-year-old female) presented with weight loss and anorexia (2 weeks). Patient 1 also had fever, acute-onset confusion and unstable gait. Both displayed pancytopenia, elevated CRP, liver enzymes, LDH, ferritin and triglycerides. Both patients had hepatosplenomegaly (patient 2 also had diffuse adenopathies). Viral/autoimmune studies irrelevant. Patient 1, initially treated for presumed urinary tract infection, diagnosed with HLH on day 10. Admitted to ICU, evolved fatally with multi-organ dysfunction despite methylprednisolone (MTP)/ anakinra and broad-spectrum antibiotics. Biopsies showed marginal zone lymphoma. Patient 2 was diagnosed with HLH on day 5, admitted to ICU in shock, evolving favourably with anakinra/MTP. Diffuse large B-cell lymphoma was diagnosed and treated, with patient survival. A brief summary of patient's findings was provided to Chat-GPT, inquiring about a most probable diagnosis and the resulting answers included the hypothesis of HLH.

Conclusions: Several factors contribute to diagnostic delay in HLH. LLM can be useful to broaden list of differentials, providing aid in diagnosing rare conditions. Physicians are required to carefully choose and interpret information provided/obtained, and should be aware that LLM too are influenced by trends or publication bias.

PARALLEL SESSION 09: SJÖGREN SYNDROME AND NOVEL THERAPIES IN AUTOIMMUNITY

18-05-2024 17:15 - 18:30

IS051 / #91

Epidemiology of Sjögren Syndrome

Roberto Gerli
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Primary Sjögren's disease (pSS) is a systemic autoimmune disease with significant impact on morbidity, mortality and quality of life. The estimation of prevalence and incidence of this disorder has been evaluated in studies mainly from Europe and Asia, but with inclusion of a low number of subjects in the majority of them. The results, moreover, have been rather variable depending on several factors including how pSS is defined, the study design (e.g., population-based vs. sample surveys) and the heterogeneity in genetic background and geographical setting of studied populations. Since the Italian National Health Service (INHS) is a universal coverage health system, representative, therefore, of the whole INHS beneficiaries community, it represent an invaluable source of epidemiological data. On this basis, prevalence, healthcare needs and related costs of pSS patients have been evaluated from the INHS perspective, taking advantage of the Research & Health Foundation's database including about 8% of the whole Italian population. The results showed that 3.8/10,000 Italian inhabitants were identified as affected by pSS in 2018. In the year following index date, a higher number of patients received ≥1 drug, with increased per capita cost with respect to controls. At least one hospitalization occurred, and at least one outpatient specialist service was performed, in a higher percentage of patients compared to controls. Overall, mean annual costs were € 1,171 per case and € 372 per control. On the basis of these data, the pSS prevalence in Italy appears to be consistent with the definition of orphan disease In addition, patients suffering from this disease have higher pharmacological, in-hospital and outpatient specialist care needs, leading to three-times higher overall cost for the INHS, compared to the general population.

IS052 / #258

Mixed Connective Tissue Diseases: Classification Criteria, Clinical Presentation and Prognosis

Luc Mouthon
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Mixed connective tissue disease (MCTD, or Sharp syndrome) is an entity defined in 1972 by Sharp et al. as a syndrome characterized by the presence of autoantibodies (Abs) directed towards ribonucleoprotein U1 (anti-U1RNP) associated with clinical features of other connective tissue diseases (CTD) such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or idiopathic inflammatory myopathies (IIM). These features include a large variety of symptoms and complications including Raynaud's phenomenon, puffy hands or fingers, arthritis, myositis, pleuritis, pericarditis, interstitial lung disease (ILD), or pulmonary hypertension (PH). The reality of MCTD as a distinct and well-defined entity has been debated since its first description and remains controversial. Due to the rarity of the disease, only few studies about MCTD are available in the literature. In a recent French multicenter study we have included 330 patients (88% females, median [interquartile range] age of 35 years [26-45]). The diagnostic criteria of Sharp or Kasukawa were met by 97·3% and 93·3% of patients, respectively. None met other classification criteria without fulfilling Sharp or Kasukawa criteria. We have identified that (i) 2 out of the 4 diagnosis criteria sets for MCTD were adequate to identify MCTD patients, (ii) 25·6% of MCTD patients progressed to a dCTD over a median follow-up of 8 years and (iii) the overall prognosis of MCTD was good with 45·2% patients achieving remission, 7·6% developing PH, and 27·9% developing ILD. MCTD identifies a heterogenous group of patients of whom roughly a quarter progress towards dCTD (especially toward SSc for patients with capillaroscopy abnormalities and SS for patients with parotid swelling) over time. PH and ILD occur in up to 30·9% and, due to their potential severity they need to be detected as early as possible at time of disease onset or during follow-up. PH and ILD are the two main causes of death in MCTD patients, although the prognosis is good.

PLENARY 02

19-05-2024 08:00 - 09:30

IS053 / #94

New Paradigms in The Management of SLE

Andrea Doria
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SLICC/ACR damage index is a surrogate measure of poor prognosis in systemic lupus erythematosus (SLE) since it predicts further damage, death, reduced quality of life, mood disorders and reduced work productivity. Damage in SLE has two major drivers: disease activity and drug-related side-effects especially those of glucocorticoids, Thus, in order to improve SLE prognosis, we should try to decrease damage due to disease activity without increasing the damage due to the standard-of-care (SoC), i.e. glucocorticoids and traditional immunosuppressants. Treat-to-target (T2T) strategy has been recently suggested in SLE patients in order to minimize the damage accrual. T2T approach in SLE should be considered as a stepwise process where the first target is to achieve clinical remission or clinical low disease activity (cLDA) and the second and third steps to minimize or even to withdrawal first glucocorticoids and then immunosuppressants. Nowadays to achieve these clinical remission or clinical low disease activity is not uncommon in our patients, but the difficulty is to maintain these two targets since disease relapses are very common in SLE. However, we know that the longer the clinical remission or the cLDA, the lower the damage accrual. Another important aspect is that damage occur early in SLE and, thus, we should try to achieve clinical remission or cLDA as soon as possible using the best therapeutical option we have since the beginning of the disease. The second step in the T2T strategy should be to minimize or even withdrawal glucocorticoids which we know to be one of the major contributors to damage accrual. It has been shown that even a small daily dosage of prednisone can contribute to damage in the long term. However, to withdrawal a low dosage of prednisone (5 mg per day) can increase the risk of disease flare. The third step in the T2T strategy is to reduce and to withdrawal immunosuppressants which are also associated with damage progression due to their side-effects. But again, the discontinuation of immunosuppressants is associated with an increased risk of disease relapse. Thus, the T2T strategy is like a tug of war; indeed, from the one side we have to reduce the disease activity and on the other side to reduce the SoC leading to frequent disease relapse without dampening the damage accrual. Indeed, the SoC alone cannot cannot allow the minimization or the withdrawal of glucocorticoids and/or immunosuppressants. This is the reason why we need a change in the paradigm of SLE management. It has recently been shown that the new biological drugs, belimumab and anifrolumab, when added to the SoC can help in decreasing disease activity and even achieving clinical remission or cLDA and at the same time to save glucocorticoids. The recent update of the EULAR recommendation for the treatment of SLE suggests an approach where one of the options in the treatment of non-renal or renal SLE is to use the combination therapy with biologics since the beginning of the disease.

IS054 / #93

Daratumumab Monotherapy for Refractory Lupus Nephritis

Dario Roccatello
University Center of Excellence on Nephrological, Rheumatological and Rare Diseases (ERK-net, ERN-Reconnect and RITA-ERN Member) including Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the, Torino, Italy

Lupus nephritis (LN) that does not respond to treatment poses a significant risk of adverse outcomes and frequently presents a life-threatening condition. In this study, we present a series of six patients (one male and five females) with a median age of 41.3 years (ranging from 20 to 61 years) who were diagnosed with refractory lupus nephritis (LN). These patients underwent renal biopsies and were subsequently administered intravenous daratumumab, an anti-CD38 monoclonal antibody (weekly for 8 weeks, followed by eight biweekly infusions and up to eight monthly infusions). The study observed a decrease in the mean disease activity, as measured by the Systemic Lupus Erythematosus Disease Activity 2000 index, in a five individuals (one patient did not show any improvement after 6 months of therapy, and daratumumab was discontinued.). Prior to therapy, the mean disease activity was recorded as 10.8, which subsequently fell to 3.6 following a 12-month period of treatment. The average proteinuria levels fell from 5.6 g per 24 hours to 0.8 g per 24 hours, and the average serum creatinine levels reduced from 2.3 mg dl-1 to 1.5 mg dl-1 after a period of 12 months. The amelioration of clinical symptoms was observed in conjunction with the seroconversion of anti-double-stranded DNA antibodies, reductions in median levels of interferon-gamma, B cell maturation antigen, and soluble CD163, as well as elevations in C4 and interleukin-10 levels. These data suggest that daratumumab monotherapy warrants further research as an effective therapy for refractory LN.

PLENARY 02 (CONT.): CHALLENGE THE EXPERT

19-05-2024 09:30 - 10:00

IS055 / #929

How Can Reporting of Autoantibody Test Results Be Improved?

Xavier Bossuyt
Laboratory Medicine, University Hospital Leuven, Leuven, Belgium

Autoantibody test results are usually reported as positive or negative based on a single cutoff value. However, such dichotomous (positive/negative) interpretation is a simplified way of test result interpretation. For many autoantibodies, the probability of disease increases with increasing antibody level. Such relationship between antibody level and probability of disease has been shown, for example, for anti-tissue transglutaminase antibodies, for rheumatoid factor and for anti-citrullinated protein/peptide antibodies (ACPA). According to the ESPGHAN guidelines for diagnosis of celiac disease in children a biopsy can be avoided if IgA anti-tissue transglutaminase antibodies exceed 10-times the upper limit of normal. For rheumatoid arthritis classification, high levels of rheumatoid factor and ACPA were assigned a higher weight than low titers of these antibodies. Although many laboratory professionals and clinicians recognize that the probability of disease enhances with increasing antibody levels, such information is not provided in the laboratory test result report. A way to communicate how strongly a test result is associated with presence/absence of disease is through reporting test result interval-specific likelihood ratios. The test result interval-specific likelihood ratios typically increase with increasing antibody levels. The likelihood ratio is the ratio of the fraction of patients with a particular test result to the fraction of controls with the same test result. For many autoantibodies, the likelihood ratio increases with increasing antibody level. A high likelihood ratio (>10) is useful to confirm the disease, whereas a low likelihood ratio (<1) is useful to exclude the disease. A test result with a likelihood ratio ~1 indicates that the test result does not help to either exclude or confirm the disease.

IS056 / #930

Can We Reliably Measure Autoantibodies that Recognize Conformational Epitopes?

Xavier Bossuyt
Laboratory Medicine, University Hospital Leuven, Leuven, Belgium

Solid phase assays are widely used for measurement of autoantibodies. Advantages of solid phase assays include automation, reproducibility and the use of well-characterized recombinant antigens. The possibility of aspecific reactivity to the solid phase is a weakness of solid phase assays. Moreover, in solid phase assays, the autoantigens are bound to the solid phase and therefore not fully accessible to the autoantibodies and/or not in their native conformation. Detecting antibodies to a multi-protein complex is difficult with solid phase assays. In immunoprecipitation, the interaction between autoantigen and autoantibody occurs in fluid phase. Thus, the native conformation of the autoantigen is preserved, thereby allowing efficient interaction with the autoantibody. Mass spectrometry can be applied to directly identify the proteins in the immunoprecipitate. Immunoprecipitation coupled to mass spectrometry or Western blotting has been successfully applied to show antibodies to complex autoantigens (e.g. multiprotein complexes), such as anti-OJ antibodies, anti-RuvBL1/2 antibodies and anti-THO antibodies.

IS057 / #931

Can The Impact of Autoantibodies in Diagnostic Criteria Be Upgraded?

Xavier Bossuyt
Laboratory Medicine, University Hospital Leuven, Leuven, Belgium

Autoantibodies are included in classification criteria for several rheumatic diseases, including rheumatoid arthritis (RA). The 2010 ACR and EULAR classification criteria for RA include anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) as serological marker for RA. The presence of ACPA or RF contributes two points if higher than the upper limit of normal (ULN) but lower than 3 times the ULN and three points if present at levels >3 times the ULN. A score ≥6 allows the classification of RA. Thus serological markers can account for up to 50% of the classification score. Sensitivities of RF and ACPA for RA are comparable (±60%), but the specificity of ACPA (±95%) is higher than the specificity of RF. Despite the differences in clinical performance characteristics, ACPA and RF are given the same weight in the classification criteria. There is some evidence that by refining the serological weight scoring, the serological scoring of the classification criteria can be improved. Such updated serological weights should take into account the nature of the antibody (RF versus ACPA), the level of antibody positivity and the presence of combined RF/ACPA positivity.

IS058 / #932

Is The Old Statement 'One Autoantibody/One Disease' Still Satisfactory in 2024?

Anti-dsDNA antibodies have long been considered the primary autoantibody and the most important biomarker for lupus nephritis (LN). The deposition of anti-dsDNA antibodies in immune complexes or their binding to planted antigens in the glomeruli has been described as the main pathogenic pathway that leads to local complement-mediated inflammatory tissue damage. In 2019, the EULAR/ACR classification included an anti-dsDNA antibody assay as a laboratory classification criterion. This assay should display ≥90% specificity for Systemic Lupus Erythematosus (SLE) against relevant disease controls. However, this statement may limit the diagnostic tools to highly specific but poorly sensitive technologies. Moreover, there are contradictory data on whether anti-dsDNA antibodies can really predict kidney involvement. Recent studies suggest that the pathogenesis of renal involvement may be related not only to autoantibodies against nucleosomal antigens but also to additional kidney-specific autoantigens such as α-enolase (ENO1), Annexin A1 (ANXA1), actinin and others. This finding is supported by studies of the analysis of glomerular micro-dissection from LN patients. Furthermore, different IgG subclasses and antibodies that display cross-reactivity between DNA and other molecules may contribute to LN pathogenesis. Therefore, the use of a panel of autoantibodies is emerging as the most promising tool for the diagnosis and characterization of kidney involvement in SLE. Anti-dsDNA antibodies have long been considered the primary autoantibody and the most important biomarker for lupus nephritis (LN). The deposition of anti-dsDNA antibodies in immune complexes or their binding to planted antigens in the glomeruli has been described as the main pathogenic pathway that leads to local complement-mediated inflammatory tissue damage. In 2019, the EULAR/ACR classification included an anti-dsDNA antibody assay as a laboratory classification criterion. This assay should display ≥90% specificity for Systemic Lupus Erythematosus (SLE) against relevant disease controls. However, this statement may limit the diagnostic tools to highly specific

but poorly sensitive technologies. Moreover, there are contradictory data on whether anti-dsDNA antibodies can really predict kidney involvement. Recent studies suggest that the pathogenesis of renal involvement may be related not only to autoantibodies against nucleosomal antigens but also to additional kidney-specific autoantigens such as α-enolase (ENO1), Annexin A1 (ANXA1), actinin and others. This finding is supported by studies of the analysis of glomerular micro-dissection from LN patients. Furthermore, different IgG subclasses and antibodies that display cross-reactivity between DNA and other molecules may contribute to LN pathogenesis. Therefore, the use of a panel of autoantibodies is emerging as the most promising tool for the diagnosis and characterization of kidney involvement in SLE.

PARALLEL SESSION 10: INFECTIONS AND AUTOIMMUNITY

19-05-2024 10:30 - 12:00

IS059 / #98

Infection and Autoimmunity - Concept and History, The Pandemic of COVID-19

Naim Mahroum
Istanbul Medipol University, International School of Medicine, Istanbul, Turkey

The etiologic and pathogenetic mechanisms involved in autoimmune diseases have been studied for decades. Genetic predisposition interacting with environmental factors is the leading and accepted concept in this regard. Having said that, infections and infectious agents constitute the main player when it comes to the environmental component. How bacteria or viruses, but mainly viruses, can trigger an autoimmune response is another part of the story. Though molecular mimicry builds up the first and the majority of the studies in the field of infection and autoimmunity, many other mechanisms have been described. Recently, the pandemic of COVID-19 brought the interaction between viruses and autoimmunity back into the center of attention. SARS-CoV-2, the causative agent of COVID-19, proved throughout the pandemic to how extent viruses can be autoimmune, as the term "autoimmune virus" was used in this regard. Generally speaking, while immunosuppressants have no place in medicine when it comes to acute viral infection; they were shown to have a great influence in improving morbidity and mortality in patients with acute COVID-19. The autoimmune phenomena seen during the acute and recovery period of COVID-19 have widened our vision and permitted areas of autoimmunity to be discovered. In addition, new terms were introduced, previous facts were questioned, and syndromes were discovered. The old and new history of infection and autoimmunity is mandatory for the present and future of the field of autoimmunity, and here is the aim behind our paper.

IS060 / #100

Post Infectious Syndromes: Spectrum and Autoımmune Mechanisms

Carmen Scheibenbogen
Institute of Medical Immunology, Charité - Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Berlin, Germany

Carmen Scheibenbogen, Institute for Med. Immunology, Charité, Berlin, Germany Many infectious diseases are associated with post-infectious sequelae. One of the best known is the late EBV infection, infectious mononucleosis which can lead to myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), a severe, incurable disease. The COVID-19 pandemic has confronted us with a new dimension of sequelae, grouped under the umbrella term "long-COVID." Following mild COVID-19 infection, approximately 3 - 5% of those affected continue to suffer symptoms 12 months after infection, with a high risk of chronicity and no effective treatment available for most patients. Post-COVID conditions are heterogeneous and vary widely in their symptom spectrum and severity. There is ample evidence that inflammation and autoimmunity are potential mechanisms in postinfectious syndromes. Several studies described autoantibodies (AAB) associated with PCS, including AABs to RAS (renin-aldosterone system) proteins, cytokines, antinuclear antibodies (ANA), G protein coupled receptors (GPCR) and other AABs commonly associated with autoimmune diseases.

IS061 / #392

The Unique Combination of Gut Microbiome and Viral Infection in FM Patients

Zaiga Nora-Krūkle[1], Santa Rasa-Dzelzkaleja[1], Lauma Ievina[1], Anda Vilmane[1], Sabine Gravelsina[1], Nikita Fomins[2], Dita Gudra[2], Viktorija Kenina[3], Davids Fridmanis[2]
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Fibromyalgia (FM) is the most prevalent type of widespread chronic pain disorders, affecting around 4.7% of population. Currently, the diagnosis of the disease is based on the patient's medical history and symptoms, which challenge diagnosing FM in a timely and correct manner. The aim of this study was to identify FM-specific measurable indicators by analyzing the gut microbiome and viral infections. The pilot-study involved a cohort of 17 patients with FM and samples from 24 healthy blood donors. Determination of human herpesviruses (HHVs) infection markers in peripheral blood mononuclear cells (PBMC)/plasma samples was performed using multiplex and real-time polymerase chain reactions, cytokines levels - using bead-based multiplex assay. The analysis of the gut microbiome - performed by constructing a genomic library and conducting next generation sequencing.The results showed a trend of HHVs being more frequently found in patients with FM than in the control group. In the FM group, patients with BMI ≥ 30 had an increase in levels of cytokines compared to the control group. Analysis of the gut microbiome revealed significant differences in β-diversity between the two groups and indicated altered relative species abundance in the FM group compared to healthy controls.The study hints at a possible link between HHVs and FM. Furthermore, changes in bacterial species composition in FM patients compared to healthy individuals suggest that investigating the role of the gut microbiome in the etiopathogenesis of FM could be a promising direction for future research.

IS062 / #103

Adaptive Immunity in COVID-19 – Two Sides of The Coin

Nina Babel
Center for Translational Medicine, Marien Hospital Herne - Universitätsklinikum der Ruhr-Universität Bochum, Herne, Germany

Infection is the fourth leading cause of death in general population and second leading cause of death in patients with chronic diseases such as chronic kidney diseases or diabetes. Sufficient function of both arms of immune systems - humoral (antibody) and cellular (T cell-driven) immunity that required for the prevention of pathogen entry and clearance infectious pathogens, respectively, can con-

trol infection. The presentation will focus on the formation of SARS-CoV-2-specific T cell immunity during natural infection or following vaccination. In context of natural infection, the role of pre-existing cross-reactive T cell immunity as well as different SARS-CoV-2 proteins will be discussed. I will present functional and phenotypic characteristics of SARS-CoV-2-specfic T cells associated with different stages and severity of COVID-19 including long COVID that might allow personalized therapy. A special focus will be on patients with chronic kidney disease - the most vulnerable patient population. In context of COVID-19 immunization, immunogenicity of COVID-19 vaccines as defined by vaccine-induced antibody and T cell response will be demonstrated in different patient cohorts including immunocompetent and immunocompromised patients. The role of immune monitoring for the vaccination recommendations in a risk population such as immunocompromised patients will be demonstrated and discussed.

PARALLEL SESSION 11: AUTOIMMUNE SYNDROME INDUCED BY ADJUVANTS (SHOENFELD'S SYNDROME) - DEDICATED TO THE LATE PROF LUIS JARA

19-05-2024 10:30 - 12:00

IS063 / #104

ASIA (Shoenfeld's Syndrome) Due to Implants: A Hype or A Real Phenomenon

Jan Willem Cohen Tervaert
University of Alberta, Faculty of Medicine, Edmonton, Canada

Implants such as breast and mesh implants can cause ASIA (Shoenfeld's syndrome). The pathophysiological mechanisms underlying this syndrome are not yet clear and the overlap it shows with other common conditions such as fibromyalgia and chronic fatigue syndrome has sparked an important debate in the scientific community regarding the existence of this syndrome. During recent years, it has been demonstrated that there is a causal relationship between these implants and ASIA as defined by the Bradford Hill criteria. Furthermore, it has been found that after explantation of implants 50 - 98% of patients report an improvement of symptoms. Despite these convincing arguments for the existence of the syndrome, many physicians state that they do "not believe" in ASIA. As with other illnesses that are not widely accepted as diseases, patients feel delegitimized. So, patients have a "double burden": they have to deal with the illness itself and also with the difficulty of finding an explanation and treatment of their symptoms. As a result, "epistemic injustice" in these marginalized patients develops resulting in large online communities. Unfortunately, in these communities patients have a dominant biomedical view on their illness. As a result, they present their biomedicalized view to their physicians which may lead to irritation especially when these physicians are "non-believers". In turn, this unfairness will increase the participation in online groups with fellow sufferers. So, I postulate that *a real phenomenon* ("ASIA due to implants") may cause *a hype* if physicians persist in contesting the existence of the syndrome.

IS064 / #109

Hyperprolactinemia in ASIA After Mineral Oil Injection and Silicone Breast Implants

Luis Jara Quezada[1,2,3], Olga Vera[3]
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[2]Division of Rheumatology, Instituto Nacional de Rehabilitación, Mexico City, Mexico
[3] Division of Rheumatology, Hospital de Especialidades Centro Médico La Raza, Mexico, Mexico

***Introduction*:** Recently, a study of immunological and endocrine parameters after 119 mammoplasty was carried out. Their results showed an increase in the levels of autoantibodies against the TSH receptor and an increase in thyroid autoimmunity after silicone mammoplasty. On the other hand, immune cells secrete prolactin (PRL). There is abundant data in humans that hyper-prolactinemia is associated with autoimmune disease, such as systemic lupus erythematosus (SLE) and other autoimmune diseases. Prolactin is elevated during pregnancy and breastfeeding in asociation with maternal-fetal complications in SLE patients. Hormonal alterations have recently been described in ASIA syndrome, especially after the COVID-19 vaccine, suggesting an adjuvant effect.

Objective: To compare serum PRL levels in patients with and without ASIA syndrome due to breast implants and mineral oil injections.

Patients and Methods: Case-control study. Cases: Patients who developed ASIA syndrome (1) after breast implant surgery or mineral oil injections for aesthetic purposes.Controls: patients without ASIA syndrome after breast implant surgery or mineral oil injections. All patients and controls had serum PRL determinations measured by radioimmunoassay (normal values: (2-20 ng/ml, Men: 17 ng/ml, Women: 25 ng/mL). Statistical analysis: Descriptive statistics were used to measure averages and standard deviation. The Chi square and Mann Withney U tests were used to compare groups. The study was carried out at the Hospital de Especialidades, Centro Médico La Raza, Mexico City, Mexico, in the period from January 1, 2015 to January 15, 2023.

Results: A total of 88 patients with breast implants and mineral oils were studied, with an average age of 51 years, with minimum exposure of one year, maximum of 47 years and average of 13 years, 85 patients were women.of the 88 patients, 50 met the criteria for ASIA, of these patients, 32 had mineral oil and 18 had breast implants. All 38 patients who did not meet ASIA criteria had breast implants. The patients were divided into 2 groups: Group 1: with ASIA (N=50). Group 2: without ASIA (N=38). The clinical manifestations were: Group 1: 15 patients had definite autoimmune disease: Rheumatoid Arthritis (3), primary hypothyroidism (5), Fibromyalgia (4), SLE (2) and Scleroderma (1). Group 2: 3 patients had defined autoimmune disease: Rheumatoid Arthritis (1), primary hypothyroidism (1) and SLE (1). The clinical manifestations of ASIA were significantly different in Group 1 vs. Group 2 (P<.001) in: muscle weakness/myositis, arthralgia/arthritis, chronic fatigue, insomnia, fever and dry mouth. Serum PRL levels were significantly elevated in Group 1:14.57 (IQR: 8.77-20.3) vs Group: 2: 8.02 (IQR: 5.5-10.6), P< .011. Of interest, 8 patients in group 1 had hyperprolactinemia (PRL > 20 ng/mL). In contrast, no patient in Group 2 developed hyperprolactinemia.

Conclusion: Patients with ASIA (breast implants and mineral oil injections) have elevated serum PRL levels and hyperprolactinemia, compared to patients without ASIA. These results suggest that A.S.I.A. is a different autoimmune entity.

IS065 / #106

Tattoo and Autoimmunity

Amir Tanay
Zabludowicz Center for Autoimmune Diseases, Tel Hashomer, Israel

Background: Tattoo's are safe based on current evidence, but Tattoo inks are currently minimally regulated for composition or purity. Unanticipated complications can arise, even decades after tattooing.

Method: Two cases are presented and the relevant current literature was screened.

Conclusions: Tattoo reactions should be evaluated by Bx with special stains. Patients with preexisting psoriasis, pyoderma gangrenosum, susceptible to the isomorphic phenomenon or pathergy - should be cautioned to avoid tattooing altogether. Susceptible individuals, are having: Autoimmune disease. Immune depression. Silicon implants. are at risk and should be advised against Tattoo. Autoimmune pathophysiology in the course of Tattoo Inflammatory Reaction can be conceptualized in the context of ASIA.

IS066 / #108

Is Vaccination in Children with Immune Mediated Diseases Safe and Immunogenic?

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Vaccination is the most effective preventive measure against infection and as such extremely important in children with immune-mediated diseases. These children are immunocompromised because of the disease itself and/or because of the therapy they are receiving. The immune system is impaired in the diseases of Inborn errors of Immunity (IEI). The field of IEI includes more than 450 diseases divided into 10 groups. The degree of immunosuppression depends on the defect itself. In children with Severe combined immune deficiencies (SCID), B and T cell response is defective. Stem cell transplantation is needed and vaccinations are not immunogenic and effective in these patients. Live attenuated vaccines are contraindicated because the children can get the infection with the attenuated vaccine virus. Children with autoimmune rheumatic diseases (ARD) are immunocompromised mainly because of the therapy they receive. The degree of immunosuppression depends on the therapy. Infections present a major danger to their health. The new update recommendations for vaccinations in children with autoimmune inflammatory rheumatic diseases were published recently. Uncertainty about safety, immunogenicity, long-term efficacy, risk of disease flare and risk of disseminated infection following vaccinations with live attenuated vaccines should be taken into account in planning the vaccinations in these patients. In general, there are no major safety concerns for vaccination with non-live vaccines, including vaccines for SARS-CoV-2, regardless of the therapy. The immunogenicity of non-live vaccines was good in published studies, however in some studies lower compared to healthy controls. Live attenuated vaccines should be withheld in some children with inborn errors of immunity. In children with ARD, treated with methotrexate, booster MMR can be safely administrated and in children treated with biologic therapy booster MMR can be considered. For VZV vaccination the level of recommendation is still low, but VZV vaccination should be strongly considered in patients treated with methotrexate and can be considered also in patients treated with biologic therapy, especially in in the case of a high risk of infection. A recent multicentre retrospective study conducted by PRES Vaccination working party provided additional evidence about the safety of booster MMR in children treated with DMARDs and biologics. A multicentre prospective study on MMR booster is ongoing.

IS067 / #107

Exploring The Exposome's Influence on Vaccination Effectiveness

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The exposome, encompassing an individual's lifelong exposure to diverse environmental, biological, and lifestyle-related factors, plays a crucial role in shaping immune responses and, consequently, the outcomes of vaccines. This presentation delves into the intricate impact of the exposome on vaccination effectiveness. It explores how internal factors like adipose tissue and microbiota, along with external elements including climatic conditions and pollution, and personal behaviors such as dietary habits, sleep patterns, and physical activity, influence the immune responses to vaccines. The insights are drawn from an extensive survey of current literature, including recent studies on obesity's effect on immune response, the role of chronic inflammation, and the influence of exercise, the gut microbiota, and nutritional factors on vaccination effectiveness. This overview aims to shed light on optimizing immunization strategies and underscores the necessity for personalized approaches in vaccine administration, considering the heterogeneous nature of the exposome and its varied impacts on different populations.

PARALLEL SESSION 12: AUTOIMMUNITY IN THE CENTRAL NERVOUS SYSTEM

19-05-2024 10:30 - 12:00

IS068 / #110

Better Understanding The Underlying Mechanism of Fibromyalgia Syndrome Using Circulating Extracellular Vesicles

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Background and aims: Fibromyalgia syndrome (FMS) is a global chronic pain condition, which affects approximately 3%–6% of the population. The underlying mechanism of FMS is unclear and there is no specific lab test to confirm its diagnosis. There is an unmet need regarding the development of a precise diagnostic marker for FMS. Extracellular vesicles (EVs), are nano-sized, cell-derived membranous particles which were found to be involved in: intercellular communications and in the pathogenesis/regulation of autoimmune diseases. Recently, an autoimmune origin had been suggested for the development of FMS. In the current study, we aimed to characterize circulating EVs derived FMS patients and to explore the protein profile of these vesicles as compared to sex and aged matched healthy controls.

Methods: Small EVs have been isolated from the plasma of women diagnosed with primary FMS (n=9) vs. age matched healthy women (n=9), using size exclusion chromatography technique. Characterization of these EVs have been conducted using nanoparticle tracking analysis, transition electron microscopy and western blot analysis. The protein profile of the EVs have been explored using proteomics analysis.

Results: We found changes in the expression of various proteins in blood-derived small EVs of FMS patients as compared to healthy controls, among them: immunological- (e.g. Complement component 1q), neurological/pain- (e.g. Cofilin-1), ribosomal protein assembly- (e.g. Nucleophosmin) and oxidative stress-(e.g. Superoxide dismutase) related proteins.

***Conclusions*:** Our results shed a light on the importance of EVs in the development of FMS and their potential to serve as a new diagnostic biomarker candidate in FMS.

IS069 / #112

The Different Clinical Manifestations of Small Fiber Neuropathy

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Traditionally, the term "small fiber neuropathy" has been applied to a clinical syndrome manifested by spontaneous and evoked pain, mostly located at the distal extremities that is frequently accompanied by disperse autonomic symptoms including dry eyes and mouth, orthostatic complaints and gastrointestinal/urinary bladder dysmotility. In small fiber neuropathy, there are no signs of large nerve fiber dysfunction therefore muscle strength and reflexes are normal. The diagnosis of small fiber neuropathy is confirmed by specifically stained skin biopsy showing superficial small nerve fiber denervation. Corneal confocal microscopy is a non-invasive procedure able to define small nerve fiber pathology. There is a clear relationship between fibromyalgia and small nerve fiber pathology. Our longstanding proposal of fibromyalgia a stress-evoked sympathetically-maintained neuropathic pain syndrome has been sustained by the reports coming from different groups of investigators showing objective evidence of small nerve fiber pathology in more than half of all patients suffering from fibromyalgia. Therefore fibromyalgia can be considered a generalized small nerve fiber neuropathic disease manifested by widespread pain, allodynia and paresthesias accompanied by various autonomic symptoms. The key issue in fibromyalgia research is to define the mechanisms whereby different psychological, physical, infectious or/and autoimmune stressors are transformed in neuropathic pain. Our group has long proposed dorsal root ganglia as the key neural hubs where different stressors can induce neuropathic pain. Evidence supporting this hypothesis will be discussed including a yet unpublished study analyzing the acute effect of fibromyalgia patients' serum on the female rat dorsal root ganglia cells.

IS070 / #113

New B Cell-Targeted Therapies for Multiple Sclerosis

Ron Milo[1,2]
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Increasing evidence suggests that B cells contribute to both regulation of normal autoimmunity and to the pathogenesis of immune mediated diseases including multiple sclerosis (MS). B cells in MS are skewed towards a pro-inflammatory profile, exhibiting excess of pathogenic memory B-cells, decrease in B regulatory cells and increase in pro-inflammatory cytokines production. B cells contribute to the pathogenesis of MS by antibody production, antigen presentation, stimulation and activation of T cells (including memory-B cell driven auto-proliferation of brain-homing autoreactive CD4+ T cells), production of pro-inflammatory cytokines, formation of ectopic germinal centers under the meninges that drive cortical pathology and contribute to neurological disability, and probably by carrying the Epstein-Barr virus (EBV), the main suspect in causing MS. The recent interest in the key role of B cells in MS has primarily been evoked by the beneficial and profound anti-inflammatory effects of rituximab, a chimeric monoclonal antibody (mAb) targeting the B cell surface marker CD20, observed in patients with relapsing-remitting (RR) MS. This has been reaffirmed by clinical trials with less immunogenic and more potent humanized and fully human B cell-depleting mAbs targeting CD20, namely ocrelizumab and ofatumumab. Ocrelizumab is the first disease-modifying drug that has shown efficacy also in primary-progressive MS, and is currently approved for both indications. Ublituximab, a movel third-generation anti-CD20 chimeric glycoengineered IgG1 mAb has recently shown high efficacy and favorable safety and is currently approved for relapsing MS. Collectively, B cell depletion with anti-CD20 mAbs was proven to be safe and highly effective in MS, without significant compromise of the normal immune reactivity. Another promising approach is the inhibition of Bruton's tyrosine kinase (BTK), a key cytoplasmic enzyme that mediates B cell activation and survival. Several 2nd generation BTK inhibitors are currently in late stages of clinical trials in all forms of MS. Frexalimab, a novel anti-CD40 ligand antibody that reduces the activation of B and other immune cells, has recently shown significantly reduced disease activity in a phase-2 trial in relapsing MS. On the other hand, targeting B cell cytokines with the fusion protein atacicept resulted in increased MS disease activity, highlighting the complex and not fully understood role of B cells and humoral immunity in MS. Finally, essentially all other approved therapies for MS, some of which have been designed to target T cells, have some effects on the frequency, phenotype or homing of B cells that may contribute to their therapeutic activity.

IS071 / #114

The Nervous System in Rheumatoid Arthritis

Christopher Edwards
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Rheumatoid arthritis (RA) was initially described as an inflammatory and destructive disease of synovial joints. However, over the last 20 years increasing focus has been directed towards the effects of chronic systemic inflammation on other organ systems. It is now clear that inflammation plays an important negative role in the development of cardiovascular disease and that DMARDs can reduce this risk. More recent research has considered the increased risk of brain related pathology such as stroke along with pain, depression/anxiety and even cognitive function. It has also been suggested that RA provides a model system to explore the consequences of chronic inflammation of relevance to all populations. This may also be true for cardiovascular disease and dementia.

PARALLEL SESSION 13: RHEUMATOID AND ARTHRITIS MYOSITIS (MUSCLES)

19-05-2024 14:00 - 15:30

IS072 / #117

Ways To Prevent Difficult-To-Treat Ra

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The prevalence of difficult-to-treat rheumatoid arthritis (D2T RA) varies between 5% and 25%, with females comprising the vast majority of patients and with no difference in patients' age between D2T and non-D2T RA cohorts. Multiple factors are usually involved in the mechanisms of RA refractoriness, with the complex interplay of inflammatory, structural, social, and psychological factors being rather discrete in each patient. No single test or study can replace the holistic clinical approach to the diagnosis and understanding of the causation of D2T RA, but more severe disease at presentation, including seropositivity and early erosion formation, and insufficiently aggressive initial treatment can contribute to the eventual development of D2T RA. Traditional in-depth clinical history and thorough clinical examination remain *sine qua non* in managing D2T RA patients, while multifaceted contribu-

tions of inflammatory and non-inflammatory components create the uniqueness of D2T RA. Prevention of D2T RA should be based on a personalized approach to every individual with RA, timely diagnosis, recognition of comorbidities, treatment goal alignment, and sufficiently aggressive treatment.

IS073 / #118

Efficacy and Safety of JAKi for The Treatment of RA in Real-Life

Carlo Perricone
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Rheumatoid arthritis (RA) is a chronic, inflammatory disease affecting the joints. An aberrant activation of the immune system, through hyperexpression of pro-inflammatory cytokines, plays a fundamental role in inducing swelling, pain, and stiffness in joints. Recently, it has been shown that blockade of cytokine signal transduction mechanisms, many of which are mediated by the Janus kinase-signal transducers and activators of transcription (JAK-STAT) pathway, may be critical in the treatment of RA. JAK inhibitors (Jakinibs) target multiple JAKs with high affinity and have a well-established rationale for clinical therapeutic use in inflammatory and autoimmune diseases by blocking multiple cytokines involved in both development and propagation of the disease. JAKi have dramatically changed the treatment scenario of RA, nonetheless a careful evaluation of patients' features needs to be performed to allow best drug performance and containment of adverse events.

IS074 / #119

Inflammatory Myopathıes and Ild

Sonja Praprotnik
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Polymyositis (PM), dermatomyositis (DM), and anti-synthetase syndrome (ASS) are conditions included among idiopathic inflammatory myopathies (IIMs), characterized by various degrees of muscle inflammation. Interstitial lung disease (ILD) is one of the most severe extra-muscular features, and the frequency and severity depend on the underlying inflammatory myopathy subtype. We aimed to identify predictors of ILD in a monocentric cohort of 213 IIM patients. Data were prospectively collected between January 2005 and June 2023. ILD was diagnosed in 77 patients, with a mean age of 63,5 years. Patients with ILD were younger then patients without (58,5 versus 65,4 P <.05). ILD was diagnosed by high resolution computed tomography (HRCT) of the lungs. The most frequent patterns are non-specific interstitial pneumonia (46% of the patients) and organizing pneumonia (20% of the patients). ILD was significantly more frequent in ASS (48/54; 88.8%) compared with other IIMs P <.001). ILD has occurred less frequently in PM (*3/16; 18,7%*) and in DM (*9/67*;13,4%), and none in statin induced myopathy. 19 of those 48 patients with ASS and ILD had the amyopathic form of the disease. This subgroup was statistically significantly associated with the combination of anti-Ro 52 and anti Jo-1 antibodies (P<.01). There have been 12 ILD in 30 overlap syndromes, but mostly overlaps with systemic sclerosis and the dominant antibody was anti PM-Scl. We did not find a relationship between any antibody in PM, DM and ILD. Microvasculopathy in nailfold capillaroscopy were also associated with DM-ILD (P<.03) In conclusion myositis antibodies and nailfold capillaroscopy provide valuable information for clinicians managing patients with ILD.

IS075 / #510

From Fat to Muscle- An Unusual Case of Myositis

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Statin induced necrotizing autoimmune myopathy (SINAM) is an exceptionally rare yet devastating complication of statin therapy that can occur at any time after initiation. Also known as anti-HMGCR myopathy. SINAM should be considered in patients who develop proximal muscle weakness and marked elevated CPK while taking statin therapy. We present a 74-year-old female, with a medical history of dyslipidemia treated with statins that presented with excessive fatigue, generalized muscle pain and weakness without dysphagia. Initial findings included elevated levels of hepatocellular liver enzymes, LDH, CPK and CRP. EMG showed myopathic fibrillation. Left deltoid muscle biopsy demonstrated necrotic and regenerative single fibers, which were scattered, compatible with mild necrotizing myopathy. Therapy was initiated with high dose steroids, prednisone 60 mg, and high dose intravenous immunoglobulin (IVIG), 2g/kg divided over 5 days. The diagnosis was confirmed later by elevated titers of anti-HMGCoA reductase antibodies. The patient continued therapy with steroids and received another course of high dose IVIG before she was discharged to a chronic care facility, where she slowly regained muscle strength and steroid therapy was tapered down. SINAM is a rare and potentially fatal autoimmune disease that often presents with progressive muscle weakness, elevated CPK levels, myonecrosis, and anti-HMGCoA reductase antibodies. Treatment includes discontinuation of the statin and initiation of immunosuppressive therapy. IVIG is beneficial for these patients. Early diagnosis can improve the prognosis. Clinicians should be aware of this devastating complication.

IS076 / #121

Correct Nutrition As Immunomodulatory Co-Therapy in Rheumatoıd Arthritis

Maurizio Cutolo
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Rheumatic and musculoskeletal diseases (RMDs) are chronic systemic immune/inflammatory conditions characterized by the interaction between gene predisposition, autoimmunity and environmental factors. A growing scientific interest has focused on the role of nutrition in RMDs, suggesting its significant contribution to the pathogenesis and prognosis of these diseases. The diet can directly modulate the immune response by providing a wide range of nutrients, which interfere with multiple pathways at both the gastro-intestinal and systemic level. Moreover, diet critically shapes the human gut microbiota, which is recognized to have a central role in the modulation of the immune response and in RMD pathogenesis, such as in rheumatoid arthritis (RA). Choosing the 'right' diet is therefore crucial and a form of self-management 'intervention' that could impact on disease expression, course and outcome. Generally, the Mediterranean diet is highly recommended in RMDs due to its anti-oxidant and anti-inflammatory properties and may be suggested as the preferred dietary pattern in both RA and SLE. Interestingly, vegetable unsaturated fatty acids (VUFA) and animal unsaturated fatty acid (AUFA) DPs were inversely related to DAS28 (Disease Activity Score on 28 joints) in RA. The study mentioned seems to show that scoring high on dietary products (DPs) based on unsaturated fats, even from

different sources, may provide independent contribution of clinical relevance on RA disease activity. Similarly, the high and regular use of fruits and vegetables, once fermented by the gut microbiota bacteria, originate the short chaid fatty acids (SCFA) that though product like piruvate exeret antiinflammatosy systemic effects and are elegible nutrients as co-theraoy in RA. On the contrary, it seems possible that high salt consumption or sugar sweetened soda, for example, may have a negative effect on gut microbiota, increasing the presence of *Prevotella copri* strains with higher Branced Chain Amino Acids (BCAA) and *Lactobacillus depletion* resulting on higher intestinal inflammation and flares in RA. To be considered that the molecular contents of beverages, including coffee, tea and wine, have been found to interfere with immune signaling pathways. Some have beneficial effects for disease progression and others not. Green tea is antioxidant and therefore a complementary beverage to act as co-therapy in RA. Red wine in low amount 1 glass a day is not proinflammatory and might be used in RA as wella s coffee 23 caps do not arm in RA. In conclusion, An appropriate and well-balanced diet does not replace the pharmacological management of disease but should at least be used as an adjuvant to medical treatment, with most evidence supporting this coming from studies in RA. Dietary counseling together with disease-modifying anti-rheumatic drugs should both form part of the early management of RA.

PARALLEL SESSION 14: THERAPEUTIC CHALLENGES IN AUTOIMMUNITY

19-05-2024 14:00 - 15:30

IS077 / #122

Helminth Derivative to Treat Autoimmunity

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Background and aims: Where there are helminthes, autoimmunity is rare. The aim of the helminthes is to protect themselves *via* immunomodulation of the host immune network. The immunoregulatory functions of helminthes were attributed to the phosphorylcholine (PC) moiety on the helminthes' secretory molecules. We have constructed a bi-functional molecule PC-tuftsin (TPC) and showed its immunomodulatory activity in murine models of autoimmune diseases and *ex-vivo* using human peripheral mononuclear cells (PBMCs) and biopsies of patients with giant-cell-arteritis (GCA).

Methods*:* Mouse models for autoimmune diseases. Cell phenotypes by FACS and RT-PCR, histology service.

Results: TPC attenuated the clinical score of murine autoimmune models|: lupus in NZ-BxW/F1 mice , collagen-induced-arthritis , DSS-induced-colitis and experimental-autoimmune-encephalomyelitis. In all the experimental autoimmune conditions, TPC decreased the secretion of inflammatory cytokines and enhanced production of anti-inflammatory IL-10 and expanded T and B regulatory cells. The immunomodulatory activity of TPC was proven also *ex-vivo* in giant-cell-arteritis (GCA), reducing the inflammatory cytokines production by patients PBMCs and in biopsies from GCA patients (3). TPC immunomodulatory activities will be discussed. In addition, TPC was able to inhibit vascular-endothelial-growth-factor (VEGF), platelet-derived-growth-factor (PDGF), Monocyte-chemoattractant-protein-1 (MCP1) and IL-8 expression by human primary aortic endothelial cells. The signaling cascade will be discussed.

Conclusions*:* Our data propose the potential for this small molecule as a novel therapy to treat patients with autoimmune diseases.

IS078 / #123

News On Janus Kinase (JAK) Function and JAK Inhıbıtıon in SLE

Martin Aringer
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Among the receptors apparently playing a role in systemic lupus erythematosus, there are several that signal via members of the Janus kinase (Jak) tyrosine kinase family. These cytokines include type I interferons, which have definitive clinical relevance in SLE, given the efficacy of blockade of their common receptor by anifrolumab, but also interferon-γ (IFNγ), interleukin-6 (IL-6), and IL-10. At least STAT1, downstream of the Jaks in IFN signaling, is clearly upregulated in SLE leukocytes, and we have data suggesting that IL-6-induced STAT3 phosphorylation is only downmodulated by more trans-signaling, transferring the effects to cells other than leukocytes and hepatocytes. Regarding controlled clinical trials, the phase III results of the Jak1/Jak2 inhibitor baricitinib were seen as disappointing and led to the termination of the program. However, one of the two sister trias showed positive results. In 2023, clearly positive phase II results of the predominant Jak1 inhibitor upadacitinib became public, and a phase III program was initiated. Moreover, there are also positive phase II data on deucravacitinib, which blocks Tyk2, the fourth member of the Jak family relevant for type I IFN signaling and for IL-12 signaling.

IS079 / #124

Autologous Stem Cell Transplantation versus Upfront Combination Therapy of Rituximab and Mycophenolate Mofetil for Progressive Diffuse Systemic Sclerosis - 2 Year Outcomes

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Objectives: Autologous hematopoietic stem cell transplantation (AHSCT) has been shown to improve long-term survival for early diffuse progressive systemic sclerosis (SSc) compared with cyclophosphamide. Cyclophosphamide, however, does not provide a long-term benefit in SSc. The combination of mycophenolate mofetil (MMF) and rituximab is a potent alternative regimen. We aimed to retrospectively compare the outcomes of SSc patients who underwent AHSCT to patients who met the eligibility criteria for AHSCT but received upfront combination therapy with MMF and rituximab.

Methods: Repeated assessments of modified Rodnan Skin Score (mRSS), forced vital capacity (FVC), and diffusing capacity (DLCO) values were conducted. Clinical improvement was defined as an mRSS decrease > 25% or an FVC increase > 10%. Event-free survival (EFS) was defined in the absence of persistent major organ failure or death.

Results: Twenty-one SSc patients in the combination therapy group were compared with sixteen in the AHSCT group. Age, sex and disease duration were similar between the two groups. Clinical improvement at 12 months was seen in 18 (86%) patients in the combination group compared with 13 (81%) in the AHSCT group (*P*= .7). The hazard ratio for EFS at 24 months favored the combination group (HR = 0.09, *P*= .04). During follow-up, both groups exhibited a significant and comparable reduc-

tion in mRSS and an increase in FVC values at each time interval up to 24 months.

Conclusion: MMF and rituximab compared with AHSCT in SSc patients eligible for AHSCT resulted in similar skin and lung clinical improvement with a better safety profile at 24 months.

IS080 / #125

Antıbody-Driven Photodynamic and Sonodynamic Therapies: A Look Into The Future of Targeted Medicine

Gary Gellerman
Chemical Sciences, Ariel University, Ariel, Israel

Photodynamic therapy (PDT) utilizes an organic dye (photosensitizer) capable of killing cancer cells in the body upon light irradiation by producing "killing" reactive oxygen species (ROS). It is one of the promising non-invasive treatment modalities for cancer. PDT is also applied against autoimmune diseases, such as rheumatoid arthritis, Lichen planus, Lichen Sclerosis, Psoriasis, Bullous dermatoses etc. Sonodynamic therapy (SDT) is a modification of PDT, in which dye (sonosensitizer) produce ROS under ultrasound irradiation. Albeit the generally similar mechanisms, the penetration depth of ultrasound into the body (~30 cm) is much greater than that of near-IR light (~3 cm), making SDT more effective than PDT for diseases located deep within the tissue. A known drawback of SDT is a side-effect caused by insufficient specificity of existing sonosensitizers and photosensitivity of patients upon treatment. We developed a new and targeted modality that provides a much safer sonotherapy. Based on our results in cancer models we will present our suggestions for applying our new approach in treatment of autoimmune diseases.

IS081 / #888

Functional Consequences of Immunological Checkpoınt Inhibitor Therapies on Lymphocytes

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Therapy with check point inhibitors has been improving prognosis of lung cancer patients but also modulates immune defense of the body. There are only limited data on the influence of different anti-cancer therapies on lymphocyte subpopulations and their relationships to survival of non-small cell lung cancer (NSCLC) and melanoma patients. We assessed the effect of immunotherapy on B cell, T cell, and NK-cell subpopulations. A total of 32 consecutive NSCLC patients were recruited at Pulmonology Clinic, Leipzig from January 2018 to March 2020 and enrolled in this study. Furthermore, 17 melanoma patients from our dermatology department were included. Immunophenotyping was done using a FACS Canto II flow cytometer (BD Biosciences) before the administration of the planned therapy and during therapy with up to 7 observational windows for each patient targeting 130 immunologic parameters. Absolute transitional B cells and activated cytotoxic T cells were significantly increased in NSCLC patients after immunotherapy ($P < .05$) or immunochemotherapy ($P < .05$). In melanoma patients, the percentage of CD8+ effector memory (CD8+CD45RA-CD45RO+CCR7-) T cells was higher in responders compared to non-responders before and immediately after the first cycle of treatment. This indicates that B as well as T cell activation have been induced by the checkpoint inhibition, independent on combination with chemotherapy. PBMC immune monitoring of immune-checkpoint inhibition (ICI) treatment appears to be a promising approach to identify early markers of treatment response and immune-related adverse events.

PARALLEL SESSION 15: EASI SESSION: THE NEW APS CLASSIFICATION CRITERIA: IMPLICATIONS IN CLINICAL PRACTICE

19-05-2024 14:00 - 15:30

IS082 / #909

Laboratory Classification Critera for Aps Are Not The Same as Diagnostic Laboratory Criteria for APS

Katrien Devreese
Coagulation Laboratory, Ghent University Hospital, Ghent, Belgium

Antiphospholipid syndrome (APS) is a rare autoimmune disease associated with autoimmune and inflammatory complications and mainly characterized by thrombotic events and pregnancy morbidity. The diagnosis of APS includes both clinical assessment of the patient and the detection of antiphospholipid antibodies (aPL). Since the clinically associated symptoms are not specific to the disease and are often caused by other underlying mechanisms, the role of the laboratory detection of aPL is crucial and most important to avoid under- and overdiagnosis. aPL is a heterogeneous group of autoantibodies, but in the classification criteria, only lupus anticoagulant (LA), anticardiolipin (aCL), and antibeta2-glycoprotein I antibodies (aβ2GPI) IgG and IgM are included as laboratory criteria. The type and combination of one or more out of the three aPL groups, as well as the titer of aCL and aβ2GPI are prognostic for the thrombotic and obstetric manifestations. Also, the clinical relevance differs between IgG and IgM aCL/aβ2GPI. Recently, new ACR/EULAR classification criteria for APS have been published. LA, aCL, and a β2GPI are still the cornerstone of the laboratory criteria. The type of laboratory parameters have principally not changed compared to the Sydney classification criteria (2006), and aCL and aβ2GPI antibody measurement is still restricted to enzyme-linked immunosorbent assays (ELISA). Also, in these new classification criteria, thresholds of moderate and high titer are restricted to the 40/80 level, and a cutoff calculated by the 99th percentile has been abandoned. The International Society on Thrombosis and Haemostasis Scientific and Standardization Subcommittee on Lupus anticoagulant/antiphospholipid antibodies (ISTH-SSC aPL) summarized a consensus (2018) on laboratory diagnosis of APS. The use of non-ELISA assays has been included and the guidance warned against a fixed cutoff value since aPL titers largely differ between solid phase assays. Nowadays, there is increasing use of measurement of aPL by methods other than ELISA, the semiquantitative reporting of titers is a matter of debate, as well as the role of the isotypes IgM and IgA, and the role of other aPL, such as antiphosphatidylserine/prothrombin antibodies. We have to differentiate between classification criteria and laboratory diagnostic criteria. Classification criteria are strict and meant for participant inclusion in studies and trials to study homogeneous populations of patients. In contrast, laboratory diagnostic criteria are broader and used in daily life to diagnose patients and optimize their management. Literature shows that classification criteria are also used as surrogate for diagnostic criteria, the more that the same parameters (LA, aCL, aβ2GPI) are included in the classification and diagnostic criteria. Patients diagnosed with a disease may or may not fulfill the classification criteria for that disease. On the one hand, improper use of classification criteria may lead to mis(under)diagnosis. On the other hand, the choice of aPL tests for the diagnosis of APS should be made wisely, avoiding adding a variety of assays with a risk for overdiagnosis of APS.

IS083 / #910

The Impact of The New Classification Critera on Pregnancy Morbidity

Savino Sciascia
University Center of Excellence on Nephrologic, Rheumatologic and Rare Diseases (erk-net, Ern-reconnect and Rita-ern Member) with Nephrology and Dialysis Unit and Center of Immuno-rheumatology and Rare Diseases (cmid), Coordinating Center of The Interregi, University of Torino, Torino, Italy

Antiphospholipid Syndrome (APS) is a systemic autoimmune disease characterized by persistent antiphospholipid antibodies (aPL). aPL are known to cause thrombosis and pregnancy complications, along with non-thrombotic symptoms such as cardiac valve disease or thrombocytopenia. Classifying APS is crucial for identifying individuals for research participation, ensuring trials include and compare similar disease states. This classification is distinct from tools used for clinical diagnosis. The APS classification criteria were last updated in 2006. However, the understanding of the disease has significantly evolved since then. The European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) collaborated to develop a new APS classification system, reflecting contemporary knowledge about the disease. This new system aims to enable the weighting of individual criteria and different risk profiles, exhibiting excellent operational characteristics with utmost specificity. The discussion will focus on the implications of releasing the new APS criteria on APS research, with a speicial focus on pregnancy complications.

PARALLEL SESSION 16: BIG DATA, PREDICTION, MONITORING AND PREVENTION

19-05-2024 15:45 - 16:45

IS084 / #152

Standardized Core Data Sets

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Systemic autoimmune diseases (CTDs) are great challenges for physicians and great burden for these patients. During the last decades, prognoses improved significantly by international collaborations, guidelines and recommendations, earlier diagnoses and also a few new medications. Most of these diseases are rare and in addition the disease expression is very heterogenous as an indication of different underlying pathophysiologic processes. A new option to overcome this heterogeneity - until now inhibiting new drug developments and successful clinical trials - is big data analysis for identifying more homogeneous subgroups and clusters, which may be evn found in more than one disease entity. In CTDs also, big data and AI may be the redeemer. But for the use of this new option qualified data are needed. In conferences, first attempts are shown using basic claims data, which are collected to regulate reimbursement. For scientific questions other data needed, which are best covered today by disease specific registries. Unfortunately, even disease specific registries content different data and file those in unharmoniized ways. The variations between registires of different disease are even bigger. For today, this challenge may be partly solved by higher numbers of data and by data curation processes. For the future, the solution should be a standardized core data set at least for all CTDs, better for all diseases. This data set should by findable, accessible, interoperable, and reusable (FAIR guiding principles) and could follow on the first, central level the 16 items set of common data elements for rare diseases registration. On a second level, the common basic assessment of all patients should be captured. The necessary items for such a level need to consented, e.g. on the basis of SNOMED nomenclature. The third level is modular disease specific and could be constructed of different sublevels for clinical observation and research. On the forth level, modules for various scientific data (genetics, proteomics etc.) should be accessible that get their final values by connection to high quality clinical data from level 1-3. In conclusion, one standardized core data set at least for all CTDs is the aim!

IS085 / #446

Precision Medicine in Systemic Lupus Erythematosus- An Update

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SLE is a heterogenous disease with different clinical and laboratory findings, including the autoimmune serology, disease course, and response to therapy. However, the physicians prescribe the available medications in a random manner according to the organ(s) involved. Precision medicine takes us some steps further; it will be possible to recognize individual variability in genetics, epigenetics, and cellular differences causing immune system aberration. By integrating molecular and biochemical markers, maybe we can identify specific personal markers that can assist in choosing the proper medication for the individual SLE patient. We reviewed the recent medical literature on SLE and precision medicine (PubMed 2020-2023). We reviewed the background genetic heterogeneity, (GWAS), interferon pathways (STAT4, IRF5, PDGF, HAS2, ITGAM, SLC5A11), all were associated with kidney involvement. Immune profiling of the innate and adaptive pathways, serum and urinary markers were also compared to clinical manifestations, disease activity, and prediction of flare. Serum CXCL10 correlated with the interferon signature, prediction of flare, disease activity, renal and neuropsychiatric involvement. Disease relevant immune subsets and peripheral blood immune-phenotyping aided in assessing disease activity and the development of stratified treatment options. Several new treatments and drug repurposing targeting these markers are under investigation. Precision medicine enables the physician to use additional tools to identify subsets of lupus patients by clinical manifestations, disease activity, severity, and treatment options.

IS086 / #156

Predictors of Severe Autoimmune Haemolytic Anaemia and Severe Thrombocytopenia in SLE

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Objective: To determine the predictors of the occurrence of severe autoimmune hemolytic anemia (AIHA) and its impact on damage accrual and mortality in SLE patients.

Methods: Factors associated with time to severe AIHA (hemoglobin level ≤7 g/dL) occurring from the onset of SLE symptoms were examined by Cox proportional hazards regressions. The association of severe AIHA with mortality was examined by logistic regression analyses while its impact on damage was by negative binomial regression.

Results: Of 1,349 patients, 49 (3.6%) developed severe AIHA over a mean (SD) follow-up time of 5.4 (3.8) years. The median time from the first clinical manifestation to severe AIHA was 111 days (IQR 43–450). By multivariable analysis, male sex (HR 2.26, 95% CI 1.02–4.75, $P = .044$), and higher disease activity at diagnosis (HR 1.04, 95% CI 1.01–1.08, $P = .025$) were associated with a shorter time to severe AIHA occur-

rence. Of the SLEDAI descriptors, only hematologic (leukopenia and/or thrombocytopenia) showed a certain trend toward significance in the multivariable analysis (HR 2.36, 95% CI 0.91– 6.13, *P* = .0772). Severe AIHA contributed neither to damage nor to mortality.

***Conclusions**:* Severe AIHA occurs during the early course of SLE. Male sex and higher disease activity at diagnosis emerged as independent predictors of a shorter time to severe AIHA occurrence. Although not statistically significant, hematological abnormalities at SLE diagnosis could predict the occurrence of severe AIHA in a shorter time. Damage and mortality did not seem to be impacted by the occurrence of severe AIHA.

IS087 / #157

Autoantibodies and Precision Medicine

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Precision Medicine aims at an individualized approach to prevention, diagnosis, and treatment by defining groups of individuals with similar characteristics. Although the term Precision Medicine is relatively contemporary, the quest for progressive individualization of diseases has been an integral part of the history of Medicine. In daily practice, physicians frequently take into account several individual characteristics of their patients, thus seeking to establish the most appropriate strategy for fine-tuning their monitoring and treatment. Lately, the increasing availability of disease biomarkers and the implementation of multiplex test platforms bring the possibility of unprecedented dissecting of discrete phenotypes of traditional diseases, thus contributing to the fulfillment of the Precision Medicine paradigm. Autoantibodies are traditional biomarkers for autoimmune diseases and can contribute to PM in many aspects, including identification of individuals at risk, disease sub-phenotyping, and the definition of prognosis and treatment. The progressive availability of multiplex platforms for testing an increasing number of autoantibodies should contribute to Precision Medicine in autoimmune diseases. Systemic lupus erythematosus (SLE) is known for the plethora of associated autoantibodies and many of those help determine specific features on an individual patient basis. Anti-SS-A/Ro60 antibodies are present in 30-40% of SLE patients but are especially associated with subacute cutaneous lupus (60-90% of patients). Anti-SS-A/Ro60 and anti-SS-B/La are associated with sicca syndrome in SLE patients. In addition, anti-SS-A/Ro60 in pregnant women is associated with an increased risk of neonatal lupus. Anti-U1-RNP antibodies are associated with scleroderma-like nail fold capillaroscopic abnormalities and Raynaud's phenomenon in SLE. Anti-Sm antibodies are associated with lupus nephritis, especially when coexisting with anti-dsDNA antibodies, neuropsychiatric lupus, serositis, pulmonary fibrosis, and peripheral neuropathy. Rising titers of antibodies to double-stranded DNA (dsDNA) and to nucleosomes are associated with imminent risk for disease flare, especially when accompanied by decreasing serum complement concentrations. The coexistence of antibodies to dsDNA and C1q is strongly associated with nephritis. Anti-P ribosomal antibodies are traditionally associated with psychosis, but this biomarker also indicates a higher probability of hepatitis and class V nephritis with a good long-term prognosis. Rheumatoid arthritis is also associated with a host of autoantibodies, although just a few are used in clinical practice. In particular, the presence of rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) are associated with more aggressive disease, extra-articular manifestations, cardiovascular disease, and premature mortality. These autoantibodies can also contribute to the selection of the appropriate therapeutic agent to be used in an individual patient. For example, RA patients with RF and/or ACPA have a higher frequency of sustained remission under rituximab and abatacept than double-negative RA patients. Systemic sclerosis (SSc) is associated with several autoantibodies, including those to topoisomerase I (Scl-70), centromere, RNA polymerase III, U3-RNP/fibrillarin, Th/To, RNA-polymerase I and II, and U11/U12 RNP. Anti-topo I is typically associated with diffuse SSc, a higher risk of severe interstitial lung disease, digital ulcers, cardiomyopathy, high skin score, and a more severe phenotype with an increased risk of mortality. Anti-centromere antibodies are associated with limited SSc, long-standing Raynaud's phenomenon, calcinosis, and a higher risk of pulmonary arterial hypertension. Anti-RNA polymerase III antibodies are associated with the diffuse SSc subset, high risk of severe, rapidly progressing cutaneous thickening, higher risk of renal crisis, gastric antral vascular ectasia, and increased possibility of underlying malignancy. Anti-fibrillarin is associated with younger age of onset, higher frequency of digital ulcers, pericarditis, and severe lower gastrointestinal involvement. Anti-Th/To is associated with a higher frequency of interstitial lung disease, pulmonary hypertension, and scleroderma renal crisis, thereby representing reduced survival of the patients. Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune disorders that affect the skeletal muscles and multiple organs. In recent years, an increasing number of autoantibodies has been identified in IMM, including myositis-specific autoantibodies (MSA) and myositis-associated autoantibodies (MAA). Several of these autoantibodies help in the phenotypic differentiation of these patients, thus contributing to Precision Medicine. Autoantibodies against aminoacyl transfer RNA synthetases (ARS) represent the most common MSA and can be detected in 22–35% of IIM patients. At least eight anti-ARS have been identified including anti-Jo-1 (anti-histidyl-tRNA synthetase), antiPL7 (anti-threonyl-tRNA synthetase), antiPL12 (anti-alanyl-tRNA synthetase), antiEJ (anti-glycyl tRNA synthetase), antiOJ (anti-isoleucyl-tRNA synthetase), antiHa (anti-tyrosyl-tRNA synthetase), antiKS (anti-asparaginyl-tRNA synthetase) and antiZo (anti-phenylalanyl-tRNA synthetase) antibodies. Anti-Jo-1 antibody is by far the most common, occurring in approximately 20% of adult patients with IIM. Anti-ARS autoantibodies are associated with the anti-synthetase syndrome, which is characterized by a spectrum of typical clinical manifestations including myositis, interstitial lung disease, arthritis, fever, Raynaud's phenomenon, and mechanic's hands. Another important autoantibody in IMM, anti-Mi-2, is associated with classic features of dermatomyositis (DM) including Gottron papules/sign, heliotrope rash, nail fold erythema, and violaceous rash including the V-sign and Holster sign. These patients tend to present with severe myositis, but they typically respond well to steroid therapy and have a good prognosis. In contrast, anti-TIF1g antibodies are strongly associated with malignancies in adult DM patients. Anti-NXP-2 is more frequent in juvenile DM (JDM) and is associated with a higher risk of developing calcinosis and severe muscle involvement. Anti-MDA-5 antibody is strongly associated with clinically amyopathic DM (CADM), rapidly progressive interstitial lung disease, and a high risk of mortality, especially in patients of Asiatic ancestry. A particularly severe form of IMM is immune-mediated necrotizing myositis (IMNM) and this form is frequently associated with antibodies to the signal recognition particle SRP and to 3hydroxy3methylglutaryl CoA reductase (HMGCR). The increasing role of autoantibodies in contributing to Precision Medicine in systemic autoimmune diseases is also observed concerning organ-specific autoimmune diseases, including autoimmune hepatitis, primary biliary cirrhosis, autoimmune encephalitis, etc. In conclusion, autoantibodies are important biomarkers and can by them-

selves indicate specific phenotypic associations. However, a more powerful definition of individual phenotypes compatible with the concept of Precision Medicine should combine autoantibodies with a host of other biomarkers, including gene polymorphism, epigenetic markers, microRNA, and microbiome. The availability of multiplex assays and the use of artificial intelligence and machine learning should contribute to the integration of these data into useful information for the management of individual patients.

IS088 / #158

ABS Against The Chemokine Receptor CXCR3 As Predictor for Mortality In A Population-Based Study

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Background and Aims: Chronic inflammation and autoimmunity contribute to cardiovascular (CV) disease. Recently**,** autoantibodies (aAb) against the CXC-motif-chemokine receptor 3 (CXCR3), a G-protein coupled receptor with a key role in atherosclerosis, have been identified. The role of anti-CXCR3 aAbs for CV risk and disease is unclear.

Methods: Anti**-**CXCR3 aAbs were quantified by a commercially available enzyme-linked immunosorbent assay in 5,000 participants (availability: 97.1%) of the population-based Gutenberg Health Study with extensive clinical phenotyping. Regression analyses were carried out to identify determinants of anti-CXCR3 aAbs and relevance for clinical outcome (i.e., all-cause mortality, cardiac death, heart failure (HF), and major adverse cardiac events (MACE) comprising incident coronary artery disease, myocardial infarction, and cardiac death). Finally, immunization with CXCR3 and passive transfer of aAbs were performed in $ApoE^{(-/-)}$ mice for preclinical validation.

Results: 4,195 individuals were included (48% female, mean age 55.5±11 years) after exclusion of individuals with autoimmune disease, immunomodulatory medication, acute infection, and history of cancer. Independent of age, sex, renal function, and traditional CV risk factors, increasing concentrations of anti-CXCR3 aAbs translated into higher intima-media-thickness, left ventricular mass, and NT-proBNP. Adjusted for age and sex, anti-CXCR3 aAbs above the 75th percentile predicted all-cause death (Hazard ratio (HR) [95%-confidence interval] 1.25 [1.02, 1.52], *p*=.029), driven by cardiac mortality (HR 2.51 [1.21, 5.22], *p*=.014). A trend towards a higher risk for MACE (HR 1.42 [1.0; 2.0], *p*=.05) along with increased risk of incident HF (HR per standard deviation increase of anti-CXCR3 aAbs: 1.26 [1.02, 1.79], *p*=.03) may contribute to this observation. Targeted proteomics revealed a molecular signature of anti-CXCR3 aAbs reflecting immune cell activation and cytokine-cytokine receptor interactions associated with an ongoing T helper cell 1 response. Finally, $ApoE^{(-/-)}$ mice immunized with CXCR3 displayed increased anti-CXCR3 aAbs and exhibited a higher burden of atherosclerosis compared to non-immunized controls. In a passive transfer model anti-CXCR3 aAb levelrs correlated with the degree of atherosclerosis.

Conclusions: In individuals free of autoimmune disease, anti-CXCR3 aAbs were associated with CV end-organ damage, predicted all-cause death as well as cardiac morbidity and mortality in conjunction with the acceleration of experimental atherosclerosis.

PARALLEL SESSION 17: AUTOANTIBODIES (ABS) - PREDICTION, PATHOGENIC AND PREVENTION

19-05-2024 15:45 - 16:45

IS089 / #129

Much More than Anti-dsDNA Antibodies for Lupus Nephritis

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Anti-dsDNA antibodies have long been considered the primary autoantibody and the most important biomarker for lupus nephritis (LN). The deposition of anti-dsDNA antibodies in immune complexes or their binding to planted antigens in the glomeruli has been described as the main pathogenic pathway that leads to local complement-mediated inflammatory tissue damage. In 2019, the EULAR/ACR classification included an anti-dsDNA antibody assay as a laboratory classification criterion. This assay should display ≥90% specificity for Systemic Lupus Erythematosus (SLE) against relevant disease controls. However, this statement may limit the diagnostic tools to highly specific but poorly sensitive technologies. Moreover, there are contradictory data on whether anti-dsDNA antibodies can really predict kidney involvement. Recent studies suggest that the pathogenesis of renal involvement may be related not only to autoantibodies against nucleosomal antigens but also to additional kidney-specific autoantigens such as α-enolase (ENO1), Annexin A1 (ANXA1), actinin and others. This finding is supported by studies of the analysis of glomerular micro-dissection from LN patients. Furthermore, different IgG subclasses and antibodies that display cross-reactivity between DNA and other molecules may contribute to LN pathogenesis. Therefore, the use of a panel of autoantibodies is emerging as the most promising tool for the diagnosis and characterization of kidney involvement in SLE.

PANEL DISCUSSION 02: DIFFICULT CASES IN AUTOIMMUNITY

19-05-2024 17:15 - 18:30

IS090 / #202

Case of Overlapping EGPA/GPA

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Background: Polyangiitis overlap syndrome is a rare systemic vasculitis with overlapping features of eosinophilic granulomatosis with polyangiitis (EGPA) and granulomatosis with polyangiitis (GPA). This systemic vasculitis cannot fit into a single category of classical vasculitis classification.

Case report: Herein we present the case of a 66-year-old woman who presented with nasal obstruction with external nose deformity ("saddle nose", figure 1) and sensorineural hearing loss. Laboratory findings included peripheral blood eosinophilia ($1.5x10^9$ cells/mcl), c-ANCA titer +++, high titer positivity for anti-PR3 (300 U/l, n.v. <10 U/l) and low titer rheumatoid factor (15.6 U/l, n.v <14). Her past medical history was notable for allergic rhinitis, while she denied asthma and nasal polyps. Other etiologies that could account for eosinophilia, such as infection or drugs, were excluded. A sinus CT revealed bilaterally thickened nasal mucosae. A chest radiography and CT revealed multiple bilateral nodules without lymphadenopathy.

Nasal septum biopsies were performed and showed exacerbated chronic inflammatory infiltrate, with microabscesses formation and some eosinophils, but apparently no granulomas or necrotizing angiitis. To further support the diagnosis, a lung atypical resection of superior right lobe was performed in correspondence of one of the nodularity highlighted by CT-scan. Histopathology not only highlighted necrotizing granulomas, but also necrotizing vasculitis showing an inflammatory infiltrate composed of numerous neutrophils and some eosinophils (figure 2). The clinical, radiographic, laboratory and pathologic findings suggested EGPA/GPA overlap syndrome, indeed both ACR2022 criteria for EGPA (score=7 points) and GPA (score=9 points) were satisfied. The overlap is due to the combination of peripheral eosinophilia (≥1x10^9/mcl) and necrotizing pulmonary granulomas associated with an eosinophilic infiltration (which favored EGPA), elevated serum PR3-ANCA levels and ORL involvement with nasal obstruction and "saddle nose" which are much more commonly seen in patients with GPA. Sensorineural hearing loss is a clinical feature that can be observed in both conditions, although rarely in EGPA and more commonly in GPA. The patient was treated with a combination of high-dose steroids (methylprednisolone 1 g e.v. daily for three days, followed by oral prednisone, 50 mg/daily) and cyclophosphamide following CYCLOPS protocol (15 mg/kg -maximum 1200 mg- at week 0, 2, 4 and then every 3 weeks for other 7 administrations). After the second administration of steroids hearing loss rapidly resolved.

Conclusions: It is important to identify patients with polyangiitis overlap syndrome of EGPA/GPA because the treatment modalities and prognosis are different. The majority of patients with EGPA achieve remission with corticosteroids alone, patients with GPA or polyangiitis overlap syndrome are usually treated with a combination of corticosteroids and immunosuppressive agents. Cyclophosphamide is the most commonly used. Polyangiitis overlap syndrome can cause irreversible multiple organ failure if not treated appropriately and promptly. As previously suggested, ANCA specificity seems the most important in determinant of the clinical outcome.

IS091 / #203

Case of Alopecia Universalis Which Improved at 1 Month of Treatment with JAK1 Inhibitor Upadacitinib

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Alopecia universalis (AU), an advanced form of alopecia areata, is a condition characterized by the complete loss of hair over the entire skin surface. Recent progresses have significantly enhanced our understanding of the pathogenesis of AU. In particular, interferon-γ (IFN- γ) and interleukin (IL)-15 seem to play a pivotal role in the pathogenesis of the disease. Nonetheless, a variety of medications has been used to treat the disease with frequently inconsistent results. Given the broad modulation of the immune system and inhibition of key molecules including IFN- γ and IL-15, oral JAK inhibitors represent a treatment option for moderate to severe cases of AA as demonstrated in case reports showing compelling evidence supporting their efficacy and tolerability. We present the case of a patient suffering from psoriatic arthritis and AU who experienced a sudden improvement in peripheral arthritis and alopecia universalis while receiving JAK1 selective treatment with upadacitinib. So far, there are very limited case reports of successful upadacitinib treatment for patients with alopecia areata, mostly in patients also suffering from atopic dermatitis. Thus, we provide evidence for efficacy of upadacitinib in managing AU in adults also in the context of an inflammatory arthritis such as PsA.

IS092 / #268

Case on LUPUS/C-APS

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This is a 22-year-old Caucasian woman diagnosed as having systemic lupus erythematosus (SLE) 8 months before the current admission. Her SLE diagnosis was based clinically on arthritis, photosensitivity, serositis, autoimmune haemolytic anaemia; and laboratory tests confirmed positive antinuclear and anti-dsDNA antibodies, hypocomplementaemia and presence of anticardiolipin IgG (57 GPL) and anti-β2-glycoprotein-I IgG (68 IU/ml) antibodies (confirmed in a second determination). Four months after the initial diagnosis, on the follow-up clinic, a kidney involvement led to a diagnosis on diffuse segmental proliferative lupus nephritis (class IV) by renal biopsy. She was treated with mycophenolic acid 720 mg (induction and then maintenance), prednisone (high-dose with tapering) 20 mg/day, hydroxychloroquine 200 mg/day and calcium. On this current admission, the patient reported 6 days of fever (39ºC), tonsillitis and general malaise. Despite amoxicillin treatment, she persisted with fever, nausea and vomiting. On physical examination, the pharynx was oedematous and presented ulcerative lesions. The abdominal examination revealed mild tenderness in the epigastrium without hepatosplenomegaly. The laboratory results showed a severe liver involvement with low grade cholestasis and no increase in the total bilirubin level; acute kidney injury and low leukocytes and platelets under 100 x 109/L. CRP was high (11.3 mg/dL), with not so high ESR (35 mm/h). An abdominal ultrasound and a thorax-abdomen computed tomography (CT) were normal. Blood cultures were performed. In the next 36 hours, the patient developed hypotension, oligoanuria, metabolic acidosis and hypoxia, resulting in transfer to the intensive care unit (ICU). Examination revealed painful hepatomegaly and laboratory tests showed a deterioration of thrombocytopenia (platelets 46 x 109/L), pretty high elevated transaminases (ALT 4,222 U/L and AST 12,658 U/L), with LDH of 31,345 UI/L and there were signs of disseminated intravascular coagulation (DIC). Despite of treatment, she developed progressive respiratory failure due to respiratory distress, myocardial dysfunction and, finally, cardiac arrest. Resuscitative efforts were unsuccessful. An autopsy was performed.

PARALLEL SESSION 18: CYTOKINES AND AUTOIMMUNITY

19-05-2024 17:15 - 18:30

IS093 / #136

IL-1BETA Inhibition in Adult Onset Still's Disease

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Interleukin(IL)-1 inhibitors represent the first-line biotechnological treatment choice in Still's disease. It should be employed since the first phases of the disease to avoid or quickly decrease glucocorticoids and

concomitant conventional immunosuppressants. Both experimental and "real-life" studies have proved to persistently control clinical and laboratory inflammatory manifestations, thus inducing a clinical inactive disease even in severe cases. The currently used IL-1 inhibitors anakinra and canakinumab have proved to be effective disregarding the age at the disease onset, the pattern of the disease (systemic versus chronic-articular course) and the biotechnological line of treatment (first-line versus second or more line) showing to be a feasible and effective strategy when used as first-line biologic strategy, but also in cases with a long disease duration. In parallel, safety data ensure about the excellent profile of IL-1 agents in terms of low frequency of adverse events and absence of severe adverse events.

IS094 / #137

IL-6, The Choroid Plexus, and The Pathogenesis of Neuropsychiatric Lupus

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Up to 50% of SLE patients experience neuropsychiatric involvement (neuropsychiatric lupus, or NPLSE) in the form of cognitive deficits, memory loss, depression, and anxiety. The pathogenic mechanisms of NPSLE have yet to be firmly established. CSF and serum levels of the inflammatory cytokine IL-6 are increased in NPSLE patients and lupus mice. Excessive IL-6, possibly entering the brain from the serum, could promote neuroinflammation by activating glial cells, including astrocytes and microglia. We then hypothesized that knocking out IL-6 would ameliorate NPSLE. We studied female MRL/lpr mice, which exhibit severe lupus-like disease and neuropsychiatric deficits. To investigate the association of IL-6 with NPSLE, we compared serum levels of IL-6 with behavioral testing scores in 18-week-old MRL/lpr mice. We repeated this battery in 14- to 18-week-old IL-6 knockout (KO; n = 15) and age-matched wildtype (WT; n = 15) MRL/lpr mice. Elevated serum IL-6 correlated with worse spatial memory, but not with depression or anxiety-like behavior. MRL/lpr IL-6 KO mice showed significantly increased novelty preference on the object placement (KO: 57.87 +/- 3.15; WT: 45.37 +/- 2.29, P = .002) and object recognition tests (KO: 67.91 +/- 3.62; WT: 48.93 +/- 4.34; P = .003), indicating improved cognition (memory). No differences were found on measures of depression or anxiety. Expression of the glial genes gfap and aif1 were significantly decreased in cortical samples from IL-6 KO compared to WT mice. Disruption of the blood-CSF barrier (B-CSFB), formed by choroid plexus (ChP) epithelia, could enable inflammatory mediators to enter the brain from the circulation. In both NPSLE patients and lupus mouse models, immune cells infiltrate the ChP and can alter normal epithelial functions through cytokine signaling, including IL-6. ATP-binding cassette (ABC) transporter function in the ChP, including P-gp, MRP1, and BCRP, is fundamental to the clearance of neurotoxic substrates from the CSF. We next assessed the effects of IL-6 on lupus derived ChP organoids to investigate the integrity of the B-CSFB in NPSLE. ChP tissue from 2-5 female KO or WT mice of ≥16 weeks of age were pooled and cultured for two weeks to generate ChP organoids, as described. A standard time-lapse permeability assay which quantified tracer fluorescence within each organoid's central vacuole was performed under various conditions. The fluorescent tracers used included two small dyes, lucifer yellow (LY) and sodium fluorescein (SF), and a larger 10 kDa dextran molecule. Importantly, LY but not SF is transported by ABC transporters. MRL/lpr-derived organoids replicated the *in-vivo* morphology and gene expression of the ChP. IL-6 rapidly increased MRL/lpr organoid permeability to LY, while IL-6 KO organoids demonstrated consistently reduced permeability. No permeability differences between IL-6 KO and WT organoids were seen for SF and 10 kDa dextran. Incubation with an anti-IL-6 receptor antibody significantly decreased LY permeability. *In-vivo* expression of *abcg2*, a constituent of BCRP, was increased in IL-6 KO MRL/lpr mice. In conclusion, we found that serum IL-6 levels correlate with worse cognition in lupus mice. Moreover, knocking out IL-6 ameliorates those deficits without altering affective features or systemic disease. IL-6 KO mice also demonstrated decreased cortical expression of inflammatory glial genes. Therefore, IL-6 may play a specific, glia-mediated role in the cognitive and memory deficits of NPSLE. Furthermore, we found that IL-6 signaling alters ChP permeability to LY. Changes in BCRP, which effluxes only LY, could explain this accumulation of LY within organoids. Therefore, the high IL-6 environment of SLE could interfere with BCRP function and hinder the ChP's ability to clear potentially neurotoxic metabolites, and thus contribute to the pathogenesis of NPSLE.

IS095 / #138

The Emerging Role of Macrophage Migration Inhibitory Family of Cytokines In Autoimmune Diseases. From Pathogenesis to New Treatments?

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Macrophage migration inhibitory factor (MIF) is a multifunctional cytokine implicated in the pathogenesis of various inflammatory and autoimmune diseases. Constitutively expressed and stored within cells, MIF interacts with a range of receptors, including CD74, JAB1, CXCR2, and CXCR4. Recently, a MIF-related protein called D-dopachrome tautomerase (D-DT) was discovered, sharing both structural and functional similarities with MIF. Functional MIF polymorphisms have been identified as significant contributors to both the susceptibility and severity of autoimmune and inflammatory diseases. The role of MIF in regulating glucocorticoid immunosuppression and its prominent function in cell survival signaling make it stand out as a key player in the host immune response. This unique position in the immune system highlights the potential impact of MIF modulation on these diseases. To harness this therapeutic potential, biologic and small-molecule therapies targeting MIF are currently undergoing clinical evaluation. The structural features of MIF, with its well-defined binding sites and functional domains, render it particularly suitable for both antibody and small-molecule antagonism. These therapies hold promise in reshaping the landscape of treatment options for patients suffering from these complex and often debilitating conditions, offering new avenues for managing autoimmune and inflammatory diseases.

PARALLEL SESSION 19: SYSTEMIC AUTOIMMUNITY, LIVER AND GASTROINTESTINAL

19-05-2024 17:15 - 18:30

IS096 / #548

Cross-Reactivity and Sequence Similarity between Microbial Transglutaminase and Human Tissue Antigens

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Microbial transglutaminase (mTG) is a bacterial survival factor, frequently used as a food additive to cross-link processed nutrients. As a result, new immunogenic epitopes are generated that might drive autoimmunity. The aims were 1. to explore epitope similarity and cross-reactivity between mTG and multiple human tissue antigens. 2. to investigate how the bacterial enzyme contributes to autoimmunity induction through epitope similarity and cross-reactivity. Emboss Matcher was used to perform sequence alignment between mTG and various antigens implicated in many autoimmune diseases. Monoclonal and polyclonal antibodies made specifically against mTG were applied to 77 different human tissue antigens using ELISA. Six antigens were detected to share significant homology with mTG immunogenic sequences, representing major targets of common autoimmune conditions like autoimmune hepatitis, Inflammatory bowel and celiac diseases and primary biliary cirrhosis. Polyclonal antibody to mTG reacted significantly with 17 out of 77 tissue antigens. This reaction was most pronounced with mitochondrial M2, ANA, and extractable nuclear antigens. The results indicate that sequence similarity and cross-reactivity between mTG and various tissue antigens are possible, supporting the relationship between mTG and the autoimmune disorders' evolvement. The implications of those cross-reactive epitopes, and sequence similarity in relation to mTG, and the potential to influence gut-related auto-immunogenesis might affect public health. The present results add two novel autoimmune mechanisms that reinforce molecular mimicry and dictate the need for control, label, and increase the transparency of the mTG in order to protect the public from autoimmune diseases. Further research is warranted to explore mTG-morbidity-induced relationships.

PLENARY 03

20-05-2024 08:00 - 09:30

IS097 / #140

Prediction and Prevention of Autoimmunity (Using Example of Rheumatoid Arthritis, Prediction Models, Review Of Status Of Preventıon Trials)

Michael Mahler
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The early identification of patients in the pre-clinical phase of rheumatoid arthritis (RA) is of high importance since early intervention can prevent disease progression and joint damage. Several ongoing studies are focused on RA prevention based on the treatment of individuals at high risk of developing RA. Although most studies are still ongoing, some have already reported promising results while others failed to demonstrate the ability to prevent RA today. Most remarkable, it was demonstrated that both vitamin D and Omega 3 have an impact on the future development of autoimmune diseases including RA. In addition, it was recently reported that Abatacept treatment in individuals at risk of RA development shows MRI improvement and prevents arthritis development. Lastly, a single infusion of rituximab significantly delayed the development of arthritis ($P<.0001$) in subjects at risk of developing RA, providing evidence for the pathogenetic role of B cells in the pre-clinical stage of autoantibody positive RA. Based on all the findings about the possible treatment in the pre-clinical phase of RA, reliable biomarkers are needed to identify patients who are on the trajectory to develop RA. Several studies have now repeatedly shown that ACPA and other biomarkers (e.g. autoantibodies, inflammatory proteins, cytokines, micro RNA) can antedate the development of RA by many years. In addition, recently, the combination of anti-citrullinated protein/peptide antibodies (ACPA), rheumatoid factor (RF) and anti-CarP (Carbamylated Peptide) autoantibodies has been shown to provide a very high Odds Ratio for RA. Although these data are intriguing, it would be more valuable to have biomarkers that predict imminent RA within 6-12 months, corresponding to the so-called 'window of opportunity'. For all prediction and prevention strategies, awareness and buy-in from individuals at risk are imperative. In this presentation, we summarize ongoing studies for the prevention of RA and provide an update on future plans for the selection of healthy individuals at risk to develop RA.

IS098 / #142

Paraneoplastic Autoimmune Laminin-332 Syndrome (PALS)

Abdul Razzaque Ahmed
Department of Dermatology, Tufts University School of Medicine, Boston, United States of America

Laminin-332 is an important component of the basement membrane. Recently, autoantibodies to Laminin-332 have been described in several autoimmune diseases. Many of these autoimmune diseases have a high incidence of malignancy. The importance of Laminin-332 autoantibodies and its relationship to malignancy is highlighted by using Laminin-332 Pemphigoid (LM-332Pg) as a prototype. To identify several autoimmune diseases that have autoantibodies to Laminin-332 present, and to determine the prevalence of malignancy in them. Using Laminin-332 Pemphigoid (LM-332Pg) as a prototype, to compare clinical profiles of LM-332Pg patients with and without cancer. By identifying the temporal detection of cancer, can the influence of autoantibodies to Laminin-332 on prognosis be determined. We identified autoimmune and inflammatory diseases in which autoantibodies to Laminin-332 were present. Autoantibodies to Laminin-332 were detected in recent studies of systemic lupus erythematosus (SLE), psoriasis, bronchiolitis obliterans (BO), graft-vs-host disease (GVH), bullous pemphigoid (BP), lichen planus (LP), epidermolysis bullosa acquisita (EBA), and membranous glomerulonephropathy (MGN). Subsequently, the rate of malignancy in these autoimmune diseases was determined. A search for publications on LM-332Pg patients to determine cancer rates and clinical outcomes to examine if a relationship can be proposed, was performed. A high incidence of cancer rate was reported in these autoimmune diseases including primary Sjögren's syndrome (pSS), systemic sclerosis (SS), dermatomyositis (DM), multiple sclerosis (MS), immune thrombocytopenia purpura (ITP), and rheumatoid arthritis (RA). Data analysis demonstrated that LM-332Pg patients had a higher risk of developing ovarian, uterine, lung, gastric cancers and leukemia. The incidence for breast cancer was lower, when compared with global cancer rates. When studied, levels of Laminin-332 autoantibodies correlated with the presence or absence of malignancy. Preliminary analysis suggests that autoantibodies to Laminin-332 are present in multiple autoimmune diseases, which also have a high incidence of malignancy. Detailed analysis of available data highlights that patients who developed LM-332Pg after cancer was diagnosed, had a more favorable prognosis, compared to patients who developed cancer when LM-332Pg was previously present. Preliminary data would suggest that autoantibodies to Laminin-332 could serve as an important biomarker in certain patients, for correlation with possible incidence of malignancy.

PLENARY 03 (CONT.): CHALLENGE THE EXPERT

20-05-2024 09:30 - 10:00

IS099 / #935

Which Is The Prevalence of Systemic Autoimmune Disorders in Patients with Autoimmune Thyroid Diseases, and Which Is The Impact on The Health of These Patients?

Poupak Fallahi[1], Valeria Mazzi[2], Giusy Elia[2], Francesca Ragusa[2], Eugenia Balestri[2], Chiara Botrini[2], Licia Rugani[2], Emilio Barozzi[2], Armando Patrizio[3], Yehuda Shoenfeld[4], Alessandro Antonelli[2], Silvia Martina Ferrari[5]

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[5]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Autoimmune thyroid diseases (AITD) are organ-specific autoimmune disorders whose main clinical presentations are Hashimoto's thyroiditis (HT), or Graves' disease (GD). HT, GD, thyroid autoantibodies and thyroid dysfunctions have been shown in patients with other organ specific and systemic autoimmune diseases. A study evaluated the prevalence of other autoimmune disorders in 3069 patients with chronic autoimmune thyroiditis (AT), with respect to two age- and sex-matched control groups. The results of the study demonstrated a significant increase of the prevalence of autoimmune disorders in AT patients (with respect to both controls), for the following diseases: chronic autoimmune gastritis (CAG), vitiligo (Vit), rheumatoid arthritis, polymialgia rheumatica (Polym), celiac disease, diabetes, sjögren disease, multiple sclerosis, systemic lupus erythematosus, sarcoidosis, alopecia, psoriatic arthritis, systemic sclerosis, and HCV-related cryoglobulinemia. Interestingly, the association of three autoimmune disorders was observed almost exclusively in AT patients. Another study evaluated prospectively the prevalence of other autoimmune disorders in 3209 GD patients, with respect to 1069 healthy controls, or 1069 patients with AT, or 1069 with multinodular goiter. On the whole, 16.7% of GD patients had another associated autoimmune disease, and the most frequently observed were: Vit (2.6%), CAG (2.4%), rheumatoid arthritis (1.9%), Polym (1.3%), multiple sclerosis (0.3%), celiac disease (1.1%), diabetes (type 1) (0.9%), systemic lupus erythematosus and sarcoidosis (<0.1%), sjogren disease (0.8%). Moreover, 1.5% patients with GD had three associated autoimmune disorders. Organ specific and systemic autoimmune diseases might have an important clinical impact in patients with AITD so a periodic screening is suggested.

IS100 / #936

Which are The New Therapies for Graves' Ophthalmopathy, and Which is The Impact on The Disease?

Poupak Fallahi[1], Francesca Ragusa[2], Giusy Elia[2], Eugenia Balestri[2], Chiara Botrini[2], Licia Rugani[2], Emilio Barozzi[2], Valeria Mazzi[2], Armando Patrizio[3], Alessandro Antonelli[2], Silvia Martina Ferrari[4]

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Graves' orbitopathy (GO) is an autoimmune disease of the retroocular tissues occurring in patients with Graves' disease. There is a broad spectrum of clinical manifestations of GO, and initially a change in appearance becomes evident. GO is a typical bilateral and rather symmetrical eye disease, however mono-lateral or asymmetrical disease may occur. The management of GO depends on severity and activity of the disease. Patients with active moderate-to-severe GO require systemic immune-modulant therapies and they should be started within 1 year from the onset in order to shorten the active phase of inflammation and stabilize quickly the disease. The first line-treatment of GO are steroids, that are rather effective in reducing swelling and redness of eyelids and conjunctiva and in improving diplopia, less so in reducing exophthalmos. Biological therapies are the new lines of intervention. Teprotumumab is a fully human immunoglobulin G1 monoclonal antibody directed against IGF-1R, thus preventing its activation by the endogenous ligands IGF-1 and IGF-2, through this mechanism it is able to reduce the pro-inflammatory cytokines production, the hyaluronan secretion, and the orbital fibroblasts activation in GO. Teprotumumab is able to reduce inflammation, proptosis and diplopia in GO patients and it was approved by the US FDA in 2020 for the treatment of GO under the name TEPEZZA. TSH-R and the IGF-1R are both the main targets for new, but still exploratory, therapeutic strategies, and clinical trials are ongoing, so further compounds are expected to be released in the near future.

IS101 / #937

Which Is The Impact of COVID-19 Infection in Patients with Thyroid Autoimmunity?

Poupak Fallahi[1], Giusy Elia[2], Francesca Ragusa[2], Armando Patrizio[3], Valeria Mazzi[2], Eugenia Balestri[2], Salvatore Benvenga[4,5,6], Gilda Varricchi[7,8,9,10], Laura Gragnani[1], Chiara Botrini[2], Emilio Barozzi[2], Licia Rugani[2], Enke Baldini[11], Marco Centanni[12,13], Yehuda Shoenfeld[14], Clodoveo Ferri[15,16], Alessandro Antonelli[2], Silvia Martina Ferrari[17]

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The SARS-CoV-2 can enter the thyroid cells via the angiotensin-converting enzyme 2 receptor. Several thyroid disorders have been associated with COVID-19 infection [subacute thyroiditis (SAT), thyrotoxicosis, and non-thyroidal illness syndrome (NTIS)] and, in part, they are believed to be secondary to the local virus replication within the gland cells. However, as for other viruses, COVID-19 seems to interfere with several aspects of the immune system, inducing the synthesis of autoantibodies and triggering latent or new onset autoimmune disease, including autoimmune thyroid disease (AITD), such as Hashimoto Thyroiditis (HT) and Graves' disease (GD). Moreover, many studies have shown a higher frequency of COVID-19 infection in patients with HT, or GD, or in general with thyroid autoimmunity. Furthermore, a more severe course of COVID-19 infection has been observed in patients with HT and/or hypothyroidism. Several mechanisms have been hypothesized to explain the induction of

autoimmunity by COVID-19 infection: the immune system hyper-stimulation, the molecular mimicry between the self-antigens of the host and the virus, neutrophils extracellular traps, and finally the virus induced transcriptional changes in the immune genes. Interestingly, COVID-19 infection could also act as environmental triggers of HT, GD and AITD in months or years following the disease, in fact a higher incidence of thyroid autoimmunity and hypothyroidism is reported in these patients. In the continuous evolving of COVID-19 scenario large, long-term, follow-up studies of thyroid disorders in COVID-19 patients are needed to better characterize the development of these diseases that could potentially affect many patients.

PARALLEL SESSION 20: NOVEL AUTOIMMUNE DISEASES

20-05-2024 10:30 - 12:00

IS102 / #145

Hypocryoglobulinaemıa: A New Entity?

Dario Roccatello
University Center of Excellence on Nephrological, Rheumatological and Rare Diseases (ERK-net, ERN-Reconnect and RITA-ERN Member) including Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the, Torino, Italy

A significant proportion of patients who exhibit strong clinical suspicions for cryoglobulinaemic vasculitis either yield negative findings in cryoglobulin detection or only exhibit minimal quantities that cannot be adequately described in terms of composition. We aimed at establishing whether the failure to detect or the detection of trace amounts of cryoglobulin with conventional methods either identifies a peculiar subset of low level cryoglobulinaemia (from now on hypocryoglobulinaemia) or represents a separate entity. Utilizing an adapted precipitation method inside a hypo-ionic medium, we conducted a prospective study to identify a total of 237 individuals (137 females) between the years 2008 and 2021. These patients, with a median age of 60.8 years (ranging from 22 to 97), exhibited a cryocrit level of less than 0.5% and were suspected of having an autoimmune illness based on clinical presentation. Out of the total sample size of 237 patients, it was found that only 54 individuals, accounting for 22.7% of the population, had a documented history of hepatitis C virus (HCV) infection. Out of a total of 237 patients, 169 individuals (71%) were found to have a pre-existing underlying disease. On the other hand, 68 patients (28.6%) who did not exhibit any laboratory markers or clinical symptoms consistent with an underlying cause were included in the study. The median age of these 68 patients was 62.9 years, ranging from 29 to 93, and there were 35 female participants. The group of 68 cases exhibiting minimal levels of cryoglobulins were classified as individuals with a potentially idiopathic hypocryoglobulinemia. Out of the total sample size of 68 patients, 19 individuals (27.9%) had a documented history of hepatitis C virus (HCV) infection. Out of a total of 68 patients, 24 individuals (35.3%) tested positive for rheumatoid factor (RF). Additionally, 25 patients (36.7%) exhibited indications of complement consumption, namely having C4 levels below 15 mg/dl and/or C3 levels below 80 mg/dl. Furthermore, 36 patients (52.9%) demonstrated elevated inflammatory indices. Out of the total sample size of 68 patients, only seven individuals had symptoms limited to arthralgia and constitutional manifestations. In contrast, the majority of patients, namely 61 out of 68 (89.7%), presented with at least one of the three primary indicators of cryoglobulinaemic vasculitis, namely skin lesions, peripheral nerve involvement, and glomerulonephritis. A total of 75% of the participants exhibited type III hypocryoglobulins. The histologic characteristics of glomerulonephritis in patients with hypocryoglobulinemia, as observed using electron microscopy, exhibited similarities to those of glomerulonephritis associated with mixed cryoglobulinemia. In summary, hypocryoglobulins frequently exhibit polyclonality and are primarily independent of hepatitis C virus (HCV) infection. Patients who exhibit a significant clinical suspicion for vasculitis, particularly glomerulonephritis, yet yield negative results for cryoglobulinemia using conventional diagnostic methods, may necessitate further study, even in the absence of hepatitis C virus (HCV) infection, rheumatoid factor (RF) activity, or indications of complement consumption.

IS103 / #146

Expanding The Spectrum of The Hyperferritinemic Syndrome, from Pathogenic Mechanisms to Clinical Observations, and Therapeutic Implications

Piero Ruscitti
University of L'Aquila, L'Aquila, Italy

From the introduction of hyperferritinemic syndrome concept, a growing body of evidence has suggested the role of ferritin as a pathogenic mediator and a relevant clinical feature in the management of patients with inflammatory diseases. From a pathogenic point of view, ferritin may directly stimulate the aberrant immune response by triggering the production of pro-inflammatory mediators in inducing a vicious pathogenic loop and contributing to the occurrence of cytokine storm syndrome. The latter has been recently defined as a clinical picture characterised by elevated circulating cytokine levels, acute systemic inflammatory symptoms, and secondary organ dysfunction beyond that which could be attributed to a normal response to a pathogen It is noteworthy that the occurrence of hyperferritinemia may be correlated with the development of the cytokine storm syndrome in the context of an inflammatory disease. In addition to adult onset Still's disease, macrophage activation syndrome, catastrophic anti-phospholipids syndrome, and septic shock, recent evidence has suggested this association between ferritin and life-threatening evolution in patients with systemic lupus erythematosus, with anti-MDA5 antibodies in the context of poly-dermatomyositis, with severe COVID-19, and with multisystem inflammatory syndrome. The possible underlying common inflammatory mechanisms, associated with hyperferritinemia, may led to the similar clinical picture observed in these patients. Furthermore, similar therapeutic strategies could be suggested inhibiting pro-inflammatory cytokines and improving long-term outcomes in these disorders. Thus, it could be possible to expand the spectrum of the hyperferritinemic syndrome to those diseases burdened by a dreadful clinical picture correlated with hyperferritinemia and the occurrence of the cytokine storm syndrome. In addition, the assessment of ferritin may provide useful information to the physicians in clinical practice to manage these patients. Therefore, ferritin may be considered a relevant clinical feature to be used as biomarker in dissecting the unmet needs in the management of these disorders. Novel evidence may thus support an expansion of the spectrum of the hyperferritinemic syndrome to these diseases burdened by a life-threatening clinical picture correlated with hyperferritinemia and the occurrence of the cytokine storm syndrome.

IS104 / #147

An Update On CPPD Diagnosis and Management

Ora Shovman
Sheba Medical Center, Affiliated with Tel-Aviv University, Ramat Gan, Israel

Calcium pyrophosphate dihydrate crystal deposition (CPPD) disease is a crystal deposition arthropathy that involves the synovial and periarticular tissues. CPPD-related arthritis is the common inflammatory arthritis especially in older age. This disease has heterogeneous presentations and sometimes represents a diagnostic challenge for clinicians. Its clinical presentation ranges from asymptomatic to acute or chronic inflammatory arthritis. This presentation reviews the etiology, clinical manifestations, differential diagnosis, diagnostic approach and management of calcium pyrophosphate deposition disease.

IS105 / #149

What's Immune in Ankylosing Spondylitis? (Or Difficult Cases)

Abdulla Watad
Department of Internal Medicine, B & Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Ramat Gan, Israel

Ankylosing Spondylitis (AS), an enigmatic immune condition, is characterised by inflammation in the axial skeleton, resulting in spinal ankylosis and functional impairment. Central to AS pathogenesis is the HLA-B27 allele, with this presentation exploring its genetic and functional implications, alongside emerging non-HLA genetic factors. The innate immune system, involving macrophages, dendritic cells, and innate lymphoid cells, is pivotal in initiating and perpetuating inflammation in AS. A detailed examination of adaptive immunity reveals the intricate involvement of T cells, interacting with autoantigens in the pathogenic process. The cytokine milieu, including TNF, IL-23 and IL-17, contributes significantly to AS inflammation, and new bone formation, impacting disease progression. Recent research highlights the influence of gut microbiota in AS, underscoring the gut-joint axis and its potential role in disease development. This comprehensive exploration aims to deepen our understanding of AS's immune intricacies, offering insights into novel therapeutic strategies and personalised treatments within the context of the autoimmune/autoinflammatory landscape.

IS106 / #150

Acquıred Hemophilia: A Too Often Overlooked Autoimmune Disease

Roberta Gualtierotti[1,2,3], Raffaella Rossio[2], Barbara Ferrari[2], Simona Siboni[3], Flora Peyvandi[1,2,3]

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Acquired hemophilia A is a life-threatening condition that is characterized by acquired factor VIII inhibitors, severe bleeding (subcutaneous, retroperitoneal, intramuscular) and prolonged activated partial thromboplastin time (aPTT). Joint bleeding is rare compared to congenital hemophilia A. In around half of cases, acquired hemophilia A is associated to an underlying condition such as other autoimmune diseases, cancer, monoclonal gammopathy of undetermined significance, or postpartum. Acquired inhibitors against factor VIII are polyclonal autoantibodies that inhibit clotting factor activity or increase clearance. Individuals with new-onset bleeding and a prolonged aPTT should undergo mixing studies and factor VIII activity testing. Management envisages hemostatic and immunosuppressive treatment and should be shared with a hematologist expert in bleeding disorders at a Comprehensive Care Center.

PARALLEL SESSION 21: SYSTEMIC SCLEROSIS

20-05-2024 10:30 - 12:00

IS107 / #133

When to Start or Escalate Treatment in SSC-ILD

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[2]University and University Hospital Zürich, Zurich, Switzerland

Interstitial lung disease associated with systemic sclerosis (SSC-ILD) occurs in about 50-60% of patients this SSc. It is the most frequent cause of death. Progression of SSc-ILD is frequent and occurs in about 70% over a 5-year period. A single episode of progression is linked to long-term mortality. The lecture is discussing how these progression events should be handled therapeutically. Should we initiate/escalate treatment after progression or should we try to prevent progression? Is progression identifying patients at risk of continuous progression? What should be done with the 30% that are stable and are not progressing over 5-years? How can we identify patients at risk? These treatment strategies will be discussed and pros and cons will be evaluated.

PARALLEL SESSION 22: NOVEL APPROACHES TO HANDLE AUTOIMMUNE DISEASES

20-05-2024 10:30 - 12:00

IS108 / #160

Modulation of Autoimmune Diseases By Targeting The Nfr2-Ho1-Co Pathway

Ferdinando Nicoletti, Katia Mangano, Gian Marco Leone, Paolo Fagone
University of Catania, Catania, Italy

The Nrf2/HO-1/CO pathway has emerged as a significant regulatory axis in the context of autoimmunity, offering novel insights into the mechanisms underlying autoimmune diseases. Nuclear factor erythroid 2-related factor 2 (Nrf2) is a transcription factor that plays a pivotal role in cellular defense against oxidative stress and inflammation. Nrf2 activation triggers the upregulation of heme oxygenase-1 (HO-1), an enzyme responsible for heme catabolism, resulting in the generation of carbon monoxide (CO) as a byproduct. Despite the existing challenges, it is important to emphasize that treatments centered around the modulation of the NFR2-HO1-CO system for diseases characterized by damaging inflammation or oxidative stress hold great promise in the context of autoimmunity. While traditional NRF2 and HO-1 inducers, exhibit potent HO-1 upregulation but are accompanied by toxicity concerns, ongoing research is dedicated to discovering safer and better-tolerated alternatives, including CO-based intervention. These efforts underscore the commitment to refining and validating these treatment approaches addressing the present limitations.

IS109 / #162

The Potential of Autologous Patient-Derived Circulating Extracellular Vesicles to Improve Drug Delivery in Inflammatory Rheumatic Autoimmune Diseases

Gilad Halpert[1], Ori Moskovitch[1], Adi Anaki[2], Tal Caller[3,4], Omer Gendelman[1,5], Abdulla Watad[6], Ruty Mehrian-Shai[7], Rachella Popovtzer[2], Boris Gilburd[1], Ori Segal[1], Yehuda Shoenfeld[8], Howard Amital[6]

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***Background and aims*:** Progress has been achieved with the introduction of biologics in the management of inflammatory/autoimmune diseases such as rheumatoid arthritis (RA), however such medications may induce immune suppression and severe side effects. Therefore, there are unmet medical needs regarding the development of novel therpeutic approaches for autoimmuine diseases. Extracellular vesicles (EVs), a cell-derived nano-sized, natural secreted particles, play a role in the development/modulation of autoimmune processes. In the current study, we hypothesized that isolation of circulating autologous tissue-specific homing EVs from RA patients - may improve the delivery of FDA-approved anti-inflammatory drugs, which will be encapsulated into these EVs. The drug-loaded EVs will be injected back to the diseased subjects and will naturally find their way to the inflamed tissue.

Methods and Results: We found that circulating EVs derived from arthritic mice (Collagen-induced arthritis model) expresses joint/synovia-specific homing receptors (e.g. αVβ3 integrin). Importantly, autologous labeled EVs, derived from blood of diseased arthritic mice (Collagen antibody-induced arthritis model), can migrate toward the inflamed synovia, using *in vivo* imaging system (IVIS). Moreover, we show that these EVs strongly expresses glucose transporter 1 (mGLUT1) which in turn, improve their therapeutic potential to be loaded with anti-inflammatory drugs using glucose-coated gold nanoparticles (GNPs). Finally, we show that EVs derived from plasma of RA patients overexpresses αVβ3 integrin and taken up by LPS/TNFα-induced activated human synovial cell line *in vitro*.

Conlusions: Overall, we show the potential of autologous circulating EVs of RA patients to serves as natural nano-carrier for current FDA-approved drugs.

PARALLEL SESSION 23: PEDIATRIC AND AUTOIMMUNITY

20-05-2024 14:00 - 15:30

IS110 / #165

Next Generation: What We Know of Children Born to Patients with Systemic Autoimmune Diseases

Angela Tincani
Department of Clinical and Experimental Science University of Brescia-italy, Rheumatology and Clinical Immunology ERN ReCONNET-ASST Spedali Civili, Brescia, Italy

We do not have much information on the long-term outcome for children born to patients with systemic autoimmune diseases. This is an unmet need for our patients often asking about their babies' future. During pre-conceptional counseling women raise several doubts or fears: what my disease can do to my baby? what could be the consequence of my treatment during pregnancy? will my children get my disease? Autoantibodies and proinflammatory cytokines of maternal autoimmune diseases can in some circumstances influence the children's long-term outcome. The most classical example is the occurrence of new cardiac problems in teenagers born to patients with anti-Ro/SS-A antibodies who already had early pacemaker implantation because of congenital heart block. However, the rate and severity of these episodes are still under investigation. The maternal drugs most discussed for their possible long-term implications for the children's long-term health are corticosteroids, reported to cause metabolic syndrome, and hydroxychloroquine for its possible responsibility in causing retinal toxicity. Both situations have been only partially investigated reaching not univocal conclusions up to now. Although maternal autoimmune disease is not directly transmitted to the child, several allergic and organ-specific autoimmune conditions have been reported by large registry studies mainly in the offspring of patients with systemic lupus erythematosus. Italian data, based on a large survey, also report an increased rate of celiac disease even if the father's family could also have a role. More studies are needed to fully clarify the "next generation" heath, but these should be performed on adult individuals of course difficult to collect and to investigate. Alternatively, data from population registries can help even if with some limitations. Up to now, we can tell the future mothers with systemic autoimmune diseases that eventual health problems of their children seem overall rare and, in any case, surmountable.

IS111 / #166

APLA- SLE- TTP- MAS- What Is The Egg and What Is The Chicken?

Sefi Uziel
Pediatric Rheumatology, Meir Medical Center- Tel Aviv University, Kfar Saba, Israel

Case presentation: A 14-year-old girl, previously healthy, presented with fever, abdominal pain, and vomiting. Physical examination revealed a moderate ill appearance, with abdominal tenderness, livedo reticularis, oral aphthous ulcers and signs indicative of shock. Laboratory findings demonstrated severe pancytopenia (WBC 2,100, hemoglobin 5.5, platelets 4,000), positive Coombs, schistocytes on blood smear, and acute renal impairment. Serological tests were positive for SLE, including ANA, dsDNA, low complement levels and triple antiphospholipid antibodies (APLA) positivity. Additional laboratory results showed undetectable ADAMTS13 activity (0) and positive ADAMTS13 antibodies. Natural Killer (NK) cell activity was substantially reduced. Abdominal CT revealed a large spleen infarct and polyserositis. Considering the diagnostic challenge, TTP, CAPS, and MAS were considered in the differential diagnosis. Upon arrival, she was admitted to the pediatric intensive care unit for immediate resuscitation and intensive monitoring. She received pulse steroids and intravenous immunoglobulin (IVIG), resulting in clinical improvement. Due to severe thrombocytopenia, anticoagulant therapy was deferred. A multidisciplinary discussion involving rheumatology, hematology, nephrology, and the plasma exchange team was conducted. As there was no central nervous system involvement, plasmapheresis was not performed, and the decision was made to initiate rituximab therapy. Rituximab treatment led to rapid improvement, allowing the initiation of low molecular weight heparin (LMWH). The patient was discharged and continued with rituximab, transitioning to belimumab. LMWH was switched to warfarin. The patient is currently in remission.

IS112 / #913

Autoimmunity in Inborn Errors of Immunity and Clinical Approaches

Tadej Avcin
Department of Allergology, Rheumatology and Clinical Immunology, University Children's Hospital, University Medical Centre Ljubljana, Ljubljana, Slovenia

The knowledge of human inborn errors of immunity (IEI) is rapidly expanding and currently we are able to classify > 500 monogenic IEI. Diseases across the entire spectrum of IEI can be associated with immune dysregulation leading to various allergic, autoimmune and inflammatory complications. These complications

can arise across all age groups and all stages of disease, ranging from presenting complaints to late complications. Based on the data from the Slovenian Registry of IEI, non-infectious and non-malignant manifestations occur in 29% patients with IEI, including autoimmune manifestations in 22%, lymphoproliferative/granulomatous in 12%, autoinflammatory in 5%, and allergic manifestations in 4% of patients with IEI. Autoimmune and autoinflammatory manifestations preceded the diagnosis of IEI in 80% of patients included in our registry, therefore, physicians treating these conditions should have a low threshold for performing the evaluation for possible underlying IEI. The clinical clues to the identification of patients with IEIs include severe or unusual infections, early or atypical autoimmune disease, positive family history or consanguinity, syndromic features, lymphoproliferation or granulomatous inflammation. On the other hand, patients with known IEIs should be regularly monitored not only for infections but also for other manifestations as they share common genetic factors for autoimmunity, lymphoproliferation, granulomatous inflammation, autoinflammation and even allergy. In the last decade, a new group of monogenic diseases with combined features of immunodeficiency, autoimmunity, autoinflammation and/or allergy was recognized. The pathogenic mechanisms in these diseases include defects of both innate and adaptive immunity as well as increased risk of infection. Characteristic examples in this group of IEI are cytoskeletal disorders, interferonopathies and relopathies. Phenotypic presentations in these diseases frequently includes combined immune- and nonimmune-mediated organ and tissue damage, such as CNS involvement in interferonopathies. With the improved diagnostics including upfront application of next-generation sequencing and additional omics technologies, we could expect earlier genetic, molecular and immune characterization of IEI and underlying autoimmune/inflammatory complications. Better knowledge and the multilayer concept of autoimmune mechanisms and manifestations in IEIs could provide also clinical guidance on the use of novel targeted therapeutic approaches.

IS113 / #274

Monogenic Causes of SLE and Related Clinical Conditions

Alexandre Belot
Pediatric Nephrology, Rheumatology, Dermatology, Hospices Civils de Lyon / Hôpital Femme Mère Enfant, BRON, France

Systemic lupus erythematosus (SLE) is a complex and chronic autoimmune disease characterized by its diverse clinical manifestations and severity. The pathophysiology of SLE involves an abnormal immune response targeting various tissues, an excess of apoptotic bodies, and an overproduction of type-I interferon. Genetic factors play a significant role, supported by evidence from monozygotic twin studies, familial clustering, and genome-wide association studies (GWAS) identifying multiple risk loci. In the 1970s, the discovery of complement deficiencies unveiled familial forms of SLE resulting from single gene defects. Advancements in high-throughput sequencing have recently disclosed an expanding field of monogenic defects associated with lupus, fostering the concept of monogenic lupus and enriching our comprehension of immune tolerance mechanisms. One can classify monogenic SLE according to disrupted pathways, including efferocytosis, interferonopathies, JAK-STATopathies, rasopathies and dysregulation in T and B cells. Suspecting monogenic lupus is crucial in cases of early-onset lupus, syndromic lupus, male patients, and familial cases. Associated clinical and biologicals features can help the clinicians to detect specific situation of monogenic lupus and propose targeted therapies.

IS114 / #276

Advances in The Management of Juvenile Idiopathic Arthritis

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In the past two decades, the treatment of juvenile idiopathic arthritis (JIA) has evolved markedly, owing to the availability of a growing number of novel, potent, and relatively safe therapeutic agents and the shift of management strategies toward early achievement of disease remission. However, JIA encompasses a heterogeneous group of diseases that require distinct treatment approaches. Furthermore, some old drugs, such as methotrexate, sulfasalazine and intraarticular glucocorticoids, still maintain a key therapeutic role. In recent years, information on the efficacy and safety of drug therapies for JIA has been enriched through the accomplishment of several randomized controlled trials of conventional, biologic and synthetic targeted disease-modifying anti-rheumatic drugs. In addition, a more rational therapeutic approach has been fostered by the promulgation of therapeutic recommendations and consensus treatment plans. A multinational collaborative effort has led to the development of the recommendations for the treat-to-target strategy in JIA. There is currently increasing interest for establishing the optimal time and modality for discontinuation of treatment in children with JIA who achieve sustained clinical remission.

PARALLEL SESSION 24: MECHANISMS IN AUTOIMMUNITY PART 2

20-05-2024 14:00 - 15:30

IS115 / #386

Auto and Allo-Immunity in Solid Organ Transplantation. Risk for Humoral Graft Rejection

Marcos López Hoyos
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One of the main barriers to the long-term success in solid organ transplantation is the increased risk of antibody mediated rejection (ABMR), mostly secondary to a poor immunosuppression adherence that facilitates the induction of ahumoral alloimmune response. The main mediator for such ABMR is the production of anti-HLA antibodies. However, there is an increasing concern among transplantation community about the role of non-HLA antibodies in the induction of ABMR, especially in organs such as lung or heart. This is mainly relevant in ABMR cases without evidence of detectable anti-HLA antibodies, but with suspicion of new onset autoantibodies. Besides, there is a number of transplanted patients in which their primary disease was of autoimmune origin and autoantibodies may relapse after transplantation and be responsible for organ damage. The possible pathogenic mechanisms, the number and the clinical relevance in the prognosis of solid organ transplantation will be discussed in the session.One of the main barriers to the long-term success in solid organ transplantation is the increased risk of antibody mediated rejection (ABMR), mostly secondary to a poor immunosuppression adherence that facilitates the induction of ahumoral alloimmune response. The main mediator for such ABMR is the production of anti-HLA antibodies. However, there is an increasing concern among transplantation community about the role of non-HLA antibodies in the induction of ABMR, especially in organs such as lung or heart. This is mainly relevant in ABMR cases without evidence of detectable anti-HLA antibodies, but with suspicion of new onset autoantibodies. Besides, there is a number of transplanted patients in which their primary

disease was of autoimmune origin and autoantibodies may relapse after transplantation and be responsible for organ damage. The possible pathogenic mechanisms, the number and the clinical relevance in the prognosis of solid organ transplantation will be discussed in the session.

PARALLEL SESSION 25: DIAGNOSTICS IN AUTOIMMUNITY

20-05-2024 14:00 - 15:30

IS116 / #171

EULAR/ACR 2019 SLE Classification Criteria – Lessons Learned in The First Five Years

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Rheumatology/ Medicine Iii, University Medical Center and Faculty of Medicine TU Dresden, Dresden, Germany

In 2024, the EULAR/ACR SLE classification criteria celebrate their 5th birthday, and it is worth looking at what we have learned in this time period. The EULAR/ACR criteria came with a new structure, i.e., positive ANA as an entry criterion and weighted criteria in 10 domains. In the validation cohort, the criteria reached a sensitivity of 96% and a specificity of 93%. Since their publication, the criteria have been externally validated in 28 different studies worldwide, including a total of 8,800 SLE patients and of 6,463 non-SLE patients. Albeit there are differences between the populations, which span worldwide and include pediatric-onset SLE and early disease, ANA were positive in 97% of the combined SLE population. The EULAR/ACR criteria had a sensitivity of 93% (8,207/8,800) and a specificity of 91%. Two additional publications from the EULAR/ACR classification criteria cohorts shed additional light on these data. In a subgroup analysis, the criteria performed very well across ethnicities and in women and men. In early disease of a duration of less than 1 year, the EULAR/ACR criteria were as sensitive as the SLICC criteria, but the 89% reached are still relevantly lower than the values reached later. Indeed, the lowest sensitivity found in an external validation study (89%) stems from an early SLE cohort. In an analysis of the impact of the attribution rule, it became clear that omitting this rule, thus counting arthritis clearly not due to SLE as an SLE criterion, for example, decreased specificity. Similarly, in a recent Chinese publication, the specificity rose from 86% to 95% after the application of the attribution rule. Beyond these reassuring data on the performance of the EULAR/ACR criteria in the classification of SLE, several publications have shown that a high criteria count predicts damage and is therefore a measure of high disease burden, also called ominosity.

IS117 / #172

Critical Issues in Autoantibody Tests Used As Classification Criteria for Autoimmune Diseases

Nicola Bizzaro[1,2], Alessio Mazzoni[3], Teresa Carbone[4], Luigi Cinquanta[5], Danilo Villalta[6], Antonella Radice[7], Giampaola Pesce[8], Maria Infantino[9]
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For almost all autoimmune diseases there are classification criteria formulated by scientific societies or international groups of experts. The purpose of these criteria is to harmonize the clinical characteristics of patients to define homogenous groups that can be compared across studies and geographic regions. Almost all criteria include laboratory tests with a weight that is sometimes very significant in the attribution of the total score needed to classify the disease. However, very often the criteria regarding serum immunological tests are not sufficiently updated and do not take into account the technological evolution of test methods. This may represent a challenge for autoimmunology laboratories that need to support their clinicians in the right classification of the disease. A wide variety of immunoassays are available for detection of autoantibodies that may differ in term of antigen composition, antigen exposure and detection method which may greatly affect the homogeneity, consistency and comparability of clinical research studies. We have reviewed the classification criteria of the main autoimmune rheumatic diseases, focusing on autoantibody tests, taking stock of the critical aspects that would require re-evaluation and updating based on the development of the technologies used today in clinical laboratories. We believe that involving laboratory experts in the multidisciplinary teams deputed to the elaboration of the classification criteria, could strengthen the contribution related to specific laboratory topics and help in a more updated definition of the best available tests.

IS118 / #923

Circulating Calprotectin: A Marker Gaining Awareness

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Calprotectin (CLP), a heterodimeric complex formed by two S100 proteins (S100A8/A9), has recently been proposed as a marker for the main autoimmune diseases. In autoimmune rheumatic diseases (ARD), the circulating calprotectin (cCLP) represents a potential prognostic biomarker mirroring local or systemic inflammation. High cCCL serum levels are associated with worse structural outcomes in rheumatoid arthritis and to a lesser extent, in spondyloarthritis. In addition, cCLP can predict disease relapse in some autoimmune diseases including systemic systemic lupus erythematosus (SLE), anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV) and some severe manifestations of connective tissue diseases, such as glomerulonephritis in SLE, AAV, juvenile idiopathic arthritis, adult-onset Still's Disease and lung fibrosis in systemic sclerosis. Therefore, cCLP levels enable the identification of patients who need an accurate and tight follow-up. Currently, there are only a few studies that evaluated the cCLP efficacy as a clinical biomarker in non-rheumatic diseases, and the results are contrasting, but surely promising. Future studies are warranted to better clarify the role of cCLP in relation to disease severity in myasthenia gravis, multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, Graves' orbitopathy, autoimmune bullous diseases and uveitis. In conclusion, from local to systemic levels, new approaches are developing and move the field of ARD management into the era of precision medicine.

IS119 / #1103

Autoantibody Standardization Committee: Priorities & Best Practices for Autoantibody Standardization

Mark Wener
University of Washington, Seattle, United States of America

The Autoantibody Standardization Committee (ASC) is a subcommittee of the International Union of Immunological Societies

(IUIS) charged with promoting autoantibody standardization and supplying validated autoantibody standardization products. ASC were surveyed for their impressions regarding priorities for standards, and best practices for building standardization reagents. Preliminary results indicate the perceived need for autoimmune myositis standards, such as standards for anti-MDA5. Standards for autoantibodies associated with systemic lupus erythematosus were also perceived as desirable, especially since the supply of some lupus-related autoantibody standards are dwindling or have been exhausted (the situation for anti-U1RNP supplied by ASC). The optimum composition of standards was also a survey topic. Standards composed by pooling a small number of individual donor specimens was the type of standard felt to provide an opportunity for representing antibody diversity while balancing expense and labor for constructing these pools. However, lack of diversity in geographic representation and genetic ancestry was felt to be a limitation for international standards composed of pools from small numbers of subjects. In addition, the risk of off-target additional antibody reactivity was also acknowledged. The potential use of monoclonal antibodies as standards was also addressed. An additional limitation of antibody standardization recognized by ASC was lack of a central repository and directory of autoantibody standards, which ASC is attempting to address. During this presentation, those attending will be asked to discuss these issues and also asked to participate in the survey.

PARALLEL SESSION 26: PEARLS IN AUTOIMMUNITY 2024

20-05-2024 15:45 - 16:45

IS120 / #280

COVID-19 Vaccine Related Autoimmune Rheumatic Diseases

Michael Ehrenfeld
Rheumatic Disease Unit, Sheba Medical Center, Ramat Gan, Israel

Since the introduction of the various COVID-19 vaccines a growing number of apparent autoimmune adverse events have been reported. Rheumatic autoimmune apparently associated adverse events compose a large group of conditions which have been reported so far, including large medium and small vessel vasculitis which will be briefly presented, adult onset Still's disease, new onset or exacerbation of arthritis, myositis, systemic lupus erythematosus and subacute cutaneous LE, Sjogren's syndrome, scleroderma, Behcet's disease and others. The cases published so far of rheumatic autoimmune diseases following COVID-19 vaccines, cannot determine if there is a causal relationship between the COVID-19 vaccines and the various described syndromes, or that they are coincidental. Despite the increasing number of reports of autoimmune syndromes following vaccination against SARS-CoV-2, their incidence is very low, considering the 13.57 billion doses of vaccine given so far and that 70.6% of the world population have received at least 1 vaccine. Fortunately, most of the syndromes are short-lived and respond quickly to steroids and other treatments, and have therefore a good prognosis, thus COVID-19 vaccine benefits dramatically outweigh this potential risk. Since many of these autoimmune and rheumatic diseases are also associated with COVID-19 infection, it can be hypothesized that the immunological mechanism leading to autoimmune diseases following the COVID-19 infection may also play a role in vaccine-induced rheumatic disease. Molecular mimicry, the production of particular autoantibodies, and the role of certain vaccine adjuvants seem to be substantial contributors to autoimmune phenomena.

IS121 / #178

Allergy and Autoimmunity, Revisited "Through The Looking Glass

Amir Tanay
Zabludowicz Center for Autoimmune Diseases, Tel Hashomer, Israel

Background and aims: Allergy and autoimmunity are two potential outcomes of a dysregulated immune system. The relationship between allergy and autoimmune disorders is complex and poorly understood. The aim of this presentation is to summarize similarities and differences of factors influencing the pathogenesis of autoimmune and allergic disease and to revise topics discussed in my previous papers about this issue. In addission, new topics of allergy and autoimmunity will be discussed.

Methods: The current literature was reviewed using key words: Autoimmunity, allergy, HLA, cytokines, autoantigens, GWAS, SNP, Tregs.

Results: Autoimmune diseases, can reflect the interplay of both Th1- and Th2-associated mechanisms. Epidemiological data indicate that the prevalence of both allergies and autoimmune diseases increase in parallel. IgE autoreactivity exists in allergy and autoimmunity, Autoantigens can trigger IgE-dependent inflammation in allergy. New evidences for non-IgE-mediated inflammation in allergy via autoimmune mechanisms was found . Shared genetic susceptibility loci and commonalities in pathways between allergy and autoimmune diseases exist, suggesting shared disease mechanisms, especially in gastrointestinal autoimmune diseases. In addition to its role in the development of autoimmune diseases, IL-17 may play a role in the development of various allergic diseases that have classically been considered to be Th2-mediated disorders.

Conclusions: Allergic and autoimmune diseases display different facets of immune dysregulation, and may coexist. Allergic and autoimmune diseases share common aspects: genes, cytokines, mast cell involvement, Treg. A reduction in number or activity of Foxp3+ Tregs triggers the activation of Th1 and/or Th2 responses, and may induce allergic and autoimmune diseases. The dichotomy between TH1 and TH2 is challenged.

IS122 / #893

Is The Syndrome of Postural Orthostatic Tachycardia Autoimmune? (Results and Review)

Zora Lazurova[1], Monika Lukacova[2], Harry Heidecke[3], Peter Mitro[2], Yehuda Shoenfeld[4]

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Introduction: Postural orthostatic tachycardia syndrome (POTS) belongs to a group of orthostatic intolerance syndromes, together with vasovagal syncope (VVS) and orthostatic hypotension. POTS is defined by the increase in heart rate ≥30 bpm or heart rate higher than 120/min during first 10 minutes after standing, without significant decrease in blood pressure. It is a rare disease, typically affecting younger females. This syndrome is associated with viral infections, vaccination, autoimmunity, pregnancy, stress or cerebral trauma. The dysreg-

ulation of autonomic nervous system plays a key role in pathogenesis. It can be caused by various neurohumoral mechanisms, receptor hypersensitivity, hypovolemia, mast cell dysregulation and last but not least, autoimmunity. The presence of autoantibodies targeted against various adrenergic and muscarinic receptors, as well, as angiotensin or endothelin receptors, has been identified in some patients with POTS. VVS is transient loss of counsciousness due to hypoperfusion of the brain caused by hypotension and/or bradycardia, that is a result of dysbalance between sympatheptic and parasympathetic activity. However, the exact pathomechanisms of VVS are also unclear. Whether autoimmune dysautonomia plays a role in pathogenesis remains unknown.

Aims: The aim of this preliminary study was to compare the levels of antibodies against receptors of autonomic nervous system between group of patients with POTS and VVS. Subjects and methods: Altogether 22 patients with orthostatic symptoms were included in this study (age 33.8 + 3.3 years, 11 females). All patients underwent the head up tilt test (HUTT) (Italian protocol; 20 minutes passive standing + 15 minutes after nitroglycerin provocation). Out of them, 8 individuals fulfilled criteria of POTS and 14 patients experienced tilt induced VVS, while POTS was excluded. Blood sampling was performed in each patient. The serum levels of alpha-1, alpha-2, beta-1 and beta-2 adrenergic receptor antibodies and M1-M5 muscarinic receptor antibodies, angiotensin receptor II (AT1RII) and endothelin receptor A (ETAR) antibodies were evaluated by ELISA method (CellTrend, Germany).

Results: POTS patients have significantly higher levels of AT1RII (10.7 ± 1.1 vs 7.1 ± 0.8 U/ml, *P* =.01) , ETAR (11.3 ± 1.2 vs 7.6 ± 0.9 U/ml, *P* = .02), alpha-1 (12.2 ± 1.5 vs 6.8 ± 1.1 U/ml, *P* = .009), beta-1 (19.7 ± 2.7 vs 9.3 ± 2.1 U/ml, *P* =.006) and beta-2 (23.7 ± 4.3 vs 10.9 ± 3.2 U/ml, *P* = .02) adrenergic receptor antibodies, out of antimuscarinic antibodies, anti-M3 (12.6 ± 1.6 vs 7.4 ± 1.2 U/ml, *P*= .01) and M4 (14.1 ± 1.8 vs 7.7 ± 1.3 U/ml, *P* = .008) were higher when compared to patients with VVS.

Conclusion: The role of autoimmunity in pathogenesis of POTS is highly debated. We have identified high levels of more types of autonomic antibodies in POTS patients when compared to individuals with VVS. If the autoimmunity might be implicated in other forms of orthostatic intolerance remains unclear. There is lack of data about possible autoimmune background of vasovagal syncope. Further studies are needed.

PARALLEL SESSION 27: NUTRITION AND LIFESTYLE IN AUTOIMMUNITY

20-05-2024 15:45 - 16:45

IS123 / #182

Emerging Role of Nutrition in The Prevention and Treatment of Autoimmune Diseases and Immunosenescence

Vânia Borba
Internal Medicine, Rehaklinik Dussnang AG, Dussnang, Switzerland

As our understanding of the intricate interplay between nutrition and immune system function deepens, an exciting frontier emerges in the realm of preventing and treating autoimmune diseases and immunosenescence. This presentation explores the dynamic relationship between nutrition and immune health, highlighting recent advancements in research and clinical interventions. The discussion will delve into the mechanisms through which specific nutrients modulate immune responses, influencing both the initiation and progression of autoimmune diseases. Additionally, it will illuminate the role of nutrition in addressing immunosenescence, the age-related decline in immune function. Drawing on cutting-edge studies, we will explore the potential of dietary interventions in mitigating inflammation, supporting immune resilience, and enhancing overall well-being.

IS124 / #549

The Food Additive: Microbial Transglutaminase Is A Potentıal Inducer of Autoimmune Diseases

Aaron Lerner[1], Carina Benzvi[2]
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Microbial transglutaminase (mTG), has recently attracted attention due to concerns regarding its potential role as an inducer of autoimmune diseases. mTG catalyzes protein cross-linking, potentially modifying endogenous naïve proteins making them immunogenic. It is classified as a processing aid and was granted the GRAS (generally recognized as safe) definition decades ago, thus avoiding thorough assessment according to current criteria of toxicity and public health safety. In contrast to the manufacturer's declarations, mTG and/or its transamidated complexes are proinflammatory, immunogenic, allergenic, pathogenic, and potentially toxic, hence, compromising public health. Most recently mTG mTG-directed cross reactivity directed against human mitochondrial M2, ANA, and extractable nuclear antigens was reported. Additionally, sequence similarity exists between the enzyme and 6 human epitopes, representing major targets of common autoimmune conditions like autoimmune hepatitis, Inflammatory bowel and celiac diseases, and primary biliary cirrhosis. Being a member of the transglutaminase family and functionally imitating the tissue transglutaminase, it is a potential inducer of celiac disease. MTG and its docked complexes have numerous detrimental effects. The manufacturers deny Those harmful aspects, claiming that the enzyme is deactivated by heating or gastric acidity and its covalently linked, iso-peptide bonds are safe. In contrast, extended thermostability and a wider pH range of mTG activity were observed recently, thus, contradicting the manufacturers' and distributers' arguments.It is hoped that the national food regulatory authorities and the scientific community will reassess the granted GRAS category of the enzyme, aiming to protect the public from the mTG health-damaging consequences.

IS125 / #184

Lifestyle Triggers of Neuroinflammation

Pedro Bastos
Center for Primary Health Care Research, Department of Clinical Sciences, Lund University, Malmö, Sweden

This presentation delves into neuroinflammation, a central mechanism in various neurological disorders, emphasizing the impact of modern lifestyle factors. It will cover how repetitive head trauma, commonly seen in contact sports, and exposure to xenobiotics such as air pollution and smoking, may promote neuroinflammation. The role of psychological stress, inadequate sleep patterns, circadian rhythm disruptions, and their neuroinflammatory consequences will be outlined, reflecting the complexities of contemporary living. The talk further examines the influence of dietary choices on neuroinflammation, particularly the typical Western hypercaloric diet, which is high in sugar, refined grains, alcohol, salt, trans fatty acids, oxidized lipids, and advanced glycation end-products, and low in various micronutrients, fiber, prebiotics, omega-3 fatty acids and phytochemicals. It will also address the

implications of obesity, insulin resistance, and hyperglycemia in this context. The impact of physical inactivity, a prevalent feature of modern lifestyle, will be discussed alongside the emerging understanding of the gut-brain axis, highlighting how changes in gut microbiota and increased intestinal permeability, often resulting from dietary and other lifestyle and environmental factors, can contribute to neuroinflammatory processes. In addition, the presentation will touch on the often-overlooked aspect of oral health in relation to neuroinflammation. By providing this helicopter view, it aims to encapsulate the multifaceted ways in which everyday lifestyle choices intersect with neuroinflammatory mechanisms. The goal is to foster an understanding of these complex interactions, offering insights into potential preventive and management strategies for neurological health in the face of evolving lifestyle patterns.

PARALLEL SESSION 28: THYROID AND ENDOCRINE SYSTEM

20-05-2024 15:45 - 16:45

IS126 / #185

Graves' Ophthalmopathy Epidemiology, Pathogenesis and New Therapies

Alessandro Antonelli[1], Silvia Martina Ferrari[2], Giusy Elia[1], Francesca Ragusa[1], Eugenia Balestri[1], Chiara Botrini[1], Licia Rugani[1], Clara Miglietta[1], Emilio Barozzi[1], Valeria Mazzi[1], Armando Patrizio[3], Poupak Fallahi[4]

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[4]Department of Translational Research of New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

Thyroid eye disease (TED), also known as Graves' ophthalmopathy, is an autoimmune disease of the orbit that generally occurs in patients with Graves' disease (GD), but in 5%-10% of patients is associated with autoimmune thyroiditis. Smoking and genetic susceptibility are important risk factors. TED is typically bilateral and when is active, it is characterized by eye redness, photophobia, eyelid swelling, proptosis and diplopia. In most severe cases, the optic nerve involvement (dysthyroid optic neuropathy) can threatens the sight, requiring immediate management. Classically, the management of TED consisted in hyperthyroidism control, local treatments, intravenous methylprednisolone pulses (IVMP) and, in selected cases, immunosuppressant medications. However, thanks to the increase of the knowledge on TED pathophysiology and the identification of new potential therapeutic targets, new biological drugs have been synthetized and introduced. They have shown high efficacy in the treatment of symptoms and sign of TED, such as teprotumumab, and others are currently under investigation with encouraging results that promise an upcoming upgrade in the disease's therapy.

IS127 / #186

Vitamin D Levels in Slovak Women with Autoimmune Thyroid Disease

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The role of vitamin D (VD) in the etiopathogenesis of autoimmune diseases (AI) is extensively studied and has been documented in various organ-specific and non organ-specific AI disorders. However, its association with autoimmune thyroid disease (AITD) is still controversial. Several studies from last decade have documented that low vitamin D status was associated with positivity of antithyroid antibodies, especially with a-TPO positivity, or were associated with various degrees of thyroid insufficiency. On the other side, some researchers did not detect any relationship between vitamin D and thyroid autoimmunity or its function.

Aim: This study was to assess the relationship between vitamin D status and thyroid autoimmunity in Slovak premenopausal women with newly diagnosed AITD.

Subjects and methods: This case-control study included 57 women with AITD and 41 age- and BMI-matched controls. All subjects were examined for serum 25(OH)D, thyroid autoantibodies (a-TPO, a-TG), fT4 and TSH concentrations. Thyroid volume was measured in all women.

Results: There were no significant differences in serum 25(OH)D levels between AITD and controls (74.04 $\pm$ 3.3 v.s. 73 $\pm$ 28 nmol/l, P =.8). No significant correlation between 25(OH) D and thyroid autoantibodies was found in the whole cohort and also in AITD group. The prevalence of VD insufficiency was 60.31% in AITD women and was similar in the control group (52.5%). There were no significant differences in the serum a-TG (P = .17**)** and a-TPO (P = .13) concentrations between VD insufficient and VD normal subjects. No significant association of VD with thyroid autoantibodies, hormonal status and thyroid volume was detected.

Conclusion: We conclude that VD insufficiency is common in Slovak premenopausal women independently on the presence of AITD. V D insufficiency is not associated with thyroid autoimmunity or thyroid volume in patients with early diagnosis of AITD.

IS128 / #187

Thyroid Autoimmunity and COVID-19

Ifigenia Kostoglou-Athanassiou

Department Of Endocrinology, Asclepeion Hospital, Voula, Athens, Greece

Thyroid autoimmunity manifests mainly as autoimmune Hashimoto's thyroiditis and Graves' disease. Subacute thyroiditis is a post-inflammatory or inflammatory thyroid disease. SARS-CoV-2 is a coronavirus, which has caused the recent pandemic. The SARS-CoV-2 virus may be related to the development of autoimmunity. Thyroid disease is a rare manifestation of SARS-CoV-2 infection. Cases of subacute thyroiditis in patients with the Covid-19 infection, have been described all over the world. Cases of thyroiditis, hypothyroidism and Graves' disease have been observed following the SARS-CoV-2 infection. The SARS-CoV-2 infection may lead to exacerbation of Graves' disease or thyroid ophthalmopathy. Vaccination against the SARS-CoV-2 virus has helped to limit the pandemic and is characterized by very few side effects. Amongst those cases of subacute thyroiditis and cases of Graves' disease have been found after vaccination against the SARS-CoV-2 virus. In conclusion, SARS-CoV-2 is a coronavirus that has been related to the development of autoimmunity. Autoimmune thyroid disease, in the form of either subacute thyroiditis, autoimmune thyroiditis and Graves' disease have been described in patients with the Covid-19 infection.

PARALLEL SESSION 29: PATHOGENESIS OF AUTOIMMUNE CONDITION

20-05-2024 17:15 - 18:30

IS129 / #194

Update On Checkpoint Inhibitors Induced Autoimmunity

Michael Ehrenfeld
Rheumatic Disease Unit, Sheba Medical Center, Ramat Gan, Israel

Immune checkpoint inhibitors (CPI) have emerged as a remarkable treatment option for diverse cancer types. However, a significant number of patients on CPI develop immune-related adverse events affecting a wide variety of organs. These events, which may reflect enhanced T-cell activation, are unpredictable, heterogeneous, and in some instances permanent or life-threatening. It is not clear whether these toxicities are distinct from conventional autoimmune diseases. An update of the rheumatic syndromes associated with CPIs will be presented including PMR-like syndromes. RA-like syndromes, myositis, Sicca syndrome, vasculitis, as well as other systemic manifestations including sarcoidosis or sarcoid-like reactions, and occasional cases of systemic sclerosis or scleroderma-like reactions, subacute cutaneous lupus erythematosus as well as SLE.

IS130 / #193

Checkpoint Proteins as A Gate between Autoimmune Rheumatic Diseases and Cancer

Maurizio Cutolo
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CTLA-4 represetnts a classical protein actig as a gate between Rheumatic diseases and cancer. In autoimmune diseases its use as fusison protein (CTLA-4Ig) is employed as therapeutical agent (abatacept) in order to block the costimulatory proteins (CD86-CD80) on surfaces of immune activated cells (ie. macrophages) and to down regulate the immune response. On the contrary in presence of cancer (ie. melanome) the use of a MoA agaist CTLA-4 (ie. ipilimumab) is employed to block the CTLA-4 and as consequence to enhance the immune response. This approach let the inventors to get the Nobel Prize for Medicine in 2018. Therefore, checkpoint proteins , at least CTLA-4 with different appeoches,can used to dowregulae or to enhence the innate immune response and to treat pathological conditions acting as a real gate for the immune response.

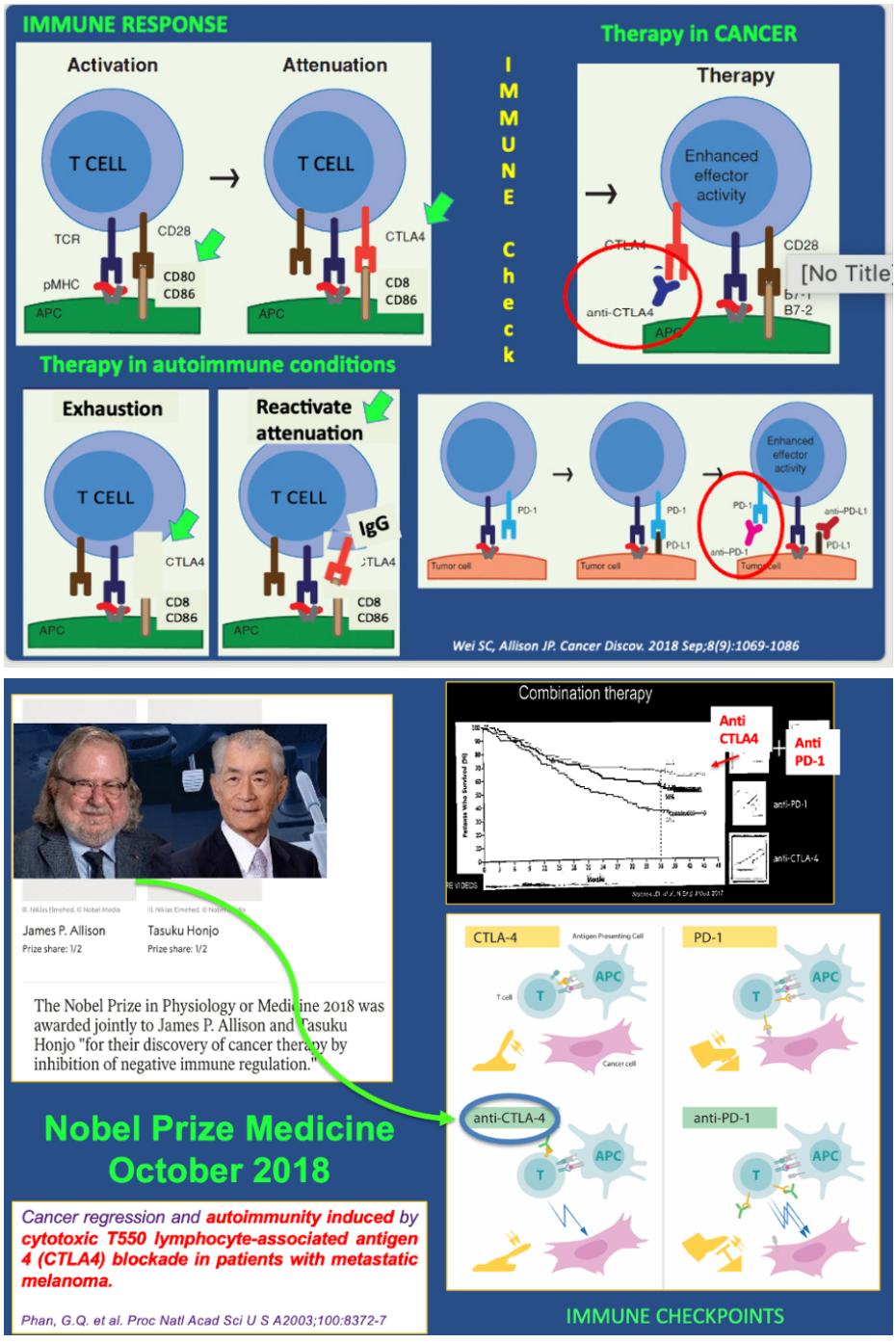

Figure 1. CTLA-4 blockade in the treatment of rheumatoid arthritis: an update.

IS131 / #283

Eosinophilic Fasciitis: From Diagnosis to Treatment

Luc Mouthon
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Eosinophilic fasciitis (EF) is a rare disease characterized by abrupt onset edema, skin sclerosis, eosinophilia, and fasciitis. Pinal-Fernandez reported the main features as they proposed diagnosis criteria, which include major criteria including skin modification or subcutaneous lesions and inflammatory fascia thickening, along with minor criteria including eosinophilia, hypergammaglobulinemia, muscle weakness, groove sign or peau d'orange and magnetic resonance imaging hyperintense fascia. The presence of both major criteria or 1 major criterion and 2 minor criteria establishes the diagnosis of EF. EF is occasionally associated with morphea, drugs, and malignancy. Morphea is reported in 20% to 40% of patients and is sometimes associated with residual fibrosis.

Hematological disorders associated with EF include myelodysplastic syndrome, myeloproliferative disorder, myeloma, lymphoma, leukemia, and aplastic anemia. Among associated cancers, melanoma, seminoma, bladder, and prostate cancers were described. However, the authors diverge on the paraneoplastic and prognosis values of such associations. Our group recently published a pharmacovigilance study of drug-induced EF (DIEF), suggesting a good prognosis for DIEF. Although diagnosis and therapeutic progress has been made, most data comes from case reports and a few case series. Therefore, EF treatment remains challenging. Glucocorticoids are considered standard therapy, and experts acknowledge good responses, but failures have been described. Moreover, some questions remain unanswered, such as disease homogeneity, the benefit of immunosuppressant drugs or methylprednisolone pulses, and relapse management.

PARALLEL SESSION 30: KIDNEY AND AUTOIMMUNITY

20-05-2024 17:15 - 18:30

IS132 / #195

Update on Therapy of Lupus Nephritis wıth Special Focus on Refractory Forms

Dario Roccatello
University Center of Excellence on Nephrological, Rheumatological and Rare Diseases (ERK-net, ERN-Reconnect and RITA-ERN Member) including Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID), Coordinating Center of the, Torino, Italy

Systemic lupus erythematosus (SLE) is distinguished by an anomalous immunological response, resulting in a highly diverse clinical manifestation that has the ability to impact several systems and organs. Although the mortality rate of systemic lupus erythematosus (SLE) has significantly declined following the implementation of steroid treatment, certain types of refractory or severe SLE still carry the risk of causing irreversible organ damage, leading to higher rates of death and morbidity. Moreover, individuals diagnosed with systemic lupus erythematosus (SLE) who have many coexisting medical conditions may encounter a complex clinical situation and experience an unfavorable prognosis. The prognosis for severe refractory systemic lupus erythematosus (SLE) can be enhanced via timely and suitable therapeutic interventions. This literature review seeks to address the lack of comprehensive data from randomized controlled studies on refractory/severe systemic lupus erythematosus (SLE) patients. Instead, it aims to provide real-world evidence from clinical research conducted at our institution, the University Center of Excellence on Nephrologic, Rheumatologic and Rare Diseases with Nephrology and Dialysis Unit and Center of Immuno-Rheumatology and Rare Diseases (CMID) in Turin, Italy. This study aims to analyze the significant clinical and prognosis characteristics, as well as therapeutic strategies, for severe and/or refractory systemic lupus erythematosus (SLE). Our investigation will incorporate our own observations alongside relevant literature, with a particular emphasis on the manifestations of dermatological, neuropsychiatric, and renal symptoms.

IS133 / #197

THE CD6/ALCAM Pathway as A Novel Biomarker and Treatment Target in Lupus Nephritis

Chaim Putterman[1,2]

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T cells are central to the pathogenesis of lupus nephritis (LN), a common complication of systemic lupus erythematous (SLE). CD6 and its ligand, activated leukocyte cell adhesion molecule (ALCAM), are involved in T cell activation and trafficking. Previously, we showed that soluble ALCAM is increased in the urine of LN patients (uALCAM), suggesting that this pathway contributes to disease. To determine the potential role of blocking CD6-ALCAM interactions as a novel therapy for SLE and lupus nephritis, we administered a monoclonal anti-CD6 antibody to MRL/lpr mice (a classic murine model of spontaneous lupus), and to non-autoimmune mice passively transferred with pre-formed polyclonal nephrotoxic antibodies (a model of induced immune-complex glomerulonephritis). In both models, anti-CD6 treatment was associated with significant decreases in kidney-infiltrating immune cells and inflammatory markers, together with an improvement in measures of nephritis. To investigate a possible role of CD6 and ALCAM as potential biomarker of lupus nephritis, urinary ALCAM (uALCAM) was examined in >1000 patients with SLE and LN from ethnically-diverse cohorts, and CD6 and ALCAM expression was assessed by single cell RNA sequencing performed on clinically-indicated kidney biopsies obtained from patients with active lupus nephritis. The analysis strongly supported uALCAM as a biomarker that distinguishes active renal involvement in SLE, irrespective of ethnicity, with better predictive power than urinary CD6. Moreover, in preliminary studies, changes in uALCAM over time predicted subsequent therapeutic responses. In kidney tissue, ALCAM was expressed by human renal structural cells, primarily tubular cells, while CD6 expression was exclusive to T cells. Moreover, patients with LN exhibited elevated numbers of CD6+ and ALCAM+ cells in the kidney. Our data demonstrate an important contribution of the CD6/ALCAM pathway to LN and SLE, supporting its use as a disease biomarker and therapeutic target.

IS134 / #199

Is Protocol Biopsy Required in Lupus Nephritis?

Mariele Gatto
Academic Rheumatology Centre, Dipartimento Scienze Cliniche e Biologiche Università di Torino - AO Mauriziano di Torino, Turin, Italy

Baseline kidney biopsy is recommended in lupus nephritis (LN) to classify different forms of LN and differentiate other forms of renal involvement, such as tubulo-interstitial nephritis, antiphospholipid-related nephropathy or thrombotic microangiopathy. Conversely, the indications for repeated protocol biopsy are more controversial. Protocol biopsy (PB) is not just rebiopsy. PB is meant to take place after a fixed period of time from index biopsy, in order to explore the extent of renal response/remission at the histological level. The need for looking into kidney tissue data along the follow-up on LN patients arises from the known discrepancy between clinical and histological response, where a remarkable proportion of patients may display persistent histological acitivty despite clinical remission. Hence, some physicians recommend PB either at 6 months in stable patients to assess the response to initial therapy, or after one-to-two years to assess treatment efficacy and tune the duration of maintenance therapy. Others recommend PB in case of incomplete response or to discriminate between active and chronic lesions. However, this practice is burdened by feasibility/safety issues and provides information that is not clearly interpretable from a prognostic point of view. While persistent activity/worsened chronicity on PB may herald flares/renal damage, it is not clear what is the optimal time frame for evaluation in clinical responders, or whether there is and which is the threshold of histological activity considered non-harmful to long-term LN prognosis. This debate is motivated by the need to translate any tissue

information into an intensification or tapering of immunosuppressive treatment, in order to avoid the risk of over- or undertreatment of LN patients. Transcriptomics and proteomics data suggest that the discrimination between responders and nonresponders in PB is possible, yet it should be defined on a molecular rather than histological basis. The issue of modulating immunosuppressive therapy in LN is highly debated. The European recommendations advise consolidating renal response for at least three years before cautiously decreasing treatment. Durable renal remission is indeed protective against subsequent renal damage. On the contrary, discontinuing the immunosuppressor in patients in clinical remission for less than three years and/or with a high steroid threshold is associated with a marked risk of flares. PB may represent a useful tool in difficult cases to evaluate the therapeutic response, modulate treatment intensity, and predict long-term renal outcome both in quiescent lupus and during flares; how to harmonize per-protocol biopsy in LN course remains challenging.

PARALLEL SESSION 31: ICAP SESSION: FOCUS ON THE CLINICAL RELEVANCE OF THE HEP-2 IFA (ANA) TEST

20-05-2024 17:15 - 18:30

IS135 / #946

Novel Clinically Relevant Patterns and Evolution of The Icap Classification Tree

Luis Eduardo Andrade
Division of Internal Medicine / Rheumatology, Universidade Federal de São Paulo, São Paulo, Brazil

The gold standard test to screen for autoantibodies in the clinical investigation of systemic autoimmune diseases is the indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA), historically known as antinuclear antibodies (ANA). The HEp-2 IFA provides information on the serum level (titer) and putative autoantibody specificities (staining pattern) in the sample. The staining pattern reflects the distribution of the target autoantigens across the cellular domains, thereby providing indirect clues on the possible autoantibody specificities in the sample. The International Consensus on Antinuclear Antibody Patterns (ICAP) was established in 2014 with the aim of promoting harmonization and understanding of HEp-2 IFA staining pattern nomenclature, as well as optimizing usage in patient care by providing interpretation guidelines for HEp-2 IFA test results. Currently ICAP has classified 30 patterns under a structured algorithm with the respective clinical and immunologic relevance (www.anapatterns.org). Each ICAP pattern has an alphanumeric code (AC, for Anti-Cell). Patterns that are easy to identify are grouped as competent-level patterns and those with more subtle features are grouped as expert-level patterns. Each expert-level pattern is under an overarching "umbrella" competent-level pattern. Thus, the operator has the option of using the expert-level or competent-level according to one's expertise and/or the nature of the image under analysis. As an ongoing initiative, ICAP promotes periodic increments in the recommendations and classification tree according to the progress in the related literature and inputs from the expert community. Accordingly, in the year 2018 ICAP implemented three novel patterns (AC-0, AC-29, and AC-XX). AC-0 refers to the staining pattern correspondent to the absence of relevant reactivity, i.e., a negative result. AC-29 is a composite pattern strongly associated with antibodies to DNA topoisomerase I (Scl-70). AC-29 comprises a specific assembly of five elements: a) nuclear fine speckled; b) metaphase chromatin also with a fine speckled staining; c) dots at the metaphase plate corresponding to the Nucleolar Organizing Regions (NOR); d) nucleolar staining; and e) cytoplasmic delicate reticular staining. The presence of these five elements is very characteristic and indicates a high probability of anti-DNA topo I antibodies. Because of its clinical relevance, this pattern was classified as the DNA topo-like pattern and received the code AC-29. AC-XX refers to unusual patterns that occur in the routine HEp-2 IFA operation in clinical and research laboratories. In recognition that one cannot rule out their potential clinical relevance, ICAP recommends that these patterns should be reported as a positive result and has created the AC-XX code for these unusual and yet unclassified patterns. For several years, investigators from different parts in the world have recognized that the nuclear fine speckled pattern (AC-4) exhibits some heterogeneity in the staining texture. Part of this heterogeneity may be related to the culturing and fixation methods used in the production of different brands of HEp-2 IFA slides. However, even using the same brand, one can notice variability in the staining texture of different samples classified as AC-4. Eventually, there were publications from different groups reporting on a specific variety of the AC-4 pattern strongly associated with anti-Ro60 antibodies. In contrast, the regular AC-4 pattern shows no particular association with anti-Ro60 antibodies. This new pattern is less frequent that the regular AC-4 pattern and is characterized by myriad discrete tiny dots spread throughout the nucleus, with no staining of the metaphase chromatin. In the year 2021, ICAP recognized this new pattern as a variant of the AC-4 pattern and the pertinent information was posted as a footnote to the AC-4 page. In 2023, during the 7th ICAP Workshop at the 32nd Dresden Symposium on Autoantibodies, ICAP recognized the myriad discrete nuclear dots as an independent pattern that has been indicated to receive the code AC-31. A similar process occurred regarding the nuclear dense fine speckled (AC-2) pattern. This pattern must be distinguished from the nuclear homogeneous (AC-1) and from other nuclear speckled patterns (AC-4, AC-5, and AC-31). In contrast to the latter patterns, the AC-2 pattern is not associated with the presence of autoantibodies relevant to systemic autoimmune diseases, but is strongly associated with anti-DFS70 antibodies, which are not associated with autoimmune diseases. The common feature in AC-2 and AC-1 patterns is the staining of the metaphase chromatin; however, they can be easily distinguished from each other by the staining texture. Other nuclear speckled patterns (AC-4, AC-5, and AC-31) are readily distinguished from AC-2 because the former do not stain the metaphase chromatin. In the last years, several investigators and specialists have noticed a variety of nuclear speckled patterns with stained mitotic chromatin that has staining texture distinct from that of the AC-2 pattern. Not surprisingly, such variants do not show association with anti-DFS70 antibodies and may occur in patients with systemic autoimmune diseases. During the 7th ICAP Workshop in 2023, a retrospective study with over 2,500 samples concomitantly assayed for HEp-2 IFA and seven relevant autoantibodies (dsDNA, nucleosome, SS-A/Ro, SS-B/La, U1-RNP, Sm, and Scl-70) showed that reactivity to at least one of these autoantibodies was present in almost 25% of samples with the AC-2 variant pattern but in only 3.4% of samples with the bona fide AC-2 pattern. Acknowledging the clinical relevance of this new pattern, ICAP has proposed the designation of the nuclear fine speckled pattern with mitotic plate under the AC-30 code. The ultimate goal of ICAP is to promote harmonization and recommendations for optimal use and interpretation of the HEp-2 IFA test, thereby contributing to the best management of patients under investigation of autoimmune diseases. Through interaction with the international community of HEp-2 IFA experts, ICAP strives to keep the classification tree updated and progressively incorporates new patterns with consistent characteristics and clinical relevance. Importantly, ICAP acknowledges that not all HEp-2 IFA images can be defined at the ultimate expert level. Therefore, as occurs with other ICAP patterns, these nov-

el patterns are under an overarching umbrella pattern that can be used as a competent-level classification.

IS136 / #947

Practical Difficulties in Fitting Some Images into The Icap Classification Tree

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Central Diagnostic Laboratory, Maastricht University Medical Center, Maastricht, Netherlands

The International Consensus on ANA Patterns (ICAP) has currently defined 31 HEp-2 IFA patterns in the categories nuclear, cytoplasmic, and mitotic. The definitions are based on the fluorescence patterns observed in distinct compartments of the cell. To support the medical community that has to deal with HEp-2 IFA results, i.e., laboratory specialists, clinicians, and scientists, the ICAP website (ana.patterns.org) has been developed. This website is regularly updated and is translated in multiple languages. Very recently also an application for mobile devices, mirroring the content of the website, has been released. The website, and hence also the application, contains multiple images representing the respective pattern. These images have been selected by the ICAP executive board. However, it is evident that the patterns differ between substrates of distinct suppliers. Therefore, each image contains information on the substrate brand that has been used. Interestingly, the images displayed on the website are not all representative of the definition of the respective pattern or of the diversity that is observed in substrates of distinct suppliers. In addition, in clinical practice many sera do not reveal a single HEp-2 IFA pattern. As such, a distinction can be made between multiple and mixed pattern based on fluorescence in a distinct or the same cellular compartment, respectively. Representative images of such situations are currently lacking, but eagerly awaited for. Supported by a number of examples, ICAP is to be challenged to broaden the set of images to acknowledge the issues raised above.

IS137 / #948

Multiple, Mixed, and Composite Patterns

Luis Eduardo Andrade
Division of Internal Medicine / Rheumatology, Universidade Federal de São Paulo, São Paulo, Brazil

The indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA), historically known as antinuclear antibodies (ANA), is the most used test to screen for autoantibodies in the clinical investigation of systemic autoimmune diseases. The HEp-2 IFA staining pattern is determined by the distribution of the target autoantigens across the cellular domains, providing indirect clues on the possible autoantibody specificities in the sample. The International Consensus on Antinuclear Antibody Patterns (ICAP) has classified 30 patterns under a structured algorithm with the respective clinical and immunologic significance (www.anapatterns.org). Each ICAP pattern has an alphanumeric code (AC, for Anti-Cell) and most of them are classified as Simple Patterns. i.e., a single cell domain is stained with characteristics distinct from other simple patterns. In contrast, there are more elaborated patterns that are classified under the Compound Pattern group, comprising multiple patterns, mixed patterns, and composite patterns. Multiple patterns refer to the co-occurrence of two or more simple patterns that can be independently identified (e.g., AC-1 and AC-23). Some multiple patterns have particular clinical interest because in the appropriate clinical context they indicate the possibility of more than one autoantibody associated with the same disease, in that way increasing the odds for those autoantibodies and that disease. For example, sera from patients with primary biliary cholangitis (PBC) may present an association of two or more of the following patterns: the cytoplasmic reticular AC-21 pattern (associated with anti-mitochondria antibodies), the nuclear multiple discrete AC-6 pattern (associated with anti-Sp100), the nuclear discontinuous envelope AC-12 pattern (associated with anti-gp210), and the centromere pattern (AC-3). Therefore, the co-occurrence of two or three of these patterns should raise the odds for the diagnosis of PBC in the appropriate clinical context. Mixed Patterns refer to the co-occurrence of two or more simple patterns staining the same cell compartment so that one cannot clearly identify any of the individual patterns. This is frequently observed when there is overlap of two or more nuclear patterns with different textures, yielding a mixed pattern with none of the original characteristic textures of either of the subjacent AC patterns. For example, sera from lupus patients frequently have multiple autoantibodies against different nuclear antigens, e.g., double-stranded DNA (AC-1 pattern), SS-A/Ro60 (AC-4), and Sm/U1-RNP (AC-5). The diffuse and blurred nuclear pattern resultant of such mixture of autoantibodies cannot be clearly classified as any of the individual AC patterns. In some cases, progressive dilution of the sample allows the identification of one or more of the individual patterns. Composite Patterns refer to the staining of more than one cell compartment caused by a single autoantibody specificity. Frequently, this is evident by comparing cells in different phases of the cell cycle. Of relevance, the unique assembly of patterns of a composite pattern is virtually specific for one autoantibody specificity. Because of this strong association, most composite patterns bear the primary target autoantigen in their names: such as the NuMA-like pattern (AC-26), the CENP-F-like pattern (AC-14), and the Topo I-like pattern (AC-29) (also see www.anapatterns.org). The lack of knowledge of the composite patterns may cause misinterpretation of the images as corresponding to multiple patterns. The proper recognition of the composite patterns is helpful in raising the suspicion of the cognate autoantibody specificity. The appreciation and identification of multiple, mixed, and composite patterns contribute to the efficiency in HEp-2 IFA pattern interpretation and add value to the laboratory investigation of patients under suspicion of systemic autoimmune diseases.

IS138 / #949

Frequently Asked Questions for Icap

Maria Infantino
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Since 2019, the International Consensus on Antinuclear Antibody (ANA) Patterns (ICAP) website has featured a "Frequently Asked Questions" (FAQ) section, facilitating a dynamic exchange between the global community and a panel of ICAP experts. This platform allows registered users to pose questions and submit IFA images that are difficult to classify, thereby receiving expert clarification and guidance. Inquiries are directed to ICAP Coordinators Edward K. L. Chan and Luis E. C. Andrade, with responses to straightforward questions provided within 24 hours, while more complex queries may involve consultation among ICAP members for consensus or diverse perspectives, extending the response time to between 72 hours and two weeks. Questions of broad interest are compiled, refined, and shared in the FAQ section of the ICAP website. Recent notable FAQs include guidance on identifying the metaphase plate and interpreting changes in anti-SS-A/Ro levels. ICAP encourages the submission of questions and discussions related to HEp-2 IFA from both research and clinical laboratories, emphasizing its role as a resource rather than offering clinical advice on individual cases.

ORAL PRESENTATIONS

PARALLEL SESSION 01: APS - WHAT'S NEW IN ANTIPHOSPHOLIPID SYNDROME?

18-05-2024 10:30 - 12:00

O001 / #378

Integrating Aβ2gpı-D1antibodies into The Clinical Practise: An Italian Multi-Center Experience

Maria Infantino[1], Silvia Foddai[2], Mariangela Manfredi[1], Maurizio Benucci[3], Irene Cecchi[4], Massimo Radin[4], Alice Barinotti[4], Elena Rubini[4], Dario Roccattello[4], Savino Sciascia[4]

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[2]Rheumatologic and Rare Diseases, University of Turin, Turin, Italy
[3]Rheumatology, San Giovanni di Dio Hospital, Florence, Italy
[4]Rheumatologic and Rare Diseases, university of Turin, Turin, Italy

***Background and Aims*:** Anti-domain I beta2-glycoprotein I IgG antibodies (aβ2GPI-D1) are a subgroup of aβ2GPI antibodies directed against one of the domains consisting of β2GPI. In APS patients these antibodies correlate strongly with thrombosis and to the lesser extent, with pregnancy complications. We evaluate the effectiveness of the reflex approach in testing for anti-β2GPI–D1 IgG antibodies (aβ2GPI-D1) of aβ2GPI positivity in a real world setting (development cohort) and validate it in an external setting (validation cohort).

Methods: Samples were tested for aPL, including ab2GPI-D1 regardless the ab2GPI status. Sera were tested by CLIA-QUANTA-Flash, Inova Diagnostics, San Diego, CA.

Results: Out of 5250 requests, 283 samples included in the development cohort resulted positive for ab2GPI (5.4%). Of those, 81 (28.6%) resulted positive for ab2GPI-D1. In the validation cohort, out of the 489 tested patients, ab2GPI antibodies resulted positive in 201 (41.1%) cases. ab2GPI-D1 antibodies were positive in 73 patients (36.3%).

Conclusions: Up to 28% and 36% of patients with ab2GPI tested positive also for ab2GPI-D1 antibodies in the development and validation cohort, respectively. Our study supports the feasibility of ab2GPI-D1 reflex algorithm to further investigate aPL positive results, especially when ab2GPI antibodies are detected to moderate-high titers.

PARALLEL SESSION 02: COVID-19, POST COVID SYNDROME AND AUTOIMMUNITY

18-05-2024 10:30 - 12:00

O002 / #1146

Asia as A Result of Suspected Post-Vaccinal Activation of Latent Infections

Background and Aims: Many pathogens that commonly infect humans are capable of triggering autoimmune responses, yet only a relatively small number of those infected consequently develop autoimmune disease. Moreover, although genetic predisposition is an important risk factor, it is not the sole determinant of autoimmunity. Research also shows that often, it is not a single infection but rather multiple concurrent infections that are responsible for the induction of autoimmunity. Notably, autoimmune and inflammatory pathologies can result not only from newly acquired infections, but also from activation of latent infections under specific circumstances.

Here presented is a case of a previously healthy, athletic 15-year old girl with no relevant personal medical history who following vaccination with the nine-valent HPV vaccine Gardasil experienced sudden onset of severe psychiatric symptoms, followed by fatigue, headache, orthostatic intolerance, sensitivity to light, sound and touch, insomnia, cognitive impairment, ataxia, and reduction in handwriting skills, executive function and athletic ability. Her labs were positive for multiple infectious agents which are well-known for their ability to cause latent infections. The patient also tested positive for autoantibodies against several nervous system antigens, including anti-MOG and anti-GABA receptor antibodies. Her diagnoses included autoimmune encephalitis, pediatric acute-onset neuropsychiatric syndrome and chronic fatigue syndrome. Comprehensive genetic testing showed that the patient had numerous relevant genetic susceptibilities in addition to HLA types associated with autoimmune disease.

Post-vaccinal activation of latent infections with autoimmune and inflammatory sequelae is a phenomenon that has previously been documented with SARS-CoV2 and influenza vaccines. Current research indicates that it may also occur following HPV vaccination. Further supporting this hypothesis, a disproportionality analysis of U.S. VAERS data shows that MedDRA codes for infections, in combination with codes for chronic fatigue, neurologic and dysautonomic symptoms with serious and disabling outcomes, are highly significantly over-represented in HPV vaccine reports compared with non-HPV vaccine reports for females aged 6-29 years.

Different triggers are capable of activating latent infections. Of those reported in the scientific literature, cellular stress including apoptosis, inflammation, and tissue damage are recognized as immunostimulatory effects of vaccinations, especially those adjuvanted with aluminum. Since the proprietary aluminum adjuvant in Gardasil is more immunoreactive than traditional aluminum adjuvants, it is possible that Gardasil vaccination may be associated with greater frequency and severity of autoimmune and/or inflammatory syndromes in genetically predisposed individuals who harbour latent infections.

PARALLEL SESSION 05: PREGNANCY AND AUTOIMMUNITY

18-05-2024 14:00 - 15:30

O003 / #267

Assesment of Ovarian Dysfunction In Adolescent Female Patients with Severe Rheumatic Disease Receiving Cyclophoshamide

Cansu Ayten Tatar[1], Gözde Özer[2], Muserref Kasap Cüceoglu[1], Ozge Basaran[1], Ezgi Deniz Batu[1], Berna Oguz[2], Seza Özen[1], Alev Ozon[3], Yelda Bilginer[1]

[1] Division of Rheumatology, Department of Pediatrics, Hacettepe University Hospital, Ankara, Turkey
[2]Department of Radiology, Hacettepe University Hospital, Ankara, Turkey
[3] Division of Endocrinology, Department of Pediatrics, Hacettepe University Hospital, Ankara, Turkey

Background and Aims: *The* aim of this study was to analyze the risk of ovarian failure in women, diagnosed with SLE and vasculitis and treated with CYC during adolescence.

Methods: This is a single-center cross-sectional cohort study involving 26 (17 SLE) patients who received CYC therapy and 15 (12 SLE) who didn't as control group. Serum FSH, LH, estradiol and AMH measurments and transabdominal pelvic ultrasonographic assessments were carried out in the early follicular phase. Analyses were done comparing the patients who received high and low doses of CYC (>3g or ≤ 3g, respectively) and who didn't.

Results: Median age of the subjects in the CYC and control groups at the time of current evaluation was similar (19 vs 18 years respectively) and median of cumulative CYC dosage was 2.3 (0,4-24) grams. With a median follow up of 6 (1-17) years, AMH was comparably lower in the group with high cumulative CYC doses compared to low doses and controls (1.86, 2.64 and 4.05 ng/mL respectively) with similar median of other hormones. Median ovarian volume was reduced significantly in the CYC group compared to the control group (4.85 and 8.30 cm^3 respectively) although mean follicular count was similar for all groups.

Conclusions: Patients receiving high cumulative CYC doses may indicate a need for watchful monitoring in terms of POF. It is thought that younger age at treatment initiation and low cumulative CYC doses reduces the risk of POF and thus using CYC in the management of pediatric rheumatic diseases may still be the choice of treatment.

O004 / #1082

Selective Suppression of Pathogenic B Lymphocytes from Hashimoto's Thyroiditis Patients by Chimeric Protien Molecules

Andrey Tchorbanov[1], Nikola Ralchev[1], Nikolina Mihaylova[1], Irini Doychinova[2], Iliyan Manoylov[1], Alexander Shinkov[2]

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[2]Medical University of Sofia, Faculty of Pharmacy, Sofia, Bulgaria

Background and Aims: Hashimoto's thyroiditis is one of the most common endocrine disorders affecting up to 20% of the adult population. No treatment or prevention exists except hormonal substitution of hypothyroidism. We hypothesize that it may be possible to suppress selectively anti-thyroglobulin (Tg) IgG antibody producing B lymphocytes from HT patients by a chimeric protein molecule containing a monoclonal antibody specific for the human inhibitory receptor CR1, coupled to peptide epitopes derived from Tg protein. We expect that this treatment will down-regulate B cell auto-reactivity by delivering a strong inhibitory signal.

Methods: Three peptides – two epitope-predicted ones derived from Tg and another irrelevant peptide – were synthesized and then coupled with monoclonal anti-human CR1 antibody to construct three chimeric molecules. The binding to CD35 on human B cells and the effects of the chimeric constructs on PBMC and TMC from patients with HT were tested using flow cytometry, ELISpot assay and immunoenzyme methods.

Results: We found that after the chemical conjugation all chimeras retained their receptor-binding capacity and the Tg epitopes could be recognized by anti-Tg autoantibodies in the patients' sera. This treatment down-regulated B cell autoreactivity and cell proliferation, inhibited Tg-specific B cell differentiation to plasmablasts and promoted apoptosis to the targeted cells.

Conclusions: The treatment of PBMCs from HT patients with Tg epitope-carrying chimeric molecules affects the activity of Tg-specific autoreactive B lymphocytes delivering to them a strong suppressive signal.

PARALLEL SESSION 06: SYSTEMIC SCLEROSIS, PSORIASIS AND SPONDYLOARTHRITIS

18-05-2024 14:00 - 15:30

O005 / #30

Cardiovascular Outcomes of Systemic Treatments in Psoriasis and Psoriatic Arthritis: A Comparative Analysis of Biological Agents

Arad Dotan[1], Niv Ben Shabat[1], Abdulla Watad[1], Galia Zacay[2], Dennis Mcgonagle[3], Howard Amital[1]

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[2]Department of Family Medicine, Meuhedet Health Maintenance Organization, Ramat-Gan, Israel
[3]The Leeds Teaching Hospitals Nhs Trust & Leeds Institute of Rheumatic And Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

Background and Aims: Major adverse cardiovascular events (MACE) are known comorbidities with psoriasis (PsO) and psoriasis arthritis (PsA). Previous studies discussed the potential of sufficient anti-inflammatory therapy for PsO and PsA in decreasing MACE incidence. We aimed to assess the risk of developing MACE in patients with pre-existing PsO treated with different treatment regimens; topical treatment, methotrexate and biologic disease-modifying anti-rheumatic drugs (bDMARDs).

Methods: We conducted a retrospective exploratory study using real-world data from the databases of the third-largest Israeli HMO, covering approximately 1.3 million subjects. A total of 61,003 PsO patients diagnosed between January 2000 and January 2020 and 244,012 healthy controls above the age 30 were included, matched for sex, age and socioeconomic status. We performed a series of Cox proportional hazards regression analyses adjusted for BMI, diabetes mellitus, dyslipidemia, and hypertension diagnoses.

Results: Our study comprised 29,067 patients, including 798 PsA patients, and a total of 107,657 matched controls. PsO patients treated with bDMARDs were at lower risk of MACE compared to matched controls (HR=0.33, *P*=.01), while those receiving topical therapy exhibited increased risk (HR: 1.15, *P*-value: .01). PsA patients treated with bDMARDs were at higher risk of MACE compared to matched controls (HR: 1.47, *P*-value: .01). Treatment with methotrexate in both PsO and PsA patients did not demonstrate a statistically significant risk of MACE compared to matched controls.

Conclusions: While topical therapy has been associated with an increased risk in PsO patients, systemic treatments, including bDMARD agents, reveal a substantial reduction in cardiovascular risk, potentially due to their targeted anti-inflammatory effects.

O006 / #39

A Machine Learning Tool for The Early Identification of Undiagnosed Psoriatic Arthritis Patients. Is It Possible?

Jonathan Shapiro[1], Benny Getz[2], Dan Underberger[2], Michael Dreyfuss[2], Ora Shovman[2], Stanley Cohen[2], Yonatan Genudi[2], Amir Ben Tov[2], Shlomit Koch[2], Yehuda Shoenfeld[2]

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Background and Aims: Psoriatic Arthritis (PsA) is an inflammatory disease affecting joints and skin. It impacts about 0.27% of adults and 20% of psoriasis patients. Early detection prevents irreversible joint damage. Previous screening tools were questionnaire-based, needing active patient-physician involvement. Leveraging machine learning, we introduced PredictAITM, which utilizes electronic medical record (EMR) data to spot undiagnosed PsA patients up to 4 years before suspicion of PSA.

Methods: We analyzed a 2008-2020 anonymized EMR dataset from Maccabi Healthcare Service, an HMO in Israel encompassing ~2.5 million members. Given PsA's prevalence among psoriasis patients, two cohorts were formed: general population and psoriasis-only. Both had distinct training and testing subsets. The study gauged our model's efficacy in identifying undiagnosed PsA patients up to 4 years pre-suspicion of PSA using prior three-year data. Exclusions were those below 18 or lacking seven continuous data years. Clinical criteria helped in PsA identification, with dermatologist diagnoses pinpointing psoriasis cases. Our model, built with Gradient boosted trees, underwent ROC, sensitivity, and PPV analysis.

Results: 2,084 patients matched PsA criteria. PredictAITM, at 90% specificity, identified PsA in the Psoriasis cohort with a 50%-38% sensitivity and 34%-30% PPV, 1-4 years pre-suspicsion of PSA. For the general population cohort at 99% specificity, the values were 42%-32% and 10%-8%, respectively. ROC plots and SHAP values presented.

***Conclusions*:** Emphasizing early PsA diagnosis is crucial. PredictAI(TM), a ML tool, assists in this, detecting half the undiagnosed PsA cases among psoriasis patients at 90% specificity, possibly preventing a year's diagnostic delay. Future research will shape its application guidelines.

PARALLEL SESSION 07: MECHANISMS IN AUTOIMMUNITY PART 1 - SESSION DEDICATED IN MEMORY OF PROF. NOEL ROSE

18-05-2024 15:45 - 16:45

O007 / #1095

Small Fiber Neuropathy in Multiple Sclerosis Patients

Background and Aims: Chronic sensory disturbances are common in patients with multiple sclerosis (MS) as well as with small fiber neuropathy (SFN). While MS patients have reduced sensation in spinal or cortical distribution, patients with SFN have painful burning and tingling sensations with a length-dependent pattern. The objective of our study was to ascertain whether MS patients who exhibit chronic distal sensory disturbances display concurrent SFN.

Methods: We conducted a retrospective observational study in a single tertiary center identifying multiple sclerosis patients who exhibited painful burning and tingling sensations. These patients underwent skin biopsy for evaluation of SFN. Skin biopsy findings of reduced epidermal nerve fiber density below the 5th percentile were considered as abnormal.

Results: Ten patients with relapsing-remitting MS who complained of painful sensory symptoms were evaluated. Skin biopsy supporting the diagnosis of SFN in 9/10 patients. All 10 patients were female, with an age of 46.6 years-old, and a median EDSS of 1.5. All patients had stable clinical and radiological findings without evidence for active disease. At the time of skin biopsy, 7 patients were on ongoing disease-modifying therapy including Teriflunomide in 4, Interferon beta, Diroximel fumarate and Galtiramer acetate, each in one case.

Conclusions: Painful burning and tingling sensations in MS patients raise concern for a spinal lesion, but when they present with a length-dependent pattern, skin biopsy commonly supports the diagnosis of SFN. The pathogenesis of this peripheral nervous system disorder may be linked to MS or other concurrent diseases and medications.

PARALLEL SESSION 09: SJÖGREN SYNDROME AND NOVEL THERAPIES IN AUTOIMMUNITY

18-05-2024 17:15 - 18:30

O008 / #681

ANTI-RO52 Antibodies and Disease Severity in Patients with Sjögren's Disease

Eléonore Bettacchioli[1,2], Christophe Jamin[1,2], Alain Saraux[1,2], Alice Tison[1,2], Divi Cornec[1,2], Maryvonne Dueymes[1,2], Nathan Foulquier[2], Sophie Hillion[1,2], Anne-Marie Roguedas-Contios[2], Anas-Alexis Benyoussef[2], Marta E Alarcon-Riquelme[3], Jacques-Olivier Pers[1,2], Valérie Devauchelle-Pensec[1,2], Cristian Iperi[2]

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[2]CHU de Brest, Brest, France
[3]Department of Medical Genomics, GENYO, Granada, Spain

Background and Aims: The diagnosis of primary Sjögren's disease (SjD) is based on a combination of clinical, histological and biological findings. Recent evidence supports that anti-Ro60 antibodies are the most specific serum marker, while the impact of anti-Ro52 antibodies remains unclear. The aim of this study was to characterize the clinical, serological, biological, transcriptomic and interferon profiles of SjD patients according to their anti-Ro52 antibody status and discuss the role of anti-Ro52 antibodies in the prognosis of SjD.

Methods: SjD patients were recruited from the European PRECISESADS (376 patients) and the Brittany DIApSS cohorts (146 patients). Four groups were defined, including double negative ($Ro52^-/Ro60^-$), isolated anti-Ro52 antibody positive ($Ro52^+$), isolated anti-Ro60 antibody positive ($Ro60^+$), and double positive ($Ro52^+/Ro60^+$) patients. Clinical information, ESSDAI, a score representing systemic activity, and biological markers linked to disease severity were evaluated. Transcriptome data obtained from whole blood by RNAseq and type I and type II interferon signatures were analysed for PRECISESADS SjD patients.

Results: In both cohorts, arthritis, parotidomegaly, increased biological marker levels (hypergammaglobulinemia, rheumatoid factor and inflammation) and higher ESSDAI were significantly more frequent in the double-positive group than in the other groups. Transcriptome analysis demonstrated that anti-Ro52 antibody positivity was associated with strong interferon pathway activation as the leading cause of the clinical associations.

Conclusions: Collectively, these results suggest that the combination of anti-Ro52 and anti-Ro60 antibodies is associated with a clinical, biological, and transcriptional profile linked to greater disease severity in SjD, through the potentiation of the interferon pathway activation by anti-Ro52 antibodies.

O009 / #648

Administration of A Novel Immune Checkpoint Molecule Tapbpl Ameliorates Autoimmune Diseases in Mice

Laijun Lai, Yujun Lin, Haiyan Liu, Zhenzhen Zhang
University of Connecticut, Storrs, United States of America

Background and Aims: Immune checkpoint molecules are critical for maintaining peripheral tolerance to avoid autoimmune disease. We have recently identified a novel immune checkpoint molecule TAPBPL that shares a significant sequence and structural similarities with existing immune checkpoint molecules. We have cloned and expressed the gene to produce recombinant TAPBPL protein and shown that the protein inhibits T cell proliferation, activation, and Th1/TH17 cytokine production *in vitro*. In this study, we investigated the ability of TAPBPL protein to ameliorate autoimmune diseases in animal models including experimental autoimmune encephalomyelitis (EAE) and collagen type II (CII)-induced arthritis (CIA), the commonly used animal models of human multiple sclerosis (MS) and rheumatoid arthritis (RA), respectively.

Methods: Mice were induced to develop EAE or CIA and injected with recombinant TAPBPL or control protein. The mice were then analyzed for EAE or CIA incidence, clinical and pathological scores, the proportion of T cells and regulatory T cells (Tregs), the expression of proinflammatory cytokines, autoantigen-specific T cell proliferation and cytokine production, and autoantigen-specific autoantibody production.

Results: Administration of TAPBPL protein ameliorated EAE and CIA, which was related to a fewer number of activated CD4 and CD8 T cells but greater number of Tregs, and a reduction of Th1/Th17 inflammatory cytokines in the mice. Furthermore, TAPBPL protein inhibited autoantigen-specific T cell growth and Th1 and Th17 cytokine expression and reduced the production of autoantibodies in the mice.

Conclusions: Our results suggest that TAPBPL protein has the potential to be used in the treatment of autoimmune diseases including MS and RA.

PARALLEL SESSION 12: AUTOIMMUNITY IN THE CENTRAL NERVOUS SYSTEM

19-05-2024 10:30 - 12:00

O010 / #967

Mechanisms of Pain Modulation by JAK Inhibition: Upadacitinib Regulates Pain-Related Pathways and BDNF Expressıon in Microglial Cells

Luca Navarini[1,2], Marta Vomero[1], Erika Corberi[1], Onorina Berardicurti[1,2], Giulia Imperatori[2], Damiano Currado[1,2], Lyubomyra Kun[1], Annalisa Marino[2], Francesca Trunfio[1], Francesca Saracino[1], Ludovica Lamberti[1], Livia La Barbera[3,4], Paraskevi Krashia[3,4], Marcello D'Amelio[4,5], Roberto Giacomelli[1,6]
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[6]Clinical and Research Section of Rheumatology and Clinical Immunology, Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy

Background and Aims: Chronic pain is a significant challenge for patients with inflammatory arthritis (IA), persisting even after improvements in joint inflammation. Microglial cells, characterized by TMEM119 expression, activate during chronic inflammation, releasing pro-inflammatory cytokines and pain-related molecules. Brain-derived neurotrophic factor (BDNF) is crucial in abnormal pain perception, and the pro-inflammatory cytokine IL-6 influences its production through JAK1 activation. Upadacitinib, a JAK1 inhibitor, effectively improves disease activity and pain. This study explores the impact of Upadacitinib on pain- and neuroinflammation-related molecules in microglia, mainly focusing on BDNF.

Methods: Microglia, differentiated from monocytes and activated into pro-inflammatory phenotype, were cultured with/without Upadacitinib (0.1 uM or 1 uM) ± IL-6. TMEM119 expression in microglia was evaluated by immunofluorescence. Intracellular BDNF levels were analyzed by flow cytometry and immunofluorescence. RNA from microglia was extracted using all prep DNA/RNA/miRNA universal kits, and bulk RNA sequencing was carried out using the Illumina system. Statistical analysis was performed using RStudio and GraphpPad Prism v.10.

Results: TMEM199 and BDNFwere expressed by microglia. Flow cytometry analysis showed that both the concentrations of Upadacitinib, alone and in combination with IL-6, reduced BDNF levels in microglial cells compared to the untreated and IL-6 conditions. Transcriptomic analysis showed that Upadacitinib is able to reduce gene expression of JAK/STAT signaling as well as neuroinflammation and chronic- and acute-pain-related pathways.

Conclusions: Upadacitinib modulates microglial gene expression, reducing JAK/STAT, neuroinflammatory, acute, and chronic pain-related pathways, and decreasing BDNF production, influencing pain perception and nociplastic mechanisms.

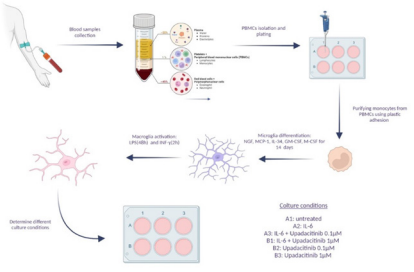
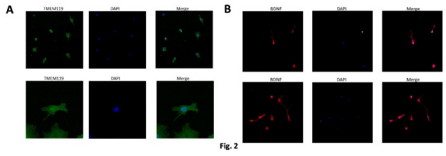


Figure 1.



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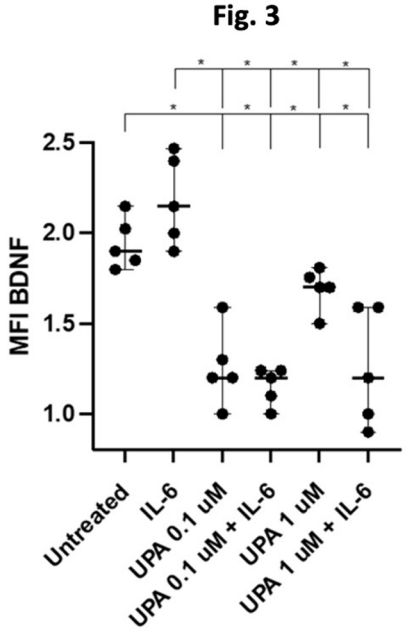

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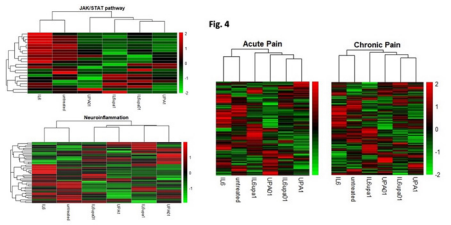

Figure 4.

PARALLEL SESSION 13: RHEUMATOID AND ARTHRITIS MYOSITIS (MUSCLES)

19-05-2024 14:00 - 15:30

O011 / #230

Functional Connectivity Associated with Response to Biologics in Rheumatoid Arthritis and Spondyloarthritis

Yuichiro Fujieda

Department of Rheumatology, Endocrinology And Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Background and Aims: Brain function orchestrates cognition and pain perception, with its dynamics significantly influencing physiopsychological states in various conditions, such as neuropsychiatric diseases or chronic pain. Notably, the dynamics of brain function captured by functional MRI-derived dynamic functional connectivity may also play a crucial role in conditions of inflammatory arthritis (IA), including rheumatoid arthritis (RA) and spondylarthritis (SpA). However, the extent and nature of its significance remain largely unexplored in patients with IA.

Methods: We conducted two studies. Structural and resting-state functional MRI data were acquired from patients with IA, osteoarthritis (OA) and heathy controls (HCs). First study was that functional connectivity (FC) was calculated using the entire BOLD signal time series. Second study was performed dynamic analysis that the time course is segmented into 36-s windows, and FC was computed in each window. We analyzed IA-specific FC measures relevant to therapeutic response to biologics.

Results: In IA patients, static functional connectivity between the left insular cortex and the anterior cingulate cortex was reduced compared to OA and HCs. This static connectivity significantly correlated with the therapeutic response to biologics. Dynamically, a distinct cluster showcasing increased corticocortical connectivity was identified. This dynamic connectivity pattern was associated with favorable therapeutic outcomes and showed a post-therapy reduction in patients responding well to treatment

Conclusions: Disease-specific resting-state FC provides a means to assess the therapeutic improvement and could predict treatment response in both RA and SpA.

O012 / #970

Role of Scleroderma/Myositis-Related Autoantibodies Detected by Immunoblot to The Diagnosis of Systemic Autoimmune Rheumatic Diseases in 410 Patients from A Single Referral Center

Mónica Renuncio-García[1,2], Juan Irure-Ventura[1,2], Diana Prieto-Peña[2,3], Carmen Secada-Gomez[2,3], Ricardo Blanco[2,3], Marcos López-Hoyos[1,2]

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Background and Aims: Immunoblot assays are mainly used in clinical practice as a diagnostic tool for systemic autoimmune rheumatic diseases (SARDs). We aim to evaluate the significance that extended analysis of scleroderma/myositis-related autoantibodies (aAbs) detected by immunoblot contributes to the diagnosis of SARDs patients.

Methods: From November 2017 to 2023, all medical records of patients who had positive immunoblot results related to scleroderma/myositis (Euroimmune AG, Lübeck, Germany) were examined. The high suspicion of SARDs in patients with nonspecific symptoms led to the request of these assays.

Results: 410 patients were positive for at least 1 aAb, and 69 of them for 2 aAbs. Main clinical features at time of immunoblot requests were: arthralgia/arthritis (n=192), Raynaud's-phenomenon (n=165), rash (n=64), myopathy (n=56) and sicca-syndrome (n=50). During follow-up, 82 patients were diagnosed with overlap-myositis, 75 with scleroderma, 52 with other inflammatory diseases, 41 with interstitial pneumonia with autoimmune features, 36 with undifferentiated-connective tissue disease, 20 with Sjögren's syndrome, 18 with dermatomyositis, 17 with systemic lupus erythematosus, and finally 1 with necrotizing myositis. In 68 patients the diagnosis of SARD was finally ruled out. Interstitial lung disease was present in 133 patients, mainly in those with anti-PL12 (*P*=.017). Cancer was detected in 35 (8.53%) patients, 20 of them were anti-Ro52+ (*P*=.01).

Conclusions: For patients with a high clinical suspicion of SARDs, immunoblot assays are very helpful in the diagnosis process. While some aAbs (anti-Mi2 and anti-Th/To), remain to be nonspecific, others including anti-PL12 and anti-Ro52 are particularly helpful in detecting SARDs patients with associated ILD and cancer, respectively.

	PL7 (n=18)	Scl70 (n=35)	PM Scl (n=56)	Ku (n=35)	PL12 (n=8)	Mi2 (n=22)	Ro52 (n=150)	Jo1 (n=23)	SRP (n=5)	Fibrillarin (n=10)	NOR90 (n=22)	CENP (n=37)	Th/To (n=11)	MDA5 (n=1)	RNA Pol III (n=11)	TIF1g (n=4)	EJ (n=3)	OJ (n=8)	Ks (n=1)	cN1A (n=8)	Ha (n=4)	SAE1 (n=1)	Zo (n=1)	NXP2 (n=2)
DM			3 (5.4)			6 (27.3)	5 (3.3)	2 (8.7)						1 (100)		1 (25.0)	1 (33.3)			2 (25.0)		1 (100)		1 (50.0)
OV	12 (66.7)		11 (19.6)	5 (14.3)	6 (75.0)	4 (18.2)	42 (28.0)	14 (60.9)		1 (10.0)	1 (4.5)	3 (8.1)					1 (33.3)	3 (37.5)		2 (25.0)			1 (100)	
IMNM									1 (20.0)															
SLE	1 (5.6)		2 (3.6)	6 (17.1)			5 (3.3)	1 (4.3)		2 (20.0)		2 (5.4)								1 (12.5)				
UCTD	1 (5.6)	3 (8.6)	5 (8.9)	3 (8.6)		1 (4.5)	18 (12.0)	1 (4.3)	1 (20.0)		2 (9.1)		1 (9.1)		1 (9.1)			1 (12.5)			1 (25)			
SS		1 (2.9)	1 (1.8)				18 (12.0)			1 (10.0)	1 (4.5)	2 (5.4)	1 (9.1)											
Scl	1 (5.6)	24 (68.6)	13 (23.2)	4 (11.4)			11 (7.3)			5 (50.0)	2 (9.1)	23 (62.2)	3 (27.3)		4 (36.4)									
IPAF		1 (2.9)	6 (10.7)	10 (28.6)	1 (12.5)	2 (9.1)	10 (6.7)				7 (31.9)	1 (2.7)			1 (9.1)	2 (50.0)		1 (12.5)			1 (25)			
Other AID		4 (11.4)	8 (14.3)	6 (17.1)		4 (18.2)	16 (10.7)	3 (13.0)	3 (60.0)		6 (27.3)	1 (2.7)	5 (45.5)			1 (25.0)			1 (100)					
Non AID	3 (5.6)	2 (5.7)	7 (12.5)	1 (2.9)	1 (12.5)	5 (22.7)	25 (16.7)	2 (8.69)		1 (10.0)	3 (13.6)	5 (13.5)	1 (9.1)		5 (45.5)		1 (33.3)	3 (37.5)		3 (37.5)	2 (50)			1 (50.0)

Abbreviations: DM: dermatomyositis; OV: overlap myositis; IMNM: immune-mediated necrotizing myopathy; SLE: systemic lupus erythematosus; UCTD: undifferentiated connective tissue disease; SS: Sjögren's syndrome; Scl: scleroderma; IPAF: interstitial pneumonia with autoimmune features ; AID: autoimmune disease

0% <25% 25-50% 50-75% >75%

Figure 1.

PARALLEL SESSION 14: THERAPEUTIC CHALLENGES IN AUTOIMMUNITY

19-05-2024 14:00 - 15:30

O013 / #1147

Therapeutic Dilemmas: Three Short Cases Employing Patient-Centered Research - Antiphospholipid Antibodies and Transverse Myelitis, Jc Virus Screening and Rituximab, Necrotizing Myositis

***Background and Aims*:** Despite data proliferation and increasing availability of evidence, individual case management often remains challenging. When the evidence does not apply or cannot be applied to the case at hand, seeking the best therapeutic approach may be time-consuming. With increasing case complexity and the burden of demands placed on clinicians, optimizing the medical care of each individual case becomes nearly impossible.

Methods: Large language models (LLMs) may assist clinicians in the management of such cases in the future. However, LLMs are usually trained on libraries (e.g. textbooks, Pubmed, CINAHL). Current models are therefore capable of competing with the average medical student in responding to medical licensing examinations. However, they are still far from able to address the challenges of complex individual decision-making.

Results: This talk presents three real-life dilemmas sent to Medint by clinicians. All the dilemmas were related to the treatment of patients with autoimmune problems. Given the nature of the cases, the clinical aspects of each case were researched using the Medint search and extraction methods, Bradford-Hill criteria and logic were applied to the findings and the summary of findings are shown as presented to the clinician in a format designed to support decision-making.

Conclusions: This work is currently performed manually by trained clinician-researchers. However, the unique method is being used to train an AI model that will emulate individual decision-making which often does not follow the traditional evidence-based approach. More details will be presented in the talk.

PARALLEL SESSION 17: AUTOANTIBODIES (ABS) - PREDICTION, PATHOGENIC AND PREVENTION

19-05-2024 15:45 - 16:45

O014 / #957

Tuftsin-Phosphoprylcholine, Based on Helminth Derivative, Decreased Il-8 Expression by Human Endothelial Cells and Temporal Artery Biopsies from Giant Cell Arteritis Patients

Stefania Croci[1], Miri Blank[2], Gary Gellerman[3], Andrii Bazylevich[3], Linoi Israel[2], Howard Amital[4], Yehuda Shoenfeld[5], Carlo Salvarani[6]

[1]Clinical Immunology, Allergy, Advanced Biotechnologies, Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Zabludowicz Center for Autoimmune DiseasesSheba medical center, Ramat Gan, Israel
[3]Chemical Sciences, Ariel University, Ariel, Israel
[4]Zabludowicz Center for Autoimmune Diseases, And Internal Medicine B, Sheba Medical Center, Tel Aviv, Israel
[5]Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Ramat Gan, Reichman University, Herzelia, Israel
[6]Unit of Rheumatology, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy

Background and Aims: Background and aims Interleukin 8 (IL-8), CXCL8, is a chemokine produced by endothelial cells, epithelial cells, macrophages and airway smooth muscle cells-sIL-8 is an important mediator of the innate immune system responses. It induces chemotaxis in target cells, primarily neutrophils, causing them to migrate toward the damaged area. IL-8 is also known to be a potent promoter of angiogenesis. Tuftsin-PhosphorylCholine (TPC) is a novel bi-specific molecule which showed anti-inflammatory activities in experimental mouse models of autoimmune diseases, such as lupus, rheumatoid arthritis, experimental autoimmune encephalomyelitis and chemically induced colitis. Ex-vivo, TPC had anti-inflammatory activities on human peripheral mononuclear cells (PBMCs) and temporal biopsies from patients with giant cell arteritis (GCA).

Methods: We addressed TPC effect on the expression of IL-8 by primary human endothelial cells. Human endothelial cells lysates were analyzed on angiogenesis-proteome-profiler. Likewise, we treated ex-vivo inflamed human temporal artery biopsies (TABs) obtained from patients with GCA with TPC.

Results: TPC treatment significantly decreased by 85% the protein expression of IL-8 by primary endothelial cells. Similarly, TPC-treated TABs from patients with GCA showed a reduction in IL-8 gene expression greater than 16 fold.

Conclusions: These data strengthen the anti-inflammatory effects of TPC. We believe that TPC could lead to the improvement of GCA and other autoimmune diseases.

O015 / #692

Transcriptomic Profiling Reveals Novel Insights into The Cellular Protective Functions of The DFS70/LEDGF Nuclear Autoantigen

Carlos Casiano[1], Pedro Ochoa[1], Evelyn Sanchez-Hernandez[1], Isaac Kremsky[2], Charles Wang[3]

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[2]Basic Sciences, Loma Linda University, School of Medicine, Loma Linda, United States of America
[3]Center for Genomics, Loma Linda University, School of Medicine, Loma Linda, United States of America

Background and Aims: Antinuclear autoantibodies (ANAs) producing the dense fine speckled (DFS) immunofluorescence pattern in HEp-2 cells typically recognize the DFS70/LEDGFp75 autoantigen. DFS autoantibodies have been detected in ANA-associated rheumatic diseases (AARD), albeit mixed with disease-specific ANAs. Conversely, monospecific DFS antibodies circulate mostly in healthy individuals or patients with non-AARD inflammatory conditions. Emerging evidence suggests that DFS antibodies have protective properties; however, the underlying mechanisms remain elusive. Understanding these mechanisms entails an in-depth knowledge of DFS70/LEDGFp75 functions. DFS70/LEDGFp75 is a protective protein, upregulated by oxidative stress-inducing agents, that plays key roles in cellular stress responses and DNA damage repair. Our aim was to obtain novel insights into the cellular protective functions of DFS70/LEDGFp75 by performing transcriptomic profiling in a drug-resistant cancer cell model that endogenously upregulates this autoantigen.

Methods: Gene expression changes resulting from DFS70/LEDGFp75 silencing in two drug-resistant prostate cancer cell lines were profiled by RNA-sequencing and robust bioinformatic analysis. Target gene validation was performed using qPCR and immunoblotting.

Results: DFS70/LEDGFp75 silencing uncovered 970 overlapping differentially expressed genes (DEGs). Bioinformatic analysis of these DEGs revealed enrichment of molecular pathways associated with cellular protection, including regulation of cell death/survival, oxidative stress response, and immune responses. Specific DEGs involved in immune regulation were validated. Ongoing transcriptomic data mining focuses on identifying and validating DFS70/LEDGFp75-target DEGs linked to cellular stress protection and anti-inflammatory responses.

Conclusions: Our results indicate that stress-induced upregulation of DFS70/LEDGFp75 triggers cellular protective anti-oxidative stress and anti-inflammatory responses. It is likely that DFS autoantibodies are sensors or even mediators of these protective responses.

PARALLEL SESSION 18: CYTOKINES AND AUTOIMMUNITY

19-05-2024 17:15 - 18:30

O016 / #894

A Hundredfold Greater Induction of IL-23 From Axial Enthesis Bone Compared to Peripheral Enthesis As An Explanation for Il-23 Blockade Failure In Ankylosing Spondylitis But Not Peripheral Psoriatic Arthritis

Paula David[1,2], Mark Harland[3], Chi Wong[3], Jake Weddell[3], Abhay Rao[4], Almas Khan[4], Jake Timothy[4], Peter Loughenbery[4], Robert Dunsmuir[4], Vishal Borse[4], Tom Macleod[3], Dennis Mcgonagle[3]

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[2]Leeds Institute of Rheumatic And Musculoskeletal Medicine (lirmm), University of Leeds, Leeds, United Kingdom

[3]Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), University of Leeds, Leeds, United Kingdom

[4]Orthopaedic and Spinal Surgery, Leeds General Infirmary, Leeds, United Kingdom

***Background and Aims*:** Both peripheral and axial spondyloarthropathy (SpA), psoriasis and inflammatory bowel disease are strongly linked to IL-23 pathway immunogenetics and immunology. Although IL-23 inhibition is efficacious in peripheral SpA, studies have been negative in axial Ankylosing Spondylitis (AS). We undertook comparative immunology of spinal, hip, and knee enthesis to test for any discrepancy in the capacity of peripheral and axial peri-entheseal bone (PEB) to produce IL-23.

Methods: Spinous process (n=5), hip capsule (n=4), and knee (n=4) PEB collected during orthopedic surgery was mechanically digested to extract entheseal immune cells. Cell subsets were phenotyped by flow cytometry and stimulated with LPS and zymosan to assess IL-23-producing capacity. Quantification of cytokine production was achieved by ELISA and LEGENDplex.

Results: Myeloid cells including monocytes and neutrophils were abundant in spine and hip PEB but scarce in knee PEB, in keeping with the fact the spine and hip are haematopoietically active whereas the knee in adults is not. Following stimulation, spine and hip PEB produced 10-100 fold more IL-23 than knee PEB per gram of tissue (spine = 659.5 pg/g, hip = 1382.1 pg/g, knee = 24.8 pg/g).

Conclusions: This comparative immunology study of adult human entheses demonstrates axial PEB, the key target of AS pathology, produces significantly more IL-23 than peripheral tissue when stimulated. Our translational findings call for trials using high-dosing regimens of IL-23 blockers that may lead to IL-23 therapy utility in axial inflammation.

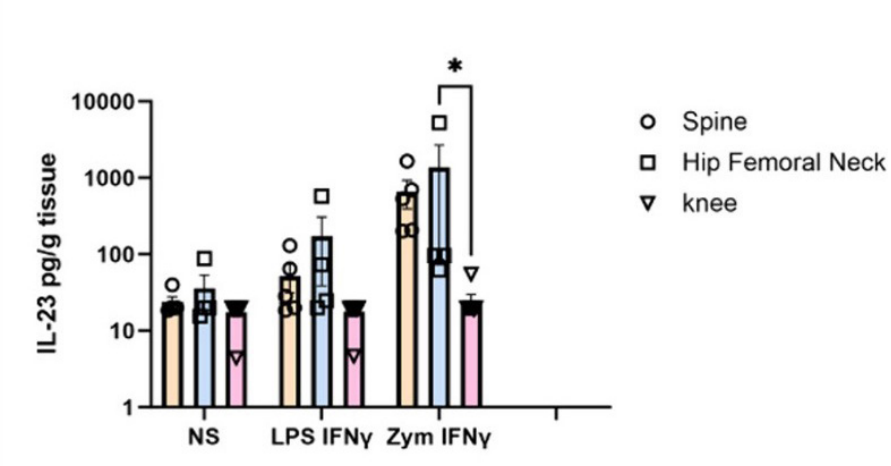

Figure 1.

PARALLEL SESSION 19: SYSTEMIC AUTOIMMUNITY, LIVER AND GASTROINTESTINAL

19-05-2024 17:15 - 18:30

O017 / #216

Cholangitis Induced by Immune Checkpoint Inhibitors: Analysis of Pharmacovigilance Data

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Background and Aims: The indications for immune checkpoint inhibitors (ICI) treatment are increasing. Due to their mechanism of action, they induce immuno-related adverse events. Among checkpoint induced liver injury, cholangitis is rarely described.

Methods: We analyzed all cases of cholangitis associated with ICI reported to the French pharmacovigilance system. The case/non-case method was used to identify a potential disproportionate reporting signal. Cases were all reports of cholangitis reported and non-cases were all other drug-related adverse reactions recorded in the WHO international pharmacovigilance database.

***Results*:** A total of 48 cases were retrieved: 24 men and 24 women of mean age 64.2 ± 13.9 years. Most patients received PD-1 inhibitors alone (n=39, 81.3%) and mean treatment duration was 8.0 ± 9.7 months. All patients presented a mixed or a cholestatic pattern. A quarter of patients had jaundice (13/48) and the duration of treatment and number of cycles were shorter in patients with bilirubin >50µmol/l. Disproportionality analyses of international data showed that cholangitis cases were 18 times more frequently reported with ICI compared to all other drugs (ROR=18.07; 95%CI: 15.85–20.59) and seven times more reported compared to all antineoplastic agents (ROR=7.02; 95%CI: 6.13–8.03).

Conclusions: This series, based on French pharmacovigilance data, provides new information

on the characteristics and evolution of ICI-induced cholangitis. Disproportionality analyses suggest that cholangitis is a specific adverse reaction induced by ICI. Future studies are needed to better understand the mechanisms of toxicity.

O018 / #433

Serum Anticardiolipin Antibodies and Endothelin-1 As Markers of Portal Hypertension in Primary Biliary Cholangitis

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***Background and Aims*:** Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease leading to progressive fibrosis and cirrhosis, in some cases with portal hypertension (PHT). Anticardiolipin antibodies (aCL) associated with presence of cirrhosis and thrombocytopenia. Endothelin-1 (ET-1) is associated with the process of tissue fibrosis, causes an increase in hydrostatic pressure, and has a proinflammatory effect. Our aim was to evaluate the concentration of endothelin-1 and the level of anti-cardiolipin antibodies in the serum of PBC patients with PHT.

Methods: The sera 37 PBC patients with PHT, 83 without PHT and 30 healthy donors were used in the study. Anti-cardiolipin antibodies and ET-1 were tested by commercial enzyme immunoassays.

Results: Elevated levels of ET -1 were detected in the sera of 87% of PBC patients with PHT, in the group of PBC patients without PHT only in 40%, $P < .001$. The concentration of ET-1 observed in the group of PBC patients with PHT was significantly higher, 6.9 ± 4.3 pg/mL vs 2.5 ± 2.9 pg/mL, $P < .001$. The majority of patients with a positive result for aCL, were patients with diagnosed portal hypertension 32% vs 12% for the group without PHT, $P = .009$. Serum aCLs were associated with more advanced cirrhosis of the liver.

Conclusions: The presence of anti-cardiolipin antibodies and high serum levels of endothelin-1 in patients with PBC and portal hypertension may be a significant marker of the risk of worse liver function, and they can be a marker of portal hypertension.

O019 / #332

Human Antimicrobial Glycoprotein-2 Expressed In Brunner Glands – A Putative Autoimmune Target of Crohn's and Coeliac Disease

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Background and Aims: Antimicrobial glycoprotein 2 (GP2) is an autoantigen in Crohn's (CD) and coeliac disease (CeD). To investigate GP2's intestinal synthesis and putative CD/CeD link, we assessed GP2-isoform ($GP2_{1-4}$) expression and reactivity to CD/CeD-related antigens.

Methods: Relative $GP2_{1-4}$-mRNA levels were analysed in intestinal biopsies of paediatric patients with CD (n=8), CeD (only small intestine, n=13), ulcerative colitis (UC) (n=4), and healthy children (HC) (n=13) by RT-PCR. GP2-protein synthesis was assessed in duodenal biopsies of 23 patients with CD, 25 with CeD, and 24 HC by immunohistochemistry. GP2-isoform reactivity was determined against native/deamidated/cleaved gliadin and phosphopeptidomannan by ELISA.

Results: $GP2_{2/4}$-mRNA levels were higher compared with $GP2_{1/3}$-mRNA in patients and HC, respectively, at almost all investigated intestinal sites. Transcription of $GP2_{1-4}$ was elevated in proximal small intestine in CeD and CD patients (only $GP2_{2/4}$) compared to jejunum (CeD/CD) and large bowel (CD) with a decreasing trend from small intestine to the colon. CeD patients demonstrated higher duodenal $GP2_{2/4}$-mRNA levels compared to HC/UC patients whereas CD patients showed higher $GP2_4$-mRNA levels compared to UC patients. Duodenal synthesis of only small GP2 isoforms was demonstrated in epithelial cells in patients/HC and, furthermore, in Brunner glands (also large isoforms) with a more frequent apical location of GP2 in CD/CeD patients. $GP2_{1-4}$ interacted with gliadin and phosphopeptidomannan whereas larger isoforms ($GP2_{1/2}$) demonstrated strongest and shorter ($GP2_{3/4}$) weakest binding. Gliadin digestion improved binding to GP2 isoforms.

Conclusions: $GP2_{1-4}$ binding to CeD/CD-related antigens, elevated $GP2_{1-4}$-mRNA transcription in duodenum, and GP2-protein secretion in Brunner glands of CeD/CD patients suggest a possible autoimmune CeD/CD link.

O020 / #754

IL-10-Producing Regulatory Cells Impact on Celiac Disease Evolution

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Background and Aims: Celiac Disease-(CD) is a T-cell mediated disorder caused by an altered immune response to gluten, characterized by mild to severe enteropathy. The mechanisms underlying CD progression remain to be fully clarified. This study aims to investigate the role of IL-10-producing regulatory cells in orchestrating the CD evolution.

Methods: We collected gut biopsies and peripheral blood from children with potential-CD (normal mucosa), with villous atrophy (acute-CD), and on disease remission (GFD). The immune cell infiltrates, levels of plasma cytokines, and magnitude of gliadin-specific T- cell responses were analyzed.

Results: An inflammatory signature with increased gliadin-specific IFN-g+ T cells characterizes CD patients regardless of mucosa damage. Nevertheless, in potential-CD patients we found an increased frequency of IL-10-secreting DC (DC-10) and of IL-10-secreting T cells specific for gliadin. Inhibition of IL-10 increased IFN-g secretion by gliadin-specific intestinal T-cell lines cells from CD patients, either with acute or potential disease. In GFD patients the levels of plasma inflammatory cytokines decreased, while IL-10-producing T cells accumulated in the gut mucosa.

Conclusions: IL-10-producing cells play a fundamental role in controlling pathological T- cell responses in the gut of CD patients, with DC-10 representing a marker of potential-CD. At this stage of disease, DC-10 protect the intestinal mucosa from damage, despite gluten-driven inflammation and infiltration of gliadin-specific IFN-g-secreting T cells are already present. Hence, in situ differentiation/recruitment of DC-10 is fundamental for mucosal homeostasis maintenance in the transition from potential- to acute-CD.

O021 / #964

Unveiling Potential Biomarkers for Inflammatory Bowel Diseases (Ibds) and Colorectal Carcinoma (CRC) Diagnosis Through Saliva Proteomic Profiling

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Background and Aims: There is an urgent demand for predictive novel biomarkers in both IBD and CRC due to their relevant health care issue: increasing incidence worldwide, young age onset, severe complications.

Methods: To uncover biomarkers, we performed proteomic analysis of saliva and faecal sample pools using LTQ-Orbitrap/MS. Twenty healthy controls (CS), 12 individuals with Crohn's Disease (CD), 13 with Ulcerative Colitis (UC), and 37 with CRC were enrolled.

Results: In saliva, 152 proteins were identified. Of these, 73 were commonly found in CRC, CD, and UC but not in CS. These proteins clustered in cell adhesion, glucose and nucleic acid metabolism based on g-profiler analysis of enriched GO terms. Seventy-nine out of 152 showed differences in abundance. Proteins highly represented in CRC, compared to CS, clustered in biological processes related to inflammation, DNA, innate and adaptive immunity. Proteins highly represented in CD with respect to CS clustered in biological processes related to DNA, immunity and oxidation. No clusters were identified for UC. Moreover, two peptides, GQ-15 and GG-17, derived from Basic Salivary Proline-rich protein 1 (PRB1), were enriched in CD stool, while in saliva PRBs were reduced in IBD and CRC. Both GQ-15 and GG-17 stimulated *in vitro* CRC cell growth and the pro-proliferative signaling pathways Erk1/2, Akt and p38.

Conclusions: In conclusion, CRC and CD share common clusters of salivary proteins involved in inflammation, immunity and DNA maintenance, and PRB1-derived peptides accumulating in CD stool can stimulate cancer cell growth. This suggests that they may play a pathogenetic role linking intestinal inflammation and cancer.

PARALLEL SESSION 20: NOVEL AUTOIMMUNE DISEASES

20-05-2024 10:30 - 12:00

O022 / #263

Autoimmunity and Endometriosis: Potential Relevance of A Novel Immunomodulating Compound

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Background and Aims: The association between endometriosis and autoimmunity is well-recognised. Endometriosis is a gynaecological disorder characterised by endometrial lesions outside the uterus and affects 5-10% of females during their reproductive age leading to pelvic pain and infertility. Natural killer (NK) cells mediate cytotoxicity towards endometrial cells in the presence of the bioactive interleukin-12 isoform (IL-12p70), that is inhibited by IL-12p40, and NK cell-mediated lysis of human K562 leukemia cells is a surrogate marker of NK cell activity in patients with endometriosis. We have developed a compound that skews IL-12 signalling towards the IL-12p70 axis in T cells via effects on both the cytokine and the receptor complex. The aim of the present study was to determine its effect on lysis of K562 cells and activation of NK cells including expression of the IL-12p70 receptor chains, β1 and β2.

Methods: The lipidic peptide, designated IK14004, was synthesised by conjugating the sequence, RSKAKNPLYR, to four dodecanoic residues. Flow cytometry studies, ELISAs and K562 co-culture assays were performed using peripheral blood mononuclear cells (PBMCs) isolated from healthy human volunteers.

Results: IK14004 activates NK cells and enhances lysis of K562 cells. Responsiveness of NK cells to IL-12p70-mediated signalling is potentially enhanced given proportionately greater increases in β2 chain expression above basal levels compared with the β1 chain.

Conclusions: Peptide IK14004 offers an opportunity to explore strategies that enhance NK cell-mediated defence against endometriosis while maintaining balanced effector - regulatory T cell responses.

PARALLEL SESSION 21: SYSTEMIC SCLEROSIS

20-05-2024 10:30 - 12:00

O023 / #487

Chronic Fatigue As A Marker of Mitochondrial Dysfunction, Hypoxic Stress and Vascular Remodelling In Early Systemic Sclerosis

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Background and Aims: A significant proportion of systemic sclerosis (SSc) patients, early in disease duration (<5 years), suffer from symptoms of myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) (SSc-CFS). In this study we investigated whether severe fatigue associated with post exertional malaise is related to increased markers of mitochondrial dysfunction, hypoxia and vascular remodelling in SSc.

Methods: ME/CFS and related symptoms were assessed by patient reported questionnaires. Clinical assessment included lung function tests, high-resolution CT (HRCT) and nailfold capillaroscopy (NVC). Mitochondrial markers, were assessed through PCR and flow cytometry.

Results: Compared to non-fatigued patients, SSc-CFS patients had altered expression of

mitochondrial genes ND4, CyB and Cox7C (P<.05). Red blood cell distribution width (RDW) was also higher in SSc-CFS patients (14.15 vs 13.25, P =.02). Statistical trends were evident for reduced $Sp0^2$ (97 vs 98, P =.06), lung single breath diffusion capacity (DLCO SB) (15.2 vs 19.28, P =.06) and capillary density in SSc-CFS patients (6.3 vs 7.75, P =.07). The frequency of telangiectasia was higher in SSc-CFS patients. Mitochondrial gene expression correlated with DLCO SB (ND4, P =.001; CyB, P =.001), and DLCO SB inversely correlated with RDW (P =.001) and telangiectasia (P =.01). No correlates were observed for interstitial lung disease.

Conclusions: Our findings suggest that symptoms compatible with ME/CFS in patients with SSc may reflect a more severe hypoxic state associated with vascular remodelling that may possibly be associated with visceral complications. Future mechanistic studies may provide added insights into our observations.

Acknowledgments: This study was funded by Dutch Kidney Foundation (17PhD01) and Scleroderma Canada (2022).

O024 / #638

Shaping Monocyte Pathogenicity in Systemic Sclerosis: The Convergence of AT1R Autoantibodies and Extracellular Vesicles

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Background and Aims: In Systemic Sclerosis (SSc), increased abundance of autoantibodies (abs) against angiotensin II type 1 receptor (AT1R) correlate with disease manifestations and is associated with increased secretion of extracellular vesicles (EVs). The importance of EVs in the pathogenesis is also based on transfer of AT1R to different tissues and immune cells. Summarily, studying GPCR abs together with GPCR-EVs in SSc pathogenesis becomes evident.

Methods: IgG and EVs were isolated from sera of systemic sclerosis patients (SSc-IgG) and healthy donors (HD-IgG) as control. Human peripheral blood monocytes of HD or monocytic cells were treated with IgG, EVs or monoclonal AT1R ab. The response of the monocytes was measured via cytokine response and migration of monocytes.

Results: Purified IgG fractions obtained from SSc patients significantly increased the release of CCL18 by monocytes compared to IgG fractions derived from HD. Likewise, SSc-derived extracellular vesicles (SSc-EVs) induced CCL18 secretion by monocytic cells and promoted monocyte migration compared to extracellular vesicles from healthy donors (HD-EVs). Additionally, a monoclonal AT1R ab triggered an inflammatory and pro-fibrotic cytokine response in peripheral blood monocytes from healthy donors. Remarkably, only co-incubation of SSc-EVs, but not HD-EVs, with the monoclonal AT1R ab on monocytes augmented their pro-inflammatory immune response.

Conclusions: The enhanced secretion of the pro-fibrotic cytokine CCL18 by human monocytes in response to SSc IgG and a monoclonal AT1R antibody suggests the involvement of anti-AT1R antibodies in the pathogenesis of systemic sclerosis. Furthermore, this effect was potentiated by SSc-derived extracellular vesicles (SSc-EVs), potentially facilitating the intercellular transfer of AT1R to recipient immune cells.

O025 / #699

The Role of CXCL4-L1, The Non-Allelic Variant of CXCL4, In Systemic Sclerosis

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Background and Aims: Chemokine (C-X-C motif) ligand 4 (CXCL4) is a biomarker of Systemic sclerosis (SSc) progression. Nano-crystalline complexes are formed by CXCL4 and DNA, which circulate in SSc-patients and efficiently trigger interferon-alpha (IFN-a) by plasmacytoid dendritic cells (pDCs), *via* TLR9-stimulation. However, the SSc expression level and interferogenic properties of CXCL4-L1, the CXCL4-non-allelic variant displaying three amino acid substitutions in its COOH-term, are unknown. The aims of this study were addressing the effect of CXCL4-L1 in complex with DNA on purified human pDCs and the CXCL4-L1 expression levels in SSc plasma.

Methods: We assess CXCL4-L1 levels in SSc plasma (by commercial ELISA) and induction, by CXCL4-L1-DNA complexes made in vitro, of IFN-a (also measured by ELISA) in purified human pDCs derived from healthy donors (HD).

Results: CXCL4-L1 was significantly more expressed in SSc plasma than in HD plasma. Plasma CXCL4-L1 positively correlated with the plasma IFN-a concentration, using Spearman's correlation test. CXCL4-L1-DNA complexes were able to stimulate pDCs to produce IFN-a.

Conclusions: We uncovered that CXCL4-L1, elevated in SSc blood, might also contribute to the SSc-IFN-a signature. Considering the blood vessel production of CXCL4-L1, these findings shed further light on SSc pathogenic mechanisms and may suggest new pharmacological interventions in SSc

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O026 / #746

Antioxidant Enzymes in Systemic Sclerosis

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***Background and Aims*:** Systemic sclerosis (SSc) is characterized by imbalance between oxidant and antioxidant molecular components resulting in increased oxidative stress. The enzymatic antioxidants comprise of superoxide dismutase, catalase and glutathione peroxidase. We aimed to analyze perturbations of these enzymes, preventing free radical formation in cells and serum of SSc patients.

Methods: Pathway enrichment analysis was performed on integrated skin tissue microarray data from 3 SSc cohorts (GSE:45485, 59785, 9285/32413) with 76 SSc and 26 healthy control (HC) skin, using lima and GSEA. Healthy human dermal fibroblasts were treated with TGF-β and analysed by RNAseq. Differentially expressed genes were computed using DeSEQ2 algorithm. Serum and erythrocyte lysates were collected from 29 SSc and 29 HC. GPX and SOD activities were measured by Cayman assay.

Results: In the analysis of skin transcriptomes, oxidoreductase activity emerged as the main downregulated molecular functional process in fibrotic SSc skin . TGF-β. stimulated skin fibroblasts downregulated many genes involved in the regulation of oxidoreductive balance Specifically, the differentially expressed genes coded for different antioxidative enzymes (*GPX1, GPX4, SOD2, SOD3, CAT, PRDX2*). These data indicated a TGF-β-induced an oxido-reductive imbalance in TGF-β-stimulated skin fibroblasts, suggesting that these cells could contribute to altered oxidoreductase gene signature in SSc skin. In addition, we observed a trend towards decreased GPX and SOD activities in serum and erythrocytes of SSc patients compared to healthy controls.

Conclusions: Multidimesional data from skin, blood and cultured fibroblast indicate the altered oxidoreductive balance is greatly potentiated in the local fibrotic environment with TGF-β-driven oxidoreductive disbalance.

O027 / #1021

Conventional Type 1 Dendritic Cells are Essential for The Development of Primary Biliary Cholangitis

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Background and Aims: Primary biliary cholangitis (PBC) is a progressive-cholestatic autoimmune liver disease. Dendritic cells (DC) are professional antigen presenting cells and their prominent presence around damaged bile ducts of PBC patients are documented. cDC1 is a rare subset of DC known for its cross-presentation abilities and interleukin 12 production. Our aim was to assess the role ofcDC1 in the pathogenesis of PBC

Methods: We utilized an inducible murine model of PBC and took advantage of the DC reporter mice *Zbtb46^{gfp}* and the *Batf3$^{-/-}$* mice that specifically lack the cDC1 subset. cDC1 cells were sorted from blood of PBC patients and healthy individuals and subjected to Bulk-MARS-seq transcriptome analysis.

Results: Histopathology assessment demonstrated peri-portal inflammation in WT mice, whereas only minor abnormalities were observed in *Batf3$^{-/-}$* mice. Flow cytometry analysis revealed a 2-fold reduction in hepatic CD8/CD4 T cells ratio in *Batf3$^{-/-}$* mice, suggesting reduced intra-hepatic CD8T cells expansion. Histological evidence of portal fibrosis was detected only in the WT but not in *Batf3$^{-/-}$* mice. This finding was supported by decreased expression levels of pro-fibrotic genes in the livers of *Batf3$^{-/-}$* mice. Transcriptome analysis of human cDC1, revealed 78 differentially expressed genes between PBC patients and controls. Genes related to antigen presentation, TNF and IFN signaling and mitochondrial disfunction were significantly increased in cDC1 isolated from PBC patients.

Conclusions: Our data illustrated the contribution the cDC1 subset in the pathogenesis of PBC and provides a novel direction for immune based cell specific targeted therapeutic approach in PBC.

O028 / #689

Analysis and Characterization of Plasma Extracellular Vescicles in Patients Affected by Systemic Sclerosis

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Background and Aims: Systemic sclerosis (SSc) is an autoimmune connective tissue disease. Cardio-pulmonary involvement is the most common cause of mortality in SSc. Extracellular vesicles (EVs) expression is altered in autoimmune diseases and merit evaluation in the pathogenesis of SSc. The aim of the study was to characterize the molecular profile of EVs in SSc by comparing EVs expression between a cohort of patients and healthy controls and between disease subgroups.

Methods: We conducted a prospective observational cohort study on 58 female SSc patients who attended the Rheumatology Clinics of the AOU "Maggiore della Carità" in Novara and 11 female controls (CT). The patients were divided into 3 subgroups: PAH (Pulmonary arterial Hypertension), ILD (Interstitial Lung Diseases) and patients without complications (SSc-NoPAH-NoILD). The MACSPLEX kit was chosen to analyze the expression of 37 epitopes on plasma EVs.

Results: At univariate analysis, CD146, CD42a and CD29 EVs were more expressed in patients (P<.05). At multivariate analysis including age only CD42a was correlated with the disease (P<.05). Comparing disease groups, CD3, CD56 and CD25 EVs were more expressed in PAH (P<.0001) *vs other groups while* HLA-DR in SSc-NoPAH-NoILD vs other groups (P <.05*)*. At multivariate analysis including demographics and clinical variables only CD3 was correlated to PAH.

Conclusions: CD42a, a marker of platelet activation, was more detectable in SSc patients than controls and may have a role in SSc pathogenesis. CD3 and CD56 (which displayed the same distribution) were found to be related to PAH-SSc and may be relevant in the pathogenesis of this complication.

PARALLEL SESSION 22: NOVEL APPROACHES TO HANDLE AUTOIMMUNE DISEASES

20-05-2024 10:30 - 12:00

O029 / #695

Novel Autoantigen Peptide Epitopes as Theranostic Targets in Incurable Autoimmune Blistering Diseases

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Background and Aims: The major obstacle to develop innovative immune therapies in rare autoimmune blistering disease bulbous pemphigoid (BP) and epidermolysis bullosa acquisita (EBA) is the identification of continuous peptide epitopes displaying high affinity binding to autoreactive B-cells receptors in the patient's peripheral blood. Using peptide autoantigen-CAR T-cell technology, one can deliver more precise immune modulation than Rituximab, which gives largely non-specific B-cell depletion and incomplete remission.

Methods: Thirty-six BP patients, 19 female and 17 male, median age 84 years (range 64-97)

having confirmed direct immune fluorescence (DIF) IgG and/or complement C3 deposition clinically associated with blisters, erosion and/or lesions on limbs and trunk were tested in enzyme linked immunoassay (MBL ELISA BP180 IgG and BP230 IgG). Twelve serum with BP180 IgG >60 U/mL or BP230 IgG > 60 U/mL were screened for reactivity in a 600 peptide array of 17mer peptides printed in duplicate derived from 16 amino acid overlapping sequences of NC16 BP180, BP180 C-terminus and BP230 C-terminus and included control peptides of polio and HA influenza viruses.

Results: The fluorescent intensities in the peptide array identified unique continuous epitopes. The performance of a novel BP180-derived peptide-streptavidin IgG ELISA evaluated on BP patients (N=36) versus autoimmune disease controls (N=36) gave 94% sensitivity and 81% specificity with LR+ of 5.5 and AUC 0.937, *P*<.0001.

Conclusions: BP180-BP230 peptides show greater sensitivity than the commercial recombinant autoantigen-based ELISA. Next generation peptide-based therapeutics which selectively target autoreactive B cells in BP are warranted for intradermal autoantibody blockade, CAR-T cells and human monoclonal autoantibodies (HuAutoMAbs).

O030 / #308

MTADV 5-MER Peptide Suppresses Lung Fibrosis, RA, IBD and MS Mouse Models and Inhibits Human Fibroblasts Biological Functions by Targeting SAA, Which Fuels Fibrosis

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Background and Aims: Focusing on therapy of chronic inflammations, we have reported that a 5-MER peptide (5-MP; Methionine, Threonine, Alanine Aspartic Acid, Valine) substantially attenuates the pathology of animal models of Rheumatoid Arthritis, Crohn's Disease/Ulcerative Colitis IBD), Multiple Sclerosis, and Idiopathic Pulmonary Fibrosis (IPF) / lung COVID 19 infection (a recent finding, to be published). The last model is termed in mice – Bleomycin-Induced Lung Fibrosis.

Methods: The 5-MP is N-acetylated C-amidated to improve its survival in the blood, thus allowing its therapeutic effects.

Results: 5-MP inhibits human Serum Amyloid A (SAA) activity, that fuels chronic inflammation and fibrosis by interfering with the formation of SAA oligomers and SAA-aggregated fibrils. Both are responsible for chronic inflammations and fibrosis *in vivo* and *in vitro* release of pro-inflammatory cytokines from *human* SAA-activated monocytes and fibroblasts. Uncontrolled fibroblast repair mechanism of injury generates fibrosis. Similarly, uncontrolled inflammation-induced activities of fibroblasts and monocytes in chronic inflammation induce fibrosis, stressing the linkage between inflammation and fibrosis. The last (fibrosis) is much less responsive to medical intervention than inflammation. However, we found, using ELISA at the protein level and qRT-PCR at the transcriptomic level, that 5-MP inhibits the activity of pro-inflammatory cytokines (IL-6 IL-1β, TNFα) in human fibroblasts and monocyte, both cell types are associated with inflammation and fibrosis. Furthermore, the *in vitro* proliferation of human stimulated fibroblasts was suppressed following their incubation with 5-MP, which explains the ability of the peptide to suppress the proliferation and accumulation of fibroblasts *in vivo*, leading to fibrosis.

***Conclusions*:** In conclusion 5-MP displays therapeutic potential in models of lung fibrosis, thus extending the anti-inflammatory potential of this peptide to fibrotic maladies, which are included in the category of "drugs unmet diseases".

O031 / #1178

Insights Into Paraneoplastic Neurological Syndromes and Beyond

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Background and Aims: Neuro-oncology is a growing field focusing on the diagnosis and treatment of primary and secondary tumors of the central nervous system (CNS) and peripheral nervous system. Additionally, neuro-oncology deals with the identification of paraneoplastic neurological syndromes (PNS) and the neurological complications of cancer therapy.

Methods: The utilization of immunotherapy in neuro-oncology is rapidly expanding encompassing immune checkpoint inhibitors (ICI) and Chimeric Antigen Receptor T cell therapy (CAR-T). Although ICI are highly effective, they can cause significant neurological adverse reactions including the induction of PNS.

Results: PNS represents a diverse group of disorders characterized by an aberrant immune response to the nervous system. The diagnosis of PNS is often challenging because of the broad range of clinical manifestations and difficulties in identification of specific paraneoplastic autoantibodies that may confirm the diagnosis. PNS can mimic other neuroimmunological disorders such as granulomatotic and demyelinating disorders which may affect both the central and peripheral nervous system. Thus, searching for PNS is essential for the early detection of hidden tumors and prompt initiation of oncological therapies.

Conclusions: The challenge in treating PNS lies in determining whether cancer therapy alone is sufficient, given the fact that some new targeted biological therapies have a short response time frame. Questions arise regarding the initiation and choice of immune-modifying therapies, their safety in patients with PNS, and the criteria for subsequent treatments.

Hereby, we aimed to describe the diagnostic challenges, clinical outcomes and therapeutic dilemmas in the management of selected cases of PNS from a large tertiary center.

PARALLEL SESSION 24: MECHANISMS IN AUTOIMMUNITY PART 2

20-05-2024 14:00 - 15:30

O032 / #702

Extracellular Vesicles in Patients with Thrombotic Antiphospholipid Syndrome Indicate Ongoing Endothelial and Platelet Activation

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Background and Aims: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombosis and/or obstetric complications and the persistent presence of antiphospholipid antibodies (aPL). Binding of aPL to the surface of endothelial cells, platelets, and monocytes triggers their activation, which also releases extracellular vesicles (EVs). Research on EVs in APS has mainly focused on medium or large vesicles, whereas research on small (sEVs) is limited. The aim of our study was to investigate different subtypes of sEVs in plasma from patients with thrombotic APS and healthy controls.

Methods: The size and plasma concentration of sEVs were determined by immunophenotypic analysis of sEVs on an ExoView® platform, and nanoparticle tracking analysis (NTA) surface protein profile was analysed by MACSPlex multiplex flow cytometry and EXOVIEW interferometric imaging.

Results: We detected sEVs with a size of less than 200 nm. The size of sEVs was comparable in patients and healthy controls, whereas we observed an increase in the total number of sEVs in patients with thrombotic APS. The frequency of endothelial cell-derived sEVs (CD144+) was increased in APS, whereas no differences were observed in the frequency of monocyte-derived sEVs (CD14+). EVs from APS patients were specifically enriched in surface expression of CD62P, indicating endothelial and platelet activation in APS. In the APS group, we also detected an increased number of sEVs positive for ICAM-1.

Conclusions: The results of increased numbers of endothelial (CD144+) and ICAM-1-positive sEVs suggest cell activation in APS, even in the absence of an acute thrombotic event.

O033 / #265

Taking The Autoimmune Sting Out Of Pd-1 Checkpoint Inhibition to Suppress Cancer Growth

Michael Agrez[1], Stephen Parker[1], Christopher Chandler[2], Darryl Turner[3], Justyna Rzepecka[3], Gavin Knox[3], Anastasia Nika[3], Andrew Hall[3], Hayley Gooding[3], Laura Gallagher[3]

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[3]Biological Sciences, Concept Life Sciences, Edinburgh, United Kingdom

Background and Aims: Exacerbation of autoimmune diseases (ADs) is the nemesis of immune checkpoint inhibitors (ICIs) such as anti-PD-1 which suppresses tumour growth by re-invigorating exhausted T cells and activating natural killer (NK) cells. While dendritic cells (DCs) are implicated in the pathogenesis of many ADs, antitumour responses induced by anti-PD-1 involve T cell: DC crosstalk that is licenced by interleukin-12 (IL-12) and interferon-gamma (IFN-γ) which also contributes to the severity of ADs. We have developed a lipidic peptide, designated IK14004, that destabilises DCs, expands the immunosuppressive regulatory T cell population and inhibits IFN-γ production yet activates cytotoxic T cells. The aim of the present study was to examine the effect of IK14004 on exhausted T cells, growth of Lewis lung cancer (LCC) and activation of NK cells.

Methods: T cell exhaustion in splenocyte-derived CD4+ T cells and LCC growth were assessed using C57BL/6 murine models. Flow cytometry and ELISAs were used to examine the effect of IK14004 on NK cells within murine splenocytes and peripheral blood mononuclear cells isolated from healthy human volunteers.

Results: In murine models, IK14004 re-invigorates exhausted splenocyte-derived CD4+ T cells and inhibits LLC growth. Human NK cells are activated by IK14004 in an IL-2-independent manner leading to expression of the natural cytotoxic receptor, NKp44, and the activating receptor, NKG2D, without enhancing IFN-γ production.

Conclusions: This novel compound offers an opportunity to gain further insight into the complexity of ICI immunotherapy so that autoimmune responses may be minimised without promoting tumour evasion from the immune system.

O034 / #309

Type 2 NKT Cells Directed Immune Regulatory Mechanism in Lupus Nephritis

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Background and Aims: Natural killer T (NKT) cells recognize lipid antigens presented by CD1d molecules and can be categorized into two subsets: type 1 or invariant (iNKT) and type 2 NKT cells. iNKT cells are reactive to αGalCer and type 2 NKT cells recognize sulfatide or lysophosphatidylcholine (LPC). We have investigated the role of type 2 NKT cells in the spontaneous development of lupus in (NZBXNZW) or BWF1 mice.

Methods: Different lipid/CD1d-tetramers were used to analyze activation and accumulation of NKT cell subsets in BWF1 mice and in lupus patients. Sulfatide and a clinically relevant NKT2 agonist was orally administered in mice to assess the importance of NKT cell-directed immune regulatory mechanism in lupus.

Results: We found that iNKT (αGalCer/CD1d-tetramer$^+$) and type 2 (sulfatide/CD1d-tetramer$^+$) NKT cells accumulate in kidney tissues with progression of disease in mice. Interestingly, iNKT cells are also activated during disease progression in both mice and lupus patients. Activation of type 2 NKT cells either via sulfatide or a structural analog of LPC, miltefosine, results in a significant inhibition of proteinuria, anti-dsDNA antibodies, proinflammatory cytokines and cellular infiltration into kidneys of BWF1 mice.

Conclusions: These studies suggest a key role for a NKT cell-based immune regulatory mechanism in the control of lupus nephritis. A novel NKT 2 cell activator structurally related to miltefosine will be dosed in an upcoming hybrid designed Phase 1 program in healthy volunteers and in patients with SLE to examine the safety and tolerability along with biomarkers to validate the role of NKT 2 cell activation in lupus.

O035 / #319

Immune-Checkpoint Inhibition and Autoimmunity: Yin and Yang

Zoltan Szekanecz[1], Enikő Sebestyén[2], Nóra Major[2], Levente Bodoki[1], Attila Makai[3], Ingrid Balogh[2], Gábor Tóth[4], Zsuzsanna Orosz[3], Péter Árkosy[2], Attila Vaskó[3], Katalin Hodosi[1], Éva Szekanecz[2]

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Background and Aims: Immune checkpoint inhibitors (ICIs) stimulate antitumor immune responses and they might trigger autoimmunity leading to immune-related adverse events (irAE). In our study, we assessed patients with malignancies who underwent anti-PD-1 treatment at the University of Debrecen, Clinical Center.

Methods: Between June 2017 and May 2021, 207 patients started ICI treatment. A total of 157 patients received nivolumab and 50 were treated with pembrolizumab. We performed binary logistic regression analysis to determine, which factors were associated with irAEs.

Results: At the time of data analysis, the mean duration of treatment was 2.03 ± 0.69 years. ROC analysis determined that 9 or more treatment cycles were associated with a significantly higher risk of irAEs. A total of 125 patients received ≥9 treatment cycles. Three times more patients were

treated with nivolumab than pembrolizumab. Of the 207 patients, 66 (32%) developed irAEs. Among the 66 patients who developed irAEs, 36 patients (55%) developed one, 23 (35%) developed two, while 7 (10%) developed three irAEs in the same patient. The most common irAEs were thyroid (33 cases), dermatological (25 cases), pneumonia (14 cases) and gastrointestinal complications (13 cases). Patients who developed irAEs received significantly more treatment cycles (21.8±18.7 versus 15.8±17.4; *P* =.002) and were younger at the start of treatment (60.7±10.8 versus 63.4±10.1 years; *P*=.042) compared to patients without irAEs. Pembrolizumab-treated patients developed more but less severe irAEs compared to those receiving nivolumab.

Conclusions: ICI treatment is very effective, however, irAEs may develop. These irAEs might be related to the number of treatment cycles and the underlying disease.

O036 / #643

The Molecular Interplay between The Transcription Factors Ets-2 And Foxp3 in Effector and Regulatory Cd4+ T-Cells Is Involved in The Development of Multiple Sclerosis (MS)

Panagiota Davoulou, Ioannis Panagoulias, Fotios Karagiannis, Ioanna Aggeletopoulou, Tassos Georgakopoulos, Athanasia Mouzaki

University of Patras, Medical School, Patras, Greece

***Background and Aims*:** Ets-2 functions as a preinduction repressor of IL-2 and other signatures cytokines that mark CD4+ T-cell lineage commitment, whereas Foxp3 is a critical regulator of CD4+ Treg development and function. We observed that in CD4+CD25+Foxp3+ Tregs from MS patients, Foxp3 is significantly reduced, while Ets-2 is significantly increased compared to Tregs from healthy controls.

***Methods*:** We investigated the effect of Ets-2 on the regulation of Foxp3 expression, as in silico analysis revealed that Ets-2 has binding sites at the Foxp3 promoter, but not vice-versa. CD4+ Jurkat T-cells were transfected with an Ets-2 or a Foxp3-overexpressing vector. Gene expression of Ets-2 and Foxp3 was examined by real-time qPCR and Western-blotting. ChIP analysis was performed to test the binding of Ets-2 to the Foxp3 promoter.

Results: Overexpression of Ets-2 resulted in a marked decrease in Foxp3 expression, and ChIP analysis confirmed the binding of Ets-2 to the Foxp3 promoter. Interestingly, overexpression of Foxp3 downregulated the expression of Ets-2, although Foxp3 does not have binding sites at the Ets-2 promoter. Further analysis revealed that this effect is mediated by STAT3, which acts as an inhibitor of Ets-2 expression. Apparently, this process is overridden in the physiological environment of MS by the increased expression of Ets-2 in Tregs.

Conclusions: In conclusion, Ets-2 is overexpressed in Tregs from MS patients and downregulates the expression of Foxp3, contributing to its decreased activity. This is the first study to show a suppressive role of Ets-2 in the development and function of Tregs and its contribution to the development of MS.

PARALLEL SESSION 25: DIAGNOSTICS IN AUTOIMMUNITY

20-05-2024 14:00 - 15:30

O037 / #977

Revolutionizing GRD Diagnosis: Novel Epitopes and Multiparametric Diagnostics to Eliminate Unnecessary Biopsies

Torsten Matthias[1], Aliaksei Shymanets[2], Jennifer Echterhagen[3], Patricia Wusterhausen[4]

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Background and Aims: Autoantibody profiles are powerful and reliable tools to correlate clinical features and therapeutic outcomes in GLUTEN-RELATED DISORDERS (GRD). The AESKUCARE® Point of Care GRD IgA (GRD-POC) and the AESKUBLOTS® GRD IgA (GRD-BLOT) are novel membrane-bound multiparametric enzyme immunoassays for overall quantitative determination of total IgA and IgA antibodies in GRDs. Evaluate the performance of two multiparametric novel test systems in a study cohort of pediatric GRDs and compare the results to well-established methods in GRD diagnostics.

Methods: GRD-BLOT and GRD-POC allow the simultaneous measurement of human-specific IgA antibodies in GRDs against human tissue transglutaminase (tTG), neo-epitopes of human tTG (tTG-neo), microbial transglutaminase (mTG), neo-epitopes of mTG (mTG-neo), deamidated gliadin-specific peptides (DGP), gliadin, Frazer's fraction, human epidermal transglutaminase (TG3) and total-IgA. Antibody titers were evaluated in a cohort of 50 pediatric GRD patients. Results correlated to EMA-IgA IFA readout, and patients clinical history.

Results: Highest AUC of antigens was 0.955 tTG IgA, followed by tTG-neo IgA and mTG-neo IgA (0.955 and 0.907 respectively). tTG-neo IgA showed the highest correlation with EMA read out (r^2=0.7453, *P*<.001). Method agreement between GRD-BLOT and GRD-POC was >93.4 %. IgA deficiency was in 100% agreement with patient history, and relevant antibodies were determined with respective IgG tests.

Conclusions: Advantage of multiparametric antibody analysis is time and cost-saving information gain. Novel antibodies like mTg-neo evaluated more quickly and integrated into routine diagnostics. In conjunction with patient's medical history, professionals can make rapid therapy recommendations, support diagnosis and avoid unnecessary biopsies, making the POC-GRD and BLOT-GRD a unique tool.

O038 / #647

Identification of Novel Antigenic Targets Using Antibody Profiling in Spinal Cord Injury Patients

Astrid Pues[1], Sven Bamps[2], Eveleen Buelens[3], Erwin Cornips[3], Jens Deckers[4], Bart Depreitere[5], Diedrik Peuskens[3], Marc Ruitenberg[6], Charlotte Van Laake-Geelen[7], Angel Arevalo-Martin[8], Lukas Grassner[9], Patrick Vandormael[10], Judith Fraussen[1], Veerle Somers[1]

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[10]VIB Center for Brain & Disease Research, Leuven, Belgium

Background and Aims: Traumatic spinal cord injury (SCI) causes damage to the nerve tissue of the spinal cord, which results in loss of motor and sensory function. Current neurological scoring systems, including the American Spi-

nal Injury Association (ASIA) Impairment Scale (AIS), and imaging techniques are insufficient to predict disease progression. Therefore, there is a high need for novel prognostic tools. This project aimed to identify and characterise novel autoantibodies as biomarkers for disease course.

Methods: A healthy and SCI spinal cord cDNA phage display library were used to screen for novel antibodies in plasma samples of SCI patients (n=12/11). Antibody reactivity against the selected antigens was validated in 303 individual plasma and serum samples of 199 SCI patients collected at baseline (T0: 0-4 days post injury [dpi]) and follow-up (T1: 21-33 dpi; T2: 34-54 dpi) and 119 age-and sex-matched healthy control (HC) samples using phage ELISA.

Results: Out of 92 identified antigens, antibody reactivity to six novel antigens (UH-SCI.104-105-106-108-109-110) was validated in individual SCI and HC samples. The antibody reactivity against UH-SCI.106-108-109 was decreased immediately after the injury (T0) when compared to HC (P<.0005) but increased over time (T1 and T2) to HC levels. Additionally, antibody reactivity against UH-SCI.104-105-108-109-110 was significantly higher at T1 in SCI patients who converted to a less severe AIS grade than in non-converters (UH-SCI.104, UH-SCI.105, UH-SCI.108, UH-SCI.110 P <0.05; UH-SCI.109 P <0.001).

Conclusions: Antibody reactivity against the novel identified antigens has prognostic biomarker potential. This could be important for patient stratification in clinical trials and clinical decision-making.

PARALLEL SESSION 27: NUTRITION AND LIFESTYLE IN AUTOIMMUNITY

20-05-2024 15:45 - 16:45

O040 / #292

The Relationship between Fibromyalgia and Nutrition- An Up to Date Review of The Literature

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Background and Aims: Objective: Fibromyalgia syndrome (FM) is a chronic, generalized pain condition usually accompanied by several associated symptoms, such as fatigue, sleep disturbance, headache, irritable bowel syndrome and mood disorders. Different medical treatments are used to treat fibromyalgia and the recent guidelines suggest that the optimal treatment consists in a multidisciplinary approach with a combination of pharmacological and non-pharmacological treatment modalities. Among non-pharmacological treatment, nutrition is a promising yet less-known tool for FM patients. The aim of this review is to update the present knowledge about fibromyalgia and nutrition.

Methods: Design: A systematic search has been performed on Medline from January 1998 to December 2017.

Results: The relationship between FM and nutrition is about a number of interest points: nutritional deficits that worsen the disease and nutritional supplements that alleviate it; Obesity and overweight, often present in FM patients, are related to the severity of FM worsening the quality of life; Food products that are found to be pain inducers or exacerbators in different neuro-metabolic pathways, such as gluten and certain amino acids; Diets rich in antioxidants, such as vegan and vegetarian diet, may have some benefits as a line of non-pharmacological treatment.

Conclusions: In summary, this review will discuss the direct and indirect relationships between FM and nutrition, and as a secondary endpoint, will reveal the potential benefit of specific dietary interventions as nonpharmacological tools as part of a multidisciplinary treatment for FM patients.

PARALLEL SESSION 28: THYROID AND ENDOCRINE SYSTEM

20-05-2024 15:45 - 16:45

O041 / #1042

Antibody-Mediated Response to SARS-COV-2, EBV, HHV-6 Superantigens and Activin-A Underpins Diagnosis of Long COVID and ME/CFS

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Background and Aims: Infections with herpes family viruses, immune dysregulation, and the persistence of inflammation, disturbance in the gut microbiome, multiple tissue damage and autoimmunity have been reported as the most common pattern for long COVID and its association with ME/CFS. Our study's aim was development of biomarkers for the early detection of long COVID and its association with ME/CFS.

Methods: Using ELISA, we measured IgG, IgA and IgM antibodies against SARS-CoV-2 superantigen amino acid sequence of 671-692, HSP60 and HSP90, which share homology with SARS-CoV-2, resulting in elevated levels of viral dUTPases and activin-A in long COVID and ME/CFS.

Results: Compared to controls, long COVID patients showed significant elevations in IgG/IgM-SARS-CoV-2 superantigen, IgE-citrullinated EBV, IgG/IgM-HHV-6 and HHV-6-dUTPase, IgA/IgM-activin-A, IgM-neural HSP60, and IgA-HSP90. Network analysis yielded a highly significant predictive accuracy of 80% for the long COVID diagnosis (sensitivity 78.9%; specificity 81.8%; area under the ROC curve = 0.876); the topmost predictors were IgA-activin-A, IgG-HHV-6, IgM-HHV-6-dUTPase, IgG-SARS-CoV-2, and IgM-HHV-6. The top predictors of CFS due to long COVID were, in descending order, IgG-HHV-6-dUTPase, IgM-activin-A, IgM-SARS-CoV-2, and IgA-activin-A (predictive accuracy: r = 0.709).

Conclusions: Detection of elevated antibodies against SARS-CoV-2 furin-cleavage site, citrullinated EBV, HHV-6 dUTPase, HSP60, HSP90 and activin-A is important in early diagnosis of long COVID and its association with ME/CFS.

PARALLEL SESSION 29: PATHOGENESIS OF AUTOIMMUNE CONDITION

20-05-2024 17:15 - 18:30

O042 / #687

Anti-Citrullinated Histone Antibody CIT-013, A Dual Action Therapeutic for Neutrophil Extracellular Trap Associated Autoimmune Diseases

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Background and Aims: Neutrophil extracellular traps (NETs) contribute to the pathophysiology of many immune mediated inflammatory diseases (IMIDs). CIT-013 is a first-in-class monoclonal antibody that specifically targets citrullinated histones H2A and H4 and shows efficacy in several pre-clinical models of NET-associated inflammation. The aims of this study were to investigate CIT-013's mechanism of action (MoA) and show target engagement in a human model of low-grade inflammation. Additionally, CIT-013's potential as treatment for rheumatoid arthritis (RA) and hidradenitis suppurativa (HS) was investigated.

***Methods*:** Confocal microscopy was used to visualize CIT-013's MoA. CIT-013's NET-targeting potential was further assessed by investigating its efficacy in a collagen-induced arthritis mouse model, as well as by the detection of NETs in RA and HS serum and tissue with ELISA and immunohistochemistry. Inhibition of NET release was investigated in LPS-challenged healthy human volunteers.

Results: CIT-013's MoA encompasses inhibition of NETosis and enhanced macrophage-mediated clearance of NETs and netting neutrophils. Elevated CIT-013 epitope levels have been demonstrated in serum and tissue of RA and HS patients. In human RA synovial tissue, NET levels correlate with inflammation grade. LPS nano-dosing in healthy volunteers induced an increase in circulating NETs which was significantly inhibited by CIT-013 treatment.

Conclusions: CIT-013 has a unique dual NET-targeting MoA, suppressing their proinflammatory properties, with therapeutic potential for IMIDs like RA and HS. This reinforces the position of CIT-013 as unique therapeutic approach for NET-associated diseases with unmet therapeutic needs. CIT-013 will enter phase 2 proof-of-concept trials in RA and HS during 2024.

O043 / #1076

Assessment of Immune Cell Activation In Pemphigus

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Background and Aims: Pemphigus is a blistering autoimmune disease of the skin and/or mucous membranes, characterised by the presence of specific autoantibodies directed against structural proteins of the human skin. Recent reports indicate that new haematological parameters, termed Extended Inflammation Parameters (EIP), can be used to assess the activation of immune cells during active inflammation. These include parameters assessing both neutrophil activation (NEUT-RI, NEUT-GI) and the number of activated lymphocytes (RE-LYMP). The aim of this study was to investigate the relationship between changes in NEUT-RI, NEUT-GI and RE-LYMP and the disease activity in patients with pemphigus.

Methods: Thirty-two patients with pemphigus and 32 sex- and age-matched control subjects were included in this study. Extended Inflammation Parameters (EIP), which include RE-LYMPH (activated lymphocytes), AS-LYMPH (antibody-producing B lymphocytes), and NEUT-RI and NEUT-GI (activated neutrophils) were analyzed.

Results: The study involved 32 patients with diagnosed different types of pemphigus. Neutrophil activation parameters (NEUT-RI and NEUT-GI) and lymphocytes (RE-LYMP) were significantly higher in these patients compared to the parameters in healthy participants (respectively $P = .0127$, $P = .0011$ and $P = .0033$). The increased quantity of activated lymphocytes (RE-LYMP) also correlated significantly with the extent of skin and/or mucosal lesions in patients assessed by the PDAI scale ($P < .02$).

Conclusions: The NEUT-RI, NEUT-GI and RE-LYMP parameters proved to be appropriate markers of inflammation severity in pemphigus, also in relation to local lesions, which was not possible with the inflammation markers (CRP, ESR) used so far on a routine basis.

ORAL DISCUSSIONS

ORAL DISCUSSIONS 01: APS: WHAT'S NEW IN ANTIPHOSPHOLIPID SYNDROME?

18-05-2024 12:50 - 13:50

OD001 / #535

Combination of Clinical Parameters Associated with Different Thrombotic Manifestations of Primary Antiphospholipid Syndrome

Gabrielle Santos[1,2], Paula David[3], Sergio Rodriguez-Rodriguez[4], Erica Okazaki[1], Marina Collela[5], Bianca Stefanello[1], Paula Prestes[1], Gabriela Yamaguti-Hayakawa[5], Cynthia Rothschild[1], Joyce Annichino-Bizzachi[5], Vanderson Rocha[1], Erich De Paula[5], Paula Villaça[1], Fernanda Orsi[1,5]

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Background and Aims: We aimed to identify demographic profiles and clinical clusters in patients with thrombotic primary antiphospholipid syndrome (t-PAPS).

Methods: Brazilian cohort of t-PAPS, data was retrieved retrospectively from the charts. Cluster analysis was used to group patients according to their clinical features.

Results: Of 263 patients, 61% were female and 17.5% were triple positive for antiphospholipids (aPL). The median age at first thrombosis was 32 years (14-77) and 75% were venous. Recurrent episodes occurred in 44% of patients, 30% of whom were on anticoagulation. The median time between first and second episode was 36 (12-103) months. Patients whose first thrombosis was arterial had more hypertension (61.2% vs. 38.8%; *P* = .003) and dyslipidemia (59.4% vs. 40.6%; *P* = .013), whereas venous thrombosis was associated with obesity (49% vs. 34%; *P* = .026) and elevated C-reactive protein (median 2.66 vs. 0.99). Cluster analysis divided our cohort into two groups. The first was composed of young women (74%), median age 26 years, with triple aPL positivity (100%), lower complement and platelet levels, mostly with venous thrombosis (~80%) and without cardiovascular comorbidities (67%) or obesity (68%). The second cluster consisted of slightly older patients (median age 36 years), single or double aPL positivity (98%), with either arterial (~27%) or venous thrombosis in unusual sites (~21%), and more cardiovascular comorbidities and obesity (50%).

Conclusions: The data provide preliminary support for at least two clusters in patients with t-PAPS. The clusters were grouped according to similar immunologic profile, comorbidities and type of thrombosis. These findings provide insight into the pathological mechanisms of different t-PAPS manifestations.

OD002 / #562

Nailfold Capillaroscopy and Pulse Wave Doppler: Relevance for the Assessment of Microvascular Damage in Antıphospholipid Syndrome

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Background and Aims: Primary Antiphospholipid Syndrome (APS) is a rare systemic autoimmune disease. The aim of this study is to compare nailfold capillaroscopy and Pulse Wave Doppler to evaluate microcirculation in APS patients and healthy controls.

Methods: We collected general data about personal hystory, laboratory, clinical and therapy features of 78 patients affected by primary APS. Subjects with multiple organ involvement, patients with active malignancy as well as asymptomatic subjects were excluded from analysis. We focused the analysis on 30 patients, equally divided in group characterized by obstetric, microvascular, arterial or venous involvement. Thirteen age and sex matched subjects were enrolled as healthy controls. Nailfold capillaroscopy was performed evaluating both capillary density and tortuosity. The pulsed wave doppler was performed analyzing the peak systolic velocity (PSV) at the base of the nail.

Results: Data analysis underlines a strong linear correlation between capillary density and PSV. In addition APS patients with non-venous involvement show both lower capillary density and PSV than APS patients with venous involvement or healthy controls. Moreover ramified/bushy capillaries are slightly increased in the APS patients as well as in the subgroup of patients with venous involvement than in patients without venous involvement.

Conclusions: Non-invasive and cost-effective imaging tests such as nailfold capillaroscopy and vascular ultrasound can be useful tools for the assessment of microvascular damage in APS patients and can guide the clinician to the choice of an individualized therapy.

OD003 / #863

Cardiac Surgery in Antiphospholipid Syndrome: A Bleeding And Thrombotic Equilibrium

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Background and Aims: Cardiovascular surgery in antiphospholipid syndrome (APS) patients has a high risk of complications, responsible for significant rates of mortality. The perioperative management of these patients is still a challenge, as there are no guidelines.

Methods: Twenty-nine years-old female with previous history of transient neurologic deficit in childhood, a venous thromboembolism episode and chronic kidney disease (CKD) of unknown etiology, was hospitalized due to severe aortic insufficiency, ventricular dysfunction and non-bacterial endocarditis. Given the clinical severity, cardiac surgery was performed with aortic valve substitution. Analytically, thrombocytopenia was evident and immunological study showed triple positivity for APS antibodies. During follow-up she presented visual loss of both superior quadrants bilaterally, with cerebral MRI showing chronic and new onset ischemic lesions and retinal angiography thrombotic microangiopathy lesions. Anticoagulation and corticotherapy was started. Kidney biopsy was not performed because of bleeding risk, so we used the ophthalmologic findings to presuppose the existence of thrombotic microangiopathy in renal circulation.

Results: We present an APS with severe organ damage, which would benefit from prophylactic measures previously, during and after surgery, if the diagnosis was confirmed sooner. With therapy, she showed slight visual and renal function improvement, but a significant impairment in quality of life remained.

Conclusions: Having our case in mind, a protocolized approach should be adopted in these patients to reduce thrombotic complications after surgery. Despite the need for more studies in the area, based on the disease severity category and catastrophic APS treatment we propose using heparin, intraoperative plasmapheresis and corticotherapy as perioperative management.

OD004 / #1069

The Prothrombotic Phenotype in Antiphospholipid Syndrome as a Crosstalk Between Innate Immunıty and Platelets

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Background and Aims: The thrombotic vasculopathy of Antiphospholipid syndrome (APS) is triggered by anti-phospholipid antibody-mediated endothelial perturbation and is amplified by other cell players. The study aimed to characterize the pathogenic role of platelets and, in particular, of platelet-leukocyte hetero-aggregates.

Methods: Thirty-seven primary APS and thirty-four normal healthy controls (NHS) were investigated. We evaluated by flow cytometry: P-Selectin, GPIIaIIIb, and ApoER2 as activation markers, cell-membrane and cytoplasmic Tissue Factor (TF) and TF pathway inhibitor expression (TFPI) as pro-coagulant phenotype, and the levels of platelet-leukocyte hetero-aggregates. Plasma C5a and C5b9 complement activation products were measured by solid-phase assays and the presence of C4d on circulating platelets and platelet-leukocyte hetero-aggregates by flow-cytometry.

Results: PAPS displayed a significantly higher percentage of platelets expressing P-selectin, GPIIbIIIa, and ApoER2 than control NHS. We found a similar increase of TF but not TFPI-positive platelets in PAPS compared to NHS. The total and TF-positive platelet-leucocyte hetero-aggregates significantly increased in patients compared to controls. ADP-activated platelets (10μM, 15 min) did not show any difference between patients and controls. PAPS[MOU2] displayed a significantly greater percentage of C4d positive platelets and platelet-granulocyte aggregates than NHS ($P = .021$ and $P = .020$). A similar, although non-significant, trend was observed in the percentage of C4d-positive platelet-monocyte aggregates. We found increased C5b9 ($P < .0001$) and higher C5a plasma levels in PAPS.

Conclusions: Platelet activation and the formation of leucocyte hetero-aggregates are hallmarks of APS. The increased expression of TF and complement split products on circulating platelets and platelet-leukocyte hetero-aggregates further supports their role in potentiating the thrombo-inflammation process associated with endothelial perturbation.

OD005 / #425

Connecting Antib2glycoprotein I Antibodies, Netosis and Endothelial Cells Activation

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Background and Aims: Although the ability of aβ2GPI to trigger endothelial cells (EC) activation is widely acknowledged in antiphospholipid syndrome (APS), the effects of NET induced by aβ2GPI on EC are yet to be determined. The aims of this study is to evaluate the interplay between NETosis, aβ2GPI and EC activation.

Methods: HD neutrophils were stimulated either with aβ2GPI isolated from APS sera, with immunoglobulin from HD or PMA. NET were stained with anti-neutrophils elastase, SYBR green and DAPI. NET quantification was performed with NETQUANT and colocalization of aβ2GPI with NET signal with JACoP. To evaluate the ability of aβ2GPI to bind to NET and prevent DNA degradation, incubation with DNase I was also performed. To study the role of aβ2GPI-induced NET on EC activation, EA.hy926 were tested for the expression of ICAM, VCAM and TF by flowcytometry after the stimulation with aβ2GPI, PMA-induced NET and aβ2GPI-induced NET.

Results: Stimulation of HD neutrophils with aβ2GPI was able to induce higher number of NET compared to stimulation with IgHD (77.6% vs 20%, $P < .0001$). Unlike IgHD, aβ2GPI binds to NET at 93.6%. Aβ2GPI binding to NET did not prevent NET degradation by DNase.

Compared with unstimulated EC, aβ2GPI-induced NET triggered robust expression of VCAM-1, ICAM-1 and TF in EA.hy926 resulting in a change-fold MFI of 6 (SE0.1), 4.2 (SE0.09), 2.3 (SE0.09), respectively. All markers were higher in EC treated with aβ2GPI-induced NET than those treated with aβ2GPI ($P < .0001$).

Conclusions: Ab2GPI play a key role in NETosis and exhibit anti-NET reactivity. Our findings unveil a novel mechanism by which NET can amplify EC activation.

OD006 / #1083

Beyond Domain I: Biological and Clinical Significance of Antiphospholipid Syndrome Igg Anti-Beta2gpi Different Domains

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Background and Aims: Antibodies against beta2 glycoprotein I (beta2GPI) Domain (D) 1 display the highest diagnostic/prognostic value for antiphospholipid syndrome (APS). On the other hand, there is evidence that antibodies specifically directed against D4,5 are not thrombogenic in animals and are not associated with APS clinical manifestations. In addition, some sera from full-blown APS neither recognize D1 nor D4,5. Aim of the study was to characterize the clinical significance of anti-beta2GPI IgG reacting with the different beta2GPI domains.

Methods: Sera from 105 APS patients classified according to the last ACR/EULAR classification criteria and 99 controls were tested by ELISA against purified human molecules, synthetic whole beta2GPI, synthetic beta2GPI molecules in which every single domain was deleted, and D4,5 complex. The thrombogenic activity of anti-D1 or anti-D5 monospecific sera was tested in the rat model as described.

Results: All the samples were positive for IgG against purified beta2GPI; most of them reacted with D1 IgG (64%), a minority against D4,5 complex (16%), and 28% were negative for both D1 and D4,5. Full-blown APS sera were polyreactive against D1, D2 and in some cases with D4 and 5 as well. No reactivity was found against D3-deleted molecules. Sera monospecific for anti-D1 IgG were thrombogenic in animals, but this was not the case for anti-D5 monospecific serum.

Conclusions: Our data show that anti-beta2GPI IgG react with different domains but not with D3 in full-blown APS. The specificity against D1 is crucial for clinical association and thrombogenic activity in animals, while monospecific anti-D5 aPL are not diagnostic/pathogenic.

ORAL DISCUSSIONS 02: AUTOIMMUNITY AND COVID-19 VACCINES

18-05-2024 12:50 - 13:50

OD007 / #355

Autoimmunity, COVID-19 Omicron Variant, and Olfactory Dysfunction: A Literature Review

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Background and Aims: Smelling is a critical sense utilized daily. Consequently, smelling impairment or anosmia may lead to a reduction in life quality.

Methods: Systemic diseases and particular autoimmune conditions can impair olfactory function; among others are Systemic Lupus Erythematosus, Sjögren Syndrome, and Rheumatoid Arthritis. Interactions between the olfactory process and the immune systems cause this phenomenon. Alongside autoimmune conditions, in the recent COVID-19 pandemic, anosmia was also described as a prevalent infection symptom. Nevertheless, the occurrence of anosmia is significantly less common in Omicron-infected patients.

Results: Several theories have been proposed to explain this phenomenon. One possibility is that the Omicron variant preferentially enters host cells via endocytosis, rather than plasma cell membrane fusion. This endosomal pathway is less dependent on the activation of Transmembrane serine protease 2 (TMPRSS2), expressed at the olfactory epithelium. As a result, the Omicron variant may have reduced efficiency in penetrating the olfactory epithelium, leading to a lower prevalence of anosmia. Furthermore, olfactory changes are known to be associated with inflammatory conditions. The Omicron variant elicits a less robust autoimmune and inflammatory response, believed to reduce the probability of anosmia.

Conclusions: Although not as common as other variants, Omicron-related olfactory dysfunction should remain a focus of further research. Olfactory issues were found to affect 10–30% of individuals throughout the Omicron-dominant era making this manifestation a public health concern.

OD008 / #417

Still's Disease and Relapsing Macrophage Activation Syndrome: Any Relevance of COVID19?

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Background and Aims: Adult-onset Still's disease (AOSD) is a rare multi-systemic auto-inflammatory disorder and MAS represents a potentially life-threatening complication of AOSD. Viral infections and vaccines might trigger AOSD and MAS.

Methods: We report the case of a healthy 41 years old woman, who developed AOSD after the second SARS-CoV-2 vaccine dose, treated with prednisone and anakinra. Due to the onset of refractory migraine, she was switched to prednisone and tocilizumab.

Results: Three weeks later after the beginning of treatment with tocilizumab, patient experienced the onset of high fever, arthralgias, skin rash together with pancytopenia, increased transaminases and ferritin (4814 ug/L) levels as well as hypertriglyceridemia and decreased fibrinogen levels. MAS diagnosis was suggested by clinical features, laboratoristical items and supported by the bone marrow biopsy. As a result anakinra 600 mg/die, dexamethasone (16 mg/die) and etoposide (100 mg) was started leading to clinical remission within one month. SARS-CoV-2 infection lead to MAS relapse and disseminated lung candidiasis leading to unresponsive multiorgan failure and patient's exitus.

Conclusions: SARS-CoV-2 infection may act as trigger of a cytokines storm leading to AOSD and MAS new onset or relapse has yet been reported as associated to such viral infection. In our case report AOSD and MAS onset occurred four months after the second SARS-CoV-2 vaccination and MAS relapsed in concomitance with SARS-CoV-2 infection and disseminated lung candidiasis. Despite the causal role of COVID-19 infection or SARS-CoV-2 vaccination cannot be proven, physicians should be aware of this potential evolution in order to promptly initiate the most appropriate therapeutic approach.

OD009 / #532

Development of Rheumatoid Arthritis After SARS-CoV-2 Infection

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Background and Aims: The SARS-CoV-2 virus has been related to the development of autoimmunity. Mechanisms possibly are molecular mimicry and the development of extracellular neutrophil traps. The aim was to describe two cases of patients who developed seropositive rheumatoid arthritis (RA) shortly after infection with the SARS-CoV-2 virus.

Methods: The cases of two female patients are described who developed late onset RA after COVID-19 infection.

Results: The first patient, aged 79, presented with arthralgias of the large joints and morning stiffness 2 months after COVID-19 infection. On clinical examination arthritis of the right shoulder and the left 3rd metacarpophalangeal joint was observed along with limited mobility of both knee joints. Laboratory examinations revealed ESR 75 mm, CRP 1.48 mg/dl (normal values <5 mg/dl), RF 256.6 U/ml (<30 U/ml), anti-CCP 584 U/ml (<5 U/ml). Late onset seropositive RA was diagnosed. Prezolon 7.5 mg/day and hydroxychloroquine 200 mg/day were administered with significant improvement. The second patient, aged 74, developed diffuse arthralgias and morning stiffness 7 months after COVID-19 infection. She had symmetric polyarthritis with tender and swollen carpal, metacarpophalangeal and proximal interphalangeal joints in both hands. Laboratory evaluation revealed ESR 44mm, CRP 1,16 mg/dl (<0,5 mg/dl), RF 23,8 U/ml (<30 U/ml), anti-CCP >200 U/ml (<5 U/ml), ANA 1/1280. Low dose corticosteroids and methotrexate 12.5 mg/wk were administered with improvement.

Conclusions: The development of seropositive RA after clinical COVID-19 infection is described. The SARS-CoV-2 virus may be related to the development of clinical autoimmune disease.

OD010 / #615

Severe COVID-19 Patients Exhibit Elevated Levels of Autoantibodies Targeting Cardiolipin and Platelet Glycoprotein with Age: A Systems Biology Approach

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Background and Aims: Age is a significant risk factor for the coronavirus disease 2019 (COVID-19) severity due to immunosenescence and certain age-dependent medical conditions (e.g., obesity, cardiovascular disorder, and chronic respiratory disease). However, despite the well-known influence of age on autoantibody biology in health and disease, its impact on the risk of developing severe COVID-19 remains poorly explored. The aim of this study was to assess the effect of aging on serum levels of autoantibodies in COVID-19 patients.

Methods: Here, we performed a cross-sectional study of autoantibodies directed against 58 targets associated with autoimmune diseases in 159 individuals with different COVID-19 severity (71 mild, 61 moderate, and 27 with severe symptoms) and 73 healthy controls. The analyses were conducted using the R programming language and its interface, RStudio. Additionally, statistical models such as linear regression, logistic regression, machine learning models (such as random forest and support vector machine), principal component analysis (PCA), descriptive statistics, and inferential statistics considering a false discovery ratio (FDR) adjusted $P < .05$ were employed.

Results: Linear regression analysis showed that severe COVID-19 patients have a significant of autoantibody levels against 16 targets. PCA and hierarchical cluster analysis based on these autoantibodies indicated a stratification of severe COVID-19 patients. Random forest analysis ranked three autoantibodies as most crucial autoantibodies for the stratification of severe COVID-19 patients. Binomial logistic regression found that two autoantibodies significantly increased the likelihood of developing a severe COVID-19 phenotype with aging.

Conclusions: These findings provide key insights to explain why aging increases the chance of developing more severe COVID-19 phenotypes.

OD011 / #1022

Transfer of Igg of Long-COVID Patients Induces Symptoms in Mice

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Background and Aims: The etiology of Long-COVID is poorly understood, but several hypotheses have been proposed to underlying Long-COVID symptoms, including autoimmunity. Yet, it remains unclear whether autoimmunity is causal or consequential in Long-COVID progression. This study aims to investigate the causal link between autoimmunity and Long-COVID.

Methods: Long-COVID patients were assessed 6-9 months post non-hospitalized SARS-CoV-2 infection. Patients were categorized into three groups based on primary symptoms and serum analysis. Total IgG was purified from blood

samples, pooled by group, and intraperitoneally injected into mice.

Results: Serum of post-exertional malaise (PEM) patients showed elevated levels of type-I IFN, pain (muscle/chest/headache) patients showed no elevated markers, while tachycardia patients showed increased neuronal damage markers and pro-inflammatory cytokines. The most pronounced effect was observed in the induction of pain-like behavior, as mice injected with Long-COVID IgG exhibited enhanced pain sensitivity, while those injected with control IgG did not. Subsequent autoantibodyome-analysis by HuProt (screening for >20,000 autoantigens) identified specific autoantibodies present in Long-COVID patients. A selection of the autoantibodies bind antigens expressed in tissues that have been described to be involved in Long-COVID pathology, including muscles. As such, we tested the functional effect of Long-COVID IgG antibodies on the functionality of heart and skeletal muscle cells. Human iPSC-derived cardiomyocyte spheroids displayed reduced contraction amplitude after exposure to pooled serum IgG from three Long-COVID patients with palpitation symptoms. Furthermore, skeletal muscle cells treated with recombinant antibodies targeting Long-COVID-specific autoantigen we identified showed mitochondrial hyper-polarization.

Conclusions: These findings provide compelling evidence for the causal role of IgG autoantibodies in Long-COVID.

OD012 / #1023

Model Building: A Roadmap From COVID-19, Post COVID and Post Vac to Chronic Fatique Syndrome

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Background and Aims: A roadmap is presented to delineate causal cofounders supposed to lead to chronic fatigue syndrome (CFS) as consequence of SARS-CoV2 infection in relation to SARS-CoV2 mRNA vaccination. Our computational CFS model integrates in-house knowledge of published and unpublished experimental data financed by public fundings covering the last 10 to 15 years.

Methods: Antibody responses against SARS-CoV2 Spike-1 and NCapsid proteins were monitored and quantitated of healthcare personal in response to mRNA vaccination and compared to antibody responses of unvaccinated individuals being infected by SARS-CoV2 variants of concern. Thirty-seven host genomes of Covid-19 patients treated in intensive-care-units were completely whole-genome -sequenced to evaluate which host genome SNPs initially published do contribute to the severity of Covid-19 disease in comparison to 503 Caucasian genomes.

Results: Our comprehensive multi-layered computational CFS disease model integrates basic knowledge of immune functions contrasting diversities of MHC class I and MHC class II peptide pathways in human patho-/physiology leading to endothelial dysfunction and to exercise intolerance. Our hypothetical autoimmune model is based on a 2-step procedure with focus on IgG trafficking, MHC peptide presentation plus a second trigger, e.g. such as long-term expression of Corona derived and/or vaccine derived SARS-CoV2 Spike-1 protein in conjunction with an inducer of inflammatory processes such as LNP itself or reactivated viral products. Our CFS model demands that CFS patients should be MHC-tissue-typed.

Conclusions: Our CSF model coincides with recently published data on SARS-CoV2 vaccine efficiencies and post-vac reports of adverse vaccination events. A Marathon mouse model is put forward to model exercise intolerance.

ORAL DISCUSSIONS 03: POST COVID SYNDROME AND COVID VACCINES

18-05-2024 12:50 - 13:50

OD013 / #438

Immune Exhaustion, Fatigue, and Long Covid Syndrome: A Comprehensive Immunological Evaluation

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Background and Aims: A substantial number of patients recovering from acute SARS-CoV-2 infection present serious lingering symptoms (long COVID (LC)). We systematically assessed LC patients >12 months after the onset of acute disease who met the classification criteria for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in two cohorts: one with patients infected with the Alpha/Delta SARS-CoV2 strains, and one with patients infected with the Omicron variant. Many patients with LC and ME/CFS also suffered from co-morbid fibromyalgia.

Methods: We compared the clinical, autoantibody, immunological and serolofical profiles of the patients from both long COVID cohorts to healthy volunteers, and to patients who were acutely infected with SARS-CoV2 and recovered (R).

Results: Compared to the recovered group, both cohorts of patients with LC syndrome had relatively increased neutrophils and monocytes with a paradoxical decrease in total lymphocyte numbers. Functionally, the T cells were exhausted, and there was an increase in the total numbers of terminal effector T cells with a reduction in circulating naïve cells. Patients with LC had significant elevations in plasma-pro-inflammatory cytokines, chemokines, and Galectin-9. Specifically in LC patients, there was a defined threshold in Galectin-9 elevation; which were clinically associated with the severity of pain and fatigue.

Conclusions: We propose that immune exhaustion associated with Galectin-9 elevation may be dysregulated in patients with ME/CFS associated with inflammatory diseases. Future studies assessing this possibility in other diseases may provide added insights into our observations.

OD014 / #515

Dysregulated Autoantibodies Targeting Vaso- and Immunoregulatory Receptors in Post COVID Syndrome Correlate with Symptom Severity

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Background and Aims: The underlying mechanisms of Post-COVID Syndrome (PCS) remain poorly understood, although emerging evidence suggests a potential involvement of immune and vascular dysregulation. Levels of homeostatic autoantibodies (AAB) targeting various G-protein coupled receptors (GPCRs) correlates to ME/CFS severity, as well as acute COVID-19 severity. Consequently, our current objective is to gain insights into the potential dysregulation of AAB and their associated targets, primarily GPCRs, as well as the interconnected pathways in PCS.

Methods: To accomplish this, we measured vaso- and immunoregulatory receptors, predominantly GPCRs, in a cohort of 80 PCS patients, with 40 of them meeting ME/CFS diagnostic criteria. Additionally, we included two control groups: 38 healthy seronegative individuals and 40 asymptomatic post-COVID-19 individuals.

Results: Our findings indicated lower levels of several AABs in PCS compared to at least one control group, along with alterations in the correlations among AABs. Notably, AABs targeting ADRB2, STAB1, and ADRA2A emerged as the most robust classifiers of post COVID-19 outcomes, with these AABs effectively stratifying patients. Furthermore, several AABs exhibited correlations with symptom severity in PCS groups, with ADRB2 AAB levels notably associated with the severity of fatigue and vasomotor symptoms in PCS/ME/CFS patients.

Conclusions: Overall, our study uncovered dysregulation of AABs against a spectrum of receptors implicated in the autonomous nervous system, vaso- and immunoregulation, underscoring their potential role in the pathogenesis of PCS.

OD015 / #516

Study of Human Microecology by Mass Spectrometry of Microbial Markers in the Blood of Patients with Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome and Post-COVID-19-Condition

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Background and Aims: The aim of our study was to analyse microbial products and metabolites encountered in systemic circulation in PCC, ME/CFS of non-COVID origin and healthy controls.

Methods: GC-MS analysis was used to identify microbial components and metabolites in blood of patients and controls

Results: In the PCC group, the levels of Enterococcus spp and Streptococcus mutans metabolites were significantly higher than in healthy controls. ME/CFS group was characterized by the higher levels of Enterococcus spp, Streptococcus mutans, Clostridium propionicum, Corynebacterium spp, Klebsiella spp, Pseudomonas aeruginosa and Cytomegalovirus metabolites, while the levels of Eggerthella and Lactobacillus spp metabolites were reduced compared to the healthy controls. Notably, that the level of endotoxin in the blood was significantly increased in ME/CFS group, but not in PCC compared to the healthy controls.

Conclusions: The concentration of microbial markers in human blood correlates with the composition of small intestine's microbiome. The similarities of the changes in the composition of the intestinal microbiome in PCC and ME/CFS is indicative of the shared immunological mechanisms in the pathogenesis of these conditions. The increased level of endotoxin in the blood of patients with ME/CFS links gut dysbiosis with chronic low-grade inflammation in this condition. Moreover, the results of our study suggest that the onset of these chronic condition alter the microbiome that then might be part of sustaining the ongoing disease, since the alteration of the microbiome was more pronounced in long-lasting ME/CFS of non-COVID origin than in new-onset PCC.

Funding: The research was funded with RSF grant 22-15-00113.

OD016 / #641

The Management of Livedoid Vasculitis Following The COVID-19 Vaccine: Two-Year Follow-Up

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Background and Aims: Livedoid vasculitis following the COVID-19 vaccine is a rare, chronic, and recurrent disease with limited effective treatments. We sought to outline the treatment and outcome in patients with livedoid vasculitis following the COVID-19 vaccine.

Methods: We conducted a prospective case series of patients diagnosed with livedoid vasculitis by their dermatologist after receiving the Moderna mRNA vaccine against the SARS-CoV-2 virus between December 1, 2021, and May 31, 2022. All patients with livedoid vasculitis following the COVID-19 vaccine were evaluated clinically follow-up for more than one year.

Results: Eight cases of livedoid vasculitis following the COVID-19 vaccine are described. Of the 4 cases with a documented outcome, withdrawal of the drug alone resulted in complete (2 patients) or partial (1 patient) recovery. For all the patients, supportive therapy was needed. The recovery period lasted from 4 weeks to 18 months. In 3 patients, continuation of treatment was possible.

***Conclusions*:** A variety of treatments with varying degrees of success have been used to treat livedoid vasculitis following the COVID-19 vaccine. Randomized clinical trials should be performed in the future to better establish these treatments in clinical practice.

OD017 / #714

Immunogenicity After COVID-19 Infection and Vaccination in Children with Autoimmune Rheumatic Diseases

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Background and Aims: Patients with autoimmune rheumatic diseases (pARD) are often immunocompromised because of the disease and the therapy they receive. As soon as the COVID-19 vaccine was licensed, we aimed to protect them through vaccination. However, many pARD got the infection before vaccination. The aim of this study was to compare the serological response after COVID-19 infection and vaccination.

Methods: Children, adolescents, and young adults, ages two to 23, were included in a prospective study conducted at the University Children's Hospital in Ljubljana, Slovenia. Data was gathered at regular visits to the rheumatology outpatient clinic. We collected demographic information, diagnosis, therapy, and timing of infection/vaccination, and conducted long-term serology (IgA/IgG) follow-ups. The anti-SARS-CoV-2 ELISA IgG/IgA test from Euroimmun, Medizinishe Labordiagnostika AG, Germany, was utilized. For statistical analysis, T-tests were performed.

Results: We collected data for 92 pARD (73% female) after infection and for 47 (64% female) after vaccination with two doses of the BNT162b2 Comirnaty (Pfizer-BioNTech) vaccine. Of those, 24 pARD experienced both infection and vaccination and were excluded from statistical analysis. Serology was available for 48 (52%) pARD after infection and for 24 (51%) after vaccination. Results are shown in Graphs 1 and 2; for most, a statistically significant difference ($P < .05$) in IgG/IgA levels was observed.

Conclusions: There was a statistically significant difference in serological response between pARD after COVID-19 infection and vaccination. Months after vaccination we observed an expected drop in antibody levels, but later the levels rose again. That could be attributed to an undetected contact of vaccinated pARD with COVID-19.

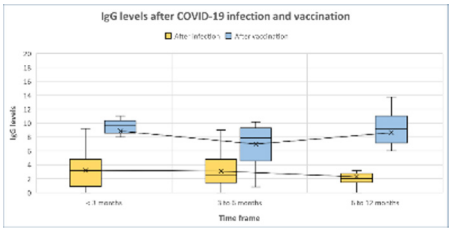

Figure 1. IgG levels after COVID-19 infection and vaccination.

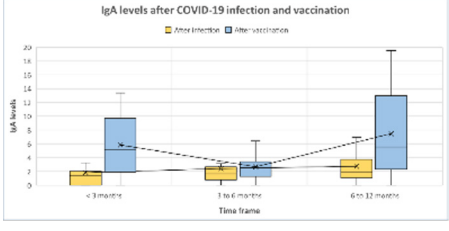

Figure 2. IgA levels after COVID-19 infection and vaccination.

OD018 / #738

Impact of COVID-19 and Vaccination Campaign on 1755 Systemic Sclerosis Patients: First Three Years of Pandemic

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Background and Aims: We investigated COVID-19 disease, and the effects of vaccination in systemic sclerosis (SSc) patients.

Methods: This prospective survey study included 1755 SSc patients (186 M, 1569F; mean age 58.7 ± 13.4 SD years, mean disease duration 8.8 ± 7.3 SD years) recruited from February 2020 to April 2023.

Results: The studied population reported a higher prevalence of COVID-19 (47.3% vs. 43.3%, $P < .000$), and a higher COVID-19-related mortality (1.91% vs. 0.72, $P < .001$) vs. the Italian general population (Igp). A significantly higher percentage of COVID-19-related hospitalization was

observed in COVID-19 positive patients with SSc-related interstitial lung involvement (ILD) vs those without (5.85% vs. 1.73%; $P < .0001$), as well as of mortality rate (2.01% vs. 0.4%; $P = .002$). Over half of patients received the first two plus one booster dose of vaccine; while only few of them had five or more doses of vaccine. An impaired seroconversion was recorded in 25.6% of individuals after the first 2 doses of vaccine, and in 8.4% of patients after the booster; the absence of T-cell immunoreactivity was observed in 3/7 patients [QuantiFERON® SARSCoV-2 Starter Set (Qiagen)]. The efficacy of vaccines, evaluated by comparing the COVID-19-related death rate recorded during pre- and post-vaccination pandemic periods, revealed a quite stable outcome in SSc patients (from 2.54% to 1.76%; P = ns), despite the marked drop in the Igp (2.95% to 0.29%; $P < .000$).

Conclusions: An increased COVID-19 prevalence and mortality rate was recorded in SSc patients; the efficacy of vaccines in term of improved outcomes was less evident in SSc compared to the Italian general population.

ORAL DISCUSSIONS 04: LUPUS UPDATE

18-05-2024 12:50 - 13:50

OD019 / #729

Myeloid Cells in Patients with Systemic Lupus Erythematosus Show Pronounced Inflammatory Signals

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Background and Aims: IFN response, plasmablasts and neutrophils are three hallmarks of systemic lupus erythematosus (SLE). The blood transcriptomic profiling of human SLE, with a focus on lymphoid (T cells, B cells and NK cells) and partial myeloid (monocytes and dendritic cells) lineages, has been uncovered. However, due to the sample processing challenge – a rapid process of fresh blood sample for optimal cell quality, the transcriptomic profiling of granulocytes remains incomplete. hence, in this study, we aim to investigate the transcriptional changes of whole myeloid cells in human SLE.

Methods: To determine cell-type specific signatures, we planned to decipher myeloid transcriptional changes in human SLE using single cell RNA sequencing (scRNA-seq). Briefly, freshly isolated white blood cells from healthy controls (n = 9) and SLE patients ($0 \leq$ SLEDAI ≤ 6, n = 9), were collected for scRNA-sq sample preparation and sequencing with BD Rhapsody single-cell partitioning technology. For data analysis, Scrublet was used for multiplet removal, BBKNN for batch correction, Python-based Scanpy pipeline for data pre-processing, visualization, clustering and differential expression testing and UMAP for data plotting.

Results: Based on Wigerblad *et al* 's work, neutrophils were clustered to 8 subpopulations. The frequency of Early_Lupus_Neu and Mid_Lupus_Neu in SLE cases was significantly higher than healthy controls. GESA and pathway analysis demonstrated that interferon, inflammatory response, IL-6/JAK/STAT3, TNF-α/NF-κB, complement, apoptosis, hypoxia and allograft rejection signals were found to be enriched in subtypes of myeloid cells.

***Conclusions*:** In SLE patients, pronounced inflammatory signals were observed in myeloid lineages, espeically in neutrophils across different development stages.

OD020 / #478

Sex Differences in Cardiovascular Risk Profile of Rheumatoid Arthritis Patients: Results From A Multicentre Cohort of the "Cardiovascular Obesity and Rheumatic Disease (Cordis)" Study Group

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Background and Aims: Rheumatoid arthritis (RA) is associated with an increased risk of cardiovascular (CV) morbidity. The gender differences in CV risk factors were assessed in the general population; however, little information exists in RA patients. Objective of this study is to characterize the CV risk of men and women with RA.

Methods: This is a cross-sectional analysis of the CORDIS cohort. For this purpose, data of consecutive patients fulfilling the 2010 American College of Rheumatology (ACR)/EULAR classification criteria for RA will be recruited for 4 years (2019-2023) in 10 different Italian hospitals.

Results: A total of 820 RA patients (193 men, 627 women) were included in the study. The mean age was 57.6 ± 0.2 years. Median RA disease duration was 143 ± 3.6 months. Hypertension was found in 49% of patients but only 35.8% of patients were treated with antihypertensive drugs. Although the males has significantly higher mean values of diastolic and systolic blood pressure than the females the percentage of patients with hypertension did not differ between sexes (54.9% in men vs (47.2%) in women ($P = .061$). Total cholesterol levels were 199.8 ± 2.4 mg/dL in males versus 207.9 ± 1.4 mg/dL in females ($P = .005$); HDL-cholesterol levels were 51.9 ± 0.8 mg/dL in males versus 59.6 ± 0.4 mg/dL in females ($P < .0001$). However, males did no differ s from the females in triglycerides concentration, blood fasting glucose, and use of anti-hypertensive drugs.

Conclusions: We registered a significantly higher prevalence of CV risk factors in males. Despite similar disease activity, male RA patients are at increased risk of CV events compared to females.

OD021 / #543

Comparative Analysis of Five Immunonutritional Indexes in Patients with Systemic Lupus Erythematosus: Across Sectional Study

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Background and Aims: Immunonutritional status in systemic lupus erythematosus (SLE) could modulate the immune cells and its inflammatory mediators. Notably, the immunonutritional status of the SLE Mexican population has not been previously described. This study aimed to assess the relationship of immunonutritional status indexes with SLE manifestations.

Methods: A cross-sectional study was conducted in 188 female SLE patients classified by the SLE ACR-1997 criteria. Clinical disease activity was evaluated by the Mex-SLEDAI index and the immunonutritional status with the CONUT, NRI, PNI, NLR, PLR, BLR, MLR, and ELR indexes.

Results: SLE patients presented a median age of 37 years. Active SLE patients had lower albumin serum levels than inactive SLE patients (3.8 *vs.* 4.04 mg/dL; $P < .001$). Moreover, active SLE patients had a lower basophil count (0.06 *vs.* 0.08 $1x10^3/\mu L$; $P = .01$), and lower A/G ratio (1.25 *vs.* 1.47; $P < .01$), ELR (0.051 *vs.* 0.071; $P = .04$), NRI (94.01 *vs.* 106.13; $P = .01$) and PNI (46.1 *vs.* 49.6; $P < .01$) scores compared to inactive SLE patients. According to Receiver Operating Characteristic (ROC) curves in which we observed that PNI index (AUC = 0.62, 95% CI = 0.53-0.71, $P < .01$), Albumin (AUC = 0.67, 95% CI = 0.59-0.75, $P < .001$), basophil count (AUC=0.66, 95% CI = 0.54-0.77, $P = .01$) ELR index (AUC = 0.65, 95% CI = 0.51-0.80, $P = .04$), and albumin/globulin ratio (AUC = 0.71, 95% CI = 0.58-0.84, $P < .01$) are adequate biomarkers to discriminate the clinical disease activity.

Conclusions: Therefore, these indexes are adequate discriminators of SLE clinical disease activity, and could be complementary biomarkers to assess the SLE clinical disease activity.

OD022 / #830

Integration of Multi-Omics Analysis Reveals Metabolic Alterations of B Lymphocytes in Systemic Lupus Erythematosus

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Background and Aims: The B cell contribution to the Systemic Lupus Erythematosus (SLE) embraces inflammatory boosting and self-antigen autoreactivity, which destroy cells and tissues in the patients. Here, the peripheral B cell transcriptome changes in SLE patients were analysed and linked with the ones occurring in their environment, including common transcriptomic changes in other cell types (cellular environment) and blood metabolites (fluidic environment).

Methods: Bioinformatics analysis was performed on the datasets from the European PRECISESADS study, including transcriptomics, metabolomics and clinical data from 363 SLE patients and 508 CTRL. The B cell transcriptome was analysed through a Deseq and GSEA, also subgrouping patients by IFN-α. The cellular environment, represented as the whole-blood transcriptome was analysed equally. Plasma and urine metabolomics peaks changes were quantified, statistically tested and annotated by the CeuMassMediator database. Common sources of variations among all the databases were identified by MOFA integration analysis.

Results: SLE cellular environment augmented in cytokines, stress response, lipidic synthesis/mobility pathways, and nucleotide degradation. B cell share these pathways, except nucleotide metabolism, which is diverted to the salvage pathway. These features are sharpened in SLE IFN-α positive patients, while other unique changes in glycosylation and LPA receptors are detected in their B cells. Schlafen proteins were found upregulated for the first time in B cells, suggesting a role in SLE disease

Conclusions: B cells showed marked metabolic changes shared with their microenvironment and unique changes directly or indirectly induced by IFN-α signalling. Linking immune cell types and changes in their microenvironment provides a novel approach to study SLE.

OD023 / #871

Exploring the Link Between TPH (CXCR5- PD-1HI), CTFH (CXCR5+ PD-1+), and DN B Cells (CD27- IGD-) in Systemic Lupus Erythematosus

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Background and Aims: Systemic lupus erythematosus (SLE) is an autoimmune disorder characterized by the generation of autoantibodies. In the pathogenesis of SLE, interleukin 21 (IL-21) is essential for the collaboration between T and B lymphocytes. It promotes the proliferation of autoreactive cells, germinal center response, differentiation of plasmablasts, and production of autoantibodies. Two specific types of T cells, peripheral helper T cells (Tph) (CD4+ PD1hi CXCR5-) and circulating T follicular helper cells (cTfh) (CD4+ PD1+ CXCR5+), are notable IL-21 producers, and their abundance is elevated in SLE patients. Among B cells, the presence of atypical B cells expressing CD11c is associated with SLE, as they are prone to differentiating into antibody-secreting cells. In our study, we evaluated the frequencies of Tph, cTfh, as well as DN B cells, including DN1 and DN2. Additionally, we investigated the intracellular expression of IL-21, IL-21R, and HLA-DR in T cells, and T-bet and CD11c in B cells.

Methods: We recruited twenty-eight SLE patients and nine healthy controls (HC) for the study. Peripheral blood mononuclear cells were isolated from blood samples, and cell staining with antibodies were performed for analysis by flow cytometry.

Results: Our findings indicated a significant increase in the frequency of Tph and cTfh cells in SLE patients compared to HC. A higher expression levels of IL-21, IL-21R, and HLA-DR. And an increase in the DN2 population, which exhibited a strong correlation with the Tph cells.

Conclusions: These results suggest that Tph and the development of atypical memory B cells are linked, potentially related to IL-21 production.

OD024 / #235

Quantification of Antiphospholipid Antibodies: The Relevance of a Clinical Based Manufacture Selection

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Background and Aims: Antiphospholipid syndrome (APS) is an autoimmune syndrome characterized by thrombosis and pregnancy loss. The 2023 ACR/EULAR classification criteria require the concomitant presence of at least persistent positivity either for lupus anticoagulant, or an IgG antiphospholipid antibody (aPL): anticardiolipin antibody, or anti-β2 glycoprotein-I antibody. The detection of aPL has commonly been carried out with enzyme-linked immunosorbent assays (ELISA), but alternative automated solid-phase techniques have been developed. As data on the agreement between these automated techniques is scarce.

Methods: Between January 2019 and November 2020, biosamples were collected and tested for aPL with two automated solid-phase methods: a fluorescence enzyme-immunoassay (M1) and a luminescence bead-based assay (M2).

Results: In a population of 1020 patients. The weighted kappa for both techniques was 0.39 (0.30-0.47). This value increased to 0.56 (0.38-0.73) when only patients with a previous diagnosis of an autoimmune disorder were included. Maybe because patients with higher titles of antibodies showed better agreement. M1 has been shown to be more sensitive and M2 slightly more specific Interestingly, only M1 obtained a significant diagnostic performance in obstetric APS. The sensibility and specificity of IgG antibodies was higher than the IgM pairs.

Conclusions: An adequate method selection for aPL quantification need to be based on the clinical suspicion and in some patients retest with a second manufacturer may be indicated. Interestingly, the detection capacity may vary considering patients' manifestations (vascular or obstetric APS) and background (autoimmune diseases history). Finally, the cut-off must be defined for each laboratory and population.

ORAL DISCUSSIONS 05: PEARLS IN AUTOIMMUNITY

18-05-2024 12:50 - 13:50

OD025 / #1033

Autoantibody Profiling in COVID-19 Reveals Altered Protein Responses and Implications for Male Reproductive Tract: Multi-Cohort Study Using Krex I-Ome Arrays

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Background and Aims: COVID-19 presents with diverse clinical manifestations, including exacerbated immune response and cytokine storm, the prodromal effects of which involve poorly understood autoantibodies. The aim of this study was to identify novel autoantibody markers that correlate with comorbidities associated with COVID-19 infection.

Methods: Employing high-throughput KREX Immunome protein-array technology, this study conducted a comprehensive analysis of autoantibody responses against 1,318 human proteins in 97 COVID-19 patients across two cohorts (Qatar and New York).

Results: Significant alterations were observed in 57 proteins in the discovery cohort and 26 in the replication cohort, compared to respective controls. Both cohorts demonstrated heightened autoantibody responses to transcription factors, immunomodulatory proteins, and disease markers, exhibiting substantial similarities (r^2 = 0.73). Consistent elevation of autoantibody responses was observed for SPANXN4, STK25, ATF4, PRKD2, and CHMP3 proteins. Validation studies confirmed the specificity of the response to SPANXN4, a crucial protein in spermiogenesis and male fertility, suggesting a potential association with COVID-19-related male reproductive tract complications. Additionally, an ICU time line study on COVID-19 patients explored approximately 100 antigens from 20 pathogens to elucidate secondary infections in ICU patients. A higher number of antibodies from secondary infections correlated with increased mortality, providing insights into the dynamics of immune responses in critically ill patients.

Conclusions: Elevated autoantibody levels were observed in discovery and replication cohorts compared with controls in immune response, structural and repair, and spermatogenesis pathways. Notably, increased autoantibodies to SPANXN4, a male fertility protein, suggest the potential for fertility complications in male COVID-19 patients who experience a severe infection.

OD026 / #1044

Anti-Polyethylene Glycol Antibodies in SARS-COV-2 Vaccinated and Unvaccinated Subjects Support Immunogenicity of Peg

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Background and Aims: PEG-lipid conjugate is used in mRNA SARS-CoV-2 vaccine to stabilize lipid nanoparticles. Humans are also exposed to PEG through many consumer products, including medicines. Incorporation of PEG into medicines is done to improve pharmacokinetics, but due to molecular size and immunogenicity, antibodies are produced against PEG and its covalent attachment to active proteins. These antibodies can potentially limit the bioavailability of drugs and possibly vaccine efficacy.

Methods: Using ELISA, we studied sera from 90 adults receiving SARS-CoV-2 mRNA vaccines for PEG-specific antibodies and compared their levels to the sera of blood donors obtained prior to the SARS-CoV-2 epidemic. We measured IgG, IgM, IgA and IgE antibodies against PEG 5K, PEG 40K, PEG-BSA, COVID vaccine ingredients and phosphatydilcholine.

Results: Analysis of data showed that at 1SD above the mean, 8%-14% of unvaccinated blood donors showed significant elevation in IgG and IgM antibodies against PEG-BSA 20K, PEG-40K, PEG-5K, vaccine ingredients and phosphatydilcholine. At the same cutoff, our

data showed that PEG-specific and vaccine ingredient antibodies were elevated in 44%-73% of mRNA-vaccinated individuals. The differences in the levels of PEG IgA and IgE antibodies between unvaccinated and vaccinated were less significant.

Conclusions: These findings support the immunogenicity, allergenicity and reactogenicity of different PEGs and phosphatydilcholine, which are major ingredients of mRNA vaccines. The measurement of antibodies against different PEGs and different vaccine ingredients is recommended in vaccinated individuals and patients with autoimmunity.

OD027 / #806

Subacute Sclerosing Panencephalitis and Autoimmune Encephalitis: Animal Models and Antibodies

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Background and Aims: Subacute sclerosing panencephalitis (SSP) is a slow infection caused by the measles virus. Latent period is up to 8 years. Subacute measles panencephalitis debuts with personality and behavior disorders, then progressive muscular-tonic, motor, visual, cognitive impairments.. Main diagnostic methods: electroencephalography,Autoimmune encephalitis (AE) affects the gray matter of the brain. With this disease, a person develops severe memory impairment, psychosis, and, as a result, inappropriate behavior over the course of several days and weeks. Symptoms are associated with the formation of antibodies to one's own nerve cells. and CNS receptors. Our goal was to study the autoimmune component of SSP, to separate its manifestations from the corresponding signs of autoimmune encephalitis in experimental mouse models of both diseases.

Methods: One group of mice (8 animals) was intrathecally injected with rabbit antibodies (AB) to the measles virus. Another mouse group was injected with ABs to rabbit NMDA receptors.

Results: The pathophysiological manifestations were different in both groups of mice. In group that received antibiotics against measles virus, severe lethargy and drowsiness were noted. At autopsy, pelvic hemorrhages were revealed in various parts of brain. In cows, the number of CD4 and CD8 cells was reduced. In group of animals with NMDA antibodies, pronounced psychomotor agitation, characteristic of the initial manifestations of AE in humans, was recorded. CD4 and CD8 were increased in these mice.

Conclusions: Thus, various experimental models of AE and SSP make it possible to trace various autoimmune processes in these two diseases and to develop the basic principles of their pathogenetic therapy.

OD028 / #1041

Extended Inflammation Parameters as Markers of Immune System Cell Activatıon in Psoriasis

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Background and Aims: Psoriasis is an inflammatory, autoimmune disease that affects approximately 2% of the population. The inflammation in psoriasis can be systemic, so despite a predominantly cutaneous manifestation, it also affects the internal organs. The diagnosis and monitoring of the disease are based on the clinical presentation. To assess the disorders of other organs, additional tests need to be performed. The main objective of the study was to search for new markers of activation of cells responsible for the immune response in psoriasis.

Methods: Thirty-one patients with psoriasis and 31 sex- and age-matched control subjects were included in this study. Extended Inflammation Parameters (EIP), which include RE-LYMPH (activated lymphocytes), AS-LYMPH (antibody-producing B lymphocytes), and NEUT-RI and NEUT-GI (activated neutrophils) were analyzed.

Results: In the study, higher values of new hematological parameters (RE-LYMPH, NEUT-RI and NEUT-GI) were observed in individuals with psoriasis ($P < .0001$) and psoriatic arthritis ($P = .002$) than in healthy controls. A statistically significant correlation was found between the values of the RE-LYMPH parameter and the severity of the disease expressed in the PASI ($P = .045$) and BSA ($P = .045$) scales.

Conclusions: Implementation of these parameters into routine laboratory analysis will likely make it possible to estimate the severity of the inflammation in psoriasis. This is of particular importance concerning the recognition of risk factors for coexisting diseases.

OD029 / #856

Immunological and Metabolomic Profile in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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Background and Aims: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are chronic systemic autoimmune diseases, of multifactorial etiology. Therefore, the objective of this study was to evaluate the immunological and metabolic profile in patients with SLE, RA, and control subjects.

Methods: Sera samples from all subjects were used to measure autoantibodies and cytokines. Additionally, the metabolic profile was analyzed using liquid chromatography-mass spectrometry to identify metabolic alterations associated with these diseases. The integration of the obtained data from the immunological and metabolic profiles will be analyzed to better understand the underlying mechanisms of RA and SLE.

Results: Significant correlations were found between some metabolites and inflammatory cytokines in SLE and RA. In SLE, a negative correlation was observed between symptom severity and Oxo_androsterone_glucuronide, suggesting a potential regulatory of this metabolite in the context of autoimmunity. Moreover, cytokines such as IL-12p70, IL-13, and TNF-α showed positive correlation with 3-Hydroxy-2-naphthoate and Benzenepropanoic-acid, -bis-dimethylethyl-hydroxy, -thio-di-ethanediyl-ester. Regarding RA, sebacic acid, showed a negative correlation with disease activity. Furthermore, C-12-NBD-Ceramide, exhibited correlations with inflammatory cytokines. Ceramides are bioactive lipids that play a crucial role in cell signaling regulation and the inflammatory response, which supports the hypothesis that this metabolite could be a

key node in a metabolic network connecting different metabolic pathways and proinflammatory cytokines in RA.

Conclusions: The metabolites selected do not appear to be directly involved in disease activity in SLE and RA. Instead, these metabolites may be more related to general metabolic processes that influence immunoregulation and cellular homeostasis in a broader context of autoimmunity.

ORAL DISCUSSIONS 06: SPONDYLOARTHRITIS

18-05-2024 12:50 - 13:50

OD030 / #460

Systemic Autoinflammatory Manifestations in Patients with Spondyloarthritis

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Background and Aims: This study aims to describe a cohort of patients with Spondyloarthritis (SpA) and systemic autoinflammatory manifestations (S-SpA cohort) against a control cohort of Still's disease (SD) patients and a further control cohort of SpA patients without systemic manifestations. Predictors of the development of SpA in patients classified as SD are also explored.

Methods: This is an observational retrospective study.

Results: Forty-one subjects were enrolled in the S-SpA cohort [21F/20M; mean ± SD age 39.0 ± 15.8 years (8.9 – 69.1)], 39 in the SD cohort and 42 in the SpA cohort. Mean ± SD latency between systemic and articular manifestations in S-SpA was 8.0 ± 10.6 years (0 – 46.2). The figure shows the comparison of systemic, articular and radiological features among S-SpA, SD and SpA cohorts. Inflammatory markers tested higher in SD than S-SpA ($P < .01$). Complete resolution of systemic symptoms was reported less frequently in S-SpA than in SD patients according to corticosteroid (Cs) ($P < .001$), methotrexate ($P = .031$) or biologic drug ($P = .047$) treatment. Articular manifestations in S-SpA and SpA patients showed similar therapeutic responses to Cs, cDMARDs and TNFα-inhibitors ($P > .05$). When considering the total 45 subjects classified as SD, a partial response to Cs in the systemic phase could significantly predict the development of SpA ($P = .001$; OR = 18.2).

Conclusions: In conclusion, SpA should be ruled out in patients with fever of unknown origin, not only in the context of undifferentiated autoinflammatory disease but also in difficult-to-treat SD. Sacroiliac MRI scans may be more valuable than spine scans in detecting the typical signs of inflammation in S-SpA.

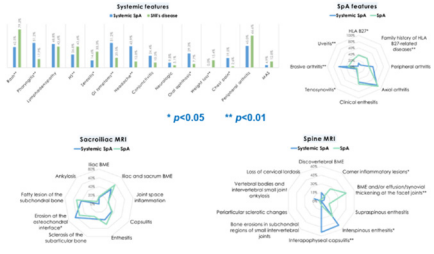

Figure 1.

OD031 / #24

Could the HLA-B27 Allele Be Associated with Gastrointestinal Manifestations in Patients with Spondyloarthritis without Inflammatory Bowel Disease?

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Background and Aims: The influence of HLA-B*27 in gastrointestinal symptoms even in those Spondyloathritis-SpA without inflammatory bowel disease has not been studied. We aim to establish the relationship between HLA genotypes and gastrointestinal variables in SpA.

Methods: Retrospective study, included patients with axial and peripheral SpA (n = 91) and healthy controls (HC) (n = 401). HLA-A, B, and DR typing was performed using PCR/SSO and Illumina Sequencing/PacBio sequencing technology. A specific questionnaire was applied asking for gastrointestinal symptoms. Clinical evaluation by rheumatologist and gastroenterologist, chromoendoscopy, magnification colonoscopy and histological analysis were performed in patients with more than two gastrointestinal symptoms. (Ethics-committee has approved this study).

Results: In total 14, 28, and 19 genotypes were identified for HLA-A*, HLA-B*, and HLA-DR* loci, respectively. Of the patients, 54% were men; mean age was 43.9 ± 11.4. The patients were classified into ankylosing spondylitis (80.2%), psoriatic arthritis (9.9%), undifferentiated spondyloarthritis (5.5%), and reactive arthritis (4.4%). In over 95% of cases, the feeding was omnivorous, and the primary gastrointestinal symptoms reported were abdominal pain (51%) and distension (53%). Additionally, 40% of individuals experienced diarrhea lasting longer than 4 weeks. HLA-B*27 occurrence in SpA individuals was significantly higher (41.8% vs. 4.2%, $P < .0001$). HLA-B*27 had a significant relation with abdominal pain ($P = .017$), intolerance to grains and dairy ($P = .046$ and $P = .045$) and ileal mucosa ulcers ($P = .024$).

Conclusions: The frequency of HLA-B*27 is lower in mestizo individuals, as observed in previous Colombian studies. HLA-B*27 is associated with early disease and significant radiographic compromise and may also affect gastrointestinal variables such as symptoms, intolerance to certain food groups and endoscopic findings.

OD032 / #627

Immunogenicity and Safety of the Booster BNT162B2 Vaccine in Patients with Axial Spondyloarthritis Treated with IL-17 and TNFα Inhibitors

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Background and Aims: Vaccination confers relatively short-term protection against severe acute respiratory syndrome coronavirus-2

(SARS-CoV-2), indicating the need for booster doses. Immunocompromised individuals with immune-mediated inflammatory diseases (IMIDs) may have pronounced immune response waning. Therefore, we investigated immune response persistence after primary vaccination and immunogenicity and safety after the BNT162b2 booster vaccination.

Methods: This prospective observational study enrolled an AxSpA cohort treated with IL-17 and TNFα inhibitors. Serum SARS-CoV-2-specific and virus-neutralizing antibodies, T-cell immune responses, and safety were assessed.

Results: Fifteen male AxSpA patients treated with TNFα (73.3%) or IL-17 (26.7%) inhibitors were enrolled. After booster vaccination humoral response increased from 905.6 (± 186.1 SD) and 409.1 (± 335.7) U/mL to 989.7 (± 12.62) and 1000 U/mL, T-cell responders from 53.3% to 80%, with no differences between AxSpA and healthy control cohorts. No severe AE occurred; the AE spectrum was comparable to the general population's.

Conclusions: Immune-response persistence after primary vaccination and immunogenicity after booster vaccination were unaffected by anti-IL17 or anti-TNFα therapy with similar AE as in the general population.

OD033 / #682

Inverse Relationship of Short Chain Fatty Acids with Secretory Immunoglobulin A Levels and Disease Activity in Patients with Spondyloarthritis

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Background and Aims: Spondyloarthritis (SpA) has been associated with dysbiotic processes, participating in the alteration of the synthesis of short chain fatty acids-SCFA, affecting humoral response and disease activity. The aim was to establish the relationship between fecal SCFA levels with serum SIgA and disease activity indices in patients with SpA.

Methods: Twenty-four adults were included,12 with SpA without Inflammatory Bowel Disease-IBD, 6 with IBD and 6 healthy controls. Patients were evaluated for the presence of gastrointestinal symptoms, disease activity, and serum secretory IgA (SIgA) levels. The quantification of SCFAs from fecal matter analyzed by ultra-high pressure liquid chromatography coupled to mass spectrometry.

Results: Non-parametric comparisons were made, finding significant differences in fecal butyric acid levels between the study groups (P = .027). It was observed that for this metabolite the healthy control and the SpA without gastrointestinal symptoms showed significant differences compared to the IBD, P = .015 and P = .009 respectively. No differences were evident between fecal SCFA levels between the SpA with gastrointestinal symptoms and IBD group. SIgA in patients with SpA without symptoms showed an inverse relationship with butyrate levels (CC = -0.900, P = .037). In patients with gastrointestinal symptoms, propionate is inversely related with IgA (CC = -0.754, P = .05). SpA with gastrointestinal symptoms shows reduced levels of all SCFAs with greater disease activity (P = .002) and BASDAI (CC = -0.776, P = .040).

Conclusions: Subclinical intestinal involvement in patients with SpA related to a reduction in SCFA. Patients with SpA and gastrointestinal symptoms present a similar profile in butyric acid levels with IBD. A differential profile observed in SCFA that discriminates patients with gastrointestinal symptoms that could modulate intestinal SIgA responses and disease activity.

OD034 / #965

Antibodies to Four Novel Peptides in New Onset Axial Spondyloarthritis

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Background and Aims: Diagnosis of axial spondyloarthritis (axSpA) is challenging and a specific laboratory diagnostic test is lacking. Previously, we identifiied immunoglobulin G (IgG) and IgA antibodies to 4 Hasselt University (UH)-axSpA peptides (UH-axSpA-IgG 4, 8 and UH-axSpA-IgA 1,10), corresponding to non-physiological peptides and to a novel axSpA autoantigen, Double homeobox protein 4 (DUX4). Validation of antibody reactivity in plasma samples of early axSpA patients (disease duration < 5 years) from 2 independent cohorts revealed antibody reactivity against at least one of these 4 peptide targets in 21.1% of early axSpA patients (30/142). Here we aim to validate the diagnostic potential of these 4 antibodies in a third independent cohort of new onset axSpA patients and controls.

Methods: Using ELISA, presence of antibodies to the 4 peptides was determined in 187 serum samples of the Belgian Inflammatory Arthritis and Spondylitis (Be-Giant) cohort and 74 controls with chronic low back pain (CLBP).

Results: The presence of antibodies against the 4 UH-axSpA peptides was confirmed in the Be-Giant cohort. Antibody reactivity against this panel of 4 antigens was present in 13.4% of newly diagnosed axSpA patients (25/187) compared to 6.2% (4/65, P = .1740) in CLBP. The LR+ for confirming axSpA using antibodies to these 4 peptides was 2.2, which is comparable to the currently used laboratory marker CRP LR+ = 2.5). So far, no correlation with clinical disease characteristics was identified.

Conclusions: The presence of antibodies to 4 UH-axSpA peptides was confirmed in the Be-Giant cohort and could be of added value for axSpA diagnosis.

OD035 / #1111

Spondyloarthropathy and Intestinal Inflammation

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Background and Aims: Inflammatory bowel disease (IBD) is generally reported to be associated with spondylarthropathies (SpA) in 5%-15% of cases. Systematic assessment by ileocolonoscopy demonstrates mucosal inflammation characteristic of Crohn disease (CD) in up to one-third of patients with SpA.

Methods: However, capsule endoscopy with evaluation of the entire small bowel may detect active inflammation in over 40% of the cases, with minimal correlation with symptoms. Nonetheless, fecal calprotectin is a re-

liable predictor of small bowel inflammation in SpA. The clinical course of asymptomatic bowel inflammation in SpA, or whether it at all constitutes IBD, is currently unclear.

Results: In the current therapeutic armamentarium for IBD, only a minority of treatment groups are effective in both IBD and SpA (anti-TNFs, JAK inhibitors). Some of the effective agents in IBD (anti-integrins, p19 inhibitors) appear to be irrelevant in SpA, posing a significant therapeutic challenge especially in anti-TNF resistant patients.

Conclusions: Thus, in patients with both SpA and IBD/ intestinal inflammation we should select whether we should focus on the primary/ clinically significant entity in patients that are lacking therapeutic options suitable for both conditions.

ORAL DISCUSSIONS 07: UPDATE IN PATHOGENESIS OF AUTOIMMUNE DISEASES

18-05-2024 12:50 - 13:50

OD036 / #341

FOXO3 Regulates the Function of Medullary Thymic Epıthelial Cells and Prevents Autoimmunity

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Background and Aims: Medullary thymic epithelial cells (mTECs) play a crucial role in central tolerance. While previous studies showed that mTECs rely on genome-protecting pathways, the underlying molecular mechanisms remain elusive. We examined the role of Foxo3 in TECs due to its known involvement in DNA damage response.

Methods: We developed a new conditional Foxo3 KO model by crossing mice carrying loxP-flanked *Foxo3* alleles ($Foxo3^{fl/fl}$) with mice expressing the Cre recombinase under the control of the *Foxn1* promoter ($Foxn1^{Cre}$).

Results: $Foxo3^{cKO}$ mice showed a disrupted mTEC compartment, particularly affecting the $CCL21^{+}$ and thymic tuft $mTEC^{lo}$ subsets. Notably, deficiency in *Foxo3* and *Aire* revealed an overarching function of Foxo3 in regulating both Aire-dependent and independent mTEC lineages. At the molecular level, Foxo3 controls specific functional modules of the mTEC transcriptome, which includes the regulation of basal DNA damage response. Consequently, *Foxo3*-deficient mTECs also presented impaired recovery after radiation-induced injury. The aforementioned changes in the TEC compartment led to alterations in regulatory T cell and iNKT cell development in the $Foxo3^{cKO}$ thymus. Lastly, aged $Foxo3^{cKO}$ mice developed signs of altered immunotolerance, which were aggravated in the *Aire*-deficient autoimmune background.

Conclusions: Our findings align with our previous study pinpointing a key role of p53 in mTEC (Rodrigues et al Blood 2017). Together, these results emphasize the connection between the DNA damage pathway, mTEC maintenance and function, and induction of immunological tolerance. Thus stdy highlights the importance of Foxo3 in preserving the genomic stability of mTECs and in supporting their role in T-cell development and prevention of autoimmunity.

OD037 / #345

Elucidating the FC Receptor and Platelet Activation Factor (PAF)-Driven Inflammatory Consequences of Anti-RBC Antibody Therapy in Autoimmunity

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Background and Aims: Autoimmune disease management often involves long-term immunosuppression, which poses significant risks. Alternatives like Intravenous immunoglobulin (IVIg) are limited by supply and side effects. Anti-RBC antibodies, notably anti-D in ITP, have emerged as a promising but pro-inflammatory alternative. This study aims to understand the role of the platelet-activating factor (PAF) pathway and Fcγ receptors in such therapies, offering insights potentially extendable to a number of autoimmune diseases.

Methods: We utilized murine ITP as a foundational model and focused on the murine RBC-specific antibody Ter119. We assessed its therapeutic and pro-inflammatory profiles through the modulation of the PAF pathway using PAF-receptor antagonists and macrophage Fcγ receptor interventions.

Results: We found that PAF-receptor antagonists effectively suppressed Ter119-induced inflammation, including changes in body temperature and chemokine production (CCL2, CCL5, and CXCL9) without affecting therapeutic activity. Macrophage depletion via clodronate liposomes and Fc-region inactivation of Ter119 significantly reduced adverse inflammatory responses.

Conclusions: Our study elucidates the critical roles of the PAF pathway and macrophage Fcγ receptors in mediating the inflammatory adverse events associated with anti-RBC antibody therapies. Although rooted in ITP, Ter119 also has substantial ameliorative effects in murine inflammatory arthritis and lung injury. The mechanisms uncovered here could serve as a blueprint for developing safer, targeted therapies across a spectrum of autoimmune diseases.

OD038 / #552

Tissue Residency and Innatelike Features Play Important Roles in CD8 Treg-Mediated Immune Regulation

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***Background and Aims*:** Understanding mechanisms by which regulatory CD8 T cells maintain homeostasis in tissues and protect them from excessive inflammation is crucial for developing effective therapies. We have investigated the molecular signature of an innate-like $Qa\text{-}1^{b}$-restricted CD8 Treg population enriched in liver and mechanisms involved in the control of autoimmune and inflammatory diseases.

Methods: $TCR\alpha\beta^{+}CD8\alpha\alpha^{+}$ Treg were sorted from liver, lung and spleen from naïve B6 mice, and the transcriptomic profile examined using single-cell RNA sequencing. Peptide agonists were defined and used to study their activation and mechanisms involved in the regulation experimental autoimmune encephalomyelitis (EAE) and hepatitis.

Results: Single cell RNA sequencing revealed that CD8 Treg is a heterogeneous Tissue Resident Memory population expressing NK inhibitory receptors (KIR), including DAP12 and transcription factors, ZBTB16, HELIOS and Tgfbr2. These cells do not express any T cell exhaustion markers, including PDCD1, CD223, HAVCR2 and CD152. They express CD122, are

dependent on IL-15 and do not express IL-12R or IL-18R. CD8Treg utilize granzymes a/b and FasL pathways in the regulation of EAE and inflammatory liver disease in mice in a Qa-1^b-dependent fashion. We have identified peptide agonists capable of activating CD8 Treg in vivo leading to prevention of immune pathologies.

Conclusions: These studies suggest a key role for a tissue-resident CD8 Treg-based immune regulatory mechanism with innate-like features in providing protection from excessive autoimmune and inflammatory tissue damage. Since CD8 Treg are present and activated in human diseases, identification of agonistic ligands has important implications for the development of novel therapeutics.

OD039 / #555

Boosting Regulatory T Cells to Suppress Autoimmunity in Generalized Vitiligo: A Role for Harmine and Kaempferol

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Background and Aims: Generalized vitiligo (GV) is an acquired skin depigmenting disease resulting due to autoimmune destruction of melanocytes. Regulatory T cells (Tregs) play critical role in curbing self-reactive CD8$^+$T-cells in GV. Current study was undertaken to assess the *in vitro* therapeutic potential of Harmine and Kaempferol as anti-vitiligo agents.

Methods: Peripheral blood and skin biopsies were collected from 52 GV patients and 50 healthy controls. Calcium levels, Calcineurin, NFATc1 and cell proliferation were assessed in patients' plasma by various kits. Transcripts (*ORAI1*, *PEIZO1*, *Calcineurin*, *GSK3B* and *DYRK1A*) and protein (IFN-γ, IL-10 & TGF-β) levels were assessed by qPCR and ELISA.

Results: Harmine and Kaempferol treatment enhances Treg suppressive capacity, NFATs and FOXP3 expression in GV Tregs ($P < 05$). Furthermore, the treatment in Tregs modulates NFAT signalling pathway, by increasing calcineurin and NFATc1 activity and decreasing DYRK1A transcripts in GV Tregs ($P < .05$). *In silico* analysis revealed that these compounds might boost Treg suppressive capacity by increasing calcineurin dephosphorylation activity, which in turn could increase NFATs activation. These compounds might increase the nuclear retention of NFATs by inhibiting DYRK1a phosphorylation activity. This treatment significantly increased melanocytes survival and proliferation in Treg:CD4+/CD8+:SK-Mel-28 cells co-culture system from GV patients ($P < .0001$).

Conclusions: This study for the first time suggests that Harmine and Kaempferol treated Tregs could control the CD8$^+$ and CD4$^+$T cells' proliferation and IFN-γ production, leading to melanocytes survival and proliferation. These compounds may serve as novel Treg-based therapeutics for vitiligo; however, future *in vivo* animal model studies are warranted to assess the safety and efficacy of these compounds.

OD040 / #597

Autoantigenomics: Exploring Patterns in the Repertoire of Autoantibody-Targeted Proteins

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Background and Aims: Autoantigenomics is a systematic approach that identifies and characterizes the repertoire of autoantibody-targeted proteins, also known as the "autoantigenome," which is a subcategory of the proteome. This promising subdomain of proteomics enables a systemic understanding of a patient's autoimmune reaction. Here, we discuss our recent research examples of using autoantigenomics to study patients with autoimmune-related neuropathies, specifically chronic inflammatory demyelinating polyneuropathy (CIDP) and sensory neuronopathy (SNN).

Methods: To obtain the autoantigenome, we utilized protein microarrays containing over 16 000 full-length proteins. We then filtered the lists of significantly targeted and study-group-specific autoantigens, and perform over-representation analyses, cluster analyses, heat maps, and pathway analyses.

Results: We present three examples of using autoantigenomics. In the first example, we found that CIDP patients who responded to intravenous immunoglobulin targeted three times more antigens than non-responders. Furthermore, we identified anchoring junction proteins as a major target in CIDP, which is a recently revealed autoimmune target in this disease. In the second example, we identified the P-body and RISC complex as significantly overrepresented in the SNN autoantigenome, which may serve as potential biomarkers for underlying autoimmune context in sensory neuronopathies. In the third example, we found that immune system pathways were significantly targeted by non-paraneoplastic SNN sera.

Conclusions: We conclude that autoantigenomics is a powerful approach that identifies global events in the repertoire of autoantibodies. It provides important insights into the underlying pathophysiology of autoimmune neuropathies. This may lead to the development of new diagnostic tools and assist treatment decisions.

OD041 / #1032

Mortality-Related Health Metrics in Systemic Autoimmune Diseases: An Epidemiological Analysis of a Nationwide Register-Based Cohort

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Background and Aims: Systemic autoimmune diseases (sAIDs) have become leading contributors to premature death. Meanwhile, regional disparities exist in capacity of rheumatology healthcare services delivery. In this study, we comprehensively analyzed mortality-related health metrics of eight sAIDs in China and examined the associations between disease burden of sAIDs and area-level socioeconomic status (including a composite indicator, human development index [HDI], and indicators in economy, healthcare, and education).

Methods: In this nationwide, register-based cohort study, we used data from Chinese Rheumatism Data Center and Nation Mortality Surveillance System between 2011 and 2021. We collected data on patient demographics, clinical status, and vital outcomes of individuals with RA, SLE, SS, IIM, SSc, BD, TAK, and AAV.

Results: Overall 156 862 individuals were included. AAV, IIM, and SSc were top three diseases with the highest fatality rates and lowest survival rates. Moreover, cardiovascular, respira-

tory (both non-infection and infection), malignancy, and digestive diseases were identified as the leading immediate causes of death in RA patients; while in the other sAIDs, cardiovascular, respiratory (non-infection), musculoskeletal, malignancy, and genitourinary diseases were leading causes of death. Generally, the overall age-, gender-, and calendar year-adjusted SMR of all sAIDs patients was 1.48 (95%CI 1.44-1.51). The adjusted SMR was highest for TAK (5.45), followed by IIM (5.08), SSc (4.94), SLE (3.50), AAV (2.97), BD (2.27), SS (1.53), and RA (0.96).

Conclusions: The mortality risk in patients with sAIDs can be in substantial excess versus general population, and sAIDs are posing more severe threat to public health as the overall society improves.

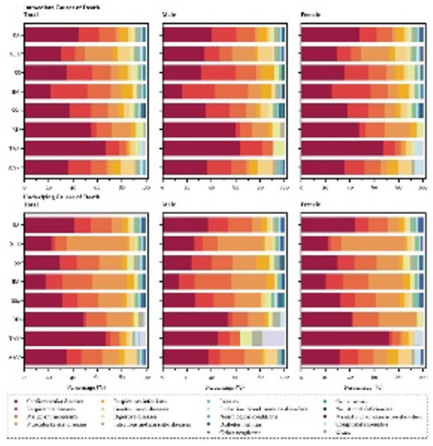

Figure 1.

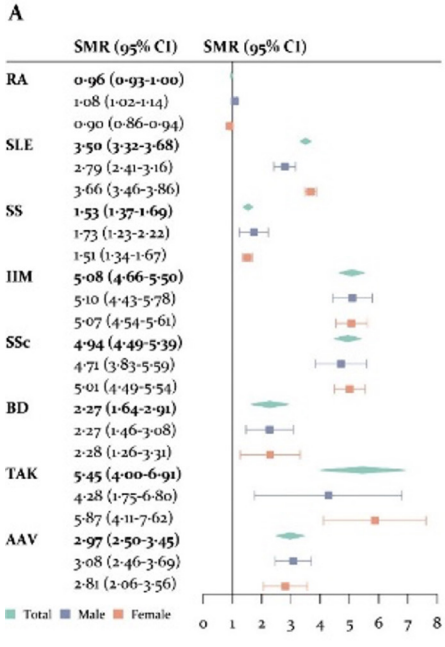

Figure 2.

ORAL DISCUSSIONS 08: VASCULITIS - UPDATE AND PREGNANCY AND AUTOIMMUNITY

18-05-2024 12:50 - 13:50

OD042 / #435

Combination of Monoclonal Antibodies Targeting Type 2 Inflammation for Severe Asthma and Eosinophilic Granulomatosis with Polyangiitis

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Division of Rheumatology, Department of Medicine Dimed, University of Padova, Padova, Italy

Background and Aims: Monoclonal antibodies targeting type 2 inflammation are promising treatments for eosinophilic-associated diseases. There is growing interest in the potential benefits of combining two biologics to treat patients with poorly controlled conditions.

Methods: We present a patient affected with a relapsing-refractory eosinophilic granulomatosis with polyangiitis (EGPA), treated with the combination of dupilumab-benralizumab. We conducted an extensive literature search in MEDLINE for original articles published until August 1st, reporting the combination of anti-type 2 biologics.

Results: A 54-year-old female ANCA-MPO EGPA patient presenting with difficult-to-treat asthma and rhino-sinusitis manifestations was referred to our Vasculitis Clinic. She was treated with several biologics, including omalizumab 300 mg, mepolizumab 100 mg, and benralizumab 30 mg. A switch to dupilumab led to significant eosinophilia (7.69×10^9/L) systemic symptoms, and a deterioration of asthma control. Therefore, a combination of dupilumab-benralizumab was started, leading to better nasal and ear outcomes, asthma control and decrease in blood eosinophils. During the 12-month treatment, no adverse effects were observed. A total of 50 cases were retrieved from the literature. Omalizumab+mepolizumab was the most frequently combination therapy (20 cases). Combination therapy led to reduction of asthma exacerbations and glucocorticoid intake, though was ineffective only for one EGPA patient. Only one patient on omalizumab-mepolizumab therapy reported a mild adverse reaction.

Conclusions: Combination biologic therapies for conditions which share pathogenic pathways appears to be both safe and effective, according to available literature. The combination approach may benefit patients with uncontrolled conditions and counter side effects of biologics, like dupilumab-related hypereosinophilia. Further studies are needed to confirm our findings.

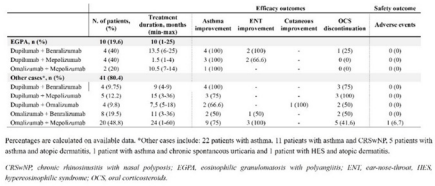

Figure 1.

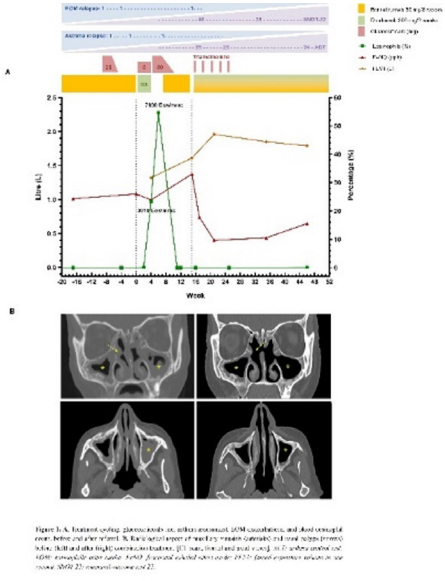

Figure 2.

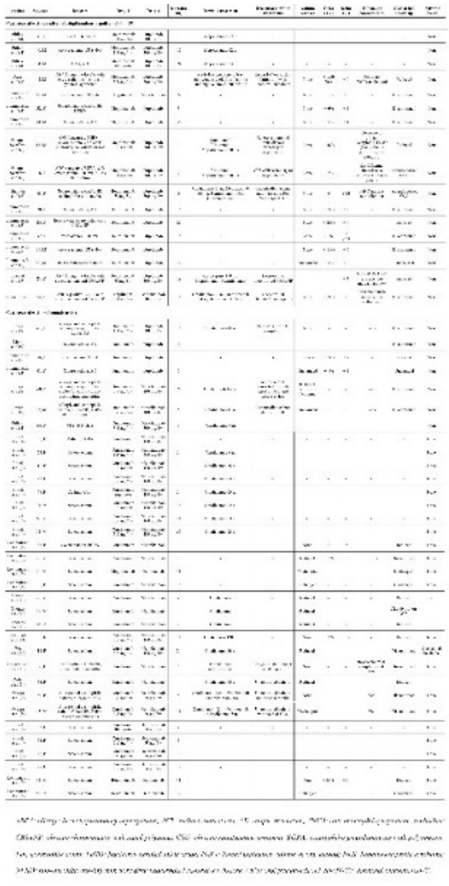

Figure 3.

OD043 / #525

Efficacy and Drug Survival of Biologic Agents in Behçet's Disease: A Real-Life Observational Monocentric Study

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***Background and Aims*:** Biologic DMARDs (bDMARDs) are effective in treating Behcet's disease (BD), with most of the evidence concerning anti-TNF, while limited data are available on long-term effectiveness and retention rate. The aim is to assess their effectiveness and 10-year retention rate.

Methods: We included patients treated with Infliximab (IFX), Adalimumab (ADA), Apremilast (APR), and Tocilizumab (TCZ) between 2009-2023. Treatment approaches were compared. Survival rates were analysed with Kaplan-Meier, and compared with Log-rank test. Japan's Behcet activity criteria were used to assess disease activity.

Results: We included 32 BD patients (34 [29-39] years, 53.1% female) exposed to 53 treatment regimens (23 = IFX, 10 = APR, 16 = ADA, 4 = TCZ), of which 68.75% received at least one cDMARD. The first bDMARD was prescribed 32.5 [13-131] months after diagnosis, with anti-TNF administered earlier (P = .044) and in individuals with ocular involvement (P = .033). Previous administration of colchicine was more frequent in patients treated with APR (P = .035). Anti-TNF treatment duration was longer compared to others bDMARDs (P = .011). Male patients exhibited a better retention rate for every bDMARD (P = .001), while there were no differences according to type of bDMARD (P = .554) or previous use of cDMARDs (P = .471). Treatment with bDMARDs resulted in a significant reduction in disease activity (92.7% vs. 44.4%, P < .001). Daily prednisone dose was significantly reduced with IFX (10 [5-21.25] vs. 5 [0-10], P = .015), while no differences were noted in acute phase reactants. Primary failure was observed in 11.3% of cases, while secondary in 24.5%. Discontinuation of bDMARDs was due to intolerance (3.7%), remission (3.7%) and adverse events (15.1%).

Conclusions: bDMARDs treatment is effective and its retention rate is affected by female sex, but not by concomitant cDMARDs.

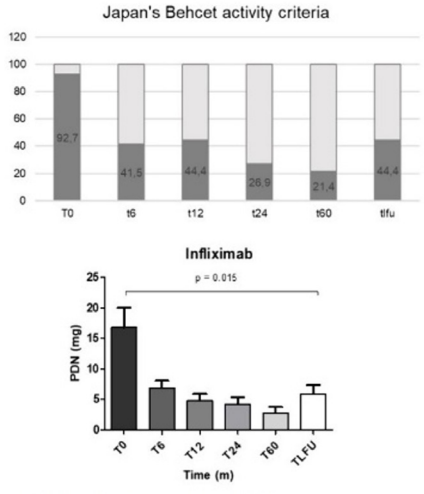

Figure 1. Overall activity according to Japan's Behcet activity criteria and prednisone dose (mg) on Infliximab during follow-up

Figure 1.

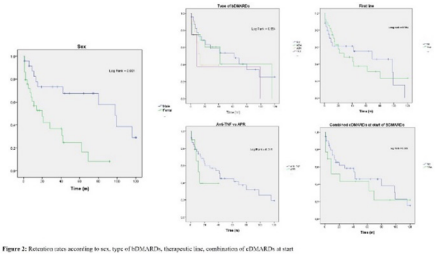

Figure 2.

Table 1: Characteristics of patients (n = 32) at baseline

Characteristics	Value
N° of patients	**32**
Sex F (n, %)	17 (53.1)
Age at diagnosis	34 (27-39)
ISG criteria 1990 (n, %)	13 (40.6)
ICBD criteria 2006 (n, %)	31 (96.9)
Risk factors, n (%)	
HLAB51	15 (60.0)
Comorbidity	19 (59.4)
Manifestations at diagnosis, n (%)	
Ocular involvement	13 (40.6)
Mucous involvement	32 (100)
Oral aphthous ulcers	32 (100)
Genital ulcers	17 (53.1)
Skin lesions	15 (46.9)
Arthritis	19 (59.4)
Epididymitis	0 (0)
Central nervous system	6 (18.8)
Vascular involvement	6 (18.8)
Arterial involvement	2 (6.3)
Venous involvement	6 (18.8)
Gastrointestinal tract	4 (12.5)
Previous treatment (before first biologic), n, %	
Prednisone	26 (92.9)
Colchicine	19 (67.9)
cDMARDs n = 0	6 (21.4)
cDMARDs n = 1	10 (35.7)
cDMARDs n ≥ 2	12 (42.9)
Azathioprine	15 (53.6)
Cyclosporine	6 (21.4)
Methotrexate	12 (42.9)
Salazopyrin	6 (21.4)
Disease duration at first biologic (m)	32.5 (13.25-131.0)
N° of therapeutic line	**53**
Infliximab (n, %)	23 (41.8)
Adalimumab (n, %)	16 (29.1)
Apremilast (n, %)	10 (18.2)
Tocilizumab (n, %)	4 (7.3)
First line bDMARDs, n, %	**28 (50.9)**
Infliximab	15 (65.2)
Adalimumab	8 (50.0)
Apremilast	5 (50.0)
Tocilizumab	0 (0)

bDMARD biologic disease-modifying antirheumatic drug, csDMARD conventional synthetic disease-modifying antirheumatic drug

Figure 3.

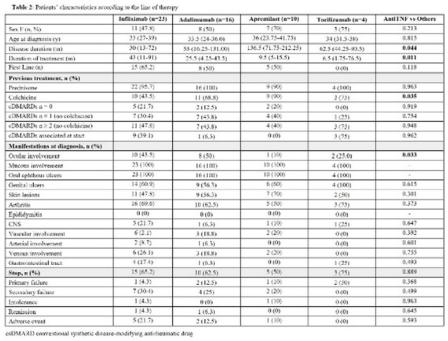

Figure 4.

OD044 / #317

Increased Interferon-Induced Genes Expression in Leukocytes of Adult Individuals with IgA Vascuiitis

Matija Bajželj[1,2], Matjaž Hladnik[2], Nika Boštic[1,3], Snežna Sodin-Šemrl[1,2], Alojzija Hocevar[1,4], Katja Lakota[1,2]

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Background and Aims: The dysregulation of immune cells biological processes in IgA vasculitis (IgAV) is not well understood. Therefore, our objective was to identify molecular pathways that are disrupted in leukocytes of IgAV patients compared to healthy controls (HC).

Methods: Peripheral blood leukocytes were collected from 6 treatment-naive adult IgAV patients at diagnosis (3 patients had IgAV limited to the skin and 3 had additional renal involvement), and 3 age-/sex-matched HC for RNA sequencing analysis. Interferon-induced genes were confirmed on the validation cohort consisted of IgAV patients with renal complications (n = 5), skin-limited disease (n = 6), and age-/sex-matched HC (n = 6) using qRT-PCR.

Results: RNA sequencing of leukocytes from IgAV patients identified an Interferon signaling pathway (p-adj = $3.01e^{-11}$) from Reactome database as differentially expressed in patients with skin-limited disease. 4/6 patients whose samples were used for RNAseq had recent /current infection. To verify the presence of interferon signaling in IgAV, we confirmed differential expression of selected interferon-induced genes by using qRT-PCR. mRNA levels of *IFIT3* (P = .0087), *GBP1* (P = .0087) and *GBP5* (P = .0152) were significantly higher in leukocytes of patients with skin-limited IgAV compared with controls. In patients

with skin-limited disease 3/6 had recent/current infection, whereas in patients with renal disease, 2/5 had recent infection.

Conclusions: Because infections are one of the possible triggers of IgAV, further analyses are needed to clarify whether the activation of the interferon signature found in our study is an integral part of IgAV or only a reflection of a possible (sub)clinical infection.

OD045 / #741

Ocular Manifestations in Juvenile Behçet's Disease: A Registry-Based Analysis

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Background and Aims: This study aims to characterize ocular manifestations of juvenile Behçet's disease (jBD).

Methods: All jBD subjects from the AIDA Network Behçet's disease registry showing ocular manifestations before 18 years were enrolled.

Results: They were 27 children (66.7% males, 45 affected eyes). The median (IQR) age at ocular involvement was 14.2 (4.7) years, with an inverse correlation between age at onset and delay of ocular manifestations (P = .02). Ocular inflammation was bilateral in 66.7% of cases. Uveitis affected 86.7% of eyes (anterior 13.3%, posterior 40%, panuveitis 37.8%), retinal vasculitis 37.8%, other manifestations 19.8%. Later onset (P < .01) and male predominance (P = .03) characterized posterior involvement; female prevalence characterized the anterior one (P = .03). Ocular complications occurred in 51.1% of eyes. Patients with complications had earlier onset (P < .01), more relapses (P = .02) and more prolonged steroidal treatment (P = .02). 74.1% of children received systemic corticosteroids, 44.4% azathioprine, 33.3% cyclosporin A, 22.2% methotrexate, 63% adalimumab and 25.9% infliximab. At the last visit, the median (IQR) BODI was 1.5 (3.3). BODI inversely correlated with age at ocular involvement (P < .01) and was higher with bilateral disease (P = .02). At the last visit, ocular damage was documented in 73.3% of eyes. The final median (IQR) BCVA was 1.0 (0.5) and blindness occurred in 15.6% of eyes. In multivariate regression analysis, HLA-B51+ independently predicted a reduction of -0.3 of the final BCVA (P = .01), while the initial BCVA (OR 0.59; P = .01) and posterior synechiae (OR 1.62; P = .01) independently predicted blindness.

Conclusions: Considering the rarity of this condition, our findings may be leveraged for potentially shaping clinical approaches and inspiring future research.

OD046 / #1072

Identification of Two Autoantigens Recognized by Circulating Autoantibodies as Potential Biomarkers for the Diagnosis of Giant Cell Arteritis

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Background and Aims: Giant cell arteritis (GCA) is a large vessel vasculitis of adults older than 50 years. Diagnosis is based on symptoms, physical examination, histopathology, blood tests, and imaging studies. It is classified as an autoimmune disorder mainly mediated by $CD4^+$ lymphocytes and macrophages, but little is known about antibody presence and autoreactivity. We aimed to identify autoantigens selectively recognized by GCA patients and to assess their potential diagnostic value.

Methods: The presence of autoantibodies was assessed by testing 11 sera of GCA patients (GCA sera) on a human protein array (>11,000 proteins), compared to 28 sera of age/sex matched healthy controls. Autoantigens selectively recognized by GCA sera, as judged by Mean Fluorescence Intensity (MFI) analysis, were validated by ELISA in expanded cohort of GCA sera (44) and Takayasu (TAK) sera (7) as a control large vessel vasculitis of young adults.

Results: Five of 59 autoantigens selectively recognized by GCA sera on the array had the highest frequency and MFI values. Two of the 5 autoantigens were also confirmed using ELISA: VSIG10L (V-set and immunoglobulin domain containing 10 like) and DCBLD1 (Discoidin). VSIG10L was positive in 25/44 patients (57%), DCBLD1 was positive in 19/44 patients (43%). Among 25 patients positive for VSIG10L, 13 (52%) also had antibodies against DCBLD1. Only 1/7 TAK sera displayed a borderline reactivity against the two proteins. Figure: GCA reactivity with target proteins.

Conclusions: We identified two autoantigens, VSIG10L and DCBLD1, recognized by GCA sera with an overall frequency of 43%-57%. Detection of GCA-specific autoantibodies may represent new and non-invasive diagnostic tools.

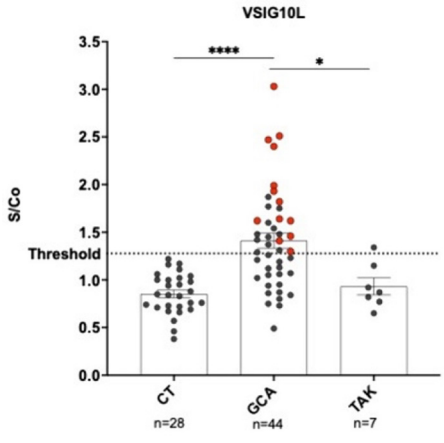

Figure 1.

ORAL DISCUSSIONS 09: SJÖGREN SYNDROME AND NOVEL THERAPIES IN AUTOIMMUNITY & AUTOIMMUNE SYNDROME INDUCED BY ADJUVANTS (SHOENFELD'S SYNDROME)

19-05-2024 12:50 - 13:50

OD047 / #397

High Expression of ICOS on Cd4+ T Lymphocytes in Peripheral Blood and Its Potential for Diagnostic Evaluation of Sjögren's Syndrome

Neža Štucin[1,2], Katja Perdan-Pirkmajer[1,3], Alojzija Hocevar[1,3], Polona Žigon[1,4], Saša Čučnik[1,2]

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[2]University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia
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[4]Famnit, University of Primorska, Koper, Slovenia

Background and Aims: Inducible-T-cell costimulator (ICOS) is a costimulatory receptor expressed on activated CD4+ and CD8+ T lymphocytes. Transcriptomic studies have shown that ICOS is upregulated in peripheral blood cells of patients with primary Sjögren's syndrome (pSS), whereas studies investigating its expression on the surface of T lymphocytes by flow cytometry are scarce. The aim of our study was to evaluate the expression of ICOS on the surface of T lymphocytes and to evaluate its diagnostic value in pSS.

Methods: We analyzed surface expression of ICOS on peripheral lymphocytes by flow cytometry in 7 patients with pSS and 7 healthy controls (HCs). The diagnostic value of ICOS expression was evaluated by receiver operating characteristic (ROC) curve analysis.

Results: A trend of increased percentage of ICOS+ cells (%ICOS+) and an increased surface expression of ICOS (MFI) was observed in the lymphocyte populations studied in patients with pSS. The increase was statistically significant in CD4+ T lymphocytes but not in total T lymphocytes and CD8+ T lymphocytes. The ROC curve analysis showed the best discriminatory ability for the %ICOS+ CD4+ T lymphocytes and the level of ICOS expression (MFI) on CD4+ T lymphocytes (AUC 0.857).

Conclusions: Our results are consistent with the presumed role of ICOS in the pathogenesis of pSS and suggest ICOS surface expression as a potential biomarker in pSS.

Population	Parameter	HC median (IQR)	SjD median (IQR)	p-value	AUC
T Lymphocytes	%ICOS+	10.40 (5.25)	15.20 (11.80)	0.0973	0.776
	MFI	2.94 (0.25)	3.41 (2.05)	0.2086	0.714
CD4+ T Lymphocytes	%ICOS+	21.30 (15.20)	35.10 (15.40)	***0.0262**	**0.857**
	MFI	4.67 (1.47)	5.98 (1.93)	***0.0262**	**0.857**
CD8+ T Lymphocytes	%ICOS+	3.94 (3.02)	7.47 (9.57)	0.0530	0.633
	MFI	2.76 (0.25)	3.05 (1.50)	0.4428	0.816

Figure 1. ICOS expression on lymphocyte populations in peripheral blood of pSS patients and HC and respective AUC values. MFI – mean fluorescence intensity; IQR – interquartile range; AUC – area under the curve.

OD048 / #786

Secretagogue Effect of PDE4 Inhibitor Apremilast on Human Salivary Gland Organoids Obtained From Primary Sjögren's Syndrome Patients

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Background and Aims: Human salivary gland organoids from pSS patients might be useful to analyze disease pathogenesis and test new drugs for glandular manifestations. This study aimed to culture vital salivary gland organoids obtained from salivary gland biopsies of pSS patients; evaluate their morphological and functional features in basal condition and after stimulation with CFTR activator Forskolin and PDE4 inhibitor Apremilast, their in vitro regenerative capacity and the immune-histological resemblance with original tissue.

Methods: Five pSS patients' salivary gland tissues were processed to obtain vital organoids; swelling assay and cell proliferation tests were performed after Forskolin and Apremilast application. Immunochemistry evaluation on original salivary gland tissue and corresponding organoids were performed, and secretomics analysis to assess their functional status.

Results: After application of Forskolin and Apremilast, we observed organoid swelling after 30 minutes, compatible with a positive functional status. In 3 cases, Apremilast induced organoid proliferation. All cases were positive for CK14 and most for CK5. A focal ductal differentiation was found in some cases, highlighted by EMA positivity. All the cases were positive for Amylase; its secretion, and thus functional status of organoids, was confirmed by its high concentration in the culture medium.

Conclusions: From pSS epithelium, differentiated cells and vital functional organoids, which recapitulate the development of original salivary glands, can be obtained. For the first time, the direct stimulating effect of PDE4 inhibitor Apremilast on pSS human salivary organoids is reported, opening new perspectives on targeting oral dryness with drugs that combine secretagogue and immunomodulatory effects.

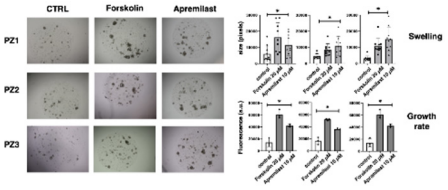

Figure 1.

OD049 / #772

My Eyes Are Burning: Insights into the Cause of Dry Eyes in Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA; Shoenfeld's Syndrome)

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Background and Aims: Many patients with ASIA due to implants complain of dry eyes which may be due to impaired tear production or increased tear evaporation

Methods: Consecutive patients with ASIA due to breast implants (n = 45), Sjogren syndrome (SS) (n = 11), and healthy controls (HC) (n =

19), were included in the study. Participants were tested with a 5-minute Schirmer test and a 5-item questionnaire (the SSSQ test), which distinguishes SS from non-SS patients as validated in the SICCA study.

Results: The 80% of our ASIA patients complained of dry eyes. 33 of 45 (73%) ASIA patients had impaired tear production (Schirmer test <15mm). Severe impairment of tear production as found in SS (Schirmer test < 5) was present in 14/45 (31%). Tear production in SS was abnormal in all patients. Tear production in ASIA was impaired when compared to HC ($P = .005$) but less impaired when compared to SS ($P = .01$). 4 SS patients and 8 ASIA patients had SSSQ scores of 7 or higher ($P = .06$). Immune deficiency was present in 26/45 (58%) of ASIA patients and in none of the SS patients. Anti-SSA was present in all SS and in only 4 ASIA patients.

Conclusions: Breast implant-induced ASIA patients have dry eyes due to impaired tear production but they do not fulfill the classification criteria for Sjogren syndrome. The SSSQ questionnaire was unable to differentiate SS from ASIA. Measurement of IgG/IgG subclass levels, however, may be helpful to differentiate sicca symptoms between ASIA and SS patients.

OD050 / #810

Safety, Immunogenicity and Effectiveness of Varicella Vaccination in Children with Juvenile Idiopathic Arthritis Treated with Anti-Cytokine Therapy

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Background and Aims: Children with juvenile idiopathic arthritis (JIA) treated with anti-cytokine therapy (AIT) are at risk for severe *Varicella zoster* (VZV) infection. Vaccination is the most effective method for protection, but data on live-attenuated vaccines in patients on AIT are scarce. The aim is to prospectively evaluate safety, long-term immunogenicity and effectiveness of varicella vaccination in children with JIA on AIT.

Methods: VZV-naÏve patients with JIA on AIT, who were at risk for varicella infection, had stable disease and normal immunoglobulin levels and lymphocyte populations, were vaccinated against VZV. Adverse events and disease activity were followed after vaccination. VZV-specific humoral and cellular immunity after vaccination were measured by Liaison and intracellular cytokine staining, respectively. Controls were healthy children after varicella vaccination.

Results: To date, 16 patients were vaccinated (12 on anti-TNFα, 3 on anti-IL6 and 1 on anti-IL1 therapy). No serious adverse events, vaccine-strain infections or increase in disease activity occurred after vaccination. Thirteen patients developed VZV-specific humoral immunity and 10/12 patients VZV-specific cellular immunity, which persisted for longer time than humoral immunity. Three patients had mild breakthrough varicella 4 months – 4.5 years after vaccination, and no controls. Another 6 patients had a documented close contact with varicella but did not contract it (mean follow-up time 7.8 ± 3.2 years).

Conclusions: Vaccination against varicella was safe, but not always immunogenic. However, it was effective in 81% of patients on AIT and prevented severe disease in all vaccinated patients. VZV-specific cellular immunity may provide additional insight into the immunogenicity of the vaccine.

OD051 / #986

Comprehensive Analysis of Anti-RO Antibodies and Antiphospholipid Antibodies in Systemic Lupus Erythematosus Patients: Implications for Secondary Sjogren Syndrome and Antiphospholipid Syndrome Coexistence

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Background and Aims: This study aimed to investigate the prevalence of anti-Ro antibodies in systemic lupus erythematosus (SLE) patients and explore their correlation with antibodies from the antiphospholipid antibody panel test. Additionally, we examined the association with secondary Sjogren syndrome and antiphospholipid syndrome.

Methods: We recruited 118 patients diagnosed with SLE and assessed the presence of anti-Ro antibodies in serum samples. Subsequently, we performed an antiphospholipid antibody panel test, including lupus anticoagulant, anti-cardiolipin antibodies, and anti-B2GP1 antibodies. Subgroup analyses were conducted for patients with confirmed secondary Sjogren syndrome and antiphospholipid syndrome. Statistical correlation analyses were employed to examine the relationships between anti-Ro antibodies and antiphospholipid antibodies.

Results: Of the 118 SLE patients, 44.9% tested positive for anti-Ro antibodies. The antiphospholipid antibody panel revealed positive results in 19.5% patients for lupus anticoagulant, 19.5% for anti-cardiolipin antibodies, and 10.2% for anti-B2GP1 antibodies. Secondary Sjogren syndrome was confirmed in 20.3% of patients, and 18.6% met the criteria for antiphospholipid syndrome. Notably, 9.3% patients exhibited coexistence of both secondary Sjogren syndrome and antiphospholipid syndrome. Our statistical analyses demonstrated a significant correlation between anti-Ro antibodies and lupus anticoagulant ($\chi2(4) = 51.536$, $P < .000$), anti-cardiolipin antibodies ($\chi2(4) = 56.859$, $P < .000$), and anti-B2GP1 antibodies ($\chi2(4) = 42.073$, $P < .000$).

Conclusions: This study reveals a notable prevalence of anti-Ro antibodies in SLE patients and their significant correlation with antiphospholipid antibodies. The coexistence of secondary Sjogren syndrome and antiphospholipid syndrome in a subset of patients underscores the intricate nature of autoimmune manifestations in the SLE population.

OD052 / #566

Unabated Type I Interferon Expedites B-Cell Activation and Anti-Drug Antibody Formation During Anti-TNF Therapy

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Background and Aims: Anti-TNFs have become a benchmark in the treatment of numerous autoimmune diseases such as rheumatoid arthritis, Crohn's disease, and psoriasis. However, TNF blockade as a therapy has its limitations. Besides well-documented side effects, anti-TNFs are associated with increased frequencies of anti-drug antibodies (ADA). ADA development represents a crucial adverse event as it often necessitates treatment cessation.

Methods: We have previously shown that TNF blockade shifts the equilibrium of TNF and

type-I interferons (Yin Yang of TNF and type-I IFN) towards an excessive type I IFN response.

Results: Here, we show that a similar pathomechanism underlies B cell-activation and ADA development during anti-TNF treatment. In fact, despite having similar immunogenicity potentials, adalimumab showed significantly higher frequency of ADA as compared to patients receiving ustekinumab. Accordingly, patients treated with the anti-TNF adalimumab but not patients treated with the anti-IL12/23 ustekinumab showed increased serum type-I IFN. Moreover, adalimumab treated patients with detectable ADA but not ADA-negative patients displayed increased serum IFN indicating a pathogenic role for anti-TNF induced type-I IFN production in ADA development. Indeed, addition of anti-TNF to co-cultures of activated pDCs and naive B cells increased type I IFN expression by pDCs and led to a stronger induction of B cell activation and IgG production. In a mouse model, activation of the type-I IFN pathway led to accelerated ADA formation during anti-TNF treatment.

Conclusions: These findings indicate that, in patients receiving anti-TNFs, unabated type I IFN production facilitates ADA formation thereby increasing the risk for secondary loss of efficacy.

ORAL DISCUSSIONS 10: INFECTIONS AND AUTOIMMUNITY

19-05-2024 12:50 - 13:50

OD053 / #473

Memory T Cell and Humoral Responses to SARS-COV2 Spike in Vaccinated and Post-Infected Patients with Systemic Lupus Erythematosus

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Background and Aims: Immune response to vaccines and pathogens remains unclear in patients with systemic lupus erythematosus (SLE).

Methods: To investigate this, a single-center retrospective study was conducted with 47 SLE patients vaccinated against COVID-19, including 13 who subsequently developed an asymptomatic/mild disease.

Results: As compared to controls, post-vaccine response against Spike was reduced in SLE patients when considering both memory T-cells in a whole blood interferon gamma release assay (IGRA-S) and IgG anti-Spike antibody (Ab) responses. The SLE-associated defective IGRA-S response was associated with a serum albumin level below 40 g/L and with the use of glucocorticoids, while a defective IgG anti-Spike Ab response was associated with lower levels of anti-dsDNA and anti-SSA/Ro 52kDa Abs. IGRA-S and IgG anti-Spike responses were independent from SLE activity and clinical phenotype, low complement, hypergammaglobulinemia, and lymphopenia. As compared to controls, SLE patients showed a rapid decay of anti-Spike T-cell memory and stable IgG anti-Spike Ab responses.

Conclusions: Both T cell and humoral anti-Spike responses were independently affected in our SLE patients cohort, which supports the exploration of both responses in the follow-up of SLE patients and especially in those receiving glucocorticoids.

OD054 / #668

The Role of Gut Microbiome in Rheumatoid Arthritis: Fecal Microbiota Transplantation as an Example

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Background and Aims: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by systemic symptoms and joint degeneration. Recent evidence has highlighted the pivotal role of the gut microbiome in the development and progression of RA, primarily through dysbiosis, which is an alteration in gut microbiota composition. Dysbiosis disrupts intestinal permeability, facilitating the movement of bacteria and their products, which subsequently triggers and exacerbates systemic inflammation. This connection between the gut microbiome and RA prompts exploration into potential therapeutic modalities.

Methods: We investigated the profound correlation between the gut microbiome and RA, emphasizing how dysbiosis acts as a trigger for this autoimmune condition. Furthermore, the therapeutic potential of manipulating the gut microbiome to modulate immune responses in RA patients was explored.

Results: Particularly, fecal microbiota transplantation (FMT), a therapeutic strategy involving the transfer of healthy fecal microbiota from a donor to a recipient, has shown promise in treating autoimmune diseases, including RA. Additionally, dietary modifications have been associated with alterations in gut microbiota composition and RA progression, expanding the range of potential interventions.

Conclusions: The findings highlight the critical role of the gut microbiome in the etiology and pathogenesis of RA and its potential as a target for future therapeutic approaches. While FMT stands out as a promising example, the need for further research and well-designed studies is emphasized to establish conclusive recommendations for clinical practice.

OD055 / #822

Autoimmune Disease as a Consequence of Microbiome Function Deficiency

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Background and Aims: Toward the end of the 20th century, a publication by David Strachan alerted the world to the onset of hay fever and asthma in children, especially in families less heavily exposed to environmental microbes. However, rather than an external immune-training agent, it is possible that the fully-functioning microbiome prevents the onset of autoimmune disease. Aim of the study is to emphasise the idea that a range of non-communicable disease, including autoimmune conditions, follows from the failure of the microbiome in the neonate.

Methods: As a hypothesis paper, this work relies only on literature review.

Results: We have developed an evolutionary mechanism to understand the development of the microbiome and its vulnerability to industrialisation. In addition, we have shown how such disruption leads to both autoimmune and adult-onset diseases of the gut-brain axis.

Conclusions: Our analysis points the way to both amelioration and prevention of disease, if key microeukaryotes can be recovered from unaffected populations.

OD056 / #1011

Molecular Mimicry Between SARS-COV-2 Spike Protein and Spermatogenesis-Related Proteins: A Possible Cause of Infertility in COVID-19 Patients?

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Background and Aims: Impaired spermatogenesis has been reported in COVID-19 patients. The purpose of this multicentre study was to investigate the possible impact of SARS-CoV-2 infection on male fertility and determine the potential reasons leading to impaired male reproductive functions.

Methods: A list of ~60 amino acid sequences containing at least five continuous identical residues shared by SARS-CoV-2 Spike glycoprotein and spermatogenesis-linked proteins were identified. Four peptides, named 1 to 4, were synthesized. Sera from acute COVID-19 and long COVID syndrome (LCS), naïve vaccinated subjects, and healthy blood donors were analysed. Immunogenicity and pathogenicity studies were performed by immunizing mice and testing their impact on mouse pregnancy.

Results: Vaccinated subjects didn't develop antibodies reacting with any of selected peptides. Infected patients with acute disease and LCS showed the highest serum reactivity with peptide 4. Antibody levels against peptide 2 were significantly higher in LCS than in acute COVID-19. Peptides 2 and 4-reacting antibodies showed differences according to age and gender of infected patients. Women with LCS presented higher levels of peptide 2 antibodies compared to those who developed acute forms. Women with LCS and chronic fatigue syndrome had higher levels of peptide 2-reacting antibodies than those with idiopathic chronic fatigue syndrome. Peptide 2 injected to male healthy mice induced abnormal fertility in heathy female mice.

Conclusions: Spermatogenesis-related antigen cross-reactive epitopes to SARS-CoV-2 Spike-protein may have adverse consequences on fertility of infected patients. These findings confirm the long-been recognized hypothesis that cross-reactivity between pathogen-related sequences and self-antigens remains an undeniable mechanism that triggers autoimmune responses.

OD057 / #1024

Effect of Human Alpha 1 Antitrypsin Intracellular Toll-Like Receptors in Dendritic Cells

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Background and Aims: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by the loss of tolerance to self-nuclear antigens leading to autoantibody production and multi-organ damage. Accumulating evidence shows that dendritic cells (DCs) activation through Toll-like receptors (TLRs), which interact with self-antigens plays a critical role in SLE pathogenesis. The maturation of TLRs requires proteolytic processing. Alpha 1 antitrypsin (AAT) is a serine protease inhibitor with anti-inflammatory and immunoregulatory properties. However, the effect of AAT on TLR maturation and the signaling is unknown.

Methods: In this study, we tested the effect of human AAT (hAAT) on DC maturation and production of inflammatory cytokines, and on TLR processing.

Results: Our results showed that hAAT inhibited TLR7/8 and TLR9 agonists-induced the expressions of costimulatory molecules CD80, CD86, and MHC-II in DCs. The treatment of hAAT also significantly reduced inflammatory cytokine productions from DCs including interleukin 12 (IL-12), type I interferon (IFN-α), and CXCL-10. Mechanistically, hAAT-treated DCs lowered the expression of interferon signature genes including MX-I, Isg-15, IRF-7, and cytokine expression such as Il-12p40 and TNF-α. Western blot analysis showed that hAAT treatment reduced the active form of TLR9 in DCs. *In vivo* studies in mouse models showed that hAAT attenuated TLR agonist-induced pathogenesis.

Conclusions: These data demonstrated that hAAT inhibited TLR7/8 and TLR9 signaling pathways in DCs, which are critical for lupus development. These findings extended the current knowledge of hAAT biology but also implied an insight into the clinical application of hAAT.

ORAL DISCUSSIONS 11: MULTIPLE SCLEROSIS

19-05-2024 12:50 - 13:50

OD058 / #436

Latent Gammaherpesvirus Infection Licenses Age-Associated B Cells for Pathogenicity in Multiple Sclerosis and Experimental Autoimmune Encephalomyelitis

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Background and Aims: While age-associated B cells (ABCs) are known to expand and persist following viral infection and during autoimmunity, their interactions are yet to be studied together in these contexts. Epstein-Barr virus (EBV) infection has long been implicated in multiple sclerosis (MS), and it is not known whether ABCs could play a role in mediating viral contribution to autoimmunity. Here, we directly compared ABCs during viral infection and autoimmunity using mouse models of EBV, gammaherpesvirus 68 (gHV68), and MS, experimental autoimmune encephalomyelitis (EAE).

Methods: Using flow cytometry and genetic mouse models, we tested our hypothesis.

Results: We observed that splenic ABCs are expanded in a sex-biased manner during both

latent virus infection and EAE, and each event drives the ABC population to opposing phenotypes. We have previously shown that latent gHV68 infection exacerbates EAE and here we show that mice lacking ABCs fail to display gHV68-enhanced disease. We then show that the circulating ABC population is expanded in people with MS and that the ABC phenotype is distinct depending on EBV infection and MS status.

Conclusions: Collectively, these findings indicate that latent viral infection and central nervous system autoimmunity differentially impact the ABC population and suggests that viral infections such as EBV prime ABCs to contribute pathogenically in MS.

OD059 / #642

Are Thymus-Resident Plasma Cells Prognostic Factors of Thymectomy in Patients with Anti-Acetylcholine Receptor Myasthenia Gravis?

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Background and Aims: Thymic abnormalities are common in anti-acetylcholine receptor-positive myasthenia gravis (AChR-MG) patients. Thymic lymphoid hyperplasia (TLH) occurs in 70% of AChR-MG patients, creating a strong argument for a causal role of the thymus in AChR-MG. The presence of ectopic germinal centers containing long living plasma cells (LLPCs) in TLH tie the link to increased autoantibodies levels in patients. Although thymectomy improved clinical outcome in non-thymomatous AChR-MG, a subcohort of patients remains resistant. Thus, there is a need to find reliable biomarkers in AChR-MG to better predict response to therapy. To explore the presence of plasma cells (PC) in the thymus as a candidate MG prognostic marker, we measured different B-cell and PC markers in thymus tissue from AChR-MG patients included in the MGTX trial.

Methods: Thymus sections (n = 23) stained for kappa, lambda and CD138. Positively stained cells were correlated with clinical outcome parameters, including prednisone dose and disease severity clinical scores (qMG, ADL), before and 6 months post-thymectomy. The percentage thymic involution was also correlated with the clinical outcome parameters.

Results: Preliminary results showed no significant correlation between PCs, disease severity and prednisone use. Data analysis based on subcohorts slightly improved correlation coefficients, indicating that the lack of significance may be due to the cohort size. Regression analysis showed no predictive value for any of the markers.

Conclusions: The presence of LLPCs in other tissues may contribute to continued autoantibody production and thus a low treatment response. Further validation of the presence of LLPS, with more accurate markers, within the follicular centers is required.

OD060 / #592

Hock Immunization, an Update of the Experimental Autoimmune Myasthenia Gravis Mouse Model

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Background and Aims: Experimental autoimmune myasthenia gravis (EAMG) is an active-immunisation model that was discovered by coincidence when rabbits injected with purified torpedo acetylcholine receptor (tAChR) to study neuromuscular junction physiology, suddenly developed signs of muscle weakness. In mice, the model requires a bilateral subcutaneous injection of tAChR in the hind footpads and over the scapulas, followed by a booster immunisation (or two) in the thighs and over the scapulas. Unfortunately, footpad injections cause severe discomfort and can lead to progressive debilitation. Instead, hock immunisation has proven to be comparable to footpad immunisation in other models, with the advantage that it does not affect mobility and for that reason can reduce discomfort and therefore be a suitable alternative.

Methods: To study this, 7-week-old female C57BL6/6J (B6) mice were injected bilaterally over the scapula and in the hocks or in the footpads for the primary immunisation. All animals received a booster immunisation 4 weeks later following the standard guidelines. Muscle strength (rack grabbing and inverted mesh), weight, disease score, autoantibody levels, pain sensitivity (Von Frey) and survival were analyzed over 12 weeks. Electrophysiological measurements during curare infusion were included in the terminal experiment.

Results: Preliminary results showed that EAMG animals presented reduced hanging time and increased percentage of decrement amplitude and area before curare infusion. Overall, no significant differences in disease incidence and severity were found between hock and footpad-immunised EAMG animals throughout the experiment.

Conclusions: In conclusion, hock immunisation provides a good refined alternative to reduce footpad-induced discomfort in the EAMG mouse model.

OD061 / #1036

Comparison Between ELISA And Cell-Based Assay for the Serological Diagnosis of Myasthenia Gravis

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Background and Aims: The diagnosis of myasthenia gravis is based on clinical symptoms and signs and can be confirmed by the detection of autoantibodies, such as anti-acetylcholine receptor (AChR) and anti-muscle-specific tyrosine kinase (MuSK), though some cases still remain seronegatives. The aim of this study was to compare ELISA for the assessment of anti-AChR (Euroimmun) and anti-MuSK (IBL International GmbH) antibodies with an indirect immunofluorescence method on transfected cells (BIOCHIP mosaic, Euroimmun) including both epsilon and gamma AChR subunits and MuSK antigens.

Methods: We analyzed 141 routine samples (76 females, mean age 59 years old, range 4-86, and 65 males, mean age 63 years old, 7-89), sent us for suspected myasthenia.

Results: The concordance between ELISA and BIOCHIP was 80.3% and 92.0% for anti-AChR

and anti-MuSK, respectively. Five patients resulted positive for anti-AChR with mosaic kit alone and three of them had myasthenia gravis. Among the twenty-one patients positives with ELISA (mean value 1.58 nmol/L, range 0.57-5.33, limit <0.50) and negatives with BIOCHIP, fourteen did not have myasthenia. Eight patients were found to be positive for anti-MuSK ELISA (mean value 0.7 U/mL, range 0.6-0.9, limit <0.4) but negative with BIOCHIP; of these three did not have myasthenia.

Conclusions: BIOCHIP approach may have potential advantages in terms of clinical specificity as compared to ELISA yielding false positive results mainly within borderline values. The role of BIOCHIP should be defined considering possible clinical significance of semi-quantitative results through sample titration in the monitoring of diseases and the inclusion of a wider panel of antigens, such as LRP4 and agrin.

OD062 / #817

Calcitonin Gene Related Peptide Beyond Migraine: Exploring Its Serum and Cerebrospinal Fluid Levels in Multiple Sclerosis

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Background and Aims: Calcitonin Gene Related Peptide (CGRP) is a neuropeptide ubiquitous in the peripheral and CNS, known for its role in vasodilation and pain transmission during migraine. It has immunomodulatory properties, both anti and pro-inflammatory effects. Multiple sclerosis (MS) is the most common non-traumatic inflammatory demyelinating disease of the CNS resulting in characteristic lesions, that lead to progressive and irreversible disability if not diagnosed and treated promptly. The aim of the study was to correlate CGRP levels, in cerebrospinal fluid (CSF) and serum, with MS progression and short-term disease severity.

Methods: We enrolled 70 patients with different MS forms: Radiological Isolated Syndrome (RSI), Clinical Isolated Syndrome (CIS) and Relapsing-Remitting (RR). We collected serum, CSF, and clinical-radiological data. During the last clinical follow-up expanded disability status score (EDSS), MS severity score (MSSS) and Age-Related MS severity (ARMSS) were assessed. CGRP levels were determined through ELISA, while neurofilaments (NFLs) levels, for neuronal damage assessment, through fluorescence-based immunoassay. None had a history of migraine at diagnosis.

Results: We found positive correlations between serum CGRP levels and the MSSS Score ($r^2 = 0.28$, $P = .0245$) and the ARMSS Score ($r^2 = 0.26$, $P = .0376$). Furthermore, serum and CSF NFLs levels were confirmed as markers of disability in EDSS ($P = .005$ and $P = .002$) and MSSS ($r^2 = 0.27$ and $P = .03$; $r^2 = 0.39$ and $P = .001$).

Conclusions: Taken together our data could suggest a possible role as marker of severity of disease of CGRP.

OD063 / #371

Subclinical and Clinical Markers in Multiple Sclerosis Patients for Prognosis and Personalized Therapy

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Background and Aims: Multiple sclerosis (MS) is complex and multifactorial autoimmune CNS disease affecting nearly three million people worldwide. Human herpesviruses (HHV) – herpes simplex virus (HSV)-1, HSV-2, varicella-zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), HHV-6A, HHV-6B and HHV-7 prevalence is at least 90% of adult population and the viruses are capable to establish lifelong latency. The aim of this study was to clarify the role of HHVs 1 to 7 in relapsing remitting MS (RRMS).

Methods: Determination of HHVs infection markers in peripheral blood mononuclear cell/ cerebrospinal fluid (CSF) samples are performed using multiplex and reverse transcription real-time polymerase chain reactions (PCR). The presence of virus-specific IgG and IgM antibodies are measured using enzyme-linked immunosorbent assays (ELISA).

Results: Preliminary research results of this study display qualitative detection of IgG and IgM class antibodies against HSV-1, HSV-2, VZV, EBV, CMV and HHV-6A/B viral antigens measured by commercially available ELISAs. Viral load semiquantitative results are obtained by Seegene Allplex multiplex real time PCR assay, whereas HHV-6A and HHV-6B are differentiated and quantified by Altona Diagnistics RealStar HHV-6 PCR Kit. Determination of activity phase of HHVs in patients with RRMS are carried out by reverse transcription real-time PCR with QIAGEN RT-PCR Kit.

Conclusions: Preliminary findings suggest a presence of HHV infections in MS patients, with serological evidence and viral load measurements indicating exposure and potential activity of these viruses. Further research is required to confirm these associations and establish their significance in the context of MS.

ORAL DISCUSSIONS 12: AUTOIMMUNITY IN THE CENTRAL NERVOUS SYSTEM

19-05-2024 12:50 - 13:50

OD064 / #376

Application of Machine Learning Algorithms for Identification of Cerebrospinal Fluid Cytokine Expression Phenotypes in Immune-Mediated Neurological Diseases: Focus on Multiple Sclerosis

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Background and Aims: Machine Learning is playing an increasingly important role in healthcare, particularly in diagnostics and therapy. Indeed, it is a promising tool to understand the pathogenetic and diagnostic role of new biomarkers, such as cytokines in immune-mediated neurological diseases. The aim of this study was to identify different cytokine expression phenotypes in a large series of patients with neurological diseases focusing on multiple sclerosis (MS).

Methods: CSF cytokines (IL-1β, IL-6, IL-8, TNF-α, CXCL10, IFN-γ, IL-10, IL-2Rα, BLC/CXCL13, IL-15 and Fractalkine) and light chain neurofilaments (NfL) were evaluated in a cohort of 141 neurological patients referred to the laboratory of immunopathology. Diagnoses were revised by Neurologists and biomarkers were analysed with customized ultrasensitive multiplex ELISA on Ella instrument (Bio-Techne, USA). Unsupervised hierarchical agglomerative clustering (HAC) algorithm was executed to identify phenotypic expression clusters.

Results: The HAC identified 9 clusters, three of which presented the best results in terms of numerosity and pathology distribution, since most diseases were spread in these 3 major expression phenotypes, one hyperinflammatory and the other two mild inflammatory. As concerns MS patients, they were spread in 3 subgroups in which IL-1β, IL-8, CXCL10, IL-15 and Fractalkine were the best discriminative markers. IL-15 has the highest discriminative power in cluster definition and shows the strongest correlation with Fractalkine ($P < .0001$).

Conclusions: Clustering analysis identified 3 different MS phenotypes in which IL-15 and fractalkine seem to play major discriminating roles. Data are preliminary but highly promising since these cytokines were already described in MS as concerns cytotoxic brain damage (IL-15) and remyelination (Fractalkine).

OD065 / #361

Antinuclear Antibodies Profile in 6759 Patients with Psychiatric Disorders

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Background and Aims: The recent paradigm of neuronal surface antibody provides an antigen-specific model linking adaptive autoimmunity to psychopathology. This study aims to explore ANAs potential significance in patients with psychiatric disorders.

Methods: ANAs using linear immunoblot assay were tested in sera from a total of 6759 in-patients between June 2020 and May 2022.

Results: Among the 6759 patients, 458 (6.8%) showed ANAs positivity with a higher rate in females than males (7.5% vs. 5.8%, $P < .05$). Anti-Ro52 (2.4%) was the most common followed by anti-SSB (1.1%) and AMA M2 (1.1%). The ANAs positivity mainly existed in patients diagnosed with schizophrenia (21.6%), depression (17.9%) and bipolar disorder (7.9%). Anti-Ro52, anti-SSA, anti-SSB and other Sjogren's syndrome-related antibodies were mainly distributed in patients with schizophrenia (20.7%), depressive episodes (18.5%), anxiety disorders (8.4%) and bipolar disorder (7.0%). While the AMA-M2 positivity was distributed in schizophrenia (22.5%), Alzheimer's disease (12.7%), depression (11.3%) and bipolar disorder (9.9%). SLE-associated ANAs such as anti-PO, anti-Sm, anti-nRNP and anti-dsDNA were distributed more frequently in patients with depression (27.5%) and schizophrenia (19.6%). Totally 32 ANA positive patients were diagnosed with autoimmune diseases, including 19 SLE cases, 9 autoimmune encephalitis, 3 Sjogren's syndrome including 1 autoimmune hemolytic anemia, and 1 immune enteritis.

Conclusions: ANAs are the common autoantibodies in patients with psychiatric disorders, such as schizophrenia and depression, a part of them combined with autoimmune diseases.

OD066 / #966

Paraneoplastic Ataxia-Ophthalmoplegia Syndrome Associated with Anti-RI Antibodies: A Case Report

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Background and Aims: Paraneoplastic neurological syndromes (PNSs) are rare autoimmune disorders caused by the remote immune-mediated effects of tumor expression. PNSs are caused by a variety of autoantibodies associated with specific tumors and different symptoms. Anti-Ri antibodies, usually associated with breast cancer, often manifest with opsoclonus-myoclonus. We report a case of anti-Ri-associated paraneoplastic ophthalmoplegia-ataxia syndrome in a patient with a breast carcinoma history.

Methods: A 60-year-old woman, with a history of infiltrating ductal breast carcinoma, was admitted to the hospital for the occurrence of subacute symptoms arising in the preceding nine months. The patient showed a severe oculomotion impairment, ataxia, a passive limitation in the mandibular opening, and mild hypophonia.

Results: Laboratory analyses showed strong positivity for anti-Ri antibodies both in serum and in CSF samples. CSF analysis showed mild protein increase with normal cellular count and positivity of BBB damage indices (Link = 0.74; Kappa-index = 10.30; BEL = 0.9). Imaging tests were normal, ruling out a new cancer diagnosis and possible recurrence of breast cancer. Treatment with intravenous immunoglobulins and high-dose intravenous corticosteroid therapy was performed, reporting limited clinical benefit.

Conclusions: The PNSs diagnosis often occurs late, treatment at an early stage may provide a good prognosis. We report a case of anti-Ri associated with an ophthalmoplegia-ataxia syndrome. Although anti-Ri antibodies are frequently associated with ataxia, rarely found in association with oculomotion impairment. However, other cases are similar to our patient in which anti-Ri identification preceded the tumor diagnosis. The laboratory plays a pivotal role, but close collaboration between the clinician and laboratory is essential to evaluate possible follow-up tests based on diagnostic suspicion.

OD067 / #701

The Relevance of Complement Activation in Myasthenia Gravis: A Quantification Study Using the Experimental Passive Transfer Myasthenia Gravis Model

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Background and Aims: In myasthenia gravis (MG), the anti-acetylcholine receptor (anti-AChR) antibody dependent activation of the classical complement pathway triggers the membrane attack complex (MAC) formation at the neuromuscular junction (NMJ). The muscle cell damage results in neuromuscular transmission deficiency, subsequent muscle weakness and fatigability. Passive transfer MG (PTMG) is a commonly used rodent model for MG research. Administration of a monoclonal antibody targeting the rat AChR (mAb35) manifests in characteristic acute muscle weakness. We aimed to characterize the complement deposition at the NMJ in PTMG rats and correlate it to the animals' disease status to investigate and compare the efficiency of (new) treatments such as complement inhibitors in the future.

Methods: Ten-weeks-old female Lewis rats were subcutaneously (s.c.) injected with 40pmol/100g mAb35; control non-MG animals received saline injections. 48 hours after disease induction the animals were euthanized, the muscle tibialis anterior (T.A.) was dissected and frozen. T.A. were used for immunofluorescence staining using anti-MAC and anti-AChR markers, and presynaptic proteins as reference. The intensity of immunofluorescence was quantified; presynaptic markers were used for normalization.

Results: In MG-animals an increase in MAC deposition was observed while AChR levels were reduced compared to non-MG animals.

Conclusions: The increase of complement proteins at the NMJ in MG-animals and the reduction in AChR indicates the activation of the classical complement pathway. The quantification of immunofluorescence raised insights about the relation of AChR reduction and complement deposition and the translation to disease severity in the animals. This methodology may become a useful tool to monitor treatment studies in MG models.

OD068 / #708

FOXP3 Gene Mutation and Decreased Cd4+Cd25+ Regulatory T Cells in Migraine: A Possible Autoimmune Link to Migraine Pathogenesis

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Background and Aims: The exact cause of migraines is uncertain, and ongoing debates link them to the immune system. In our previous clinical studies, we observed reduced levels of regulatory T cells (Tregs) in migraine patients. Furthermore, a preliminary meta-analysis of Treg populations in migraine patients shows significant reductions. Treg reduction and FOXP3 gene mutations are associated with other autoimmune diseases, but their relevance to migraines is unexplored. To bridge this gap, we conducted a focused pilot study on FOXP3 gene mutations in migraine patients.

Methods: A total of 20 participants, including ten cases and ten controls, were recruited for the study. Familial clinical history was collected for pedigree analysis, and blood samples were obtained from each participant for the gene mutation study.

Results: The prevalence of the AG genotype for rs2232365 was found to be 50% among the patients and 20% among the controls (OR = 4.0, CI = 0.54-29.09, 95%, *P* = .17). For rs3761547, the AG genotype was observed in 60% of the patients and 10% of the controls (OR = 13.5, CI = 1.19-152.2, *P* = .03), while the AC genotype was found in 70% of the patients and only 10% of the controls (OR = 21.0, CI = 1.77-248.1, *P* = .01).

Conclusions: Our pilot study indicates a possible association between FOXP3 gene variance and migraine predisposition, specifically, AG and AC genotypes at rs3761547 and rs3761548 SNPs, respectively. Further studies are required to gain a deeper understanding of the role of autoimmunity in migraine.

OD069 / #795

Deposition of the Membrane Attack Complex and IgG Subclasses at the Neuromuscular Junction in LRP4-Antibody-Positive Myasthenia Gravis

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Background and Aims: Involvement of the complement system in the pathogenesis of myasthenia gravis (MG) depends on the IgG subtype. Treatment with complement inhibitors is restricted to acetylcholine receptor (AChR)-antibody positive-MG that mainly belong to the IgG1 subtype with strong capacity for complement activation. The main pathomechanism of LRP4-antibodies (ab) is thought to be the disruption of AChR-clustering at the postsynaptic membrane. However, LRP4-ab have found to be of the IgG1 or IgG2-subtype with different capacities to activate the complement pathway. This study investigated the role of the complement pathway and IgG subclasses in LRP4-ab+-MG at the neuromuscular junction (NMJ) of intercostal muscle biopsies.

Methods: In a cross-sectional study of six patients with LRP4-ab+-MG, external intercostal muscle was biopsied and analyzed by immunohistochemistry, double-immunofluorescence as well as gene expression analyses of complement factors via qPCR. Results were compared to 'disease controls' (AChR-ab-positive MG) and 'non-disease controls' (NDC, scoliosis patients).

Results: Mean age was 41.5 years, 5 (83.3%) were female. Disease severity ranged from MGFA class IIb-V, two patients were double seropositive for LRP4-ab and AChR-ab. In 5 out of 6 patients, C5b-9 (MAC) was identified at the NMJ. IgG subtyping was performed in 4 patients, all evidenced co-localization of MAC with IgG1. Gene expression of complement factors was increased in LRP4-ab+- as well as AChR-ab+-MG ('disease controls) patients compared to NDC.

Conclusions: Our data suggest a crucial role of the complement system in LRP4-ab+-MG. Targeted complement inhibition might therefore be a therapeutic option in LRP4-ab+-MG.

ORAL DISCUSSIONS 13: RHEUMATOID ARTHRITIS

19-05-2024 12:50 - 13:50

OD070 / #324

Novel Antibodies that Predict Failure to Reach Early and Sustained Remission or Low Disease Activity after First-Line Therapy in Rheumatoid Arthritis

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Background and Aims: One-third of RA patients do not respond to first-line treatment (methotrexate and glucocorticoids). Therefore, this study aimed to identify novel antibody biomarkers that can predict lack of response to first-line therapy in RA.

Methods: Two cDNA phage display libraries from RA hip and knee tissues representing RA synovial antigens, were screened for antibody reactivity in baseline sera from RA patients of

the CareRA trial, failing to reach remission at week (w)8. Antibody reactivity to identified University Hasselt (UH)-RA antigens was validated using ELISA in 177 samples. To test if antibody reactivity against a panel of three antigens can predict failure to reach remission or low disease activity (LDA) according to the DAS28CRP/DAS28ESR/CDAI/SDAI, multivariate analyses including age, gender and RF/ACPA status were performed. IHC was carried out on synovial sections from one RA patient using purified human anti-UH-RA antibodies to determine tissue expression of the UH-RA antigens.

Results: A panel of 3 antigens, UH-RA.305/318/329, could discriminate between RA patients not reaching w8 DAS28CRP remission and those that did (31% vs. 15%, *P* = .015). In all patients, baseline anti-UH-RA.305/318/329 antibody reactivity predicted failure to reach w8 DAS28ESR remission (OR = 2.64, *P* = .0116), SDAI/CDAI sustained remission (SDAI = OR = 9.09, *P* = .0038, CDAI = OR = 8.11, *P* = .0063) and sustained DAS28CRP LDA (OR = 2.82, *P* = .008). In RF/ACPA seronegative patients, failure to reach w8 DAS28CRP remission (OR = 13.3, *P* = .0036), w8 SDAI LDA (OR = 9.78, *P* = .0028), and SDAI sustained LDA (OR = 14.4, *P* = .0033) could be predicted by baseline antibody reactivity. Notably, human anti-UH-RA.305/329 antibodies targeted synovial lining in knee synovial tissue.

Conclusions: We identified 3 antibody biomarkers that predict failure to achieve remission/LDA after first-line RA therapy.

OD071 / #960

"Properties of a New Biologic (Ab-IPL-IL-17™) for IL-17-Mediated Diseases: From Preclinical to Clinical Evidence"

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Background and Aims: Interleukin (IL)-17A and IL-17F are key drivers of inflammation that are functionally dysregulated in several immune-mediated inflammatory diseases (IMIDs). Targeting these cytokines has some therapeutic benefits, but issues associated with low therapeutic efficacy and immunogenicity for subgroups of patients or IMIDs reduce their clinical use. Therefore, there is an urgent need to improve the coverage and efficacy of antibodies targeting IL-17 family.

Methods: Here, we identified a bioactive 20 amino acid IL-17A/F-derived peptide (nIL-17™) that mimics, *in vitro* and *in vivo*, the pro-inflammatory actions of the full-length protein. Subsequently, we generated and characterized a novel anti-IL-17 neutralising monoclonal antibody (Ab-IPL-IL-17™).

Results: We demonstrated that nIL-17™ displays more pro-inflammatory effects than parental protein IL-17A, in both NIH-3T3 mouse embryonic fibroblast cell line and human macrophages. Furthermore, nIL-17™ promoted leucocyte recruitment to pre-inflamed tissues. In addition, Ab-IPL-IL-17™ not only was able to reduce significantly the biological effects evoked by IL-17 cytokines but, more importantly, it displayed less off-target effects than the current gold-standard biologics. Finally, we compared the therapeutic efficacy of Ab-IPL-IL-17™ with reference anti-IL-17 antibodies in preclinical murine models and samples from RA and IBD patients. We found that Ab-IPL-IL-17™ could effectively reduce clinical signs of arthritis and neutralise elevated IL-17 levels in IBD patient serum.

Conclusions: Collectively, our preclinical and (in vitro) clinical evidence indicates high efficacy and therapeutic potency of Ab-IPL-IL17™, supporting the rationale for large-scale clinical evaluation of Ab-IPL-IL-17™ in patients with IMIDs.

OD072 / #963

Novel Autoantibodies as Potential Diagnostic Markers for Seronegative Rheumatoid Arthritis

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Background and Aims: Rheumatoid arthritis (RA) is an autoimmune disease characterized by the presence of rheumatoid factor and anti-citrullinated protein antibodies which are present in approximately 70% of patients. Aiming to find novel diagnostic markers particularly for seronegative RA we have used in previous studies a 16k protein array presenting 6371 human proteins for de-novo discovery of potential autoantigens.

Methods: Differentially reactive proteins (n = 742) were used to generate a high density peptide array containing 73 160 peptides including 12 951 citrullinated peptide variants. Out of these a set of 313 differentially reactive peptides was selected for generation of a Luminex bead array and subsequently characterised employing 464 samples from seropositive RA, seronegative RA, disease controls and healthy subjects.

Results: Twenty-five native peptides were recognized by seronegative patients but less frequently by seropositive patients and disease controls. Remarkably, the presence of reactivities against ≥3 peptides proved highly specific for RA. Thus, 13.5% of seronegative patients but only 2.4% of controls showed multiple reactivities resulting in a positive likelihood-ratio of 5.5. As expected, significant reactivity against several citrullinated peptides was preferentially seen in seropositive patients but some peptides were also recognized by a subset of seronegative RA patients. Importantly, 4% of seronegative patients showed ≥3 reactivities whereas such patterns were not observed in disease controls. Thus, altogether almost 20% of seronegative patients showed multiple reactivities against native and/or citrullinated peptides.

Conclusions: The newly identified autoantigens will allow development of a diagnostic assay for identifying a subset of hitherto seronegative RA patients enabling earlier diagnosis and treatment.

OD073 / #1079

Impact of Jak-Stat Inhibitors on T-Cells Subsets in Rheumatoid Arthritis

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Background and Aims: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation that can be treated with the JAK-STAT inhibitors (jakinibs). This work aims to determine the impact of jakinibs in circulating T-cell subsets measured by flow cytometry in RA patients.

Methods: Seventy-five RA patients treated with jakinibs were recruited. Two sex and age

matched groups of 20 healthy donors and 20 RA patients treated with biological treatment were enrolled as controls. Multiparametric flow cytometry was performed in peripheral blood mononuclear cells for T-cell immunophenotyping.

Results: Within the jakinib group, 36 (48.00 %) patients were treated with baricitinib, 13 (17.33%) with tofacitinib, 19 (24.00%) with filgotinib and 8 (10.67%) with upadacitinib; in the RA control group: 11 patients were treated with tocilizumab and 9 with abatacept. The percentage of Effector Memory (EM, CD3+CD4+CD45RA-CD62L+) and Terminally-differentiated CD45RA (TEMRA, CD3+CD4+CD45RA+CD62L-) T-helper cells were increased in patients treated with jakinibs in comparison with healthy and RA controls [(20.51 (15.05-31.13), 10.79 (7.16-16.25), and 12.12 (7.62-17.05); $P < .0001$ and $P < .0001$)] and [1.51 (0.67-3.27), 0.38 (0.14-1.55) and 0.33 (0.14-1.18), $P = .004$ and $P = .002$] respectively. In addition, the percentage of Central Memory T-helper cells (CM, CD3+CD45RA+CD62L+) was decreased in the jakinib group in comparison to healthy and RA controls [38.4 (43.82-45.66), 48.87 (42.07-56.52), and 48.32 (43.82-58.8), $P = .002$ and $P = .001$]. Naïve T-cells (CD3+CD45RA+CD62L+) and regulatory T-cells (CD3+CD4+CD127-CD25+) were analysed but no statistically significant differences were found.

Conclusions: JAK-STAT inhibition shifts T-helper subsets towards a more exhausted phenotype. Further functional studies should be addressed to elucidate the impact of jakinibs in T-cell subsets.

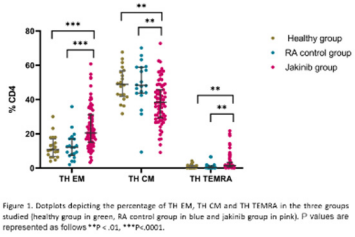

Figure 1. Dotplots depicting the percentage of TH EM, TH CM and TH TEMRA in the three groups studied (healthy group in green, RA control group in blue and jakinib group in pink). P values are represented as follows **P< .01, ***P< .0001.

Figure 1. Dotplots depicting the percentage of TH EM, TH CM and TH TEMRA in the three groups studied (healthy group in green, RA control group in blue and jakinib group in pink). P values are represented as follows: **P< .01, ***P < .0001.

ORAL DISCUSSIONS 14: CYTOKINES AND AUTOIMMUNITY

19-05-2024 12:50 - 13:50

OD075 / #41

Cerebrospinal Fluid Cytokines: Set-Up of Reference Ranges and Clustering Analysis to Identify Different Phenotypic Expression in Immune-Mediated Neurological Disorders

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Background and Aims: Standard cerebrospinal fluid (CSF) analysis may be uninformative in cases of suspected autoimmune neurological disease and specific autoantibodies are rarely identified, while certain CSF cytokines could be of great help in guiding diagnosis and therapy. The aim of this study was to validate reference ranges of cytokines concentration in CSF and identify different phenotypic expression in neurological diseases.

Methods: CSF cytokines ((IL-1β, IL-6, IL-8, TNF-α, CXCL10, IFN-γ, IL-10 and IL-2Rα) were analysed in 201 consecutive patients (110M/91F; age range 0 - 85 years) referred to the laboratory with suspected immune-mediated and/or neurodegenerative diseases from April 2020 to January 2023. Diagnoses were revised by Neurologists and cytokines were measured using customized ultrasensitive multiplex ELISA on Ella instrument (Biotechne, USA). Two clustering models (hierarchical agglomerative and K-means) were employed to identify phenotypic expression.

Results: In the absence of truly normal CSF, we set-up cytokine expression reference ranges using data obtained from all the CSF series, considering values between minimum and 25th percentile as low levels (presumably close to physiologic), between 25th percentile and median as intermediate levels (+), between median and 75th percentile as high levels (++) and above 75th percentile as very high levels (+++). Both the clustering models identified particular cytokine expression profiles in which CXCL10, IL-8 and IL-6 retained the greatest discriminative power.

Conclusions: We set-up CSF cytokines reference ranges suitable for diagnostic purposes in immune-mediated neurologic diseases. Data are preliminary, but clustering analysis appears to be a very promising approach to identify complex expression phenotypes useful for differential diagnosis and targeted therapy.

OD076 / #579

Interaction Between MCP-1 Chemokine, Oxidative Stress, and Antioxidant Status: Possible Pathogenic Role in Primary Biliary Cholangitis

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Background and Aims: Primary biliary cholangitis (PBC) is a slowly progressing, autoimmune liver disease leading to liver failure. Oxidative stress plays a significant role in the pathogenesis of chronic liver diseases. We determined markers of oxidative injury, antioxidant components like glutathione, and MCP-1 concentration, which may be associated with oxidative stress. Our aim was also to evaluate whether the degree of lipid peroxidation, measured by the serum level of 8-isoprostane influences the PBC progression and study the correlation between level 8-isoprostane, MCP-1, and specific autoantibodies.

Methods: We determined MCP-1, 8-isoprostane, aldehydes, 3-nitrotyrosine, myeloperoxidase, and glutathione in the serum of 40 patients with PBC and 20 healthy subjects.

Results: PBC patients had significantly higher levels of aldehydes (MDA and 4-HNE) and superoxide dismutase (SOD) activity compared to healthy controls, $P = .03$ and $P = .2$, respectively. GSH was significantly reduced ($P \leq .001$). Serum 8-isoprostane was elevated in PBC - 238.9 [3.8–500.0] pg/mL as compared to healthy controls - 12.3 [1.6–22.1] pg/mL, $P < .001$. 8-isoprostane and MCP-1 levels increased and glutathione levels decreased gradually with progression from mild fibrosis to cirrhosis.

Conclusions: PBC patients had increased levels of all lipid and protein oxidative injury products compared to controls. A major contribution of oxidant/antioxidant imbalance can provide to the progression of liver injury in PBC, which suggests the involvement of oxidative damage. Our findings suggest an interaction between MCP-1 and oxidative stress in PBC. Interesting results indicate that serum 8-isoprostane might be a candidate marker for the prediction of the degree of liver fibrosis.

OD077 / #958

Dissection of Anti-Inflammatory and Immunomodulatory Activity of Mangifera Indica Extract: From Cd4+Cd45rbhigh T Cells Transfer Model of Colıtıs to Inflammatory Bowel Disease Patients

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Background and Aims: Inflammatory bowel diseases (IBDs) are chronic intestinal disorders mainly characterized by an immune dysregulation. Increasing evidence demonstrates that dietary polyphenols from *Mangifera indica* L. (commonly known as mango) mitigate intestinal inflammation and splenic Treg/Th17 ratio. Therefore, in this study, we aimed to dissect the anti-inflammatory and immunomodulatory activity of this plant extract (here referred as MIE).

Methods: Rag1$^{(-/-)}$ mice, transferred with CD4^{+}CD45RB^{high} T cells, were treated daily with MIE (90% in mangiferin, 10 mg kg^{-1}, p.o.) for 4 weeks. Thereafter, severity of colitis was evaluated coupled with the assessment of the cellular infiltrate's phenotype. Moreover, FITC-dextran assay was employed to determine intestinal permeability in addition to western blot analysis for tight junction proteins. Finally, an analysis of main proinflammatory cytokines was performed on sera from IBD patients stimulated with LPS (0.1 μg ml^{-1}) and treated with MIE (0.03-10 μg ml^{-1}).

Results: Treatment with MIE revealed a reduction of body weight loss and clinical score coupled to a significant modulation of both infiltrated and splenic Th1, Th17 and Treg cells. These data were consistent with the modulation of several pro/anti-inflammatory cytokines on colonic *lamina propria* and a mitigation of the gut permeability/functionality. Interestingly, MIE significantly reduced TNF-α and, in part, IL-17 levels on IBD sera.

Conclusions: Our results demonstrate a beneficial activity of MIE on the immunological perturbance during the onset of colitis and on the systemic inflammatory reaction typical of IBD patients, paving the way for its rationale use as nutraceutical and/or functional food.

OD078 / #973

JAK Inhibitors Improve ATP Production and Mitochondrial Function in Rheumatoid Arthritis: A Pilot Study

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Background and Aims: Rheumatoid arthritis (RA) is a chronic, autoimmune disease associated by inflammation of the synovial tissue. Several studies describe the presence of mitochondrial dysfunction in RA, but few of them follow the dynamics in energy parameters after therapy. The aim of our investigation is to evaluate the direct effect of JAK inhibitors on cellular metabolism in RA patients.

Methods: Peripheral blood mononuclear cells (PBMCs) and plasma from ten newly diagnosed RA patients were isolated before and 6 months after therapy with JAK inhibitors. A real-time metabolic analysis was performed to assess mitochondrial function and cell metabolism in PBMCs.

Results: A significant decrease in proton leak after therapy with JAK inhibitors was found. The increased production of ATP indicates improvement of cellular bioenergetics status.

Conclusions: These findings could be related to the catalytic action of JAK inhibitors on oxidative phosphorylation which corresponds to the amelioration of clinical parameters after treatment. Our study is the first to establish the dynamics of mitochondrial parameters in PBMCs from RA patients before and after *in vivo* therapy with JAK inhibitors.

OD079 / #1031

Endogenous Retroelement Activation is Implicated in IFN-A Production and Anti-CCP Autoantibody Generation in Early Rheumatoid Arthritis

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Background and Aims: Endogenous retroelements (EREs) stimulate type 1 interferon (IFN-I) production but have not been explored as potential interferonogenic triggers in Rheumatoid Arthritis (RA). We investigated ERE expression in early RA (eRA), a period where IFN-I is increased.

Methods: ERE expression in DMARD naïve eRA whole blood (LINE1; RT-PCR) and bulk synovial tissue (LTR5, LINE1, SINE; Nanostring) was examined alongside IFN-α activity. Circulating lymphocyte subsets, including B cell subsets, from eRA patients and early psoriatic arthritis (PsA), were flow cytometrically sorted and similarly examined. Existing established RA and osteoarthritis (OA) synovial single-cell sequencing data was re-interrogated to identify repeat elements, and associations explored.

Results: There was significant co-expression of all ERE classes and *IFNA* in eRA synovial tissue (n = 22, $P < .0001$) and significant positive associations between whole blood LINE1 expression (n = 56) and circulating IFN-α protein ($P = .018$) and anti-CCP titres ($P < .0001$). ERE expression was highest in circulating eRA B cells, particularly naïve B cells compared with PsA, with ERE regulation by SAMDH1 implicated and associations with *IFNA* again observed. Finally, in established RA synovium, LTRs, particularly ERVK, were most increased in RA compared with OA where, for all synovial subsets (monocytes, B cells, T cells and fibroblasts), ERE expression associated with increased IFN-I signalling ($P < .001$).

Conclusions: Peripheral blood and synovial ERE expression is examined for the first time in eRA highlighting both a potential causal relationship between ERE and IFN-I production and an intriguing association with anti-CCP autoantibodies. This suggests EREs may contribute to RA pathophysiology with implications for future novel therapeutic strategies.

ORAL DISCUSSIONS 15: NOVEL AUTOIMMUNE DISEASES

19-05-2024 12:50 - 13:50

OD080 / #743

Rheumatic Immune-Related Adverse Events Induced by Immune Checkpoint Inhibitors: Management and Treatment in an Italian Single-Center Cohort

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Background and Aims: While immune checkpoint inhibitors (ICIs) have revolutionised cancer therapy, their immunomodulatory actions

may lead to immune-related adverse events (irAEs). The purpose of this paper is to describe a single-center cohort of oncologic patients who experienced rheumatic irAEs (Rh-irAEs).

Methods: We prospectively collected oncologic patients treated with ICIs and admitted to Rheumatology Unit of Udine due to Rh-irAEs from January 2019 to September 2023.

Results: A total of 35 patients (22 males,13 females; mean age: 69.8 ± 11.2 years) were collected. The mean time to onset of Rh-irAEs was 15.4 ± 20.4 weeks, with an average severity grade of G2. The main Rh-irAEs observed were musculoskeletal manifestations (30/35), followed by myositis (3/30). Additionally, half of the patients developed antibodies without symptoms. Two-thirds of patients (24/35) discontinued ICI, and all patients required glucocorticoids. A rechallenge was attempted in 7 patients, with recurrences of Rh-irAEs in two of them. Among the 35 patients, 27 required additional treatments due to steroid resistance or dependence. Patients with myositis required high-dose intravenous immunoglobulins, one patient required mycophenolate mofetil due to concomitant myocarditis, and the third one began cyclosporine. During the follow-up period, 6 patients achieved oncological response (3 partial and 3 complete), 14 patients experienced tumor progression, and 15 had a stable disease. Overall, 9 patients died, with two of them having myositis and associated myocarditis.

Conclusions: Rh-irAEs often necessitate discontinuation of ICI and treatment with immunosuppressive drugs that might impact the antitumour response. Myocarditis can be life-threatening and Rh-irAEs often evolve into a chronic inflammatory condition.

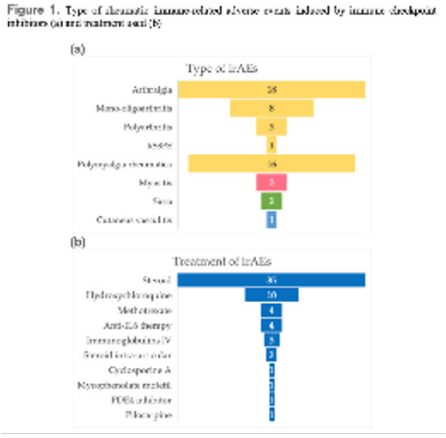

Figure 1. Type of rheumatic immune-related adverse events induced by immune checkpoint inhibitors (a) and treatment used (b).

OD081 / #777

Prevalence of Autoantibodies in Sarcoidosis Patients: A 5-Year Case Revision on A Clinical Laboratory

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Background and Aims: Sarcoidosis is a multisystem granulomatous disease of unknown etiology affecting individuals worldwide. Most researchers agree to the possible autoimmune or immune-mediated core of the disease. Accumulation of non-necrotizing granulomas, lung and other organ fibrosis, accounts for the clinical manifestations that vary widely, depending on organ involvement. Approaching autoantibodies prevalence in sarcoidosis patients, depends as if we expect coexistence of autoimmunity like connective tissue diseases or other like rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, Sjogren's syndrome and spondyloarthropathies or the triggering effect of some of those diseases in sarcoidosis manifestation.Immune function disorders as well as autoantibody production, including rheumatoid factor and antinuclear antibodies, are seen in sarcoidosis and in connective tissue diseases, suggesting a common immunopathogenic mechanism.

Methods: Retrospective evaluation of the association of ECA values and autoantibodies detection by IFI in Hep2 Cells and immunoblotting for SARDS (Euroimmun™) ds-DNA by FEIA (Thermofisher ™) with confirmatory IFI with Crithidia luciliae (Euroimmun™). Liver autoimmune diseases study by IFI in Liver mosaic 9 (Euroimmun™) and liver immunoblotting profile by Euroimmun™. Systemic sclerosis and Myosites autoantibody profile by immunoblotting (Euroimmun™). CCP antibodies and RF evaluation by Elia, Thermofisher ™.

Results: The authors present 5 years revised casuistic from October 2018 to October 2023 as a reference clinical laboratory center in autoimmune diseases diagnosis, focusing on associated ou concomitant autoantibodies appearance in the context of clinical manifestations of sarcoidosis.

Conclusions: The authors present an eventual association between sarcoidosis and multiple autoimmune diseases, revealing the need to careful screen, evaluate and monitor all these patients for concomitant autoimmunity or complicated disease forms.

OD082 / #974

Autoantibodies Targeting G Protein-Coupled Receptors in Sjögren's Syndrome

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Background and Aims: G protein-coupled receptors (GPCR) participate in various pathophysiological processes and were previously described to be involved in different autoimmune diseases. In primary Sjögren's Syndrome (pSS), autoantibodies against muscarinic acetylcholine receptor 3 (M3) may impair secretion of saliva and tears in exocrine glands and neural transmission in gastrointestinal tract. We aimed to investigate the role of autoantibodies targeting other GPCRs in pSS, in particular to simplify diagnostic procedures in pSS patients lacking Ro/SSA autoantibodies.

Methods: IgG autoantibodies against angiotensin receptor (AT1R), endothelin receptor (ETAR), adrenergic receptors (α1AR, α2AR, β1AR, β2AR), muscarinic receptors (M1-M5) and the chemokine receptor CXCR3 were measured by ELISA in pSS (n = 347) using commercially available kits (CellTrend GmbH, Luckenwalde, Germany), and were compared to healthy individuals (HC, n ≤ 50) and patients with other rheumatic diseases (AID, n≤67), including Rheumatoid Arthritis and Systemic Lupus Erythematosus.

Results: IgG antibodies against the M1-M5 and CXCR3 were significantly increased ($P \leq .05$) in pSS compared to HC. These GPCR-autoantibodies were identified in up to 43% of all pSS patients and in up to 33% of pSS patients lacking anti-Ro/SSA (n = 99). Anti-M1, anti-M2, anti-M4 and anti-CXCR3 were also significantly associated with pSS when comparing with other AID. Additionally, reactivity of GPCR-autoantibodies may correlate with disease characteristics, such as neurological involvement.

Conclusions: Autoantibodies against the muscarinic receptors (M1-M5) and the chemokine receptor CXCR3 are associated with pSS including its Ro/SSA negative subset. These autoantibodies could be helpful in diagnosing this subset of pSS patients and may have pathogenic

relevance since they are associated with few disease manifestations.

OD083 / #976

Exploring the Role of Environmental Exposure in the Causality of Chronic Illness and Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/ CFS)

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Background and Aims: The accumulation of toxic substances in the body induces disease through several distinct mechanisms. The case study of a patient with ME/CFS and a history of exposure to environmental pollutants describes the need for an environmental evaluation during the workup of complex multisystem disorders.

Methods: A 66-year-old male with ME/CFS and a 10-year history of pseudodementia presented to the clinic with chronic fatigue, muscle and joint pain, severe post-exertional malaise, and cognitive decline. The patient also revealed disordered sleep and orthostatic intolerance. The fatigue assessment scores placed his physical function well below average compared to the general population. A workup confirmed environmental exposure with extremely high Arsenic level of 1329 ug/24 hr, Mercury 25 ug/24 hr, Aluminum 125 ug/24 hr, and abnormal levels of trichothecene and gliotoxin groups of mycotoxins in urine.

Results: The treatment was focused on gentle chelation via dietary modifications and nutraceuticals to strengthen the patient's antioxidative and detox capacity. The patient improved his symptoms shortly after starting treatment, particularly fatigue and cognitive symptoms.

Conclusions: Extrinsic toxins like asbestos, benzenes, pesticides, persistent organic pollutants, molds, food additives, and intrinsic toxins produced from the digestive process, intestinal dysbiosis, yeasts, fungi, and parasites can upregulate inflammatory processes and lead to a greater intensity of neurological symptoms. This case study highlights potential dangers associated with exposure to mixed molds, heavy metals, and other environmental pollutants, leading to many symptoms involving multiple body systems and may cause a debilitating chronic disease.

OD084 / #997

Chronic Pain as an Autoimmune Disease

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Background and Aims: Autoimmune diseases occur with greater frequency in women, with a parallel sexually dimorphic trend reported in sufferers of chronic pain. In females, the immune system may be continuously "primed", potentially due to the presence of two X chromosomes, each bearing a plethora of genes involved in immune responsiveness. Estradiol is both neuroprotective and neurodegenerative, with reproductive cycle and age-dependent outcomes. Modulating immune cells could therefore be a means to promote nerve recovery, with sex-specific outcomes. Understanding biological sex differences that maintain, or fail to maintain, neuroimmune homeostasis may inform selection of specific treatment regimens for women or men for chronic pain management.

Methods: After 14 consecutive days of intraperitoneal CBDA-ME administration at 0.01, 0.1 and 1 $\mu g \cdot kg^{-1}$, commencing 1 day after surgically implanting a sciatic nerve-constricting cuff to induce NEP, the anti-nociceptive efficacy of this cannabinoid was assessed in male and female Sprague–Dawley rats relative to vehicle-treated counterparts. In females, 2 and 4 $\mu g \cdot kg^{-1}$ daily doses of CBDA-ME were also evaluated. Behavioural tests were performed for hind paw mechanical and thermal withdrawal thresholds once a week for 8 weeks. At endpoint, in vivo electrophysiological recordings were obtained to characterize soma threshold changes in primary sensory neurons.

Results: In males, CBDA-ME elicited a significant concentration-dependent chronic anti-hyperalgesic effect, also influencing both nociceptive and non-nociceptive mechanoreceptors, which were not observed in females at any of the concentrations tested.

Conclusions: Initiating treatment of a peripheral nerve injury with CBDA-ME at an early stage post-surgery provides anti-nociception in males, warranting further investigation into potential sexual dimorphisms underlying this response.

ORAL DISCUSSIONS 16: NOVEL APPROACHES TO HANDLE AUTOIMMUNE DISEASES

19-05-2024 12:50 - 13:50

OD085 / #266

The Metabolic Effects of Semaphorin3A on Human T Cells During Homeostasis and Immune-Mediated Diseases

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***Background and Aims*:** Semaphorin3A (sema3A) is a regulatory immune protein found to be expressed and secreted from on T and B regulatory cells. The effect of Sema3A on T and B cells in the metabolic level has not yet been studied. The aims of this study were to understand how Sema3A affects glycolysis and OXPHOS and to understand how Sema3A affects the PI3K-AKT-mTORC1 axis in activated T cells.

Methods: Mitochondrial and glycolysis stress tests were used to investigate Sema3A's effect on OXPHOS and glycolysis, in healthy and rheumatoid arthritis patients. Mass Spectrometry was used in order to understand how Sema3A effects different metabolites' production during glycolysis. Glucose uptake, ATP production and Fatty Acid Oxidation (FAO) were evaluated using glucose assay, ATP determination and Fatty Acid Oxidation assay kits, respectively. Western blot analysis was used to investigate Sema3A's effect on the AKT-mTORC1 pathway.

Results: Sema3A downregulates OXPHOS and glycolysis in activated T cells in both rheumatoid arthritis patients and healthy control. In addition, Sema3A downregulates glucose uptake as well as lactate and pyruvate production, leading to the reduction of ATP production. Furthermore, Sema3A inhibits the phosphorylation of both AKT and mTORC1. Finally, Sema3A upregulates FAO in activated T cells.

Conclusions: Sema3A downregulates glycolysis by direct inhibition of AKT and mTOR phosphorylation which leads to the reduction of glucose consumption and the inhibition of the glycolytic pathway and its byproducts. As a result, ATP is downregulated as well. Activated T cells treated with Sema3A undergo metabolic reprogramming and switch to FAO as an alternative pathway to insure their survival.

OD086 / #665

Update on the Emerging Application of Fecal Microbiota Transplantation in Autoimmune Diseases

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Background and Aims: The gut microbiota dysbiosis has been attributed to play a crucial role in the development and progression of several autoimmune diseases, such as inflammatory bowel disease, autoimmune thyroid and liver diseases, systemic lupus erythematosus, and type 1 diabetes mellitus, among others. Nevertheless, Fecal microbiota transplantation (FMT) has only been recently studied as a valuable tool to provide a better understanding of the role of microbiome in the pathogenesis of autoimmune diseases, besides being a possible valuable method to treat autoimmune diseases.

Methods: Fecal microbiota transplantation is a procedure referring to transferring the fecal microbial material from a healthy donor's gut containing microorganisms responsible for immune balance to the gut of a patient with autoimmune disease. The procedure is performed therapeutically to restructure and repopulate the microbiome of the host with beneficial microbes in an aim to combating certain illnesses.

Results: In our paper, we will be providing an overview of more than 12 autoimmune diseases where FMT was performed, and promising outcomes were documented. Furthermore, proposed mechanisms of actions leading to a specific change in the composition of gut microbiota found in selected autoimmune disorders have been discussed.

Conclusions: This extensive review will be a valuable tool to understand FMT from a wide view and to present many newer applications specifically in autoimmune diseases.

OD087 / #675

Treatment with Immune Checkpoint Inhibitors and Immune-Related Adverse Events

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Background and Aims: A new therapeutic approach against cancer is based on the use of immune checkpoint inhibitors (ICI). Different clinical trials are ongoing on patients with different types of tumor, that show promising results. These drugs are monoclonal antibodies (mAbs) that act against immune checkpoints allowing the immune system to react against tumor cells, such as: Ipilimumab against CTLA-4 placed on T cell surface; nivolumab, pembrolizumab, and cemiplimab against PD-1 found on immune cells; durvalumab, atezolizumab, and avelumab acting against PD-L1 on tumor cells and on macrophage; or relatlimab whose target is LAG-3 on immune cells. The immune-related adverse events (irAEs) caused by ICIs are different from those caused by chemotherapies.

Methods: We have performed a review of the literature on Pubmed by using keywords such as immune checkpoint inhibitors, cancer immunotherapy or endocrine disorders.

Results: Thyroid dysfunctions, hypophysitis, type 1 diabetes mellitus and adrenalitis are the most common endocrine irAEs. Thyroid dysfunctions are mainly associated to anti-PD-1 mAb, whereas hypophysitis mostly to an anti-CTLA-4 treatment. Type 1 diabetes mellitus and adrenalitis are rare irAEs. The combination of anti-CTLA-4 plus anti-PD-1/PD-L1, or anti-LAG-3 plus anti-PD-1 could increase the risk and prevalence of endocrine irAEs.

Conclusions: ICIs are promising therapies for the treatment of cancer, but can also cause mild to fatal irAEs. Therefore more investigations are necessary for a better understand of the mechanisms at the basis of the induced endocrine irAEs, and for a better management of these disorders.

OD088 / #740

MRNA Technology for the Development of Car T Cells Targeting Fibrotic Diseases

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***Background and Aims*:** Engineered T cells expressing chimeric antigen receptors (CARs) have already been proven to be an effective treatment in cancer immunotherapy. For this reason, recent research approaches are investigating the use of CAR T cell therapies in non-malignant immune-mediated diseases such as infectious diseases, and autoimmune or fibrotic diseases. Fibrotic diseases are characterized by the overgrowth, hardening, and/or scarring of various tissues caused by excessive deposition of extracellular matrix components. The main cellular mediators of fibrotic diseases are activated fibroblasts, which express the surface antigen "fibroblast activation protein" (FAP). In this project, we aim to generate transient anti-FAP CAR T-Cell targeting activated fibroblasts for the treatment of fibrotic diseases.

Methods: Most CAR-T cells in development are based on stable genetic modification by viral vectors. An alternative to stable genetic modification is the transient modification of cells by introducing an mRNA encoding the CAR protein into the cells. mRNA-based CAR cell therapies thus offer the possibility of a safe and pharmacokinetically controllable immunotherapy.

Results: The work includes the screening of various aFAP CAR constructs and the optimization of the aFAP CAR mRNA for prolonged CAR expression and reduced immunogenicity. In addition, novel image-based cytotoxicity assays using live cell microscopy have been developed, providing new insights into the kinetics of CAR T cell killing.

Conclusions: Our mRNA-based aFAP CAR-T cells are able to effectively kill activated fibroblasts. In the future, it is conceivable to produce further mRNA-based transient CAR-T cells to combat other non-malignant diseases or autoimmune diseases such as rheumatoid arthritis or lupus erythematosus.

OD089 / #916

Anti-RO and Anti-LA Seropositivity Is Associated with Increased Rates of Ischemic Heart Disease in Adults- Results from a Large Population-Based Study

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[7]Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva, Israel
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Background and Aims: Emerging evidence suggests an arrhythmogenic effect of Anti-Ro/SSA (anti-Ro) and anti-La/SSB (anti-La) antibodies in adults, potentially involving a subclinical intracardiac inflammatory process. Despite the established association between inflammation and ischemic heart disease (IHD), it is noteworthy that as of now no study has delved into the potential link between these antibodies and IHD. This population-based study aimed to examine the association between anti-Ro/La seropositivity and IHD in the general adult population.

Methods: We conducted a retrospective study using electronic medical records from the largest health maintenance organization in Israel. Patients with positive serology for either or both anti-Ro and anti-La antibodies were included, along with matched controls. Multivariate logistic regression models were utilized to assess the odds of IHD in seropositive patients compared to controls.

Results: Among 17,231 seropositive patients and 84,368 controls, the rate of IHD was significantly higher in the seropositive group (9.7% vs. 8.1%, OR = 1.23; 95%CI 1.14-1.31; *P* < .001). The association was more pronounced in younger patients [<40 years old (OR = 3.36; 95%CI 1.66-6.82; *P* < .001), 40-49 years old (OR = 1.85; 95%CI 1.26 -2.73; *P* < .01), 50-59 years old (OR = 1.87; 95%CI 1.55-2.26; *P* < .001), 60-69 years old (OR = 1.26; 95%CI 1.11-1.42; *P* < .001), ≥ 70 years old (OR = 1.11; 95%CI 1.03-1.20; *P* < .01)]. As well as in patients with fewer traditional cardiovascular risk-factors (none: OR = 1.29; 95% CI 1.09 to 1.77; *P* < .01, 1-2: OR = 1.30; 95% CI 1.19 to 1.41; *P* < .001, ≥3: OR = 1.09; 95% CI 0.99 to 1.21; *P* = .076).

Conclusions: Our study demonstrates for the first time a positive association between anti-Ro/La seropositivity and IHD in the general adult population, especially among younger individuals with fewer traditional cardiovascular risk factors.

ORAL DISCUSSIONS 17: PEDIATRIC AND AUTOIMMUNITY

20-05-2024 12:50 - 13:50

OD090 / #981

Revolutionizing GRD Diagnosis: Novel Epitopes and Multiparametric Diagnostics to Eliminate Unnecessary Biopsies

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Background and Aims: Autoantibody profiles are a powerful and reliable tool to correlate clinical features and therapeutic outcomes in Gluten-Related Disorders (GRD). The AESKUCARE® Point of Care GRD IgA (GRD-POC) and the AESKUBLOTS® GRD IgA (GRD-BLOT) are novel membrane-bound multiparametric enzyme immunoassays for the overall quantitative determination of total IgA and IgA antibodies in GRDs. Evaluate the performance of two multiparametric novel test systems in a study cohort of pediatric GRDs and compare the results to well-established methods in GRD diagnostics.

Methods: GRD-BLOT and GRD-POC are in-vitro-immunoassays for the simultaneous measurement of human-specific IgA antibodies in GRDs against human tissue transglutaminase (tTG), neo-epitopes of human tTG (tTG-neo), microbial transglutaminase (mTG), neo-epitopes of mTG (mTG-neo), deamidated gliadin-specific peptides (DGP), gliadin, Frazer's fraction, human epidermal transglutaminase (TG3) and total-IgA in heparinized or Na-EDTA venous or capillary whole blood, plasma or serum. Antibody titers were evaluated in a cohort of 50 CD, 5 Morbus Chron, and 15 Ulcerative Colitis pediatric patients. Results were correlated to AESKUSLIDES ® EMA IgA IFA readout, and clinical history of the patients, Receiver-Operating Characteristic (ROC) curves, method agreement, and Pearson correlation were calculated.

Results: Using cut-offs estimated from ROC curves, the highest area under the curve (AUC) of antigens was 0.955 tTG IgA, followed by tTG-neo IgA and mTG-neo IgA (0.955 and 0.907 respectively) on the GRD-BLOT IgA. tTG-neo IgA showed the highest correlation with EMA read out (r^2 = 0.7453, *P* < .001) followed by tTG-IgA and mTG-neo IgA (0.7035, *P* < .001; *P* < .5504, *P* < .001 respectively). Overall method agreement between GRD-BLOT and GRD-POC counting all antigens on the multiparametric tests was >93.4 %. IgA deficiency was detected in 100% agreement with patient history, and the relevant antibodies were determined with respective IgG tests.

Conclusions: The advantage of multiparametric antibody and autoantibody analysis is a time and cost-saving information gain. New, potentially clinically relevant antibodies like mTg-neo can be evaluated more quickly and integrated into routine diagnostics. In conjunction with the patient's medical history, professionals can make rapid therapy recommendations, like e.g., dietary changes or support diagnosing GRDs and avoid unnecessary biopsies, making the POC-GRD and BLOT-GRD a unique tool.

OD091 / #219

Stratification of Pediatric Patients Suspected of Sjögren's Disease by Integrative Machine Learning

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Background and Aims: Childhood Sjögren's disease (cSjD) is a rare disease. This data-driven study with integrative machine learning models stratified patients suspected of cSjD, proposing the novel Florida Scoring System (FSS).

Methods: A rare cohort of 217 patients who visited Pediatric Rheumatology at the University of Florida between January 2018 and March 2022 were enrolled. Following comprehensive evaluations, the diagnosis of cSjD was made following the 2016 ACR/EULAR criteria due to the lack of pediatric criteria. Latent class analysis (LCA) analyzed 196 clinical and laboratory variables stratifying heterogeneous patient classes. Machine learning models ranked variable importance and predict LCA-derived patient classes. Causal graph learning selected key features to build the final FSS.

Results: The LCA model identified three distinct patient groups based on their clinical and laboratory features, including Class I (Highly symptomatic with Positive labs, HP, n = 27), Class II (Highly symptomatic with Negative labs, HN, n=98), and Class III (Mildly symptomatic with Negative labs, MN, n = 92). Machine learning models, including random forest, gradient-boosted decision tree, partial least square discriminatory analysis, LASSO-penal-

ized ordinal regression, and artificial neural network, accurately predicted three classes and ranked variable importance consistently. Causal graphic model discovered key variables for constructing a 3-level FSS. Our analyses revealed salivary gland ultrasonography as a non-invasive alternative to a lip biopsy in young children.

Conclusions: Unprecedented in the field, our study with robust and cross-validated machine learning models applied to the pediatric cohort resulted in a physician-friendly scoring system, which can assist clinical reasoning for long-term monitoring.

OD092 / #705

Long-Term Neurodevelopmental Outcome of Children, Born to Mothers with APS

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Background and Aims: Children of mothers with APS are generally considered healthy, but studies have shown that they are prone to cognitive abnormalities. The aim of this study was to assess long-term neurodevelopmental outcomes in a Slovenian cohort of children of mothers with APS.

Methods: Consecutive children of mothers with APS, referred to the UMC Ljubljana for immunologic evaluation between 2001 and 2023 were included. Data of babies and mothers were recorded. Antiphospholipid antibodies (aPL) were checked at birth and at follow-up. Neurologic and cognitive development was assessed at every visit. In addition, the children were evaluated by a psychologist using general health questionnaire, the Child Behavior Check List and age appropriate Wechsler Intelligence Scale.

Results: A hundred-and-eight children (56 boys) were included. The mean follow-up was 4.5 years (3 months-20 years). None developed SLE, APS or thrombosis. At birth 35.1% had positive aPL. Neurodevelopmental abnormality was detected in 36 % of patients, in 50.1% of those followed for at least 3 years and in 54 % of those followed for at least 6 years. Of the 37 children assessed by psychologist, 13.5 %, exhibited behavioural and emotional abnormalities, 33.3 % had significantly dicrepant cognitive profiles. Elements of ADHD were noted in 36.3%, one third of which was pretem. Speech/verbal abnormalities were detected in 21.2% and 6.1% children had problems with graphomotorics.

Conclusions: Children of mothers with APS are at risk of neurodevelopmental abnormalities, when they reach school-age, in more than 50% of cases. Close follow-up and early interventions would be beneficial.

OD093 / #757

Postnatal Health of Infants Born to Mothers with Autoimmune Diseases when Treated with Hydroxychloroquine

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Background and Aims: The purpose of this retrospective cohort study was to observe the postnatal health in infants born to mothers with autoimmune diseases treated with hydroxychloroquine (HCQ) during pregnancy.

Methods: A total of 312 pregnancies of patients who suffered from different systemic autoimmune diseases were considered. Pregnancy data were collected; a telephone follow-up questionnaire was successfully carried out in 182 infants to detect the long-term pediatric outcome. The women who took hydroxychloroquine during pregnancy were defined as "HCQ group" and were compared to women who did not take hydroxychloroquine, "non-HCQ group".

Results: Higher prevalence of women with multiple maternal diseases was detected in the HCQ group, in comparison to that of non-HCQ group ($P = .0015$). Despite HCQ group consisted of more complicated maternal conditions, the obstetrical and neonatal outcomes were similar between the two groups. Regarding the postnatal health, 40% of infants of HCQ group revealed no pathologies *versus* 25% of the children in non-HCQ group ($P = .0368$).

Conclusions: The observation of a protective role on infants born to mother that took HCQ during pregnancy is an interesting finding that needs better elucidating in prospective long-term studies.

ORAL DISCUSSIONS 18: MECHANISMS IN AUTOIMMUNITY

20-05-2024 12:50 - 13:50

OD094 / #170

Immune Checkpoints Inhibitors and the Epidemiology of Autoimmune Disease, the Impact of COVID-19

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Immune checkpoint inhibitors (ICIs) have been used for years in the field of oncology contributing to better prognosis and survival in previously fatal malignancies. By blocking signals of tumor cells, ICIs inhibit cell activation causing malignant cell death. Among others, cytotoxic T-lymphocyte antigen number 4 (CTLA-4) inhibitor is one of the oldest ICIs, followed by the anti-PD-1 (pembrolizumab and nivolumab) and anti-PD-L1 antibodies (atezolizumab, durvalumab, avelumab). Throughout the years the side effects of ICIs have been extensively reported particularly the immune-related ones. Known collectively as immune-related adverse events (irAEs) of ICIs, irAEs were described in various incidences and severities, and affecting almost every organ system. For instance, hepatitis, colitis, abnormal thyroid function, and central nervous system (CNS) manifestations were all reported. Interestingly, the irAEs were shown to behave differently than the well-known epidemiology of autoimmune diseases. For example, as females are affected more commonly in autoimmune diseases, some in young ages such as lupus, and some in older age like giant cells arteritis; ICIs were suspected to alter these recognized patterns. In fact, while the mechanisms of action of ICIs is based on immune alteration, the concerned link seems understandable. The question if the pandemic of COVID-19 has contributed to this correlation needs to be addressed. The epidemiology of autoimmune diseases under ICIs during the pandemic of COVID-19 is our main topic.

OD095 / #410

Altered Tissue Resident Memory-Regulatory T Cells and Antigen-Specific Regulatory T Cells Compromise Survival of Skin Melanocytes in Generalized Vitiligo

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Background and Aims: Generalized vitiligo (GV) is an autoimmune disorder characterized by loss of functional melanocytes. Altered tissue Resident Memory T (TRMs) and regulatory T cells (Tregs) have been implicated in GV pathogensis. The study was aimed to assess TRM-Tregs and antigen (Ag)-specific Treg cells' suppressive activity and melanocyte survival in GV.

Methods: $CD4^+$/$CD8^+$ TRMs, TRM-Treg cells, and Ag-specific Tregs were isolated from 25 GV patients and 20 controls using Treg/TRM Isolation Kit. TRM cells, Ag-specific Tregs frequencies and cytokines (IL-17, IL-15, TGF-β, IL-10, IFN-γ, Granzyme B, & Perforin) were assessed by flow cytometry, IHC and ELISA kits, respectively. TRM-Tregs & Ag-specific Tregs' suppressive capacity was assessed by BrdU cell proliferation assay.

Results: Percentage of $CD4^+$ & $CD8^+$TRM cells was significantly increased whereas percentage of TRM-Tregs and Ag-specific Tregs were significantly reduced in GV skin compared to controls. IHC analysis revealed significantly high percentage chromogenic intensity of IL-17A and IL-15 whereas reduced percentage chromogenic intensity of TGF-β and IL-10 within Lesional skin of GV patients. Moreover, percentage TRM-Treg and Ag-specific Treg mediated suppression of $CD4^+$ and $CD8^+$TRMs was significantly reduced in GV skin compared to controls. Additionally, percentage of SK-Mel-28 cells proliferation was also significantly reduced in skin of GV patients compared to controls in different co-culture systems alongwith decreased TGF-β and IL-10 levels and increased IFN-γ, Perforin and Granzyme B levels.

Conclusions: The study for the first-time reports that TRM-Tregs & Ag-specific Treg fails to suppress $CD4^+$ & $CD8^+$ TRMs cytotoxic function and proliferation affecting the melanocytes survival, suggesting the role of altered TRM-Tregs & Ag-specific Tregs in pathogenesis and progression of GV.

OD096 / #756

Abnormal Glycosignature of Host Tissue Trigger Pathogenic Recognition Through Gamma Delta T Cells/Il-17a Axis in Autoimmunity

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Background and Aims: Autoimmune diseases are life-threatening disorders with increasing disability. Systemic Lupus Erythematosus (SLE) as many other autoimmune diseases arise when immune stimuli override mechanisms of self-tolerance. Glycans are master regulators of the inflammatory response being important molecules for the discrimination between "self"/"non-self". We here explored whether lupus nephritis (LN) exhibit an altered cellular glycosylation aiming to identify a unique glycosignature that characterizes LN pathogenesis and disclosuring a novel immunopathogenesis mechanism.

Methods: A comprehensive tissue glycomics characterization was performed in a cohort of human biopsy-proven LN clinical samples from SLE patients. A combination of advanced tissue mass spectrometry imaging (MSI); *in situ* glyco-characterization and *ex vivo* glycophenotyping of human kidney biopsies were performed to structurally map the *N*-glycans repertoire in LN samples. Mechanistically, in vitro primary cell cultures were used to teste the immunogenicity of glycobiomarker. Moreover, glycoengineered mice models as well as ex vivo glycoreprograming of SLE kidney fresh biopsies were performed and analyzed by flow cytometry and cytometric bead array.

Results: LN presented a distinctive glycan signature, marked by an increased abundance mannose-enriched glycans (typically found in lower microorganisms). We demonstrated that abnormal exposure of these microbial-associated mannose structures on kidney tissue surfaces triggers recognition by γδT-cells, prompting a pathogenic IL-17a-mediated autoimmune response. Furthermore, metabolic glycoreprogramming of kidney tissue, inhibited γδT-cells from producing IL-17a, effectively controlling disease progression.

Conclusions: Taken together, this work revealed an unique immunological mechanism based in mannose-glycans/γδT-cells/IL-17a axis in SLE immunopathogenesis, proposing glycans as a strategy to reprogram the glyco-metabolic profile of tissues as a next-generation targeted-therapy for autoimmune diseases treatment and prevention.

OD097 / #796

Heterozygous Truncating RC3H1 Mutations Predispose to Systemic Auto-Immunity

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Background and Aims: Our understanding of the molecular mechanisms disrupting immune tolerance remains limited. Identifying monogenic triggers for autoimmune diseases offers vital insights into these complex conditions and is a valuable resource for tailoring personalized treatments. Recently, we provided first evidence for the role of RC3H1 in human immune disease by describing a patient carrying a homozygous truncating RC3H1 mutation afflicted with intellectual disability and relapsing hyperinflammation closely resembling hemophagocytic lymphohistiocytosis. In the present study we aim to characterize

patients with immune dysregulation and autoimmune features harboring heterozygous truncating mutations in RC3H1.

Methods: We identified heterozygous truncating variants in RC3H1 using whole exome sequencing in patients with a suspected monogenic cause of immune dysregulation and autoimmunity. PBMCs and serum from these patients were analyzed using flow-cytometry and proximity extension assay, respectively. The functional defect of the RC3H1 variants was studied using complementation assays in murine knock-out T cells.

Results: Heterozygous truncating RC3H1 mutations segregate with autoimmune disease in 3 unrelated families. Immunoprofiling of the RC3H1 carriers shows dysregulation of known RC3H1 targets such as ICOS and OX40. Complementing RC3H1 knock out murine T cells with the identified variants confirm the inability to regulate canonical RC3H1 targets.

Conclusions: Our comprehensive dataset illustrates that heterozygous truncating mutations in RC3H1 can be singularly attributed as monogenic causes in the realm of human systemic autoimmune disorders—a field traditionally considered multifactorial in etiology. Our findings emphasize the potential for genetic studies in families afflicted by auto-immunity and is a striking example of the uncovered heterogeneity of diseases such as SLE and Sjögren syndrome.

OD098 / #867

Transcriptome Analysis Defines Combinatory Pathway Activity in Keratinocytes Necessary for Split Formation in Pemphigus Vulgaris

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Background and Aims: Pemphigus vulgaris (PV) belongs to the group of autoimmune blistering diseases of the skin and/or mucous membranes. After the loss of tolerance, autoantibodies are produced, which predominantly target either desmoglein 3 (Dsg3) or Dsg1/3. Autoantibodies targeting these proteins disrupt cell-cell-adhesion, leading to blister formation. PV pathogenesis is not known in detail yet, so we here unravel want to unravel the early onset of split formation, focusing on the first steps occurring right after autoantibody binding.

Methods: Here, we study the transcriptome and proteome changes occurring after autoantibody binding and split formation under single-chain variable fragment (scFv) PX43 (directed against Dsg1/3) stimulation in a human skin organ culture (HSOC) model.

Results: Keratinocytes respond within 24 hours with activation of NFκB, JAK-STAT, EGFR/MAPK, and TGFβ, as well as Interferon α/β signaling on the transcriptome and proteome level. Repression of split formation through targeted inhibition of either p38 MAPK, MEK, PIK3, VEGFR, or the NGF receptor TRKA resulted in inhibitor-specific pathway (de-)activation. While NFκB and JAK-STAT remained unaffected with all inhibitors as a general stress response, secondary to split formation, inhibition of p38 MAPK. TRKA or VEGFR inhibition activated upstream WNT signaling, and MEK inhibition downregulated the upstream EGFR/MAPK pathways. PIK3 signaling was negatively affected through PI3K, p38 MAPK, and VEGFR inhibition.

Conclusions: The results hint at different pathways and pathway combinations necessary for PV cell detachment. The results will help to define the clinically relevant transcellular tissue communication code driving tissue remodeling during injury and shedding light on the pre-disease state of PV.

OD099 / #778

Plasma Biomarkers of Neurogenesis Are Increased Among People with HIV After COVID-19

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Background and Aims: The interactions between HIV-1 and SARS-CoV-2 in the CNS remain a threat. Moreover, the long-term outcomes of COVID-19 in people with HIV-1 (PWH) are unknown and require further examination. In the present study, we investigated the longitudinal impact of an existing HIV-1 infection on post-COVID-19 recovery, assessing plasma levels of circulating inflammatory, neurogenesis, and BBB biomarkers.

Methods: Samples from forty-four participants with or without HIV were obtained approximately 10 days after the initial COVID-19 diagnosis (t = 0) and then three (t = 1) and six (t = 2) months later. Biomarkers of blood brain barrier (BBB) and vascular dysfunction, neurogenesis, and inflammatory responses were assessed by multiplex profiling and ELISA.

Results: The majority of inflammatory biomarkers either decreased or remained unchanged over time. The BBB disruption and vascular dysfunction biomarkers (S100β and soluble ICAM1, respectively) increased at t = 1 and then returned to basal levels, suggesting transient alterations. IL-17A (at t = 0) and sICAM-1 (at t = 1), were increased in PWH, whereas IL-9 and TNF-α (both at t = 2) were reduced in PWH compared to people without HIV. Among biomarkers of neurogenesis, eotaxin/CCL11 was upregulated at t = 0 and t = 1, FGF-2 was increased at t = 2, and G-CSF was elevated at all time points studied in PWH when compared to people without HIV.

Conclusions: BBB and vascular dysfunction occurs after COVID-19 and may be implicated in the development of post-COVID conditions. HIV-1 infection may potentiate post COVID-19-induced neuropathology by impairing neurogenesis.

ORAL DISCUSSIONS 19: DIAGNOSTICS IN AUTOIMMUNITY

20-05-2024 12:50 - 13:50

OD100 / #307

Performance Characteristics of a Novel, Fully Automated Multiplexed Immunoassay Microarray for the Serological Qualitative Detection of Eleven Autoantibodies Commonly Found in Connective Tissue Diseases

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Background and Aims: There is a limited offer of fully-automated multiplexed devices for testing autoantibodies associated with connective tissue diseases (CTD). We assessed the performance characteristics of the novel MosaiQ™ AiPlex CTD microarray (AiPlex-CTD), used with the fully-automated MosaiQ system, for simultaneous qualitative detection of eleven autoantibodies commonly found in CTD.

Methods: A comparator study was conducted at Hôpital Pitié-Salpêtrière (Paris, France), using anonymized serum samples, characterized as non-reactive for all analytes (n = 445) or reactive for ≥1 analytes included in the assay (n = 466) with a composite of CE-marked devices, as part of AiPlex-CTD evaluations towards CE mark under IVDR. For dsDNA, samples were reactive by HEp-2000®-IgG-FLUORESCENT-ANA-Ro, (ANA-IFA) (ImmunoConcepts, USA) and Anti-dsDNA-IgG-ELISA (DRG, Germany). For other analytes, samples were reactive by ANA-IFA and FIDIS™-Connective-Profile (FIDIS) (Theradiag, France) or were reactive by ANA-IFA and/or ANAscreen (ANA-ELISA) (ORGENTEC-Diagnostika-GmbH, Germany) but FIDIS non-reactive or equivocal. Non-Reactive samples were characterized with both ANA-IFA and ANA-ELISA.

Results: After discordant analysis, compared with composite comparator results, AiPlex-CTD showed Positive Percentage Agreement (PPA) ranging from 78.4% for SCL-70 to 100% for SS-A 60. Negative Percentage Agreement (NPA) ranged from 97.2% for dsDNA to 100% for Jo-1, SS-B and Sm/RNP. Performance details for each individual analyte are shown in the table.

Conclusions: MosaiQ AiPlex-CTD demonstrated high concordance with compared CE-marked devices, for the automated simultaneous qualitative detection of the eleven autoantibodies included in the assay. This platform has the potential to contribute to the advancement of CTD testing. Further ongoing steps include the addition of other autoantibodies to the microarray and semi-quantification.

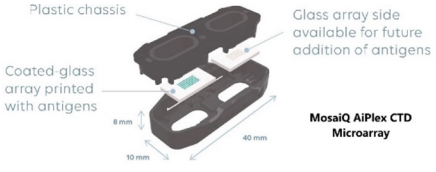

Figure 1.

Table 1. Performance of MosaiQ AiPlex CTD versus Composite Comparator Results

Performance of MosaiQ AiPlex CTD versus Composite Comparator Results

Analyte	Agreement Reactive (PPA) (%) n/N [95% CI]	Agreement Non-Reactive (NPA) (%) n/N [95% CI]	Agreement Overall (OPA) (%) n/N [95% CI]
dsDNA	98.9 172/174 [95.8, 99.8]	97.2 411/423 [95.1, 98.5]	97.7 583/597 [96.1, 98.7]
CENP-B	97.5 78/80 [91.3, 99.7]	99.3 420/423 [97.9, 99.9]	99.0 498/503 [97.7, 99.7]
Jo-1	96.1 28/31 [79.8, 99.8]	100 420/420 [99.1, 100]	99.3 448/451 [98.1, 99.9]
Ribosomal P	98.9 89/90 [94.0, 100]	99.5 422/424 [98.3, 99.9]	99.4 511/514 [98.3, 99.9]
SS-A 60	100 175/175 [97.9, 100]	99.8 422/423 [98.7, 100]	99.8 597/598 [99.1, 100]
TRIM21 (SS-A 52)	99.4 153/154 [96.4, 100]	98.3 417/424 [96.0, 99.3]	98.6 570/578 [97.3, 99.4]
SS-B	91.9 79/92 [77.1, 92.3]	100 424/424 [99.1, 100]	97.5 503/516 [95.7, 98.7]
Sm	88.6 78/88 [80.1, 94.4]	99.8 423/424 [98.7, 100]	97.9 501/512 [96.2, 98.9]
Sm/RNP	95.1 121/127 [90.0, 98.0]	100 425/425 [99.1, 100]	98.8 546/552 [97.7, 99.4]
Scl-70	78.4 29/37 [61.8, 90.2]	98.3 404/411 [96.5, 99.3]	95.7 433/448 [94.5, 98.1]
U1RNP	80.5 103/128 [72.5, 86.8]	98.3 417/424 [96.6, 99.3]	94.2 520/552 [92.3, 96.0]

Two-sided 95% CI using Clopper-Pearson Exact Method. Counts of Indeterminate and Data Reduction Error Results not included in % agreement calculations. Results after retesting of discordant results in the comparator device (applicable for frozen samples). n/N= Samples correct/samples tested. CI: Confidence Interval; NPA: Negative percent agreement; PPA: Positive percent agreement; OPA: Overall percent agreement.

OD101 / #335

Insights Gained from a Decade of Autoantibody Testing Harmonization: Reflections from the UK Neqas External Quality Assurance Program

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Background and Aims: External quality assurance programs are crucial for standardizing laboratory practices and improving autoantibody detection in autoimmune diagnostics. Our study analyzed UK NEQAS EQA reports from 2012 to 2021 to assess harmonization levels and identify areas for improvement.

Methods: We focused on anti-nuclear antibodies (ANA), anti-dsDNA, anti-centromere, and anti-extractable nuclear antigens (ENA) antibody tests.

Results: Despite the rise of solid-phase immunoassays (SPA), most laboratories still prefer indirect immunofluorescence (IIF) on HEp-2 cells for ANA testing (80% in 2012, 79% in 2021). Many laboratories adopted ICAP nomenclature and automated ANA pattern recognition systems for harmonization. SPAs such as fluoroenzyme immunoassay increased slightly (10% in 2012, 12% in 2021 for ANA and from 29% to 39% for ENA), while ELISA dropped from 7% to 3% for ANA and from 36% to 8% for ENA, replaced by chemiluminescence and Luminex methods.

Conclusions: In summary, autoimmune diagnostics have evolved with new tests and technologies, but standardization remains a work in progress, especially for exercises utilizing target antigens not included in the single SPA profile or those not easily recognizable by means of the IIF method (e.g., Jo1). Also the introduction of ICAP nomenclature improved classification within the UK NEQAS scheme. This shift may have contributed to the reduced number of misclassified cytoplasmic patterns that were categorized as ANA negative. Lastly, it cannot be overlooked that the increased standardization may be attributed to the marked reduction in assay manufacturers. In fact while in 2012 more than 20 assay kit manufacturerss were involved, in 2021 95% of participants used only five of these.

OD102 / #343

High-Throughput Proteomics to Identify Novel Biomarkers in Autoimmune Diseases

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***Background and Aims*:** There is a need for novel disease-specific, organ-associated and prognostic biomarkers to improve the management of patients with autoimmune diseases. High-throughput multiplex technologies such as protein arrays and proximity extension assays allow to profile a large number of autoantibodies and proteins and identify new candidate biomarkers to improve patients´ management and clarify the underlying molecular landscape of these diseases.

Methods: Our studies are based on antigen arrays including 42 000 protein fragments representing 18 000 unique human proteins, as well as 2000 full-length versions of secreted proteins from the Human Protein Atlas. We performed proteome-wide screenings and verification of autoantibodies in plasma and serum samples from 281 patients with vasculitis and 83 patients with systemic sclerosis. Moreover, Olink Explore HT technology was used to profile 5300 proteins in 100 plasma samples from vasculitis and 100 from systemic sclerosis patients. Samples were selected from deeply characterised cohorts available through well established international collaborations with expert clinicians.

Results: In ANCA-associated vasculitis, we identified new candidate biomarkers associated to subgroups of patients with specific clinical features and helpful in predicting relapse events. A screening of sclerosis patients allowed to identify novel candidate biomarkers that could possibly improve the diagnosis and subclassification of patients with skin and lung fibrosis in the future.

Conclusions: The combination of clinical expertise and high throughput cutting-edge technology allows to identify new proteins and autoantibodies as candidate biomarkers associated to specific clinical features in autoimmune inflammatory conditions. Moreover, these data can deepen the understanding of mechanisms and etiology in vasculitis and systemic sclerosis.

OD103 / #539

Serum Calprotectin Levels Measured by Chemiluminescence Immunoassay as an Inflammation Biomarker in Rheumatoid and Psoriatic Arthritis in Relation to Other Biochemical and Disease Activity Parameters

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Background and Aims: Several studies reported correlation among ELISA serum calprotectin (cCLP) levels, biochemical inflammatory parameters and disease activity in rheumatoid (RA) and psoriatic (PsA) arthritis. Recently, a chemiluminescence immunoassay (CLIA) for fecal CLP was successfully adapted to measure cCLP. We aimed to assess CLIA cCLP levels as inflammatory and activity marker and to study its relation with other biochemical parameters in RA and PsA patients.

Methods: Eighty-eight subjects were studied: 1) RA patients treated with disease modifying drugs (DMARD) with low or no activity by common clinical indexes (rRA = 11), 2) RA patients candidate to start treatment with biological DMARD (aRA = 23), 3) PsA patients treated with DMARD with low or no activity by common clinical indexes (rPsA = 11), 4) PsA patients candidate to start treatment with biological DMARD (aPsA = 10) and 5) non-disease controls (n = 33). Disease activity scores were DAS28 (RA) and DAPSA (PsA). Different serum and plasma inflammatory parameters were also analyzed. Statistical GraphPadv7.0S and SPSSv26 programs were used.

Results: cCLP concentrations were significantly increased in aRA and aPsA *vs* controls, as well as in aRA *vs* rRA. cCLP levels were directly correlated with other biochemical inflammatory parameters (erythrocyte sedimentation rate, C-reactive protein, Serum Amyloid-A), and DAS28 activity index in RA groups. Area under curve (AUC) of 0.66 ($P = .047$) and 0.92 ($P < .0001$) were obtained for cCLP to classify active/remission RA and PsA patients, using a ROC analysis with DAS28 and DAPSA indexes, respectively.

Conclusions: In RA and PsA patients, cCLP is a suitable inflammation biomarker, well correlated with other biochemical inflammatory parameters and the disease activity degree.

OD104 / #659

ChatGPT and Autoimmunity: A New Wepon in the Battlefield of Knowledge

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Background and Aims: The field of medical research has been always full of innovation and huge leaps revolutionizing the scientific world. In the recent years, we have witnessed this firsthand by the evolution of Artificial Intelligence (AI), with ChatGPT being the most recent example. ChatGPT is a language chat bot which generates human-like texts based on data from the internet. If viewed from a medical point view, ChatGPT has shown capabilities of composing medical texts similar to those depicted by experienced authors, to solve clinical cases, to provide medical solutions, among other fascinating performances. Nevertheless, the value of the results, limitations, and clinical implications still need to be carefully evaluated.

Methods: In our current paper on the role of ChatGPT in clinical medicine, particularly in the field of autoimmunity.

Results: We aimed to illustrate the implication of this technology alongside the latest utilization and limitations.

Conclusions: In addition, we included an expert opinion on the cyber-related aspects of the bot potentially contributing to the risks attributed to its use, alongside proposed defense mechanisms. All of that, while taking into consideration the rapidity of the continuous improvement AI experiences on a daily basis.

OD105 / #653

Tattoo: An Environmental Culprit of Triggering Autoimmune Diseases

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Background and Aims: Although our understanding of autoimmune diseases has taken a huge leap in the past years, there is still a lot to unravel in the interplay of genetic, immunological and environmental factors. While some environmental factors as silica dust, industrial solvents, or dietary components, have been significantly implicated in triggering autoimmune diseases, many others are still not taken into enough consideration.

Methods: For instance, several case reports have reported autoimmune reactions occuring after applying tattoos yet no significant data is available to look in depth into the possibility of such relation. Complications following the application of a tattoo are quite common including various dermal infections, allergic disorders as psoriasis, allergic dermatitis and on the long run even tumors. The composition of tattoo ink with pigments made of substances as cobalt, mercury and aluminum among others raise suspicion of a correlation between tattoos and autoimmune diseases.

Results: In our study, we provide our own insight through the investigation of 120 participants all with tattoos. While some participants were in fact patients with known autoimmune diseases, that were diagnosed after the application of the tattoos that were visiting the clinic to follow-up with their conditions, the others were either newly diagnosed or are healthy with no known medical conditions.

Conclusions: In addition, we review present literature on tattoos, their capabilities and mechanisms in triggering autoimmune disease.

OD106 / #1054

Autoimmune Diseases in Centenarians: A Paradox

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Background and Aims: Age is a crucial risk factor for both the onset and severity of autoimmune diseases (ADs). The aim of this study was to describe the preliminary results of ADs in the COOLCEN, a cohort of centenarians in Colombia. Additionally, the study aimed to review the literature on autoantibodies in centenarians

Methods: Prospective nationwide cohort study. A simple random sampling method was used to identify and conduct face-to-face interviews with centenarians and their relatives. Search was done through PubMed

Results: Fifty centenarians were included, of whom 74% were females, the average age was 100.9 (±1.9) years. 70% of the centenarians had no formal education, whilst 86% had a poor or extremely low economic status. 86% had comorbidities, with essential hypertension being the most prevalent at 86%. 74% were vaccinated against COVID-19. COVID-19 was observed in 16%, with only one requiring emergency assistance without complications. One patient had post-COVID syndrome. 56% had a history of smoking, and 34% had a history of alcohol consumption. There were no patients who had a personal or family history of AD. Nine studies were reviewed (involving 520 centenarians). Despite the occurrence of various autoantibodies, with ACA IgG being the most prevalent (58%), no AD cases were documented.

Conclusions: Although it is inferred that centenarians should exhibit ADs and other types of pathologies related to immunosenescence and immune resilience, this is not supported by the evidence, resulting in a paradox of age-related autoimmunity foundations.

ORAL DISCUSSIONS 20: ENDOCRINE SYSTEM AND THYROID

20-05-2024 12:50 - 13:50

OD107 / #854

Risk Assessment of the Development of Pre-Nosologic Autoimmune Processes in Cosmonauts

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Background and Aims: The specificity of space flight factors is associated with several groups of pathogenic and stressogenic effects on the astronaut's organism, which could be linked to the risk of autoimmune diseases.

Methods: Seven male cosmonauts examined (mean age 56.9 ± 5.6 years, last flight more than 180 days ago) were clinically healthy during biomaterial collection. The following parameters were studied: CRP, IL-6 and -8, TNF-α, angiotensin-converting enzyme, and prolactin. Qualitative determination of antineuronal paraneoplastic autoantibody panels using the EUROLINE Paraneoplastic Neurological Syndromes 12 Ag kit (Euroimmun, Germany) and semi-quantitative determination of a panel of autoantibodies to antigens expressed by nervous tissue using the ELI-N-test-12 diagnostic kit (Medical Research Center "Immunculus", Russia) following the manufacturer's instructions was performed.

Results: Studying immunobiochemical levels in cosmonauts revealed increased TNF-α levels (7.90 (3.96-11.08) pg/mL, with the norm <6 pg/mL). Overexpression of TNF-α is known to be significantly correlated with neuroinflammation. The rest of the immunobiochemical parameters studied were within the physiologic normal range. Some cosmonauts had borderline, weakly positive results for anti-GAD65, anti-SOX1, anti-Yo, and even sharply positive results for anti-Hu. Some cosmonauts had abnormal peaks of individual autoimmune reactivity to individual antigens of nervous tissue (GFAP, β-endorphin, NF-200, serotonin, and glutamate receptors). Similar test results suggest a tendency toward increased autoimmune reactivity.

Conclusions: Studying the spectrum and intensity of autoimmunity and cytokine status allows us to assess the risk of autoimmune processes and neuroinflammatory processes at the prenosologic stage. This restrains the depreciation of labor resources and contributes to the professional longevity of space labor specialists.

OD108 / #538

Transverse Myelitis and COVID-19 Disease in a Patient with Hashimoto's Thyroiditis

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Background and Aims: The SARS-CoV-2 virus has caused the recent pandemic. In some patients the SARS-CoV-2 infection was characterized by neurological manifestations. One of these is transverse myelitis thought to be caused either by the virus itself as the SARS-CoV-2 virus may be neuroinvasive or by an autoimmune reaction due to molecular mimicry between the viral and host proteins. The aim was to describe the case of a male patient with Hashimoto's thyroiditis who developed transverse myelitis in the course of COVID-19 illness.

Methods: The case of a 52 year-old male patient is described who developed transverse myelitis after COVID-19 infection.

Results: The patient presented with Hashitoxicosis approximately 15 years ago. TSH was 0.01 μIU/ml, anti-Tg and anti-TPO antibodies were positive, while a thyroid ultrasonogram revealed loss of homogeneity. Unimazole was administered. During the course of the disease the patient developed hypothyroidism and thyroxine was administered. Approximately a year ago he presented with COVID-19 disease and a rather severe illness. The patient was admitted to a COVID-19 department. During hospitalization he started to feel numbness in the lower extremities and subsequently the lower extremities were paralyzed. Transverse myelitis was diagnosed and prednisolone was administered. Over the course of two months prednisolone was tapered and the patient improved. He is able to walk independently without the use of walking aids.

Conclusions: Transverse myelitis in the course of COVID-19 disease has been described. The disease may be due to the virus itself, as it may be neuroinvasive or to an autoimmune reaction due to molecular mimicry.

OD109 / #645

The Type 1 Diabetes-Associated A946t Single Nucleotide Polymorphism in IFIH1 Results in Increased Basal Type I Interferon Signaling

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Background and Aims: The *IFIH1* gene encodes for melanoma differentiation-associated protein 5 (MDA5), a cytoplasmic dsRNA sensor that detects replication intermediates of RNA viruses. Stimulation of MDA5 by dsRNA mediates a cellular antiviral response, driven by type I interferons (IFNs). Infections Coxsackievirus B (CVB) viruses are implicated as environmental triggers for Type 1 diabetes (T1D). CVB infections often coincide with T1D onset, and an antiviral gene signature is frequently detected in the peripheral blood shortly before autoantibody development. Interestingly, a non-synonymous single nucleotide polymorphism (SNP), rs1990760, in the *IFIH1* gene is identified as a risk factor for T1D. This SNP results in an amino acid change from alanine to threonine at position 946 (A946T) in MDA5, which may have functional consequences on antiviral responses. The objective is to determine how the A946T SNP affects the response to CVB infections and contribute to T1D initiation. We hypothesize that the A946T SNP results in exacerbated MDA5 signaling and increased type I IFNs during CVB infections.

Methods: We infected peripheral blood mononuclear cells from healthy donors with or without the the $IFIH1^{A946T}$ variant and measured subsequent IFN response. We also overexpressed the $IFIH1^{A946T}$ variant in beta-Lox5 cells and a type I IFN reporter cell line.

Results: We found that CVB3 induced type I IFNs and IFN-stimulated gene (ISGs) expression and overexpression of the $IFIH1^{A946T}$ variant led to increased basal expression of type I IFNs and ISGs.

Conclusions: This increased basal expression of type I IFNs may lead to beta-cell stress and hyperreactive immune cells, which contribute to T1D initiation.

OD110 / #636

Immune-Modulatory Effect on Th1 and Th2 Chemokines Secretion by Rapamycin, Mycophenolic Acid, or Glucocorticoids in Retro-Orbital Cells of Patients with Graves' Ophthalmopathy

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Background and Aims: Cytokines and chemokines have a key role in the pathogenesis of Graves' Ophthalmopathy (GO), and cytokines stimulate the T-helper (Th)1 and Th2 chemokines release from retro-orbital cells. We aimed to investigate the effects of rapamycin, mycophenolic acid and/or glucocorticoids on the secretion of Th1 and Th2 chemokines in GO orbital cells.

Methods: We obtained primary cultures of retro-orbital fibroblasts, preadipocytes and myoblasts from 6 GO patients, and we tested the effect of increasing concentrations of rapamycin and/or mycophenolic acid and/or glucocorticoids (alone or in combination) on the secretion of the prototype Th1 (CXCL10) and Th2 (CCL2) chemokines.

Results: In the primary GO retro-orbital cells, CXCL10 was undetectable in the supernatants, and it was induced dose-dependently by interferon (IFN)-gamma, but not by tumor necrosis factor (TNF)-alpha, while their combination had a significant synergistic effect on CXCL10 secretion. On the other side CCL2 was present at low level in basal condition, and it was induced dose-dependently by TNF-alpha (but not by IFN-gamma alone); TNF-alpha+IFN-gamma had a significant synergistic effect on CCL2 release. Adding mycophenolic acid, rapamycin, or glucocorticoids (in a pharmacological range) in presence of IFN-gamma+TNF-alpha, a dose-dependent inhibitory effect on the chemokines release was observed. Furthermore, the combination of mycophenolic acid or rapamycin and/or with glucocorticoids, had a synergistic inhibitory effect on chemokines release.

Conclusions: Our data showed the therapeutic role of mycophenolic acid or rapamycin with glucocorticoids, that could be reached through their immune-modulatory effect on Th1 and Th2 chemokines secretion in orbital cells of GO patients.

OD111 / #797

The Incidence of New Not-Thyroid Autoimmune Disorders in Patients with Graves' Disease

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Background and Aims: No study has evaluated the incidence of new cases of not thyroid autoimmune disease (NTAD) in Graves' disease (GD). In this study, we show the incidence of new cases of NTAD in female GD patients (GDp).

Methods: We have evaluated the appearance of new NTAD in 600 female GDp without previous NTAD in comparison with 300 gender-and age-matched controls with multinodular goiter followed in our unit for ≥2 years.

Results: In this longitudinal study, we have shown a significantly higher incidence ($P < .05$) of new cases of vitiligo, chronic autoimmune gastritis, rheumatoid arthritis, polymyalgia rheumatica, celiac disease, and Sjögren syndrome in comparison to the control group, despite a significantly longer observational period in the control group.

Conclusions: In this study, we first show a higher incidence of new cases of NTAD in female GDp in comparison to the control group. These results suggest that female GDp should be periodically evaluated for NTAD.

OD112 / #407

Thyroid Polyautoimmunity in Spain: Focusing on Celiac Disease and Autoimmune Atrophic Gastritis

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Background and Aims: Autoimmune thyroid disorders (AITD) are one of the most common organ-specific autoimmune diseases. Although AITDs can present as a single AD (autoimmune disease), they frequently coexist with additional ADs, a condition known as polyautoimmunity (PolyA). In fact, polyA in ADs is thought to be most frequently associated with AITD. Our aim is to study the prevalence of polyA in patients with AITDs from our influence area.

Methods: Observational prospective study, including 226 sera from patients with a clinical suspicion of AITD. All patients were tested for tissue transglutaminase (Ttg) IgA (EliA™ Celikey), parietal cells autoantibodies (APCA) (EliA™ Parietal Cells), intrinsic factor autoantibodies (IFA) (EliA™ Intrinsic Factor) and TSH receptor autoantibodies (TRAbs) (EliA™ TSH-R). Clinical records were thoroughly reviewed to identify previous clinical diagnoses of other AITDs.

Results: Out of the 226 patients included a total of 5 individuals were identified as having Celiac Disease (CD), and 3 patients with Autoimmune Atrophic Gastritis. Notably, all clinically diagnosed CD patients suffered from Graves' Disease. Serological results revealed 44 patients with positivity to more than one autoantibody, resulting in 19.4% of latent/overt polyA. APCA was found to be the predominant autoantibody associated with latent polyA.

Conclusions: We should consider polyA in patients diagnosed with AITDs in our area. The definition diagnostic algorithms based on the most prevalent ADs associated with AITD could be the next step to foster early diagnosis and improve patient management.

ORAL DISCUSSIONS 21: PATHOGENESIS OF 1AUTOIMMUNE CONDITION

20-05-2024 12:50 - 13:50

OD113 / #29

Molecular Mimicry Studies Involving SARS-COV-2

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Background and Aims: Since the beginning of COVID-19 pandemic, there had been many studies involving molecular-mimicry as a possible means of the pathogenicity mechanism upon getting infected with SARS-CoV-2. Here we aim to make a discussion of molecular mimicry through the sudies involving SARS-CoV-2.

Methods: The study involves comparative evaluation and general discussion of the literature selected through presentations at the Friday Mosaic of Autoimmunity International Online Meetings and through PubMed literature search.

Results: Literature of interest reveals molecular-mimicry as a possible autoimmunity-related mechanism of SARS-CoV-2 pathogenicity. Molecular mimicry searches in the literature reveals that they are performed with different targets and search algorithms, leading to varying results, not in the sense of a conflict, but in the sense of grasping different aspects. Experimental validations are generally lacking. Yet, although experimental proofs are strong assets, lack of evidence even in presence of experimental work does not necessarily mean that the risk is absent. Experimental studies may not represent the *in vivo* condition and studies on live organisms can lack the organism with a certain genetic susceptibility. Experimental studies may also not reveal a possible reaction merely due to the complexity or stochastic nature of the organismic responses even if the right tools are utilized.

Conclusions: Molecular mimicry-based autoimmunity induction upon SARS-CoV-2 infection is complex. The present literature suggests that it can lead to development of severe illness in susceptible patients even through certain vaccines, which saved the lives of the millions of others. Understanding the underlying mechanisms can lead to effective treatments.

OD114 / #35

Post-Traumatic Stress Disorder as a Potential Autoimmune Condition

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Background and Aims: The association between post-traumatic stress disorder (PTSD) and autoimmunity is a complex interplay mediated by autonomic dysregulation, characterized by attenuated parasympathetic and elevated sympathetic functions. In this review, we investigate how pathological stress levels in PTSD act as key mediators contributing to autonomic dysfunction, thereby leading to autoimmune disorders like systemic lupus erythematosus, rheumatoid arthritis, and type 1 diabetes.

Methods: We conducted a review of the literature, aiming to understand the relationship between autoimmunity and PTSD, with a specific focus on the interplay with the autonomic nervous system.

Results: The findings of this review highlight a bidirectional influence where certain autoimmune diseases can increase the susceptibility to develop PTSD. Furthermore, the overlaps in pathogenesis between fibromyalgia and PTSD reveal stress as a significant shared component, offering new insights into potential therapeutic targets.

Conclusions: The understanding of chronic low-grade inflammation, high concentrations of cytokines, and other inflammatory biomarkers in PTSD patients paves the way for innovative treatment strategies. We propose these factors as potential targets and biomarkers, advocating for their inclusion in PTSD diagnostic criteria. Our review opens new perspectives in understanding the multifaceted relationship between stress, PTSD, and autoimmunity, emphasizing further research needs. This review indicates a need for investigating anti GPCR antibodies in this condition. In light of these findings, we will embark on a targeted research project on anti GPCR antibodies in PTSD and autoimmunity, to uncover underlying mechanisms and therapeutic applications.

OD115 / #228

Lung Alveolar Epithelial Barrier Injury by Electronic Cigarettes and Alcohol Exposure via P2X7R Purinergic Receptor

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Background and Aims: E-Cig use has grown substantially since inception, particularly among adolescents and coincides with alcohol consumption. This study established an *in vitro* model of e-Cig exposure of human lung epithelial (LEpC) exploring the mechanism of AEB injury by e-Cig or ethanol (ETH).

Methods: LEpC were exposed to ETH (100 mM), its main metabolite, acetaldehyde (ALD, 100 mM), or e-Cig coil generated vape (e-liquid nicotine concentrations of 0% or 1.8%) in conditioned media. We investigated e-Cig, ETH or ALD induced mitochondrial impairment (Seahorse assay), Ca^{2+} accumulation, extracellular vesicle (EVs) release, P2X7r expression and ATP content in EVs.

Results: ETH, ALD and e-Cig induced 30-42% reduction in spare respiration (mitochondrial stress). We found 20-30-fold increase in intracellular Ca^{2+} levels in ETH, ALD or e-Cig treated LEpC. ETH, ALD and e-Cig (1.8%) stimulation increased numbers of EVs (2-3-fold) and particle size (20%-30%). P2X7r expression in EVs was increased 6-fold by ETH or e-Cig (1.8%) and 8-fold after ALD stimulation. ATP levels in isolated EVs were increased by ETH (55-fold), ALD (70-fold) and e-Cig (110-fold). To check functional effects, EVs were applied on brain microvascular endothelial cells (BMVEC). EVs from ETH exposed LEpC increased BMVEC Ca^{2+} levels by 2-fold, while ALD and e-Cig (1.8%) EVs escalated BMVEC Ca^{2+} levels 4-fold. P2X7r antagonist significantly reduced all above-mentioned effects after e-Cig, ETH or ALD exposure of LEpC. 0% e-Cig had no effects on functional changes in LEpC.

Conclusions: We uncovered mechanisms of AEB injury by e-Cig and alcohol via mitochondrial dysfunction and P2X7r activation.

OD116 / #44

The Impact of T Cells on Kidney Disease in MRL/LPR Mice: Lessons from a Phenotypic Drift in the Strain

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Background and Aims: Murphy Roths Large/lymphoproliferation (MRL/lpr) mouse model is recognised for mimicking human systemic lupus erythematosus. Mice carrying the *lpr* mutation show a marked acceleration of the disease compared to MRL+/+ mice. They develop systemic autoimmunity, massive lymphadenopathy and splenomegaly associated with proliferation of aberrant T cells, abnormalities in B cells, anti-Smith and anti-dsDNA/chromatin circulating autoantibodies, immune complex glomerulonephritis, and arthritis. In early 2021, an unexpected phenotypic drift was noted in our MRL/lpr in-house colony, periodically revitalised with Jackson Lab's mice. Our investigation focused on differences between the two strains with a particular emphasis on T cells in the kidney.

Methods: Biochemical and cellular assays combined with genetic and pathological analyses were used to compare both MRL/lpr strains.

Results: At cellular level, mutant MRL/lpr mice exhibited reduced counts of leukocytes, total lymphocytes, B and T cells, both peripherally and in kidneys. Mutated mice displayed decreased proteinuria levels with low C3 deposits, and fewer skin lesions; their survival rate was improved. However, serum total IgG and IgG2a levels, and anti-dsDNA IgG titers remained unaffected.

Conclusions: These results confirm the pivotal role of T cells in renal tissue damages and renal failure observed in MRL/lpr mice, but show that their impact on the whole autoimmune phenotype is limited.

OD117 / #416

Association between NOS2 RS2297518 Polymorphism and Lupus Nephritis

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Background and Aims: Systemic lupus erythematosus (SLE) is a chronic, multisystemic, autoimmune disease. Lupus nephritis is a frequent manifestation affecting up to 50% of patients. Studies showed that expression of the iNOS enzyme is increased in the glomeruli of patients suffering from proliferative lupus nephritis. This enzyme is coded by the *NOS2* gene. *NOS2* rs2297518 polymorphism is a missense variant that leads to substituting serine with leucine, leading to increased iNOS activity in A allele carriers. The study aimed to analyze associations between *NOS2* rs2297518 polymorphism and SLE susceptibility and clinical manifestations.

Methods: Our study included 94 SLE patients diagnosed and treated at the Clinic of Allergology and Immunology, University Clinical Center of Serbia, Belgrade, and 128 controls without autoimmune diseases. Genotypisation for *NOS2* rs2297518 polymorphism was performed using TaqMan assays.

Results: Among our patients 6 (6.4%) had AA genotype, 33 (35.1%) carried AG and 55 (58.8%) had GG genotype, while in controls 6 (4.7%) participants had AA genotype, 46(35.9%) carried AG genotype and 76 (59.4%) had GG genotype (p=0.858). The presence of lupus nephritis was recorded in 20 patients, who were A allele carriers more often than patients without lupus nephritis (70% vs. 35%; $P = .005$).

Conclusions: The findings of this study suggest that *NOS2* rs2297518 polymorphism could be associated with renal manifestation in SLE. Further studies in larger populations are needed for a definitive conclusion.

OD118 / #996

ALPHA-1 Antitrypsin for the Control of Autoimmunıty

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Background and Aims: Although the pathogenesis of autoimmune diseases is complex and elusive, inflammation is commonly involved in the development of these diseases. Therefore, anti-inflammatory approaches hold great potential for the treatment of autoimmune diseases. However, long-term control of inflammation is challenging and most of the currently used drugs have side effects. Alpha-1 antitrypsin (AAT) has anti-inflammatory and immune-modulatory functions.

Methods: We have tested the effect of AAT on the control of autoimmunity in several animal models.

Results: We have shown AAT protein and gene therapy prevent and reverse type 1 diabetes (T1D) in mouse models, and delay rheumatoid arthritis (AR) in collagen-induced arthritis (CIA) mouse model. We have recently shown that AAT gene therapy prevents lupus development and extended life span in spontaneous lupus-prone mouse models. Our mechanistic studies have shown that AAT treatment inhibits: (1) dendritic cell (DCs) maturation and functions by inhibiting intracellular toll-like receptors (TLRs) activation, and (2) inflammatory cytokine production by inhibiting NF-kB sig-

naling pathways. Importantly, AAT treatment reduced autoantibody productions in autoimmune disease models.

Conclusions: Our findings extend the current understanding of AAT functions and provide insight into new applications of AAT in the control of autoimmunity.

ORAL DISCUSSIONS 22: GENETICS AND OTHER MECHANISM OF AUTOIMMUNITY

20-05-2024 12:50 - 13:50

OD119 / #564

Celiac Disease Associated HLA: The Double-Edged Sword in COVID-19

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Background and Aims: The SARS-CoV-2 pandemic is still active, although it has changed its course and become less violent and has taken a more chronic course, with the appearance of new mutations in different parts of the world. Many high-risk conditions have been described but fewer protective factors have been evaluated. Interestingly, it appears that CD patients are not more susceptible to COVID-19, compared to the normal population. The hypothesis is that the HLA-DQ 2\8 protects the CD population from attracting SARS-CoV-2 and its short and long-term consequences. The aims were to 1. Explore whether the CD-associated genetic background, namely HLA-DQs, protect them from COVID-19 severity and outcome. 2. To suggest mechanisms to explain HLA-DQ2\8-SARS-CoV-2 cross-talks.

Methods: In the present study, we investigated whether SARS-CoV-2 epitopes can potentially cross-react with human-associated common cold coronaviruses (CCC) and assessed the binding affinity of these epitopes to HLA-DQ 2\8. Using computational methods we examined sequence similarity between SARS-CoV-2 and 4 distinct CCC.

Results: Thirty-seven epitopes of 15mer length that display at least 67% identity and exhibit significant binding affinity to HLA-DQ 2\8, were identified. Various mechanisms are suggested to explain such protection.

Conclusions: If substantiated, it might increase our understanding of the gene-environment enigma and viral-host autoimmune relationship and open new therapeutic strategies to fight the ongoing SARS-CoV-2 pandemic. Interestingly, SARS-CoV-2 is considered an auto-immunogenic virus, but, on contrary, its susceptible genes are protective against COVID-19. This controversy deserves much more studies.

OD120 / #476

Toll-Like Receptor (TLR) 7 Variants Associate with Disease Activity State in Patients with Juvenile-Onset Systemic Lupus Erythematosus

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Background and Aims: Among the immune-related genes on the X chromosome, the Toll-like receptor (TLR)-7 locus is centrally involved in the activation of the type I interferon pathway, a key pathogenic pathway in systemic lupus erythematosus (SLE).

Methods: In order to investigate genetic variability of TLR-7 (X: p22; 23.3 kb), 319 juvenile (j) SLE patients were included (51 boys, 268 girls) from the UK jSLE Cohort Study. Using new generation sequencing approaches, identified variants were associated with demographic and clinical features.

Results: Damaging TLR7 variants, with stops codons present in the endosomal domain, were recorded in 2/319 (0.6%) patients from both sexes. Three SNPs with minor allele frequencies ≥5%, rs2302267 (n.-20T>G-promoter), rs179008 (Gln11Leu), and rs3853839 (c.*881C>G-3'UTR) were retrieved. When compared to publicly available ethnic cohort data, SLE risk associated with rs3853839 GC/GG was increased in female African/Caribbean (OR: 1.8; 95% CI: 1.2-2.8), while reduced in female European jSLE patients (OR: 0.5; 95% CI: 0.4-0.7). Finally, the non-random TT-CC haplotype resulting from negative linkage disequilibrium between the rs79008 T and the rs3853839 C alleles was associated with increased disease activity (pBILAG-2004), constitutional and musculoskeletal involvement.

Conclusions: In conclusion, TLR7 variants contribute to jSLE risk, and some predict organ domain involvement. Findings require to be confirmed in larger independent cohorts.

OD121 / #629

Genetic Variants of Vitamın D Genes in Systemic Lupus Erythematosus: Relationship of RS2282679 GC SNV with Risk of Hypovitaminosis D, Clinical, and Renal Activity

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Background and Aims: Systemic lupus erythematosus (SLE) is the prototypical autoimmune disease where vitamin D deficiency is associated with higher clinical disease activity. This study aimed to evaluate the association of 5 single nucleotide variants (SNVs) in key genes of vitamin D metabolism with disease susceptibility, clinical activity and vitamin D metabolites in SLE.

Methods: A comparative cross-sectional study was conducted in 224 SLE patients and 201 healthy female subjects (HS). By allelic discrimination with TaqMan probes, the genotypes of SNVs rs3794060 *DHCR7*, rs2282679 *GC*, rs10741657 *CYP2R1*, rs10877012 *CYP27B1*, and rs4809959 *CYP24A1* were identified. ELISA assays were performed to quantify: Vitamin D binding protein (VDBP), calcidiol, and calcitriol. Multifactor dimensionality reduction (MDR) analysis was used to determine epistasis.

Results: The rs2282679 in *GC* was the best SNV to identify vitamin D deficiency as well as renal activity in SLE. Notably, the AC genotype of rs2282679 *GC* was associated with higher risk to vitamin D deficiency (OR = 2.22; *P* = .01), active SLE (OR = 1.93; *P* = .04), and renal activity (OR = 2.94; *P* = .02), compared to carriers of AA genotype. Furthermore, the C allele at rs2282679 *GC* was associated with higher risk of vitamin D deficiency (OR= 1.74; *P* = .02) in HS. In SLE patients carriers of the CC genotype in rs2282679 *GC* had lower VDBP serum levels compared to AC and AA genotypes carriers (189.2 vs. 206.4 and 218.8 mg/dL respectively; *P* = .03).

Conclusions: The rs2282679 *GC* was associated with higher clinical and renal activity, as well as with lower calcidiol and VDBP levels in SLE patients and HS.

OD122 / #449

Molecular Classificatıon and Prognosis of Systemic Lupus Erythematosus-Associated Pulmonary Arterial Hypertension Based on Rare Variants in Pah Risk Genes

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***Background and Aims*:** Pulmonary arterial hypertension (PAH) is severe complication of systemic lupus erythematosus (SLE). This study aimed to identify the value of rare variants in PAH genes on clinical phenotype and outcomes of SLE-associated PAH.

Methods: Two houndred and thirty seven patients with SLE-associated PAH confirmed by right heart catheterization from the multicenter prospective CSTAR-PAH cohort were included and analyzed for whole-exome sequencing. Deleterious rare variants among 28 PAH risk genes were annotated. The primary outcome was all-cause mortality. Reaching a low-risk profile of PAH was the secondary outcome.

Results: Over all, PAH rare variants were detected in 51 (21.5%) patients with SLE-associated PAH. SLE-associated PAH patients carrying PAH rare variants had shorter PAH duration from SLE onset (3.0 ± 3.1 vs. 5.3 ± 5.2 years, *P* = .004), lower rate of serositis (11.8% vs. 29.6%, *P* = .010), lupus nephritis (17.6% vs. 34.4%, P=0.022), and positive anti-U1 RNP antibodies (45.1% vs. 65.6%, *P* = .008), and lower SLE disease activity index (2.31 ± 2.02 vs. 5.03 ± 2.81, *P* = .047). After adjusting confounding factors, carrying PAH rare variants was identified as a independent prognostic factor of mortality (HR = 3.18, 95% CI, 1.12-9.02, *P* = .030) and reaching low-risk profile of PAH (HR = 0.40, 95% CI, 0.28-0.90, *P* = .020). Furthermore, a significant interaction was found between carrying PAH rare variants and baseline serositis on the prognosis.

Conclusions: This is the first study investigating deleterious rare variants of PAH risk genes in SLE-associated PAH. Analyzing PAH rare variants helped the molecular classification of SLE-associated PAH in distinguishing "vasculopathy"(carrier) and "vasculitis"(non-carrier). Carrying PAH rare variants also independently predicted the long-term outcomes of SLE-associated PAH.

OD123 / #1058

Preexisting Autoantibodies as Predictor of Immune Related Adverse Events (Iraes) for Advanced Solid Tumors Treated with Immune Checkpoint Inhibitors

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***Background and Aims*:** Immune checkpoint inhibitors (ICIs), used alone or as a combination are standard of care in many cancers but they can generate immune related adverse events (irAEs). Objective: To assess the association between preexisting autoantibodies and occurrence of irAEs.

Methods: Setting and participants: all consecutive patients receiving ICIs for advanced solid tumors between May 2015 and July 2021 and for which routinely used autoantibodies (ANCA, ANA, RF, anti-TPO and anti-TG) have been tested.

Results: Two houndred and twenty one patients were included. Treatments received were PD-(L)1 monotherapy (n = 162) and PD(L)1-combinations (n = 59). 129 patients (58%) had preexisting autoantibodies (positive group). Grade >1 irAEs were more frequent among patients with preexisting autoantibodies (OR = 3.5; *P* = 2.4*10-5) in the positive vs negative group respectively. IrAEs occurred earlier in the positive group: 13 weeks vs. 28.5 weeks in the negative group (*P* = .01). Twelve patients (9.4%) experienced multiple (≥2) irAEs in the positive group vs. 2 (2%) in the negative group (OR = 4.5, *P* = .04). Positive and negative groups did not differ in terms of ICIs exposure (*P* = .95). After a median follow-up of 25 months, median PFS and OS were longer among patients experiencing irAE (*P* = .00034 and *P* = .016, respectively), but did not differ according the presence or absence of preexisting autoantibodies (*P* = .09 and *P* = .66, respectively).

Conclusions: The presence of preexisting autoantibodies is significantly associated with the occurrence of grade >1 irAEs in patients treated with ICIs. Thus, autoantibody detection should be part of the work-up prior to ICI initiation in order to identify patients most at risk of developing irAEs.

ORAL DISCUSSIONS 23: SYSTEMIC AUTOIMMUNITY, BIG DATA AND THERAPEUTIC CHALLENGE

20-05-2024 12:50 - 13:50

OD124 / #365

The Prospective Associations of Autoimmune Diseases with Major Morbidity and Mortality

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Background and Aims: Autoimmune diseases (AD) comprise a diverse group of chronic conditions. While it is well-recognised that some individual AD are associated with other chronic diseases (e.g. inflammatory bowel disease with colorectal cancer), these risks are not well-characterised for AD as a whole. We examined the prospective associations between ADs and major morbidity and mortality.

Methods: China Kadoorie Biobank (CKB) is a population-based cohort study with prospective follow-up of approximately 0.5 million residents aged 30-79 years, recruited between 2004 and 2008 from 10 diverse regions in China. We identified participants with one or more of 33 AD. Multivariable Cox regression was used to estimate hazard ratios (HR) for incident

major chronic diseases (cardiovascular disease [CVD], cancer, type 2 diabetes [T2D]) and all-cause mortality associated with time-varying exposure to AD, with adjustments for socio-demographic and lifestyle factors.

Results: After excluding participants with a history of major chronic disease at baseline, 438,389 participants remained, including 17,050 (3.9%) with an AD. Participants with AD had higher risks of CVD (n = 3.101; adjusted HR 1.16, 95% CI 1.12-1.21), cancer (n = 1,409; 1.24, 1.18-1.31), T2D (n = 1.380; 1.51, 1.43-1.59) and all-cause mortality (n = 2.049; 1.23, 1.17-1.28) when compared to individuals without any AD. In sensitivity analyses excluding type 1 diabetes from the AD exposure, the association with T2D was attenuated to 1.30 (1.23-1.38).

***Conclusions*:** AD was associated with significantly higher risks of major morbidity and death from any cause in this adult Chinese population. Further research on underlying mechanisms and the role of targeted preventative measures is needed.

OD125 / #851

Unsupervised Machine-Learning Identifies Distinct Clusters Based on B Cell Phenotyping and Autoantibody Profiles in Patients with Systemic Lupus Erythematosus

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Background and Aims: To assess the aggregation of systemic lupus erythematosus (SLE) patients into different clusters according to B cell immunophenotype and serology within the frame of the BLISS-SC phase III trial.

Methods: We analysed data from 796 patients with SLE from the phase III BLISS-SC clinical trial of belimumab. Using an unsupervised machine-learning algorithm,we stratified patients into discrete clusters based on autoantibody profile and B cell immunophenotype.Analysis of variance was used to compare the characteristics of the clusters.

Results: Cluster 1 (n = 193) was characterised by significantly higher proportions [mean (SD)] of $CD19^+CD24b^+CD27^+$ regulatory [35.79%, (12.57)], $CD19^+CD20^+CD27^+$ bulk memory [32.03%, (9.94)], $CD19^+CD20^+CD69^+$ activated B cells [0.21%, (0.34)], $CD19^+CD20^-CD138^+$long-lived plasma cells [0.65%, (0.99)], and $CD19^+CD-38b^+CD27b^+$ SLE-associated plasma cells [6.57%, (7.01)].Cluster 2 (n = 358) was characterised by higher proportions of $CD19^+CD-24b^+CD38b^+CD27^-$transitional [6.49%, (9.21)], and $CD19^+CD20^+CD27^-$ naïve B cells [85.52%, (7.19)]. Cluster 3 was characterised by a higher proportion of $CD19^+CD20^+CD138^+$ short-lived plasma cells [0.11%, (0.15)] and was the most serologically active with respect to low C3 and C4 levels and anti-dsDNA positivity compared to clusters 1 and 2.Cluster 2 was dominated by musculoskeletal and mucocutaneous manifestations when compared to cluster 1 and cluster 3 ($P < .001$).Cluster 2 displayed the highest proportion of LLDAS attainment throughout week 52.Cluster 3 showed the highest proportion of SLEDAI-2K and mean prednisone dosage throughout week 52. No significant differences were captured across the 3 clusters with regard to SRI-4 and DORIS remission.

Conclusions: Three different clusters were identified among SLE patients based on B cells and autoantibody profiles, which are not captured on the basis of sole clinical classification and which may have implications with regard to treatment response.

OD126 / #28

Cannbinoids and Immunity-Promising Pre-Clinical Findings Open the Door to Significant Clinical Applications

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Background and Aims: In recent years, a wide range of cannabinoid-based treatments are offered to patients. Therefore, it is crucial to explore the various biological effects of these treatments. Phyto-cannabinoids possess a wide range of immune-regulatory properties, mediated by the endocannabinoid system. A variety of pathological conditions involve dysregulation of the immune system. In autoimmune diseases and Graft versus Host Disease (GvHD), increased immunological activity causes inflammation and tissue damage. Immuno-modulating therapies can regulate the immune system; suggesting cannabinoids use in the therapy of immune related disorders. We aim to compare the effects of cannabinoid treatments on innate and adaptive immune response.

***Methods*:** First, we compared the influence of D9 tetrahydrocannabinol (THC) and cannabidiol (CBD) and cannabis extracts on lymphocyte activation *in vitro* and in murine models for bone marrow transplantation and GvHD. Next, we tested these cannabinoids on LPS activated peritoneal macrophage and in a murine colitis DSS model.

Results: The *in vitro* studies clearly indicate differential effects of the cannabinoid- based treatments on both lymphocytes and macrophage activation. In the murine models for GvHD and colitis, we identified superior anti-inflammatory activity of the cannabis extracts over the pure cannabinoids. In the murine model for bone marrow transplantation, we demonstrated that all treatments, pure THC in particular, inhibit lymphocyte reconstitution after transplantation and showed the inhibitory role of the cannabinoid receptor CB2.

Conclusions: Our results highlight both similarities and differences between various cannabis-based treatments. Revealing of the reciprocal relationship between cannabinoids, the endocannabinoid system and immunity is essential to design therapeutic strategies with improved efficacy.

OD127 / #1030

Cannabis Sativa Modulates Proliferation of Peripheral Blood Mononuclear Cells and M1 to M2 Polarisation of Macrophages Isolated from Patients with Rheumatoid Arthritis

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Background and Aims: Rheumatoid arthritis (RA) is a chronic disabling autoimmune disease with a high prevalence worldwide (0.46%). Currently, patients with RA are treated with different drugs, such as non-steroidal anti-inflammatory drugs (NSAIDs) or disease-modifying anti-rheumatic drugs (DMARDs), which provide clinical improvement at the cost of multiple adverse effects. Therefore, research and development of new integrative therapies, including phytomedicines or compounds derived from immunomodulatory plants such as *Cannabis* are required. Aim: To establish the *ex vivo* immunomodulatory activity of different *Cannabis sativa* chemotypes on peripheral

blood mononuclear cells (PBMCs) and pro-inflammatory macrophages (M1) from patients with RA

Methods: PBMCs and M1 macrophages were cultured with *Cannabis* extracts obtained by the supercritical fluid method. The IC50 of *Cannabis* extracts and their effect on the proliferation of phytohemagglutinin (PHA)-stimulated PBMC were determined by the colorimetric MTT assay. Immunophenotypic variations of M1 macrophages and cytokine production were evaluated by multiparametric flow cytometry. Immunomodulatory *Cannabis* extracts were chemically characterized by HPLC and GM-MS.

Results: *Cannabis* extracts exhibited low cytotoxic activity (≥ 100 ug/mL) and reduced the proliferation of PHA-stimulated PBMCs at concentrations between 12.5 and 50 ug/mL. In addition, pro-inflammatory-M1 macrophages (CD16+/CD86+/CD80+/CD209-/TNFα+) polarized towards an anti-inflammatory M2 profile (CD16+/CD206+/CD163+/lL10+) when exposed to *Cannabis* extracts. These immunophenotypic changes were significantly higher in cell cultures exposed to extracts derived from *Cannabis* chemotypes containing CBN ≥ CBD ≥ Δ9THC.

Conclusions: *Cannabis sativa* extracts immunomodulate *ex vivo* the proliferation of PBMCs and the M1 to M2 polarisation of macrophages isolated from patients with RA. This modulatory effect could be related to particular *Cannabis* chemotypes.

OD128 / #1105

Real-World Drug Survival of Biologics and Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs Among Psoriatic Arthritis Patients

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Background and Aims: To evaluate the real-world adherence, drug survival and discontinuation risk of biologics and targeted synthetic DMARDs among psoriatic arthritis patients, comprising both young and elderly patients.

Methods: A retrospective study using a computerized database. Treatment-naïve and treatment-experienced PsA patients, younger and older than 60 years, who initiated treatment with bDMARDs (TNF-α inhibitors, IL-17 inhibitors, IL-12/23 inhibitors or tsDMARDs (PDE-4 inhibitor Apremilast) during 2015–2018 were included. Adherence was assessed using the proportion of days covered (PDC) method. Time to discontinuation was analyzed using Kaplan-Meier estimates. Risk of discontinuation was estimated by Cox proportional hazard model.

Results: We identified 427 eligible patients. 22.2% were older than 60 years old, utilizing 673 treatment lines. The proportion of adherent patients (PDC ≥0.8) was similar (62.1% to 66.5%) across all lines of therapy and across different biologics (70.0%-72.0%), while apremilast, showed the lowest, in both treatment-naïve and experienced settings (43.6% and 25.5%, respectively). The Kaplan-Meier analysis showed that in the treatment-naïve, TNF-αis had higher drug survival compared with apremilast ($P = .032$). Apremilast also had the lowest drug survival in the treatment-experienced group ($P < .0001$). Kaplan-Meier analysis by age groups, showed similar drug survival rates in elderly (≥60 years) and non-elderly (<60 years) patients, regardless of treatment-experience status. The multivariable model showed that apremilast had increased risk for discontinuation compared with TNF-αis.

Conclusions: Adherence, drug survival and risk for discontinuation were similar for all included bDMARDs, regardless of treatment-experience status, while apremilast, showed lower rates and increased risk. Drug behavior was similar in elderly and non-elderly patients. With the variety of MoA available for PsA patients, these findings may assist caregivers in selecting the appropriate treatment.

ORAL DISCUSSIONS 24: MYOSITIS AND PSORIASIS

20-05-2024 12:50 - 13:50

OD129 / #318

The Association Between Psoriasis Disease Severity and Inflammatory Bowel Disease and Psoriasis: A Population-Based Analysis

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Background and Aims: The skin-gut axis, characterized by bidirectional communication between the skin and gut, plays a crucial role in the pathogenesis of psoriasis and inflammatory bowel diseases (IBD). We aimed to explore the association between psoriasis and IBD and identify predictors associated with IBD development among patients with psoriasis

Methods: A retrospective study which utilized electronic database from the Meuhedet Health Maintenance Organization (MHMO) in Israel. Psoriasis was categorized as severe if any systemic agent or phototherapy was administered. Univariate and multivariate logistic regressions were used to identify specific predictors for IBD, with adjustments made for potential confounders. The study received approval from the Ethical Committee of the MHMO.

Results: A total of 61 003 adult patients who were diagnosed with psoriasis between 2000 to 2022 were included. Among them, 1495/61 003 patients (2.4%) were diagnosed with IBD, as compared to 3834/244 012 patients (1.6%) in the non-psoriasis group. Spondyloarthropathies, including psoriatic arthritis (OR 0.49, 95% CI 0.34-0.72, $P < .001$) and ankylosing spondylitis (AS) (OR 1.78, 95% CI 1.29-2.45, $P < .001$), were associated with a higher prevalence of IBD. Severe psoriasis was significantly associated with a higher likelihood of IBD, compared to mild psoriasis (OR 16.03, 95% CI 11.02-23.34, $P < .001$). Anti-nuclear antibody (ANA) was not found to be in significant correlation (aOR 0.99 95%CI 0.65-1.54 $P = .9$).

Conclusions: A strong association between psoriasis and IBD was demonstrated, including its subtypes: Crohn's disease and ulcerative colitis. Moreover, such association was dependent on severity of psoriasis as determined by treatment used.

OD130 / #773

Pathogenic Effects of Angiotensin IL Type 1 Receptor (AT1R) Autoantibodies on Endothelial and Immune Cells in Systemic Sclerosis

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Background and Aims: In systemic sclerosis (SSc), a chronic autoimmune disease, functional autoantibodies (Abs) targeting G protein-coupled receptors (GPCRs) such as angiotensin II type 1 receptor (AT1R) promote the increased expression of vascular adhesion molecules and release of cytokines that cause recruitment of inflammatory immune cells into the skin of SSc patients, leading to vasculopathy and fibrosis. Here, the effect of AT1R Abs on endothelial function, neutrophil adhesion, and immune response of monocytes are examined.

Methods: Human umbilical vein endothelial cells (HUVEC) were treated with monoclonal AT1R antibodies for 24h and changes in glycocalyx thickness and neutrophil adhesion to HUVEC were assessed. Further, a monocyte-like cell line (U937) and HUVECs were stimulated by the mAbs and the corresponding isotype control for 24h. The pro-inflammatory response of U937 cells was explored by examining the CC-chemokine ligand 18 (CCL18) release.

Results: HUVEC stimulated by mAbs recognizing AT1R reduced the glycocalyx thickness by approximately 29% compared to the isotype. Examining if this decrease may facilitate the adhesion of inflammatory cells like neutrophils to endothelial cells indicated that autoantibodies alone may not affect the adhesion of neutrophils and they do not adhere to the vascular endothelial cells. Moreover, the mAbs induce an inflammatory and pro-fibrotic CCL18 cytokine response in monocytes stimulated by AT1R antibodies (196 pg/ml) but not with isotype controls (105,7 pg/ml).

Conclusions: AT1R antibodies induce the release of CCL18 by U937 cells and alter the glycocalyx structure of vascular endothelial cells. These data indicate that AT1R antibodies are involved in the pathogenetic mechanisms of SSc.

OD131 / #711

The Tyrosıne Kinase-2 Subunit Is the Main Mediator of the JAK/STAT3 Downstream in Inflammatory Idiopathic Myositis

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Background and Aims: The importance of the JAK/STAT pathway is established in different autoimmune diseases, and JAK inhibitors represent an effective therapeutic opportunity. The aim of this study was to assess the in vitro role of the four Janus kinase (JAK) subunits on phosphorylation of STAT3 in PBMC from patients with inflammatory idiopathic myositis (IIM).

Methods: Blood samples from n.5 healthy donors (HD) and n.5 IIM patients with active disease and naive to corticosteroids and immunosuppressive treatment were collected. After PMBC separation, the effects of JAK-1, -2, -3, and tyrosine kinase-2 (TYK-2) selective inhibition were assessed by quantification of phosphorylated-STAT3 (p-) with FACS analysis in CD4pos and CD14pos cells at baseline and after incubation with selective inhibitors.

Results: At baseline IIM patients had significantly higher pSTAT3 levels both in CD4pos and CD14pos cells, compared to HD ($P < .05$). After selective JAK inhibition we observed a significant reduction in pSTAT3 levels of CD4pos and CD14pos only from IIM patients. Of note a different effect of selective JAK-inhibitors on pSTAT3 modulation was observed. Specifically, the JAK-1 and TYK-2 selective inhibitors were more effective in CD4pos-pSTAT3pos cells, while only the selective TYK-2 inhibition determined a dramatic reduction in CD14pos-pSTAT3pos cells.

Conclusions: The JAK/STAT3 pathway is significantly activated in PBMC from IIM patients. The high activation of pSTAT3 can be modulated by selective inhibition of JAK1 and TYK2. Our findings are consistent with the pivotal role of IFN-I signaling in IIM pathogenesis, and evidence a potential role to consider selective JAK1/TYK2-inhibitors as innovative therapeutic strategy in IIM patients.

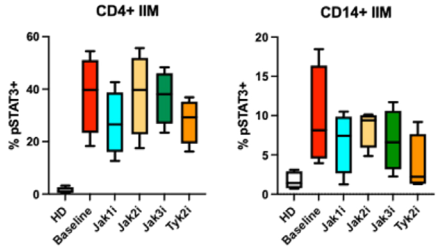

Figure 1.

OD132 / #821

Evaluation of the Seasonal Incidence of Myositis-Specific and Myositis-Associated Antibodies in Italy

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Background and Aims: Idiopathic inflammatory myositis (IIM) are a heterogeneous group of autoimmune disorders characterized by chronic inflammation of the muscle. Identification of myositis-specific (MSA) and myositis-associated (MAA) antibodies contributed to

the definition of clinical-serological clusters of IIM. The exposition to triggering environmental agents in genetically susceptible individuals represents the most likely pathogenic mechanism for IIM development. The aim of this study is to evaluate the seasonal pattern of incidence of MSA and MAA in Italy.

Methods: The distribution among the months of the year of the positive results obtained from 65026 myositis immunoblot performed between 2018 and 2020 was analyzed.

Results: Some MSA and MAA display an heterogeneous pattern of distribution in the different months of the year: anti-MDA-5 antibodies have been detected preferentially between October and November; anti-Mi2b between September and October; anti-PM-Scl-75 peak in autumn and winter; anti-TIF-1g in autumn.

Conclusions: Data of this study demonstrate that some MSA and MAA are seasonal expressed. Regarding anti-MDA-5 antibodies, our observations are in agreement with those of other studies performed on different ethnicities. For other autoantibodies (anti-PM-Scl-75, anti-TIF-1g) this is the first description of a seasonal pattern of incidence. Regarding anti-Mi2b, the observation of a peak immediately after summer is in agreement with literature data showing the increased incidence of anti-Mi2 autoantibodies in populations living at latitudes particularly exposed to solar radiations. In conclusion, our data suggest that environmental agents typical of different seasons can influence the development of MSA and MAA. Additional studies are needed to understand the biological mechanisms responsible of this phenomenon.

OD133 / #603

Anti-CN1A in the Real Life: Is It Truly a Myositis Specific Antibody?

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Background and Aims: Anti-cytosolic 5'nucleotidase 1A (anti-cN1A) autoandibodies were proposed as specific diagnostic markers for inclusion body myositis (IBM), but they were also demonstrated in other autoimmune diseases and to a small extent in healthy people. Our study aims to verify the diagnostic accuracy of anti-cN1A, analyzing its prevalence and clinical correlation in patients who came to our attention for suspected idiopathic inflammatory myopathies (IIM).

Methods: We recently introduced in our laboratory a test to assess the presence of anti-cN1A antibodies by lineblot method as part of an extended profile (Euroline 9G by Euroimmun) for autoantibodies associated with autoimmune myopathies. We collected laboratory and clinical features of all cN1A positive cases from nov 2022 to Sept 2023.

Results: Twenty five patients (88% females; mean age = 51 ± 24 years, range 3-86 years) tested positive for anti-cN1A. 7 were high positive, 7 moderate and 11 low. Only 10/25 (40%) were positive only for cN1A, while the majority presented also other autoantibodies (mostly Ro60 and Ro52, but also PM/Scl75 and 100, U1RNP, Scl70, Ku, Jo1, SSB, HA, MJ/NXP2 and Mi2-beta). Only 2/25 (8%) patients were diagnosed as myopathies (one polymyositis and one in overlap with scleroderma and MCTD), while 9 presented other connective tissue diseases (lupus, scleroderma, vasculitis, polymyalgia), 2 autoimmune thyroiditis and 12 other unrelated diseases (mostly neurologic). Anti-cN1A antibodies were high positive both in myopathies and in unrelated diseases.

Conclusions: In our experience, anti-c1NA are rarely present in isolation and as myositis-specific antibodies. They can be frequently found at high titer also in other autoimmune and non autoimmune diseases.

E-POSTER VIEWING

E-POSTER VIEWING 01: BASIC MECHANISMS: AUTONOMIC NERVE SYSTEM AND AUTOIMMUNITY AND DYSAUTONOMIA

EP001 / #789

Proteomics in Patients with Fibromyalgia Syndrome: A Systematic Review of Observational Studies

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Background and aims: Fibromyalgia is a disease of unknown pathophysiological mechanisms with the diagnosis being made by clinical criteria. Proteomics offer a revolutionary way of collecting data regarding protein markers or therapeutic targets. The present systematic review aimed to synthesize the available evidence regarding the proteome of adult patients with fibromyalgia, using data from observational studies.

Methods: An extensive literature search was conducted in the MEDLINE/Pubmed, CENTRAL and clinicaltrials.gov databases, from conception until November 2022. The study protocol was published in OSF. All studies were examined according to the PRISMA 2020 guidelines and extracted data involved characteristics of the patients and controls, pain and quality of life scales and identified proteins.

Results: Eleven studies fulfilled the protocol criteria and a total of 3328 proteins were identified, 149 of which were demonstrated at different levels in patients with fibromyalgia compared to controls. Controls included both healthy controls and patients with pain (inflammatory and non-inflammatory). The identified proteins involved plasma, serum, blood, CSF and saliva samples. The most important proteins were transferrin, fibrinogen chains, profilin-1, transaldolase, PGAM1, apolipoprotein C3, complement C4A and C1QC, immunoglobin parts and acute phase reactants. The quality of the individual studies was moderate to good.

Conclusions: Fibromyalgia seems to be related with protein dysregulation in the complement and coagulation cascades, as well as in iron metabolism.

EP002 / #848

Cardiovascular Dysautonomia as One of the Post-COVID Syndrome Manifestations

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Background and aims: The presence of dysautonomia has become increasingly common among the manifestations of the post-COVID syndrome. Aim of this research was to evaluate cardiovascular dysfunction in patients with post-COVID syndrome.

Methods: 56 patients (38 women, 18 men) with an average age of 21.0 (20.0;24.5) years with verified COVID-19 have been examined. Heart rate variability (HRV) was performed in all patients using the "VNS-spectrum" analyzing system (Neurosoft, Russia). Total spectral power (TP), very low frequency power (VLF), low frequency power (LF), high frequency power (HF, ms2/Hz), LF/HF ratio, 30:15 ratio were studied. Results have been statistically processed.

Results: TP at rest has higher than normal mean value (6140 (3277;10607) ms2/Hz) but after verticalization it decreases 3 times (1938 (1047;3371) ms2/Hz). Women at rest had higher prevalence of HF (2203 (993;4595) ms2/Hz) then men. LF after verticalization decreases (1530 (969;2719) and 863 (392;1758) ms2/Hz) respectively) demonstrating the abnormal orthostatic reaction. LF/HF ratio at rest had lower, than normal mean value and, especially in women (0.835 (0.450;1.32)), alluded the presence of dysautonomia.

Conclusions: The presence of dysautonomia was observed, primarily in women, in the form of hyperactivation of parasympathetic nervous system. Abnormal orthostatic reaction with lower sympathetic reactivity was described.

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E-POSTER VIEWING 02: BASIC MECHANISMS: COVID-19, POST COVID SYNDROME, VACCINES AND AUTOIMMUNE ADVERSE EFFECTS

EP003 / #442

The Incidence of Pediatric Type 1 Diabetes and Diabetic Ketoacidosis at Onset Post COVID-19 Pandemic: Findings from a Tertiary Care Teaching Hospital, Oman

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Background and aims: It has been reported that COVID-19 infection may lead to the pathogenesis of some autoimmune diseases, including Type 1 diabetes mellitus

(T1DM). Here, we aimed to evaluate the incidence and acute complications among T1DM pediatric patients attending the endocrine pediatric clinic at a tertiary care teaching hospital in Oman before and after the COVID-19 pandemic outbreak.

Methods: We conducted a retrospective cross-sectional study in which we identified the newly diagnosed subjects with T1DM among pediatric patients for a period of six years, before (Jan 2017- Dec 2020) and after (Jan 2020- Dec 2022) the COVID-19 pandemic. Data were collected from the electronic medical records.

Results: A total of 142 children (<16 years old) were newly diagnosed with T1DM during the study period. Forty-eight patients were diagnosed before the COVID-19 pandemic, and 94 were diagnosed during it. The incidence of T1DM was higher during COVID-19 compared to the years before (83.56 vs. 38.31 per 10, 000 respectively). The most prevalent complication in the sample during the pandemic was Diabetic ketoacidosis (DKA) (61.70%), with significant increase in its prevalence and severity in the sample during the pandemic (*P*-values of .041). Moreover, during the COVID-19 outbreak, severe presentation of DKA was significantly associated with ICU admission and hospital stay.

Conclusions: Here, we report an increase in T1DM incidence during the COVID-19 pandemic. Our findings indicate potential autoimmune long-term complications post–COVID–19. Further studies are required to decode whether the elevation in T1DM rates after the COVID-19 outbreak was caused by SARS-CoV-2 infection.

EP004 / #662

EBV and SARS-CoV-2 – Two Sides of The Same Coin of Autoimmunity

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Background and aims: The development of autoimmune diseases is driven by two main factors: genetics, and environmental factors. Epstein-Barr virus (EBV) is among the many bacterial and viral infectious agents that can trigger autoimmune disease. Similarly, SARS-CoV-2, the causative agent of COVID-19 has been extensively studied for its involvement in various autoimmune diseases.

Methods: Since the beginning of the COVID-19 pandemic huge efforts were made to understand the mechanisms of the infection and learn more about the virus, during which several COVID-19 patients tested positive for EBV.

Results: Actually, EBV usually remains dormant in humans after the initial infection under the so-called "latent infection". The virus remains inactive unless a patient becomes an immunocompromised allowing viral reactivation presenting with various manifestations. Interestingly, it was demonstrated recently that EBV reactivation is one of the causes of long COVID syndrome, seen in patients recovering from acute COVID-19. Studies have also showed that patients with SARS-CoV-2 infection with concomitant EBV reactivation had higher levels of CRP, D-dimer and calcium levels as well as higher incidence of acute respiratory distress syndrome (ARDS) and respiratory failure.

Conclusions: Therefore, due to the substantial similarities between EBV and SARS-CoV-2 in terms of autoimmune implications, hereby we view EBV reactivation with COVID-19 patients by illustrating similar mechanisms in inducing autoimmune diseases.

EP005 / #666

The Autoimmune Mechanisms of the Psychological Features in Post-COVID

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Background and aims: While the world is breathing a relief following the declaration of the world health organization (WHO) regarding the end of the COVID-19 pandemic; the long lasting effects of COVID-19 are still vivid. The so-called post-COVID syndrome was extensively reported in patients recovering from acute COVID-19.

Methods: Such manifestations include long lasting fatigue, inability to return to pre-infection activity, residual shortness of breath and chest pain, to name a few. Of importance, a variety of psychological or psychiatric symptoms were shown to be experienced by certain groups of people infected with SARS-CoV-2. For instance, insomnia, anxiety, depression, and stress were all reported in patients following acute infection.

Results: The latter is in addition to the exacerbation of pre-existing disorders or symptoms in the affected individuals. Among others, the mechanisms proposed in this regard direct viral penetration into the central nervous system (CNS), and psychological and social stress induced by the illness itself and the lockdown with social distancing. In terms of autoimmunity, the induction of immune-dysregulation by SARS-CoV-2 has been studied. Furthermore, some autoantibodies appear to be acquired during the acute phase of COVID-19, including autoantibodies against different G protein-coupled receptors (GPCRs) of the nervous system.

Conclusions: Therefore, we described hereby in our work the autoimmune mechanisms behind the psychological features seen in patients after the recovery from acute COVID-19. The lights shed on those aspects assist in diagnosing and dealing with the burden of the patients after the pandemic came to an end.

EP006 / #289

SARS-CoV-2 Gut-Targeted Epitopes: Sequence Similarity and Cross-Reactivity Join Together for Molecular Mimicry

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Background and aims: The SARS-CoV-2 virus, known for its auto-immunogenic properties, not only targets the respiratory system but also heavily infects the gastrointestinal tract, thereby potentially influencing gut-associated autoimmune diseases. Despite this, there remains a paucity of research exploring the molecular mimicry between the virus and intestinal epitopes. The present study aimed to illuminate the sequence similarities between SARS-CoV-2 antigens and human enteric sequences, focusing on known areas of cross-reactivity.

Methods: SARS-CoV-2 epitopes that cross-react with human gut antigens were analyzed us-

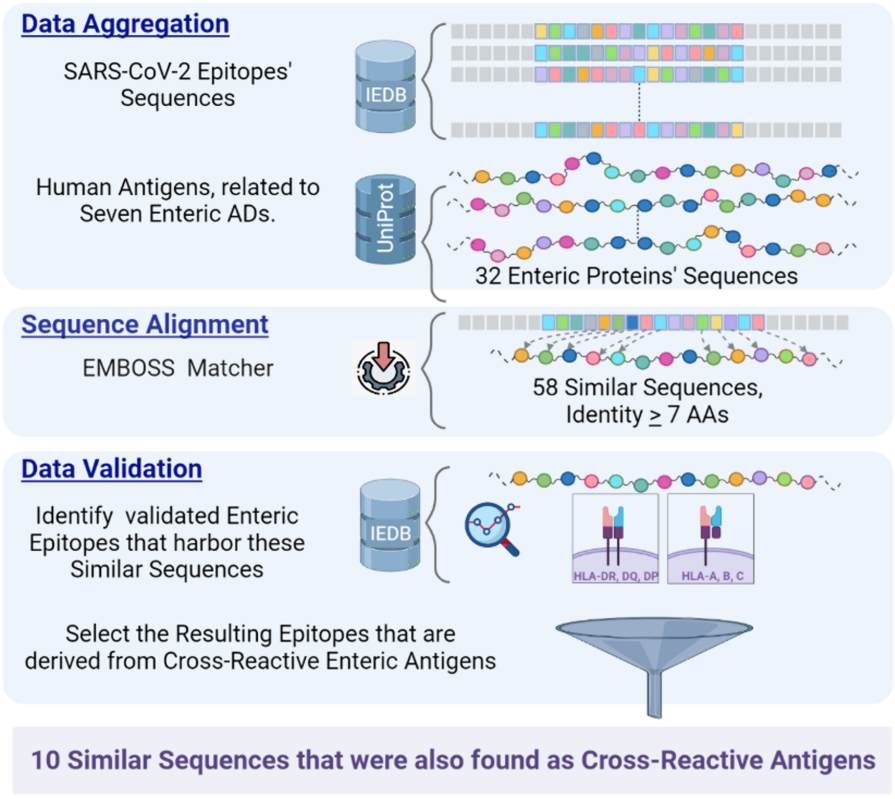

Figure 1.

ing data aggregated from the Immune Epitope Database (IEDB) and enteric antigens sourced from the UniProt Knowledgebase. Utilizing EMBOSS Matcher, a pairwise local alignment tool, sequence similarities were identified among SARS-CoV-2 epitopes and enteric antigens. The similar sequences were then validated as enteric epitopes, and compared with cross-reactive antigens.

Results: Of the 58 pairs of similar sequences, 10 were confirmed as validated epitopes and are associated with cross-reacting antigens specific to four distinct SARS-CoV-2 proteins. These epitopes are linked to seven enteric antigens connected to various autoimmune conditions: one with UC, three with PBC, one with CD, and five with AIH; interestingly, one is linked to two ADs.

Conclusions: The findings demonstrate a notable correlation between antibodies created against viral proteins and those cross-reactive with human gut antigens, which play crucial roles in several cellular functions. The implications of these cross-reactive epitopes, in relation to SARS-CoV-2, and the potential for them to influence gut-related auto-immunogenesis are discussed, paving the way for deeper understanding and further research into this critical enigmatic area.

Table 1.

Vitamin D levels	Deficiency (<10.0ng/mL)	Relative Deficiency (10.0-30.0ng/mL)	Sufficiency (>30.0ng/mL)
Regular COVID Unit (487 patients)	116 patients-23,8% (mean 6.9ng/mL)	274 patints-56,3% (mean 19.9ng/ml)	97 patients-19.9% (mean 39.7ng/mL)
COVID ICU (87 patients)	27 patients-31,0% (mean 6.1ng/mL)	56 patients-64,4% (mean 18.2ng/mL)	4 patients-4,6% (mean 32.5ng/mL)
Total	143 patients	330 patients	101 patients

EP007 / #614

Investigation of Vitamin D Levels in Hospitalized Patients with COVID-19

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Background and aims: Vitamin D levels are considered to contribute to the proper functioning of the immune system and may be related to the body's susceptibility to infections. The aim of this study is to investigate the levels of vitamin D in patients with COVID-19.

Methods: The study included 574 patients hospitalized due to COVID-19 infection for a period of 26 months. Of these, 487 patients were admitted to the regular COVID-19 clinic, while the remaining 87 were admitted to the COVID-19 ICU. During their hospitalization, serum levels of vitamin D were measured. The measurement of vitamin D levels was performed using the 25-OH Vitamin D Reagent kit (ABBOTT) on the Alinity i analyzer using the chemiluminescence method. Depending on vitamin D levels, the participants were divided into three groups: sufficiency, relative deficiency and deficiency.

Conclusions: The majority of hospitalized patients have relative deficiency in vitamin D with a mean value of 19.6ng/mL. A significant portion of all patients exhibits vitamin D deficiency, particularly in the COVID ICU, where this percentage reaches one-third of hospitalized patients. The percentage of COVID ICU patients with sufficiency in vitamin D is extremely low (<5%).

EP008 / #655

COVID-19 as Autoimmunity Trigger

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Background and aims: Throughout the pandemic of COVID-19, the medical community composed of its clinicians and researchers, has learned regarding the capabilities of infections, particularly viruses, in triggering autoimmunity and autoimmune disorders. Though the correlation between viral infections and autoim-

mune diseases was reported extensively in the medical literature decades before the appearance of the causative agent of COVID-19, the SARS-CoV-2; the autoimmune manifestations of SARS-CoV-2 infection have been shown to affect almost every organ system. The involvement of various systems of the body secondary to the autoimmune phenomena was found to occur during the acute COVID-19 as well as the recovery phase, to an extent of contributing to the post-COVID syndrome according to recent studies.

Methods: Many mechanisms were reported in regard to the way SARS-CoV-2 infection can trigger autoimmunity including immune dysregulation, autoantibody production, hyperferritinemia, and cytokine storm, among others. Of importance is renal involvement, as both glomerular and non-glomerular renal diseases were described with higher rates including collapsing glomerulonephritis and membranous nephropathy.

Results: Such an implication of autoimmunity in SARS-CoV-2 infection, including renal and non-renal involvement, is critical and of paramount as it serves as a base for diagnosis, therapy, and prognosis.

Conclusions: We aimed to focus on the role of SARS-CoV-2 infection in provoking autoimmunity and autoimmune diseases by illustrating the mechanisms described and presenting the systemic involvement of the COVID-19.

EP009 / #509

Demographic Features of the Lipid Spectrum Before and During the COVID-19 Epidemic

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Background and aims: The aim of this cross-sectional study was to evaluate the influence of COVID 19 infection on lipid parameters in the urban population.

Methods: Lipid profiles of 57536 patients aged 13-94 in 347 cities of European Russia estimated before COVID 19 epidemic in 2016 year and those from 65500 patients during 2020-2021 years were compared with usage of descriptive statistics, sample comparison, and two-factor analysis of variance.

Results: The average level of total cholesterol (TC), as well as LDL-C, was the highest in the age group of 43-62 years for both sexes in both compared samples: before and during the COVID-19 epidemic. The peaks of the average values of TC and LDL-C in men appeared 10 years earlier than in women in both the pre-epidemic and epidemic populations. The average values of TC and LDL-C decreased with age and reached their minimum in the elderly. Nevertheless mean HDL-C levels in men increased monotonously with age, while levels in women rose sharply from a minimum at age 13 to a maximum at age 25, followed by a slight decrease with age and a downward trend across all age groups during the epidemic. Mean HDL-C levels in COVID-19 positive patients were significantly reduced: 1.39 [1.35, 1.43] compared with 1.47 [1.45, 1.48] in patients with negative test results ($P<.001$).

Conclusions: The results of a cross-sectional study showed a statistically significant dependence of lipid parameters on sex, age and COVID 19 infection.

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EP010 / #679

Prevalent and Persistent New-Onset Autoantibodies in Mild to Severe COVID-19

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Background and aims: While the underlying and likely diverse causes of post-COVID-19 condition remain unknown, pre-existing and new-onset autoantibodies are major hypotheses. We analyzed the autoantibody repertoire emerging after COVID-19 in 525 healthcare workers (HCW) and hospitalized patients followed at 5 visits over 16 months.

Methods: We performed an initial proteome-wide screening of the autoantibody repertoire of 32 HCW which informed a targeted analysis of 372 antigens in the full longitudinal cohort. Two machine learning approaches were used to identify new-onset autoantibodies. Using peptide arrays, we performed epitope mapping of 6 autoantibodies and validated detected epitopes in an independent cohort of neuro-COVID and controls.

Results: New-onset autoantibodies were detected in 55% of baseline seronegative individuals. Of these, 60% remained elevated after 12 months. Twenty-two new-onset autoantibodies emerged in >1% of the cohort. Among these, ten had increased prevalence in patients. Three prevalent autoantibodies were associated to increased severity of neuropsychiatric symptoms post-COVID-19. Three epitopes were validated in the independent cohort and two displayed sequence similarity to the Spike protein fusion peptide.

Conclusions: Prevalent and persistent new-onset autoantibodies emerged after COVID-19 and persisted for 12 months with several being more common after severe disease. Three new-onset autoantibodies were associated to neuropsychiatric symptoms post-COVID-19. Epitope mapping revealed potential molecular mimicry between highly prevalent new-onset autoantibodies and the fusion peptide. These results show that a complex autoantibody repertoire develops after COVID-19 and provide a clear rationale for further investigation of new-onset autoantibody repertoires in other infectious diseases, as well as for continued study of the presented new-onset autoantibodies.

EP011 / #715

Multisystem Inflammatory Syndrome in Children (Mis-C): Clinical Manifestations and Therapy

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Background and aims: In children, COVID-19 is usually mild. However, in rare cases, children can be severely affected and develop a significant systemic inflammatory response, which has been termed multisystem inflammatory syndrome in children (MIS-C). The aim of our study was to evaluate clinical manifestations and therapy in patients with MIS-C.

Methods: A single small center study was performed. Included were patients with MIS-C treated at our pediatric clinic from November 2020 till March 2022. WHO/CDC diagnostic criteria for MIS-C were used. Data was collected retrospectively from patients' medical records.

Results: A total of 12 patients were included. The mean age was 8.9 years. Female and male patients were equally affected. In addition to fever and myocardial dysfunction, which were present in all patients, gastrointestinal involvement was the most common clinical manifestation. 6 patients had conjunctivitis, 5 had rash, 2 sore throat and 1 lymphadenopathy. All our patients were treated with intravenuous immune globulin (IVIG) and aspirin. 9 patients (75%) were put on glucocorticosteroids. Anticoagulation with a low-molecular-weight heparin was used in 11 patients. We didn't use biologics in any of our patients. All 4 patients (33.3%) presenting with shock required intensive care treatment. 1 girl who presented with COVID-19 pneumonia recieved antiviral therapy with remdesivir.

Conclusions: All of our patients with MIS-C achieved full recovery. Because the disease can present as a severe shock-like illness early diagnosis and prompt treatment are of significant importance.

EP012 / #654

COVID-19 and SLE: Infection and Autoimmunity At Its Best

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Background and aims: If one had any doubts before the pandemic regarding the correlation between infections and autoimmunity, COVID-19 left us fascinated on the strong bond between the two entities. The immune and autoimmune reactions seen in patients infected with SARS-CoV-2 have served as a base for this assumption. Later on, the use of immunosuppressants such as systemic glucocorticoids, among other biological agents, turned this assumption to a fact. This was no different when it comes to the vaccines against COVID-19. Through several postulated mechanisms these vaccines, although generally considered safe, are thought to have the potential to result in autoimmune reactions making them not more innocent than the infection itself. When Systemic lupus Erythematous (SLE) is viewed as a classical autoimmune multisystemic disorder, the connection with SARS-CoV-2 infection and COVID-19 vaccination, is of extreme importance. This is because early reports during the pandemic has shown.

Methods: Increased rates of SARS-CoV-2 infection among patients known previously to have SLE and much more interestingly, cases of new-onset SLE after COVID-19 has been documented in the literature.

Results: Subsequently vaccines against COVID-19, those mRNA based and adenovirus-vector based, were reported to induce new SLE cases, trigger immune thrombocytopenia or lupus nephritis, two common presentations of SLE, or exacerbate flares.

Conclusions: In our paper, we concluded various aspects of available and recent data regarding SLE and COVID-19 as both an infection and vaccination.

EP013 / #801

Multiplex and High-Throughput Autoantibody Profiling and Multi-Disease Serology

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Background and aims: Viral infections have been associated with the development of autoimmune disorders. The recent COVID-19 pandemic affected a large number of people and there is a risk for autoimmune complications, some of which may have already presented as long-COVID. There is therefore an urgent demand for serological platforms that can combine high-throughput serology and multiplex screening for novel autoantigens.

Methods: A high-throughput multiplex bead-based serological assay was established by evaluating more than hundred representations of SARS-CoV-2 proteins, before a final set of antigens was selected with a sensitivity of 99.7% and a specificity of 99.4%. This assay is currently being extended to include other viruses in addition to SARS-CoV-2, such as influenza virus, respiratory syncytial virus, parainfluenza virus, adenovirus, and metapneumovirus. Additionally, by utilizing human antigens this high-throughput platform allows for studies focusing on finding new-onset autoantibodies following infection.

Results: Our serological assay has been used to assess serostatus in over 250,000 samples as well as contributing to over 30 publications the last three years. In addition, we have identified new-onset autoantibodies associated with increased severity of neuropsychiatric symptoms post-COVID-19.

Conclusions: To enable broad and high-throughput studies on seroprevalence we are extending our highly specific and sensitive multiplex COVID-19 serological assay to also include a broad range of other viral infections with pandemic potential or association, and further combine this with autoimmune responses after infection.

EP014 / #323

COVID-19 Morbidity and Mortality in Immunocompromised Patients

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Background and aims: In Hungary, the HUN-VE3 study determined the comparative effectiveness of various primary and booster vaccination strategies during the Delta COVID-19 wave. Immunocompromised (IC) individuals have increased risk for COVID-19. We wished to estimate the risk of SARS-CoV-2 infection and COVID-19 related death in IC individuals compared to healthy ones and the effectiveness of the BNT162b2 vaccine by reassessing HUN-VE 3 data.

Methods: Among the 8,087,988 individuals undergoing follow-up in the HUN-VE3 cohort, we selected all the 263,116 patients with a diagnosis corresponding with IC and 6,128,518 controls from the second wave, before vaccinations started. The IC state was defined as two occurrences of corresponding ICD-10 codes.

The control group included patients without chronic diseases. Data have been obtained from the National Public Health Center.

Results: Out of the 263,116 IC patients 12,055 patients (4.58%) and out of the 6,128,518 healthy controls 202,163 (3.30%) acquired SARS-CoV-2 infection. Altogether 436 IC patients and 2141 healthy controls died in relation to COVID-19. The crude incidence rate ratio (IRR) of SARS-CoV-2 infection was 1.40 (95%CI: 1.37-1.42). The crude mortality rate ratio was 4.75 (95%CI: 4.28-5.27). The BNT162b2 vaccine was more effective in IC patients compared to controls. Primary vaccine effectiveness (VE) was higher in IC patients compared to controls and the booster restored VE after waning. VE regarding COVID-19 related death was less in IC patients compared to healthy individuals.

Conclusions: There is increased risk of SARS-CoV-2 infection and COVID-19 related mortality in IC patients. Moreover, booster vaccination using BNT162b2 might restore impaired VE in these individuals.

EP015 / #1071

The DUhTP Marathon Mouse: An Animal Model for Studying COVID-19 Related Metabolic Dysfunction Exacerbated by Exertion - Possibly a Model for Post-Exertional Malaise (PEM)

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Background and aims: The IndyMed CFS model (ISBN: 978-0-85466-172-5) is hypothesized to be due to inflammatory autoimmune processes supported by IgG trafficking / MHC class I and enhanced class II allele-specific peptide presentation in concert with a second trigger of inflammatory leading to endotheliitis, impaired oxygen diffusion and post-exertional malaise (PEM). The Marathon mouse model (DUhTP) initially selected for high treadmill performance is envisaged to serve as CFS animal model on its own or as F1 hybrid crossed with current ACE2 and forthcoming humanized transgene disease models.

Methods: DUhTP Marathon mice display an exceptional running capacity associated with lipid-dependent metabolism compared to unselected controls (DUC) derived from the same genetic background. Both lines underwent three weeks of high-speed treadmill training or were sedentary. Muscle and plasma samples were analyzed. Transcriptional networks were determined by next generation transcriptome sequencing of femoral muscle tissue.

Results: Three weeks of DUhTP high-speed training, that favors anaerobic glycolytic utilization, resulted in oxidative fatty acid utilization due to metabolic adaptation without alterations in muscle fiber types. The latter observation mirrors the histology of muscles in human PEM, implicating that DUhTP exercise capabilities provide an excellent model to study exertional exhaustion due to SARS-CoV2 infection, possibly induced by mRNA vaccines or LNPs alone or in concert with other inflammatory agents.

Conclusions: Marathon mice alone or as hybrids with ACE2 / Spike 1 transgenics are put forward to serve as a pertinent model for investigating Post-Exercise Malaise (PEM) induced by confounders such as SARS-CoV-2 infection, post-vaccination responses, or Lipid Nanoparticle (LNP) exposure.

EP016 / #828

Investigation of the Genetic Association of ACE2 (Rs2285666) and Tmprss2 (RS12329760, RS2070788 and RS383510) Gene Polymorphisms with Cell-Mediated Immunity Against COVID-19 in Rheumatic Patients

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Background and aims: The present study attempted to assess the possible association of four ACE2 and TMPRSS2 gene polymorphisms with the cell-mediated immunity of rituximab-treated rheumatic patients with impaired seroconversion, who had previously been vaccinated against SARS-CoV-2.

Methods: Whole blood samples were collected from 47 rituximab-treated rheumatic patients (37 female, 8 male, age 31-94y) and 22 healthy individuals (12 male, 10 female, age 42-95y), 3–6 months after last vaccination against SARSCoV-2. Four tetra-primer, ARMS-PCR protocols, each specific for the ACE2 polymorphism RS2285666 and the TMPRSS2 polymorphisms RS383510, RS12329760 and RS2070788, were designed and implemented. Cell-mediated variant-specific SARS-CoV-2 immunity (CMI) was assessed by the interferon-γ release assay Covi-FERON FIA.

Results: Seventy percent of the rituximab-treated patients and 64% of the healthy individuals had an active, CMI against SARS-CoV-2. All genotypes studied deviated from the Hardy–Weinberg equilibrium, with the prevalence of the heterozygous genotype in 3 polymoprhisms (except RS2070788). No significant statistical association was observed between any of the gene polymorphisms and the absence of CMI in both patients and healthy individuals.

Conclusions: There are still contrasting results regarding the role of these four genetic polymorphisms in the severity of SARS-CoV-2 infection and during the present study, they were not associated with the development of CMI. Deviation of the genotypes from the Hardy–Weinberg equilibrium has also been extensively found in previous studies, something that may be due to the action of other selection forces. The small sample size of the present study warrants further investigation of these polymorphisms.

EP017 / #1040

Levels of Liver-Related Autoantibodies in Patients with Possible Post-COVID Syndrome

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Background and aims: The liver is among the organs affected by the SARS-CoV-2 virus during acute COVID-19 and, likely, in a post-COVID period. Our study aimed to assess the association between liver functional tests (LFT), circulating liver-related autoantibodies, and possible post-COVID syndrome at 2.5 years after the first COVID-19.

Methods: The study included 77 patients (mean age was 54 ± 13 years, 41 females). Among them, 55 patients had non-severe, 17 – severe, and 4 – critical disease courses. At 2.5 years follow-up, patients were clinically examined and interviewed regarding their long-lasting symptoms and reinfections with SARS-CoV-2. Serum tests included the detection of LFT (ALT, AST, SF, GGT), C-reactive protein (CRP), the total immunoglobulin G (IgG), antinuclear antibodies (ANA IgG), anti-liver kidney microsomal type 1 antibodies (anti-KLM1), antibodies against soluble liver antigen (anti-SLA) detected by ELISA.

Results: Forty-seven patients reported new long-lasting symptoms, and 28 patients reported reinfections. Despite clinically insignificant levels of LFT, total IgG (median 11.0 g/l), ANA IgG (median 0.3), anti-LKM1 (median 2.0 U/l), and anti-SLA (median 1.2 U/l), the presence of long-lasting symptoms was associated with higher levels of ANA IgG (*P*=.24) and anti-LKM1 (*P*=.045). Reinfections were associated with a higher level of total IgG (*P*=.028). The levels of autoantibodies were not related to COVID-19 severity, age, CRP, and LFT, except for a relationship between total IgG and GGT (r_s=0.25, *P*<.05).

Conclusions: Despite the exclusion of autoimmune hepatitis after COVID-19, higher levels of anti-LKM1 and ANA IgG were positively associated with possible post-COVID syndrome.

E-POSTER VIEWING 03: BASIC MECHANISMS: ENVIRONMENT, OBESITY, SMOKING, EXERCISE AND AUTOIMMUNITY

EP018 / #825

Cellular Inflammation Mechanisms Induced by Air Pollution on Rheumatic Autoimmune Diseases

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Background and aims: The mechanisms through which air pollutants modify the immune response and contribute to the pathogenesis of autoimmune diseases (ADs) still need to be fully understood. Therefore, the objective of this study was to comprehend the in vitro cellular mechanisms by which particulate matter (PM), 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), and silica induce a pro-inflammatory immune response that could potentially trigger and/or exacerbate autoimmune rheumatic diseases**.**

Methods: Peripheral Blood Mononuclear Cells (PBMCs) from patients with rheumatoid arthritis, systemic lupus erythematosus, and Sjögren's syndrome as well as control subjects were stimulated with PM, TCDD, and silica, both in the presence and absence of an Aryl hydrocarbon Receptor (AhR) antagonist. We assessed the cytokine and chemokine profile in the culture supernatants, analyzed the activation and maturation of innate and adaptive immune cell populations, and examined signaling pathways, including AKT, NF-κB, p38, STAT1, and STAT3.

Results: PM, silica, and TCDD triggered the activation of monocytes, dendritic cells, NK cells, CD4 and CD8 T lymphocytes, along with an effector and central memory CD4 and CD8 T cell phenotype. These contaminants induced the release of cytokines such as IL-6, IL-10, IL-1b, IL-17, MCP-1, and G-CSF through the activation of STAT-1, NF-κB, and P38. TCDD-induced inflammation was AhR-dependent. There were no significant differences between patients with ADs and control subjects.

Conclusions: Air pollutants activate and mature immune cells, induce the production of inflammatory mediators, and activate specific signaling pathways. Nevertheless, the cellular mechanisms triggered by these pollutants are similar between patients with autoimmune conditions and healthy individuals.

EP019 / #561

Anti-Inflammatory and Regenerative Properties of Adiponectin and AdipoRon in Human Cultured Skeletal Muscle Cells and Fibroblasts

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Background and aims: Muscle involvement in systemic rheumatic diseases patients is common. The level of adiponectin, a hormone secreted by adipose tissue with favourable metabolic and muscle regenerative properties, is perturbed in most rheumatic patients. Our objective was to explore the molecular responses in cultured primary human skeletal muscle cells and muscle fibroblasts after exposure to adiponectin with a focus on inflammation and muscle regeneration and to test if AdipoRon, a synthetic adiponectin receptor agonist, could reconstitute/replace the adiponectin signalling.

Methods: Human primary skeletal muscle (CD56+) cells and muscle fibroblasts (CD56- cells), prepared from samples of *semitendinosus* muscle, were exposed to adiponectin or AdipoRon, followed by gene expression analysis by quantitative PCR. Using western blotting, we examined activation of inflammatory mediator NFkB and activation of metabolic and inflammatory mediator AMPK. As adiponectin receptors have ceramidase activity, sphingosine-1-phosphate (S1P), a ceramide-derived lipid with anti-inflammatory and regenerative effects, and interleukin-6 (IL-6) were quantified in the conditioned medium by ELISA.

Results: Adiponectin-stimulated muscle fibroblasts and skeletal muscle cells secreted IL-6, which is known for its positive impact on muscle regeneration. Notably, the stimulated muscle fibroblasts secreted more S1P. Conversely, AdipoRon had no impact on S1P or IL-6 secretion. Nevertheless, it suppressed NF-kB and activated AMPK in both cell types, suggesting anti-inflammatory properties.

Conclusions: Cultured skeletal muscle cells and fibroblasts responded to adiponectin and AdipoRon with distinct molecular changes associated with anti-inflammatory and muscle regeneration processes. These findings highlight the importance of further studies of adiponectin pathway involvement in muscle manifestations of inflammatory rheumatic diseases.

EP020 / #865

Analysis of the Cardiovascular Disease Risk in Rheumatoid Arthritis Patients: Relationship with Clinical Disease Activity

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Background and aims: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint damage. Cardiometabolic status is a key factor in cardiovascular disease risk (CVD) mortality in RA. This study aimed to assess the association of cardiometabolic risk status with clinical variables in RA patients.

Methods: This study was conducted in Mexican women: 154 RA patients and 201 control subjects (CS). Anthropometry, biochemical, and cardiometabolic indexes were evaluated.

Results: RA patients had higher levels of triglycerides (*P*<.001), albumin and uric acid (*P*=.03), as well as a higher score of CMI index (*P*<.001), Triglycerides/HDL-C ratio (*P*<.001), LAP score (*P*<.001), WHR index (*P*<.001), WHtR index (*P*<.001) and Hs-CRP (*P*<.001) than CS. Likewise, ESR levels (*P*<0.01) and waist circumference (*P*<.01) are higher in RA patients with high CVD risk by Hs-CRP levels. In contrast, albumin levels are lower (*P*<.001). Besides AR patients showed higher cardiometabolic risk to a waist ≥80 cm (OR=2.9; *P*<.001), BMI ≥25 kg/m^2 (OR= 3.5; *P*<.001), a high body fat (OR= 3.5; *P*<.01), a average muscle mass (OR= 2.02; *P*<.01), high CMI index ≥1.188 (OR= 4.3; *P*<.001), LAP index ≥31.06 (OR= 5.3; *P*<.001), WHR index ≥ 0.5 (OR= 4.03; *P*<.001), WHtR index ≥ 0.85 (OR= 5.5; *P*<.001), Hs-CRP ≥ 3mg/L (OR= 6.9; *P*<.01), and to have metabolic syndrome (OR= 2; *P*= .03).

Conclusions: In conclusion, AR patients have higher CVD risk than the general population.

EP021 / #507

Metabolomics and Immunologic Profiling Unravel the Impact of Diet on Autoimmune Disease Susceptibility

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Background and aims: The increasing incidence of autoimmune diseases has sparked growing interest in understanding the complex relationship between diet and autoimmunity. Recent research has shown that dietary interventions have therapeutic potential in managing autoimmune diseases, with evidence of improvements in conditions like rheumatoid arthritis through dietary restrictions. However, the precise molecular mechanisms underlying these effects remain incompletely understood. Prior studies have provided valuable insights into this relationship, especially in the context of lupus. It was observed that dietary restrictions could protect mice from developing lupus, while a high-fat diet increased susceptibility to the disease. These effects were closely associated with changes in the gut microbiota and the expression of specific disease-related genes.

Methods: To further explore these findings, a meticulous experiment involving 160 mice was conducted over a 40-week period. The mice were divided into groups and subjected to four different diets, ranging from high-fat to restricted control diets. Various physiological parameters, including weight, proteinuria, and blood counts, were monitored throughout the study. Additionally, a wide range of organs and tissues were collected and will be analyzed using various techniques. The study's results showed that dietary composition had a profound impact on health and susceptibility to autoimmune pre-disease conditions.

Results: This study revealed significant variations in metabolic indicators, such as body weight and glucose levels, and intriguing immunological characteristics, such as alterations in blood cell counts and spleen length.

Conclusions: Molecular analysis is currently underway on various organs to gain a deeper understanding of the underlying mechanisms.

EP022 / #485

Vitamin D in Psoriatic Arthritis and Sjogren's Disease – A Systematic Review and Meta-Analysis

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Background and aims: This systematic review and meta-analysis aimed to summarize current evidence on vitamin D status in patients with psoriatic arthritis (PsA) and in patients with Sjögren's disease (SD) with a particular focus on disease activity and clinical manifestations. Vitamin D effects depicted in Figure 1.

Methods: PubMed, Web of Science, Scopus and Cochrane Library databases were searched for studies that investigated vitamin D levels in PsA and in SD. Included studies were cohorts or observational studies, and those assessing the level of 25(OH)D3 with control group consisting of healthy or, in PsA case, psoriasis (Pso) patients. Nottingham-Ottawa Quality Scale was used to assess methodological quality. Random effects meta-analysis model was applied with inverse variance weighting and mean difference with 95% CI was calculated.

Results: For PsA, four studies including 264 PsA patients and 287 healthy controls and five studies including 225 PsA patients and 391 Pso patients were eligible for meta-analysis. Vitamin D levels were lower in PsA patients compared to the healthy group, while higher compared to Pso patients. For SD, nine studies totaling 670 SD patients and 857 healthy controls were eligible for meta-analysis. A high prevalence of hypovitaminosis D was observed in SD patients when compared to healthy controls. Results depicted in Figures 2 and 3.

Conclusions: In conclusion, PsA and SD patients have lower vitamin D levels than the general population. However, further studies are essential to understand the role of vitamin D in the development and disease severity of PsA and SD.

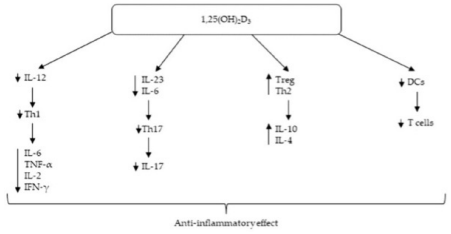

Figure 1.

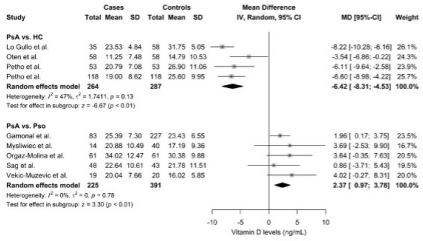

Figure 2.

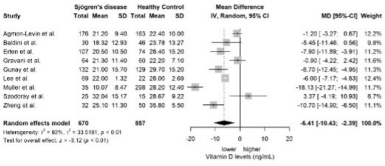

Figure 3.

EP023 / #609

Temperature, Ph Dependency and Activity of Microbial Transglutaminase and Its Gliadin Cross-Linked Neo-Complexes

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Background and aims: Microbial transglutaminase (mTG) is a survival factor for bacteria and is heavily used as a food additive in the processed food industry. Being an enzyme, its temperature and pH range of activity are sensitive. Study the mTG temperature and pH operating ranges by exploring its capacity to cross-link gliadin peptides.

Methods: After optimizing the conditions to cross-link gliadin peptides by mTG (Zedira, Germany), temperature and pH dose-response curves were explored. Gliadin peptides, mTG, and cross-linked products were analyzed on SDS gels.

Results: mTG showed activity at 60°C by cross-link gliadin peptides. Also, various processed food products are not boiled during production processes. On the other hand, the mTG-gliadin docked complexes turn more immunogenic when heated to 90°C. Most probably, more epitopes are exposed to the immune system during denaturation. Concerning the pH impact on mTG activity, the enzyme is active at pH 4.0 and above.

Conclusions: Generally, during processed food preparation, the mTG cross-linked complexes are created before heating or boiling. The resulting covalent isopeptide bonds are incredibly resistant to the luminal proteases. During meal intake, gastric acidity is neutralized, and the pH can reach 4.5. Many children and adults consume acid-suppressive medications, infants and the elderly have a higher gastric pH, and alkaline reflux is not rare. Temperature and pH do not jeopardize the mTG induced cross-linking of gliadin peptides during food preparation. The stomach pH allows those cross-linked complexes to pass and reach the gut lumen.

E-POSTER VIEWING 04: BASIC MECHANISMS: EXPERIMENTAL AUTOIMMUNE MODELS

EP024 / #560

Update of the Guidelines for Passive Transfer Myasthenia Gravis Rat Model: The Use of Subcutaneous Administration

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Background and aims: The passive transfer myasthenia gravis (PTMG) is a passive immunization model induced by injecting monoclonal antibody 35 (mab35) intraperitoneally (i.p.) or intravenously (i.v.). These two injection methods cause moderate pain and the risk of needle misplacement is high, making the model less reproducible. Subcutaneous (s.c.) administration could be a more robust technique to use. We aimed to establish a refinement of the PTMG model using s.c. administration.

Methods: A total of 32, 11-week-old, female Lewis rats were used. Following guidelines, one group was injected i.p. with 20pmol/100g BW mab35 and euthanized 48h post-immunization. Other animals were injected s.c. 20 or 40 pmol/100g BW with mab35 and were euthanized 48h or 72h post-immunization. Control groups received 0.5 mg/kg IgG1 isotype control s.c. or i.p. and were euthanized 48h post-immunization. Blood samples were taken and muscle weakness, fatigue, weight and disease scores were recorded daily up to the time point of euthanasia. Electrophysiological measurements during curare infusion and post-mortem assays were performed to determine AChR-muscle content.

Results: Signs of muscle weakness and fatigue were observed in all animals injected with mab35, while no signs were observed in the animals injected with isotype control. No differences were observed between the group's 20pmol/100g BW i.p. and 40pmol/100g BW s.c., suggesting that the increased dose compensated for the reduced absorption rate in s.c. injections.

Conclusions: Thus, administration method as well as dosage influences disease induction. The results from this study show that s.c. administration could be considered as a refined method to induce myasthenia gravis in rats.

EP025 / #812

Age-Dependent Changes of Thymocyte and Peripheral T Cell Composition, Activation and Apoptosis in NZB Mice

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Background and aims: Spontaneous autoimmune mouse models, like the New Zealand Black (NZB) strain is used to investigate the pathogenesis of the disease. In a previous study we found age-related changes in the natural- and pathological autoantibody network during the development of autoimmune hemolytic anemia (AIHA). Now our goal was to follow the age-dependent changes of thymocyte- and peripheral T cell composition, activation and apoptosis.

Methods: We used female NZB mice at different ages. Cells isolated from the thymus, spleen and lymph-nodes were labeled with fluorochrome-conjugated anti-CD3,-CD4,-CD8,-CD25 and CD69 antibodies for analysis using a FACSCanto-II flow cytometer. We measured the apoptosis frequency of thymocytes after 4 hours in vitro DX treatment with anti-cleaved caspase-3,8,9 staining.

Results: In the thymus we found increased ratio of DN, and SP and diminished DP thy-

mocytes with ageing. Caspase activation in untreated DP and SP thymocytes was similar in young and old animals, only in DN thymocytes decreased with ageing. DX-induced caspase activation in DP thymocytes diminished in old animals. In peripheral lymphatic organs elevated ratio of DN T cells and activated CD69+ Tc and Th cells were observed at 9 months, while the ratio of CD4+ Th- and Treg cells decreased with ageing.

Conclusions: During the age-associated development of AIHA in NZB mice, we observed an elevated ratio of activated $CD8^+$ and DN T cells accompanied with a decrease of Tregs, which might be the results of the dysregulated selection (apoptosis) process of DP thymocytes.

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EP026 / #959

LatY136F Mice: A Preclinical Model for Igg4-Related Disease, Autoimmune and Inflammatory Disorder

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Background and aims: Experimental preclinical models are powerful research tools to explore autoimmune diseases as well as the efficacy and mechanism of action for novel therapeutics.

Methods: Mice with a loss-of-function mutation in the LAT adaptor (LatY136F) develop an autoimmune and type 2 inflammatory disorder called defective LAT signalosome pathology (DLSP). DLSP manifestations involve accumulation of Th2 effector cells triggering polyclonal B cell activation, IgG1/IgE hypergammaglobulinemia and systemic autoimmunity with nephritis showing IgE autoantibody deposits and severe proteinuria.

Results: Most previously described T cell–mediated autoimmune manifestations require persistent TCR input. In contrast, the autoreactive TCR expressed by LatY136F CD4+ T cells hand over their central role in T cell activation to CD28 costimulatory molecules. As a result, all subsequent LatY136F DLSP manifestations, including the production of autoantibodies, solely rely on CD28 engagement By using single cell omics, we recently showed that T follicular helper cells, CD4+ cytotoxic T cells, activated B cells and plasma cells were found in LatY136F spleen and lung. Such cell constellation entailed all the cell types causative of human IgG4-related disease (IgG4-RD), an autoimmune and inflammatory condition with LatY136F DLSP-like histopathological manifestations. Our findings elucidate the etiology of the LatY136F DLSP and qualify it as a model of IgG4-RD and autoimmune disorder.

Conclusions: Our model is a useful tool to facilitate therapeutic target discovery and the preclinical evaluation of drug candidates intending to treat IgG4-RD, type 2 immune disorders and inflammatory fibrotic conditions in the hopes of developing more effective, more targeted and less toxic therapies for treatment and prevention.

EP027 / #962

LatY136F Mice: A Preclinical Model for Igg4-Related Disease, Autoimmune and Inflammatory Disorder

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Background and aims: Experimental preclinical models are powerful research tools to explore autoimmune diseases as well as the efficacy and mechanism of action for novel therapeutics.

Methods: Mice with a loss-of-function mutation in the LAT adaptor (LatY136F) develop an autoimmune and type 2 inflammatory disorder called defective LAT signalosome pathology (DLSP). DLSP manifestations involve accumulation of Th2 effector cells triggering polyclonal B cell activation, IgG1/IgE hypergammaglobulinemia and systemic autoimmunity with nephritis showing IgE autoantibody deposits and severe proteinuria.

Results: Most previously described T cell–mediated autoimmune manifestations require persistent TCR input. In contrast, the autoreactive TCR expressed by LatY136F CD4+ T cells hand over their central role in T cell activation to CD28 costimulatory molecules. As a result, all subsequent LatY136F DLSP manifestations, including the production of autoantibodies, solely rely on CD28 engagement By using single cell omics, we recently showed that T follicular helper cells, CD4+ cytotoxic T cells, activated B cells and plasma cells were found in LatY136F spleen and lung. Such cell constellation entailed all the cell types causative of human IgG4-related disease (IgG4-RD), an autoimmune and inflammatory condition with LatY136F DLSP-like histopathological manifestations. Our findings elucidate the etiology of the LatY136F DLSP and qualify it as a model of IgG4-RD and autoimmune disorder.

Conclusions: Our model is a useful tool to facilitate therapeutic target discovery and the preclinical evaluation of drug candidates intending to treat IgG4-RD, type 2 immune disorders and inflammatory fibrotic conditions in the hopes of developing more effective, more targeted and less toxic therapies for treatment and prevention.

EP028 / #1037

Validation of the Specificity of T-Cell Receptors Associated with Type I Diabetes

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Background and aims: Type 1 diabetes mellitus (T1D) is a chronic autoimmune disease characterized by the destruction of the pancreas β-cells and, as a result, insulin deficiency. Despite advances in medicine, glycemic control is not optimized for most T1D patients, and many cannot even receive basic care due to the high cost of therapy. Autoimmunity against β-cells is mediated and regulated by CD4+ T cells. "Miseducated" T-helper cells, with T-cell receptors (TCRs) specific to autoantigens, recruit adaptive and innate immune cells. CD8+ T cells are the main effectors that destroy β-cells. In our study, we focus on the role of TCRs associated with T1D detected within the Russian population.

Methods: The aim of this work is to develop approaches for confirmation the specificity of TCRs associated with the T1D pathogenesis. For this purpose, we designed lentiviral TCR system. TCR specificity was validated on various Jurkat cell lines, transduced with TCRs of interest, by flow cytometry (FACS) and enzyme immunoassay (ELISpot).

Results: Detection of TCR-dependent expression of reporter fluorescent proteins in re-

sponse to antigen-specific stimulation of the target TCRs in the Jurkat76 cell line TCR-null showed the most reproducible results. FACS confirmed the specificity of TCRs in Jurkat76 CD4+ line in response to stimulation with the GAD65 antigen in the context of the diabetes-associated HLA II haplotypes - DR3-DQ2/DR4-DQ8 that indicates a possible association of these TCRs with the T1D development.

Conclusions: The insight of the TCR specificity in T1D pathogenesis could open the way for new therapeutic approaches to substitute broad-spectrum unspecific immunotherapies.

EP029 / #774

Measurement of Complement Deposition at the Neuromuscular Junction in Myasthenic Rat Models

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Background and aims: Myasthenia Gravis (MG) is an autoimmune disorder, triggered by autoantibodies against proteins in the neuromuscular junction (NMJ), most commonly the acetylcholine receptor (AChR). One of the most relevant mechanisms of action of such antibodies is the activation of the classical pathway of the complement system, leading to membrane attack complex (MAC) formation at the NMJ and tissue damage. This results in neuromuscular transmission impairment, leading to muscle weakness and fatigability. Commonly used rodent models for MG research are the experimental autoimmune MG (EAMG) and the passive transfer MG (PTMG). To analyze complement deposition at the NMJ in these models, we optimized an immunofluorescence (IF) staining using the tibialis anterior (T.A.) muscle and different complement markers.

Methods: Disease induction was performed according to the standardized guidelines and recommendations for EAMG and PTMG, respectively. Animals were euthanized and the TA were dissected and frozen in melting isopentane. Fine sections of 10 µm were used for the IF staining for complement proteins. Anti-MAC and anti-C3 antibodies, as well as markers for AChR (alpha bungarotoxin) and presynaptic proteins for normalization.

Results: For both, EAMG and PTMG animals, clear NMJ complement deposition was visualized while AChR levels were reduced compared to non-MG animals.

Conclusions: IF staining combines several advantages as being an easy practice, allowing multifactorial analysis and quantification options. To assess the activation of the common complement effector pathway and therefore full complement activity, C3 and MAC are excellent targets. Moreover, additional applications of this methodology may be to test the efficacy of different complement inhibitory therapies.

E-POSTER VIEWING 06: BASIC MECHANISMS: GENETICS AND EPIGENETICS IN AUTOIMMUNITY

EP030 / #369

Exploring Heterozygous NLRP3 Gene Mutation in a Family with Autoimmune Diseases and Immunodeficiencies: Uncovering Uncharted Territory

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Background and aims: This text discusses a family grappling with autoimmune diseases and immunodeficiencies, particularly focusing on a heterozygous mutation in the NLRP3 gene. Typically, this mutation leads to cryopyrin-associated periodic syndromes (CAPS), characterized by overactive inflammasomes and excessive interleukin-1 β production. However, this family exhibits a diverse range of autoimmune diseases (AIDs) and hypogammaglobulinemia among its members, despite carrying the same NLRP3 gene mutation. In this particular family, three related women carry the c.598G>A mutation of the NLRP3 gene, each exhibiting a different spectrum of AIDs, with two of them also experiencing hypogammaglobulinemia.

Methods: The case report highlights a 16-year-old female with autoimmune thrombocytopenia (PTI), who later developed celiac disease and selective IgA deficiency. Her mother also presented with autoimmune hemolytic anemia (AIHA) and later she developed hypogammaglobulinemia. Given the occurrence of autoimmune diseases and hypogammaglobulinemia in these two patients, we investigated possible genetic mutations within the family. A paternal aunt of the mother had oligo-LES.

Results: Remarkably, genetic testing of all three women in the family, conducted via blood samples, revealed the presence of the same NLRP3 gene mutation.

Conclusions: In existing literature, the NLRP3 gene c.598G>A mutation has not typically been associated with AIDs but rather with familial cold autoinflammatory syndrome. Nevertheless, our clinical observations suggest a connection between this variant and the complex spectrum of AIDs and hypogammaglobulinemia. Further clinical research and functional analyses are needed to understand the relationship between this gene mutation and the broader range of autoimmune diseases and immunodeficiencies observed in this family.

EP031 / #610

Association of Global DNA Methylation Status with Cardiometabolic Risk in Patients with Systemic Lupus Erythematosus

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Background and aims: Epigenetic factors such as global DNA methylation could affect the expression of genes related to the immune system and contribute to the pathophysiology of autoimmune diseases such as systemic lupus erythematosus (SLE), as well as their associated cardiometabolic comorbidities. This study was aimed to evaluate the association between global DNA methylation status with cardiometabolic risk and clinical disease activity in patients with SLE.

Methods: A comparative cross-sectional study was carried out in women: 204 patients with SLE and 201 control subjects (CS). SLE patients

were classified according to the 1997 SLE-ACR criteria, and the clinical disease activity, according to the Mex-SLEDAI index. The percentage of global DNA methylation was determined using the 5-mC-Zymo DNA ELISA kit.

Results: Active SLE patients had a lower global DNA methylation status than inactive SLE patients (active SLE = 3.4% *vs.* inactive SLE =5.09%; *P*=.04), global DNA methylation status was also higher in SLE patients positive for anti-nuclear antibodies (ANAs) than in SLE patients negative to ANAs (positive ANAs = 4.09% vs. negative ANAs =13.7%; *P*=.01). Notably, a high global DNA methylation status was associated with higher HDL-C levels (β coefficient = 6.8; CI=2.1-11.5; R=0.05; *P*<.01) and a lower LDL/HDL ratio (β coefficient = -0.37; CI= -0.66 to -0.08; R=0.03; *P*=.01).

Conclusions: In conclusion, high global DNA methylation status was associated with low cardiometabolic risk in patients with SLE.

EP032 / #685

Study of HLA-DQB1-AS1, the Antisense Long Non-Coding RNA: A Possible Function in the Regulation of HLA-DQ2.5 Risk Genes of Celiac Disease

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Background and aims: The genes encoding the HLA-DQ2.5 molecules are the main risk factors associated to Celiac Disease (CD), with a key pathogenic role, as the DQ2.5 present the gliadin peptides to inflammatory T cells. We demonstrated a higher expression of DQA1*05/DQB1*02 alleles in Antigen Presenting Cells-(APC) respect to the DQ alleles not CD-associated (1,2) and observed a variation in the mRNAs amount, following in vitro gliadin stimulation (3). Our objective is to investigate the HLA-DQB1-AS1, the antisense non-coding RNA complementary to intron-4/exon-5 of DQB1 gene, and the modulation of its expression upon gliadin challenge.

Methods: We quantified, by qPCR, the expression of DQA1*05/DQB1*02 and the DQB1-AS1 RNA in peripheral blood mononuclear cells (PBMC), monocytes-derived macrophages, and B cells from adult patients with acute CD and on remission. The patients enrolled either homozygous for DQB1*02 (DR3-DR3 or DR3-DR7), or heterozygous (DR5-DR7), with only one copy of DQB1*02.

Results: We demonstrated that DQB1-AS1 expression varies according the genotype and is higher in APC with two copies of DQB1*02 allele. Moreover, we found that gliadin stimulation causes a decrease of DQB1-AS1 in parallel to HLA-DQB*02 mRNA reduction. Silencing and overexpression experiments are in progress to investigate the DQB1-AS1 function.

Conclusions: Our data support the function of DQB1-AS1 as regulator of CD risk alleles. The antisense RNA might represent a target of a regulatory mechanism that affects DQB1*02 mRNA amount and, as consequence, DQ2.5 molecule expression in CD.

EP033 / #594

Methyl-Donor Supplementation Modify IL-27R Methylation Levels in an Animal Model of Lupus

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Background and aims: IL-27R has an immunosuppressive function and inhibits production of pro-inflammatory cytokines, such as IL-10, providing a regulatory mechanism to control autoimmunity and tissue inflammation. Considering the significant role of IL-10 in the pathogenesis of systemic lupus erythematosus (SLE), IL-27 may also play an important role in this disease. DNA methylation process can inhibit binding of the transcription machinery, promoting gene silencing and also may be regulated by the availability of methyl group donor nutrients. Thus, the objective was to evaluate if a methyl-donor supplementation may alter DNA methylation levels of IL-27R gene in animal model of lupus.

Methods: For this, 14 female NZBWF1/J mice (25g, aged 8 weeks) were randomly into two groups: standard diet group that received regular food and supplemented diet group that received the same diet but supplemented with folic acid and vitamin B12. Animals received the diets for twelve weeks. At the end of the experiment, adipose tissue samples were collected and DNA methylation was analyzed by Infinium Mouse Methylation BeadChip. Statistical analyzes were performed using the independent t test.

Results: DNA methylation levels of cg07906995 of IL-27R gene was hypomethylated in those animals that received supplemented diet (2.7±0.3%) compared to those received standard diet (9.0±0.3%; *P*=.004).

Conclusions: Methyl-donor supplementation led to a hypomethylation of cg07906995 of IL-27R gene which may be related to the gene overexpression. Considering that IL-27R control the production of proinflammatory cytokine (IL-10), the use of nutrients may be an adjuvant treatment to SLE.

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EP034 / #474

Knowledge and Current Practices in Monogenic Uveitis: An International Survey by IUSG and Aida Network

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Background and aims: This study aims to explore awareness, knowledge, and diagnostic/therapeutic practices in monogenic uveitis (mU) among uveitis experts.

Methods: This is an explorative, cross-sectional survey study. An anonymous, semi-structured, electronic survey was delivered to uveitis experts from the AIDA Network and International Uveitis Study Group (IUSG). We included respondents answering ≥50% of the survey.

Results: Seventy-seven participants rated their knowledge of mU as proficient (3.9%), adequate (15.6%), sufficient (16.9%), or poor (63.6%). When asked about the first mU gene they thought of, 60.4% mentioned *NOD2*, 3.9% mentioned *NLRP3* or *MEFV*, and 49.4% provided incorrect or no answers. Success rates in clinical scenarios varied from 15.6% to 55.8% and were higher for ophthalmologists working in multidisciplinary teams ($P<.01$). Genetic testing was ordered for suspected mU by 41.6% of physicians. The availability of molecular techniques did not significantly differ based on geography ($P>.05$). The public healthcare system ensured a higher percentage of tests prescribed were obtained by patients compared to private insurance ($P<.001$). In terms of immunosuppressive drugs (ISD), Tumor Necrosis Factor α inhibitors were the most familiar to uveitis experts. The difficulties with off-label therapy procedures were the primary barrier to ISD prescription for mU patients and correlated inversely with the obtained/prescribed drug ratio for interleukin-1 ($P=.006$) and interleukin-6 ($P=.007$) inhibitors.

Conclusions: This survey identifies proficiency areas, gaps, and opportunities for targeted improvements in mU patient care. The comprehensive outputs may inform evidence-based guidelines empowering clinicians with standardized approaches, and drive an AIDA Network – IUSG unified effort to advance scientific knowledge and clinical practice.

EP035 / #841

A Knowledge-Based Data-Mining Tool to Investigate Disease Pathogenesis: Sjögren's Syndrome, Rheumatoid Arthritis, Systemic Lupus Erythematosus

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Background and aims: Sjögren's syndrome (SS), Rheumatoid arthritis (RA), and Systemic Lupus Erythematosus (SLE) are autoimmune diseases with both overlapping and distinct clinical and molecular features. Our aims were: 1. to develop an online tool for analysis of human gene-disease associations; 2. to explore possible bacterial involvement in disease pathogenesis in relation to human gene-disease associations.

Methods: Data infrastructure was established on a Postgres database using $\text{Python}_{v3.8}$ packages: $\text{Plotly}_{v5.17.0}$ and $\text{Streamlit}_{v1.27.2}$. The $\text{Diseases}_{v2.0}$ and GTEx_{v8} databases were utilized, providing searchable disease names, affiliated gene symbols, confidence scores, and gene expression across 54 human tissue types. The microbe-set enrichment analysis database provided context about bacteria possibly affecting human gene expression associated with autoimmune disease pathogenesis.

Results: We found the following numbers of gene-disease associations: SS (n=2,000), RA (n=6,837), and SLE (n=5,171). There were 1,421 genes in common between SS, RA and SLE, encompassing gene-disease linkages across all genomic sources. In SS, minor salivary gland gene expression showed under-expressed STAT4, BLK, KCP, BTNL2, and C6orf10 and over-expressed GPX3, HLA-DRA, HLA-DRB5, and ATP6V1F. In addition, bacterial involvement determination showed STAT4 expression to be possibly affected by 14 bacterial genera including *Streptococcus*, *Lactobacillus*, *Staphylococcus*, *Mycobacterium*, *Porphyromonas*, and *Helicobacter*.

Conclusions: We developed a data mining tool, applied to SS, RA and SLE in this study, designed to view common gene-disease associations, gene expression, and possible human gene-bacterial interactions. The tool will also allow users to investigate any disease of interest. For SS, further investigation into the role of bacteria affecting disease progression is underway in our laboratory.

EP036 / #373

Transcriptional Factors and MicroRNAs as an Important Factor for Th17/Treg Balance in RA Patients– miR-26 and miR-155 as a Potential Biomarker for RA

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Background and aims: The aim of this study was to understand the potential impact of the selected microRNAs expression profiles on Th17 and Treg cells frequency, RA phenotype, and expression profile of selected transcriptional factors: SOCS1, SMAD3, STAT3, STAT5 in RA and OA patients and in healthy controls (HCs).

Methods: The study was conducted on 14 RA patients, 11 OA patients, and 15 HCs. Treg and Th17 frequency were established by flow cytometry. microRNAs and transcriptional factors expression was estimated by qPCR.

Results: The expression of miR-100 and miR-326 was not detected in Th17 and Treg cells. miR-126 expression was detected only in RA Th17 cells. miR-24 expression was higher in RA patients with DAS-28 >5.1 than in RA patients with DAS28 ≤5.1. In RA Treg cells we observed a negative correlation between miR-26 and miR-126, and STAT5A. In HCs Treg cells we observed a negative correlation between miR-155, and STAT3 and SMAD3, and between miR-24 and miR-126, and SOCS1. Based on the ROC analysis, the diagnostic potential of miR-26 was determined at AUC 0.92 for distinguishing RA patients from HCs and at AUC 0.75 for distinguishing RA patients from OA. The diagnostic potential of miR-155 was determined at AUC 0.80 for distinguishing RA patients from HCs and at AUC 0.75 for distinguishing RA patients from OA.

Conclusions: miR-26 and miR-155 may play a role as a potential prognostic biomarker for RA.

EP037 / #383

Aging and the Impact of Global DNA Methylation, Telomere Shortening, and Total Oxidative Status on Sarcopenia and Frailty Syndrome

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Background and aims: Aging is a biological event which influences many organs and systems. Both sarcopenia and frailty syndrome refer to the geriatric conditions with overlapping phenotypes. Many mechanisms are involved in the aging process such as: DNA methylation telomeres which are susceptible to oxidative stress, and inflammations which result in telomere shortening, leading to chromosomal instability. The study goal was to determine the associations between these processes, frailty and sarcopenia syndrome.

Methods: Global DNA methylation was analyzed using the ELISA method. Telomere length was analyzed using qPCR. Total oxidative status (TOS) was analyzed using a colorimetric method.

Results: We found a positive correlation between ASMM and 5-mc in patients with sarcopenia (r=0.69, *P*=.03), and a negative correlation between the level of FI-CGA and BMI in geriatric control (r=-0.38, *P*=.049). In the analysis of the correlation between the level of vitamin B12 and the percentage of methylated DNA in patients with frailty syndrome, we found a positive correlation (r=0.70, *P*=.0001). Significantly higher levels of methylation were noted in patients with sarcopenia when compared to the healthy subject aged 25-30 (*P*=.01) and the healthy subject above 50 years old (*P*<.0001). Patients with frailty syndrome were characterized by significantly higher global methylation levels than healthy subjects above 50 years old (*P* <.0001). Additionally, global methylation was statistically higher in geriatric patients than in healthy subjects aged 50+ (*P*=.003).

Conclusions: Present study revealed that the main factor affecting methylation, telomeres length and level of total oxidant stress was age.

EP038 / #591

Placental Overexpression of VGLL3 Drives Preeclampsia-Like Disease in Mice

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Background and aims: Etiology of preeclampsia (PE), a hypertensive disorder in pregnancy, involves poorly-understood immune dysregulation. Failure of immune tolerance in PE parallels autoimmune signaling in the non-pregnant state. Our group discovered that VGLL3, a Hippo pathway transcription cofactor that orchestrates female-specific inflammation, can drive systemic lupus erythematosus in mice when overexpressed in skin. Endogenous VGLL3 expression is greatest in placenta, where its dysregulation is hypothesized to cause autoimmune-associated complications, such as PE. Indeed, murine *Vgll3*-null placentas exhibit a transcriptomic dampening of lymphocyte-mediated immunity. We aimed to determine whether placental overexpression of *Vgll3* can drive PE-like disease in mice.

Methods: PE characteristics, including hypertension and blood and urine parameters, were assessed in dams with placenta-specific overexpression of *Vgll3*. Placentas were subjected to bulk and single-cell RNA-Seq and histological analyses and integrated into our PE patient data for comparison. HTR8 trophoblast cells were cultured with Hippo inhibitors followed by RNA-Seq.

Results: Dams with placental overexpression of *Vgll3* developed hypertension and hematologic changes. Placentas exhibited microthrombi and fibrinoid necrosis within and around fetal capillaries in the labyrinthine placenta that were occasionally accompanied by immune cells aggregates. VGLL3 was elevated in cytotrophoblasts of PE patients. Transcriptomic signatures of murine stromal and immune cells from *Vgll3*-overexpressing placentas were mirrored in human PE placentas. Chemical inhibition of VGLL3 induced a major transcriptomic shift in trophoblasts targeting PE-linked molecular pathways.

Conclusions: Overexpression of *Vgll3* in placenta causes PE-like presentation in mice, driving a transcriptomic shift that is parallel to what we observe in PE patients and that may be targetable.

EP039 / #42

Evolutionary Adaptations and Genetic Risk for Autoimmunity: Two Sides of The Same Coin

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Background and aims: Causal variants for inflammatory diseases might have been under pathogen-driven natural selection. While this hypothesis has important implications for biomedicine, its application in practice has been hindered by challenges with pinpointing (prioritizing) the targets of selection (mutations). Our project aim was to prioritize disease variants under natural selection for functional experiments. Such variants point to gene variants that strongly impacted the immune response in the past.

Methods: We used fully sequenced genomes of 2,500 donors from the Estonian biobank to analyze the evolution of 593 risk loci associated with 21 autoimmune disorders, cumulatively testing 4838 candidate SNPs. We reconstructed the evolutionary scenario of each risk loci by applying a new class of methods based on the inference of ancestral recombination graphs.

Results: We found that 204 out of 593 risk loci contain at least one candidate SNP with evidence for natural selection. Inferred selection coefficients suggest that these SNPs were likely under weak and moderate selective sweep.

Such sweeps leave flanking variation, making it possible to fine-map the target of selection. We next fine-mapped likely targets of natural selection among candidate risk SNPs (57 loci out of 204) and also identified hitchhiking scenarios. We conclude by discussing an adaptive mutation in the FCRL3 gene that was likely protective against mucosal barrier infections but currently contributes to various autoimmune diseases.

Conclusions: Our findings support the idea that inflammatory disease variants contributed to pathogen resistance endophenotypes and are promising for functional analyses since natural selection picks mutations with a tangible effect on the phenotype.

E-POSTER VIEWING 07: BASIC MECHANISMS: INFECTION AND AUTOIMMUNITY: MICROBIOME, INFECTOME AND INTERACTOME

EP040 / #845

Antigen-Specific Immune Responses Against Epstein-Barr Virus, Human Cytomegalovirus & Helicobacter Pylori Antigens in Patients with Myasthenia Gravis

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Background and aims: Myasthenia Gravis (MG) is an autoimmune disease with muscular weakness which can be triggered by infections. The aim of our study was to investigate the possible correlation between concurrent humoral antigen-specific immune responses against Epstein-Barr virus (EBV), Human Cytomegalovirus (HCMV) and *Helicobacter pylori (HP)* in patients with MG.

Methods: Eighteen patients with MG and 22, 36 and 49 healthy controls (HC) were tested for antigen-specific IgG antibody reactivity against EBV, HCMV and *HP* respectively by immunoblotting (Euroimmun, Germany).

Results: Concerning EBV in MG, higher reactivities and magnitudes were shown against p79. EBNA-1 (100% *P*=.053, 57.8±21.3 AU *P*=.053) and p41.VCA (55.6% *P*=.004, 21.7±8.1 AU *P*=.006), compared to HCs (77.3% *P*=.053, 74.9±28.4 AU, *P*=.053 and 9.1% *P*=.004, 12.5±0.7 AU *P*=.006 respectively). Accordingly, for HCMV in MG only anti-UL57 (38.5%, *P*<.001) and anti-UL83 antibodies (61.5%, *P*=.011) showed a lower frequency in MGs compared to HCs (96.2%, *P*<.001 and 96.2%, *P*=.011 respectively). Finally, for *HP* in MG anti-p120-CagA (52.5±28.7 AU, *P*=.034), anti-p67-FSH (24.8±9.6 AU, *P*=0.004), anti-p50 (19.2±7.1 AU, *P* <.001), anti-p41 (22.5±0.7 AU, *P*=.004), anti-p29-OMP (26.0±6.1 AU, *P*=.003), anti-p19-OMP (19.4±5.2 AU, *P*=.05) and anti-p17 (21.0±4.6 AU, *P*=.018) antibodies had lower magnitudes in MGs compared to HCs (77.7±42.3 AU, *P*=.034, 46.4±32.1 AU, *P*=.004, 40.8±22.1 AU, *P*<.001, 43.1±24.4 AU, *P*=.004, 61.8±49.8 AU, *P*=.003, 42.7±32.1 AU, *P*=.05) and (42.2±24.1 AU, *P*=.018) respectively.

Conclusions: In contrast to HCMV and *HP,* antigen-dependent EBV reactivities were more prevalent and stronger in MG compared to HCs pointing towards a putative role in that disease.

EP041 / #599

Infective Endocarditis or Anca Associated Vasculitis: The Importance of a Correct Differential Diagnosis

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Background and aims: Autoimmunity and infection are strongly related and considered as expression of a double-edged sword. In this setting differentiation between Infective Endocarditis (IE) and ANCA Associated Vasculitis (AAV), such as Granulomatosis with Polyangiitis can be particularly tricky, since the absence of clear diagnostic criteria.

Methods: Here we present the case report of a young patient with particular clinical features both resembling to Infective Endocarditis or granulomatosis with polyangiitis. We propose a revision of the literature with the aim to better clarify any possible relation or differentiation from the two different pathologies. We searched the MEDLINE database (National Library of Medicine, Bethesda, MD) and selected articles, over the last 12 year, with the headings "granulomatosis with polyangiitis", "Wegener's granulomatosis", "heart", "cardiac involvement", "valve", "valvular", "endocarditis", "vasculitis", "ANCA", "ANCA associated Vasculitis" to identify cases of IE mimicking GPA and/or GPA mimicking IE.

Results: This review enlightens the challenge in the differential diagnosis between IE, and AAV. Ear-nose-throat involvement seems to be the best differentiation factor between infectious and autoimmune disease; other intriguing criteria may be resembled by kidney involvement, valvular alteration, and blood tests, including ANCA positivity.

Conclusions: The review of the literature highlighted that differential diagnosis between infective endocarditis and granulomatosis with polyangiitis may be critical and need to be clearly analyzed.

EP042 / #23

Specific Dysbiosis in Spondyloarthritis According to Subtype, Disease Activity, and Treatment: A Fecal Microbiota Study

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Background and aims: Variability in microbiota composition could induce metabolic changes influencing clinical activity and inflammatory status in spondyloarthritis-SpA. The aim was to compare the diversity and composition of fecal microbiota in SpA patients.

Methods: 16S ribosomal RNA gene MiSeq sequencing was performed on DNA isolated from feces. Patients with simultaneous SpA and IBD were excluded. Differences in richness and diversity indices were evaluated using QIIME2™. Differences between means > 0.2% and p-value < 0.05 were assumed to be significant. Approval from institutional ethics committee was obtained.

Results: 69 individuals included, 49 with SpA (ankylosing spondylitis-AS 72.9%, psoriatic arthritis-PsA 18.8%, reactive arthritis-ReA 8.3%), 5 positive controls-dysbiosis, and 15 controls-eubiosis. Conventional treatment use was 42.9%, anti-TNF 40.8%, and anti-IL-17 16.3%. Diversity and richness showed significant differences for AS and high activity. The number of ASVs were higher for anti-IL-17 (*P*=.025) and a trend for anti-TNF (*P*=.09). AS vs PsA; increased Clostridium clostridioforme (*P*=.002), Gemmiger formicilis (*P*=.009), Roseburia inulivorans (*P*=.008), and Lachnospira pectinoschiza Lachnospira (*P*=.005) in AS. AS vs ReA; increased L. pectinoschiza (*P*=.009), Ruminococcus callidus (*P*=.006), Clostridium ruminantium (*P*=.031), and G. formicilis (*P*=.034) in AS. In anti-TNF decreased C. clostridioforme (*P*=.023), G. formicilis (*P*=.030), and R. callidus (*P*=.003). In anti-IL-17 decreased Alistipes indistinctus (*P*=.012). In high activity, decreased Bacteroides eggerthii (*P*=.0003), C. ruminantium (*P*=.026), and Alistipes putredinis (*P*=.035).

Conclusions: There are differences in diversity for the subtypes of SpA and disease activity. Treatment with anti-TNF and anti-IL-17 can influence the microbiome environment affecting microbiota restoration.

Acknowledgment: Asociacion Colombiana de Reumatologia - Asoreuma for presentation financial support.

EP043 / #847

Oral Microbiome Constitutes a Multi-Marker Signature in Patients with Sjögren's Syndrome

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Background and aims: Sjögren's Syndrome (SS) is a long-term autoimmune disease, causing dry eyes/mouth and systemic complications. SS treatment includes prevention of ocular/oral symptoms. Our objective was to compare oral microbiome profiles in patients with SS, *sicca* syndrome and healthy controls (HCs).

Methods: Oral samples (saliva (S), buccal mucosa (B), tongue (T), and/ or supragingival plaque (P)) were collected from HCs (N=38), SS patients (N=19), and *sicca* patients (N=10). Samples were sequenced using 16S rRNA gene amplification to determine the relative abundance of bacterial taxa. Data from SS and *sicca* patients' saliva samples were combined to constitute a hyposalivary dysfunction group (HSD: N=29). *Alpha*- and *beta*-diversities were determined to compare HC *vs.* SS (BPST and S sample site combinations), SS *vs.* sicca (S sample site) and HC *vs.* HSD (S sample site). LEfSe analysis was performed for each comparison. ROC curves were plotted for significant species per Mann-Whitney U-test (*P*<.05). CombiROC plots were completed for species with an AUC>0.75.

Results: All *alpha-/beta*-diversity comparisons were significant. LEfSe showed *Gemella sanguinis* to be a common pSS differential species among all comparisons. In the SS *vs.* sicca comparison, *Rothia mucilaginosa* was a differential species for *sicca* patients. *Prevotella fusca* and *Prevotella buccalis* were HC differential features. CombiROC analysis using multiple species resulted in AUCs>0.90 for all comparisons with HC group.

Conclusions: There were significant differences in oral microbiome profiles of patients diagnosed with SS, *sicca*, and healthy controls. The differential species identified, possibly constitute a multi-marker signature of SS.

EP044 / #785

Is Helicobacter Pylori Involved in the Excistence of Ana in Psoriatic Disease?

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Background and aims: In patients with psoriatic disease, ANA are frequently found even before the initiation of the triggering biologic therapy but their origin remains unclear. We considered *Helicobacter pylori* (Hp) infection as their initiating factor and assessed this hypothesis. Our aim was to assess antigen-specific antibody responses against Hp in ANA positive and ANA negative patients with psoriatic disease.

Methods: A total of 87 psoriatic disease patients (51 with psoriasis, Ps and 36 with psoriatic arthritis, PsA stratified in 28 ANA positive patients (15 with PsA) and 59 ANA negative patients (21 with PsA). Antibody reactivity to Hp-specific antigens was tested by western immunoblotting (Euroimmun).

Results: Overall, anti-Hp reactivity did not differ between ANA positive and ANA negative. Antibodies against p120-CagA, p95-VacA, p75, p67-FSH, p66-UreB, p57, p54-flagellin, p50, p41, p33, p30-OMP, p29-UreA, p26, p19-OMP and p17 antigens of Hp were found in 53.8%, 0%, 30.8%, 84.6%, 92.3%, 100%, 76.9%, 30.8%, 53.8%, 23.1%, 23.1%, 100%, 53.8%, 30.8% and 23.1% in ANA positive compared to 60%, 8%, 28%, 56%, 100%, 92%, 72%, 36%, 48%,28%, 24%, 92%, 64%, 16% and 16% in ANA negative patients with psoriatic disease, respectively (*P*>.05, for all comparisons). Also, no correlation was found between anti-Hp serostatus and ANA titre or ANA pattern. Finally, no correlation was found between anti-Hp reactivity and clinical features amongst ANA positive and ANA negative patients.

Conclusions: Our data do not support any significant association between antibody responses to specific Hp antigens and ANA seropositivity, suggesting an unlikely role for Hp infection in autoantibody production.

EP045 / #229

Cannabinoid Receptor 2(CB2) Agonists Alter Immune Responses and Decrease Neuroinflammation in Chronic HIV Infection in A Humanized Mouse Model

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Background and aims: Despite effective control of HIV replication by antiretroviral therapies, a significant number of patients develop HIV-associated neurologic disorders (HAND).

HAND is attributed to chronic immune activation, ongoing neuroinflammation and blood brain barrier (BBB) compromise. We have shown before that factors implicated in HAND pathogenesis (chronic neuroinflammation, secretion of pro-inflammatory factors and BBB impairment) could be mitigated by CB_2 stimulation. In this study we aimed to demonstrate that HIV-infected humanized huNSG mice are a reliable and relevant model for longitudinal studies of HIV-1 infection.

Methods: We have tested the effectiveness of three novel non-toxic, orally bioavailable CB_2 agonists in chronic HIV infection using the huNSG mouse model. Using non-forceful feeding as the method of daily administration, we studied effects on HIV infection up to 12 weeks. Viral load and human cytokine were measured in blood. Changes in immune markers on T cells during chronic HIV infection in the huNSG mice were analyzed by flow cytometry.

Results: All tested CB_2 agonists attenuated immune activation markers in the blood; however, none had an effect on HIV viral loads *per se*. The CB_2 agonists helped to diminish immune activation in the spleen and normalized cytokine profile in the blood. CB_2 agonists dampened microglial activation and improved expression of tight junction protein that stabilize the BBB.

Conclusions: Our study indicates that novel orally bioavailable CB_2 agonists have potential in suppression of immune activation in chronic HIV infection, both systemic and in the brain, and warrant further investigation as candidates to be included in a HIV treatment regimen.

EP046 / #802

Deciphering HTLV-Induced Phenotypic Variations: Insights from Integrative Systems Immunology Analysis

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Background and aims: The human T-cell lymphotropic virus (HTLV) is a retrovirus responsible for a widespread infection, affecting an estimated 10 to 20 million people worldwide. While most HTLV cases are asymptomatic, some individuals develop serious conditions such as adult T-cell leukemia/lymphoma (ATL) or autoimmune diseases like spastic paraparesis/HTLV-associated myelopathy (HAM/TSP), a chronic myelopathy associated with HTLV. The reasons behind this divergence remain unclear.

Methods: To shed light on this issue, we conducted an analysis of publicly available whole transcriptome data from 237 individuals. This group included 49 healthy controls (HC), 45 asymptomatic carriers, 117 ATL patients, and 26 HAM/TSP patients. To ensure data accuracy, we performed metanalysis for batch effect correction and employed Fisher's method to combine p-values for information integration. Subsequently, we examined enriched biological processes by identifying meta-differentially expressed genes (meta-DEGs).

Results: In asymptomatic individuals, we observed an enrichment of meta-DEGs associated with the regulation of responses to biotic stimuli, mononuclear cell differentiation, and various biological processes related to innate immunity, such as myeloid leukocyte activation, positive regulation of TNF, phagocytosis, and macrophage activation. In contrast, ATL patients displayed meta-DEGs mostly enriching the regulation of cell-cell adhesion, positive regulation of cytokine production, and various T cell-specific processes, including leukocyte differentiation, regulation of activation, proliferation, and adhesion. HAM/TSP patients primarily exhibited enrichment in processes related to the response to viruses, mononuclear cell differentiation, and various biological processes associated with the negative regulation of cell-cycle-related processes and checkpoint signaling.

Conclusions: These findings offer a comprehensive understanding of the distinct phenotypic outcomes induced by HTLV infections.

E-POSTER VIEWING 08: BASIC MECHANISMS: INNATE AUTOIMMUNITY, TLRS AND AUTOIMMUNITY

EP047 / #601

Effect Of Poly I:C In Human Thyrocytes in Culture, Implications for Autoimmune Thyroiditis

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Background and aims: The pathways and mechanisms that trigger the thyroid autoimmune response have not been able to be deciphered, although they have been able to link factors that are specific to the immune system, such as pro-inflammatory cytokines, were the expression is regulated by activation of different Toll-like receptors (TLR), after the union of molecular pattern associated with pathogen (PAMP) of bacteria and virus.

Methods: In the present study, we work with two human thyroid cell lines, NThy-ori 3-1 and TPC-1 (Papillary thyroid cancer cell line). Both cell lines were stimulated with bacterial lipopolysaccharide (LPS) and/or polycytidylic acid (poly I:C). Subsequently, the expression of different genes was analyzed by conventional RT-PCR and Immunohistochemistry. The expression of genes related to thyroid function (thyroid peroxidase (TPO) and thyroid hormone receptors (TSH-R), Toll-like receptors (TLR3, TLR4 and TLR9) and inflammatory cytokines (IL-1b and TNF-alfa).

Results: The results show that treatment with LPS and Poly I:C does not produce changes in thyroid function genes, but shows an increase in the expression of the TLR3 and TLR4 in both cell lines. Also the treatment in the two cell produce an increase in the expression of IL-1β and TNF-alfa.

Conclusions: Demonstrating that PAMPs of viral origin as a bacterial would be helping to trigger an autoimmunity at the level of the thyroid, producing changes in the thyroid microenvironment, leading to that the thyrocytes obtain the ability to act as antigen-presenting cells, which favors the development of Hashimoto's thyroiditis.

EP048 / #706

Decreased CD180 Signaling Via The PI3K/Akt/ NF-kB Pathway in B Cells Might Be Associated with Altered Baff Receptor Expression in Systemic Sclerosis

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Background and aims: Differential expression and functions of Toll-like receptor (TLR) homologue CD180 on B cells have been associated with autoimmune disorders. TLRs can alter the expression of B-cell activating factor (BAFF) receptors and also signal via the phosphatidylinositol-3-kinase (PI3K)/ Akt/ the mammalian target of rapamycin (mTOR)/ NF-κB pathways. Our aim was to investigate whether CD180 signaling contributes to cell dysfunction in diffuse cutaneous systemic sclerosis (dcSSc).

Methods: Peripheral blood mononuclear cells of dcSSc patients and age-matched healthy controls (HC) were isolated using Ficoll gradient centrifugation. To investigate the effects of activation via CD180 the cells were stimulated with anti-human CD180 antibody. The expression of CD180 and BAFF receptors and the changes in the phosphorylation of Akt, S6 and NF-κB were detected by flow cytometry.

Results: We found that CD180 expression of dcSSc B cells was significantly lower than in HC B cells. Stimulation via CD180 increased the phosphorylation of Akt and NF-κB in B cells to a lower extent in dcSSc B cells compared to HC. Anti-CD180 antibody treatment had opposite effects on the expression of BAFF receptors in HC B cells, resulting in similar levels found in dcSSc without stimulation.

Conclusions: Our results suggest that the TLR homologue CD180 molecule may be involved in B cell dysfunction in early dcSSc. B cell activation via CD180 utilizes the PI3K/Akt/mTOR/ NF-κB pathway in dcSSc and may contribute to a pathological BAFF signaling.

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EP049 / #644

Autoantibodies Targeting The Alarmin High-Mobility Group Box Protein 1 (HMGB1) in Systemic Lupus Erythematosus: Prevalence and Characterization

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Background and aims: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease, characterized by the presence of circulating autoantibodies directed against self-antigens. Recent studies showed involvement of HMGB1, a nuclear protein which can act as an alarmin when released into the extracellular environment and anti-HMGB1 autoantibodies (Abs) among SLE patients. According to these data, we aimed to assess anti-HMGB1 Abs relevance in SLE patients and to evaluate Abs specificities against HMGB1 fragments.

Methods: Anti-HMGB1 Abs were measured in 146 SLE patients' sera by ELISA. 66/146 patients had quiescent disease. Of 80 patients with active disease, 40 had nephritic exacerbation and 40 had rheumatoid exacerbation. Antibody specificity was also investigated using different fragments of HMGB1.

Results: Of the 146 SLE patients, 40.4% (59/146) presented anti-HMGB1 Abs, the majority of them with active disease (39/80). Interestingly, active disease was significantly associated with the presence of anti-HMGB1 Abs (*P*=.034). Titers of anti-HMGB1 Abs were significantly higher in rheumatoid exacerbation than in quiescent patients (*P*=.007). Moreover, anti-HMGB1 Abs positively correlated with anti-dsDNA Abs (r=0.2; *P*=0.019) but not with SLEDAI (r=0.17; *P*=.05). Regarding antibodies specificities, all positive for anti-HMGB1 Abs targeted HMGB1 AB Boxes, A Box and B Box fragments. Interestingly, 84% negative for anti-HMGB1 Abs presented Abs against these fragments.

Conclusions: Anti-HMGB1 Abs might be interesting new biomarkers for diagnosis and follow-up as they were found more frequently in active than in quiescent SLE patients. Moreover, these Abs could impact the HMGB1 inflammatory functions and this part needs to be investigated.

EP050 / #362

C1q and Galectin-3: A Novel Interaction

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Background and aims: C1q is a key initiator of the complement system and plays a vital role in preserving the immune system's normal functioning. It mediates the clearance of cell debris and interacts with a wide variety of ligands. Currently, no experimental data exists on the molecular mechanism of interaction between C1q and the molecules from the galectin family. Gal-3 is known to control intercellular and extracellular molecular interactions during immunological responses. Thanks to its carbohydrate binding domain and its proline-rich N-terminal domain, Gal-3 can interact with ligands as a protein or/and a lectin.

Methods: We investigated the possible recognition between C1q and Gal-3 by ELISA and fluorescence spectroscopy. Additionally, molecular docking and molecular dynamics simulations were performed to further identify biding site amino acids.

Results: The data showed that C1q and Gal-3 had a pronounced affinity for interaction and supramolecular binding. When the active AAs of the two proteins interacted, electrostatic attraction, aided by a plethora of hydrogen bonds, was dominant for the stabilization of the complex. When the contact of C1q and Gal-3 was not limited according to active residues, the complex between them was stabilized mainly by Van der Waals interactions and fewer but stronger hydrogen bonds. Fluorescence spectroscopy gave quantitative assessment to the recognition with Kd value of 0,04μM.

Conclusions: Galectin-3 is a new ligand of C1q. It is a protein-protein interaction between the globular "head" regions of C1q and the backside of the lectin domain of Gal-3. Acknowledgement: The experimental work was financed by Grant KP-06-N41-9 of the Bulgarian NSF.

EP051 / #1145

Anti-Citrullinated Histone Antibody CIT-013, a Dual Action Therapeutic for Neutrophil Extracellular Trap Associated Autoimmune Diseases

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Background and aims: Neutrophil extracellular traps (NETs) contribute to the pathophysiology of many immune mediated inflammatory diseases (IMIDs). CIT-013 is a first-in-class monoclonal antibody that specifically targets citrullinated histones H2A and H4 and shows efficacy in several pre-clinical models of NET-associated inflammation. The aims of this study were to investigate CIT-013's mechanism of action (MoA) and show target engagement in a human model of low-grade inflammation. Additionally, CIT-013's potential as treatment for rheumatoid arthritis (RA) and hidradenitis suppurativa (HS) was investigated.

Methods: Confocal microscopy was used to visualize CIT-013's MoA. CIT-013's NET-targeting potential was further assessed by investigating its efficacy in a collagen-induced arthritis mouse model, as well as by the detection of NETs in RA and HS serum and tissue with ELISA and immunohistochemistry. Inhibition of NET release was investigated in LPS-challenged healthy human volunteers.

Results: CIT-013's MoA encompasses inhibition of NETosis and enhanced macrophage-mediated clearance of NETs and netting neutrophils. Elevated CIT-013 epitope levels have been demonstrated in serum and tissue of RA and HS patients. In human RA synovial tissue, NET levels correlate with inflammation grade. LPS nano-dosing in healthy volunteers induced an increase in circulating NETs which was significantly inhibited by CIT-013 treatment.

Conclusions: CIT-013 has a unique dual NET-targeting MoA, suppressing their proinflammatory properties, with therapeutic potential for IMIDs like RA and HS. This reinforces the position of CIT-013 as unique therapeutic approach for NET-associated diseases with unmet therapeutic needs. CIT-013 will enter phase 2 proof-of-concept trials in RA and HS during 2024.

E-POSTER VIEWING 09: BASIC MECHANISMS: MECHANISM AND ETIOLOGY OF AUTOIMMUNE DISEASES – FROM BENCH TO PATIENTS

17-05-2024 08:00 - 23:50

EP052 / #393

Evaluation of Mitochondrial Interplay and Linked Mechanisms in Regulating The Multiorgan Pathology in Murine Lupus

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Background and aims: The complexity of systemic lupus erythematosus (lupus) is still an enigma. Mitochondrial dysfunction and oxidative stress are known to be important aspects that can regulate lupus etiology. However, their role in regulation of organ manifestation in lupus is unknown. This study is based on comprehend the interplay between AMPK/PGC-1/SIRT-1 axis, mitochondrial complex activity and anti-oxidants levels in lupus organ pathology.

Methods: The study was carried out on Pristane-induced Balb/c mice lupus model (LM). Evaluation of anti-oxidants (Superoxide Dismutase and catalase), mitochondrial complexes, pro-inflammatory cytokine levels (IL-1β, IFN-Ɣ, IL-17A), biochemical parameters were assessed. Immunohistochemistry was performed on tissue sections for detection of immunocomplex deposition. The AMPK/PGC-1/SIRT-1 mRNA axis was analysed by q-PCR and flowcytometry. Analysis of reactive oxygen species (ROS) among white blood cells (WBCs) was performed by using various dyes (DCFDA, Mitosox, JC-1) on flowcytometry.

Results: Immune complexes in tissue sections, anti-nuclear antibodies in serum and pro-inflammatory cytokines were significantly high while anti-oxidants were considerably reduced in LM as compared to control. Biochemical parameters depicted altered organ pathology in LM which was accompanied by dysregulated mitochondrial complex and anti-oxidant activity and lupus nephritis was predominant. Differential expression of the AMPK/PGC-1/SIRT-1 axis was detected in tissue and its correlation with mitochondrial and antioxidant activity emerged which was negative in LM while positive in controls. A close association was observed between ROS, mitochondrial membrane potential and AMPK/PGC-1/SIRT-1 axis in WBCs.

Conclusions: This study points towards a plausible role of interplay between AMPK/PGC-1/SIRT-1 axis, mitochondrial function, and oxidative stress in affecting organ pathophysiology.

EP053 / #859

Antibody Reactivity Against Human Cytomegalovirus Antigens in Patients with Sjogren Syndrome

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Background and aims: Human Cytomegalovirus (HCMV) infection is considered as one of the potential causes of Sjögren's syndrome (SjS) he disease. Until now a detailed analysis of antibody reactivity against all HCMV antigens has not been performed. The aim of our study was to detect the specific antibody immune response against all immunodominant (n=6) HCMV antigens in patients with SjS.

Methods: Sera from 37 SjS and 44 matched healthy controls (HC) were tested for the presence of IgG anti-HCMV antibodies by Western immunoblotting (Euroimmun AG, Germany).

Results: Ab positivity against HCMV was found in 24 (64.9%) patients with SjS vs 31 (70.5%) HCs (*P*=NS). Reactivity against antigens of HCMV was comparable in SjS patients and HCs Concerning the magnitudes of antibody responses, antibodies against p38 were found statistically lower in SjS patients compared to HCs (37 ± 7.9 AU vs 50.1 ±16.8 AU, *P*=.030).

Conclusions: Antibodies against p38 antigen of HCMV were found in lower titers in patients with SjS compared to HCs. The pathophysiological significance of these finding requires more investigation testing larger number of patients with SjS.

EP054 / #1065

An Innovative Multi-Compartmental Dynamic 3D Model to Investigate the Pathogenesis of Systemic Sclerosis as a Prototype of Fibrotic Vasculopathies

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Background and aims: The development of 3D models partially overcomes the limitations of 2D *in vitro* cultures and *in vivo* models, allowing to recreate the tissue/organ architecture and cell-cell cross-talk. We set up a 3D multi-compartmental dynamic system for culturing endothelial cells (ECs) and fibroblasts to reproduce the vascular and connective structures. ECs and fibroblasts are the main actors in Systemic Sclerosis (SSc), the prototype of vas-

culopathies. Using traditional 2D cultures, we previously demonstrated the pathogenic role of SSc immune complexes (SSc-ICs). We aimed to apply our 3D model to investigate the SSc pathogenesis more deeply in an environment as close as possible to the *in vivo* milieu.

Methods: We grew human ECs and skin fibroblasts in acellularized hydrogel and dermal scaffold, respectively, into two bioreactors interconnected via a dynamic flow from ECs to fibroblasts. We then incubated 3D ECs with SSc-ICs/healthy-ICs with the EC-conditioned medium flowing throughout 3D fibroblasts. Sections of ECs/hydrogel and fibroblasts/scaffold were evaluated by histological analysis and indirect immunofluorescence by confocal microscopy.

Results: Treatment with SSc-ICs resulted in poorly organized vascular structures and increased deposition of collagen and a-SMA together with a fibrotic phenotype typical of Scleroderma, at variance with healthy-ICs which induced the formation of vascular-like structures by ECs and a derma-like homogeneous architecture by fibroblasts.

Conclusions: The proposed dynamic 3D platform simulating the in vivo EC-fibroblasts cross-talk is a valuable model for studying the pathogenesis of SSc and other vasculopathies. It can be used to develop novel therapies that may improve patient management.

EP055 / #479

Relevant Cell Populations in COVID Patients with Autoimmune Manifestations

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Background and aims: Common variable immunodeficiency (CVID) is the most prevalent inborn error of immunity (IEI) with clinical relevancy. It involves a wide range of manifestations and includes disorders such as systemic autoimmune diseases and autoimmune cytopenias. The Euroclass classification offers a correlation between CVID clinical profile and some relevant cells populations. In this communication we analyse multiple cytometry cell populations and their relation with autoimmune disease incidence in our cohort of 22 CVID patients.

Methods: In the moment of the CVID diagnose, blood test was extracted from patients in order to do a cytometric analysis of the memory B-cell compartments, plasmablasts, CD21low B cells and transitional cells.

Results: In our cohort of 22 patients, 9 had autoimmune manifestations, which were mainly arthritis and cytopenias. From those 9 patients, 4 had a decreased number of LB switch class; 6 had B-cell CD21low increased percentage and 2 had augmented transitional B cells. The 13 CVID patients without previous diagnosis of autoimmunity had the following distribution: 8 had a decreased number of LB switch class; 6 had LB CD21low increased and 2 had increased transitional B cells. There were no significant differences between both groups' populations.

Conclusions: In our cohort, patients with autoimmune pathology had greater proportion of CD21low B-cells when compared with no autoimmune manifestations group although it is not statistically significant. Other relevant populations were similar between both CVID profiles. Despite further investigation on this topic is required, our results suggest that B-cell compartment analysis might be a useful tool to complement CVID autoimmune follow-up.

EP056 / #464

Characterization of Circulating Extracellular Vesicles and Their Micro-RNAs Cargo in Idiopathic Inflammatory Myopathies Reveals a Potential Role as Biomarkers Across Clinically Diagnosed Myositis Subsets

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Background and aims: Idiopathic inflammatory myopathies (IIM) are rare systemic autoimmune disorders. Extracellular vesicles (EVs) are cell-derived nanoparticles involved in intercellular signaling. MicroRNAs regulate gene expression in several autoimmune diseaseswhich belong to EVs cargo. This study aims to investigate the potential role of circulating EVs and EV-microRNAs as IIM biomarkers.

Methods: EVs isolated from platelet-free plasma of IIM and healthy donors (HD) were quantified by nanoparticles tracking analysis (NTA) and EV-microRNAs investigated through Next-Generation Sequencing (NGS).

Results: Circulating EVs concentration was significantly higher in IIM patients (n=64) than HD (n=65) (*P*=.0073), and in patients in clinical remission vs. active disease (*P*=.0087). Cancer associated myositis (CAM) displayed higher EV levels vs. no-CAM (*P*=.0128). EVs levels were reduced in patients receiving rituximab than other treatments (*P*<.0001). NGS detected differences in EV-miRNA between patients and HD. Patients displayed up-regulated miR-223-3p (*P*=.019), miR-15a-5p (*P*=.0189), miR-451a (*P*=.0074), miR-486-5p (*P*=.0052), miR-32-5p (*P*=.0146), and miR-222-3p (*P*=.0282) and down-regulated miR-141-3p (*P*=.0313), miR-142-3p (*P*=.0244), and let-7a-5p (*P*=.0003). Among IIM patients, miR-143-3p was selectively up-regulated in CAM (*P*=.0085); miR-148a-3p (*P*=.0171) and miR-335-5p (*P*=.0171) in dermatomyositis; miR-222-3p (*P*=.002) and miR-151-3p (*P*=.0233) up-regulated and miR-363-3p (*P*=.0001), miR-374a-5p (*P*=.0258), miR-144-3p (*P*=.0170), miR-181a-5p (*P*=.0037) down-regulated in patients with an active disease. miR-4433b-5p (*P*=.0439), miR-92a-3p (*P*=.0111), let-7f-5p (*P*=.0304) were up-regulated and miR-27a-3p (*P*=.0486) down-regulated in patients receiving only glucocorticoids vs. glucocorticoids and immunosuppressants.

Conclusions: Our results suggest a differential miRNA footprint between patients and HD and across IIM subsets, thus potentially submitting EVs and EV-miRNAs as biomarkers for IIM phenotyping and treatment response.

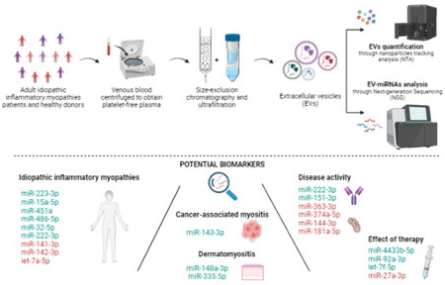

Figure 1.

EP057 / #667

Chronic Stress as a Cause of Autoimmunity - A Holistic Approach

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Background and aims: Autoimmune diseases have multifactorial etiologies and complex pathogenesis. Nevertheless, immune dysregulation is a critical event in the development of autoimmune diseases particularly in genetically susceptible individuals exposed to the destructive effects of chronic stress on mental and physical health. Chronic stress is a continuous or recurrent "fight-or-flight" state which leads to various physiological imbalances such as continuous low-grade inflammation, hypothalamic-pituitary axis (HPA) over-activation and cortisol desensitization as well as sympatho-adrenergic system hyperstimulation, to name a few. We aimed to elucidate the mechanisms by which psychological and physiological stressors exert their effects on the immune system, how to prevent these triggers and how to use their shared mechanisms as avenues for treating autoimmune diseases.

Methods: Navigating through current medical literature we have studied the link between chronic stress and the resultant reactions progressing to autoimmune diseases.

Results: The accumulation of the allostatic load is dependent on psychological resilience and social support of individuals but also their epigenetic tendency for inflammation and immune dysregulation which includes genetics, environmental factors, lifestyle, and physical health. Instead of depending on pharmacological immunosuppression, more emphasis should be placed on establishing healthy sleeping, eating, and breathing habits, psychological resilience and pharmacological modulation of inflammation as well as gut microbial health.

Conclusions: Finally, we recommend for the current medical consensus to consider alternative, more holistic treatment options next to the current mainstay of autoimmune treatment that is exogenous corticosteroids.

EP058 / #506

Selective Monovalent Blockade of Human Fc [Gamma] Riii in a Humanized-Murine ITP Model: A New Frontier in Autoimmune Therapeutic Strategies?

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Background and aims: Fc gamma receptor IIIA (FcγRIIIA) is integral to both immune defense and the pathology of autoimmune diseases such as immune thrombocytopenia (ITP). While blockade of FcγRIIIA can increase platelet counts in ITP patients, it can also induce adverse inflammatory reactions. This study aims to develop and test a high-affinity monovalent single chain variable fragment (scFv) designed to selectively bind and inhibit human FcγRIIIA, mitigating both platelet destruction and adverse events.

Methods: A monovalent scFv, 17C02, was engineered to target human FcγRIIIA. This scFv was expressed in three formats: a monovalent fusion protein with albumin, a one-armed human IgG1 antibody, and a standard bivalent antibody. In vitro phagocytosis assays were conducted using human ITP-serum-sensitized human platelets, and in vivo studies were performed on FcγR-humanized mice to evaluate the efficacy of these therapeutic approaches.

Results: Both monovalent therapeutics effectively prevented the phagocytosis of ITP-serum-sensitized human platelets in vitro. In vivo studies corroborated these findings, with both therapeutics elevating platelet counts in FcγR-humanized mice. The monovalent albumin fusion protein did not induce any adverse events as evidenced by stable body temperature, whereas the one-armed antibody led to minor thermoregulatory shifts despite the Fc region being functionally impaired by LALA mutation.

Conclusions: Our data demonstrate that targeted, monovalent blockade of human FcγRIIIA effectively mitigates platelet phagocytosis and could potentially serve as a therapeutic strategy for ITP patients. Importantly, monovalent approaches appear to circumvent the adverse events commonly associated with bivalent antibody treatments, providing a safer and more efficacious autoimmune therapeutic avenue.

EP059 / #605

Generation of mABS Against tTG and mTG Neo Epitopes

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Background and aims: Gluten-related diseases occur in 5% of the population. An increase in diagnosis seems to be due to a real increase in the incidence rather than the increased use of food additives, such as microbial transglutaminase (mTG). Gliadins are cross-linked by tissue transglutaminase (tTG) and/or mTG to form complexes, exposing immunogenic neo-epitopes, triggering the production of anti-neo-epitope antibodies. Detection of these antibodies is a powerful tool in early detection of enteric damage in pediatric CD. Anti-neo-epitope transglutaminase antibodies represent a new generation of markers offering several advantages like better diagnostic performance, a higher reflection of intestinal damage, better predictability at an early age, more diverse epitopes, and less false positivity. Recently, we generated monoclonal antibodies specifically recognizing tTG/mTG neo-epitopes.

Methods: In a first-of-its-kind attempt to generate mAbs against tTG/mTG neo epitopes, we injected mice with the tTG-gliadin and mTG-gliadin complexes. The resulting antibodies were tested for specificity using tTG-Neo, tTG, mTG, mTG-Neo, and gliadin ELISAs. Cell lines generating specific mAbs against tTG neo, tTG, mTG, mTG neo, and gliadin were identified and cultured to produce large quantities of the mAbs. These mAbs were purified and stored until further use.

Results: IFA EMA slides using anti-tTG- and mTG-neo mAbs revealed new patterns, previously not observed, different from the well-known tTG honey-comb pattern, as well as the gliadin pattern.

Conclusions: The purified mAbs are specific to the neo-epitopes and can be used for various research applications.

EP060 / #850

Antibody Reactivity Against Human Cytomegalovirus Antigens in Patients with Psoriasis

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Background and aims: Various pathogens have been considered instrumental for the development of Psoriasis (Ps), including human *Cytomegalovirus* (HCMV), but the fine specificity of anti-HCMV antibody responses has not been assessed in great detail. The aim of our study was to comprehensively assess antigen specific antibody responses against the immunodominant antigens of HCMV in patients with psoriasis and to correlate the detection of anti-HCMV antibodies with clinical features.

Methods: Sera from 51 patients with Ps and an equal number of demographically matched healthy controls (HC) were tested. IgG anti-HCMV antibodies were tested by Western immunoblotting.

Results: Positivity against HCMV was found in 33 (64.7%) patients with Ps and in 34 (66.7%) HCs, (*P*=ns). Amongst positive individuals, antibodies against UL57 and against UL83 were significantly less frequent in patients with Ps than in HCs (51.5% vs 94.1%, *P*<.001 and 57.6% vs 88.2%, *P*=.006 respectively). Concerning the magnitudes of antibody responses, not significant differences were found between patients with Ps and HCs.

Conclusions: Antibodies against UL57 and UL83 of HCMV were less frequent in Ps patients compared to HCs, suggesting an unlikely immunopathogenic role for HCMV in psoriasis.

EP061 / #674

Gas6/Tam System: Potential Prognostic Biomarkers for Multiple Sclerosis

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Background and aims: The protein growth arrest specific 6 (Gas6) and its tyrosine kinase receptors Tyro-3, Axl, Mer (TAMs) are ubiquitous proteins involved in inflammation. Gas6 and TAMs have been associated with neuronal remyelination and stimulation of oligodendrocyte survival. We evaluated the correlations between soluble levels of these molecules, both in cerebrospinal fluid (CSF) and serum, with Multiple Sclerosis (MS) progression and short-term disease severity.

Methods: We enrolled 64 patients with different forms of MS: Radiological Isolated Syndrome (RIS), Clinical Isolated Syndrome (CIS) and Relapsing-Remitting (RR). At diagnosis, we collected serum, CSF, and clinical-radiological data. During the last clinical follow-up expanded disability status score (EDSS), MS severity score (MSSS) and Age-Related MS severity (ARMSS) were assessed. Gas6 and TAMs concentrations were determined by ELISA, while neurofilaments (NFLs) levels, for neuronal damage assessment, through fluorescence-based immunoassay.

Results: At diagnosis, RIS and CIS showed higher values of sMer and sTyro-3, compared to RRMS (*P*= .007 and *P*= .018). Serum sAxl was higher in patients untreated or first-line disease modifying treatments (DMTs) versus patients with high-efficacy DMTs (*P*= .04). Serum Axl was associated with EDSS ≤ 3 at diagnosis (*P*= .037). High levels of Gas6 in CSF were associated with EDSS ≤ 3 at diagnosis (*P*= .04), and high levels of Gas6 in serum to a lower MSSS (r^2 = -0.32 and *P*= .01).

Conclusions: Gas6 and its receptors, particularly Axl, might have a neuroprotective role and prognostic potential in MS.

EP062 / #572

In Early Rheumatoid Arthritis, Anti-Citrullinated Peptide Antibodies Associate with Low Number of Affected Joints, and Rheumatoid Factor with Systemic Inflammation

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Background and aims: To investigate how individual autoantibodies associate with different signs and symptoms at the time of RA diagnosis.

Methods: Sixteen individual ACPA reactivities, anti-CCP2, IgA, IgG and IgM RF were analyzed centrally in baseline sera from 1600 RA patients classified according to the 1987 ACR criteria. The results were related to CRP, ESR, number of swollen and tender joints, 28-joint disease activity scores (DAS28 and DAS28CRP), global disease activity evaluated by the patients, and health assessment questionnaire obtained at baseline.

Results: Individually, all autoantibodies except IgG RF associated with low counts of swollen and tender joints, and with high ESR. In IgM RF negative patients ACPA associated strictly with low number of swollen and tender joints. This association persisted in multiple regression, where IgM and IgA RF instead associated with increased inflammatory markers, especially ESR. The ACPA microarray detects residual ACPA positive patients in the anti-CCP2 negative subjects, and among subjects without any ACPA peptide reactivity there was no association between RF isotypes and ESR. The effect of RF on ESR increased with the number of ACPA, the effect being most prominent for IgM RF.

Conclusions: In early RA, ACPA associate with low counts of affected joints and IgM RF associates with elevated ESR in an ACPA-dependent manner. Our findings may be related to different roles for ACPA and RF in RA aetiology. Future studies in early RA may benefit from evaluating the impact of individual autoantibodies in seropositive patients as well as distinct DAS28 components separately.

EP063 / #453

Serological Biomarkers of Extracellular Matrix Remodeling Are Elevated in Patients with Immune-Mediated Alopecia

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Background and aims: Remodeling of extracellular matrix (ECM) proteins, together with genetic predisposition, hormonal dysfunction and localized microinflammation, are key events in hair loss. ECM protein synthesis is predominantly done by dermal fibroblasts, in an orchestrated manner with keratinocytes. This exchange takes place in the basement membrane zone (BMZ), located at the epithelial-mesenchymal interface in the hair follicle. The BMZ is mainly composed by nidogen, laminin, and type IV and VII collagen. The aim of this study is to investigate blood-based ECM biomarkers in patients with alopecia and compare to healthy controls.

Methods: In serum from patients with immune-mediated alopecia (n=25) and healthy controls (n=20), ECM loss and remodeling was quantified using serological biomarkers quantifying formation of type VII (PRO-C7), and degradation of type IV and type VII collagens (C4M, TUM and C7M), turnover of type IV collagen (PRO-C4), and nidogen degradation (NIC). The difference between the two groups was assessed using Mann-Whitney U test, where a p-value below 0.05 was considered significant.

Results: Patients with alopecia has elevated levels of PRO-C7 (P=.008), TUM (P=.049), and NIC (P<.0001) compared to healthy donors. No statistically significant difference was observed between alopecia patients and healthy donors for PRO-C4, C4M and C7M (P=.848, P=.408 and P=.136, respectively).

Conclusions: This study identified an altered ECM turnover in patients with alopecia by blood-based biomarkers. Such biomarkers could be novel objective, and potentially predictive, biomarkers of disease activity and severity.

EP064 / #239

Skeletal Muscle Cell Bank Development and Clinical Data Collection in a Cohort of Patients with Idiopathic Inflammatory Myopathies

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Background and aims: The pathophysiology of idiopathic inflammatory myopathies (IIM), which remains incompletely understood, can be studied at the cellular level using cultured skeletal muscle cells obtained from IIM patients. Our aim is to create a cell bank comprising these cells and characterise the cohort by analysing the clinical data of the patients.

Methods: Skeletal muscle cells are isolated from the remains of muscle biopsies taken as part of the standard diagnostic procedure for patients with suspected IIM. The muscle tissue is cleaned of adipose and connective tissue. The CD56+ myogenic cells are then isolated according to the established protocol. Simultaneously, the clinical data of the patients are collected.

Results: Our cell bank consists of skeletal muscle cells from 27 IIM patients, of whom 70.4% were female. A third of all patients were seronegative. Patients with immune-mediated necrotising myopathy had the highest serum levels of creatine kinase and aldolase and the lowest muscle strength. Additionally, less than half of the patients in each subgroup had elevated C-reactive protein (CRP), with no apparent differences in levels of inflammatory markers observed between the subgroups. Notably, 23.9% of patients had vitamin D deficiency.

Conclusions: Our continuously expanding cell bank consists of samples covering the heterogeneity of IIM. The clinical data are consistent with the expected values, suggesting our cohort is representative and appropriate for further experiments.

Table 1. Characteristics of patients with idiopathic inflammatory myopathies

Patient characteristics	
Total – N (%)	**27 (100)**
Female	**19 (70.4)**
Male	**8 (29.6)**
Age in years – mean ± SD	**64.6 ± 12.6**
Disease subtype – N(%)	
Dermatomyositis	**9 (33.3)**
Polymyositis	**2 (7.4)**
Antisynthetase syndrome	**4 (14.8)**
Immune-mediated necrotising myopathy	**4 (14.8)**
Inclusion body myositis	**1 (3.7)**
Overlap syndrome	**7 (25.9)**
Immunoserology – N (%)	
Seropositive	**17 (63.0)**
Seronegative	**10 (37.0)**
Manual muscle testing score (/150) – median (interquartile range)	**127 (108 – 143)**
Muscle damage markers – median (interquartile range)	
Creatine kinase – *μkat/L*	**34.0 (7.3 – 78.4)**
Aldolase – *nkat/L*	**213.0 (110.3 – 725.3)**
Inflammatory markers – median (interquartile range)	
C-reactive protein – *mg/L*	**5 (2.5 – 34.0)**
Erythrocyte sedimentation rate – *mm/h*	**29 (12 – 45)**
Serum level of 25-OH vitamin D – *nmol/L* – median (interquartile range)	**42 (30 – 56)**

EP065 / #672

An Imbalance of L-Selectin Expression on Peripheral Blood Leukocytes in Sjögren's Syndrome

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Background and aims: L-selectin is a cell adhesion molecule expressed on most peripheral blood leukocyte populations and is an indispensable player in the process of leukocyte extravasation. L-selectin could be involved in the process of leukocyte infiltration into the salivary glands in primary Sjögren's syndrome (pSS). The aim of our study was to evaluate expression of L-selectin in peripheral blood of pSS patients.

Methods: We enrolled 8 pSS patients and 7 healthy controls (HCs) and analyzed surface expression of L-selectin on leukocytes in peripheral blood by flow cytometry.

Results: The expression of L-selectin on leukocytes was different in pSS compared to HCs, furthermore, the direction of altered expression differed between different leukocyte subpopulations. There was a trend toward increased L-selectin expression on granulocytes in pSS compared with HC. Expression of L-selectin on B lymphocytes was significantly decreased, whereas expression on T lymphocytes showed a trend of increase. L-selectin expression was significantly decreased in total monocytes, in classical and intermediate monocytes, but not in non-classical monocytes.

Conclusions: Although all peripheral blood leukocytes were exposed to the same systemic inflammatory environment in pSS, the expression of L-selectin differed among considered subpopulations.

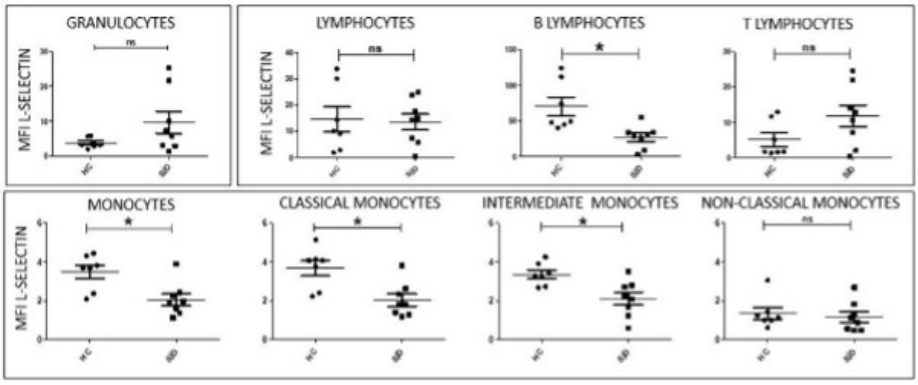

Figure 1. L-selectin expression on leukocyte subpopulations in SjD patients and HC. MFI - mean fluorescence intensity; ns – not statistically significant; (*) – P value <.05.

EP066 / #748

Proteome Analysis of Minor Salivary Glands from Sjögren Syndrome Patients

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Background and aims: Sjögren's syndrome (SS) is an under-researched autoimmune disease with many unmet clinical needs, no approved therapies and little knowledge of the underlying pathomechanisms. To better understand the molecular nature of SS, we investigated the proteome of minor salivary gland (MSG) tissues.

Methods: Proteome analysis was performed by mass spectrometry on flash frozen MSG tissue from 18 patients with SS, fulfilling the 2016 ACR/EULAR classification criteria, and 6 controls experiencing sicca symptoms but not fulfilling the criteria. Proteins were identified using the Spectronaut software. Differentially expressed proteins were identified using the Bayes test. Pearson correlation analysis was performed to identify proteins that correlate with clinical features of the disease.

Results: We identified 5577 proteins, 7 of which were differentially expressed between groups (log2 FC>2, *P*-adjusted<.05). All 7 proteins were upregulated in SS compared to sicca controls. Pearson's correlation analysis revealed a strong positive correlation of PTPRCAP, CD3E, SH2D1A and DOCK10 protein expression with the focus score (r>0.5, *P*-adjusted<.05).

Conclusions: The number of proteins identified in our analysis exceeds that of previous studies and allows us to provide the first list of differentially expressed proteins in MSG tissues in SS and controls that correlate with SS-relevant measures. This is a first step towards a better understanding of SS pathophysiology.

Table 1. Differentially expressed proteins and their correlation with the focus score. r – correlation coefficient; (*) – r>0.5 and *P*-adjusted<.05.

Protein	r	p-adjusted
PTPRCAP	0.5854*	0.0138*
IKZF1	0.3150	0.1448
CD3E	0.6158*	0.0091*
HDAC3	0.4480	0.0565
PIK3CD	0.4128	0.0750
SH2D1A	0.6705*	0.0038*
DOCK10	0.5400*	0.0237*

Figure 1.

EP067 / #290

Soluble CD72 Is a Specific Signaling Ligand for CD6 on CD4+ T Cells, Inducing T Cell Proliferation and Pro-Inflammatory Cytokines

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Background and aims: CD72 is a highly required regulatory receptor on B cells. In contrast, soluble CD72 (sCD72) is reported to be a stimulatory molecule for T cells, and as a result is found to be increased in autoimmune diseases such as SLE and in association with lupus nephritis. To establish a preliminary finding that sCD72 is a specific ligand for CD6 on T cells, and that this binding induces T cell proliferation and the production of pro-inflammatory cytokines.

Methods: Activated CD4+ T cells were isolated from peripheral blood mononuclear cells of 15 healthy individuals, and incubated with purified sCD72 for 48 hours. Next, we assessed the status of CD4+ T cell proliferation and expression of pro-inflammatory cytokines. We also performed Co-IP experiments with the objective of showing that CD6 is indeed a specific receptor for sCD72 on activated T cells.

Results: We were able to demonstrate that sCD72 significantly increases the expression of pro-inflammatory cytokines, namely IL-17 and IFN-γ in activated CD4+ T cells. Furthermore, in a dose-dependent manner, sCD72 increases the proliferation of CD4+ T cells and induces more than 5 cycles of division in 70% of cells compared to only 15% of the control cells. We validated the sCD72-CD6 interaction and demonstrated that CD6 is a specific receptor for sCD72 on activated T cells.

Conclusions: The sCD72- CD6 axis on activated CD4+ T cells is a new signaling pathway in the induction of immune-mediated diseases.

Targeting sCD72 may become a useful therapeutic tool in many autoimmune diseases.

EP068 / #325

Evidence for a Role of the Aryl Hydrocarbon Receptor Identified in a Simple 2-D Model of Systemic Sclerosis

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Background and aims: New therapeutic approaches are urgently needed for systemic sclerosis (SSc). The transcription factor aryl hydrocarbon receptor (AHR) is critical for skin homeostasis, but very little is known regarding SSc. We used TGFß-treated dermal fibroblasts deficient for AHR to query a possible role of AHR in the production of matrix metalloproteinases 1 protein (MMP1) and collagen type 1 (COL1A1).

Methods: AHR-negative human fibroblast (HDF) and keratinocyte (HaCat) cell lines (KO lines) were generated with Crisp/Cas9. Cells were treated with TGFβ (25ng/ml) for 24h/48h. Differential gene expression was determined using Droplet Digital PCR (ddPCR™). In addition, MMP1 and COL1A1 were measured by ELISA. Expression of AHR protein was assessed by western blotting.

Results: At basal level, fibroblasts produced more COL1A1 than the keratinocyte cell line HaCaT. After 48 h, as expected, TGFß induced COL1A1 secretion, but more in the HDF-KO than in the HDF-WT. AHR protein itself also increased upon TGFß treatment. Curiously, adding the skin-typical AHR-agonist, FICZ, to the HDF-WT reduced AHR protein, but not *AHR* mRNA. Finally, secretion of MMP1 decreased in the absence of AHR in HDF.

Conclusions: A simple SSc model based on treatment of fibroblasts with high concentrations of TGFß for several days increased COL1A1 secretion. Both deficiency of AHR and activation of the AHR signaling pathway affected expression levels of MMP1 and COL1A1 induced by TGFß. As AHR expression itself was also sensitive to TGFß, this may reflect on a role exploitable in the regulation of the fibrosis process, which needs to be studied further.

E-POSTER VIEWING 10: BASIC MECHANISMS: OTHER

EP069 / #843

Mitochondrial Metabolism in Patients Affected with Fibromyalgia Syndrome Is Impaired and Correlates with Disease Severity

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Background and aims: Fibromyalgia syndrome (FMS) is a musculoskeletal syndrome characterized by chronic widespread pain. There is growing evidence suggesting that dysfunction in the mitochondria may play a role in the development and maintenance of symptoms. Our aim was to study the mitochondrial function of patients with FMS.

Methods: Adult primary FMS patients with 2016 criteria at any time in the clinical history were included. The fibromyalgia severity score (FSS) was used to classify severity. Mitochondrial activity was measured in peripheral blood mononuclear cells by the Agilent Seahorse XF Cell Mito Stress Test, which measures the oxygen consumption rate (OCR) of cells. The bioenergetic health index (BHI) - calculated as ATP-linked respiration x reserve capacity/proton leak x non-mitochondrial respiration for each experiment - expresses the global mitochondrial function, with lower values corresponding to greater impairment.

Results: Twenty-eight patients with FMS were enrolled (median age 58, min 34 - max 80 years; median total FSS 20.5, min 12 - max 26). We found significantly different BHI values (P=.002) in subjects with an FSS >20 (n=14) vs FSS <20 (n=14). BHI was moderately correlated with the total FSS (Spearman's rho -0.6, P<.002). No difference was found in total FSS and BHI of patients treated (n=10) vs not treated (n=18) with drugs currently recommended for FMS.

Conclusions: In this study, we found that the mitochondrial metabolism in patients affected with fibromyalgia syndrome is impaired and correlates with disease severity but not with treatment. Our study paves the way for future larger studies on mitochondrial function in fibromyalgia syndrome.

EP070 / #556

The Potential Harmful Effects of the Horizontal Gene Transfer of Genetically Engineered Microorganisms (GEMs) On the Intestinal Microbiome/Dysbiome Balance

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Background and aims: The main mechanism of bacterial evolution is horizontal gene transfer (HGT) and the acquisition of new traits can be achieved through mobile genetic element (MGEs) exchange. Introducing GEMs might break the harmonic microbiome balance in the intestinal compartment. The present objective is to reveal the role played by GEMs' HGT in the changing landscape of enteric eubiosis, resulting in chronic human diseases, autoimmune ones in particular.

Methods: A search of articles published in PubMed/MEDLINE, EMBASE from 2000 to 2023, using the following MeSH entry terms: "GEMs" or " MGEs" or " HGT" and "harmful effects" or "detrimental effects" or "side effects" and "intestinal microbiome" and "public health", was conducted.

Results: Antibiotic resistance genes, microbial-engineered enzymes represented mainly by microbial transglutaminase, probiotics, and genetically modified plants can exchange harmful MGEs. Autoimmune, neurodegenerative, metabolic, allergic, cancerous, neurodevelopmental, behavioral and infertility diseases can appear. The long-term symbiotic evolution of the enteric pro- or eukaryotic cells inhabitants can be in danger. The regulatory authority's safety control of GEMs is not enough to protect public health. Viability and biocontainment, GEMs genetic instability, differential individual microbiome variations, competition with the stable communities, uncontrolled growth,

metabolic abnormalities, and their toxic effects, limiting the viability of the inhabitant GEMs and clearing the foreign MGEs topics were not adequately explored.

Conclusions: Extensive studies are required to explore this multi-directional communication between gut homeostasis and the newly introduced GEMs to protect public physical health and mental behavior. Always remember that " primum non nocere" is the name of the game.

EP072 / #380

Females Systemic Sclerosis Patients Show An Increase in Frequency of "Age-Associated B-Cells" and Type I Interferon Signature

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Background and aims: The incidence of some autoimmune diseases, including systemic sclerosis (SSc), is very high in women, likely due to sex hormones and defective X chromosome inactivation (XCI). Tlr7 is a X-linked gene whose increased dosage triggers autoimmunity in mice. TLR7-triggering, in addition to TLR9-triggering, plays a role in Type I interferon (IFN-I) signature/inflammation in SSc. TLR7 is also implicated in the activation/differentiation of "age-associated B-cells" (ABC), cells that accumulate prematurely in autoimmune diseases. Here we aimed to address the currently unclear ABC frequency in SSc female/male patients and IFN-I expression.

Methods: We assessed the frequency of ABC cells in PBMCs from SSc patients compared to healthy donors, (HD) by flow cytometry, using specific markers (CD11c and Tbet). We tested IFN-I levels in SSc and HD plasma by ELISA.

Results: Of a total of 47 patients, 11 females out of 42 (26%), but none of the males, had significant increased frequency of ABC cells as compared to expression in HD (sorted by sex). The Pearson's correlation test showed that frequency of ABC cells in females SSc patients correlated with IFN-a levels in plasma. None of the males had an IFN-a increase either.

Conclusions: These preliminary results are consistent with an increased TLR7 response in females SSc patients, leading to increased ABC cells frequency and IFN-a concentration in blood. Future correlations between ABC frequency and several disease parameters warrant deep investigation in SSc.

EP073 / #1062

Complement Activation Products and Antiphospholipid Antibodies Throughout Pregnancy

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Background and aims: Pregnancies in Systemic Autoimmune Rheumatic Diseases (SARD) still display an increased risk of obstetric complications despite therapy/close monitoring according to guidelines. Therefore, the identification/validation of predictive biomarkers for obstetric risk is an unmet need. Antiphospholipid antibodies (aPL) are the most important predictive factors for obstetric morbidity and are associated with complement activation. Indeed, complement levels have been suggested as useful biomarkers, with an emerging role in plasma complement activation products (C3a, C5a, sC5b9) than serum C3/C4. Our aim was to investigate the usefulness of a large panel of laboratory antiphospholipid syndrome (APS) criteria and complement levels before, throughout, and after pregnancy to validate diagnostic/prognostic algorithms.

Methods: 59 SARD pregnant women (18 APS, 10 aPL carriers, 7 SLE aPL neg, 12 non-SLE connective tissue diseases, 12 inflammatory arthritis) and 20 healthy pregnant controls were followed during the pregnancy. aPL criteria tests, anti-PS-PT and anti-B2GPI domain(D)1/D4,5 antibodies, total circulating immunoglobulins and complement proteins (C3a, C5a, sC5b9, C3, C4) were measured.

Results: aPL titers were stable during the pregnancy, displaying a small decrease during the 2nd and 3rd trimesters that disappeared after partum with behavior comparable to the whole Ig and albumin serum levels. We observed an increase in aCL, anti-B2GPI and anti-D1 IgG titers, and increasing values in C3a, C5a, and sC5b9 in the 2nd trimester of pregnancy in women with aPL.

Conclusions: Our findings suggest that the 2nd trimester of pregnancy may be the crucial period during which complement-mediated aPL damage to the placenta occurs.

EP074 / #780

Unveiling the Age-Associated Dynamics of the Autoantibodyome: Insights from Health and Disease

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Background and aims: The autoantibodyome represents the entirety of autoantibodies within an organism, pysiologically abundant molecules which are influenced by factors such as age and disease. This study sought to delineate the relationship between the autoantibodyome and age within various health contexts, including neurodegenerative, proliferative, and autoimmune diseases.

Methods: To achieve this, we curated publicly available protein array datasets of autoantibodies from the Gene Expression Omnibus repository. Autoantibodies exhibiting Spearman's correlations with age > 0.5 or < -0.5 were identified, associated to their respective targets, underwent duplicate removal, and the functional enrichment analysis was performed with EnrichR.

Results: Our findings reveal that the correlation between the autoantibodyome and age follows an overall symmetrical normal distribution, but can be increased and/or decreased in kurtosis and mean within different disease states. We identified, across the different study cohorts, 3,887 autoantibodies against unique targets in healthy control subjects that correlated with age, exhibiting associations with processes such as protein and histone deacetylation and deacylation, as well as cytoskeleton, actin, and actomyosin organization. In samples from individuals with multiple sclerosis, the targets were associated with protein modification and phosphorylation processes. Notably, we found that autoantibodies targeting EPB41L1 and BAIAP2, which respectively interact with dopamine and insulin receptors in the brain, decreased with age in Parkinson's disease samples.

Conclusions: This study provides a comprehensive view on the intricate relationship between the autoantibodyome and age across various health conditions, highlighting the physiological presence of these molecules and the dysregulation of autoantibodies and biological processes in the context of disease.

EP075 / #367

ICAP Classification Patterns Under the Magnifying Glass of Multiplex Antibodies Detection

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Background and aims: In 2009, the American College of Rheumatology ANA Task Force position statement recommended the indirect immunofluorescence assay (IFA) using HEp-2 substrate as the "gold standard" for primary antinuclear antibodies (ANA) detection. Each laboratory can decide whether a competent or expert level are using to interpret and raport the results. For an acurate diagnostic, in both cases, the autoantibodies confirmatory tests are necesarly to completed the puzzle toghether with clinical manifestations. Starting from ICAP classification patterns we wondered if a microblot array in a microplate format, could shed light for the clinician on the way of diagnosis.

Methods: For a period of six month, 150 ANA Hep 2 positive serum samples with a titer >/= 1/320 and different ICAP patterns were tested on Microblot-Array ANA Plus with 44 recombinant antigens. Data analysis of array results was performed using a reader and the results are evaluated by interactive software (TestLine Clinical Diagnostics, Czech Rebublic). For IFA slides we are using a Nikon E200 microscop equipped with a Mshot MSX2-C camera.

Results: Antigens associated with different ICAP patterns were confirmed by this new generation immunoblot array. Some simple nuclear/ cytoplasmic aspects hightlights the presence of more than one autoantibody. We can observed, for some ICAP patterns, a good correlation between the microblot antibody value and ANA hep 2 titer.

Conclusions: Further studies are needed to evaluate if this type of technology can be used only for the diagnosis or even for monitoring the therapy because the result also enable identification of specific antibody and quantitative (U/ml).

EP076 / #481

Homocysteine in Systemic Sclerosis - A Systematic Review and Meta-Analysis

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Background and aims: Homocysteine (Hcy) is hypothesized to be a contributing factor in systemic sclerosis (SSc) pathogenesis through inducing vascular damage. Therefore, the aim of this review is to explore current evidence regarding the association between Hcy and SSc.

Methods: Databases PubMed, Web of Science, and Scopus were searched on 12 July 2023. All included studies provided data on serum Hcy measurements in SSc patients and healthy controls (HC). The only study designs included were cohort and observational studies. Risk of bias assessment was conducted using the Newcastle-Ottawa scale. For meta-analysis, mean difference with a 95% confidence interval was obtained and results were depicted as forest plots.

Results: of 148 retrieved results, 9 fulfilled inclusion and exclusion criteria and were included in a random-effects meta-analysis totalling 489 SSc patients and 319 HC. Overall, even though Hcy levels were somewhat higher in SSc patients than in HC, the difference did not reach statistical significance (MD = 1.46, 95% CI -0.45, 3.36; P= .13) with present high heterogeneity between studies (I^2 = 99%; P < .01). Detailed results are depicted in Figure 1.

Conclusions: Even though this review study did not find statistically significant elevation in Hcy levels in SSc, there is a need for further structured research regarding Hcy as there is a high heterogeneity present between included studies. Further evaluation of Hcy levels in SSc will enable deeper understanding of vascular damage pathogenesis and therefore possibly improve clinical care of these patients.

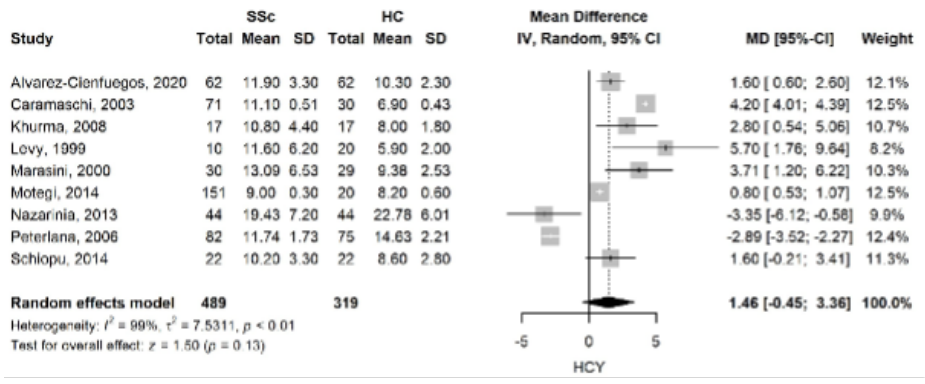

Figure 1.

EP077 / #658

Herpes Simplex Virus and SLE: The Hidden Aspect

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Background and aims: The relation between infectious agents and autoimmunity has been extensively studied. The association was emphasized during the COVID-19 pandemic. SLE represents a chronic systemic autoimmune disease affecting almost every organ system. In terms of etiology, infectious agents, especially viruses, were linked to its emergence.

Methods: For instance, a significant correlation between SLE and hepatitis C virus (HCV) compared to controls was reported. Moreover, infections were found in remarkable association with SLE besides increasing the mortality rate in hospitalized patients. Herpes viruses are widely spread DNA viruses infecting high proportion of the general population causing latent and active infection determined by the competency of the immune system.

Results: Herpes viruses were found to provoke autoimmunity through several mechanisms: the capability of lysing infected cells, causing irregular expression of the histocompatibility molecules presenting self-antigens, and molecular mimicry leading to cross-reactive T cells. Interestingly, Herpes Simplex Virus (HSV) was directly and indirectly linked to SLE. Evaluating the presence of HSV-1 and HSV-2 in SLE patients with atypical symptoms was highly recommended by experts.

Conclusions: Despite the fact that HSV-1 and HSV-2 are not as common as other herpes viruses in connection to SLE; their implication in SLE should not be underestimated due to the critical importance of CNS infection in SLE, which carries high mortality rate and constitutes a challenge in the differential diagnosis of SLE-related CNS disease. While the latter is treated with high doses of immunosuppression, the high mortality in the former could be worse under immunosuppressive treatment.

EP078 / #443

The Role of Aryl Hydrocarbon Receptor in Methotrexate Metabolism. Potential Interaction with Il-6 Receptor Inhibitor

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Background and aims: Aryl Hydrocarbon Receptor (AhR) as a transcription factor plays an important role in drug metabolism but also in immune response. It regulates the expression of drug metabolising enzymes and transporters, such as reduced folate carrier (SLC19A1/RFC1) - crucial in influx transport of methotrexate (MTX) and ABC transporters, responsible for efflux transport and drug resistance. Moreover, treatment with IL-6 receptor inhibitor (tocilizumab, TCZ) may be helpful to overcome the low-dose MTX resistance. In the present study, we have explored this association.

Methods: The cryo-EM structure of the human indirubin-bound AHR complex (PDB code: 7ZUB) was used for docking performed with Flare software (Cresset, UK). PBMC and HepG2 cells were cultured as spheroids and treated with MTX, TCZ, IL-6 and a combination of these reagents. Gene expression was analyzed by ddPCR. Flow cytometry was used to detect AHR and drug impact on cells.

Results: Computational docking analysis revealed that MTX is bound in the binding pocket. Treatment with drugs had on different PBMC subtype cells variable impact. *AhR* mRNA was downregulated after MTX treatment, and upregulated after cytokine IL-6. TCZ increased *AhR* expression in PBMC cells. Compared to HepG2, TCZ dysregulated correlation between mRNAs: *AHR* and *SLC19A1* in PBMC. However, HepG2 response after treatment with IL-6 and MTX was more evident through increased levels of *SLC19A1* and *ABCG2* than PBMC.

Conclusions: MTX is AHR's ligand, however possible mechanism of interaction may depend on cell type. Regulation of the expression of drug transporter genes involved in MTX treatment response appears to depend on AhR activity.

E-POSTER VIEWING 11: CLINICAL PRACTICE - DIAGNOSTICS: ASIA SYNDROME, BREAST IMPLANTS AND AUTOIMMUNITY

EP079 / #664

Antiphospholipid Syndrome in the Era of COVID-19

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Background and aims: Far from the typical flu-like presentation, COVID-19 has showed association with many autoimmune diseases such as systemic lupus erythematous and antiphospholipid syndrome (APS).

Methods: The hypercoagulable state SARS-CoV-2 has contributed to in patients with acute COVID-19 and the critical role of anticoagulant treatment in these patients answer part of the question regarding the correlation between APS and COVID-19. The second part, or the main part, is the role of autoimmunity in this association particularly with the data available regarding the triggering effect of SARS-CoV-2 in terms of autoimmunity described in COVID-19 patients. This is furtherly strengthened when patients with COVID-19 were found to have antiphospholipid antibodies from different types.

Results: Moreover, on the severe side of the APS spectrum, catastrophic APS was shown to have overlapping characteristics with severe COVID-19 like cytokine storm and multi-organ failure. In addition, COVID vaccine-induced autoimmune reactions and diseases reported by many studies have further pointed to the association between COVID-19 and APS. Whether the antiphospholipid antibodies were present or de novo, COVID vaccine-induced vascular thrombosis in certain individuals necessitates further investigations regarding the possible mechanisms involved.

Conclusions: In our current paper, we aimed to shed light on the associations mentioned, their implications, importance, and consequences. What is obvious, the correlation between APS and COVID-19 is more than merely a coincidence, rather it is infection and autoimmunity again.

EP080 / #661

The Mosaic of Autoimmunity – Tattoos as Part of the Story

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Background and aims: Autoimmune diseases stem from a complex interplay of genetic susceptibility, environmental triggers, and immune dysregulation. Tattoos, once purely decorative, have gained recent popularity and are proposed as potential environmental triggers for autoimmune conditions. We explored the mechanisms underlying tattoo-induced autoimmune hyperstimulation, emphasizing immune dysregulation.

Methods: One mechanism involves the introduction of foreign substances into the skin dermis during tattooing. Tattoo pigments, comprising microparticles and nanoparticles, impact macrophages responsible for particle clearance. The pigments induce varying effects on the cells, subtly but significantly secreting inflammatory factors like tumor necrosis factor. Additionally, they induce lasting changes in macrophage membrane markers, influencing cell adhesion and immunological tolerance, even at non-toxic levels.

Results: Certain tattoo pigments, especially those with iron oxide and carbon black, associate with granulomatous reactions, potentially leading to sarcoidosis. Vigilant monitoring and early detection of sarcoidosis manifestations are essential in this regard. Another mechanism involves molecular mimicry as pigments may contain epitopes that mimic self-antigens prompting autoantibody production. This, combined with tattoo pigment persistence in the skin, could lead to sustained immune system activation.

Conclusions: Understanding these mechanisms is vital for recognizing potential tattooing risks, especially in those genetically predisposed to autoimmune conditions. It underscores the need for caution during cosmetic tattooing and further research to identify specific compounds causing tattoo complications. By clarifying these mechanisms, we aim to illuminate the intricate link between tattoos and autoimmune hyperstimulation, contributing to a better comprehension of autoimmunity complex origins.

EP081 / #663

Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA): Now More Than Before

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Background and aims: An adjuvant is a substance aimed to enhance the effect of an agent given concomitantly. Adjuvants were shown to carry their modulating effect by boosting the immune response and can be commonly found in therapeutic/medical devices such as vaccines, silicone breast implants, mineral oils, and cosmetics, among others.

Methods: Even though adjuvants are safe most of the time, the administration of adjuvants may trigger an autoimmune response particularly in genetically susceptible and predisposed individuals. Therefore, the innate and adaptive immune response following the exposure to an adjuvant is one of the main criteria of ASIA syndrome. In fact, before ASIA was coined by Shoenfeld, the prevalence of autoimmune diseases has been heavily studied regarding silicone breast implants and tattoos, along with vaccines, all which fall under the term "autoimmune/inflammatory syndrome induced by adjuvants" now.

Results: Indeed, the interaction between silicone and the human body has risen with the use of silicone implants for reconstructive and cosmetic purposes. Recently, ASIA was reported in association with mineral oil and cosmetic exposure as injectable oily substances, such as paraffin, which have been used for a long time.

Conclusions: Therefore, we aim to provide higher awareness into the substances introduced to our bodies, especially in this era of cosmetic perfection.

EP082 / #498

Life-Threatening Cardiac Manifestation of Silicone Breast Implants

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Background and aims: Autoimmune/inflammatory Syndrome Induced by Adjuvants (ASIA) is a disease with typical autoimmune symptoms that occurs as a result of exposure to environmental immune stimulatory factors in genetically susceptible individuals. The purpose of this case report is to describe the diagnostic and treatment characteristics of severe cardiac manifestations resulting from silicone breast implants.

Methods: Case report and discussion.

Results: The medical history of our 42-year-old female patient includes silicone breast implants in 2005 and replacement in 2015. In 2018, she was diagnosed with heart failure with a left ventricular ejection fraction of 20%. In 2019, endomyocardial biopsy confirmed lymphocytic myocarditis, on the basis of which the patient received five therapeutic plasma exchanges. She was admitted to our institute in 2022 due to low cardiac output syndrome and multiorgan failure. A biventricular assist device (BiVAD) was implanted. Chest CT revealed an intracapsular rupture of the breast implants. Based on her lymphocytic myocarditis and the suspected ASIA syndrome, we started high-dose steroid treatment, therapeutic plasma exchanges, and intravenous immunoglobulin (IVIG) therapy. The silicone breast implants were surgically removed, after which the patient improved significantly, and could be weaned of the BiVAD. Malignant ventricular arrhythmia and subsequent resuscitation necessitated an ICD implantation. After 127 days of intensive therapy, the patient was discharged with improved cardiac function and monthly IVIG therapy. The cardiogenetic testing of our patient revealed a heterozygous variant in the LMNA gene.

Conclusions: Aesthetic breast implants may trigger serious cardiac complications, especially in individuals with underlying predisposing factors.

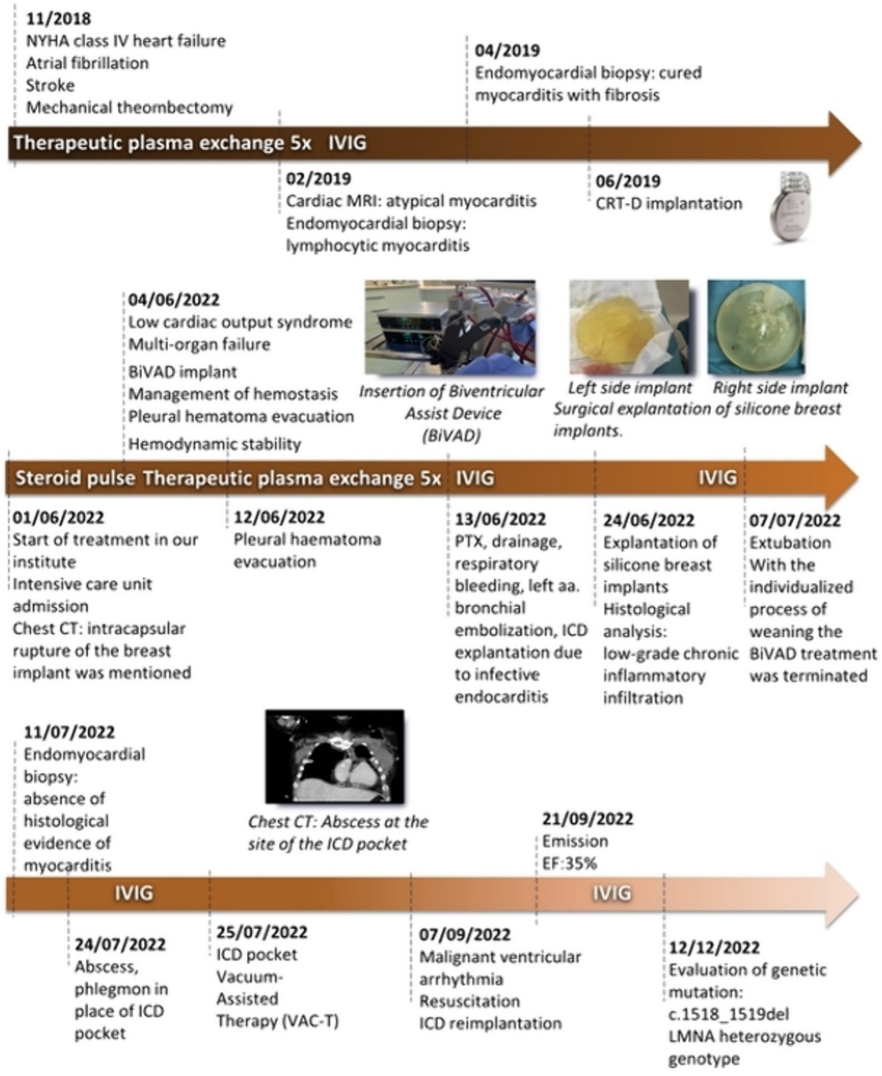

Figure 1.

E-POSTER VIEWING 12: CLINICAL PRACTICE - DIAGNOSTICS: CANCER AND AUTOIMMUNITY

EP083 / #622

Rheumatologic Disease as Paraneoplastic Syndrome – Case Series from a Single Center

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Background and aims: Rheumatic syndromes and malignancy may coexist. Although paraneoplastic disease means no tumour or metastasis invasion, there is an inquire into the link of these conditions. Emerging knowledge reveal intricate autoimmune mechanisms of both diseases. Accurate early diagnosis of each condition and sound medical judgement determine "the right treatment for the right patient at the right moment" with the best patient outcome.

Methods: We studied a total of 25 consecutive patients in longitudinal medical care in our unit during the last 5 years (2018-2022).

Results: The series included 9 male and 16 (64 %) female patients. Solid malignancies were present in 18 cases (72%) and hematologic malignancies in 7 cases. The most frequent sites for solid tumours were breast (24%), uterus, prostate, lungs. Rheumatologic syndromes were heterogeneous: 40% rheumatoid arthritis (RA), 8% systemic sclerosis (SS), 8% dermato-/polymyositis (DM), 24% vasculitis (polymyalgia rheumatica-PMR, granulomatosis with poliangeitis - GPA) and other (ankylosing spondylitis, remitting seronegative symmetrical synovitis with pitting oedema, systemic lupus erythematous). Most malignancies were diagnosed after rheumatism diagnosis (60%). Most malignancies were diagnosed within the first two years after the rheumatic disease onset (60%). Rheumatic diseases had either typical or atypical patterns, with presence of biologic markers of disease (70% - positive for RF but only 30% ACPA positive).

Conclusions: All kind of rheumatic autoimmune disorders may accompany malignancies. A careful approach for main disease and comorbidities at first presentation and during Rheumatologic follow up is mandatory for a tailored treatment of both diseases.

EP084 / #374

Increased Serum Levels of TIM-3, VISTA, PTX3 and CD27 in Patients with Dermatomyositis with and without Cancer

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Background and aims: Among autoimmune diseases, dermatomyositis (DM) has the highest association with cancer. This study aimed to identify novel biomarkers, which could help to discriminate DM patients with cancer from DM patients without cancer.

Methods: DM patients without cancer (n=19), with cancer (n=15) and healthy controls (CTR, n=17) were enrolled. Serum samples were analyzed to search for antibodies against plasma membrane proteins using Human Skeletal Muscle Myoblasts (HSMMs) as targets in flow cytometry assays. Twenty soluble immune checkpoints were quantified in sera by Luminex assays. Fisher's exact test and Mann-Whitney U test with Bonferroni correction were used for pairwise comparisons.

Results: Patients with DM showed higher percentages of cells stained with serum IgG antibodies than CTR, while patients with DM with

and without cancer showed similar percentages. CD27, CD80, LAG-3, MICA, PD-L2, TIM-3, PTX3, CD40L, PD1 and VISTA were higher in DM patients than CTR. Moreover, IDO, CD137 and CD40 were detected more frequently in patients. No differences comparing DM patients with and without cancer were observed. VISTA, CD27, PTX3 and TIM-3 were the best classifiers of patients with DM by ROC curve analysis.

Conclusions: Our data suggest the presence of IgGs against membrane proteins of HSMMs. Several soluble immune checkpoints resulted increased in patients with DM, suggesting a potential pathogenic role. The investigated biomarkers did not allow discrimination of DM patients with and without cancer.

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EP085 / #691

Cancer in Systemic Sclerosis: Results from a Single Centre in Northwest Greece

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Background and aims: Systemic Sclerosis (SSc) is a complex autoimmune disease, with both cutaneous and internal organ involvement. SSc is associated with an increased risk for malignancy compared to the general population. However, conflicting results have been reported, possibly due to the differences across populations. The aim of our study was to evaluate the frequency and possible factors associated with cancer development in a cohort of Greek SSc patients.

Methods: Consecutive patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were included. Demographic, clinical and serological characteristics, along with information regarding cancer development were recorded.

Results: In total 188 patients participated, of whom 66.8% had limited SSc. Thirteen of the patients (6.9%) developed cancer. More specifically, 3 patients developed lung cancer, 3 gastrointestinal malignancy, 3 B-cell lymphoma, 2 follicular carcinoma of the thyroid gland, 1 prostate malignancy and 1 non-melanoma skin cancer. Median time for cancer development was 11.6 years. Mean age of SSc diagnosis was 54.0 years for those who developed cancer and 46.9 years for those who did not develop. Patients with cancer had more frequently pulmonary fibrosis, pulmonary hypertension and left ventricular diastolic dysfunction. No statistically significant difference was observed regarding sex, smoking status, disease subtype and the use of calcium channel blockers, while a trend for previous cyclophosphamide exposure was observed.

Conclusions: In accordance with the literature, an increased risk for malignancy development among SSc patients was observed, irrespectively of disease subtype. Thus, careful screening and follow-up is required especially in patients with pulmonary and heart involvement.

EP086 / #752

New Evidence for Neutrophil Extracellular Traps and Neutrophil-Related Mediators in Human Thyroid Cancer

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Background and aims: Neutrophils play central roles in inflammation and cancers. They contain and release several mediators, including myeloperoxidase (MPO), pentraxin-3 (PTX3) and matrix metalloproteinase-9 (MMP-9), and neutrophil extracellular traps (NETs). The aim of our study was to evaluate NETs and neutrophil-related mediators as possible biomarkers in thyroid cancer (TC) patients.

Methods: We enrolled 22 healthy controls (HCs), 26 multinodular goiter (MNG) patients, 20 differentiated TC (DTC) patients, and 26 de-differentiated TC (De-DTC) patients. We evaluated serum levels of free DNA (dsDNA), nucleosomes, citrullinated histone H3 (CitH3), and MPO-DNA complexes (which represent NETs indicators), and MPO, PTX3, MMP-9 and granulocyte-monocyte colony-stimulating factor (GM-CSF) (as neutrophil-related mediators).

Results: All NETs indicators showed higher serum levels in DeDTC patients (vs HCs). Unlike HCs and MNG patients, CitH3 levels were elevated in DeDTC and DTC patients. MPO-DNA complexes and nucleosomes were elevated in DeDTC patients (vs HCs and MNG patients); and MPO-DNA complexes resulted increased in DeDTC patients (vs DTC patients also). MPO levels were elevated in DeDTC patients (vs HCs). PTX3, MMP-9 and GM-CSF levels were increased in DTC and DeDTC patients (vs HCs). Additionally, dsDNA, nucleosomes and MPO-DNA complexes levels resulted higher in patients with metastatic disease at diagnosis with respect to non-metastatic patients.

Conclusions: Conclusion: NETs appear to be related to the malignancy and severity of TC. These findings, in addition to the levels of neutrophil-related mediators found to be elevated in TC compared to MNG and HCs, confirm that neutrophilic inflammation may be involved in TC.

EP087 / #570

Increased Levels of Natural Antibodies in Non-Infectious Benign Pleural Effusions Compared to Malignant Pleural Effusions

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Background and aims: Natural antibodies (NAbs) are present in serum and secretions under healthy conditions, in the absence of deliberate immunization. NAbs belong to all Ig-classes and are mainly polyreactive by being able to recognize structurally unrelated antigens, such as nucleic acids, proteins, carbohydrates and haptens. NAbs present a major homeostatic and regulatory function in mucosal immunity of inner body cavities. The pleural cavity is involved in several clinical entities that manifest as pleural effusions (PE). Our aim was to investigate the detectability of NAbs in human pleural fluid of patients with benign and malignant PE and to assess potential differences between groups.

Methods: Pleural fluid from 29 patients with benign and 29 with malignant PE were analyzed regarding IgM, IgA and IgG NAb levels

by in-house indirect ELISA against actin, hyaluronidase, carbonic anhydrase, DNA, Trinitrophenyl (TNP) and lipopolysacharide (LPS). Total Ig class concentration was also measured by in-house sandwich ELISA and a normalization step regarding Ig class concentration was applied.

Results: We found significantly increased levels of IgM and IgA NAbs, in non-infectious benign compared to malignant PEs, against several antigens of our panel. This increase was independent of the total Ig class concentration and possibly linked to autoimmunity-induced PE frequently occurring in these patients.

Conclusions: Our findings provide the basis for the exploitation of pleural fluid NAb measurements, since the significant differences found herein support their potential application in PE management.

E-POSTER VIEWING 13: CLINICAL PRACTICE - DIAGNOSTICS: COMPLEMENT IN AUTOIMMUNITY

EP088 / #366

Study On the Correlation Between Phospholipase A2 Activity and the Presence of Autoantibodies to Complement Proteins C1q, C3 and Factor H in SLE Patients

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Background and aims: Increased activity of phospholipase A2 enzymes (PLA2) like calcium-independent PLA2 (iPLA2), secretory PLA2 (sPLA2) and cellular PLA2 (cPLA2) has a crucial role in the maintenance of inflammatory process during the course of systemic lupus erythematosus (SLE). We studied whether an elevated PLA2 activity correlated with the presence of autoantibodies against the complement proteins C1q, C3 and Factor H in sera of SLE patients.

Methods: Sera from 48 SLE patients were analyzed spectrophotometrically for PLA2 activity and for the presence of autoantibodies to complement C1q, C3 and Factor H by ELISA. Data were compared using Pearson's coefficient of correlation. A cohort of sera samples with elevated PLA2 activity were further analyzed with Western Blot in order to determine the type of PLA2 enzyme present in them.

Results: PLA2 enzyme activity weakly correlated with the presence of anti-C1q autoantibodies (r = 0.088, *P*= .550), anti-C3 autoantibodies (r = 0.232, *P*= .113) and anti-Factor H autoantibodies (r = 0.057, *P*= .698). Western Blot analysis revealed the presence of PLA2 enzyme with molecular mass of 260 kDa in all tested sera.

Conclusions: The PLA2 activity in SLE is weakly influenced by the presence of anti-complement autoantibodies. Other factors contribute as well to the increase of PLA2 activity. A possible presence of iPLA2 enzymes or oligomeric form of sPLA2/cPLA2 enzymes were detected.

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EP089 / #857

The Relevance of C1q in Systemic Lupus Erythematosus Patients - Single Center Pilot Study

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Background and aims: Systemic Lupus Erythematosus (SLE) is an autoimmune disorder mediated by complement. Flares of SLE are characterized by consumption of C3 and C4 but also C1q component of the complement. The aim was to investigate if low levels of C1q and C4 correlate with global and renal disease activity.

Methods: C1q was determined in serum samples of 41 patients with SLE using a N Latex C1q Kit (Trimero Diagnostics, Spain) on Atellica®NEPH630 (Siemens Healthineers, Germany). C4 concentrations were measured with Alinity c Complement C4 Reagent Kit (Abbott, USA).

Results: According to obtained C1q values, patients were divided into four groups: I. (N=4) below the manufacturer reference interval (RI) (<15.7 mg/dL); II. (N=8) lower RI range (15.7–23.0 mg/dL); III. (N=24) upper RI range (23.1-30.6 mg/dL) and IV. (N=5) above RI >30.6 mg/dL. Group I. had also lower C4 concentrations, but only 1/4 had active SLE and 1/4 renal involvement. Majority patients in group II. had lower C4 (6/8) together with renal involvement (6/8) and SLE activity (6/8). All pathological parameters were present in 5/8 patients. In group III. 5/24 had lower C4 but none of the 24 patients showed simultaneously active disease with renal involvement. All patients in group IV. had normal C4.

Conclusions: C1q as a component of the complement can be used to assess the activity of SLE especially in patients with the renal disease. Our pilot study found the tendency of lower serum levels of C1q and C4 in patients with active SLE and in patients with renal involvement (group II.).

EP090 / #400

Sera of Healthy First-Degree Relatives of SLE Patients Contain Autoantibodies to Globular Domains of C1q

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Background and aims: SLE is an autoimmune disorder caused by genetic and environmental factors. The clinical manifestation marks the accumulation of various types of autoantibodies, anti-C1q among them. We aimed to correlate the genetic predisposition with the presence of anti-C1q in healthy relatives of SLE patients.

Methods: We analysed by ELISA sera from 48 SLE patients and 48 healthy first-degree relatives (FDR) of SLE patients. Along with the intact C1q we tested the globular fragments constituting its globular domain (gC1q) - ghA, ghB and ghC. They were applied in two experimental designs - as immobilised and as soluble antigens.

Results: In the SLE group we detected 50% positive sera to at least one of the immobilised antigens, which were 31% anti-C1q, 17% anti-ghA, 8% anti-ghB and 8% anti-ghC positive. The same group had 54% positive sera to at least one of the soluble antigens, which were 6% anti-C1q, 33% anti-ghA, 31% anti-ghB

and 8% anti-ghC positive. In the FDR group we detected 67% positive sera to at least one of the immobilised antigens, which were 38% anti-C1q, 31% anti-ghA, 25% anti-ghB and 40% anti-ghC positive sera. The same group had 52% positive sera to at least one of the soluble antigens, which were 17% anti-C1q, 23% anti-ghA, 35% anti-ghB and 13% anti-ghC positive. Among the positive sera in both groups we found double- and triple-positive ones.

Conclusions: Both immobilised and soluble C1q is targeted by autoantibodies specific for gC1q. The anti-soluble gC1q autoantibodies might be a contributing factor for triggering SLE in genetically predisposed humans.

E-POSTER VIEWING 14: CLINICAL PRACTICE - DIAGNOSTICS: DIAGNOSTIC MEASUREMENTS IN AUTOIMMUNITY

EP091 / #775

Prevalence of Ds-Dna Autoantibodies in Patients without Systemic Autoimmune Rheumatic Diseases (SARDS): A 5-Year Case Revision on a Clinical Laboratory

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Background and aims: Anti-ds-DNA antibodies are generally included in screening algorithms for autoimmune diseases. The high prevalence of autoantibodies in healthy populations, or at least those who currently do not present with systemic autoimmune disease, is widely described in the literature. The positivity of ds-DNA tests using current laboratory methods (CLIA, FEIA or Elisa) still requires confirmation by IIF in Crithidia luciliae. The specificity of this method makes it possible to eliminate false positives from ds-DNA screening tests. Ds-DNA antibodies are complex molecules, referring to different nucleic acids and non-DNA structures. This is revealed by comparing several analytical methods which can give different test results depending on the type of assay, the antigen used or the variable avidity of anti-dsDNA antibodies.

Methods: ANA screening with IIF in Hep-2 cells (Euroimmun™); ds-DNA by FEIA (Thermofisher ™) with confirmatory IIF with Crithidia luciliae (Euroimmun™). Immunoblotting for SARDS (Euroimmun™). Liver autoimmune diseases study by IIF in Liver mosaic 9 (Euroimmun™) and liver immunoblotting profile by Euroimmun™. Systemic sclerosis and Myositis autoantibody profile by immunoblotting (Euroimmun™).

Results: The authors present 5 years revised casuistic from October 2018 to October 2023 as a reference clinical laboratory center in autoimmune diseases diagnosis, focusing on the prevalence os ds-DNA autoantibodies appearance in the context of patient without systemic autoimmune rheumatic diseases (SARDS).

Conclusions: Anti-ds-DNA antibodies are generally associated with LES, although in rare cases, anti-dsDNA antibodies are also found in patients with other autoimmune diseases like autoimmune hepatitis.

EP092 / #236

Eosinophilic Granulomatosis with Polyangiitis After Benralizumab Discontinuation for Severe Eosinophilic Asthma- A Case Report

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Background and aims: Eosinophilic granulomathosis with polyangiitis (EGPA) is a small to medium-vessel necrotizing vasculitis with eosinophilic inflammation. Benralizumab, an anti-IL-5 receptor monoclonal antibody, has been used for therapy of severe eosinophilic asthma, that is one of the features of EGPA. Only few case reports have showed EGPA onset after biologics discontinuation. It is unclear whether anti IL-5 therapy for severe asthma can prevent, mask, or delay EGPA development.

Methods: A case report of a patient who developed EGPA after benralizumab was stopped for severe asthma treatment.

Results: A 41 years top athlete with severe eosinophilic asthma and three times nasal polypectomy, was treated with benralizumab for one year with good response. The treatment was stopped due to lack of medication in our hospital. Three months later he presented with moderate asthma exacerbation, eosonophila (40.2%), fatigue, muscle pain, numbness and tingling in feet. Due to persistent hypereosinophila hematological conditions have been excluded. Immunoserological analysis were positive for myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody (ANCA) antibodies. Electroneuromyography revealed severe sensorimotor polyneuropathy, computerized tomography (CT) showed chronic inflammation in all paranasal sinuses. Lung CT scan and echocardiography were normal. There were no signs of kidney damage. The EGPA diagnosis was confirmed based on severe long term corticosteroid dependent asthma, hypereosinophila, chronic sinusitis, nasal polyposis, sensorimotor polyneuropathy and positive MPO ANCA. Immunosuppressive therapy was introduced: methylprednisolone 1mg/kg with gradual dose tapering and cyclophosphamide pulse therapy that led to clinical improvement.

Conclusions: In patients with severe eosinophilic asthma, discontinuation of benralizumab might be the trigger for EGPA development.

EP093 / #869

Clinical Comparison of Five Assays for the Detection of Anti-dsDNA Antibodies and Their Correlation with Complement Consumption

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Background and aims: Anti-dsDNA antibodies are highly specific and part of the classification criteria for systemic lupus erythematosus (SLE). They correlate with disease activity and contribute to the pathogenesis of lupus nephritis (LN). This study aimed to compare five methods for anti-dsDNA antibody detection and to estimate their association with complement consumption.

Methods: 186 samples were collected at Labcorp and tested on five assays: *Crithidia luciliae* indirect immunofluorescence test (CLIFT, Euroimmun, Lübeck Germany), BioPlex 2200 dsDNA (BioRad, Hercules, US), QUANTA Lite HA dsDNA ELISA, QUANTA Flash dsDNA chemiluminescent immunoassay (CIA), and Aptiva dsDNA, a particle-based multi-analyte technology (PMAT) immunoassay (all 3 assays, Inova Diagnostics, USA). Complement C3 and C4, measured with Cobas c 502 (Roche Diagnostics, USA), were used as serological surrogates and compared to each assay to assess the correlation with disease activity.

Results: The quantitative agreement varied between 0.60 (BioPlex vs. CLIFT) and 0.96 (Aptiva vs. QUANTA Flash) (Table 1). The C3 agree-

ment from highest to lowest was: HA dsDNA ELISA, CLIFT, QUANTA Flash, Aptiva, then BioPlex 2200. The findings were compared to qualitative results derived from CLIFT testing, since CLIFT is often used as the confirmation assay for anti-dsDNA. The highest area under the curve (AUC) from the receiver operating characteristic (ROC) curve was found for QUANTA Flash (0.95) followed by Aptiva and HA ELISA (both 0.94) and then BioPlex (0.87).

Conclusions: Anti-dsDNA antibodies measured using different methods showed varying agreement with CLIFT and complement consumption. Aptiva and QUANTA Flash dsDNA were highly correlated and in strong concordance with low C3 levels.

Table 1. Agreement between methods for anti-dsDNA detection

	CLIFT	BioPlex 2200	HA ELISA	BIO-FLASH	Aptiva
CLIFT					
BioPlex 2200	0.60 (0.38-0.76)				
HA ELISA	0.87 (0.78-0.93)	0.67 (0.47-0.80)			
BIO-FLASH	0.80 0.67-0.89)	0.72 (0.54-0.83)	0.86 (0.76-0.92)		
Aptiva	0.78 (0.64-0.87)	0.66 (0.46-0.80)	0.83 (0.72-0.91)	0.96 (0.94-0.98)	

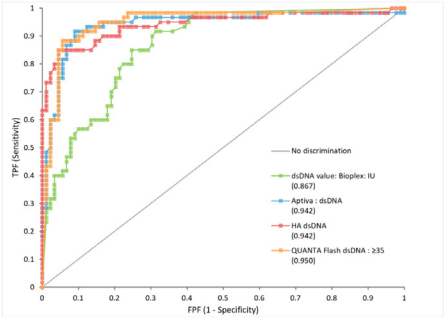

Figure 1. Receiver operating characteristic (ROC) curve analysis comparing four anti-dsDNA assays with CLIFT

Figure 1. Receiver operating characteristic (ROC) curve analysis comparing four anti-dsDNA assays with CLIFT.

EP094 / #872

Detection of Myositis Specific Autoantibodies Using the Novel Particle-Based Multi Analyte Technology on Cohorts of Suspected and Well-Defined Idiopathic Inflammatory Myopathies

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Background and aims: Myositis specific antibodies (MSA) represent not only important diagnostic tools but help in the stratification of idiopathic inflammatory myopathy (IIM) patients into clinical phenotypes, according to treatment responses, and disease outcomes. MSA have the potential to be included in the classification criteria thus standardization of MSA detection is of high importance. Many laboratories use immunoprecipitation (IP) for MSA detection but due to potential regulatory challenges, reliable alternatives to IP are mandatory. This study aimed to evaluate the performance of a novel particle-based multi-analyte technology (PMAT) for the detection of MSA on cohorts previously screened for myopathies.

Methods: A total of 609 patients consisting of individuals sent for myopathy screening [suspected IIM (n=215), clinically defined IIM (n=189)] and relevant disease controls (n=205) were included. MSA were measured with Autoimmune Myopathy research use only (RUO) reagents (PMAT, Inova Diagnostics, San Diego, USA; Mi-2, TIF1y, PL-12, SAE-1, EJ, MDA-5, HMGCR, Jo-1, PL-7, SRP54, NXP-2, and OJ). Using preliminary cut-offs identified in the receiver operating characteristic (ROC) curves, the clinical performance parameters and prevalence of each marker were calculated.

Results: The clinical performance of the 12 assays on the IIM screening cohort and controls are summarized in table 1. The frequency of each MSA on clinically defined IIM are in table 2.

Conclusions: The Autoimmune Myopathy (RUO) PMAT showed good performance at >99.5% and expected MSA prevalence among clinically defined and suspected IIM patients. The novel PMAT detecting a spectrum of MSA in IIM on a fully automated system represents a potential alternative to other diagnostic assays.

Table 1. Performance of the Autoimmune Myopathy (RUO) PMAT analytes on IIM screening (n=609) and controls (n=205)

Parameter	EJ	HMGCR	Jo-1	MDA5	Mi-2	NXP2	OJ	PL-12	PL-7	SAE	SRP	TIF1-y
Sensitivity (n=189)	1.1%	3.7%	6.3%	13.8%	5.8%	9.0%	2.1%	1.1%	1.6%	3.2%	1.6%	5.3%
Sensitivity (n=404)	1.2%	4.0%	5.0%	8.7%	4.2%	7.4%	8.2%	1.7%	1.7%	3.2%	1.5%	4.2%
Specificity (n=205)	100.0%	100.0%	100.0 %	100.0%	100.0 %	100.0 %	99.5%	100.0%	100.0%	100.0%	99.5%	99.5%
Likelihood ratio (+)	+∞	+∞	+∞	+∞	+∞	+∞	16.75	+∞	+∞	+∞	3.04	8.63
Likelihood ratio (-)	0.99	0.96	0.95	0.91	0.96	0.93	0.92	0.98	0.98	0.97	0.99	0.96
Odds ratio	+∞	+∞	+∞	+∞	+∞	+∞	18.2	+∞	+∞	+∞	3.1	9.0
Youden's index	0.012	0.040	0.050	0.087	0.042	0.074	0.077	0.017	0.017	0.032	0.010	0.037

Table 2. Prevalence of each MSA on clinically defined IIM (n=189) broken down by disease subtype

Parameter	EJ	HMGCR	Jo-1	MDA5	Mi-2	NXP2	OJ	PL-12	PL-7	SAE	SRP	TIF1-y
Sensitivity (n=189)	1.1%	3.7%	6.3%	13.8%	5.8%	9.0%	2.1%	1.1%	1.6%	3.2%	1.6%	5.3%
Sensitivity (n=404)	1.2%	4.0%	5.0%	8.7%	4.2%	7.4%	8.2%	1.7%	1.7%	3.2%	1.5%	4.2%
Specificity (n=205)	100.0%	100.0%	100.0 %	100.0%	100.0 %	100.0 %	99.5%	100.0%	100.0%	100.0%	99.5%	99.5%
Likelihood ratio (+)	+∞	+∞	+∞	+∞	+∞	+∞	16.75	+∞	+∞	+∞	3.04	8.63
Likelihood ratio (-)	0.99	0.96	0.95	0.91	0.96	0.93	0.92	0.98	0.98	0.97	0.99	0.96
Odds ratio	+∞	+∞	+∞	+∞	+∞	+∞	18.2	+∞	+∞	+∞	3.1	9.0
Youden's index	0.012	0.040	0.050	0.087	0.042	0.074	0.077	0.017	0.017	0.032	0.010	0.037

EP095 / #767

Pediatric Rheumatological Diseases in Nepal- Maiden Himalayan Cohort

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Background and aims: The availability of advanced courses, subspecialists, diagnostics, and therapeutics has shifted the paradigm for the diagnosis, and management of pediatric rheumatological diseases (PRDs) including autoimmune diseases in developing countries.

Methods: Case records of patients diagnosed and treated (including HSCT) for PRDs at the tertiary private care center in Kathmandu from Aug 2020 to November 2023 were analyzed. Lead author (DB) collated data from all patients. Diagnosis and treatments were based on internationally acclaimed criteria.

Results: A total of 527 patients with PRDs were diagnosed. The mean duration from initial symptoms to diagnosis was 12.5 months. Juvenile idiopathic arthritis (n = 281), connective tissue disorders (n = 213), vasculitides (n = 204), immune dysregulation & lymphoproliferation (n = 61) constituted the major proportions. Monogenic causes were diagnosed in 27 patients. Monogenic disorders included various etiologies including rare ones e.g., A20 haploinsufficiency, *ARPC1B* deficiency, Blau syndrome, *PIK3CD* mutation, TRAP syndrome (*TNFRSF1A)*, and PAPA syndrome. Almost 60% of children with autoimmunity and/or arthritis had visited dermatologists or orthopedicians before referral. We also diagnosed 69 children with inborn errors of immunity (IEIs). Autoimmunity was observed among 24 patients with IEIs. Observation of oligoarthritis in X-linked agammaglobulinemia (XLA) was a peculiar finding.

Conclusions: We present the first cohort of PRDs from Nepal. Significant phenotypic variations were noted. There are significant challenges to the diagnosis and treatment of PRDs and IEIs in resource-limited settings. Various socioeconomic factors coupled with a lack of awareness of PRDs accounted for a late presentation with severe state, increased morbidity, disability and mortality.

EP096 / #389

Possible Role of Lung Ultrasonography in SSc-Related ILD Follow-Up. Strong Correlation Between Warrick's Score and B-Lines in Patients Affected by Systemic Sclerosis

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Background and aims: HRCT is the *Gold Standard* to diagnose and study SSc-related ILD but its use must be limited related to radiological risk. In this study we aimed to evaluate the possible role of lung ultrasonography (LUS) to identify and quantify lung involvement in SSc.

Methods: We studied 27 patients (23 females and 3 males) with a mean age of 59.69 (±13.33) years and a disease duration of 14.46 (±9.91) years. Each patient underwent clinical assessment, HRCT, LUS, respiratory functional test and heart ultrasonography (HUS). Warrick score (Ws) was estimated by HRCT images. Through LUS we calculated the full B-lines count (BLC) and we created a B-line score (BLs) considering full B-lines count in respect of the number of thoracic available spaces. Based on normal distribution of variable, correlations were studied either with Pearson's R or Spearman's rho tests. A p-value of 0.05 was considered significant.

Results: We found a strong positive correlation between BLC and Ws (R=0.82, $P<.001$), similarly to BLs and Ws (R=82, $P<.001$). Unsurprisingly, Ws negatively correlated with spirometry's values particularly with $FEV_{1,}$ FVC, DLCO and TLC whereas as strong relation between the same spirometry values and BLs is demonstrated.

Conclusions: The correlation between Ws, BLC and BLs underline the potential role of LUS in SSc-related ILD typization. Moreover, the presence of strong relation between LUS and functional tests suggested the possibility to create an imaging-functional integrated score useful to predict ILD involvement and to personalized therapy in SSC patients.

EP097 / #613

Study of the Frequency of Positive Antinuclear Antibodies in A General Hospital in the Last Six Years

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Background and aims: The purpose of this study is to investigate the frequency of positive antinuclear antibodies (ANA) in our hospital over the last six years.

Methods: The study included 15,017 adult individuals (hospitalized patients in various clinics) who were examined for the presence of ANA over the last six years. The examination of ANA was performed using indirect immunofluorescence with HEp-2 Cells as the substrate (ANA Test ZENIT-autoimmunity), and samples with ANA titers >1/160 were considered positive. The fluorescence pattern was also recorded.

Conclusions: The number of individuals examined for ANA in our hospital remained high and relatively stable over the last six years. The percentage of ANA(+) during 2018, 2019, and 2020 remained stable (24.8%-26.0%), while in the last three years, it showed a slight increase (27.9%-31.5%). Two-thirds of ANA(+) were detected in females, with a stable frequency over the past six years. The mean age at which positive ANA were detected in females is 55.3 years, while in males, it is 62.0 years (approximately 7 years earlier in females). The speckled pattern of ANA remained the most common pattern throughout all the years.

Table 1.

Year	2018	2019	2020	2021	2022	Up to 9/2023
Patients	2438	2694	2457	2559	2729	2140
ANA(+)	26.0%-(635)	25.3%-(681)	24.8%-(609)	29.5%-(755)	31.5%-(859)	27.9%-(597)
Females	71.8%-(456)	72.8%-(496)	68.6%-(418)	69.1%-(522)	67.5%-(580)	66.3%-(396)
Average age (years)	51.1	54.9	58.1	54.8	54.8	57.8
Males	28.2%-(179)	27.2%-(185)	31.4%-(191)	30.9%-(233)	32.5%-(279)	33.7%-(201)
Average age (years)	55.1	66.8	65.3	65.0	60.5	59.2
Speckled pattern	48.7%-(309)	57.6%-(392)	58.3%-(355)	65.4%-(494)	58.6%-(503)	62.1%-(371)

EP098 / #1057

Relationship Between Neuropsychiatric Symptoms and the Presence of Anti-Ribosomal P Antibodies in Patients at the University Hospital of Uruguay

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Background and aims: Anti-ribosomal P antibodies (Ab. anti-P0) are specific for Systemic Lupus Erythematosus (SLE); they are not detected in healthy individuals or in other rheumatic diseases. Patients with SLE often suffer from anxiety and depression during the disease, which makes treatment difficult and affects the prognosis of the disease. Ab. anti-P0 is associated with neuropsychiatric manifestations and plays an important role in its pathogenesis. Evaluate the presence of neuropsychiatric symptoms in patients with positivity for Ab. anti-P0.

Methods: In all anti-nucleocytoplasmic Ab (ANA) requests from the period 2020-2023, those with positivity for Ab. anti-P0 were selected. Medical records of the selected patients were reviewed in search of neuropsychiatric pathology. The same number of patients with negativity for Ab. anti-P0 were used as controls, randomly selected and whose medical records of these pathologies was also sought. The data were analyzed using the Chi-square test.

Results: 2862 ANA were performed obtaining 31% positivity. Based on the institutional protocol, 822 Extractable nuclear antigens (ENAs) were carried out, obtaining 40% positivity. Positivity for Ab. anti-P0 was obtained in 0,7% of patient with ANA. Ab. anti-P0 that corresponded to 2.4% of the ENAs performed. The 20 Ab. anti-P0 corresponded to 18 patients. Of them, 34% presented neuropsychiatric symptoms. In the control group, 26% presented neuropsychiatric symptoms. A p-value of 0.64 was obtained.

Conclusions: Despite what is stated in the literature no significant difference was observed between the two groups and the presence of neuropsychiatric symptoms.

EP099 / #523

Performance Assessment of the New Euroline Neurologic Syndrome 15 Ag (Igg) for the Determination of Autoantibodies Associated with Neurological Disorders

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Background and aims: Many paraneoplastic as well as non-paraneoplastic autoantibodies (AAbs) have been described in neurological disorders in the last decade. By integrating the associated antigens into existing assays, the diagnostic work-up of patients is being improved and diagnostic gaps reduced. Here, we assess the performance of the new EUROLINE Neurologic Syndrome 15 Ag (IgG) which expands the EUROLINE Paraneoplastic Neurologic Syndrome 12 Ag by adding CDR2L (together with CDR2 targeted by anti-Yo), AK5, and Neurochondrin (NCDN).

Methods: Sensitivity of each AAb was analyzed using a total of 194 clinically and diagnostically pre-characterized samples. Specificity of each AAb was investigated using a minimum of 100 sera from healthy blood donors.

Results: Using the EUROLINE Neurologic Syndrome 15 Ag, autoantibody positivity was confirmed in 89-100% of samples. In particular, all samples for which clinical and tissue-based indirect immunofluorescence assay pre-characterization indicated anti-Yo positivity were anti-CDR2 and -CDR2L double positive. Anti-AK5 was determined in serum and cerebrospinal fluid (CSF) with a sensitivity of 90 and 100%, respectively, and anti-NCDN with a sensitivity of 100%. The individual specificities were ≥99%.

Conclusions: The EUROLINE test kit provides a tool for the qualitative *in vitro* determination of AAbs against a large panel of 15 different neuronal autoantigens to support the diagnosis of neurologic syndromes. The parallel detection of anti-CDR2 and anti-CDR2L (both anti-Yo) increases the diagnostic significance, as double positivity is strongly related to paraneoplastic cerebellar degeneration.

EP100 / #526

Simultaneous Detection of Multiple Purkinje Cell Antigens Using the Euroline Purkinje Cell Profile (Igg)

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Background and aims: In several neurologic syndromes, autoantibodies (AAbs) are directed against antigens in the cerebellum, including those expressed exclusively in Purkinje cells. These AAbs can be associated with inflammation, altered neurotransmission and cerebellar degeneration. They are commonly detected by means of indirect immunofluorescence assays (IFA) using tissue cryosections and confirmed by blot assay. Here, we report the assessment of the new EUROLINE Purkinje Cell Profile (IgG) (EUROIMMUN) line blot which enables simultaneous detection of multiple autoantibodies against Purkinje cell antigens.

Methods: Sensitivity of the line blot was determined using pre-characterized (tissue-based IFA, cell-based IFA, or immunoprecipitation) patient sera that showed a biomarker-specific

immunofluorescence signal on cryosections. Sera were positive for anti-Yo (indicating positivity for anti-CDR2 and anti-CDR2L, n=14), anti-Tr (DNER) (n=14), anti-PRKCG (n=3), anti-ARHGAP26 (n=3), anti-Homer-3 (n=5), anti-RGS8 (n=3), anti-RYR2 (n=3) and anti-AP3B2 (n=3). Specificity was tested using 150 control sera from healthy blood donors.

Results: Presence of AAbs against Yo (CDR2 and CDR2L[1]), PRKCG, ARHGAP26, Homer-3, RGS8, RYR2 and AP3B2 was confirmed in all sera. Anti-Tr (DNER) positivity was detected in all but one serum. A specificity of 100% was found for anti-Tr (DNER), anti-PRKCG, anti-Homer-3, and anti-RGS8, of 99.3% for anti-ARHGAP26 and anti-AP3B2, and of 98.7% for anti-RYR2.

Conclusions: The EUROLINE Purkinje Cell Profile (IgG) provides excellent sensitivity and specificity for the determination of AAbs against nine Purkinje cell antigens, including the seven newly developed substrates CDR2L, PRKCG, ARHGAP26, Homer-3, RGS8, RYR2, and AP3B2. The simultaneous detection of relevant AAbs supports fast serodiagnosis of autoimmune neurologic syndromes.

EP101 / #530

Evaluation of the Performance of the Euroimmun Anti-Gabaa Receptor Ifa in Patients with Suspected Autoimmune Anti-Gabaar Encephalitis

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Background and aims: Autoantibodies (AAbs) against Gamma-aminobutyric acid receptors A and B ($GABA_AR$, $GABA_BR$) are found in patients with autoimmune anti-GABAR encephalitis. Because of the rareness of anti-$GABA_AR$ encephalitis the full spectrum of symptoms is still unknown. Most patients suffer from seizures accompanied by status epilepticus. Treatment of epileptic seizures might be ineffective without simultaneous autoimmune therapy, demonstrating the importance to diagnose this rare form of encephalitis. This study analyzes the performance of a cell-based anti-$GABA_AR$ indirect immunofluorescence assay (IFA; for research use only, EUROIMMUN) using sera from patients with suspected anti-$GABA_AR$ encephalitis.

Methods: Clinically pre-characterized sera from 30 patients with suspected anti-$GABA_AR$ encephalitis were tested for presence of anti-$GABA_AR$ and anti-$GABA_BR$ AAbs with specific cell-based IFAs using $GABA_AR$- or $GABA_BR$-transfected cells. Anti-GABAR-positive sera were further investigated with tissue-based IFAs using cryosections of rat hippocampus as well as rat and monkey cerebellum. Serologically pre-characterized samples from 21 patients positive for encephalitis-specific AAbs other than anti-$GABA_AR$ served as controls.

Results: Of the 30 patient sera, one serum was positive for anti-$GABA_AR$ and one for anti-$GABA_BR$ AAbs. AAb positivity was confirmed using tissue-based IFA. All control samples were anti-$GABA_AR$-negative in the cell-based anti-$GABA_AR$ IFA, indicating an analytical specificity of 100%.

Conclusions: This cell-based anti-$GABA_AR$ IFA shows excellent analytical specificity for the detection of anti-$GABA_AR$ AAbs in human serum. Thus, the test provides a diagnostic tool to support recognition of rare anti-$GABA_AR$ encephalitis.

EP102 / #631

Verification of the New Immunoassay for Anti-Cardiolipin Igg and Anti-Cardiolipin Igm Antibodies

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Background and aims: Cardiolipin autoantibodies are, among other, an important criterion for the diagnosis of antiphospholipid syndrome (APS).The aim of this study was the verification of the ELISA-based immunoassay for anti-cardiolipin IgG (aCL-IgG) and anti-cardiolipin IgM (aCL-IgM) on Alegria 2 instrument, (Orgentec Diagnostika GmbH by Sebia, Mainz, Germany) including precision and comparison with ELISA assays for aCL-IgG and aCL-IgM (Orgentec Diagnostika GmbH, Mainz, Germany).

Methods: For precision evaluation, we tested confirmed negative pool sample and pathological commercial controls for five days in triplicate. Precision criterion declared by the manufacturer was 5.5 % for repeatability and 8.6 % for total within-laboratory precision for aCL-IgG and 3.7% repeatability and 5.7 % for total within-laboratory precision for aCL-IgM. Thirty sera samples were used for method comparison. Results were categorized as positive/negative and Cohen's kappa test was used for agreement testing (criterion: kappa >0.60).

Results: Repeatability CV% 0.030 and 2.280 and within-laboratory precision CV% 0.118 and 2.998 was gained for normal and pathological samples for aCL-IgG, and CV% of 0.110 and 1.81 and within-laboratory precision CV% 0.212 and 3.616 for aCL-IgM respectively. Kappa coefficient was 1.000 for both aCL-IgG and aCL-IgM.

Conclusions: Precision results met the criteria declared by the manufacturer and our calculated CV indicates rather small relative variability and proving the new method suitable for the routine use. Excellent agreement between methods is very reassuring but expected due to the same manufacturer. Lack of standardisation in autoimmune diagnostics imposes that information about methodological differences must be clearly stated on laboratory report.

EP103 / #804

Serum Immunoglobulin Heavy/ Light Chain Levels in Systemic Autoimmune Rheumatic Diseases

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Background and aims: The heavy/light chain (HLC) assays are used for the quantification of individual heavy and light chain isotypes in serum i.e. IgGk, IgGλ, IgAk, IgAλ, IgMk, IgMλ. HLC assays are a sensitive tool which have been shown to improve the management of multiple myeloma, particularly in the regcognition of minimal residual disease. The objective of our study was to investigate the distribution of immunoglobulin isotypes in patients with various systemic autoimmune rheumatic diseases (SARD).

Methods: We conducted a retrospective study, including patients with SRAD such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), primary Sjögren's syndrome (SSp) and sarcoidosis. We used patient frozen samples

which were previously stored at Biobank of Picardie. HLC assays were assessed with polyclonal antibodies targeting epitopes between heavy-chain and light-chain constant regions (Hevylite®, Binding Site, Birmingham, UK). We collected data on disease course (occurrence of lymphoma, monoclonal gammopathy of undetermined significance (MGUS) and multiple myeloma).

Results: This study included 88 patients : 14 RA patients ; 31 SLE patients ; 33 SSp patients and 10 patients with sarcoidosis. The median age at sample collection was 49.5 [18-83] years. In patients with SSp, the development of MGUS was associated with an increase of IgGk/λ ratio. Elevated concentrations of IgA, IgAk and increased IgAk/λ ratio were significantly associated with the development of lymphoma in SSp patients.

Conclusions: Elevated IgA, IgAk and IgAk/λ ratio could be predictive factors of lymphomagenesis in Sjögren's syndrome. However, further studies are needed to confirm these preliminary data.

EP104 / #518

Serodiagnosis of Anti-Glomerular Basement Membrane Disease Using a Newly Developed Chemiluminescence Immunoassay

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Background and aims: Autoantibodies against the glomerular basement membrane (GBM) are important markers in the diagnosis and monitoring of autoimmune glomerulonephritides. Fast and reliable detection of these autoantibodies is crucial as anti-GBM disease can progress rapidly with fatal outcome. Here, we investigated the diagnostic performance of a newly developed, standardized anti-GBM chemiluminescence immunoassay (ChLIA).

Methods: The diagnostic performance of the EUROIMMUN Anti-GBM ChLIA (IgG), processed on a fully automated random-access device, was assessed using sera from 67 clinically characterized anti-GBM disease patients and 221 disease controls. Results were compared with those obtained by the EUROIMMUN Anti-GBM ELISA (IgG). Inter-assay concordance, measurement range and interference were determined in a subset of samples.

Results: The ChLIA reached 100% sensitivity at a specificity of 98.6%, while the ELISA was less sensitive (89.6%) and more specific (100%). High qualitative concordance between both assays was evidenced by positive and negative agreement rates of 100% and 95.6%, respectively, and a kappa score of 0.901. The ChLIA showed linearity within a measurement range of 3.8-517.3 CU/ml. Coefficients of variation were calculated as 1.2-3.3% (intra-lot) and 1.6-4.2% (inter-lot). No interference was observed for hemolyzed, lipemic or icteric samples.

Conclusions: These validation results demonstrate a high quality of the novel Anti-GBM ChLIA. Given its excellent performance compared to the corresponding ELISA, it represents a promising alternative tool for accurate anti-GBM assessment in routine diagnostic settings with the advantage of rapid turnaround time and fully automated random-access processing. Future studies will address the assay's suitability for monitoring anti-GBM levels during follow-up.

EP105 / #521

Performance Assessment of aNewly Developed Chemiluminescence Assay for Anti-CCP Determination

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Background and aims: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by painful, swollen joints with limited movement and progressive joint destruction. Approximately 70% of RA patients develop autoantibodies (AAbs) against citrullinated peptides (ACPA) which are detected using primarily cyclic citrullinated peptides (CCP). This study aimed to assess the performance of the novel EUROIMMUN Anti-CCP chemiluminescence assays (ChLIA) based on clinical data and in comparison with an anti-CCP ELISA.

Methods: Sera from 185 patients with clinically diagnosed RA and from 281 control patients with various autoimmune and infectious diseases were analyzed for the presence of anti-CCP AAbs. The results obtained using the EUROIMMUN Anti-CCP ChLIA (IgG), processed on the IDS-i10 (Immunodiagnostic Systems), and the EUROIMMUN Anti-CCP ELISA (IgG) were compared.

Results: The Anti-CCP ChLIA yielded a sensitivity of 64.9% (120/185) with a specificity of 97.9% (275/281), while the anti-CCP ELISA yielded a sensitivity of 61.6% (114/185) with a specificity of 96.1% (270/281). Assay comparison resulted in a positive, negative, and overall agreement of 93.6%, 97.4% and 96.4%, respectively.

Conclusions: High agreement rates were observed between the anti-CCP ChLIA and the anti-CCP ELISA, with increased sensitivity and slightly higher specificity for the anti-CCP ChLIA. Thus, the Anti-CCP ChLIA is an excellent tool to support the diagnosis of RA. Results should always be interpreted together with those of further laboratory diagnostic procedures and based on the clinical picture.

EP106 / #730

Evaluation of a New Prototype Elisa for the Detection of Autoantibodies Against IA2 in Patients with Type 1 Diabetes Mellitus

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Background and aims: Autoantibodies against insulinoma-associated antigen-2 (anti-IA2) are an important marker for diagnosis and prediction of new-onset type 1 diabetes mellitus (T1DM). Here we report on the performance of a new prototype Anti-IA2 ELISA with shorter total incubation time (3h15min) compared to the established EUROIMMUN Anti-IA2 ELISA (minimum 17h40min).

Methods: The clinical performance of the prototype ELISA was evaluated using a sensitivity panel comprising sera from 32 patients with suspected T1DM and 111 patients with confirmed T1DM, and a specificity panel consisting of sera from 50 suspected cases each of connective tissue disease and celiac disease, and from 210 healthy donors. for method comparison, 32 samples from suspected T1DM cases

and a subset of 100 samples from confirmed T1DM patients were additionally analyzed using the established EUROIMMUN Anti-IA2 ELISA and the Medipan CentAK anti-IA_2 M radioimmunoassay (RIA), respectively.

Results: The clinical sensitivity of the prototype ELISA amounted to 73.4% (105/143) at a specificity of 99.4% (308/310). Method comparison revealed a sensitivity of the prototype of 93.3% (28/30) referring to the established ELISA and 93.8% (61/65) referring to the RIA, while the overall agreement was 90.6% (29/32, ELISA) and 90.0% (90/100, RIA).

Conclusions: The results suggest that the new Anti-IA2 ELISA will be a valuable tool in supporting the serodiagnosis of T1DM. Reducing the processing time to a few hours minimizes the time required for laboratory testing, reinforcing the prototype's suitability to replace the established ELISA. Additionally, the new assay enables easier automation in conjunction with other ELISA with similar timelines on EUROIMMUN Analyzer I or EUROLabWorkstation ELISA.

EP107 / #762

Management Approach of Neuroendocrinology and Immunology in Children with Juvenile Idiopathic Arthritis

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Background and aims: The study of interactions between neuroendocrinology and immunology, or immunoendocrinology, is a recent field. Few studies investigated autoimmune diseases associated with organ non-specific rheumatological disorders in children with juvenile idiopathic arthritis (JIA). No study has yet established independent predictor variables for autoimmune endocrine disease in JIA. The aim of this study was to evaluate pituitary autoimmunity and endocrine function in children with JIA. The novelty and originality of this paper is that for the first time, pituitary antibodies were evaluated in JIA patients.

Methods: This study included 97 patients with a JIA diagnosis. Patients with any other chronic conditions were excluded from the study. We made a baseline assessment and clinical follow up. The study protocol was approved by Doctoral School Ethics Committee.

Results: We noticed several peculiarities regarding pituitary hormones and their correlations with JIA characteristics. TSH medium value is greater in prepubertal than in pubertal children (P<.0001). We revealed TSH differences between children with sJIA vs oJIA (P<.05), and between oJIA and RF negative polyarthritis (P<.01). Hyperprolactinemia was statiscally higher in children with JIA onset below 3 years old and prolonged disease duration (P=.002). Gonadotropes correlate moderately, inversely proportionally with childs' age, r=-0.339 for LH and r=-0.468 for FSH. Autoimmune pituitary involvement through indirect immunofluorescence wasn't revealed in our cohort of patients.

Conclusions: Endocrine dysfunction remains underestimated in JIA patients. This study analyzed the impact of autoimmunity on pituitary function and its relationship with JIA-related clinical manifestations. Further studies are needed to elucidate interrelation between neuroendocrinology and cytokines profile.

EP108 / #37

How Importance Is the Knowledge of Autoantigen Structure in Autoimmunity: Regarding a Case

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Background and aims: JC virus is responsible for Progressive Multifocal Leucoencephalopathy (LMP) in immunodepressed patients that causes demyelination of Central Nervous System structures. Onconeural antibodies (OncoAb) are responsible for Paraneoplastic Neurological Syndromes such as Cerebellar Degeneration (CD) by Yo antibodies (YoAb). YoAb recognize two proteins of Purkinje cells (CDR2 and CDR2 like), and 90–98% of patients have cancer detected. Both are included in differential diagnosis of subacute ataxias.

Methods: Literature and patient's clinical history review.

Results: A 33-year-old man was referred for progressive weakness on his left arm and leg. A positive serology for HIV 1(viral load: 331000 copies) and syphilis were observed. Magnetic Resonance Imaging (MRI) showed unspecific findings, although in the context of HIV immunosuppression might suggest LMP among other causes. JC virus PCR in cerebrospinal fluid (CSF)was performed, and also serological and autoimmunity study in serum and CSF. OncoAb results showed an intense band for YoAb (Euroimmun Immunoblot) in serum and CSF. Both samples were send to confirm, but weren't. JC virus PCR was positive and confirmed LMP.

Conclusions: CDR2L has recently been identified as the main antigen of YoAb. However, has a 45% sequence identity with CDR2. Latest revisions propose that reactivity for both proteins must be observed. We have confirmed with Euroimmun company that their immunoblot only contains CDR2, while confirmation immunoblot, contains both and was only positive for CDR2, probably due to cross-reactivity with JC virus. It is important to know the composition of commercial immunoblots, especially in OncoAb due to its high association with cancer, and to confirm any positivity by a second technique.

EP109 / #700

Interleukin-6 in Cerebrospianl Fluid as Biomarker of Inflammation and Infection of Central Nervous System: Validation of Its Analysis on the Eclia Roche Platform

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Background and aims: Our preliminary data in several pathological conditions involving the central nervous system suggested IL-6 as a promising CSF biomarker for diagnosis and prognosis, but there are no certified method to measure IL-6 in CSF. The aim of this study was to validate the IL-6 dosage in CSF in a automated platform.

Methods: IL-6 was analysed by electrochemiluminescence immunoassay (ECLIA) on Roche platform, currently certified only for serum and plasma. CSF samples were pooled to obtain 4 different IL-6 concentrations and distributed in aliquots to measure IL-6 before and after storage at 25°C, 4°C, -20°C, with multiple freezing and thawing cycles. for repeatability and within-laboratory precision, we performed a protocol based on 5 days of testing, with 5 replicates per day, using 2 instruments, following CLSI guidelines (document EP05-A3. Wayne PA, 2014).

Results: IL-6 is stable in CSF samples stored at 25°C and 4°C for at least 48 hrs, and at -20°C for at least 14 days, also after 4 cycles of freezing and thawing. The mean repeatability CVs% ranged from 5,2% (lowest IL-6 level) to 0,84% (highest), while the mean within-laboratory CVs% ranged from 5,4% (lowest IL-6 level) to 0,94% (highest). Repeatability and precison were in line with that declared by the Manufacturer using serum samples.

Conclusions: IL-6 is a very stable molecule in CSF. At our knowledge, this is the first study which has validated IL-6 CSF analysis in ECLIA on Roche platform, that allows its dosage also in emergency, so we can plan to introduce IL-6 testing in CSF standard analysis.

EP110 / #742

Anti-Hmgcr Myopathy – Cardiologist Should Know More About Statins

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Background and aims: Anti-HMGCR (Anti-3-hydroxy-3-methylglutaryl coenzyme A reductase) myopathy is a rare form of immune mediated necrotizing myopathy characterised by muscle fibre necrosis without significant inflammatory infiltrate that was initially described in patients with a history of statin exposure. It is characterized by proximal muscle weakness with marked creatine kinase elevation and anti-HMGCR autoantibodies.

Methods: A 70 year-old female with a past medical history of myocardial infarction (2010) and hyperlipidaemia on atorvastatin 80mg (4 years) reported to rheumatologist a 1 month history of progressive, painless, weakness of lower extremities. Her labs were significant for elevated creatine kinase, myoglobin and troponine without inlammatory markers and she was send and admitted to the emergency with suspection for second myocardial infarction. Neither electrocardiography nor coronarography confirm diagnosis and during few days she was discharged from the hospital with diagnosis mild myocardial infarction to follow up with rheumatology and cardiology.

Results: One month later she presented worsening muscles soreness and weakness of all extremities and due to concern for statin-induced myopathy (her daughter works in immunology lab) discontinued atorvastatin (despite doctors´ recommendation) and asked lab for testing anti-HMGCR autoantibodies.

Conclusions: The test was positive and subsequent biopsy confirm diagnosis of immune mediated necrotizing myopathy.

EP111 / #860

Comparison of a Point-of-Care Method and An Elisa to Assess Infliximab and Adalimumab Drug and Autoantibodies Levels for Therapeutic Drug Monitoring (TDM)

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Background and aims: Anti TNF-a drugs infliximab (IFX) and adalimumab (ADA) are widely used to treat severe immunological disorders; they are monoclonal antibodies that may trigger the production of autoantibodies directed against the drug that diminish its effect by decreasing its concentrations in blood.

Methods: In this study we compared two methods for therapeutic drug monitoring (TDM) of IFX and ADA and the levels of anti-drug antibodies (anti-IFX and anti-ADA): an ELISA method (IDKmonitor, Immundiagnostik, Germany) and a point-of-care (POC) method on time-resolved fluorescence (TRF) (ez-track1, Theradiag, France). Diagnostic leftovers from 21 samples were tested for IFX and anti-IFX and 19 samples were tested for ADA and anti-ADA. Anti-drug antibodies were classified as positive if >10 AU/mL or negative if ≤10 AU/mL.

Results: IFX levels ranged 0.1-45 with ELISA and 0.2-46.5 µg/mL with TRF; ADA were 4.4-25 and 4.7-30.3 µg/mL. Mean values between ELISA and TRF were different both for IFX and for ADA (IFX 9.7±10.6 vs. 11±11.1 µg/mL, *P*= .006; ADA 11±5.4 vs. 12.8±6.7 µg/mL, *P*= .0002). A strong correlation was found between single values: linear regression $r^2 = 0.971$, p <.0001 for IFX and $r^2 = 0.959$, p <.0001 for ADA. Anti-IFX values had a fair agreement with a Cohen's Kappa = 0.35; anti-ADA were all negatives for both methods except for one sample that was 13.2 AU/mL with TRF and 2.5 with ELISA.

Conclusions: A POC method might be reliably used to assess anti TNF-a drug levels, while for anti-drug concentrations the inter-methods agreement should be further studied.

EP112 / #348

Peptides from the Variable Domain of Immunoglobulin G as Biomarkers in Chronic Inflammatory Demyelinating Polyradiculoneuropathy

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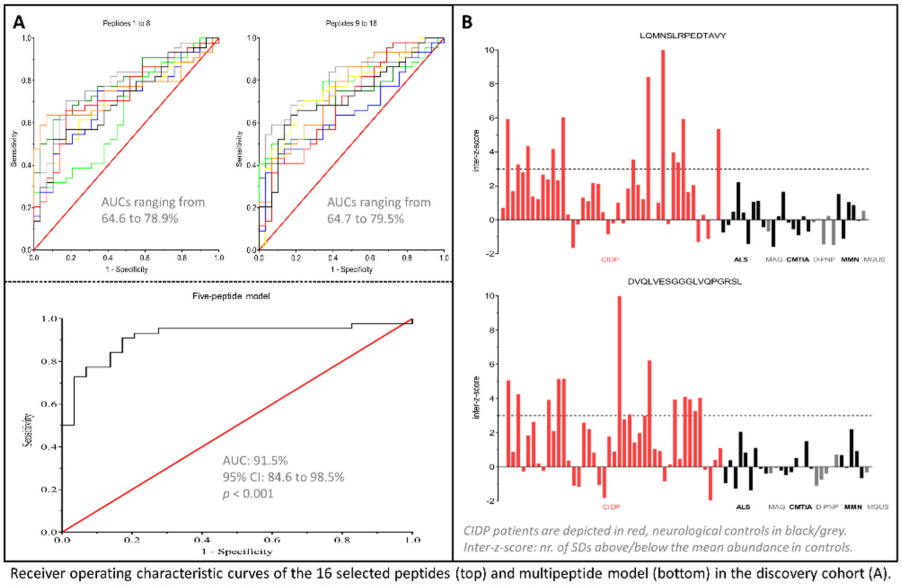
Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a clinically heterogeneous disease for which diagnostic biomarkers are currently lacking. Peptides derived from the immunoglobulin G (IgG) variable domain have earlier been shown to be shared among patients with the same immunological disease. As humoral immune factors are likely involved in the pathogenesis of CIDP, we aimed to evaluate IgG variable domain–derived peptides as diagnostic CIDP biomarkers.

Methods: IgG-derived peptides were determined in prospectively collected sera of patients with CIDP and neurological controls via mass spectrometry. Peptides of interest were selected through statistical analysis in a discovery cohort. Next, diagnostic performance was evaluated for both individual peptides and a multipeptide model, followed by performance reassessment in a validation cohort.

Results: Sixteen promising IgG-variable domain-derived peptides were selected in a discovery cohort of 44 CIDP patients and 29 neurological controls. All 16 peptides were shown to be significant predictor variables for CIDP in univariate logistic regressions and ROC

curve analysis (AUC range: 64.6% to 79.6%). 13/16 peptides were also retained in multivariable logistic regression models including age and sex. A model composed of 5/16 peptides showed strong discriminating performance (AUC 91.5%; p < 0.001). In the validation cohort containing 45 patients and 43 controls, 2/16 peptides were retained as predictor variables for CIDP, while the five-peptide model now demonstrated an AUC of 61.2% (*P*= .064).

Conclusions: IgG variable domain–derived peptides showed a valid source for diagnostic biomarkers in CIDP, albeit with challenges toward replication. Our proof-of-concept findings warrant further study of IgG-derived peptides as diagnostic CIDP biomarkers.



Receiver operating characteristic curves of the 16 selected peptides (top) and multipeptide model (bottom) in the discovery cohort (A). Inter-z-score profiles of two selected peptides of interest showing upregulation in CIDP (B).

Figure 1.

EP113 / #349

Paranodal Antibodies Against Contactin-1, Neurofascin-155 and Neurofascin-186 in Neuromuscular Disorders Other Than Chronic Inflammatory Demyelinating Polyradiculoneuropathy

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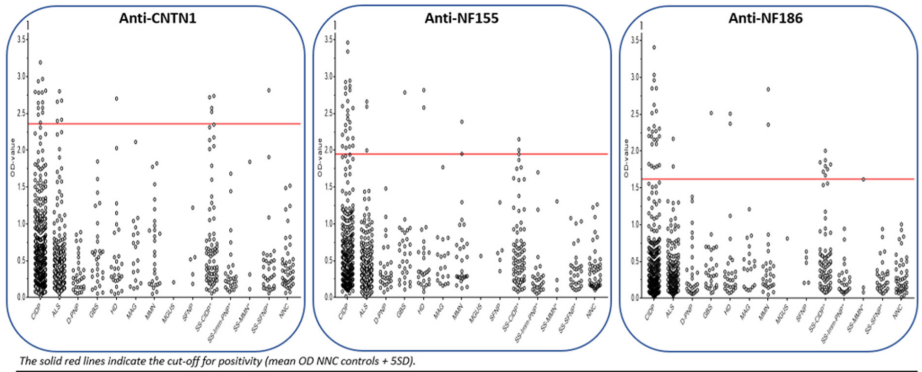
Background and aims: Paranodal antibodies (PNAb) against contactin-1 (CNTN1), neurofascin (NF)155 and NF186 are reported in 1-10% of patients diagnosed with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) but are sporadically also reported in non-CIDP-like disorders. In this study, we explored the specificity of PNAb for CIDP-like pathology by measuring these antibodies also in extensive cohorts of patients with various other neuromuscular disorders. Additionally, the presence of PNAb was investigated in patients with both Sjögren's syndrome (SS) and peripheral neuropathy.

Methods: Serum of adult patients with CIDP and neurological controls with or without SS was prospectively collected at the Neuromuscular Reference centers of Leuven (Belgium) and Hannover (Germany) and was evaluated in a 1/100 dilution on the presence of antibodies against CNTN1, NF155 and NF186 via in-house developed ELISA's utilizing recombinant human antigens and rabbit anti-human IgG HRP-labeled secondary antibody. Samples were measured in duplicate and considered positive when optical density (OD)-values exceeded the (mean+5SD) OD-value measured in non-neuropathy controls.

Results: In total, 462 patients with CIDP (incl. 74 SS-patients), 462 patients with other neuromuscular disorders (incl. 59 SS-peripheral neuropathy patients and 266 amyotrophic lateral sclerosis (ALS) patients) and 41 non-neuromuscular controls were included. PNAb were detected in 46 CIDP patients (incl. 9 SS-CIDP) (10.0%) but also in 15 patients with other neuromuscular disorders (3.2%) (ALS, n=8; Guillain-Barré syndrome, n=1; multifocal motor neuropathy, n=2; hereditary disorders, n=3; SS-small-fiber neuropathy, n=1).

Conclusions: While the prevalence of PNAb was most pronounced in the CIDP groups, detection of PNAb in disorders not resembling CIDP challenges their specificity for CIDP-like pathology.



The solid red lines indicate the cut-off for positivity (mean OD NNC controls + 5SD).

Cohort	N included (N positive)	Cohort	N included (N positive)	Cohort	N included (N positive)	Cohort	N included (N positive)	Cohort	N included (N positive)
CIDP	388 (37, 9.5%)	Guillain-Barré syndrome (GBS)	29 (1, 3.4%)	Multifocal motor neuropathy (MMN)	27 (2, 7.4%)	Sjögren's syndrome (SS) - CIDP	74 (9, 12.2%)	SS-SFNP	31 (1, 3.2%)
ALS	266 (8, 3.0%)	Hereditary disorders (HD)	27 (3, 11.1%)	MGUS-related neuropathy	1 (0)	SS-immune mediated neuropathy	25 (0)	Non-neuropathy controls (NNC)	41 (0)
Diabetic peripheral neuropathy (D-PNP)	30 (0)	Anti-MAG neuropathy (MAG)	18 (0)	Small-fiber neuropathy (SFNP)	5 (0)	SS-MMN	3 (0)		

Figure 1.

EP114 / #697

Prevalence and Clinical Relevance of Anti-DFS70 Antibodies in a Ecuadorian Cohort

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Background and aims: Anti-DFS70 autoantibodies are primarily found in healthy individuals and are used to rule out systemic autoimmune rheumatic diseases (SARD). The clinical significance of detecting anti-DFS70 autoantibodies remains uncertain. This autoantibody is not associated with any specific clinical manifestations and its prevalence is mutifactorial. To study the prevalence of anti-DFS70 as well as its clinical relevance and its relationship with other autoimmune disease biomarkers in a group of Ecuadorian individuals.

Methods: Anti-DFS70 levels using ELISA techniques, line quantitative immunoassay (LIA) and Antinuclear antibodies (ANA) using indirect immunofluorescence (IFI) were tested. N: 312 patients.

Results: Prevalence of anti-DFS70: 9.6% (30/312). Average age: 41.23 years (range:8-79 years). 36.7% had some form of autoimmune disease. Most common diseases associated with the presence of anti-DFS70 were lupus erythematosus (SLE):64% and rheumatoid arthritis (RA):36%. All positive samples were tested using IFI (Hep-2 cells). A typical fine dense speckled (AC-2) pattern was observed in 28/30 samples. Two samples showed discordant patterns, specifically homogeneous patterns with positive results for anti-nucleosomes and anti-histones. The median titer of anti-DFS70 was 1/160. Most common laboratory abnormality: low C3 levels in 27% of the patients. Interestingly, the AC-2 pattern was not the most frequently observed pattern in our cohort, accounting for only 2.08% (28/1346 ANA samples).

Conclusions: The pattern was easily identified, even in the presence of other antibodies. Individuals with autoimmunity, particularly those with SLE, had a higher incidence of anti-DFS70. Although rare, it is important to continuously evaluate its effects on clinical outcomes until we fully comprehend its significance. To our knowledge, this is the first study conducted in Ecuador.

EP115 / #1080

Comparison of Manual with Artificial Intelligence Aided Interpretation of HEp-2 IFA Patterns

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Background and aims: The determination of antinuclear antibodies (ANA) using immunofluorescence assays (IFA) on HEp-2 cells is an essential laboratory test for the diagnostics of systemic rheumatic diseases. So far, this technique was labour-intensive and required trained laboratory experts for interpretation of ANA. To overcome these difficulties, automated analysers have been developed which apply artificial intelligence (AI) for ANA evaluation.

Methods: In total, 1332 consecutive serum samples of routine ANA screening were included into this study. Detection of ANA was performed using AKLIDES ANA Plus (Medipan GmbH, Blankenfelde-Mahlow, Germany), an AKENOMIneo (Medipan) automated liquid handler for sample preparation and an akironNEO automated fluorescence microscope (Medipan) for ANA analysis. Each ANA image was manually re-evaluated by two experts and the results were compared with automated interpretation.

Results: A total of 16 different nuclear, cytoplasmic and mitotic competent level ANA patterns were identified in the sample collective by manual and automated interpretation. The most frequent pattern was AC-4/5 (speckled). Kappa coefficient of agreement of the results between human observers was 0.884 (almost perfect agreement). Agreement between automated and individual observer interpretation was also almost perfect (kappa=0.870 and 0.837, respectively). AI detected patterns in all classification groups even barely discernible patterns such as AC11,12 (nuclear envelope) and multiple patterns, e.g., AC3+AC21 (centromere+antimitochondrial antibody).

Conclusions: AI-aided analysis of ANA patterns in combination with automated sample processing and interpretation reduces the time to result. The standardization of the whole workflow reduces inter-observer variability and improves the analytical performance of ANA testing.

EP116 / #531

Septin-3 as a Novel Autoimmune Target Antigen in Patients with Paraneoplastic Cerebellar Ataxia

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Background and aims: Septin-5 autoantibodies are associated with non-paraneoplastic cerebellar ataxia, and septin-7 autoantibodies with encephalopathy with prominent neuropsychiatric features. Here, we report on newly identified septin-3 autoantibodies in patients with paraneoplastic cerebellar ataxia.

Methods: Sera from three patients producing similar immunofluorescence patterns on neuronal tissue sections were subjected to immunoprecipitation and MS. The identified candidate antigens, all septins, were expressed in HEK293 cells either individually, as complexes, or combinations missing individual septins, for use in recombinant cell-based indirect immunofluorescence assays (RC-IFA). Specificity for septin-3 was confirmed by tissue IFA neutralization. Tumor sections were analyzed for septin-3 expression.

Results: Immunoprecipitation with rat cerebellum lysate revealed septin-3,-5,-6,-7, and -11 as candidate target antigens. All three patient sera reacted with cells co-expressing septin-3/5/6/7/11, while none of 149 healthy controls was similarly reactive. In RC-IFAs, patient sera recognized only cells expressing septin-3. Incubation of patient sera with five different septin combinations, confirmed the autoantibodies' specificity for septin-3. The tissue IFA reactivity of patient serum was

abolished by pre-incubation with HEK293 cell lysates overexpressing the septin-3/5/6/7/11 complex or septin-3 alone. All three patients had cancers, presented with progressive cerebellar syndromes, and responded poorly to immunotherapy. Expression of septin-3 was demonstrated in resected tumor tissue.

Conclusions: Septin-3 is a novel autoantibody target in patients with paraneoplastic cerebellar syndromes. RC-IFA with HEK293 cells expressing the septin-3/5/6/7/11 complex may serve as a screening tool to investigate anti-septin autoantibodies in samples with a characteristic staining pattern on neuronal tissue sections. Autoantibodies against individual septins can then be confirmed by RC-IFA expressing single septins.

EP117 / #537

Identification of Dagla as an Autoantibody Target in Cerebellar Ataxia

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Background and aims: We aimed to investigate the clinical, imaging and fluid biomarker characteristics in patients with anti-diacylglycerol lipase alpha (DAGLA)-autoantibody-associated cerebellitis.

Methods: Serum and CSF samples from four index patients (age 18-34) were subjected to comprehensive autoantibody screening by indirect immunofluorescence assay (IIFA). Immunoprecipitation, mass spectrometry and recombinant protein assays were used to identify the autoantigen. As controls, sera from 101 patients with various neurological symptoms and a similar tissue staining pattern as the index patient samples, and 102 healthy donors were analyzed in recombinant cell-based IIFA (RC-IIFA) with the identified protein. Epitope characterization of all positive samples was performed.

Results: All index patients suffered from pronounced gait ataxia, dysarthria, and visual impairments. Paraclinical hallmarks in early-stage disease were inflammatory CSF changes and cerebellar cortex hyperintensity in MRI. Severe cerebellar atrophy developed in 3/4 patients within 6 months. All patient samples showed a similar unclassified IgG reactivity with the cerebellar molecular layer. DAGLA was identified as the target antigen and confirmed by competitive inhibition experiments and DAGLA-specific RC-IIFA. Serum positivity for anti-DAGLA was also found in 17/101 disease controls, including patients with different clinical phenotypes than the one of the index patients, and in 1/102 healthy donors. Epitope characterization revealed that 17/18 anti-DAGLA-positive control sera reacted with a C-terminal intracellular DAGLA 583-1042 fragment, while the CSF samples of the index patients targeted a conformational epitope between amino acid 1-157.

Conclusions: We propose that anti-DAGLA autoantibodies detected in CSF with a characteristic tissue IIFA pattern represent novel biomarkers for rapidly progressive cerebellitis.

EP118 / #403

Detection of KLHL11 Autoantibodies Using a New Cell-Based Indirect Immunofluorescence Assay

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Background and aims: Autoantibodies against kelch-like protein 11 (KLHL11) were first described in 2019 as markers of paraneoplastic encephalitis. Early diagnosis and treatment are imperative to improve prognosis and outcome of affected patients. Rat brain immunohistochemistry was reported to be not useful in routine screening for KLHL11 antibodies. This study evaluates the performance of a new recombinant cell-based assay for the standardized detection of KLHL11-specific IgG and reports the characteristics of the examined patients.

Methods: Serum (n=9), CSF (n=5) and/or plasmapheresis (n=1) samples from 10 patients with clinical presentations compatible with anti-KLHL11 encephalitis as well as sera from 100 healthy blood donors were analyzed using a prototype indirect immunofluorescence assay (IFA; EUROIMMUN) based on recombinant HEK293 cells expressing human KLHL11.

Results: KLHL11 autoantibodies were detected at high titers in all samples (serum >1:1,000; CSF >1:320; plasma >1:100,000) from all (10/10) patients but in none (0/100) of the blood donors, indicating 100% sensitivity and specificity. Anti-KLHL11-positive patients had a median age of 52 years (range 27-71) and 80% were male. The most common reported clinical presentations were cerebellar syndrome (ataxia), brainstem diencephalic encephalitis, rhombencephalitis and limbic encephalitis. Testicular or ovarian tumors were found in 87.5% (7/8) of the cases with available results from malignancy screening.

Conclusions: The new cell-based IFA enables the sensitive and specific detection of KLHL11 autoantibodies, thus supporting the diagnosis of patients with predominantly paraneoplastic brainstem cerebellar syndrome. Future studies will evaluate assay performance in larger patient cohorts to address the reported association of KLHL11 autoimmunity with a wider spectrum of syndromes and tumors.

EP119 / #484

"De Novo" Glomerulonephritis Associated with IgA Anti-GBM Alloantibodies After Kidney Transplantation in Alport Syndrome: Diagnostic Implications

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Background and aims: Alport syndrome (AS) is caused by mutations in Type IV collagen (CIV) genes. The α3α4α5(CIV) heterotrimer is defective causing kidney, hearing and ocular abnormalities. Some AS patients who undergo kidney transplantation develop anti-GBM disease by alloantibodies (AlAb). We present a patient with glomerulonephritis after kidney transplant associated to AlAb of IgA isotype against CIV.

Methods: A biopsy of the kidney graft was studied by electron microscopy and direct immunofluorescence (DIF). Chemiluminescence / indirect immunofluorescence (IFI) and bead-based immunoassay were performed to detect anti-GBM and anti-HLA antibodies, respectively. Reactivity of serum against CIV chains was evaluated by Western Blot. Genetic sequencing of AS genes was made.

Results: Kidney graft biopsy showed thrombotic microangiopathy with changes supporting humoral rejection. DIF showed crescents, linear positivity for IgA and weak staining for IgG. Anti-HLA AlAb to the graft were negative, as were chemiluminiscence and IFI for IgG anti-GBM antibodies. However, IgA antibodies were demonstrated by IFI on kidney sections. Western Blot showed only IgA AlAb, mainly to α5 and α3 CIV chains. A new biallelic variant in *COL4A4* gene (c.1343G>T) was found, causing an aminoacid change which alters the CIV triple helix.

Conclusions: This is the first case, to our knowledge, of an AS patient who developed rejection associated with IgA anti-GBM AlAb after kidney transplant. It should be pointed out that commercial tests only detect IgG antibodies to α3 CIV chains. Additional tests are mandatory to detect antibodies to GBM of other immunoglobulin subclasses or with different targets.

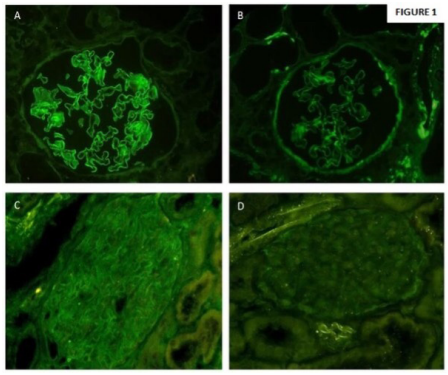

Figure 1.

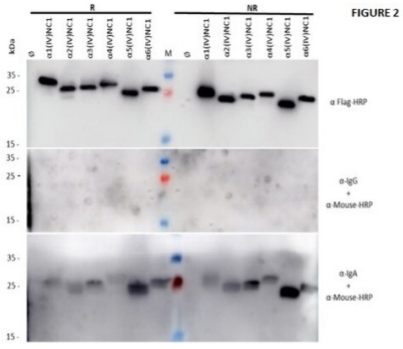

Figure 2.

EP120 / #40

Longitudinal Serological and Clinical Investigations in Patients with Anti-IgLON5 Disease Suggest Clinical and Prognostic Relevance of Intrathecally Produced IgLON5-IgG4

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Background and aims: Anti-IgLON5 disease is a rare neurological disorder hallmarked by autoantibodies against IgLON5 and clinical and histopathological features of neuroinflammation and neurodegeneration. The IgLON5 autoantibodies are predominantly of the IgG4 subclass, with distinct pathogenic effects in vitro reported for IgG1 and IgG4.

Methods: We longitudinally analyse IgLON5-specific IgG subclass levels in 46 sera and 20 cerebrospinal fluid (CSF) samples from 13 HLA-subtyped anti-IgLON5 disease patients using a cell-based assay and flow cytometry. We correlated antibody levels with immunotherapy and outcome. Our findings led us to develop a quantitative method for intrathecal anti-IgLON5 IgG4 synthesis.

Results: IgLON5-specific IgG4 predominated in in 38/46 serum and 11/20 CSF samples, IgG1 in 1/46 serum and 1/20 CSF samples. CSF anti-IgLON5 IgG was always considerably lower than the corresponding serum levels. CSF anti-IgLON5 IgG4 levels prior clinical improvement were significantly lower than in those without. Immune therapy was associated with reduced IgLON5 antibody levels whereas no treatment was associated with unchanged or increased antibody levels, and decreased IgG1 and IgG4 in serum and CSF were most frequently observed after combination therapy. Lastly, we developed a novel method to measure intrathecal synthesis (IS). IgLON5-specific IgG4 IS was present in all of five patients studied and decreased upon successful immunotherapy in two.

Conclusions: Initiation of immunotherapy was associated with lowering IgLON5-specific IgG4/IgG1 levels. Prominent lowering CSF IgLON5-specific IgG levels, also reduction of IgLON5 IgG4 IS and CSF taken prior to clinical improvement showed significantly lower IgLON5-IgG4 titres than CSF samples before patients remained stable or clinically worsened.

EP121 / #388

Combining Anti-CCP Antibody and Rheumatoid Factor Isotype Specific Test Results Increases the Diagnostic Confidence of Rheumatoid Arthritis

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Background and aims: Analyzing patient samples for anti-CCP autoantibodies and rheumatoid factor (RF) IgM represents a pivotal aid in the diagnosis of rheumatoid arthritis and has been included in the 2010 ACR/EULAR rheumatoid arthritis classification criteria. In the early phases of RA, its differential diagnosis from other diseases can be difficult. Some studies suggested an increase in diagnostic confidence by additionally testing for RF IgA and combining test results. We aimed to contribute to the ongoing scientific debate about the combination of test results by analyzing samples from early RA patients for anti-CCP, RF IgM and RF IgA autoantibodies.

Methods: A sample cohort of 100 rheumatoid arthritis patients with symptoms of less than two years and 149 disease controls were analyzed for the above mentioned serological markers with the respective EliA™ tests.

Results: In this study, anti-CCP, RF IgM and RF IgA autoantibodies were measured in 62%, 62% and 50% of early RA patients at a specificity of 95.3%, 90.6% and 91.9%, respectively. 56 % of the RA samples but only 1.3% of the disease controls were positive for both anti-CCP and RF IgM leading to a positive likelihood ratio (LR(+)) of 41.72 and a positive predictive value (PPV) of 0.97. Triple positivity for all three autoantibodies was detected in 45% of the RA samples and only 0.7% of the controls. The calculated LR(+) and PPV was 67.1 and 0.98, respectively.

Conclusions: The combination of anti-CCP, RF IgM and RF IgA autoantibody testing can provide higher diagnostic confidence of RA than testing for either marker alone.

EP122 / #394

A Potential Risk of False Positive Results When Utilizing Purified Human Thyroid Peroxidase as Antigen in Anti-Thyroid Peroxidase Antibody Tests

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Background and aims: The antigen quality is one of the important factors affecting the reported results of an *in vitro* diagnostic test. The isolation from human/animal tissue or the recombinant expression are two commonly used sources for protein antigens. In this study, we aim to compare anti-thyroid peroxidase (anti-TPO) antibody tests using different TPO antigens: recombinant human versus purified from human thyroid gland. The latter has been reported to contain traces of thyroglobulin (TG).

Methods: Samples containing anti-TPO and/or anti-TG were measured with two anti-TPO tests using TPO from these different sources. To analyze the effect of anti-TPO and anti-TG on the reported results, the anti-TPO or anti-TG antibodies were sequestered by pre-incubating the samples with recombinant TPO or TG prior to the measurement with the anti-TPO tests.

Results: For the sample negative for anti-TG antibodies, the depletion of anti-TPO antibodies clearly reduced the reported result for both anti-TPO tests. For two samples containing both anti-TPO and anti-TG antibodies, the reported results were only clearly reduced for the test using recombinant TPO upon the depletion of anti-TPO antibodies. In contrast, the reported results of the anti-TPO test using TPO purified from the human thyroid gland were clearly reduced when these two samples were depleted of anti-TG antibodies. This effect was not observed when the anti-TG antibody depleted samples were analyzed with the anti-TPO test using recombinant TPO.

Conclusions: The results of this study highlight that the antigen quality can significantly affect the reported results of an antibody test.

EP123 / #811

Evaluation of Requested Tests for Myositis Specific Antibodies During the COVID-19 Pandemic Period

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Background and aims: During the COVID-19 pandemic, it is recorded that SARS-CoV-2 infection or vaccination has influenced the request for Myositis-specific/associated autoantibodies (MSAs/MAAs), in the context of clinical investigation, as well as their positivity against specific antigenic targets. Study, registration and evaluation of requested tests for MSAs/MAAs in a cohort of patients with suspected myopathy, during the pandemic period (2020-2022) compared to the pre-COVID period (2018-2019).

Methods: 432 serum samples (group I, period 2018-2019) and 732 serum samples (group II, period 2020-2022) were studied for MSAs/MAAs in the diagnostic approach of Idiopathic Inflammatory Myopathy (IIM). The MSAs/MAAs were sought with Immunoblotting Assay (IB-Euroimmun panel for anti-PL-7, PL12, EJ, OJ, Mi-2, SRP, PM/Scl, Ku, TIF1g, MDA5, NXP2, SAE1, Ro52).

Results: A gradual increase in the requested parameters was observed in the pre-pandemic and pandemic period. Positive samples were recorded at a rate of 4.1% and 4.6% for the years 2018 and 2019, respectively, while positivity for the years 2020,2021,2022 was recorded at 6.5%, 10.4% and 12.2%, respectively. A predominance of anti-Jo1 and anti-Ro52 antibodies was detected, while a great diversity was observed in the specificity of the antibodies against the other antigenic targets.

Conclusions: Our study shows that while a small increase in the request for MSAs/MAAs during the pandemic period is observed, nevertheless it is recorded a significant increase in their positivity. This fact highlights the need for further investigation about the possible involvement of the COVID-19 or vaccination in the incidence of IIM.

EP124 / #650

Identification of Autoantigens for Biliary Atresia Using Human Proteome Microarrays

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Background and aims: Autoimmune-mediated injury of bile ducts is recognized as the primary cause to persistent cholangitis in children with biliary atresia (BA) and autoantigens are unclear.

Methods: A human proteome microarray was used to screen autoantigens in a cohorts (20 BA, 5 disease controls, 5 healthy controls) by serum "mixed pool" method. Then a focused microarray was fabricated with these newly identified candidates to further verify the specific autoantigens. Finally, ELISA detecting autoantibodies to the specific antigens was established and tested in sera from 120 BA patients and 233 controls, for diagnosis.

Results: Forty-nine BA-related differential autoantigens were identified by the screening criteria of fold change>2 and stable expression. GO functional analysis revealed that these differential autoantigens mainly involved in the regulation of cell development, proliferation, apoptosis and the formation of biliary tracts. With the focused microarray it showed that under the premise of ensuring 90% specificity, the sensitivity such as RBPJ and CNPY4 to distinguish NC and DC was 50% and 30%, respectively. The levels of anti-RBPJ antibodies detected by ELISA in sera of 120 patients with BA showed that the overall OD value of BA group was significantly higher than that of the control group (P<.001), with the AUC of BA and non-BA diagnosed by anti-RBPJ antibody at 0.694 (P<.001, 95%CI: 0.633 ~ 0.754), sensitivity 55.8% and specificity 78.1% .

Conclusions: RBPJ and CNPY4 have been screened as the specific autoantigens for biliary atresia using by human proteome microarray, and anti-RBPJ could be used as a novel serum biomarker to distinguish BA from non-BA.

EP125 / #646

Prevention and Early Diagnosis of Rheumatoid Arthritis – The DigiPrevent Project

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Background and aims: Rheumatoid arthritis (RA) is a chronic and debilitating disease that affects over five million people in Europe and often requires lifelong and expensive treatment. Prevention and early curative treatment for RA is the aspired solution for patients and society, but the current healthcare structure in Europe rarely enables prevention or optimal early treatment. The DigiPrevent project is a research collaboration between academia, healthcare providers, patient organizations, payors, and industry that receives funding from EIT Health. The aim is to develop tools to improve the identification of individuals with an increased risk for RA and to improve the referral from primary- to secondary care.

Methods: The project includes a digital screening tool, called *Rheumatic?* which can be used by individuals with musculoskeletal complaints at primary care level or earlier for identification of individuals at risk for RA or with early signs of RA.

Results: The information from *Rheumatic?* will be combined with serologic- and genetic information into an algorithm that will improve the quantification of risk for RA and enable earlier diagnosis and better referrals. The tools will be evaluated in health care systems in Sweden, the Netherlands, and Germany.

Conclusions: The DigiPrevent developed tools will improve identification of individuals at risk for RA and with early signs of RA. This will enable prevention efforts that could reduce the numbers of RA by 20-50%, based on current knowledge of modifiable lifestyle factors and impact of existing therapies in individuals at very high risk of developing RA.

EP126 / #444

Calprotectin – A Robust and Sensitive Marker of Inflammation in Ra Patients

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Background and aims: Calprotectin (S100A8/S100A9, MRP8/MRP14) in plasma has been shown to be more sensitive than Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP) in reflecting inflammatory activity in patients with rheumatoid arthritis (RA). The aim of this study was to explore the robustness of the laboratory examination and the correlation with clinical examinations of inflammation.

Methods: Plasma samples from early (n=220, mean disease duration 7.2 months) and established RA (n=177, mean disease duration 10.0 years) patients were analyzed for calprotectin levels at baseline and after 1, 2, 3, 6 and 12 months using either Enzyme-linked immunosorbent assay (ELISA, Calpro AS, Norway) or fluoroenzyme immunoassay (FEIA, measured on EliA™ platform (Thermo Fisher Scientific, Sweden)). Clinical measures as number of swollen joints and examiner's global score (EGA) by use of visual analogue scale (VAS) were included as well as Ultrasound performed by an experienced sonographer.

Results: The two methods detecting calprotectin showed high correlation (Spearman correlation 0.91 and 0.96 for early respective established RA). When comparing number of patients in remission having normal calprotectin compared to normal CRP levels, there was a higher percentage of agreement for calprotectin compared to CRP, 93-96% vs 71-85% depending on timepoint and remission criteria.

Conclusions: Calprotectin has been shown to be a better marker of inflammation in RA than the commonly used inflammatory markers and may therefore be widely included in clinical laboratories. The present study supports the robustness of the analyses, showing similar calprotectin measures across different analytical methods and better correlation with remission than CRP in RA patients.

EP127 / #1068

The Diagnostic and Predictive Value of Autoantibody Profile in Systemic Sclerosis

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Background and aims: Autoantibodies can serve as diagnostic and predictive tools in systemic sclerosis (SSc). This multicenter study aimed to analyse the relevance of autoantibodies to disease phenotypes and course.

Methods: Patients' data were collected from a retrospective review of medical records (2013-2023) of SSc patients followed at seven tertiary care hospitals in Turkey. HEp-2 IIF was used for ANA pattern and ENA profile ELISA and ENA blot (Euroimmun, Germany) for specific autoantibody determination.

Results: A total of 360 SSc patients (239 limited cutaneous sclerosis-lcSSc), 84 diffuse cutaneous sclerosis-dcSSc) were enrolled. 90.2% were females; mean age 54.64 years (SD 13.98). The most frequent pathology in the dcSSc group was ILD (66.3%); in the lcSSc group was gastrointestinal involvement (56.5%). Autoantibody profiles were available for 303 patients. Anti-Scl70 positivities were 74.8, 56.1, 53.7, 70.1, 48.7, 53.9 and 83.1, respectively, in ILD, PAH, gastrointestinal involvement, digital ulcers, Raynaud's phenomenon, telangiectasia and joint contractures. Anti-Scl70 and anti-CENP-B positivities were equal in cardiac involvement (each 47.8%). Anti-Scl70 positivity was significantly associated with ILD (P<.001) while there was a significant negative association with CENP-B (P<.001). PAH did not show any significant association with either anti-Scl70 or anti-CENP-B. There was a significant negative association with CENP-B positivity and gastrointestinal involvement (P<.001). CENP-B was positive in 51.6% of Sjögren overlap, 77.8% of rheumatoid arthritis overlap and 68.8% of cancer patients.

Conclusions: Organ involvement was higher in anti-Scl-70 positive SSc patients. Autoantibodies could be used as valuable biomarkers for disease stratification in SSc patients and might be used for the precision of disease course.

EP128 / #557

Comparison of Three Different Assays for the Detection of Mpo/Pr3 Anca Antibodies

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Background and aims: Autoantibodies targeting PR3 and MPO proteins (ANCA) in primary granules of neutrophils are essential for the diagnosis and classification of ANCA-associated vasculitis (AAV). We aimed to compare our in-house direct ELISA with the capture ELISA (Svar Life Science) and the chemiluminescent assay (QUANTA Flash MPO and PR3, Inova Diagnostics) for the detection of MPO and PR3 ANCA.

Methods: Three different ANCA assays were performed in the sera of 39 patients with AAV, 55 patients with various non-AAV vasculitides, and 66 patients with different connective tissue diseases. The agreement and correlations between the results of the assays were calculated, and their clinical performance for AAV was determined.

Results: The agreement between negative and positive results of the assays for the detection of MPO and PR3 ANCA ranged from 97.5-98.8% with Cohen`s kappa coefficients between 0.861 (0.728-0.995) and 0.947 (95% CI 0.875-1.000), indicating near perfect agreement between negative and positive results. The Spearman's rank correlation coefficient of positive results ranged from 0.451-0.914, indicating moderate to strong correlations. The diagnostic sensitivity, specificity, and diagnostic accuracy (determined as area under the ROC curve - AUC) of ANCA antibodies for AAV of the assays tested were comparable (in-house ELISA 89.7%, 95.0%, and 0.937; capture ELISA 92.3%, 98.3%, and 0.939; and QUANTA Flash 89.7%, 95.9%, and 0.972).

Conclusions: With this study, we have shown that the commercial assays provide comparable results to the in-house ELISA that we have been performing in our laboratory for more than a decade.

EP129 / #558

Implementation of aNew Protocol for the Detection of Cryoglobulins

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Background and aims: Cryoglobulins (CG) are important for the diagnosis of cryoglobulinemic vasculitis. Our aim was to introduce a new, more sensitive and specific protocol for the detection of CG.

Methods: In the Department of Rheumatology (UMC Ljubljana), samples were routinely analyzed for CG according to the protocol using the Folin-Ciocalteu reagent. With the new protocol, the type of CG was determined by immunofixation on visually observed positive samples, and the concentration of CG (IgG, IgM, and/or IgA) was measured by immunonephelometry. The verification included precision and analytical sensitivity for immunofixation and precision of IgG, IgM and IgA. The agreement and correlation between the results of the two protocols were calculated.

Results: The analytical sensitivity of immunofixation was 2.23 mg/L for IgG, 2.62 mg/L for IgM, and 2.34 mg/L for IgA. The commercial control was tested on three gels with identical results, polyclonal IgG, IgM, and IgA, confirming precision between runs. For a patient sample (polyclonal IgG and monoclonal IgM kappa), identical results were obtained 4 times on one gel, confirming within-run precision. The precision of nephelometric measurements using commercial controls within and between runs was: 2.9% and 3.4% for IgG, 2.0% and 2.2% for IgM, and 3.3% and 3.3% for IgA. Using results from 258 samples, the agreement between the two protocols was 86% and Cohen`s Kappa was 0.483 (95% CI 0.346-0.619) with a Spear-

man correlation coefficient of 0.692 (95% CI 0.370-0.865).

Conclusions: With the new precise protocol, we have improved the detection and quantification of CG in our laboratory.

EP130 / #749

Testing Antibodies Against Domain I B2gpi in Aps Patients Positive for Classification Criteria Antibodies Has No Additional Benefit

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Background and aims: Antibodies against domain I of β2GPI (anti-D1) are considered the true pathogenic antibody subset of anti-β2GPI but are not included in the new EULAR/ACR classification criteria for APS. The aim of this study was to evaluate the added value of anti-D1 testing in APS patients.

Methods: Our study included 125 samples from APS patients (99 chronic patients with a median disease duration of 7 years and 26 newly diagnosed) screened at the Department of Rheumatology (UMC Ljubljana) between 2019 and 2020. Sera were tested for aCL and anti-β2GPI (IgG, IgM) and anti-D1 (IgG) using QUANTA Flash CLIA (Inova Diagnostics, San Diego, CA). Thresholds for moderate/high were set according to the new EULAR/ACR classification criteria for APS and are shown in Table 1A.

Results: The results of all aPL tested are shown in Table 1A. 49/125 (39.2%) patients had at least one positive aPL test in the low/moderate/high range. 24/49 (49.0%) aPL-positive patients had positive levels of anti-D1, and 21 (87.5%) of them had high levels of both aCL IgG and anti-β2GPI IgG. 2/24 (8.3%) patients had moderate aCL IgG and high anti-β2GPI IgG, and 1/24 (4.2%) had low positive anti-β2GPI IgG (Table 1B). We found one patient who met the laboratory domain classification criteria for APS with moderate aCL IgG and high anti-β2GPI IgG but no anti-D1 antibodies.

Conclusions: According to our study, testing for anti-D1 in patients with moderate or high positive aCL and anti-β2GPI IgG does not add value in classifying patients as APS.

Table 1.

A

Thresholds (CU)	aCL IgG	aCL IgM	anti-β2GPI IgG	anti-β2GPI IgM	anti-D1 IgG
Low (manufacturer`s cut-off)	20	20	20	/	30 (99th percentile of HBD)
Moderate	30	30	60	20	
High	100	100	120	40	
No. of pos. (n=125)					
Low	5	4	13	/	24
Moderate	7	15	4	6	
High	21	9	25	14	

B

Combinations of aCL and anti-β2GPI IgG in APS patients	High aCL and High anti-β2GPI	Moderate aCl and High anti-β2GPI	Moderate aCL and Moderate anti-β2GPI	Moderate aCl and Low anti-β2GPI	Low aCL and Low anti-β2GPI	High/moderate/low aCL or High/moderate/low anti-β2GPI	Negative
No. of patients* (% of all patients)	21 (16.8)	3 (2.4)	1 (0.8)	1 (0.8)	1 (0.8)	22 (17.6)	76 (60.8)
No. of anti-D1+ (% of *)	**21 (100)**	**2 (66.7)**	**0**	**0**	**0**	**1 (4.5)**	**0**
No. of single/double low/moderate/high+ IgM (% of *)	13 (61.9)	0	0	0	0	7 (31.8)	8 (10.5)

EP131 / #524

Adequation of a Novel Chemiluminescence Immunoassay (CLIA) Method to Determine Serum Calprotectin Levels in Rheumatoid and Psoriatic Arthritis Patients

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Background and aims: Calprotectin (CLP) is a heterodimeric protein, secreted mainly by neutrophils, that has been traditionally used as a fecal marker of inflammation (fCLP) in the gastrointestinal tract. Recently, circulating calprotectin (cCLP) levels, mainly determined by ELISA methods, have been found elevated in rheumatoid (RA) and psoriatic (PsA) arthritis patients correlating with disease activity. The objective of this work was to assess the suitability of an adapted fCLP CLIA method to measure cCLP levels in RA and PsA patients.

Methods: Serum calprotectin levels were measured by CLIA (Liaison, Diasorin), in comparison with a standardized ELISA (Bülhmann, Palex), in seventy-eight subjects recruited by Rheumatology area as follows: 1) RA patients (n=32), 2) PsA patients (n=21), both clinically diagnosed, and 3) non-arthritis controls (n=25). Both methods were realized according to the manufacturer instructions, except for a 1:5 initial sera dilution in CLIA. Statistic analysis was done with GraphPadv7.0 and SPSSv26, while methods were compared with MedCalc (v20.218) program.

Results: cCL*P value*s of study subjects (mean age: 58, women: 74%) were similar in ELISA and CLIA, with a strong correlation between results (r=0.97, *P*<.0001). Moreover, Bland-Altman plot showed a mean bias of 1.09 and 95% limits of agreement of -2.84 and 5.03. Kappa agreement index was 0.84 (almost perfect agreement). ELISA and CLIA cCL*P value*s were also similar in every studied group (RA, PsA and controls), without showing statistical differences between methods (*P*>.05).

Conclusions: Therefore, CLIA resulted to be a fast and reliable alternative method to determine cCLP levels both in RA and PsA patients.

EP132 / #326

The First Determination of Anti-PLA2R by Indirect Immunofluoresence Can Help in Membranous Nephrophaty Diagnosis

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Background and aims: Membranous nephropathy (MN) is the most common cause of nephrotic syndrome (NS) in adults. It is important to differentiate MN in to primary MN (pMN) and secondary MN (sMN) type since their treatment and prognosis are different. M-type phospholipase A2 receptor (PLA2R), the target antigen present in glomerular basement membrane (GBM) is commonly associated with pMN. Renal biopsy being an invasive procedure, noninvasive biomarkers such as anti-PLA2R antibody in serum can be helpful and preferable to differentiate and monitor pMN vs sMN. A thirty two - year old female has a history of proteinuria (12 g/day) about three years ago. She has refused renal biopsy, so serological testing for anti-PLA2R is requested for this case.

Methods: The detection of anti-PLA2R was accomplished through Indirect Immunofluoresence Test (IIFT), EUROIMMUN. The anti-PLA2R IgG IIFT contains 2 BIOCHIPs: transfected cells expressing recombinant PLA2R/control-transfected cells. The serum was diluted 1:10-1:80 in PBS -Tween.

Results: The anti-PLA2R resulted negative but we observed the positivity on transfected cell nuclei in all dilutions. Then we determined the Antinuclear Antibody (ANA) on Hep-2 cells. ANA resulted positive >1:320 and the speckled pattern was observed. This positivity and the pattern was associated with positivity of anti-Smith and the positivity of anti-RNP. Our patient was diagnosed with Lupus MN.

Conclusions: We can say that IIFT gives more information not only for anti-PLA2R. IIFT can detect the lower titre of anti-PLA2R and helps in early diagnosis of pMN.

EP133 / #461

A Comparative Study of Microblot-Array (MBA) with Conventional Routine Methods for the Detection of Antibodies Associated with SLE and SCL in Czech Population

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Background and aims: Autoimmune diseases (AIDs) include a wide range of disorders, demanding multiple antibody tests for[PI1] different AIDs. Traditional ANA tests like Immunofluorescence (IFA) and BLOTs methods have separate limitations in efficiency (antigens distribution), sample volume, and accuracy. MBA ANA can analyze 44 markers simultaneously, monitor antibody levels, and provide insights into specific AIDs.

Methods: The primary objective of this study was to assess MBA's diagnostic capabilities and explore its potential in ANA diagnostics. The distribution of antibodies was monitored in sera samples from 533 patients, which are stored in the Institute of Rheumatology) - 261 with Systemic scleroderma (SCL) and 332 with Systemic lupus erythematodes (SLE), diagnostically characterized by laboratory routine methods (screening by indirect immunofluorescence IIF – IMMUNOCONCEPT and by Blot – Euroimmun and Human Diagnostika). Correlation of the different laboratory routine methods with MBA was determined.

Results: In patients with SCL, agreement between all three methods was 87.8%, on the MBA and IIF methods 92.2% and on the MBA and BLOT 92.2%. In patients with SLE, agreement on all three methods was 87.5%, on the MBA and IIF 87.5% and on the MBA and BLOT 88.75%.

Conclusions: A detailed comparison showed that MBA is a reliable method for diagnosing AIDs, aligning well with traditional tests like BLOT and IFA. This signals a new era in ANA testing, with MBA offering precision and efficiency. It can detect multiple disorders in one test, speeding up diagnostics, promising quicker, personalized treatment, and improved patient lives.

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EP134 / #457

Urinary Soluble CD163 and Anti-C1q Antibodies Are Independently Useful in Lupus Nephritis Follow-Up

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Background and aims: Lupus nephritis (LN) diagnosis and follow-up requires noninvasive biomarkers. Therefore, the added value of anti-C1q antibodies (Abs) and urinary soluble (s) CD163 needs to be evaluated in a real-world clinical practice, the aim of the study.

Methods: A monocentric and retrospective study was conducted in 105 SLE patients with biopsy-proven nephritis having an active LN (LN-A, n=47, SLEDAI-2K≥6) or not (n=58), as well as 57 non-renal SLE patients (SLEDAI-2K range: 0-14). The panel of LN biomarkers included: 14 serological biomarkers (e.g., anti-C1q Abs, anti-dsDNA Abs, complement C3 fraction), and 2 urinary parameters (spot proteinuria/creatinuria ratio [PCR] and sCD163/creatinuria ratio).

Results: Among serological markers (n=14), anti-C1q Abs (AUC=0.770; *P*<10-4 and 71.7% sensitivity) best predicted proliferative LN-A. Urinary sCD163/creatinuria ratio (AUC=0.959; *P*<10-4 and 100% sensitivity threshold=325 ng/mmol) outperformed PCR for monitoring renal activity allowing prediction of impending flares and remissions in follow-up. Last but not least, a sustained and increased anti-C1q Ab positivity, but not sCD163/creatinuria ratio, during follow-up indicates risk for developing an end-stage kidney disease.

Conclusions: In addition to the kidney biopsy, which is invasive and presents contraindications that restricts its usage, the detection of SLE-associated biomarkers is important at the time of LN diagnosis, and part of them can be used to monitor LN activity and in turn to provide guidance for therapeutic response, flare, and ESKD evolution. Results from our study support the consideration of anti-C1q Abs and urinary sCD163/creatinuria as independent factors in the list of classical LN biomarkers in addition to anti-dsDNA Abs, C3 complement fraction, PCR and eGFR.

EP135 / #334

Over-Expression of LEDGF/P75 in HEp-2 Cells Enhances Autoreactive Igg Response in Patients with Benign Prostatic Hyperplasia – Evidence of a Novel Autoimmune Disease in Men?

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Background and aims: Lens epithelium-derived growth factor-splice variant of 75kDa (LEDGF/p75) is an au-toantigen over-expressed in solid tumors and acts as a stress-related transcriptional co-activator. Participation of autoimmune responses in the pathophysiology of benign prostatic hyperplasia (PBH) and a corresponding immunosuppressive therapy by TNFalpha antagonists has been recently suggested. Thus, autoAb testing could aid in the diagnosis of BPH patients profiting from such therapy.

Methods: We generated CRISPR/Cas9 modified HEp-2 LEDGF knock-out (KO) and HEp-2 LEDGF/p75 over-expressing (OE) cells and examined IgG autoantibody reactivity in patients with prostate cancer (PCa, n=89), bladder cancer (BCa, n=116), benign prostatic hyperplasia (BPH, n=103), and blood donors (BD, n=60) by indirect immunofluorescence assay (IFA) and line immunoassay (LIA).

Results: We could not detect elevated binding of autoAbs against LEDGF/p75 in cancer patients, but autoAb reactivity to LEDGF/p75 OE cells in about 50% of patients with BPH was unexpectedly significantly increased. Furthermore, a LIA enabling the detection of 18 different autoAbs revealed a significantly increased occurrence of anti-dsDNA autoAbs in 34% of BPH patients in contrast to tumor patients and BD. This finding was confirmed by anti-mitochondrial (mDNA) autoAb detection with the Crithidia luciliae immunofluorescence test that also showed a significantly higher prevalence (34%) of anti-mDNA autoAbs in BPH.

Conclusions: Our study provided further evidence for the occurrence of autoimmune responses in BPH. Furthermore, LEDGF/p75 over-expression renders HEp-2 cells more autoantigenic and an ideal target for autoAb analysis in BPH with a potential therapy consequence.

EP136 / #584

Autoantibody Profiles in Patients with Musculoskeletal Complaints

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Background and aims: Timely and rapid stratification of musculoskeletal complaints is essential to ensure accurate care and to prevent irreversible negative outcomes for the patients. In this study autoantibody profiles of patients are studied as part of larger models that aim to improve the stratification of patients with musculoskeletal complaints.

Methods: 159 samples from an ongoing collection of samples from patients with musculoskeletal complaints referred to rheumatology outpatient clinics in the Netherlands were analyzed for autoantibodies with EliA™ technologies (Phadia AB, Sweden; CCP IgG, CCP IgA, RF IgM, RF IgA and CTD screen) and a research multiplex chip (citrullinated RA associated peptides and individual CTD associated proteins).

Results: In this patient cohort, 15% of samples were RF IgM positive, 12% were positive for the CTD Screen and 7% were CCP IgG positive. Only 2% were positive for both CTD screen and CCP IgG. The most common positive chip reactivities in CTD screen positive samples were Ro 60 (in 42%) and RNA pol III (in 32%). Within CCP IgG positive samples, the most common RA associated autoantibodies were directed against citrullinated filaggrin (Fil 307-324, 73%) and fibrinogen (Fib 36-52, 64%) peptides.

Conclusions: In this study, many autoantibody reactivities were found in samples from patients with musculoskeletal complaints. In the future, antibody reactivities will be correlated to clinical diagnosis and used for evaluation in models for earlier stratification of patients with musculoskeletal complaints to enable earlier diagnosis and treatment start.

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EP137 / #339

Addressing Diagnostic Delay in Axspa by Implementing Patient Self-Sampling from Remote Human Leucocyte Antigen-B27 (Hla-B27) Analysis

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Background and aims: Axial spondyloarthritis (axSpA) is a rheumatic disease with a prevalence of 0.3-1.4%. Medical treatment is important to improve prognosis, quality of life and avoid functional disability. Thus, the current diagnostic delay of 3-11 years is a major challenge. Human leukocyte antigen B27 (HLA-B27) is part of the diagnostic approach – particularly for the screening of patients with inflammatory back pain. This prospective study assesses the feasibility and acceptance of unsupervised home-sampling for HLA-B27 analysis by individuals with inflammatory back pain and suspected axSpA.

Methods: We enrolled 36 newly referred patients with suspected axSpA, providing them with a CE-certified upper-arm device (TAP II, YourBio Health, USA) for unsupervised home blood sample collection post-consultation. Genomic DNA extraction from whole blood samples enabled real-time PCR for HLA-B27 analysis using the Applied Biosystems™ TaqMan™ (Thermo Fisher Scientific, USA) assay. As endogenous control globin and human growth hormone were measured and Ct values over 35 were considered as undetermined. Patient acceptability for home sampling was assessed using the Net Promoter Score (NPS).

Results: Among 36 patients, 31 (88.6%) returned their samples. HLA-B27 analysis yielded definite results in 29 of the 31 samples. The concordance with standard hospital-based venous analysis was 100%. Patient acceptance was remarkably high, with an NPS of +35.5%.

Conclusions: This study demonstrates the accuracy, feasibility, and high patient acceptance of unsupervised remote blood sample collection for HLA-B27 analysis in individuals with suspected axSpA. These results provide an important basis for the implementation of screening and triage tools to reduce the diagnostic delay.

EP138 / #861

Clinical Evaluation and Method Comparison of Novel Assays for the Detection of Antibodies Associated with Connective Tissue Diseases

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Background and aims: The detection of antinuclear antibodies (ANA) is important in the diagnosis of ANA-associated rheumatic diseases (AARD). Newer technologies and methods for detecting ANAs are becoming more available, offering wider analytical measuring ranges (AMRs), smaller footprint, and random-access capabilities. Leveraging broad antibody profiles with new laboratory technology platforms can help to deliver more efficient diagnosis in patients affected by connective tissue diseases (CTDs). This study aimed to evaluate the performance of Aptiva® CTD Essential Reagent based on a novel fully automated particle-based multi-analyte technology (PMAT) in comparison with other reference methods.

Methods: A total of 1269 samples were collected from various AARDs and disease controls. All samples were tested on the Aptiva® CTD Essential Reagent (PMAT, Inova Diagnostics, USA). Additionally, a subset of samples were tested using chemiluminescent immunoassays for dsDNA, RNP, Ro60, Ro52, SS-B, Scl-70, Jo-1 and Centromere (CIA, QUANTA Flash, Inova Diagnostics, USA) and ELISAs using Orgentec Sm (ORGENTEC Diagnostika GmbH, Germany) and QUANTA Lite Ribo-P (Inova Diagnostics, USA). Qualitative correlations were calculated, and clinical performance was assessed.

Results: Method comparison showed Cohen's *kappa* values between 0.71 (dsDNA) and 0.98 (Ribo-P). The clinical evaluation focused on disease specific markers for all analytes showing good discriminations between the target disease and relevant disease controls.

Table 1. Method comparison result between PMAT and CIA or ELISA methods

	Comparator method	Kappa (95% CI)	NPA (95% CI)	PPA (95% CI)	TPA (95% CI)
dsDNA (n=428)*	CIA	0.71 (0.63-0.78)	91.3 (88.2-94.4)	78.9 (70.8-85.1)	88.1 (84.7-90.8)
RNP (n=480)	CIA	0.77 (0.71-0.84)	90.6 (87.3-93.2)	97.9 (92.6-99.4)	92.1 (89.3-94.2)
Sm (n=418)	ELISA	0.82 (0.72-0.92)	98.2 (96.3-99.1)	85.7 (70.6-93.7)	97.1 (95.0-98.4)
Ro52 (n=1028)	CIA	0.93 (0.91-0.96)	97.8 (96.6-98.6)	97.6 (94.5-99.0)	97.8 (96.7-98.5)
Ro60 (n=551)	CIA	0.88 (0.84-0.92)	91.8 (88.5-94.3)	98.5 (95.6-99.5)	94.2 (91.9-95.9)
SS-B (n=550)	CIA	0.88 (0.82-0.93)	96.3 (94.1-97.7)	96.7 (90.8-98.9)	96.4 (94.5-97.6)
Scl-70 (n=435)	CIA	0.90 (0.84-0.96)	97.6 (95.4-98.7)	95.5 (87.6-98.5)	97.2 (95.2-98.4)
Jo-1 (n=416)	CIA	0.96 (0.90-1.00)	99.7 (98.6-100.0)	96.0 (80.5-99.3)	99.5 (98.3-99.9)
Centromere (n=449)	CIA	0.94 (0.90-0.98)	98.3 (96.2-99.2)	96.2 (90.6-98.5)	97.8 (95.9-98.8)
Ribo-P (n=387)	ELISA	0.98 (0.93-1.00)	99.7 (98.5-100.0)	100.0 (85.7-100.0)	99.7 (98.6-100.0)

*Indeterminate range for dsDNA as positive
NPA = negative percent agreement, PPA = positive percent agreement, TPA = total percent agreement, CI =confidence interval

Table 2. Clinical performance results for Aptia CTD Essential Reagent

	Target	Sensitivity % (95% CI)	Specificity % (95% CI)	Odds Ratio (95% CI)
dsDNA* (n=1269)	SLE	50.4 (44.0-56.8)	90.1 (88.1-91.8)	9.2 (6.6-12.9)
RNP (n=1039)	MCTD	65.1 (58.0-76.8)	94.8 (93.2-96.1)	39.2 (23.2-66.3)
RNP (n=1178	SLE	37.4 (31.4-43.8)		11.0 (7.4-16.2))
Sm (n=1269)	SLE	10.4 (7.1-15.1)	99.6 (99.0-99.9)	30.1 (10.8-84.0)
Ro52 (n=531)	SjS	60.3 (52.0-68.0)	96.7 (94.4-98.0)	44.8 (23.1-83.6)
Ro52 (n=620)	SLE	24.2 (19.3-30.3		9.3 (5.0-17.4)
Ro52 (n=607)	SSc	15.2 (11.0-20.6)		5.2 (2.7-10.0
Ro52 (n=481)	MCTD	19.8 (12.9-29.1		7.2 (3.4-15.1)
Ro52 (n=481)	IIM	19.0 (14.2-25.0		6.8 (3.5-13.0))
Ro60 (n=531)	SjS	66.7 (58.5-73.9	94.9 (92.2-96.7)	37.0 (20.9-65.3
Ro60 (n=620)	SLE	52.2 (45.7-58.5)		20.2 (12.0-33.8)
SS-B (n=1039)	SjS	46.8 (38.8-55.0)	96.5 (95.1-97.6)	24.6 (15.1-40.0)
SS-B (n=1128)	SLE	15.7 (11.5-20.9)		5.2 (3.1-8.6)
Scl-70 (n=1269)	SSc	30.4 (24.7-36.8)	94.3 (92.7-95.5)	7.2 (4.9-10.7)
Jo-1 (n=1269)	IIM	11.5 (7.5-16.7)	99.1 (98.7-99.7)	19.7 (8.5-45.6)
Centromere (n=1269)	SSc	47.0 (40.5-53.6)	97.0 (95.7-97.8)	28.3 (18.2-43.9)
Ribo-P (n=1269)	SLE	11.7 (8.2-16.5)	99.7 (99.2-99.9)	45.9 (14.6-143.7)

*Indeterminate range for dsDNA as positive
SjS=Sjogren's syndrome, SLE = systemic lupus erythematosus, MCTD = Mixed connective tissue disease, SSc = systemic sclerosis, IIM=Idiopathic Inflammatory Myopathy, CI =confidence interval

Conclusions: Our data show good agreement between results obtained using the novel PMAT assays and reference methods varying between substantial and perfect agreement for each assay. All analytes, including dsDNA, RNP, Sm, Ro52, Ro60, SSB, Scl-70, Jo-1, Centromere and Ribo-P showed good clinical performance.

EP139 / #1087

Clinical Performance of Aptiva® PR3 and Aptiva MPO for the Detection of Anti-Neutrophil Cytoplasmic Antibodies (ANCA) Using a Particle-Based Multi-Analyte Technology

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***Background and Aims*:** Anti-neutrophil cytoplasmic antibodies (ANCA) are important biomarkers in the diagnosis of ANCA-associated vasculitis (AAV), more specifically anti-proteinase-3 (PR3) antibodies in granulomatosis with polyangiitis (GPA) and anti-myeloperoxidase (MPO) antibodies in microscopic polyangiitis (MPA). Due to the progressive nature of the disease, rapid detection of ANCA is crucial for the diagnosis and treatment of AAV patients. This study aims to evaluate the clinical performance of the Aptiva PR3 and MPO assays on the novel particle-based multi-analyte technology (PMAT) in comparison to other methods.

Methods: The study cohort included a total of 344 patient samples: 115 from patients with AAV or from routine ANCA testing, and 229 from disease controls consisting of non-AAV controls. All samples were tested on the Aptiva PR3 and MPO PMAT assays (research use only, inova Diagnostics, USA) as well as QUANTA Flash PR3 chemiluminescent immunoassay (CIA) and QUANTA Lite MPO ELISA for method comparison (inova Diagnostics, USA).

Results: The PR3 and MPO PMAT assays showed similar clinical performance compared to the CIA and ELISA methods. Good quantitative and qualitative agreement was found between the PMAT assays and CIA/ELISA methods.

***Conclusions*:** The Aptiva PR3 and MPO PMAT assays demonstrated good clinical performance in comparison to the commercially available methods. Additionally, high agreement was observed between the Aptiva PR3 PMAT assay to the PR3 CIA method and between the Aptiva MPO PMAT assay to the MPO ELISA. The Aptiva Vasculitis panel for the detection of PR3 and MPO demonstrates a promising alternative to screening for ANCA in high-volume laboratories.

Table 1. Performance Characteristics of The Aptiva PR3 and MPO PMAT Assays, QUANTA Flash PR3 CIA, and QUANTA Lite MPO ELISA

Performance Characteristic	PR3 PMAT	PR3 CIA	MPO PMAT	MPO ELISA
Sensitivity % (95% CI) All samples (n=115)	63.2 (58.5-72.0)	52.9 (47.8-56.4)	60.5 (55.1-64.7)	37.2 (31.8-44.9)
Sensitivity % (95% CI) in GPA (n=40) for PR3, in MPA (n=6) for MPO	72.5 (68.3-81.2)	65.0 (58.1-71.2)	83.3% (58.5-95.7)	83.3% (58.5-95.7)
Specificity % (95% CI)	100.0 (98.5-100.0)	99.1 (97.8-100.0)	100.0 (97.3-100.0)	100.0 (97.3-100.0)
Likelihood Ratio (LR+)	∞	60.1	∞	∞
Likelihood Ratio (LR-)	0.37	0.47	0.40	0.63
Odds Ratio (95% CI)	∞	126.6	∞	∞
Area under the curve (AUC) 95% CI	0.904 (0.844-0.963)	0.855 (0.793-0.917)	0.996 (0.991-1.00)	0.889 (0.816-0.963)
Overall Agreement	97.3 (94.7-98.6)		95.6 (92.5-97.5)	
Cohen's *kappa*	0.887 (0.810-0.964)		0.716 (0.565-0.867)	
Spearman's *rho*, *p*-value	0.855 (0.790-0.917) *p*<0.0001		0.823 (0.776-0.889) *p*<0.0001	

EP140 / #1090

Evaluation of a Novel Particle-Based Multi-Analyte Technology for the Detection of Antiphospholipid Antibodies

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Background and Aims: Antibodies to antiphospholipids (aPL) and associated proteins are a hallmark in the diagnosis of antiphospholipid syndrome (APS). Besides the classification criteria markers anti-cardiolipin (aCL) and anti-beta-2 glycoprotein I (aβ2GPI) IgG and IgM, aCL and aβ2GPI IgA are increasingly recognized as important markers in the diagnosis of APS. This study aimed to assess the clinical performance of a novel particle-based multi-analyte technology (PMAT) that has been developed for the detection of aCL and aβ2GPI IgA.

Methods: A total of 585 samples from APS patients (n=153) and relevant disease controls (n=432) were tested for aCL and aβ2GPI IgA using Aptiva® APS IgA (investigational use only, inova Diagnostics, San Diego, CA, USA). Clinical sensitivity and specificity, positive and negative predictive values, and positive and negative likelihood ratios were calculated for aCL and aβ2GPI IgA.

Results: The clinical performance for the novel aCL IgA and aβ2GPI IgA assays is outlined in Table 1. The sensitivity and specificity were 31.4% and 97.9% for aCL IgA and 32.0% and 98.6% for aβ2GPI IgA. The Odds ratio was 21.49 for aCL IgA and 33.45 for aβ2GPI IgA.

Conclusions: Our data shows good clinical performance of the novel Aptiva® APS IgA for the detection of antiphospholipid antibodies as an aid in the diagnosis of APS.

Table 1. Clinical Performace of Aptiva APS IgA

Parameter	aCL IgA	aβ2GPI IgA
Sensitivity (n=153)	31.4% (95% CI: 24.6 - 39.1%)	32.0% (95% CI: 25.2 - 39.8%)
Specificity (n=432)	97.9% (95% CI: 96.1 - 98.9%)	98.6% (95% CI: 97.0 - 99.4%)
Positive Predictive Value	84.2% (95% CI: 72.9 - 91.4%)	89.1% (95% CI: 78.2 - 94.9%)
Negative Predictive Value	80.1% (95% CI: 78.3 - 81.7%)	80.3% (95% CI: 78.6 - 82.0%)
Likelihood ratio (+)	15.06 (95% CI: 7.69 - 29.62)	23.06 (95% CI: 10.34 - 51.71)
Likelihood ratio (-)	0.70 (95% CI: 0.62 - 0.77)	0.69 (95% CI: 0.61 - 0.76)
Odds ratio	21.49 (95% CI: 10.34 – 44.58)	33.45 (95% CI: 14.26 – 78.34)
Youden's index	0.29	0.31

EP141 / #1052

Age Differences in DFS70 Positive Patients Referred for Routine ANA Screening at the Niguarda Metropolitan Hospital in Milan

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Background and Aims: in the context of systemic autoimmune diseases, screening for anti-nuclear antibodies (ANA) by indirect immunofluorescence on Hep-2 cells remains essential for diagnosis. The dense fine speckled pattern (DFS), often linked to a DFS70 antibody specificity, is commonly found in clinical practice. However, its significance and distribution in the population remain unclear. Notably, an isolated anti-DFS70 antibody specificity has been proposed as an exclusion factor in the diagnosis of ANA-associated rheumatic diseases (AARD). This study aimed to characterize anti-DFS70 positive population, comparing with anti-DFS70 negative control population.

Methods: Subjects investigated for ANA from January 2021 to December 2023 at Niguarda Hospital in Milan and suspected for DFS pattern were tested for anti-DFS70 antibody by fluorescence enzyme immunoassay (Thermofisher Scientific). Demographic and laboratory data were retrospectively collected from hospital database. Stratification by anti-DFS70 status (positive vs negative, cutoff value 10 U/ml). Wilcoxon-Mann-Whitney test performed to identify any statistically significant differences between the two groups.

Results: of 188 subjects included, 153 were anti-DFS70 positive and 35 negative. DFS70 positive subjects were younger (median age 45.19, IQR 28.76-56.99) than negative ones (median age 62.78, IQR 51.12-67.28). Age difference was statistically significant ($P < .001$). No other significant differences between the two groups were found.

Conclusions: in this preliminary study, DFS70 positive subjects were younger than negative ones, without significant sex difference. Results must be confirmed with a larger sample size. Young subjects undergoing laboratory tests

are more frequently healthy and this finding could be in agreement with the hypothesis of using anti-DFS70 as an exclusion criterion for AARD.

EP142 / #776

Evaluation of Specific Tests Demand After a First Positive Screening Result in Autoimmunity

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***Background and Aims*:** Screening tests for systemic autoimmune diseases should begin with a ANA test by Immunofluorescence on Hep2 cells. After a positive result, high titer with specific pattern with correlation to clinical manifestations, the clinician should go for further studies with high specificity, searching for specific autoantibodies. These evaluations are performed by innumerous methodologies ranging from ELISA, immunoblotting or solid phase assays. The communication between the laboratory and the clinicians has always been a priority for us. Helping the clinician to interpret and give the best use to the given result is key for patient orientation and diagnosis. The type of additional information printed in the lab report is determinant and should be carefully chosen and given. It is our practice to issue small texts referring prevalence's and pattern association with autoimmune disease making the following requests for specificity, easier and more efficient.

***Methods*:** Retrospective 2-year evaluation of autoimmunity first positive results in a hospital referral autoimmunity consult. Time evaluation for specific requests, eventual novel ANA screening confirmation,concordance between first and second results and second prescription maker evaluation.

***Results*:** The authors present 2 years revised casuistic from October 2021 to October 2023 as a reference clinical laboratory center in autoimmune diseases diagnosis, focusing on key issues regarding laboratory interaction in the clinical setting.

***Conclusions*:** Communication between the autoimmunity laboratory and prescribing physician is essential for patient guidance. This is particularly important if the prescribing doctor is a general practitioner. Small guiding messages allows efficient result interpretation, reducing time for diagnosis as well as efficient patient follow up.

EP143 / #673

The Role of RA33 Isotypes in Early Rheumatoid Arthritis Diagnostics

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***Background and Aims*:** Early diagnosis of rheumatoid arthritis (RA) leading to effective treatment is essential to improve prognosis and to prevent disease progression. Anti-CCP antibodies and RF have a similar sensitivity (~70%), but a reduced sensitivity at early stage of disease (~60%). Anti-RA33 IgG is known to be a specific biomarker for RA. This study's objective was to evaluate the prevalence of anti-RA33 isotypes (IgM, IgA, IgG) in early RA (eRA) in comparison to anti-CCP antibodies and RF within four independent European eRA cohorts.

***Methods*:** The evaluation cohort from Austria included 257 eRA patient and 357 disease controls samples. To validate the data, two eRA patient cohorts from Sweden (Swedish Rheumatology Quality Register biobank, n=156) and UK (n=100) were analyzed in comparison to controls (n=448). A third validation cohort from Germany included 37 eRA and 121 controls. Serum samples were analyzed for the presence of anti-RA33, anti-CCP and RF (each IgM, IgA, IgG) using the EliA™ platform (Thermo Fisher Scientific, Sweden).

***Results*:** Up to one third (27-30%) of eRA patients were positive for at least one of the anti-RA33 isotypes, revealing a diverse distribution of the isotypes among eRA patients and little overlap between the immunoglobulin classes. The combination of anti-RA33 isotypes detected 21-28% of the CCP IgG- and RF IgM-negative RA patients with a specificity of each isotype of ≥90%.

***Conclusions*:** The combination of anti-RA33 isotypes provided a considerable added value for the diagnosis of eRA in the anti-CCP- and RF-negative group and revealed a distinct patient group positive for anti-RA33 antibodies.

EP144 / #1064

Myositis Autoantibodies: Clinical Relevance and ANA HEp-2 IIF Pattern Association

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***Background and Aims*:** Detection of myositis-specific autoantibodies (MSA) and myositis-associated autoantibodies (MAA) is valuable for the diagnosis of idiopathic inflammatory myopathies (IIM). The aim of this retrospective study was to investigate the MSA/MAA profiles in IIM patients and to examine their correlation with HEp-2 IIF patterns.

***Methods*:** Patients positive for any of the myositis antibodies with EUROLINE Myositis profile 3 (Euroimmun, Germany) between 2017 and 2023 were included. ANA patterns were determined by HEp-2 IIF. Demographic and relevant laboratory data were extracted from medical records.

***Results*:** A total of 656 patients with positive MSA/MAA were analyzed. 67.5% had IIM, 17.1% systemic autoimmune disease (SAID) and 15.4% non-IIM/SAID. 73.8% of IIM patients had MSA, 10.1% MAA and 5.0% both MSA and MAA. A significant correlation was detected for anti-TIF1g and anti-NXP2 and DM ($P < .05$). Similar correlation was also identified for anti-Ku (MAA) in DM ($P < .05$). Anti-SRP positivity was significantly associated with PM ($P < .05$). The probability of DM was 0.36 (95% CI: 0.2-0.66) times higher in patients with Ro52 accompanying any MSA/MAA. HEp-2 IIF results were available for 275 patients. In MSA and MAA positive groups the most common pattern was AC-4 (43.6-41.2%, respectively) and 37.1-37.3% of the patients, respectively, were AC-0.

***Conclusions*:** HEp2 IIF patterns did not provide clues to help guide for MSA or MAA. While anti-TIF1gamma and anti-NXP2 were associated more with DM, anti-SRP seemed to support diagnosis of PM. Myositis antibody profiling may help the diagnosis of IIM and also support to identify related unique syndromes.

EP145 / #739

Associations Between ICAP Image of Anti-Nuclear Antibodies Determined by Indirect Immunofluorescence and Specific Autoantibodies Determined by Immunoblot and/or ELISA Method in Bulgarian Patients

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Background and Aims: The indirect immunofluorescence (IIF) technique is a significant screening tool and "golden standard" for detection of anti-nuclear antibodies (ANA), important in diagnosis of autoimmune diseases. This method permits detection of a broad variety of autoantibodies directed against different cellular structures grouped according to the international Consensus on ANA Patterns (ICAP) in 30 morphological patterns. However, the second step in the autoimmune diseases diagnosis algorithm is detection of specific ANA, performed on Solid-phase immune assays, including immunoblots and ELISA. The aim of our study was to investigate the correspondence between immunoblot and/or ELISA and ANA-IIF patterns on different titers.

***Methods*:** IIF of HEp-2 cells was used to identify ANA titer and ICAP pattern. Detection of specific autoantibodies was performed by enzyme-linked immunosorbent assay (ELISA) and immunoblot analysis.

***Results*:** in 2022, 1244 consecutive patients referred to the laboratory were tested by both ANA-IIF and immunoblot and/or ELISA analisis. 65% of these patients were found to be positive for ANA-IIF titter (>1:160) and 48% were found to be positive for specific autoantibodies. The patients positive for specific autoantibodies increase with ANA-IIF titer elevation: from 12% in the group of ANA-IIF negative patients (<1:160) to 75.2% in the group of ANA-IIF high positive patients (≥1:1280). In ANA-IIF positive patients we established the following discordances between ICAP images and specific autoantibodies: 3.8% in the group of ANA-IIF titer 1:320; 2.7% in the group of ANA-IIF titer 1:640 and 2.4% in the group of ANA-IIF titer ≥1:1280.

***Conclusions*:** The results of our study display minimal disparity between ANA-IIF ICAP pattern and the corresponding specific autoantibodies.

EP146 / #466

Diagnostic Accuracy and Clinical Utility of Anti-DsDNA Assays in Childhood Onset Systemic Lupus Erythematosus

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Background and Aims: Childhood onset Systemic lupus erythematosus (cSLE) is a severe heterogeneous autoimmune disease. Antibodies against double-stranded DNA (anti-dsDNA) are present in 50-70% of cSLE patients and play an important role in diagnosing cSLE. To date, limited information is available on the diagnostic accuracy of anti-dsDNA assays in children and it is not known whether these tests fulfill the ACR-EULAR requirement for anti-dsDNA assays to achieve ≥90% specificity in cSLE. Here, we determined the diagnostic accuracy and clinical utility of a FEIA dsDNA assay as well as a combined detection strategy based on the FEIA dsDNA assay and the CLIFT assay in patients previously diagnosed with cSLE.

Methods: In this single-center retrospective cohort study, fifty-seven cSLE patients and 380 age-matched disease controls were included.

Results: The FEIA dsDNA assay showed a low sensitivity (43.9%) and low positive predictive value (PPV, 43.8%) and a high specificity (95.0%) and high negative predictive value (NPV, 96.4%) for the diagnosis of cSLE. False-positive results occurred in 18/380 of controls and, given the rarity of SLE, these outnumbered the true positive results in cSLE in the same time period. The combined approach achieved a comparable sensitivity (44.4%) and NPV (96.0%) compared to the FEIA dsDNA assay, but a substantially increased specificity (99.5%) and PPV (85.7%).

Conclusions: The FEIA dsDNA assay fulfills the ACR-EULAR requirement for anti-dsDNA assays to achieve ≥90% specificity in cSLE, which supports its use for diagnosing cSLE. Moreover, the occurrence of false-positive results can be reduced by applying a combined approach based on the FEIA dsDNA/CLIFT assay.

EP147 / #1043

Brain Autoimmunity Is Strongly Associated with Long COVID and ME/CFS

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Background and Aims: Many people who have had COVID-19 reported a range of neurocognitive symptoms, including brain fog, poor memory and severe fatigue months after their initial illness. It is estimated that 40% of individuals infected with SARS-CoV-2 may develop long COVID; in about half these individuals, their illness looks like a neurological disease. Change in the gut microbiome and neuroinflammation at the blood-brain barriers (BBB) may be responsible for long COVID manifestation in the brain. The aim of this study was to assess if antibodies directed against BBB proteins and neural antigens are involved in the induction of long COVID/ME/CFS.

Methods: IgG, IgA and IgM antibodies were measured by ELISA method against S100B, claudin-5, and five different neural antigens in the blood of 90 controls and 90 patients with long COVID.

***Results*:** We found that long COVID was associated with significant increase in IgG antibodies directed against MBP, MOG and synapsin, followed by IgM antibodies to BBB proteins, MBP and MOG. SARS-CoV-2 antibody titer correlated significantly with levels of neuronal antibody. Binary logistic regression analysis showed that both IgG and IgM MBP antibody levels were the best predictors of long COVID.

***Conclusions*:** Brain-targeted autoimmunity contributes significantly to the pathogenesis of long COVID and its severity. Measurements of IgG and IgM antibodies against MBP, MOG, synapsin, S100B and claudin-5 are recommended for detection of long COVID in the brain.

EP148 / #441

Validation of a Clinical Protocol including Ferritin Levels to Assess Disease Severity in Patients with COVID-19

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Background and Aims: We established an admission protocol to identify patients with severe COVID-19. This protocol included clinical and laboratory findings, and we added ferritin levels. We defined the severity of COVID-19 at the beginning of hospitalization and started treatment, without delay, in accordance with the guidelines of the infectious disease unit. Specifically, we evaluated ferritin levels as a guide to severity and outcome of patients.

***Methods*:** We conducted a retrospective study, at Wolfson Medical Center, Israel, for a period of 19 months (2020-2021). The protocol parameters included demographic data, comorbidities, immune status, oxygenation level, lymphopenia, levels of CRP, LDH, D-DIMER, creatinine, AST, ALT and ferritin.

***Results*:** The study included 407 patients of which 207 (50.9%) were men and 200 (49.1%) were women; the average age was 62 years old (range-18-101). Most patients had co-morbidities. While only 7.1% required mechanical ventilation, 48% required an oxygen supplement including high-flow ventilation. Over 58% of the patients, were never vaccinated for COVID-19. A very elevated level of ferritin, over 1000 ng/dl, was one of the strongest and most significant predictors for disease severity in COVID-19 patients ($P < .001$). In addition, lymphopenia, elevated levels of CRP, ALT, AST, LDH and creatinine correlated with severe disease, complications, and death.

***Conclusions*:** The addition of ferritin level to our protocol at hospital admission was effective in identifying high-risk patients for severe COVID 19 infection. Elevated ferritin levels correlated with the other known markers as significant and clear indicators of the development of severe COVID 19 disease.

EP149 / #470

Proficiency Testing in Autoimmune Disease Diagnoses: Ensuring Accuracy and Reliability

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***Background and Aims*:** The diagnosis of autoimmune diseases presents unique challenges to clinicians and laboratorians alike. More than 80 recognized autoimmune conditions, particularly collagenoses like systemic lupus erythematosus (SLE) or Sjögren's syndrome, pose diagnostic challenges due to their diverse clinical presentations and reliance on autoantibody markers. Proficiency testing, a cornerstone of laboratory quality assurance, plays a pivotal role in ensuring the precision and reliability of autoantibody detection in these complex disorders.

***Methods*:** The participating laboratories were provided with native human samples, obtained under ethically impeccable conditions at our dedicated study site. The samples were tested for a panel of extractable nuclear antigen (ENA) autoantibodies that can be detected in cases of collagenoses like Sjögren's syndrome, systemic lupus erythematosus (SLE) or polymyositis.

***Results*:** revealed a high overall accuracy rate in autoantibody detection, with variations observed between laboratories depending on the specific autoantibodies tested. Laboratories exhibited an exceptionally high accuracy in semiquantitative detection of anti-SS-A / Ro autoantibodies, a hallmark of SLE and Sjögren's syndrome. Inter-laboratory variations underscore the need for ongoing quality improvement efforts, regarding the accuracy of diagnostic assays. Herein, proficiency testing feedback reports served as valuable tools to highlight optimization potentials.

***Conclusions*:** in the face of the diagnostic challenges posed by collagenoses, proficiency testing offers a pathway to consistency, competence, and ultimately, better patient outcomes. Our observations reinforce the commitment to maintaining rigorous standards in autoimmune disease diagnostics, with the aim of providing patients with the accurate and timely diagnoses they deserve.

EP150 / #703

Utility of Various Serological Parameters in Antiphospholipid Syndrome and Their Association with a High-Risk Profile

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***Background and Aims*:** Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized with vascular thrombosis and obstetric morbidity. To better understand the underlying molecular nature and identify possible biological markers of this disease, we have investigated levels of several serological markers in plasma of patients with APS.

***Methods*:** We enrolled 44 patients with APS (median disease duration 7 years), 12 newly diagnosed APS patients (disease duration 3 months) and 27 healthy controls (HCs) and analyzed levels of 14 serological markers using Luminex xMAP technology (Luminex 200) in coordination with R&D Systems' Human Premixed Multi-Analyte Kit Luminex immunoassay, next to lupus anticoagulant (LA), anticardiolipin (aCL) antibodies (immunoglobulin G [IgG] and IgM), and anti-beta-2 glycoprotein 1 (anti-β2GP1) antibodies (IgG and/or IgM).

***Results*:** We found 8 markers significantly elevated in patients with APS compared to HCs. GDF-15, VCAM-1, and Kallikrein5 were most increased in APS patients compared to healthy controls, with their levels increasing with multiple aPL positivity. Levels of TFPI were statistically significantly decreased in patients with APS compared to healthy. None of the parameters were statistically significantly different between newly diagnosed and chronic patients.

***Conclusions*:** GDF-15, VCAM-1 and Kallikrein5 were most significantly increased in APS patients potentially related to endothelial dysfunction which is a key pathological component of APS.

Table 1. Levels of Biomarkers in Plasma of Aps Patients and Healthy Controls

	Newly diagnosed median (IQR) n=12	Chronic patients median (IQR) n=44	Healthy control median (IQR) n=27	p-value Healthy control vs. newly diagnosed	p-value Healthy control vs. Chronic patients
Age (y)	39 (37-52)	44 (34-56)	41 (31-55)	0.923	0.531
Female/Male	9/3	29/15	19/8		
vWF (ng/mL)	5.4 (2.8-7.5)	6.3 (4.1-8.9)	3.9 (3.1-5.8)	0.299	***0.001**
ADAMTS13 (ng/mL)	1170.3 (862.8-1568.8)	933.9 (662.5-1159.1)	981.2 (810.5-1092.8)	0.791	0.096
CSA(ng/ml)	22.4 (19.3-32.6)	28.07 (20.3-44.5)	29.4 (25.1-34.1)	0.495	0.979
Kallikrein5 (ng/mL)	5.2 (4.7-6.5)	5.2 (4.2-6.1)	4.2 (3.5-4.7)	***0.017**	***0.003**
CCL2/MCP (ng/mL)	0.1 (0.1-0.2)	0.2 (0.1-0.2)	0.1 (0.11-0.2)	0.938	***0.005**
VEGF (ng/mL)	0.5 (0.04-0.055)	0.1 (0.04-0.1)	0.1 (0.04-0.1)	0.925	0.660
Syndecan-1 (ng/mL)	3.24 (2.85-4.46)	3.5 (3-4.1)	3.3 (2.7-3.7)	0.387	0.124
E-selectin (ng/mL)	27.6 (20.1-87.8)	26.5 (18.4-36.5)	21.2 (12.9-34.1)	0.088	***0.010**
P-selectin (ng/mL)	57.9 (57.9-57.9)	40.3 (23.8-57.9)	28.3 (23.2-46.6)	***<0.001**	0.258
VCAM-1 (ng/mL)	1609.7 (736.8-2218.0)	782.7 (673.5-1297.9)	530.4 (401.1-720.3)	***0.014**	***0.009**
ICAM (ng/mL)	491.9 (293.1-544.2)	824.7 (521.3-1276.4)	759.9 (586.3-929.3)	0.906	0.481
TFPI (ng/mL)	11.1 (3.9-19.8)	10.8 (7.7-16.7)	16.9 (11.1-25.5)	0.860	***0.011**
GDF15 (ng/mL)	1.8 (0.9-3.7)	0.96 (0.5-82.1)	0.4 (0.3-0.4)	***0.018**	***<0.001**
CXCL7 (ng/mL)	0.35 (0.35-1.27)	1.26 (0.35-2.3)	0.35 (0.35-1.00)	0.848	***0.003**

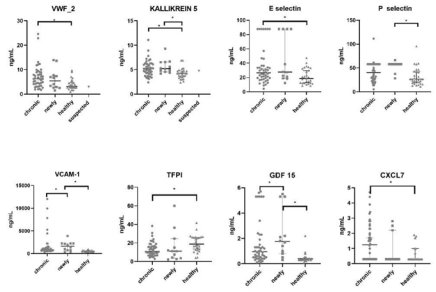

Figure 1. Eight Significantly Changed Biomarkers in The Plasma of APS Patients Compared To Healthy Control.

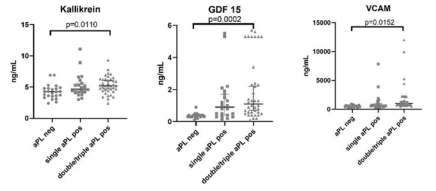

Figure 2. Biomarker Levels in Association with The Number of APL Positivity.

E-POSTER VIEWING 15: CLINICAL PRACTICE - DIAGNOSTICS: GASTROINTESTINAL AUTOIMMUNITY

EP151 / #1009

Five-Year Seropositivity of Autoantibodies Used in the Diagnosis of Autoimmune Liver Diseases

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***Background and Aims*:** Early diagnosis and treatment of autoimmune liver diseases are crucial. Medical Microbiology laboratories should implement diagnostic algorithms that include the necessary methods and tests for diagnosis, closely monitor seroprevalence data, and contribute to the creation of both institutional and national data. We aimed to analyze our five-year data retrospectively to establish our institutional data and contribute to national data.

***Methods*:** Between 01/01/2019 and 31/08/2023, data from patients who were tested for the autoimmune liver disease diagnostic panel; anti-nuclear antibody, anti-mitochondrial antibody, anti-smooth muscle antibody, and anti-liver-kidney microsomal antibody, were retrospectively analyzed. Tests were performed on the IF Sprinter device according to the manufacturer's recommendations using the Liver Mosaic: Basic Profile EUROPattern indirect Immunofluorescent Antibody Assay (IIF) kit and evaluated with the EUROStar III Plus (Euroimmun, Germany) fluorescence microscope.

***Results*:** Our study included 2459 patients, with varying numbers and rates of positivity detected in 185 patients; AMA was positive in 106 (4.31%) patients, ASMA in 73 (2.97%) patients, LKM in 1 (0.04%) patient, AMA+ASMA concurrently positive in 3 (0.012%) patients, and AMA+LKM concurrently positive in 2 (0.08%) patients.

***Conclusions*:** We aim to report the seropositivity rates of autoimmune liver diseases in our institution and emphasize the need for seroprevalence and incidence data for this group of diseases in our country.

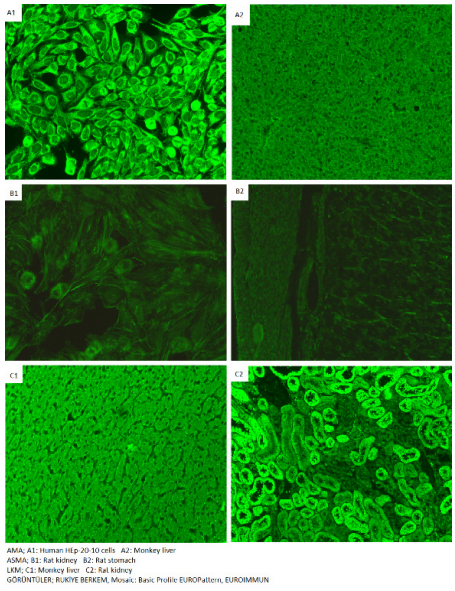

Figure 1.

EP152 / #618

In Patients with High Anti-Smooth Muscle Antibody Titres, Clinical Context Remains Key to Diagnose Autoimmune Hepatitis

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Background and Aims: Autoimmune hepatitis (AIH) is a rare liver condition where diagnosis remains challenging. We aimed to assess the diagnostic accuracy of using autoimmune profiles in the intelligent Liver Function (iLFT) platform which standardises investigation of abnormal LFTs using algorithms.

***Methods*:** Patients who had an autoimmune profile performed through iLFT between 09/03/2016-20/1/2023 were included in the study (n=5277). The clinical records of those with immunology consistent with autoimmune hepatitis (at least one of: ASMA, ANA or LKM) were retrospectively interrogated (n=1427).

***Results*:** During the study period iLFT identified 19 patients with AIH of which 14 were new diagnoses. Mean [SEM] ALT in the newly diagnosed AIH patients was significantly higher ($P < .0001$) than in all other patients (independent of aetiology) (446.8U/L [133.1] vs 100.3U/L [1.858]). 68% (n=13) of patients with AIH had a high ASMA (>1:160). The commonest diagnosis in patients with an ASMA>1:160 was steatotic liver disease (52% [66/126]) and AIH made up only 7% (13/126) patients with a high ASMA. The specificity of an ASMA > 1:160 was 97.9% (95% CI: 97.4-98.2) but sensitivity was 68.4% (95% CI: 43.5-87.4).

***Conclusions*:** in a large cohort of patients screened for liver disease using iLFT, ALT was most significantly associated with a diagnosis of AIH. ASMA remained relatively specific but even at high titres it is of low sensitivity. This study re-emphasises the importance of clinical context when making a diagnosis of AIH and the lack of sensitivity of ASMA as a screening tool despite its high specificity.

EP153 / #493

Exploring the Association Between KIR Genes and Non-Celiac Gluten Sensitivity

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***Background and Aims*:** Non-celiac gluten sensitivity (NCGS) is a clinical condition characterized by gastrointestinal and extraintestinal symptoms triggered by gluten ingestion

without celiac disease and wheat allergy. Despite advancement of knowledge in NCGS, the pathogenesis is still poor understood. Recently, the role of Natural Killer (NK) cells is emerged. KIRs (Killer Immunoglobulin-like Receptors) regulate NK cell activation through their interaction with Human Leucocyte Antigens (HLA). Both KIRs and HLA loci are highly polymorphic, and two KIR haplotypes have been identified: A and B. The aim of the present study is to evaluate the influence of KIRs genealterations on NCGS.

***Methods*:** We performed a retrospective case-control study including 40 patients with a certain diagnosis of NCGS and 32 healthy blood donors as controls. KIR genotyping was performed using the KIR SSO Genotyping Test kit (one Lambda, inc. Canoga Park, CA, USA) on Luminex technology.

***Results*:** We observed a significantly higher frequency in healthy controls than NCGS patients for the following genes: KIR2DL1 (96.87% vs. 55%, $P = .0024$, OR= 25.36; 95% CI = 3.15-204.35); KIR2DL2 (65.62% vs. 32.5%, $P = .006$; OR =3.95, 95% CI=1.48-10.6); KIR2DL3 (81.25% vs. 22.5%, $P \leq .0001$; OR = 14.92, 95% CI=4.69-47.47); KIR2DL5 (62.5% vs. 10%, $P \leq .0001$; OR = 15, 95% CI=4.27-52.7). Furthermore, we found that 85% of NCGS patients have a type B haplotype, while controls have predominantly type A and AB haplotype, 31.25% and 56.25%, respectively.

***Conclusions*:** Our study suggests that KIR genotypes may be involved in the pathogenesis of NCGS.

EP154 / #596

Gluten-Induced Inflammation in Gut Mucosa of Celiac Disease Patients Is Downregulated by IL4: New Therapeutic Perspective for Celiac Disease

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Background and Aims: Childhood celiac disease (CD) is characterized by two main forms: acute-CD (positive anti-tissue transglutaminase-tTG antibodies and intestinal villous atrophy) and potential-CD (positive anti-tTG and normal mucosa architecture). We recently observed an expansion of IL4-producing T cells in the gut biopsies of potential-CD children that inversely correlated with anti-tTG antibody titers and histological scores of mucosal damage. In this follow-up study, we investigated the regulatory role of IL4 in the preventing the inflammatory response to gluten in CD.

***Methods*:** Short-term T-cell lines (TCLs) were generated from gut biopsies of children with acute- and potential-CD by cyclic stimulation with gliadin and growth factors, in absence or presence of exogenous IL4 (control-TCLs and IL4-TCLs, respectively). Changes in cytokine production profile, cell infiltrates and gliadin recognition pattern were evaluated in control- and IL4-TCLs.

***Results*:** IFN-γ release was significantly reduced, whereas IL10 production was increased, in IL4-TCLs culture supernatants, collected over time up to 6 weeks. IL4 induced a significant expansion of CD4+ T-helper cells, and a decrease of CD8+ T cells and TCR γ/δ+ T cells. A significant inhibition of IFN-γ production in response to whole gliadin and immunogenic peptides was measured in IL4-TCLs compared to control-TCLs.

***Conclusions*:** Our study demonstrated a hitherto unexplored immunoregulatory function of IL4 on gluten-induced inflammation in gut mucosa of CD patients. Studies aimed to dissect the role of IL4 in preventing villous atrophy in CD-predisposed individuals are ongoing.

EP155 / #452

Comparison of Two Immunoassays for the Detection of Intrinsic Factor Autoantibodies

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***Background and Aims*:** The study of autoantibodies directed to intrinsic factor (APCA) aids in the diagnosis of AAG (autoimmune atrophic gastritis) that may develop into pernicious anemia (PA) and helps to differentiate PA from other anemia etiologies. IFA are characterized by high specificity (up to 100%) but low sensitivity. The aim of this study was to compare the performance of two immunoassays for the detection of IFA.

***Methods*:** Observational prospective study, including samples received for IFA testing in our laboratory. According to our routine test results (Biermer-Atrophic Gastritis Dot, Alphadia), samples were selected until a minimum of 50 IFA positive sera and 100 IFA negative sera were collected. Serum samples were then analyzed using EliA™ intrinsic factor (Thermo Fisher Scientific). Discrepant results (understood as positive vs. negative) were evaluated using a third method: IFAb ELISA (Demeditec Diagnostics GmbH). The tests correlation was evaluated using Pearson analysis.

***Results*:** Discrepancies were found in 4 samples. ELISA analysis revealed that 3 out of 4 were negative for IFA, and 1 was positive. Considering ELISA as the index test, Dot blot resulted in 3 false positives results and 1 false negative result. In contrast, EliA showed 100% agreement with ELISA. The correlation coefficient obtained was r=0.857. Additionally, Dot blot reported more clustered results than EliA due to their lower dynamic range.

***Conclusions*:** Considering that both tests are valid methods for routine IFA analysis, the EliA test has higher concordance with ELISA and reports more coherent and accurate quantitative results.

EP156 / #456

Comparison of Two Immunoassays for the Detection of Parietal Cells Autoantibodies

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***Background and Aims*:** The study of autoantibodies directed to parietal cells (APCA) aids in the diagnosis of AAG (autoimmune atrophic gastritis) that may develop into pernicious anemia (PA) and helps to differentiate PA from other anemia etiologies. ACPA are characterized by high sensitivity (80-90%) in PA early disease stages, but low specificity. The aim of this study was to compare the performance of two immunoassays for the detection of ACPA.

***Methods*:** Observational prospective study, including samples received for ACPA testing in

our laboratory. According to our routine test results (Biermer-Atrophic Gastritis Dot, Alphadia), samples were selected until a minimum of 100 ACPA positive sera and 100 ACPA negative sera were collected. Serum samples were then analyzed using EliA™ Parietal Cell (Thermo Fisher Scientific). Discrepant results (understood as positive vs. negative) were evaluated using a third method: Triple Tissue IIF (Biocientífica). The test correlation was evaluated using Pearson analysis.

***Results*:** Discrepancies were found in 15 samples. Verification through IIF (gold standard) revealed that 14 out of 15 were negative for ACPA, and just one patient was positive. ACPA negative samples: 9 were correctly classified by EliA (5 false positives) and 5 by Dot blot (9 false positives). ACPA positive sample: correctly identified by EliA, while being negative for Dot Blot. Correlation coefficient obtained was r=0.816. Additionally, Dot blot reported more clustered results than EliA due to their lower dynamic range.

***Conclusions*:** Considering that both tests are valid methods for routine ACPA analysis, the EliA test has higher concordance with IIF results while reporting more coherent quantitative results.

EP157 / #606

Don't Let Gluten-Related Issues Slow You Down - Read on to Learn More!

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Background and Aims: Looking for a quick and efficient way to diagnose gluten-related diseases? Look no further! Check out this intriguing case report on a brand-new Point of Care (POC) tool that could save you time and hassle. Define the antibody profile of a woman suffering from unrecognized celiac disease for 10 years or longer using the AESKUCARE® POC GRD IgA (GRD-POC) test and confirm diagnosis.

***Methods*:** AESKUCARE® GRD IgA is a near-patient in-vitro-immunoassay for the simultaneous measurement of human-specific IgA antibodies against human tissue transglutaminase (tTG), neo-epitopes of human tTG (tTG neo), microbial transglutaminase (mTG), neo-epitopes of mTG (mTG neo), deamidated gliadin-specific peptides (DGP), gliadin, Frazer's fraction, human epidermal transglutaminase (TG3) and total-IgA in heparinized or Na-EDTA venous or capillary whole blood, plasma or serum.

***Results*:** A woman with unclear gastrointestinal symptoms performed GRD-POC self-test 2020-02-19 resulting in multiple positive GRD profile. She was placed on a gluten-free diet after medical examination and genetic-confirmation of HLA-DQ3 + HLA-DQ8, and received iron, folic acid, and vitamin B12. After one-year GFD follow-up on the GRD-POC test, no GRD antibodies were detectable. Re-examining her stored sample from 2011 with GRD-POC already showed high antibody levels against tTG neo, mTG neo, and DGP with high levels.

***Conclusions*:** If GRD-POC test had been performed earlier, accurate and rapid diagnosis could have saved the woman at least a decade of suffering. In conjunction with patient's medical history, professionals can make rapid dietary recommendation or support diagnosing GRDs, making the AESKUCARE® GRD IgA a unique tool.

EP158 / #327

Loss of Mucosal Tolerance to Glycoprotein 2 Is a Potential Diagnostic Biomarker in Cholangiocarcinoma without Concomitant Primary Sclerosing Cholangitis

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***Background and Aims*:** Anti-Glycoprotein 2 (anti-GP2) IgA and antineutrophil-cytoplasmic antibodies to proteinase 3 (PR3-ANCA) are predictive markers of cholangiocarcinoma (CCA) in patients with primary sclerosing cholangitis (PSC) but their occurrence in CCA without PSC is yet elusive.

***Methods*:** Discovery (118 Chinese patients) and validation (38 Polish patients) cohorts with CCA without PSC were compared with 49 patients with pancreatic ductal adenocarcinoma (PDAC), 21 patients with benign pancreatic neoplasms (BPN), 45 patients with hepatocellular carcinoma (HCC), and 75 healthy controls (HC) for the occurrence of PR3-ANCA, IgA and IgG to large (anti-$GP2_1$) and short (anti-$GP2_4$) GP2 isoforms, and carbohydrate antigen 19-9 (CA19-9).

***Results*:** Anti-$GP2_1$ IgA was the most prevalent autoantibody in both CCA cohorts (discovery: 65/118, 52.6%; validation: 17/38, 44.7%) and corresponding levels were significantly elevated compared to other controls except PDAC patients. Anti-$GP2_4$ IgA levels were significantly increased in CCA patients compared with PDAC patients and HC. Both IgA autoantibody levels were not significantly correlated with CA19-9 levels or CCA differentiation status. of all autoantibodies, anti-$GP2_1$ IgA demonstrated the best diagnostic performance for the differentiation of CCA from disease controls and HC by receiver-operating characteristic-curve analysis. Compared with tumor markers, anti-$GP2_1$ IgA demonstrated also the highest performance although not significantly different from that of CA19-9. Anti-$GP2_1$ IgA was an independent predictor of CCA with old age and gamma-glutamyl aminotransferase and anti-$GP2_4$ IgG as confounders by logistic regression.

***Conclusions*:** Mucosal loss of tolerance in the form of anti-$GP2_1$ IgA distinguishes CCA from BPN and HCC and is an independent risk predictor for the occurrence of CCA.

EP159 / #404

Coeliac Disease Autoimmunity in Children with Diabetes Mellitus: Not Always Coeliac Disease

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***Background and Aims*:** To evaluate the efficiency of coeliac disease (CD) autoantibodies for CD diagnosis in children with Diabetes Mellitus (IDDM).

***Methods*:** We reviewed the files of IDDM patients referred to our pediatric Gastroenterology Unit because of positive IgA transglutaminase antibodies (tTG) (EliA Celikey) or symptoms. Sera stored at -80ºC were retrieved and IgA endomysial antibodies (EMA), IgA and IgG deamidated gliadin peptides antibodies (DGP) (EliA Gliadin DP) and IgG tTG antibodies (EliA Celikey) were determined.

***Results*:** Out of 36 patients, 15 had tTG-IgA > 10 times upper limit of normal (ULN), all were IgA-EMA positive, and in 13 CD was confirmed. Additionally, 11 cases had tTG-IgA -3x ULN, 5 also with positive IgA-EMA, but only in 2 of them was CD confirmed. In all negative IgA-EMA CD was ruled out after clinical and serological follow up. IgG DGP antibodies were positive in all CD patients, levels being > 10x ULN in 4 and 1-2 x ULN in 3 cases. All non-CD children were negative for IgG-DGP. of note, 1 patient (father with CD) had persistent IgA-tTG >10x ULN, repeated positive IgA-EMA, and DGP-IgG 1-2 x ULN, and no histological lesions on 2 consecutive Biopsies; afterwards, as a young adult, CD was diagnosed.

***Conclusions*:** Negativity of IgG-DGP and/or IgA-EMA could be useful to rule out CD in IDDM children with positive IgA-tTG provided our results are confirmed in a larger study population.

EP160 / #406

Incidence of Celiac Disease Over Time in a Southern Europe Population: Impact of Serological Testing

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***Background and Aims*:** Celiac disease is a chronic immune-mediated disorder, with an increasing incidence of up to 7.5% during the last decades, but it is still considered undiagnosed. The implementation of screening programs and non-biopsy diagnostic approach-based algorithms is essential for accurate diagnosis. Our aim is to study the incidence evolution of CD across age and the usefulness of a diagnostic algorithm combining non-biopsy approach with risk patient screening.

***Methods*:** from 2012 to 2019, 19.564 consecutive samples belonging to CD suspected and risk group patients from Lugo area, were analyzed using our standardized algorithm. EliA Celikey (Thermo Fisher Scientific) was used to quantify serum TG2-IgA (grey zone: 2-4U/ml, bordeline positive: 4-8U/ml, cut-off positive: >8 U/ml, 10XULN> 80 U/ml). Serum EMA-IgA titers were measured by IFI (AESKU-Diagnostics).

***Results*:** Over the 8-year period, 294 additional CD patients were diagnosed. 23 (8.01%) were first-degree patient relatives. Children's incidence was continuously higher than that of other age groups. The adult and senior age groups saw an increase in annual incidence rates. The incidence rate per 100 000 individuals increased from 6.79 in 2012 to 16.55 in 2019. The correlation between the TG2-IgA and EMA-IgA titers was statistically significant (*P* .001), and all patients with TG2-IgA titers > 80U/ml tested positive for EMA.

***Conclusions*:** The non-biopsy testing strategy is relevant for adults as well, and when combined with risk group screening, enables early detection while being cost-effective. Additionally, TG2-IgA measurement in a second sample can be used to corroborate TG2-IgA-based CD Diagnosis without the requirement for EMA-IgA testing, if TG2-IgA < 80 U/ml.

EP161 / #611

Results of a Novel Multiparametric Test for Gluten Related Diseases in a Pediatric Cohort

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***Background and Aims*:** The AESKUBLOTS® Gluten Related Diseases (GRD) is a novel membrane-bound multiparametric enzyme immunoassay for the overall quantitative determination of total IgA and IgA antibodies against gliadin, DGP, tTG, tTG neo-epitope (tTG crosslinked to gliadin peptides), TG 3 (tissue transglutaminase 3), mTG neo-epitope (microbial transglutaminase crosslinked to gliadin-peptides), mTG and PT-gliadin (Frazers Fraction) in human serum or plasma. Evaluate the performance of a novel test system in a study cohort of pediatric GRDs and the correlation of the results to well-established methods in GRD diagnostics.

***Methods*:** Antibody titers of AESKUBLOTS® GRD IgA were evaluated in a cohort of 50 CD, 5 Morbus Chron, and 15 Ulcerative Colitis pediatric patients. Results were correlated to AESKUSLIDES ® EMA IgA IFA read out, and AESKUBLOT® Gastro Pro IgA / IgG, ROC-curves, method agreement, and Pearson-correlation were calculated.

***Results*:** Using cut-offs estimated from ROC curves, highest AUC of antigens was 0.955 tTG IgA, followed by tTG-neo IgA and mTG-neo IgA (0.955 and 0.907 respectively) on the AESKUBLOTS® GRD IgA. tTG-neo IgA showed highest correlation with EMA read out (r^2=0.7453, $P < .001$) followed by tTG-IgA and mTG-neo IgA (0.7035; 0.5504, $P < .001$ respectively). IgA deficiency was matched to 100% with clinical diagnosis, and relevant antibodies were determined with respective IgG tests.

***Conclusions*:** This novel test system is a unique and powerful tool to support diagnosing and monitoring of GRDs, such as celiac disease or non-celiac-wheat sensitivity. Excellent correlation with the highly specific EMA IFA and comparability to well-established markers show its superior performance as a screening assay.

E-POSTER VIEWING 16: CLINICAL PRACTICE - DIAGNOSTICS: HEMATOLOGICAL DISEASE AND AUTOIMMUNITY

EP162 / #418

The Strange Case of Dr Wiskott and Mr Aldrich: An Adult Diagnosis of Wiskott Aldrich Syndrome

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***Background and Aims*:** Wiskott-Aldrich syndrome (WAS) is a rare primary immunodeficiency, caused by a mutation of gene WASP; clinically it is characterized by eczema, immunodeficiency and thrombocytopenia. The WAS survival without a hematopoietic stem cell transplantation (HSCT) is poor.

***Methods*:** We report the case of a 27-year-old man, referred to our Center with the aim to evaluate a possible immunodeficiency since of his medical history characterized by multiple infections, aortitis and refractory immune thrombocytopenic purpura treated with splenectomy.

***Results*:** on the basis of blood sample analysis showing hypogammaglobulinemia, IgM's deficit, thrombocytopenia, we firstly confirmed the hypothesis of immunodeficiency and started intravenously Ig supplementation. A few years later we performed the genetic investigation by NGS that highlighted the mutation in WAS gene, and two heterozygote mutations not yet reported in literature (RAG1- JAK3). We also confirmed the reduction of the expression of WAS protein in B- cells. At the same time an EBV-related lymphoma was diagnosed and therapy with Rituximab was started with good clinical and response. Together the genetic evidence, the past medical history and the new evidence of malignant disease we can confirm the diagnosis of Wiskott-Aldrich syndrome with classical phenotype.

***Conclusions*:** This case underline the relevance of genetic investigations, which can drastically change the therapeutic approach. The best therapeutic approach in adult diagnosis of WASP isn't yet defined, but HSCT seems to be the best therapeutic option in case of persistent and confirmed good response to Rituximab.

EP163 / #634

Severe Lactic Acidosis Caused by Autoimmune Hemolytic Anemia

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***Background and Aims*:** Autoimmune hemolytic anemias are rare and heterogeneous disorders characterized by hemolysis, which is a well-recognized risk factor for thrombosis. Multiple pathophysiological mechanisms for thrombosis have been proposed, involving hemolysis itself and additional effects of the immune system. This case report emphasizes the differential diagnosis of lactic acidosis to include severe anemia, and spleen infarct and necrosis as presented in this case

***Methods*:** A 53-year-old female, was referred to the ER due to extreme weakness. On admission, she appeared somnolent and pale, vital signs were within normal range except for tachypnea, her examination revealed jaundice and palpable spleen. she was preventively intubated. Laboratory tests showed a severe high anion gab metabolic acidosis, with high lactate (18.32 mmol/L), a macrocytic anemia combined with high reticulocytes, indirect bilirubin and LDH, haptoglobin undetectable. Lactic acidosis caused by severe autoimmune hemolytic anemia was further diagnosed, confirmed by coombs test.

***Results*:** An infectious and autoimmune investigation ruled out differential diagnosis causing AIHA.Imaging study of the abdomen and chest revealed an enlarged inhomogenous spleen, and free peritoneal fluid. After consultation with a surgeon she underwent a splenectomy. Pathology showed extensive areas of parenchymal necrosis, Consistent with hemorrhagic infarct. No evidence of lymphoproliferative disease.

***Conclusions*:** The presence of elevated lactate levels in critically ill patients has important implications for morbidity and mortality. Usually increased due to tissue hypoxia caused by systemic or local hypoperfusion, increased glycolysis, critical decrease in oxygen delivery (DO2) and carrying capacity e.g. severe anemia, are associated with anaerobic metabolism and, therefore, lactic acidosis.

EP164 / #421

The Challenges of Evans Syndrome

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***Background and Aims*:** Evans syndrome is an autoimmune condition that presents with two or more cytopenias, which most commonly include autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), with or without immune neutropenia. The aim of this work is to present the various challenges facing diagnosis, treatment and management of patients with Evans Syndrome. A 56-year-old male patient presents to the ER with bleeding for the last 3 days, weakness and fatigue which had worsened during the last week, and fever. Past medical history showed nothing relevant, no smoking, no drugs abuse, no other treatments or concomitant diseases.

***Methods*:** When evaluating Evans Syndrome checking for autoantibodies agains RBCs and other blood components is important. A bone marrow biopsy in order to determine whether it is primary or secondary to lymphoma/CLL, should be performed. Viral checks, previous autoimmune diseases should be excluded. Peripheral blood should be checked regularly until the patient is stable, and during follow up.

***Results*:** Upon presentation the patient had: Hgb 6.9 g/dL, PLT 7000/mm3, ANC 3900/mm3. AST and ALT were elevated, total bilirubin 8.2 mg/dL, LDH 4020 U/L. ICT (++) DCT (++++) both positive. Blood structure eeCckk. Autoantibodies agains 'e' were found in circulation. Transfusion was quiet impossible. Due to corticotherapy the patient had major intestinal bleeding. Total body CT normal. Bone marrow biopsy and aspiration normal.

***Conclusions*:** Evans syndrome is difficult to diagnose and manage. Even if the patient responds to treatment complications can arise, and relapses are common. A careful follow up is equally important.

E-POSTER VIEWING 17: CLINICAL PRACTICE - DIAGNOSTICS: POLYMYOSITIS, MYASTHENIA GRAVIS AND MULTIPLE SCLEROSIS

EP165 / #922

Kappa Index Screening Effectively Improves Oligoclonal Band Testing Response in a Clinical Laboratory

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***Background and Aims*:** Kappa free light chains in cerebrospinal fluid (CSF) have been extensively explored for their ability to reflect intrathecal chronic inflammation in multiple sclerosis. Automated analytical methods providing fast, cost-effective, and metric results support their widespread use, helping over-

come technical and result interpretation difficulties in oligoclonal band (OCB) determination. Previously, we demonstrated kappa index utility as a screening step for OCB analysis (2.55 cut-off) and have established it in our practice since March 2023. We aimed to evaluate the impact of kappa index on laboratory workload and turnaround times for OCB analyses, as well as the agreement between methods in adults with elevated kappa index (≥21.4).

***Methods*:** The number of OCB determinations and turnaround times were assessed retrospectively in homologous periods in 2022 and 2023 (April to October) by consulting the LIS. Agreement between methods was determined in adults with elevated kappa index.

***Results*:** in 2023, among 351 adult samples 28.5% required OCB determination based on kappa index results. A 56% decrease in OCB testing was observed in the first seven months using kappa index screening with concomitant improvement in average turnaround time from 36 to 14 days. Most patients (94%) presenting with kappa index above 21.4 were also positive for OCB (minimum two CSF-specific OCB).

***Conclusions*:** in our laboratory kappa index screening has proven an effective strategy to decrease OCB testing workload and improve turnaround time, which is particularly valued in multiple sclerosis suspected cases. An elevated kappa index (≥21.4) was generally associated to positive OCB results.

EP166 / #837

Ro-52/SSA Positivity Is Associted with ICU Mortality in Rapidly-Progressive Interstitial Lung Disease in Anti-MDA5+ Dermatomyositis Patients: Data from a Single-Center Cohort

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***Background and Aims*:** The aim of this study was to describe clinical and laboratory data in patients with Anti-MDA5 positive antibodies, with a specific focus on factors associated with mortality.

***Methods*:** Anti-MDA5+ patients included in a monocentric cohort of 95 idiopathic inflammatory myopathy adult patients were enrolled in this observational study. Skin and joint involvement were assessed by clinical judgement, lung involvement by clinical and radiological imaging; RP-ILD was defined as hypoxemia and dyspnea associated with radiological worsening within 3 months from ILD onset. Muscular involvement was assessed by Manual-Muscle Test and/or muscle enzymes.

***Results*:** 16 patients, mean age 54.7±3.7, mean follow-up of 2.5±1.3 years were included. Associated autoantibodies were found in 63% of cases: Ro-52/SSA 56.3%, ACCPa 18.8%, RF 12.5%, JO-1 6.3% and PM/Scl-75 6.3%. Skin, joint, muscular and lung manifestations were fund in 67.5%, 18.8%, 18.8% and 87.5%, respectively. Radiological ILD-pattern were OP 43.8%, OP/NSIP 25%, NSIP 12.5% and UIP 6.3%. Fifteen patients had ILD (93.8%), 8 displayed RP-ILD (50%); of whom 6 (75%) were admitted to the ICU; 4 died due to respiratory failure or infection (83.3%), one underwent lung transplant. The mean time from ICU admission to death was 2.1±0.5 months. Mortality was particularly distributed in the first two months from diagnosis. Three deceased RP-ILD patients displayed Ro-52/SSA+ compared to none of the survived (Chi-squared; $P = .035$); no significant difference in Ro-52/SSA+ between RP-ILD and non-RP-ILD patients ($P = .086$) was found.

***Conclusions*:** Ro-52/SSA seropositivity was associated with ICU-mortality in RP-ILD anti-MDA5+ DM patients.

EP167 / #751

Frequency of Myositis-Specific and Myositis-Associated Autoantibodies

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***Background and Aims*:** Idiopathic inflammatory myopathies (IIMs) are heterogeneous conditions characterised by muscle inflammation and weakness, skin rashes and systemic complications. Knowledge on IIM has evolved in recent years with the identification of myositis-specific (MSA) and myositis-associated (MAA) antibodies. MSA are associated with particular clinical syndromes within the IIM spectrum.

***Methods*:** In our study conducted in the period from 07/2021-01/2023, a total of 447 serum samples from patients suspected of having IIM were analyzed for the specific MSA or MAA. Sixteen MSA and MAA (Mi-2α, Mi-2ß, TIF1γ, MDA5, NXP2, SAE1, Ku, PM-Scl 100, PM-Scl 75, Jo-1, SRP, PL-7, PL-12, EJ, OJ, Ro-52) were tested with the Euroline myositis line–blot assay (Euroimmun, Lübeck, Germany).

***Results*:** In 116 of 239 antibody-positive samples one MSA/MAA was detected. 76 samples were presented with two autoantibodies while 32, 9, 2 and 1 samples with 3, 4, 5 and 7 autoantibodies respectively. Antibodies to Ro52 were the most frequently detected MAA, (68/239;28,5%). Among MSA antibodies, the most common were antibodies to the MDA5 antigen (64/239;26,8%) mostly borderline positive, 30 samples were positive for TIF1γ (12.6%), of which 13 were strongly positive, and 24 for Jo-1 (10%), of which 12 were strongly positive.

***Conclusions*:** MSA/MAA autoantibodies were found in the majority of serum samples from patients suspected of having IIM. Unlike previous studies, this study showed that the most common MSA antibodies were against MDA5 and TIF1 γ antigen, both regarded as dermatomyositis autoantibodies and associated with interstitial lung disease and malignancy, respectively.

EP168 / #587

Diagnostic Potential of Blood-Based Biomarkers in Multiple Sclerosis

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***Background and Aims*:** Multiple Sclerosis (MS) is an immune-mediated inflammatory disease affecting the central nervous system (CNS). It presents significant inter- and intra-individual heterogeneity in clinical presentation, progression, and therapy response. The extracellular matrix (ECM) is a network of molecules supporting the cells in CNS. The aim of the study was to investigate the utility of extracellular matrix -related serological biomarkers in MS.

***Methods*:** in serum from patients with MS (n=23) and healthy controls (n=18), we quantified the levels of MMP-degraded biglycan (BGM), Cathepsin-S degraded nidogen (NIC) and MMP degraded secreted protein acidic and rich in cysteine (SPARC-M). The difference between the two groups was evaluated by Mann-Whitney U test, and the diagnostic accuracy was evaluated by the area under the

receiver operating characteristics (AUROC) curve. An AUC=0.85 was considered clinically relevant.

***Results*:** The mean age of 23 patients with MS (8 males, 15 females) was 35.7 years (SD=3.7), and the 18 healthy donors (9 males, 9 females) had a mean age of 35.8 (SD=3.8) years. BGM, NIC, and SPARC-M, were elevated in patients with MS compared to healthy donors (P =.028, P = .004, and P < .0001, respectively). All biomarkers showed separation between patients diagnosed with MS and healthy donors: BGM AUROC of 0.717 (95%CI: 0.547-0.888, P = .028), NIC AUROC of 0.765 (95%CI: 0.601-0.928, P = .005), and SPARC-M AUROC of 0.875 (95%CI: 0.764-0.987, P < .0001).

***Conclusions*:** This study identified an increase in extracellular matrix degradation in patients with MS using blood-based biomarkers. Such biomarkers may be useful for assessing patients' eligibility for targeted treatments.

Table 1. Demographic Table

	Healthy (N=18)	MS (N=23)	p-value
Age, mean (SD)	35.8 (3.8)	35.7 (3.7)	0.908
Sex, Male (%)	9 (50%)	8 (34.78%)	
BMI	25.6 (2.96)	24.8 (3.25)	0.426
Caucasian (%)	25 (100%)	24 (100%)	1.000
Smoking, Current smokers (%)	0 (0%)	2 (8.7%)	
Years since diagnosis (SD)	NA	1.3 (2.22)	

Categorical variables are written as numbers (percentage), while continuous variables are mean (standard deviation). BMI, body mass index

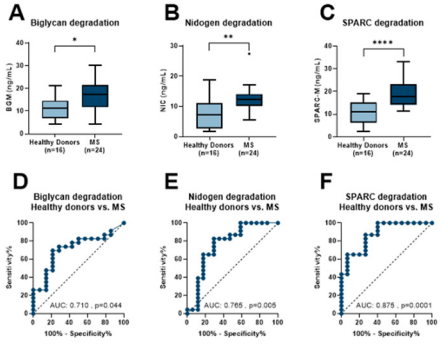

Figure 1. Levels of BGM, NIC, and SPARC-M in Serum from Healthy Donor and Patients with MS.

EP169 / #527

Clinical Features of Patients with Antisynthetase Syndrome - Retrospective Single Center Analysis

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***Background and Aims*:** Antisynthetase syndrome (ASyS) is a subtype of idiopathic inflammatory myopathy, characterised by interstitial lung disease (ILD), myositis, arthritis, Raynaud phenomenon and mechanics hands, in association with anti-aminoacyl-transfer-RNA (anti-ARS) antibodies. The clinical picture and prognosis of the disease depends on the presence of specific anti-ARS antibody.

***Methods*:** This retrospective study included 15 patients in whom anti-ARS antibodies were detected in the period from 4/2018 to 4/2023 with follow up with at least 6 months, when myositis antibody panel become avaliable in the Clinical Institute for Laboratory Diagnostics of UHC Rijeka.

***Results*:** The median age of patients was 59.4 years, while the ratio of women to men was 11:4. Among 15 patients, 9 had anti-Jo-1 (60%), 5 anti-PL-7 (33,3%), 1 anti-PL-12 (6,7%) antibody, while 1 patient with anti-PL-7 also had anti-OJ antibody. Anti-Jo-1 antibody positive patients initialy presented with arthralgia/arthritis (88.9%), myositis (77.8%), ILD (33.3%), Raynaud phenomenon and mechanics hands (22.2%). In anti-PL-7 positive patients, clinical features of arthralgia/arthritis (80%) and ILD (60%) dominated, and other clinical manifestations included myositis (40%) and Raynaud phenomenon (20%). The patient with anti-PL-12 antibody, as well as the one with anti-OJ and anti-PL-7 antibody, had predominantly ILD. At two-year follow up, one anti-Jo-1 and one anti-PL-7 antibody positive patient had newly developed ILD.

***Conclusions*:** in the studied cohort, anti-Jo-1 antibody positive patients predominate, while arthralgia/arthritis, myositis and ILD were the most common clinical manifestations. The frequency of anti-PL-7 positive patients is significantly higher compared to previous data from bigger cohorts of patients with AsyS.

EP170 / #356

The Prevalence of Dementia Among Dermatomyositis and Polymyositis Patients – A Big Retrospective Cohort Study

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***Background and Aims*:** Polymyositis (PM) and dermatomyositis (DM) are inflammatory mediated myopathies characterized by progressive symmetric proximal muscle weakness and associated with extra-muscular involvement. CNS complications are rarely reported with these diseases. The aim of this study is to investigate the association between dementia and PM/DM.

***Methods*:** A retrospective cohort study was conducted using Clalit Health Care database, the largest health maintenance organization in Israel. Patients with a first recorded diagnosis of PM/DM were included and were compared with age, gender matched controls in a ratio of 1 to 5. The prevalence of dementia among PM/DM patients compared to controls was assessed using a univariate and a multivariable model. Binary logistic regression analysis was conducted to assess association of different factors with dementia within the PM/DM cohort.

***Results*:** The study included 2085 PM/DM cases (17.0%) and 10 193 age- and gender-matched controls (83.0%). During the follow-up time, 36 PM/DM patients were diagnosed with dementia compared to 160 controls, with a univariate HR of 1.10 (95%CI 0.77-1.58). within the PM/DM cohort, significant predictors for the development of dementia included increased age at diagnosis (5 years increment; OR=1.86; 95%CI 1.57-2.21; P < .001), and treatment with glucocorticoids (OR=5.40; 95%CI 1.67-17.67; P = .005).

***Conclusions*:** in our cohort, inflammatory myopathies were not associated with dementia. Age, and treatment with glucocorticoids were associated with dementia. Therefore, if dementia is diagnosed in patients with inflammatory myopathies other systemic causes should be sought.

EP171 / #876

Frequency and Characteristics of Ha, Ks, and Zo Antibody-Positive Patients in an Unselected Cohort

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***Background and Aims*:** Autoantibodies to Ha, Ks, and Zo are associated with anti-synthetase syndrome (ASyS), a myositis subtype characterized by muscle weakness and interstitial lung disease. Our aims were to establish the frequency, demographic and clinical characteristics of Ha, Ks, and Zo antibody-positive patients in a referral setting, and to evaluate the performance of a line immunoblot assay (LIA) for detection of these antibodies.

***Methods*:** Consecutive samples received at ARUP Laboratories for myositis antibody testing were screened by protein immunoprecipitation (IP) of S^{35}-labeled K562 cells. Samples with distinct bands suspicious of Ha, Ks, or Zo, samples positive for other autoantibodies associated with myositis or other autoimmune diseases, and samples from healthy donors were tested by LIA. Clinical and laboratory data for Ha, Ks, and Zo antibody-positive patients were sought to confirm diagnosis.

***Results*:** We report on the frequency of detection of Ha, Ks and Zo antibodies in a reference laboratory setting, agreement between LIA and IP for the detection of these antibodies and the clinical characteristics of patients positive for Ha, Ks, and Zo antibodies.

***Conclusions*:** Identification of Ha, Ks, and Zo antibodies is important for diagnosis, prognosis, and disease management in patients with ASyS. Testing for Ha, Ks, and Zo antibodies is currently only performed by a small number of labs, primarily on a research basis. LIA confirmed the presence of Ha, Ks, or Zo antibodies in patients with corresponding bands observed in the IP assay. Combined use of both methods improves reliability for the diagnosis of ASyS in patients undergoing evaluation for inflammatory myopathies.

E-POSTER VIEWING 18: CLINICAL PRACTICE - DIAGNOSTICS: PRECISION (PERSONALIZED) MEDICINE IN AUTOIMMUNITY

EP172 / #704

Fibromyalgia Sine Inflammation Is Syne-Immune

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***Background and Aims*:** The etiopathogenesis of fibromyalgia syndrome (FMS) is unclear. Recent studies show that immunoglobulins' transfer from patients with FMS may induce pain in mice via human anti-satellite glial cells. Pro-inflammatory cytokines (as TNF-tumor necrosis factor) play crucial role in autoimmune/inflammatory rheumatic arthritides (AIIRD), are target for biological therapies. Some cytokines have potent nociceptive effects. FMS is frequent in AIIRD; about third of Rheumatoid Arthritis (RA) and Psoriatic (PSA) patients. Modulating cytokines involved in inflammation and nociception could benefit AIIRD with co-morbid FMS. JAK/STAT inhibitors (JAKi) in RA, show an additional analgesic benefit over Adalimumab, an anti-TNF antibody, regardless of rheumatic clinical response (RCR) and remission.

***Methods*:** We report a case-series with AIIRD and secondary co-morbid FMS, on anti-rheumatic treatment, with sustained both good RCR and relief of FMS symptoms (diffuse pain, fatigue, non-refreshing sleep).

***Results*:** Table 1, summarizes a total of 11 patients, mainly women with seropositive-RA and FMS, who achieved bi-modal clinical effects. The JAKi group (Upadacitinib) is the main treatment of benefit.

***Conclusions*:** Anti-inflammatory treatment in rheumatic diseases, especially JAK/STAT inhibitors, is beneficial for FMS symptoms, irrespective of therapy-timing, whether early or late after other drug failures. This is presumably through its anti-nociceptive mode of action. This observation underscores an immune-mediated aspect in Fibromyalgia pathogenesis, involving cytokines and antibodies.

Table 1. Cdmard's=Conventional Disease-Modifying-Anti-Rheumatic-Drugs, Spa=Axial-Spondylo-Arthropathy, +:Rf=Rheumatoid Factor, ++:Acpa=Anti-Citrullinated-Peptide-Antibodies/Rf.

Case(no.)/Gender/Age(Y)	AIIRD-Type/Disease-duration(Y)	Anti-Rheumatic Drug:Treatment-Line after cDMARD's(n)/Retention-time(m)
1/Female/57	SPA/5	Etanercept:1/30
2/Female/57	RA+/20	Upadacitinib:6/24
3/Female/36	RA+/18	Upadacitinib:2/30
4/Female/52	RA++/17	Etanercept:1/168
5/Female/36	RA++/13	Upadacitinib:2/30
6/Female/62	RA++/21	Tocilizumab:2/24
7/Female/67	RA+/17	Sarilumab:6/24
8/Female/57	RA+/30	Upadacitinib:6/23
9/Male/66	PSA/unknown	Adalimumab:1/72
10/Male/42	SPA-Uveitis-Colitis/15	Upadacitinib:5/10
11/Female/59	RA+/37	Abatacept:2/56

EP173 / #497

The Minimization of Immunosuppression in Liver Transplant Recipients: Personalization of Immunosuppressive Therapy

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***Background and Aims*:** The introduction of potent immunosuppression (IS) has increased the one-year survival rates post liver transplantation to over 90%. However, due to the deleterious side effects associated with IS, no substantial progress had been made in prolonging their long-term survival. The liver's unique ability to autoregulate its immunological response, makes it possible to minimize IS in liver transplant recipients (LTRs). Minimization aims to identify the minimal dose of IS, in an individual LTR, that is sufficient to prevent rejections and simultaneity doesn't cause clinically significant side effects. In our study, IS minimization protocols were introduced in LTRs to identify, based on clinical and laboratory characteristics personalized IS requirement.

***Methods*:** from February 2018, ninety-seven adult LTRs were recruited with a non-autoimmune primary liver disease, stable graft func-

tion for >3 years and no evidence of rejection. The dose of IS was minimized in 3-month intervals with laboratory tests performed after each dose reduction to evaluate liver function.

***Results*:** IS minimization was feasible in 87.6% of LTRs. After 36 months of follow-up, 76 out of 97 LTRs were on monotherapy, with 47 of them being on subtherapeutic doses of calcineurin inhibitors and 2 were on spacing protocols with tacrolimus. In 12/97 LTRs (12.4%), liver function tests (LFTs) increased, (in those who had indications, a liver biopsy was performed confirming immunological changes) necessitating the return to the previous IS level which resulted in normalization of LFTs in all patients.

Conclusions: Minimization of IS seems to be a safe procedure to personalize the IS therapy in eligible LTRs.

Table 1. Immunosuppression Therapgy at Baseline and After 36 Months.

	AT BASELINE (N=97)	AT 36 MONTHS (N=97)
COMPLETE WITHDRAWAL	1 (1.03%)	1 (1.03%)
SPACING*	0	2 (2.06%)
SUBTHERAPUTICAL#	24 (24.7%)	47 (48.5%)
MONOTHERAPY		
TAC	24 (24.7%)	45 (46.4%)
CsA	0	2 (2.06%)
MONOTHERAPY	55 (56.7%)	76 (78.4%)
TAC	43 (44.3%)	58 (58.8%)
CsA	5 (5.15%)	9 (9.28%)
MMF	6 (6.19%)	9 (9.28%)
EVE	1 (1.03%)	0§
DUAL THERAPY	39 (40.2%)	18 (18.6%)^
TAC + GCS	17 (17.5%)	6 (6.19%)
TAC + MMF	13 (13.4%)	9 (9.27%)
TAC + EVE	2 (2.16%)	1 (1.03%)
CsA + GCS	2 (2.06%)	0**
CsA + MMF	4 (4.12%)	2 (2.06%)
MMF + GCS	1 (1.03%)	0+++
TRIPLE THERAPY	2 (2.06%)	2 (2.06%)
TAC + GCS + MMF	1 (1.03%)	0****
CsA + GCS + MMF	1 (1.03%)	1 (1.03%)
TAC + GCS + EVE	0	1 (1.03%)*****

* TAC 0.5mg taken 5 times a week
# serum concentration of TAC <5ng/ml or CsA <50ng/ml
§ patient switched to monotherapy with TAC
^ decrease in number due to the patients being converted to monotherapy
** patients converted to monotherapy with cyclosporine A
*** patient converted to monotherapy with MMF
**** patient converted to dual therapy with tacrolimus and MMF
***** addition of everolimus with the intent of withdrawing tacrolimus after consultation with oncological team
Abbreviations used: CsA cyclosporine A, EVE everolimus, GCS glucocorticosteroids, MMF mycophenolate mofetil, TAC tacrolimus

EP174 / #344

New Insights Into Early and Established Rheumatoid Arthritis Subtypes Through Serologic Biomarker Profiling – Part of the Scandra Project

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Background and Aims: Rheumatoid arthritis (RA) is a chronic inflammatory disease with variable clinical presentation, response to therapy, and long-term outcomes. Currently, there is a lack of predictive biomarkers to guide an individualized treatment strategy. Combinations of conventional and novel serological biomarkers might stratify patients for a more personalized approach. We aim to identify new serologic biomarkers by testing samples from large RA patient cohorts, in order to develop algorithms that bring personalized medicine into clinical rheumatology practice.

***Methods*:** We included 808 baseline samples from Norwegian patients with RA, including 319 early RA (eRA) and 483 with established RA (estRA). We used EliA™ technology (Thermo Fisher Scientific, Sweden) to measure anti-CCP IgG/A, RF IgM/A/G, and the RUO assay anti-RA33 IgM/A/G. Novel biomarkers were investigated using an in-house research multiplex chip assay containing native, citrullinated or acetylated peptides.

***Results*:** in both eRA and estRA patient samples, 70% were positive for both anti-CCP IgG and RF IgM. Among the remaining 30% (called seronegative group), a significant amount was positive for anti-RA33 IgM/A/G (42% in eRA and 33% in estRA patient samples). The measurement with our multiplex chip revealed additional biomarkers that were positive in the seronegative group: the most promising candidate was a peptide variant of fibrinogen with a sensitivity of 15% and 10% in eRA and estRA patient samples, respectively.

***Conclusions*:** Our study highlights the value of combining different technologies and datasets, resulting in the identification of possible biomarkers that can be used to create a unique algorithm with potential benefits for patients and the medical community.

E-POSTER VIEWING 19: CLINICAL PRACTICE - DIAGNOSTICS: BIG DATA, PREDICTION, MONITORING AND PREVENTION

EP175 / #528

Risk Factors Associated with the Development of Interstitial Lung Disease in Rheumatoid Arthritis in A Guatemalan Outpatient Clinic

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Background and Aims: Pulmonary manifestations affect 5 to 10% of RA patients. Some of the associated factors that have been described are advanced age, being men, RA activity, anti-cyclic citrullinated peptide (Anti-CCP) or Rheumatoid factor (RF) positivity, and environmental factors such as smoking. The objective of this study was defining risk factors associated with the development of interstitial lung disease (ILD) in patients with rheumatoid arthritis.

***Methods*:** Cross-sectional, retrospective study of patients with diagnosis of RA fulfilling the 2010 ACR/EULAR criteria, evaluated in the Rheumatology outpatient clinic, from December 1st, 2008, to May 31st, 2023. ILD was diagnosed by high-resolution computed tomography or biopsy.

***Results*:** A total of 322 files were reviewed, of which a total of 14 cases (4.35%) were defined as ILD associated with RA. The main characteristics are shown in Figure 1. Data was analyzed using multivariable logistic regression, obtaining a global prediction of 75% for ILD development, with significant ORs for the variables time of diagnosis of ILD, use of glucocorticoids, methotrexate, and positivity Anti CCP, as observed in Figure 2. A survival and risk analysis by Kaplan Meier and Hazard Plot was used for the appearance of ILD in association with time of RA diagnosis, showing that the risk of ILD increases after of 10 years of the diagnosis, with a risk of 2.18 (6.021-14.6) as shown in Figure 3.

***Conclusions*:** The risk factors associated with AR-ILD in our population, behave in a similar way to other latitudes of the world, especially the RA disease duration at the diagnosis of ILD.

Table 1.

	RA-ILD n:14	Non ILD-RA n:14	P value
Age mean (+/- SD) *	63.4 (11.0)	63.3 (14.7)	0.98
Female (%)	14 (100)	9 (64.3)	0.014
RA disease duration (+/- SD) *	14.14 (8.71)	12.86 (7.14)	0.63
Mean age of RA diagnosis (+/- SD) *	49.29 (11.7)	50.5 (17.7)	0.13
Current smokers n (%)	5 (35.7)	3 (21.4)	0.40
Smoking Index (+/- SD)	1.69 (3.48)	0.19 (0.53)	0.015
BMI			0.40
Underweight n (%)	1 (7.1)	2 (14.3)	-----
Normal n (%)	6 (42.9)	1 (7.1)	-----
Overweight n (%)	3 (21.4)	6 (42.9)	-----
Obese n (%)	3 (21.4)	9 (28.6)	-----
Extremely Obese n (%)	1 (7.1)	1 (7.1)	-----
Treatment			
Glucocorticoids n (%)	14 (100)	11 (78.6)	0.067
csDMARDs n (%)	14 (100)	14 (100)	1
MTX n (%)	12 (85.7)	14 (100)	0.54
Dosis media de MTX (+/- DS)	9.64 (5.53)	12.6 (4.43)	0.41
Tiempo medio uso MTX (+/- DS) **	59 (54.36)	120.43 (84.73)	0.31

	OR	95% IC
Age >50 years	2.18	0.17 - 27.07
Sex	0.39	0.23 - 0.65
Current Smokers	2.037	0.37 - 3.9
Obesity	0.27	0.052 - 1.4
Mena age or RA diagnosis	1.8	0.39 - 8.18
RA Diseases duration**	10.31	6.02 - 14.6
Disease activity		
Remission	0.68	0.12 - 3.85
Mild	1.63	0.22 - 11.70
Moderate	0.48	0.32 - 0.71
High	0.48	0.32 - 0.71
Erosive disease	2.03	0.37 - 10.9
Glucocorticoids	2.27	1.46 - 3.53
MTX	2.16	1.43 - 3.28
Biologic DMARs	1.38	0.56 - 3.41
RF Positive	2.16	0.17 - 27.08
Anti CCP Positive	10.8	1.69 - 68.93

Table 2.

	OR	95% IC
Age >50 years	2.18	0.17 - 27.07
Sex	0.39	0.23 - 0.65
Current Smokers	2.037	0.37 - 3.9
Obesity	0.27	0.052 - 1.4
Mena age or RA diagnosis	1.8	0.39 - 8.18
RA Diseases duration**	10.31	6.02 - 14.6
Disease activity		
Remission	0.68	0.12 - 3.85
Mild	1.63	0.22 - 11.70
Moderate	0.48	0.32 - 0.71
High	0.48	0.32 - 0.71
Erosive disease	2.03	0.37 - 10.9
Glucocorticoids	2.27	1.46 - 3.53
MTX	2.16	1.43 - 3.28
Biologic DMARs	1.38	0.56 - 3.41
RF Positive	2.16	0.17 - 27.08
Anti CCP Positive	10.8	1.69 - 68.93

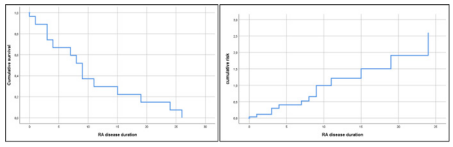

Figure 3.

EP176 / #766

Left Ventricular Diastolic Dysfunction Correlates with Pro-Autoimmune Pattern in Essential Arterial Hypertension

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***Background and Aims*:** Low-grade systemic inflammation facilitating autoimmunity is an important mechanistic component of heart failure (HF) with preserved left ventricular (LV) ejection fraction (EF) (HfpEF). The aim of this study was to estimate serum proinflammatory biomarkers (C-reactive protein (CRP), tumor necrosis factor alpha (TNF-α), and interleukin-6 (IL-6)) in middle-aged males (M) and females (F) with essential hypertension (HTN) depending on LV diastolic dysfunction (LVDD).

***Methods*:** The main group comprised 55 M and 49 F with the first- to second-severity grade HTN with LV EF ≥50%. Patients had sinus rhythm, the 1st or the 2nd severity degree LVDD, LV hypertrophy, left atrium dilatation, and NT-proBNP >125 pg/mL. Comparison group: 30 hypertensives without HF; control group: 31 normotensives. Quantitative features were compared using the Mann–Whitney test, median χ2, ANOVA module. Spearman's rank correlation coefficients were determined to identify the relationship between the proinflammatory pattern and exercise tolerance.

***Results*:** Hypertensive M had markedly higher CRP, TNF-α, and IL-6 levels compared to F. All mean values corresponded to reference range. In patients with second-degree LVDD, CRP, TNF-α, and IL-6 levels were significantly greater than in subjects with the 1st degree LVDD (both within M and within F samples). Significant negative associations between CRP, IL-6, TNF-α levels and the 6 min walk test existed both in hypertensive M and F.

***Conclusions*:** The study demonstrated a close relationship between the proinflammatory/pro-autoimmune pattern of serum markers and LVDD or exercise tolerance indicators, regardless of the patients' sex. LVDD pathogenesis may include systemic inflammatory/autoimmune links.

EP177 / #839

Biomarkers of Endothelial Injury in a Child with Raynaud's Phenomenon and Newly Diagnosed Systemic Lupus Erythematous: Case Report

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Background and Aims: Systemic lupus erythematosus (SLE) is a systemic autoimmune condition with multisystem involvement. Literature data suggest that increased levels of biomarkers of endothelial injury and hypercoagulability may correlate with disease activity.

Methods: We describe a case of a 17-year adolescent with longstanding Raynaud phenomenon who developed generalized edema and acute kidney injury, followed by a diagnosis of juvenile SLE.

Results: An adolescent female with longstanding isolated Raynaud phenomenon was admitted to nephrology unit of a reference hospital complaining on progressive, generalized edema. She had rapidly progressive increase in creatinine and urea, and nephrotic-range proteinuria. She was diagnosed with acute glomerulonephritis but due to Raynaud phenomenon and severe renal disease, she was seen by rheumatologist. Antinuclear antibodies, anti-double stranded DNA and anti-Smith ab were ordered and returned positive. Complement fractions were reduced. Antiphospholipid antibodies were negative. A diagnosis of jSLE was made, with a SELENA-SLEDAI index of 45 points, indicating high disease activity. D-dimers were high. Capillaroscopy revealed non-specific pattern and capillary sludging. Von Willebrand factor and tissue plasminogen levels were abnormal, suggesting endothelial injury and hypercoagulable state. She was treated with high dose prednisolone and cyclophosphamide with clinical and laboratory improvement, but still presenting signs of vasculopathy.

Conclusions: Emergent literature data suggest that dysregulated endothelial markers are promising biomarkers for monitoring disease activity and even subclinical inflammation. More studies are needed to understand the correlations.

EP178 / #379

Haptoglobin As a Novel Marker of Adult IgA Vasculitis Renal Involvement

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Background and Aims: Adult immunoglobulin A vasculitis (IgAV) is a small vessel leukocytoclastic vasculitis, characterized by variable clinical presentation. Currently used markers are suboptimal in predicting severe renal involvement and the need of aggressive treatment vs. mild and self-resolving skin limited disease. Our aim was to identify potential biomarkers through RNA sequencing of IgAV leukocytes and skin.

Methods: Peripheral blood leukocytes and skin biopsy samples were collected from treatment-naïve adult IgAV patients at the time of diagnosis with: 1) IgAV nephritis (n=3), 2) skin-limited IgAV (n=3), and age-/sex-matched HC (n=3) for RNA sequencing analysis. Haptoglobin serum level was measured in 157 treatment-naïve adult IgAV patients (31% with IgAV nephritis).

Results: in both leukocytes and skin of IgAV patients with nephritis, we found 45 overlapping differentially expressed genes, thereby

representing renal-associated IgAV pathology. on the other hand, in skin-limited IgAV 12 overlapping genes were identified as differentially expressed in comparison to HC. In IgAV nephritis patients haptoglobin was identified as a hub gene, based on protein-protein interaction network. Haptoglobin protein serum level was elevated in IgAV nephritis cases ($P = .015$). Positive correlation was observed between haptoglobin and SAA ($r_s = 0.62$, p-adj < 1 x 10^{-3}), CRP ($r_s = 0.60$, p-adj < 1 x 10^{-3}), and BWAS ($r_s = 0.248$, p-adj = 2 x 10^{-3}).

Conclusions: Haptoglobin might be a novel marker of renal involvement in adult IgAV associated with disease severity.

EP179 / #1038

Tcrgrapher: A Software for the Identification of Antigen-Specific TCRs

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Background and Aims: Understanding TCR specificity could open up novel avenues for target treatment of autoimmune diseases and diagnostics. Our study aims at benchmarking established tools for the antigen-specific TCR identification from a single repertoire snapshots, highlighting their limitations, and providing recommendations for analysis and experimental design.

***Methods*:** We designed the "TCRgrapher" R library for the identification of specific TCRs. TCRgrapher includes a unified framework that can run ALICE, TCRNET, tcrdist3, and GLIPH2 with a flexible set of controls and parameters. We applied TCRgrapher to three sets of TCR repertoires: post-LCMV infection data published by Shlesinger et al., our data of mice vaccinated with Sputnik V, and our data of lung-infiltrating CD4+ T cells collected at the peak of tuberculosis infection. Each dataset had an experimentally obtained repertoire enriched with antigen-specific TCRs, used as a positive set.

***Results*:** Among the single-repertoire analysis methods scrutinized, ALICE and TCRNET performed best on mice TCRβ repertoires. Furthermore, we found minor differences between ALICE performance with different TCR generation models and with corrections to clonotype abundance. TCRNET performance by clonotype grouping was mostly identical. TCRNET showed higher precision in the area of low recall with real data used as the control sample compared to the OLGA-generated control. GLIPH2 gave satisfactory results only in cases of clusters formed by one nucleotide mismatch and only being run locally.

***Conclusions*:** TCRgrapher provides a user-friendly way to find condition-specific clonotypes and compare the results from different tools. We hope that our work will be useful to a wide range of researchers in the field.

EP180 / #469

Autoantibody Profiling and Serology Testing of Human Body Fluids Using High Density Protein Arrays

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***Background and Aims*:** The Autoimmunity and Serology Profiling facility at SciLifeLab (www.scilifelab.se) provides infrastructure and technologies for analysis of antibody repertoires and serostatus in various body fluids, and antibody validation through custom designed protein and peptide arrays, to both Swedish and international academia as well as to industry.

***Methods*:** Supported by the resource of more than 42 000 unique human protein fragments generated within the Human Protein Atlas (www.proteinatlas.org), representing over 18 000 human protein coding genes, our services encompass proteome-wide autoantibody reactivity screening on large microarrays for individual or pooled samples, as well as solutions for investigation of autoantibody repertoires and serostatus in hundreds of patient samples in parallel. We offer expertise and instrumentation for generating customized spotted protein microarrays and conducting measurements and analyses on commercially available protein microarrays.

***Results*:** in addition to offering the world's largest recombinant protein microarray, we provide high-throughput bead-arrays for directed screening of large sample cohorts with high multiplexing capabilities. These microarrays, in combination with our infrastructure and knowledge, have proven to be an important tool for large-scale screening of sample cohorts relating to various fields such as autoimmunity, allergy, neuroproteomics and cancer, as well as for affinity binder validation and epitope mapping.

***Conclusions*:** The SciLifeLab Autoimmunity and Serology Profiling facility have so far contributed to nearly 60 publications during the past three years, showcasing its success. In addition to providing access to essential equipment for microarray production and analysis, we also offer invaluable expertise, extending our services to the academic and industrial sectors, both nationally and internationally.

EP181 / #353

Dissecting the Connection Between Uveitis and Psoriasis: The Mediating Role of Spondyloarthropathies

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***Background and Aims*:** The association between uveitis and spondyloarthropathy (SpA) related conditions is well-established. However, evidence describing the link between uveitis and psoriasis, and psoriasis without concomitant SpA-related-conditions is conflicting. This large-scale population-based study sought to describe the prevalence and features of uveitis among psoriasis patients in Israel as well as investigating the risk for uveitis in different subgroups of psoriasis patients compared to the general population.

***Methods*:** We conducted a retrospective study utilizing the electronic database of the Meuhedet Health Maintenance Organization. The study included all patients diagnosed with psoriasis between 2000-2020, each patient was matched with four controls. Logistic regression models were employed to assess the association between psoriasis and uveitis while adjusting for the presence of SpA-related conditions.

***Results*:** 61 003 psoriasis patients and 244 012 matched-controls were included. The prevalence of uveitis was 1.3% vs. 1.1% respectively (OR=1.12; 95%CI 1.10-1.30; $P < .001$). When adjusting to psoriasis severity, concurrent SpA, and psoriasis treatment no significant association was found. The rates of uveitis among psoriasis patients with concurrent SpA-related condition was 3.2% compared to 1.4% in controls without psoriasis or SpA (OR=2.38; 95%CI 2.00-2.83; $P < .001$), while in psoriasis patients without SpA, rate of uveitis was 1.0% and was similar to controls.

***Conclusions*:** Our findings suggest that the positive association between psoriasis and uveitis is primarily mediated by the coexistence of other SpA-related conditions. These findings imply to the presence of a shared pathogenetic mechanism and set the direction for a phenotypic-targeted screening strategy**.**

E-POSTER VIEWING 21: CLINICAL PRACTICE - DIAGNOSTICS: STANDARDIZATION OF DIAGNOSTICS

EP182 / #1012

Do We Recognize the AC-29 (Topo Like-1) Pattern?

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Background and Aims: Recently identified DNA topoisomerase I has been designated under the code AC-29 (Topo-like I) in ICAP; it includes staining in five cellular regions. Studies have found AC-29 pattern to be particularly specific for systemic and widespread cutaneous sclerosis. The aim of this study is to define AC-29 pattern and conduct follow-up tests, particularly demonstrating the presence of the Scl-70 antibody in the diagnosis of systemic sclerosis and widespread cutaneous scleroderma, and to emphasize its importance in diagnostic approaches.

***Methods*:** Data from patients who were requested ANA testing between 01/01/2021-31/08/2023, were analyzed. Tests were performed on IF Sprinter device using IIFT:ANA Mosaic 1A EUROPattern kit and evaluated with EUROStar III Plus fluorescence microscope. For follow-up tests, EUROLINE ANA Profile Mi-2, Ku, DFS70 (IgG) kit was used, and tests were conducted on EUROBlot Master 44 (Euroimmun, Germany) device.

***Results*:** 27 patients were identified with AC-29 pattern; 24 were female and 3 were male, aged between 16-89 years. Nine of them had a diagnosis/presumptive diagnosis of Scleroderma/SLE/Raynaud's Syndrome, seven had joint diseases, five had dermatitis, three had Sjögren's Syndrome, one had iridocyclitis, and two were identified with other diseases. Nine female patients tested positive for Scl-70 antibody, with seven diagnosed with scleroderma, one with SLE and scleroderma, and one with Raynaud's Syndrome. Strong/very strong positivity for AC-29 pattern was associated with Scl-70 positivity, whereas lower levels of positivity were not.

***Conclusions*:** Our findings underscore the diagnostic significance of identifying AC-29 pattern and detecting Scl-70 antibody. Experts should closely monitor advancements in diagnostic testing and integrate them into their diagnostic approaches.

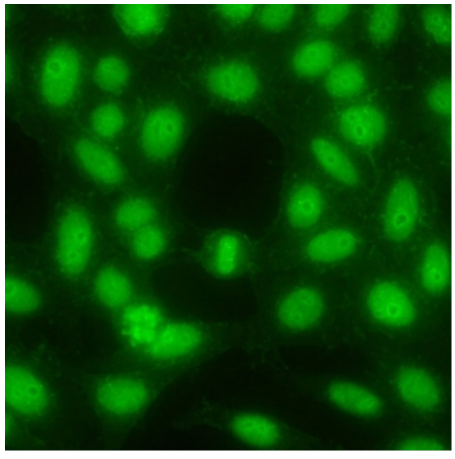

Figure 1.

EP183 / #492

Harmonization of ANA Testing Challenge: Quantification Strategy to Accurately Predict End-Point Titers Avoiding Serial Dilution

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***Background and Aims*:** Despite the advantages of automated systems for antinuclear antibody (ANA) analysis, the prediction of end-point titers avoiding serial dilutions is still in progress. The aims of this study were to set a conversion table providing discriminant ranges of fluorescence signal intensity values (FI) corresponding to the end-point titers and validate this tool in a real-life laboratory setting.

***Methods*:** 894 serum samples were analyzed for ANA using Image Navigator system. In order to classified FI into non-overlapping groups corresponding to conventional end-point titers, statistical discriminant analysis was used. Validation study was performed calculating agreement and error rates between visual readings and conversion table of 1119 routine ANA positive samples.

***Results*:** Setting of FI ranges corresponding to the end-point titers for different staining patterns was computed. For samples showing single pattern, the overall agreement between visual readings and conversion table was 98.4% for all titers ranging from 1:160-1:2560, of which 68.0% had the same titer and 30.4% were within ±one titer difference. Concordance rates according to ANA patterns were as follows: 1) nuclear 98.4%, of which 67.0% had the same titer and 31.4% ± one titer; 2) cytoplasmic 100%, of which 72.7% had the same titer and 27.3% than ±one titer; 3) mitotic 66.6%, of which 33.3% had more ± one titer.

***Conclusions*:** Our study developed a quantification method for autoantibodies titers assessment based on just one single sample dilution instead of traditional serial dilution approach, providing significant advantages in routine laboratory in terms of reduction in hand-on time and harmonization of results.

EP184 / #838

Comparison of Five Different Reagents for dsDNA Antibodies Determination

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Background and Aims: Anti-double stranded DNA (anti-dsDNA) antibodies play an important role in the diagnosis, classification and management of systemic lupus erythematosus (SLE). Our aim was to compare the results of five different methods for anti-dsDNA in different hospital centers.

Methods: The study included 50 patients with history or suspicion of SLE. Anti-dsDNA was measured using 5 different reagents: Anti-dsDNA-NcX ELISA on Euroimmun Analyzer I-2P (EUROIMMUN AG, Lubeck, Germany), dsDNA chemiluminiscent immunoassay (CLIA) on IDS iSYS (IDS ISYS, Pouilly en Auxois, France), QUANTA Flash® dsDNA CLIA on BIO-FLASH® (inova Diagnostics inc, San Diego, USA), Anti- dsDNA on Alegria2 ELISA like method (Orgentec, Mainz, Germany), and Anti-dsDNA ELISA on BEP 2000 analyzer (Orgentec, Mainz, Germany). Results were categorized as positive or negative and we calculated kappa statistics as well as intraclass correlation coefficient (MedCalc version 14.8.1).

Results: intraclass correlation coefficient showed good degree of consistency in average (0.8495 (95%CI: 0.7716- 0.9066)) but only moderate reliability on single ratings (0.5302 (95%CI: 0.4033-0.6599). Separate Cohen`s kappa testings revealed fair to moderate agreement for most reagent combination and substantial agreement between Alegria2 ELISA like anti-dsDNA and Orgentec anti- dsDNA ELISA (kappa=0.722) as well as between CLIA methods, QUANTA Flash® and IDS iSYS dsDNA (kappa=0.629).

Conclusions: Our results showed mostly moderate comparability between anti-dsDNA methods. Considering our results it is obviously possible to obtain different results of anti-dsDNA for the same patient regardless of the standardisation of the anti- dsDNA method. Considering that, it is important to follow up the patient with the same method.

EP185 / #879

Clinical Evaluation of a New Multiparametric Microdot Array Panel for Systemic Autoimmune Diseases Diagnosis

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***Background and Aims*:** The early and reliable detection and quantification of autoantibodies plays an important role in autoimmune diseases diagnosis and in disease course monitoring. Novel technologies such as multiplexed determination of autoantibodies have been recently introduced. The aim of this study was to evaluate the performance of a new RUO microdot array-based multiparametric assay (ZENIT AMiDot) to correctly classify patients with multiple Connective Tissue Diseases (CTDs) and healthy controls (HC), also comparing with fluorescence enzyme immunoassay (FEIA) for the detection of anti-ENA and anti-dsDNA antibodies.

***Methods*:** The study involved 125 patients with systemic autoimmune diseases (n=75) as well as HC (n=50). ZENIT AMiDot CTD panel was designed from Cambridge Life Sciences. Tests were run on automated slide processor ZENIT FLOW (A. Menarini Diagnostics), then slides were imaged and analyzed using ZENIT fast (A. Menarini Diagnostics).

***Results*:** The diagnostic sensitivity and specificity of the microdot array were 83% and 84%, respectively. The new method showed a good agreement with FEIA for the anti-ENA antibodies (average agreement: 95.7%, ranging from 90.1% for anti-SSB/La antibodies to 100% for anti-CENP B and anti-Jo1 antibodies), and a lower agreement for anti-dsDNA antibodies (79%). Mean agreement among methods assessed by the Cohen's kappa was 0.71.

***Conclusions*:** ZENIT AMiDot CTD and FEIA methods showed good qualitative agreement. The microdot array showed good clinical performance and could be a valuable aid in the detection of CTDs patients, offering an alternative to line immunodot assay or to other methods largely in use such as FEIA.

EP186 / #921

The Impact of ICAP Nomenclature in the Harmonization of Anti-Nuclear Antibodies (ANA) within UK NEQAS, A Global EQA Scheme

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***Background and Aims*:** External quality assurance (EQA) programs play a pivotal role in standardizing laboratory practices, allowing us to evaluate how intra-method and inter-methods variability changes over time. The objective of our study was to analyze the UK NEQAS EQA reports for the "Antibodies to Nuclear and Related Antigens" programme between 2013 and 2023 to assess the overall level of harmonization in autoimmune diagnostics and to identify issues where improvement actions are needed.

***Methods*:** Despite solid-phase immunoassays (SPA) with well-characterized antigens are gaining popularity in autoimmunity laboratories, the indirect immunofluorescence on HEp-2 (IFA HEp-2) cell substrate remains the predominant method used for anti-nuclear antibodies (ANA). There has been a migration over time from the use of rodent substrate to HEp 2/2000 cells.

***Results*:** During the last decade, the international Consensus on ANA Patterns (ICAP) initiative promoted harmonization and understanding of HEp-2 IFA staining pattern nomenclature. Most laboratories (60%) have adopted the use of ICAP nomenclature when reporting ANA patterns. There appears to be some harmonisation in the screening dilutions utilised by laboratories but end point dilution varies greatly. This is dependent upon individual patient samples as well as ANA pattern type. Currently available computer-aided diagnosis (CAD) systems for the detection of ANA by HEp-2 IFA assay enable a standardized measurement of system-specific fluorescent intensity measures.

***Conclusions*:** Our analysis showed there is an increasing number of laboratories using these systems to interpret ANA patterns. However, there are some discrepancies between manual and automated reading results, especially for mixed patterns.

EP187 / #390

Enabling Laboratories to Do More with Less: Assessment of Workflow Efficiencies Through Instrument Consolidation in an Immunology Lab

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***Background and Aims*:** one way to ensure current laboratory processes and technology are fully optimized is to perform a Workflow Analysis Study. Geisinger Medical Center (GMC) recognized an opportunity to consolidate their immunology laboratory for allergy and autoimmune testing.

***Methods*:** To measure the impact of the instrument consolidation and integration of Phadia250™ systems, operational data was collected through direct workflow observations, time and motion studies, and targeted interviews. The baseline study encompassed seven separate platforms that GMC utilized for autoimmune and allergy testing. The following systems were included: Two DYNEX DSX® Two Werfen BIO-FLASH® Two Siemens IMMULITE® 2000 one ZEUS IFA™

***Results*:** The workflow assessment resulted in GMC consolidating down to three platforms for autoimmune and allergy testing: Two Phadia250 ZEUS IFA™ A total of 361 square feet of laboratory space was saved equating to a 57% improvement over the baseline metric. After consolidating most of the testing to the two Phadia250 systems, the total daily manual time went from 4.2 hours to just over 2.5 hours. The combined workflow assessment resulted in saving a total of one full time employee (FTE).

***Conclusions*:** To keep up with growing testing demands, laboratories must continue to produce high-quality results in an efficient manner. Instrument consolidation is a viable strategy to save on technologist time, space and costs. This can result in not only economic savings to the laboratory, but also allows medical technologist to be funneled to other more needed areas of the laboratory, while saved space can be used for test expansion.

E-POSTER VIEWING 22: CLINICAL PRACTICE - DIAGNOSTICS: THYROID AUTOIMMUNITY

EP188 / #745

Perspective Study of Specific Autoantibodies Against Thyroid Antigens in a Cohort of Patients invastigated for Graves' Disease

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Background and Aims: Graves' disease (GD) is an organ specific autoimmune disease and the most common cause of hyperthyroidism; it is more prevalent in woman aged 40-60 years old. Autoantibodies (Aabs) directed against the TSH receptor (TRAb), Thyroid Peroxidase (anti-TPO) and Thyroglobulin (anti-TG) are the specific markers detected in patient serum samples in the context of clinical assessment. The aim of our study was to detect and evaluate the presence of autoantibodies against specific thyroid antigens (TRAb, TPO and TG) and their comparison to the TSH levels in patients investigated for GD based on clinical and other serological parameters.

***Methods*:** in 194 patients ages between 18-87 (average age 52.7 years) with suspected GD samples were collected during an one year period. Anti-TPO, anti-TG, TSH were investigated by chemiluminescence (CLIA) and TRAb by ELISA.

***Results*:** in 78 (40.2%), TRAb were positive and their levels were between 1.6-77.2 IU/L (cut off 1.5 IU/L). Among them, 50 (64.1%) had hyperthyroidism (TSH<0.2), 16 (20.5%) had euthyroidism while 12 (15.4%) hypothyroidism, and the mean of TRAb were 19.3, 9.9 and 6.2, respectively. Anti-TPO and anti-TG Aabs were both negative in 21 patients (26.9%), in 14 (17.9%) positive anti-TPO were detected, whereas both positive anti-TPO και anti-TG Aabs were determined in 55.1% of the samples.

***Conclusions*:** The detection of high levels of autoantibodies and in particular TRAb is a marker for the diagnostic approach of Graves' disease while their early determination is essential for treating patients with hyperthyroidism.

EP189 / #716

Evaluation of Genetic Factors Triggering the Onset and Severity of Graves' Orbitopathy

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***Background and Aims*:** Graves' orbitopathy (GO) is a complication of Graves' disease, affecting around 40-60% of the cases. Unfortunately, there is no complete understanding of the exact mechanism involved. Some factors can predispose more to the severe or mild onset of GO. Therefore, our study aims to establish the genetic factors that would determine the probability and severity of the disease onset.

***Methods*:** Our research group includes orbital fibroblasts collected from 19 Graves' orbitopathy patients (7 in active and 12 in inactive stage). Additionally, 5 control materials were collected from patients during blepharoplastic surgery. Fibroblasts from the orbital tissue were cultured to obtain fully functional cells, and subsequently, RNA was isolated. Fibroblast transcriptome was assessed using the NGS technique.

***Results*:** First, we observed that active fibroblasts differ in the general transcriptome profile based on their clinical activity score (CAS) classification. Comparing active-stage fibroblast with the control group, we did determine a significant difference in the metabolic pathways using the WIKI pathway tools. We also found essential variations in the B cell receptor signaling between the mentioned groups. Furthermore, comparing the active stage with the inactive stage, we observed differences in the chemokine signaling pathways and the degradation process of selected amino acids.

***Conclusions*:** Determination of the genetic factors contributing to Graves' orbitopathy pathophysiology is of great importance. Establishing the role of these elements in the disease would be a crucial step toward developing novel targeted therapeutics.

EP190 / #864

Should We Assess Routinely an Ovarian Reserve in Girls and Young Women with Autoimmune Thyroid Disease?

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***Background and Aims*:** Some studies report that reproductive aged women with autoimmune thyroid disease (AITD) have a significantly higher risk of diminished ovarian reserve. What is the best time to assessed it in females with AITD? To find the answer we assessed ovarian reserve in girls and young women with AITD.

***Methods*:** There were 77 patients with AITD, 7.6-23.5 yr-old, mean 14.3±3.7 years with mean AITD duration time of 3.2±2.1 years and 29 age-matched healthy controls, 3.1-24.5 year-old, mean 15.1±6.5 years included to the study. In all participants FSH, luteinizing hormone (LH), E2, prolactin, SHBG, TSH, fT4, anti-TPO, AMH, and inh-B, if possibly in 3-5th day of the menstruation cycle were measured.

***Results*:** There were no differences in assessed hormones between patients with HT and healthy controls. Any correlations between AMH and other biochemical parameters, age of participants, AITD duration nor SDS of BMI were found. We found a significantly positive correlation between AMH and inh-B (r=0.56, *P* = .01) in AITD patients and between inh-B and FSH (r=0.55, *P* = .01) in both groups.

***Conclusions*:** The results of our study did not indicate that young patients with HT have impaired ovarian function and ovarian reserve. It makes no clinical sense to evaluate the ovarian reserve in teenagers and young women with AITD.

Table 1

	AMH	inh-B	FSH	LH	E2	SHBG	TSH	fT4	Prolactin
AITD	5.7±4.3	55.6±4.3	5.6±2.3	6.2±5.4	52.6±44.6	84.8±46.7	3.5±4.8	15.8±4.2	176.1±88.9
Controls	4.5±2.8	66.3±5.7	5.2±3.0	4.8±4.2	59.8±43.2	102.7±34.4	3.6±5.4	15.0±2.2	204.3±175
P	0.2	0.5	0.6	0.3	0.6	0.2	0.9	0.3	0.6

E-POSTER VIEWING 23: CLINICAL PRACTICE - DIAGNOSTICS: TYPE 1 DIABETES MELLITUS

EP191 / #1035

Performance of a New Prototype ELISA for the Detection of Autoantibodies Against Gad 65 in Patients with Type 1 Diabetes Mellitus

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Background and aims: Autoantibodies against the 65 kDA isoform of glutamic acid decarboxylase (GAD) are an important marker for diagnosis and prediction of new-onset type 1 diabetes mellitus (T1DM) and GAD65 antibody-associated neurological diseases, especially stiff-person syndrome. We developed a new prototype Anti-GAD ELISA that requires a lower amount of serum (5µl) and has a shorter total incubation time (2h15min) compared to the established EUROIMMUN Anti-GAD ELISA (25 µl, 2h40min) and evaluated the performance of the prototype assay.

***Methods*:** The clinical performance of the prototype ELISA was evaluated using a sensitivity panel comprising sera from 100 T1DM patients and 20 patients with a suspected neurological disorder, and a specificity panel comprising sera from 48 ANA-negative patients, 74 patients with suspected thyroid disorder, and 227 healthy donors. Agreement between the prototype and the established ELISA was analyzed using 36 sera from suspected T1DM patients. Agreement between the prototype and the Medipan CentAK anti-GAD_{65} M radioimmunoassay (RIA) was analyzed using 100 sera from T1DM patients.

***Results*:** The clinical sensitivity of the prototype ELISA was 86.7% at a specificity of 98.6%. The prototype and the established ELISA agreed 100% (Cohen's κ=1). The prototype ELISA and the RIA detected anti-GAD autoantibodies in 86% and 75% of T1DM patients, respectively (moderate agreement, κ=0.5).

***Conclusions*:** The new Anti-GAD ELISA showed a promising performance compared to the established ELISA. Shorter processing time and a lower amount of serum reinforce the prototype's suitability to replace the established ELISA. Additionally, the new ELISA enables easier automation in conjunction with other ELISA on EUROIMMUN instruments.

EP192 / #818

Analysis of Autoantibodies in Children with Type 1 Diabetes Following SARS-COV-2 Infection: Padova Hospital Experience

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Background and Aims: The main players in DM1 are: genetic predisposition, environmental factors, including viruses, and the action of the immune system.

The aim of our work is to investigate whether during the COVID-19 pandemic, SARS-CoV-2 infection was related to an increased autoimmune response associated with pediatric DM1.

***Methods*:** We identified two cohorts of patients: with DM1 at onset and with already diagnosed DM1. In both cohorts, anti GAD and anti IA-2 autoantibodies were determined. We also determined anti insulin, anti ZnT8 and anti pancreatic insula autoantibodies, PCR and IL-6 in patients subdivided into IgG negative and positive (vaccinated and unvaccinated) on the basis of SARS-CoV-2 Spike's anti-RBD IgG.

***Results*:** Differences among the three groups (IgG negative, IgG positive unvaccinated, and IgG positive vaccinated), failed to reach significance with regard to the number of autoantibodies at onset, the extent of weight loss, the presence of asthenia, familiarity, pH, blood glucose, the presence of DKA, antibodies to GAD, anti IA-2, anti ZnT8, and anti insula, and PCR. Ketonemia and IL-6 in the vaccinated was significantly lower than in the unvaccinated and the level of pre- and post-COVID anti GAD did'nt change, instead the level of anti IA-2 decreased significantly.

***Conclusions*:** Vaccinated children, at the time of onset, appear to have slightly different diabetes from classical diabetes, with less familiarity, greater seronegativity, and generally fewer autoantibodies. In addition, asthenia and weight loss appear more infrequent and milder in vaccinees, who also have significantly lower ketonemia than others, and are significantly less inflamed.

E-POSTER VIEWING 24: CLINICAL PRACTICE - DIAGNOSTICS: OTHER

EP193 / #598

Psychological Diagnostics in Autoimmune Patients

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***Background and Aims*:** It is very well known that autoimmune disorders are often followed by neuropsychiatric symptoms. These symptoms mimic neuropsychiatric disorders very well and patients often end up with diagnosis of neuropsychiatric disorder. Differential diagnostics becomes an important parameter in helping these patients. We need to recognize and differentiate autoimmune patients with neuropsychological symptoms and autoimmune patients with developed neuropsychiatric disorder as comorbidity.

***Methods*:** We are at the disposal of wonderful psychological instruments with fantastic psychometric properties and by applying them we can make full neuropsychological evaluation. We can use Luria-Nebraska Neuropsychological Battery, for checking intellectual Functioning and Cognitive Abilities we can use Pearson's WAIS- IV, for Personality Functioning besides MMPI-2, we have Morey's PAI, for different psychological symptoms we have a variety of Beck's Scales, Spielberger's Scales, for Psychobiological Symptoms there is old Cornell index and variety of Pain Scales.

***Results*:** Three patients with autoimmune disorders went through detailed neuropsychological evaluations using before mentioned methods. Results of these evaluations are presented in the form of psychological findings and opinions, so they can be of practical service to medical staff in hospitals and ambulances. The aim is to show how concrete psychological results are of great benefit for therapy outcome in medical settings.

***Conclusions*:** This short oral presentation will try to present psychological diagnostic instrument that provide information of psychological functioning and how these data can be used in a psychological and other medical treatments for neuropsychologic symptoms considering autoimmune problems. At the end you will be able to hear short interviews with patients.

EP194 / #582

Prevalence of Sarcoidosis in Colombia: An Analysis of the Ministry of Health Databases

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Background and Aims: The implementation of the SISPRO system allows it to be executed as a tool capable of collecting information of interest to the health system. A descriptive analysis was performed emphasizing demographic variables of the Colombian population to estimate the prevalence of sarcoidosis from the records collected between January 2017 and December 2021.

***Methods*:** An observational-descriptive cross-sectional study was carried out in which the international Classification of Diseases (ICD-10) was used as keywords for this purpose the diagnoses for Sarcoidosis (D860) associated with lymph nodes and unspecified site (D861, D862, D863, D863, D868, D869, G532, M633) were used and reported with variables such as sex, age, and prevalence distribution.

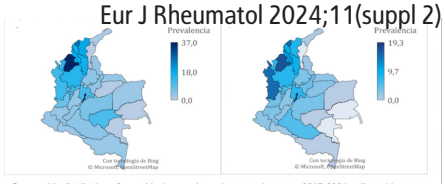
***Results*:** During 2017 to 2021, 6317 patients with sarcoidosis were registered in Colombia, for a female: male ratio of 2.07 and an unadjusted prevalence of patients seen of 12.1 per 100 000 inhabitants with a higher distribution in women in a proportion of 67.48% of cases. A pattern of prevalence's distribution was found in the groups from 30 to 39 years. A similar upward curve was found for the male sex from 20 to 29 years of age. In relation to the Sarcoidosis distribution by states, it was identified that the areas with the highest total concentration of patients corresponded to Bogotá, Cordoba and Atlántico. The states with the lowest concentration were Cesar, Guajira, Casanare and Vichada. This is attributed to less development and lower population density.

***Conclusions*:** This is the first study that describes the prevalence of a disease such as sarcoidosis in a Latin American country.

Table 1. Number of Registered Patients with Primary Fiagnosis of Sarcoidosis According To Age Group Between 2017-2021.

Age group	Men (n)	Women (n)	Total (n)	Total Prevalence
0 - 19	313	416	729	3,38
20 - 29	188	484	672	6,56
30 – 39	311	578	889	9,87
40 - 49	336	741	1077	14,49
50 - 59	372	950	1322	19,60
60 a 69	340	728	1068	21,75
70 a 79	191	364	555	19,30
80 years old and more	83	156	239	15,27
Total	2054	4263	6317	12,13

The total patients column corresponds to the number of patients seen in the five-year period. Prevalence is calculated from the ratio per 100,000 patients seen during the same period. Source : Own elaboration



Geographic distribution of sarcoidosis prevalence between the years 2017-2021, adjusted by sex by departments in Colombia. Prevalence is calculated with the average population served as denominator per 100,000 inhabitants A) Women B) Men. Source: Own elaboration

Figure 1. Geographic Distribution in Colombia of Sarcoidosis Prevalance Between Years 2017-2021.

EP195 / #1026

Biomarkers Reflecting the Pathogenesis, Clinical Manifestations, and Guide Therapeutic Approach in Systemic Sclerosis

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***Background and Aims*:** Systemic sclerosis (SSc) is a progressive autoimmune disorder that mainly affects the skin. There are other clinical manifestations as renal, pulmonary, cardiovascular, and gastrointestinal tract involvements.

***Methods*:** Based on the skin involvement there are two subtypes of SSc, as limited cutaneous SSc (lSSc) which involves the acral part of the body and diffuse cutaneous SSc (dSSc) resulting in significant skin thickening of the body. Despite of the extensive research the patomechanism is not fully clarfied, how Ssc develops, moreover identifying biomarkers to predict the clinical outcome and prognosis still remains challenging.

***Results*:** Circulating biomarkers can be crucial to define the diagnosis, to predict the prognosis and monitor the clinical course. However, only some patients are responsive to the therapy in SSc, and there is a need to reach the ideal therapy for any individual to prevent or slow down the progression in early stages of the disease.

***Conclusions*:** in this review, we summarize the potential biomarkers in Ssc, describe their role in the diagnosis, and patomechanism, as well as clinical course.

EP196 / #788

A Follow Up Study of Autoimmune Diseases and Macrophage Activation Syndrome as Non-Cardiogenic Complications in 151 Children with Kawasaki Disease

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***Background and Aims*:** Our aim was to evaluate the presence of autoimmune diseases (AIDs) in patients after Kawasaki disease (KD) and to compare clinical, demographic and laboratory characteristics between patients who developed AIDs (group A) and patients who did not (group B).

***Methods*:** A single-center, retrospective cohort study with longitudinal follow-up of all children newly diagnosed with KD between June 2006 and December 2019 was performed.

***Results*:** in total, 151 children with KD were included. Sixteen (10.6%) developed AIDs after KD including 6 juvenile idiopathic arthritis (JIA), 6 macrophage activation syndrome, 3 coeliac diseases, 1 ulcerative colitis, 1 psoriasis, 1 hypothyroidism, and 1 demyelination. Three patients presented with more than one AID. We found no difference in age distribution, clinical characteristics, and incidence of coronary artery abnormalities (CAAs) between the two groups. Group A had significantly lower median serum sodium (135 vs. 137 mmol/L, P = .002), lower median platelet count (262 vs. 363 x10^9/L, P = .026), higher neutrophil to lymphocyte ratio (NLR) (9.4 vs. 4, P = .009) and a higher percentage of IVIG resistance (37.5% vs 12.6%, P = .022). Moreover, we found that children with KD had twice as many AIDs compared to CAAs on long-term follow-up (10.6% and 5.3% respectively).

***Conclusions*:** in our cohort, children with KD had twice as many AIDs as CAAs on long-term follow-up, with a significantly higher percentage of IVIG resistance. Additional studies are necessary to clarify the possible role of sodium, platelet count, and NLR for risk stratification of AID after KD.

EP197 / #832

Association of Positive Lupus Anticoagulant, Anti-Cardiolipin and Anti-β2 GPI Antibodies with Thrombotic Events in Patients with Antiphospolipid Syndrome

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Background and Aims: Antiphospholipid syndrome (APS) is a prothrombotic disorders clinically manifested with increased risk of thrombosis and pregnancy complications. APS is characterized with persistent presence of antiphospholipid antibodies: lupus anticoagulant (LA), anti-cardiolipin (aCL) and/or anti-β2-glycoprotein I antibodies (anti-β2 GPI). The study aimed to investigate the diagnostic accuracy of LA1/LA2 ratio, aCL IgG, aCL IgM and anti-β2 GPI values in APS patients with confirmed positive LA in the assessment of thrombotic events.

***Methods*:** in this retrospective study a review of positive LA findings (LA1/LA2 ratio >1.40) together with aCL IgG, aCL IgM and anti-β2 GPI results, in the period from November 2022 to July 2023 was performed. Among 3200 of total requests for LA, 124 (3.9%) were positive. The study included only patients who, in addition to positive LA, had also requests for immunological tests (69/124). Finally, patient's histories were reviewed and thrombotic events data were extracted.

***Results*:** Two groups of patients were observed, with or without any thrombotic event. No statistically significant difference of LA1/LA2 ratios was observed between these two groups, whereas a statistically significant difference of aCL IgG (P = .001) and anti-β2 GPI values (P = .001) was demonstrated. Subsequently, ROC analysis was performed for each parameter separately.

***Conclusions*:** Statistical analysis showed that patients with positive LA and higher concentrations of aCL IgG and anti-β2 GPI had higher risk of developing thrombotic events. ROC curve analysis confirmed aCL IgG and anti-β2 GPI as the best parameters for the assessment of thrombotic events in APS patients with confirmed positive LA .

Table 1. Results of Statistical Analysis of investigated Parameters (Expressed As Medians interquartile Ranges) in Patients with Positive Lupus Anticoagulant with Or without Thrombotic Events.

Parameter	Unit	With trombotic events (N=28)	Without trombotic events (N=41)	P-value
LA1/LA2	ratio	1.84 (1.59-2.19)	1.80 (1.65-1.89)	0.566
aCL IgG	CU	334.6 (217.8-622.1)	11.2 (4.0-195.3)	**0.001**
aCL IgM	CU	7.3 (4.2-17.6)	12.6 (2.9-24.6)	0.970
anti-β2 GPI	CU	1453.2 (673.4-2527.2)	33.7 (9.2-580.4)	**0.001**

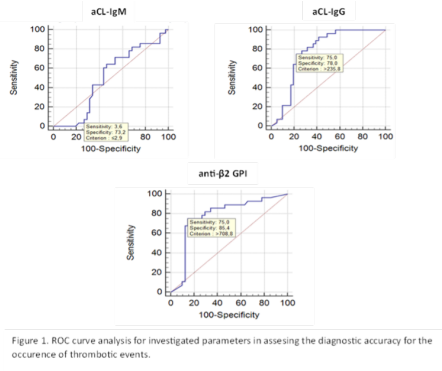

Figure 1. ROC curve analysis for investigated parameters in assesing the diagnostic accuracy for the occurence of thrombotic events.

Figure 1. ROC Curve Analysis for Investigated Parameters in Assessing the Diagnostic Accuracy for the Occurence of Thrombotic Events.

EP198 / #1029

Humoral Response to SARS-COV-2: A Perspective Study in Vaccinated Subjects and COVID-19 Patients

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Background and Aims: In December 2020 the anti-SARS-CoV-2 vaccination campaign started worldwide. In Italy there were 4 vaccines: Pfizer; Moderna; Astrazeneca (AZ); Johnson&Johnson (J&J). This study investigated the quantity/persistence of humoral response in vaccinated subjects (VS) and COVID-19 patients (CP).

***Methods*:** In total 179 individuals were enrolled. For 169/179 subjects (19-95 years) we had all the samples: 114 VS and 55 CP. Blood samples were collected through a dried blood spot for one year and the antibodies levels were checked by ELISA.

***Results*:** We found that Moderna and Pfizer had a similar kinetic (peak at 7 and 6 wafd [weeks after the first dose]). AZ administered in homologous and heterologous manner gave the same trend (peak at 15 and 13 wafd). However, AZ heterologous subjects had antibodies concentration ten times higher than AZ homologous. J&J maintained a constant trend

just above the cut off. CP responded similarly after 1 or 2 doses of vaccine (peak at 2 and 5 wafd). CP with two doses had double IgG levels and remained longer. 132/169 volunteers received the booster: 91 VS and 41 CP. The booster increased the IgG levels in AZ homologous, AZ heterologous and J&J. In all the VS and CP, the IgG levels persisted longer.

***Conclusions*:** In conclusion, the vaccine type influences the humoral response. Moderna and AZ heterologous showed the highest antibodies concentrations. The number of doses is fundamental to maintain/recall a humoral response and its persistence over time. The heterologous vaccination might be more effective to achieve a good humoral response (i.e. IgG concentration).

EP199 / #602

Iron Deficiency in Familial Mediterranean Fever: A Study on 211 Adult Patients from the JIR Cohort

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***Background and Aims*:** Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease in the world. Fatigue is known to trigger attacks of the disease. Currently, there is no association between iron deficiency and fatigue in FMF patients. Our aim was to evaluate the prevalence of iron deficiency in FMF patients and its association with clinical and laboratory parameters.

***Methods*:** A retrospective evaluation of homozygous patients followed prospectively at the French National Reference Centre for Adult Autoinflammatory Diseases was performed. All patients consented to the anonymous collection of their medical data via the JIR cohort.

***Results*:** Of 211 patients, 67 (31.8%) had a serum ferritin level < 27 ng/mL and were defined as iron deficient. of these, 61 (91%) were female with a mean age of 36.81 (± 17.03) years. FMF patients with iron deficiency had lower levels of hemoglobin ($P < .001$) and body mass index ($P = .023$) and were significantly younger than those without iron deficiency ($P = .004$), but they did not have more elevated inflammatory biomarkers. Female gender ($P = .0015$) was associated with lower ferritin levels.

***Conclusions*:** Iron deficiency, which mainly affects young women regardless of their level of inflammation, may be secondary to excessive gynaecological losses. Iron-deficient FMF patients may be more fatigued, which may increase FMF attacks. It may be important to correct iron deficiency because this condition alone can cause asthenia. Interestingly, ferritin doesn't seem to have pro-inflammatory properties in FMF. This work highlights the importance of measuring ferritin levels in FMF patients to detect iron deficiency in the absence of anaemia.

EP200 / #875

Long-Term Outcome of Patients with MIS-C in Slovenia

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***Background and Aims*:** Multisystem inflammatory syndrome in children (MIS-C) is a serious complication of SARS-CoV-2 infection. Short-term outcome is mostly favourable, but less is known about the long-term sequelae. The aim of this study was to evaluate a long-term outcome of patients with MIS-C.

***Methods*:** A cohort study included children up to 18 years of age diagnosed with MIS-C at Children's hospital University Medical centre Ljubljana, Slovenia, between September 2020 and May 2022. Their possible organ involvement as well as neuropsychological and psychosocial status were regularly assessed and finally checked at the last follow-up visit 1,5-3 years after initial presentation, using clinical, laboratory, imaging evaluations and neuropsychological tests battery measuring attention, executive function, memory and fine motor skills.

***Results*:** Out of 78 enrolled patients, 5% reported non-specific symptoms at the final follow-up, such as headache and fatigue. We observed individual cases of weight gain, arterial hypertension, nodules on the vocal cords and allergic rhinitis. Cardiac involvement was observed in 67/78 children (86%) at initial presentation, with residual changes in 4/67 (6%) of these patients. No MIS-C recurrence was noted after SARS-CoV-2 reinfection or COVID-19 vaccination. 60/78 (77%) patients were included in neuropsychological and psychosocial assessment, in which we found cognitive deficits beyond the expected baseline levels specfic domains.

***Conclusions*:** The long-term outcome of MIS-C in slovenian patients was generally favourable, with no recorded deaths. Non-specific symptoms, residual cardiac changes and cognitive deficits were identified, but no recurrence of MIS-C was noted post-reinfection or COVID-19 vaccination.

EP201 / #783

Ocular Complications in Juvenile Idiopathic Arthritis-Associated Uveitis in Children: Retrospective Analysis

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***Background and Aims*:** Within the diverse clinical spectrum of Juvenile Idiopathic Arthritis (JIA), JIA-associated uveitis stands out as a particularly challenging complication, characterized by inflammation of the eye. Uveitis in children often progresses quietly, concealing the potential for severe ocular complications that can profoundly affect a child's visual health and overall quality of life. This retrospective analysis seeks to provide a comprehensive evaluation of the ocular complications linked to JIA-associated uveitis in pediatric patients.

***Methods*:** In this study, we conducted a retrospective analysis of ocular complications in patients with JIA associated with uveitis. We reviewed the medical records of 124 patients aged up to 18 years who had been diagnosed with JIA and were admitted to the Rheumatology Department between January 2022 and June 2023.

***Results*:** In our study of 124 pediatric JIA patients, 20 (16.13%) were diagnosed with uveitis, predominantly females (80%) with an average age at JIA onset of 6.28 ± 4.18 years and uveitis onset at 6.75 ± 3.24 years. Oligoarticular JIA was the most common subtype (70%), with positive ANA testing in 75% of cases. Ocular complications were prevalent in 85% of patients, with posterior synechiae (75%), cataracts (55%), and giant macular cystoid edema (25%) being the most common. Additional complications included glaucoma, band keratopathy,

optic nerve atrophy, vitreous body destruction, and retinal detachment.

***Conclusions*:** This study highlights the critical significance of early detection and proactive management of uveitis in Juvenile Idiopathic Arthritis patients, emphasizing the need to prevent severe ocular complications in the pediatric population.

EP202 / #713

Coexistence of Autoimmune Diseases in Patients with Juvenile Idiopathic Arthritis

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Background and Aims: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. The aim of our study was to evaluate the prevalence of coexistent autoimmune diseases in children with JIA.

***Methods*:** A retrospective, single small center study was performed. All patients diagnosed with JIA who were examined at our pediatric clinic during 10 years period were enrolled. Data was collected from patients' medical records.

***Results*:** A total of 111 patients were included. The mean age was 8.1 years. 71 patients (64%) were female. 24 patients with JIA (21.6%) had coexistent autoimmune disease. The most common was uveitis (13 patients, 11.7%). Psoriasis and celiac disease were present in 3 patients, 2 patients had autoimmune thyroid disease. Inflammatory bowel disease, idiopathic thrombocytopenic purpura and Henoch- Schonlein purpura were present in only 1 patient. 28 patients (25.2%) presented with a family history of autoimmune disease. Associated autoimmune diseases were most frequent in patients with oligoarticular type of JIA whereas patients with systemic JIA (Still disease) had none of them. This confirms the hypothesis that systemic JIA is considered an autoinflammatory and not an autoimmune disease.

***Conclusions*:** Our study demonstrated that autoimmune diseases are frequently coexistent in children with JIA. Therefore, all these patients should be regularly screened for associated autoimmune diseases.

EP203 / #696

Severe Acute Respiratory Syndrome Coronavirus-2 Variants and Antibody Responses in Bangladesh

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***Background and Aims*:** Novel SARS-CoV-2 variants are emerging at an alarming rate. The Delta variant and Omicron variants of concern (VoC) carry spike (S)-protein mutations, which have the potential to evade protective immunity, to trigger break-through infections after COVID-19 vaccination, and to propagate future waves of COVID-19 pandemic.

***Methods*:** Unique SARS CoV-2 variant spike protein mutations in nasopharyngeal swabs of RT-PCR-positive COVID-19 infections in Dhaka and Chittogram Bangladesh were identified by post-RT-PCR melting curve analysis and next generation sequence analysis. To assess the anti-SARS CoV-2 antibody responses, the levels of the anti-S -proteins and anti-N-protein IgG were measured by ELISA.

***Results*:** SARS CoV-2 Omicron variants of asymptomatic or mild COVID-19 replaced Delta variant infections requiring hospitalization and oxygen support. The omicron XBB became predominant in July 2022 and associated with cough, headache or body ache and loss of smell; 47 of 68 (69%), 30 of 68 (44%) and 27 of 68 (40%) respectively at higher frequency than BA.1 / BA.2; 16 of 88 (18%), 13 of 88 (15%) and 0 of 88 (0%) $P < .01$, $P < .01$ and $P < .0001$. Linear regression analysis reveals no associations between the number of previous infections and the number of symptoms, r=-0.084, $P = .68$. The levels of anti-nucleoprotein (N)-protein-IgG post COVID-19 and anti-Spike (S) protein-IgG post-COVID-19 vaccination were similar between BA.2, BA.4/BA.5 and XBB.

***Conclusions*:** Omicron XBB subvariants emerged in Bangladesh two months prior to previous reports and include unique patterns of S-protein mutations not assigned in PANGO lineage. The sustained antibody responses indicate natural re-infections and are consistent with persistent SARS CoV-2 omicron immune escape during extensive nation-wide vaccine coverage.

EP204 / #717

Gender Differences in Systemic Manifestations of Sjögren's Syndrome - Single Centre Experience

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***Background and Aims*:** Sjögren's syndrome (SS) is a chronic autoimmune disease, more common in women, that affects multiple organ systems. Our aim was to assess differences in clinical manifestations and comorbidities between males and females with SS treated in our centre over a 10-year period.

***Methods*:** The medical records of the patients diagnosed with SS were collected from outpatient clinics, department and day hospital of the Department of Rheumatology and Clinical Immunology of University Hospital of Split. For statistical analysis, the Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA) was used. $\chi 2$ test, Fisher's test, univariate and multivariate logistic regression were used for analysis.

***Results*:** The study included 317 subjects, 300 (94.6%) females. Men were more prone to pulmonary involvement, vasculitis, and lymphoma, while women more frequently had hypothyroidism. Vasculitis manifested as cryoglobulinemic (29%), leukocytoclastic (17%), CNS and systemic vasculitis (12%), nodular and urticarial vasculitis (6%). Interstitial lung disease (ILD) was the most frequent pulmonary disease, classified as NSIP (40%), UIP (20%), sarcoidosis (16%), with fewer cases of bronchiolitis obliterans with organizing pneumonia (8%). All evaluated lymphomas were the non-Hodgkin type. Younger patients showed an association with thrombocytopenia and antiphospholipid syndrome (APS), while older patients were associated with cardiovascular diseases (CVD), hypertension, osteoporosis, diabetes, dyslipidaemia, rheumatoid arthritis, systemic sclerosis. We confirmed the connection of primary SS (pSS) with male gender and younger age.

***Conclusions*:** Despite the fact that men less likely develop pSS, male patients have more severe disease than women. The research highlights differences in the clinical course of SS between genders which might influence therapeutic approaches.

EP205 / #608

Differences in HRQoL and Fatigue in Patients with Sjogren's Syndrome and Systemic Lupus Erythematosus

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***Background and Aims*:** Studies comparing health-related quality of life (HRQoL) in patients with Sjogren's syndrome (SS) to patients with other autoimmune rheumatic diseases have produced conflicting results. We aimed to compare HRQoL and fatigue in patients with SS and systemic lupus erythematosus (SLE) and to evaluate the influence of disease activity and clinical manifestations on HRQoL in patients with SS.

***Methods*:** The study included 135 patients with SS and 65 patients with SLE. The Short Form Health Survey-36 (SF-36) questionnaire was used to evaluate HRQoL. The fatigue Severity Scale (FFS) was used to assess fatigue.

***Results*:** The total SF-36 score in patients with SS was 49.65 (±23.35), Mental Component Summary score (MCS) was 52.64 (±24.19), and Physical Component Summary (PCS) score was 38.44 (25-100). Compared to SLE patients, only the PCS score was significantly lower (38.13 (6.26-97.5); $P = .028$) in SLE patients (SF-36 - 47.09 (±22.12), $P = .117$; MCS 51.47 (±22.85), $P = .784$). Most patients (69.63%) with SS had pathological values of FFS - 4.67 (±1.96), which was similar to SLE patients 4.98 (±1.84). There was a significant correlation of ESSDAI and ESSPRI with the SF-36, PCS, and MCS scores. The strongest correlation was found between the ESSPRI pain subscale and SF-36 (rho=-0.602, $P < .001$) and ESSPRI fatigue subscale and PCS (rho=-0.702, $P < .001$).

***Conclusions*:** Patients with SS have reduced HRQoL to a similar extent as patients with SLE, except for better scores in the physical domain. Disease activity has a negative impact on HRQoL in SS, with pain and fatigue as significant contributors.

EP206 / #391

The Impact Novel Patterns Between Autoimmune Disease and Coronavirus Disease 2019 Have Made on the Laboratory

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***Background and Aims*:** Epidemiological data from 2015 highlights a surge in autoimmune disease incidence rates within the last thirty years, with some increasing as much as 7% per year. Just as coronavirus infections have increased in prevalence so has autoimmune diseases. In relation, laboratories are seeing staff shortages worse than ever before. The magnitude of laboratory management is increasing and continued studies in this area can help to provide the tools and resources necessary to ensure on-going quality patient care.

***Methods*:** A survey will be emailed to laboratory managers, supervisors or directors of U.S. laboratories (hospital-based and reference) that manage autoimmune disease testing. The survey will be distributed in November 2023 and results will be analyzed in January 2024. The survey questions focused on pre-covid (2019) vs current (2023) for autoimmune disease testing volumes, staff shortages, and lab priorities.

***Results*:** For this study, we will identify the relationship between pre-covid (2019) and current autoimmune disease testing volumes (2023), positivity rates, and staff shortages. The statistical significance of the correlation coefficients will be assessed using a t test. How laboratory management goals/priorities have changed will be summarized and analyzed for similarities, differences, and trends.

***Conclusions*:** increasing efficiency will increase revenue for the laboratory. Non-specified testing, lack of screening practices, and symptom difficulty can further delay a patient's treatment journey. Bringing awareness to the increase in autoimmune disease prevalence to the laboratory and providers they can ensure proper lab tests are offered with high quality results and providers are aware of what lab tests should be requested.

EP207 / #779

Assessment of HLA Antibody Dynamics in Patients Awaiting Kidney Transplantation

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***Background and Aims*:** Although preexisting anti-HLA antibodies are regularly monitored for changes in kidney transplant (KT) candidates, their natural dynamics over time are not well understood. This study examined the dynamics of anti-HLA in kidney transplant candidates.

***Methods*:** The study reviewed anti-HLA single antigen bead (SAB) test results of 4130 patients between June 2020 and June 2023. Among these patients, 213 patients met the inclusion criteria, which required having undergone SAB assay measurement on at least two occasions, with a minimum interval of 6 months before KT, and no history of immunosuppression. The SAB results were categorized by the peak mean fluorescence intensity (MFI) levels into different grades: strong (>10 000), moderate (5000-10 000), weak-moderate (3000-5000), weak (1000-3000), and negative (<1000).

***Results*:** Of 213, 144 (67.6%) showed no changes in class I and 133 (62.4%) in class II MFI grades. For class I, 46 (21.6%) patients had increased MFI, and 24 (11.3%) patients decreased. For class II, 22.1% increased, and 16.4% decreased. Significant MFI changes, defined as changes of two or more grades, were found in 12 (5.6%) patients for class I and 11 (5.2%) for class II antibodies. one patient experienced spontaneous resolution of HLA antibodies, despite no documented targeted interventions or immunosuppression during the pre-transplantation evaluation period.

***Conclusions*:** Anti-HLA antibody dynamics are mostly stable, but significant changes can occur, including rare cases of spontaneous resolution. These findings highlight the individualized nature of anti-HLA antibody dynamics and emphasize the complexity of alloimmunity. Further researches into the underlying mechanisms and their impact on kidney transplant outcomes are necessary.

EP208 / #439

When Psoriasis Turns into Lupus: Diagnostic Challenges

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***Background and Aims*:** Cutaneous lupus erythematosus (LE) can manifest in a variety of skin morphologic presentations. We aim to highlight the occurance of psoriasis-like lesions in LE patients.

***Methods*:** This report presents two LE cases where psoriasiform skin morphology delayed accurate diagnosis finding.

***Results*:** The first case involved a 36-year-old patient initially diagnosed with psoriasis due to red, scaly plaques on the extensor forearms, nail changes and facial lesions. Further inves-

tigations revealed LE, supported by interface dermatitis changes and lupus band in dermatohistology and positive ANA. Systemic treatment for lupus resulted in significant improvement. The second case featured a 77-year-old male with a history of chronic lymphatic leukemia and skin lesions mimicking psoriasis. Over two years, various diagnoses were considered, including immune complex vasculitis and Pityriasis lichenoides. Ultimately, LE was confirmed through immunofluorescence and serology, leading to successful treatment with hydroxychloroquine. This case likely presents as paraneoplastic LE.

***Conclusions*:** These cases underscore the challenges in diagnosing LE, given its diverse skin manifestations, which can resemble other conditions like psoriasis. Healthcare providers should thoroughly assess all skin morphologies presented by patients, as prompt and accurate diagnosis is crucial for effective management. LE should always be considered, even in cases initially suggestive of other dermatological conditions.

EP209 / #401

SARS-COV-2 Infection in Patients with Sjögren's Disease–A Single Centre Experience

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***Background and Aims*:** Sjögren's disease (SD) patients have some specific features that could make them even more prone to COVID 19 infection (mucosal dryness, altered exocrine gland excretions), but the data are limited. The aim of our study was to determine clinical and epidemiological characteristics of *SARS-CoV-2* infection in a well-defined cohort of patients with SD.

***Methods*:** Patients diagnosed with SD based on the ACR/EULAR 2016 classification criteria[1] between January 2016 and December 2019 were included. In March 2022 retrospective reviews of patient's medical record were performed regarding *SARS-CoV-2* infection in the period between March 2020 and February 2022. All patients with a confirmed *SARS-CoV-2* infection were contacted by phone to fulfill a questionnaire regarding their infection course.

***Results*:** Among 169 SD patients (94% female, mean age 58.2 ± 14.0 [23-88]) 66 patients had at least one *SARS-CoV-2* infection documented (39%). Most patients (48/66, 72.7%) had mild *SARS-CoV-2* infection. Five patients (7.5%) had severe infection requiring hospitalization. There were no death and thrombotic events due to infection. Males and younger patients were more at risk for *SARS-CoV-2* infection. We found no differences in baseline sicca symptoms, functional tests or ESSDAI at diagnosis in SD patients with and without SARS COV-2 infection.

***Conclusions*:** Almost 40% of our SD patients had at least one *SARS-CoV-2* infection during the 24month observation period. We did not find any association between the objective severity of mucosal dryness nor baseline systemic disease activity and the risk of SARS-COV-2 infection.

EP210 / #593

A Prospective Single-Centre Two-Year Follow-Up Study on the Detection of Antinuclear Antibodies (ANA) in Healthcare Workers After MRNA-Based Anti-SARS-COV-2 Vaccines

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***Background and Aims*:** This two-year follow-up study aimed to assess the persistence of antinuclear antibodies (ANA) in healthcare workers (HCWs) who received the BNT162b2 and mRNA-1273 vaccines.

***Methods*:** 155 HCWs were enrolled in the study. only 77 participants (60 females and 17 males, age range 26-67 years, median age 48) completed all scheduled blood draws and received 3 doses of either these mRNA vaccines. Blood samples were collected before vaccine administration (T0), at 3 (T1), 12 (T2), and 24 months (T3) after the first dose. ANA were assessed using indirect immunofluorescence on Hep-2 cells.

***Results*:** Out of the initial population, 52 subjects who tested negative for ANA at T0 were included in the final analysis. Among them, 35 participants completed sample collection until the last follow-up (T3). After excluding subjects who contracted COVID-19 between T2 and T3, the final population for analysis comprised 17 subjects. Two individuals, positive at T1, maintained their positivity until T3. At T2, 6 subjects became ANA positive, resulting in a total of 8 ANA-positive subjects . At T3 the total number of positive subjects became 7. All participants who were negative for ANA at T0 were surveyed to determine if they had undergone specialized rheumatology examinations.

Conclusions: Our research observed the onset of ANA in a subset of individuals who were initially ANA-negative. Actually, the follow-up showed that two participants displayed clinical manifestation of arthralgia. Further investigations would be necessary to understand the clinical implications of ANA development in vaccinated individuals.

EP211 / #718

Anti-Annexins Antibodies and Arterial Calcifications in Systemic Lupus Erythematosus

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***Background and Aims*:** Cardiovascular disease due to premature and accelerated atherosclerosis represents a major cause of morbidity and mortality in systemic lupus erythematosus

(SLE). Traditional risk factors do not fully explain accelerated atherosclerosis seen in SLE. It has been shown that annexin A2 and annexin A5 could have atheroprotective effects. The aim of our study was to evaluate the association between anti-annexins antibodies and arterial calcifications in patients with SLE.

***Methods*:** No pregnant women with SLE were enrolled prospectively in this study. Several imaging examinations have been employed to assess cardiovascular calcifications: multislice computed tomography, carotid ultrasound imaging, abdominal aorta ultrasound imaging, leg arteries ultrasound imaging, echocardiography. Anti-annexin A2 antibodies (aANXA2) and anti-annexin A5 antibodies (aANXA5) were detected by ELISA.

***Results*:** We included 69 patients. The median age at inclusion was 43.3 [22-74] years. Vascular calcifications in at least one arterial territory were detected in 47.5% of the SLE patients. The prevalence of vascular calcifications according to the arterial territory was as follows : coronary artery calcifications (26%), thoracic aorta calcifications (33.3%), abdominal aorta calcifications (26%), carotid artery calcifications (7.3%), leg arteries calcifications (7.2%) and valvular calcifications (14.4%). The prevalence of aANXA2 and aANXA5 was 10.4% and 6% respectively. We observed an association between the presence of aANXA2 and the presence of coronary calcifications ($P = .0095$).

***Conclusions*:** We observed a high prevalence of arterial calcifications in SLE. The association between antibodies directed against annexin A2 and coronary calcifications suggests that these autoantibodies could have a pro-atherogenic role. Further studies are needed to confirm these preliminary results.

EP212 / #299

Monogenic SLE

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***Background and Aims*:** SLE is an autoimmunity characterized by a set of clinical features. Its diagnosis is supported by laboratory, with anti dsDNA autoantibodies as the most critical finding. Recently, a small, well-defined group of SLE has been defined where a defect in a single gene defines *monogenic SLE*. The specification of genetics has elucidated several key mechanisms leading to the manifestations of SLE. These include complement defects, interferonopathies, DNA clearance defects, and defects in tolerance particularly of B lymphocytes. Clinical features overlapping with the SLE may also be seen in rasopathies, relopathies and some other monogenic diseases, especially those accompanied by vasculitis.

***Methods*:** Retrospective analysis of patients with complement disorders and positive anti dsDNA autoantibodies in a single center, analysis of genetic testing in the Immunodeficiency/Autoimmunity Panel at the national level.

***Results*:** Monogenic SLE is a rare disease. Mentioned methods detected a family with vasculitis, cutaneous presentation, neuropathy and cytopenias due to the mutation of TREX1. TREX1 is a 3'-exonuclease with an important role in DNA degradation and apoptosis. The aetiology has not yet been clearly established in other patients, and analysis of candidate genes and investigation of other indicated SLE patients is now underway.

***Conclusions*:** Mongogenic SLE is a very rare disease caused by defects in genes with important roles mainly in intracellular processes including cell defence and nucleic acid degradation. The list of about 30 genes currently described in this context is growing. Here we present the proven etiology in one family and ongoing genetic testing in other candidates.

EP213 / #877

Incomplete Systemic Lupus Erythematosus: Characteristics and Clinical Outcome

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Background and Aims: Incomplete systemic lupus erythematosus (iSLE) is a condition of patients with clinical and immunological signs of lupus who do not fulfill classification criteria for SLE

***Methods*:** iSLE (n=60) was defined by rheumatologists as clinical diagnosis, not fulfilling ACR or SLICCcriteria and had no classification or specific symptoms of other rheumatic diseases. The majority of the iSLE patients were female (97%), aged 38 [26-47] years.

***Results*:** The median age of iSLE diagnosis was 33 [25-42] years, disease duration was 12 [2-29] months. The clinical manifestations were as follows: Fever–30%, acute cutaneous lupus – 21%, subacute – 7%, discoid-2%, panniculitis-3%, non-scarring alopecia–10%, Raynaud phenomenon-5%, oral ulcers – 9%, joint involvement – 55%, serositis – 8%, nephritis – 10%, psychosis – 5%, migraine – 17%, leukopenia – 21%, thrombocytopenia – 14%, autoimmune hemolysis – 7%. Autoantibody profiles revealed the presence of ANA in 82% cases, anti-dsDNA - in 45%, anti-Sm - none, antiphospholipid antibodies (aPL) – in 37% of patients. Eighteen patients (30%) exhibited low complement. Evolution of iSLE to SLE occurred in 15 (25%) of these patients, 2(3%) - to antiphospholipid syndrome, 2 (3%) – to osteoarthritis, 1 (2%) - to Sjögren's syndrome, 11(18%)-to none-rheumatic diseases, with a median interval of 14 [5-35] months between iSLE onset and the other definite diagnosis. Twenty seven patients (45%) continue to be observed by a rheumatologist with a diagnosis of iSLE.

***Conclusions*:** The most commonly clinical features in patients with iSLE are joint involvement (55%), fever (30%), hematological manifestations (28%) and cutaneous lupus (23%); among immunological disorders are positive ANA,anti-dsDNA, more than a third of iSLE patients had aPL and hypocomplementemia. only quarter of iSLEpts were diagnosed with definite SLE within 14 months. Some patients with iSLE have serious organ involvement: nephritis (10%), serositis (8%), and up to 5% have neurologic symptoms. This may explain why iSLE patients should be treated with immunomodulatory medications.

EP214 / #1081

Immunological Disorders in Skin and Mucosal Lesions in Patients with Systemic Lupus Erythematosus

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***Background and Aims*:** In patients with SLE, the skin lesion is the second most common manifestation after the musculoskeletal system. The aim is to study the association between skin lesions and immunological markers of SLE.

***Methods*:** The study included 200 patients (169 women and 31 men), average age was

35.0 [26.0-43.0] years old. The duration of the disease was 63.0 [22.0; 158.0] months. APS was secondary in 39 patients. All patients were evaluated for skin lesions and its appendages. The immunological examination included a-dsDNA, C3 and C4 complement components, a-Sm, Ro/SS-A, La/SS-B, RNP-70, IgM and IgG aCL, IgM and IgG aß2HP1 by ELISA.

***Results*:** Active skin lupus and mucosal lesion was significantly associated with a-dsDNA, a-Sm positivity and low C3 and C4 levels. Acute CLE, chronic CLE, lupus chilblain and periungual erythema were associated with a-Sm positivity and low C3 and C4 levels. Significant associations were found between alopecia and low C3 levels, Ro/SS-A positivity. Low C3 and C4 levels were strongly associated with mucocutaneous vasculitis. Positivity for IgG-aCL, IgG-aß2GP1 was associated with livedo and comminuted hemorrhages. No significant associations were found between skin lesions in SLE and positivity for La/SS-B, RNP-70, IgM aCL, and IgM aß2GP1.

***Conclusions*:** SLE is always associated with immunological disorders, which is one of the important parts for diagnosis. The study of immunological markers is crucial not only for assessing activity, but also for predicting the development of skin manifestations of SLE.

Clinical manifestations	Immunological marker	χ^2_1 p; OR [95% CI]
Active skin lupus	a-dsDNA	12,56; 0,0004; 2,79 [1,57-4,96]
	a-Sm	7,48; 0,006; 3,44 [1,45-8,11]
	low C3 levels	11,29; 0,0008; 2,74 [1,15-4,96]
	low C4 levels	10,08; 0,001; 2,55 [1,44-4,57]
Acute cutaneous lupus erythematosus	a-Sm	9,01; 0,003; 3,27 [1,47–7,59]
	low C3 levels	7,49; 0,006; 2,84 [1,32-6,11]
	low C4 levels	6,59; 0,008; 2,40 [1,24-4,65]
Chronic cutaneous lupus erythematosus	a-Sm	10,18; 0,001; 3,46 [1,57–7,65]
	low C3 levels	13,33; 0,0003; 3,35 [1,72–6,53]
	low C4 levels	9,41; 0,002; 2,51 [1,39–4,52]
Lupus chilblain	a-Sm	10,34; 0,001; 5,53 [1,98-15,45]
	ow C3 levels	4,7; 0,03; 5,36 [1,19-24,00]
	low C4 levels	13,56; 0,0002; 9,00 [2,51-32,23]
Periungual erythema	a-Sm	7,03; 0,008; 4,89 [1,95-12,28]
	low C3 levels	9,22; 0,002; 8,23 [1,88-36,01]
	low C4 levels	10,71; 0,001; 4,69 [1,86-11,84]
Alopecia	Ro\SS-A	4,52; 0,03; 1,96 [1,05–3,66]
	low C3 levels	3,9; 0,049; 1,92 [0,99–3,69]
Mucosal lesion	a-dsDNA	6,99; 0,008; 4,44 [1,48-13,31]
	a-Sm	4,94; 0,03; 3,05 [1,23–7,54]
	low C3 levels	10,67; 0,001; 6,30 [1,84-21,63]
	low C4 levels	13,31; 0,0001; 4,98 [2,08-11,93]
Livedo	IgG-aCL	5,81; 0,02; 3,18 [1,29–7,84]
	IgG-aß2GP1	8,57; 0,003; 4,56 [1,65-12,58]
Comminuted hemorrhages	IgG-aCL	8,67; 0,003; 6,11 [1,89-19,78]
	IgG-aß2GP1	8,83; 0,003; 6,19 [1,91-20,02]
Mucocutaneous vasculitis	low C3 levels	4,44; 0,04; 4,60 [1,02-20,86]
	low C4 levels	10,53; 0,002; 7,57 [2,08-27,51]

Figure 1. The Relation of Immunological Markers and Skin Lesions in SLE.

EP215 / #311

Interstitial Lung Involvement in Rheumatoid Arthritis

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***Background and Aims*:** Rheumatoid arthritis (RA) is a systemic inflammatory disease primarily affecting synovial joints. Interstitial lung disease (ILD) is the most common manifestation of rheumatoid lung disease. Clinically significant RA-ILD occurs in nearly 10-15% of patients with RA. The aim of this study was to characterize the patients in the diffuse lung disease (DLD) consultation with RA-ILD and to identify the most frequent patterns of RA-ILD on high-resolution chest CT (HRCT).

***Methods*:** Retrospective analysis of patients in the DLD consultation with a diagnosis of RA-ILD.

***Results*:** N=8 patients, 62.5% female and 37.5% males, with an average age of 67.63 years old. 75% of patients had respiratory symptoms such as exertional dyspnea (37.5%) and dry cough (37.5%). The other 25% of patients were asymptomatic. All patients presented HRCT findings suggestive of interstitial pulmonary involvement. At the multidisciplinary team meeting was established that the patterns of RA-ILD on HRCT were: Usual interstitial pneumonia (UIP) (25%), fibrosing non-specific interstitial pneumonia (NSIP) (25%), ground glass opacities (25%) and bilateral centrilobular opacities (12.5%). one of the patients (12.5%) who had a diagnosis of RA combined with Sjogren's syndrome, presented with bilateral cysts on HRCT suggestive of lymphoid interstitial pneumonia (LIP). The most used therapeutic scheme was corticosteroid plus corticosteroid sparing agent in 75% of patients. one patient (12.5%) was under antifibrotic therapy.

***Conclusions*:** ILD is a serious complication of RA contributing to significantly increased morbidity and mortality. The predominant HRCT patterns are UIP or NSIP. Immunosuppressants remain the mainstay of therapy, but ongoing studies are exploring the role of antifibrotic therapy in patients with progressive fibrotic ILD.

EP216 / #328

Interstitial Lung Involvement in Systemic Sclerosis

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***Background and Aims*:** Systemic sclerosis (SSc) is a progressive and often devastating disease characterized by autoimmune dysfunction, vasculopathy, and fibrosis. Interstitial lung disease (ILD) is identified in the majority of patients with SSc and is the leading cause of SSc-related mortality with a prevalence of up to 30% and a 10-year mortality of up to 40%. The aim of this study was to characterize the patients in the diffuse lung disease (DLD) consultation with SSc-ILD and to identify the most frequent patterns of SSc-ILD on HRCT.

Methods: Retrospective analysis of patients in the DLD consultation with a diagnosis of SSc-ILD.

***Results*:** N=4, 50% female, with an average age of 62.75 years old. Three patients (75%) had respiratory symptoms: exertional dyspnea (50%) and dry cough (25%). one patient (25%) was asymptomatic. All patients presented HRCT findings suggestive of interstitial pulmonary involvement. At the multidisciplinary team meeting was established that the patterns of SSc-ILD on HRCT were: ground glass opacities (75%) and fibrosis with honeycomb in the lower lobes (25%). The most used therapeutic scheme was corticosteroid plus corticosteroid sparing agent (mycophenolate mofetil/methotrexate) in 75% of patients. The patient with a HRCT pattern of fibrosis is undergoing therapy with nintedanib.

***Conclusions*:** As ILD is the leading cause of death in SSc, screening for its presence with HRCT is essential. The data from the SENSCIS trial (2023) showed that nintedanib slows the progression of pulmonary fibrosis in patients with SSc-ILD irrespective of risk factors for progression. These results support the prompt initiation of nintedanib in patients with fibrosing SSc-ILD to preserve lung function and improve patient outcomes.

EP217 / #296

Granulomatosis with Polyangiitis Associated with Peripheral Vascular Disease

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***Background and Aims*:** Incidence of peripheral vascular disease was not well represented among patients with granulomatosis with polyangiitis (GPA). We present a case of

76-year-old female without underlying atherosclerotic risk factors, who presented with claudication history.

***Methods*:** Recently diagnosed GPA treated with immunosuppression on remission, currently presented with two weeks of claudication, significant weight loss, early satiety, and exertional dyspnea.

***Results*:** (Previous investigations) PANCA present Anti-MPO 85RU/ml (0-29RU/ml) PR3 34U/ml (0-20U/ml) Nasal biopsy proven lymphoplasmacytic inflammation eosinophil count <5 per hpf. Clinical and investigations confirmed GPA. Treated with immunosuppressant IV hydrocortisone and oral prednisolone, later achieved remission. This admission Arterial doppler ultrasound proven peripheral vascular disease. Recently hemoglobin dropped from 12.8 g/dL to 10.6 g/dL. Ferritin 1003 ug/L, ESR 80 mm/hr, CRP 61.9 mg/L, Anti-MPO 124 RU/ml. No tumor mass shown in CTAP PET-CT scan normal. Esophago-gastro-duodenoscopy and colonoscopy no active bleeding. Currently patient in relapse. No cardiovascular risk factor; normal blood pressure, total cholesterol 4.34 LDL 2.26 Hba1c 5.7%.

***Conclusions*:** GPA could predispose peripheral vascular disease in our case, which warrants early cardiovascular and peripheral vascular disease screening and risk factor control.

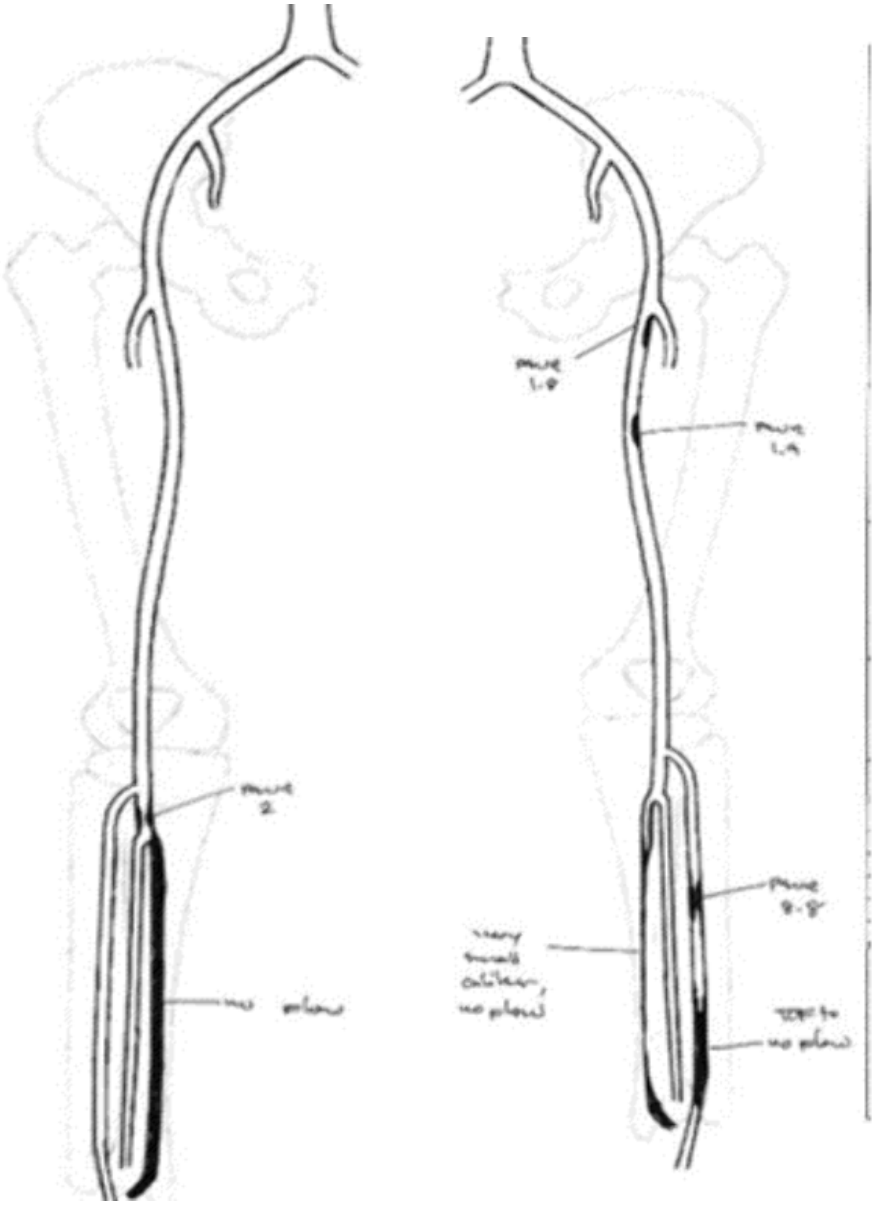

Figure 1. Arterial Doppler Ultrasound of Bilateral Lower Limb Showed Total Occlusion of Bilateral Posterior Tibial Artery and Occlusion of Left Distal Anterior Tibial Artery.

EP218 / #459

Chronic Urticaria Subtypes in Children: Intertwining the Causes and Continuing Despite Trigger Identification

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***Background and Aims*:** In chronic urticaria (CU) mast cell activation, incuding autoimmunity, play a role. The aim of our study wasto evaluate the causes and natural course of CU subtypes after defining triggers.

***Methods*:** 30 children's data (1-18 years old, an average age 9, 8 years, female predominance (67%)), diagnosed with CU between August 2019 -2023, were analysed.

***Results*:** Different potential triggers were simultaneously present in 83% of children with CU (in 15/5/3/2 children 2/3/4/5 different triggers, respectively). Specific IgE to inhalant allergens were present in 67% but in 65% of them they have no clinical meaning. In only two children CU worsened after contact with pets but avoiding them did not diminish CU. Infectious trigger was suspected in 47%. Children with parasitosis had less symptoms after the mebendazole treatment. In one child treated with macrolides CU ended afterwards but in others CU continued after antibiotic. Low serum diamine oxidase (DAO) level was found in 31% children with CU. All children benefited from low-histamine diet. In one girl with celiac disease gluten-free diet did not influence CU course. Half of CU cases had a physical trigger (53% cold urticaria, 33% dermographism). All children with inducible urticaria had also other triggers of CU. Detectable autoimmune antibodies were present in 10% of children with CU. one girl with CindU had previously systemic juvenile arthritis.

***Conclusions*:** Different potential triggers were found in 83% of children with CU. Low-histamine diet, mebendazole and sometimes macrolide treatment was associated with less symptoms of CU.

E-POSTER VIEWING 26: CLINICAL PRACTICE - THERAPY: CENTRAL NERVOUS SYSTEM AND AUTOIMMUNITY: EYE, SMELL AND PSYCHIATRY

EP219 / #288

Retinal Vasculitis: A Window to Neurolupus

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Background and Aims: Systemic lupus erythematosus (SLE) can be manifested by vasculitic phenomena, being retinal involvement rare. Which can be a signal of central nervous system affection.

***Methods*:** 33 year-old women with a history of cutaneous lupus without treatment, was admitted with bilateral retinal occlusive arterial and venous vasculitis with macular damage, oral prednisolone (1mg/kg) was started. on the reevaluation it was evidence of progression and she was hospitalized for further investigation. A physical examination revealed: cicatricial alopecia, chronic vasculitic lesion in the right malleolar region, active vasculitic lesion in the hallux and arthritis of the distal metacarpophalangeal joints. Laboratory workout showed thrombocytopenia, C4 consumption (9 mg/dL), positive antinuclear (1/1000) and dsDNA (213.6 UI/mL). Infection cause was excluded with evaluation of both blood and aqueous humors. The cranioencephalic magnetic resonance revealed a deep right temporal white matter lesion, suggesting inflammatory/vascular lesions and the positron emission tomography (PET) showed hypometabolism in the occipital cortex. Induction therapy was started with methylprednisolone pulses and maintenance therapy with rituximab, due concerns over fertility.

***Results*:** We are presented with a case of neuropsychiatric lupus (NPSLE) and once the treatment with glucocorticoids and rituximab was started no progression of lesions was reported.

***Conclusions*:** NPSLE treatment is controversial, being high-dose glucocorticoids and intravenous cyclophosphamide the cornerstone. Rituximab is considered a rescue therapy, although in young women with severe manifestations we considered that it has potential to become the first line therapy. This case also highlights the relevance of PET in the imagiologic diagnosis of NPSLE.

EP220 / #612

Cyclosporine Induced Neurotoxicity in a Patient with Behcet Disease

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***Background and Aims*:** Behcet's disease (BD) is chronic, multisystemic, inflammatory syndrome characterized by recurrent attacks of oral-genital ulcers, skin lesions, and ocular, musculoskeletal, vascular, central nervous system and gastrointestinal involvement. The aim of this abstract is to present the worsening of neuro Behcet disease, probably caused by a neurotoxicity of cyclosporine A, in a 33-year-old caucasian female patient with a severe ocular BD with recurring neurouveitis and secondary glaucoma.

***Methods*:** Her symptoms started 8 years ago with temporary loss of vision, together with aphtous and genital ulcers. The diagnosis was delayed and after some time she finally received intravenous methylprednisolone 120 mg/day which was tapered to 5 mg/day combined with cyclosporine A 5 mg/kg, administered by ophtalmologist. A few days after patient was admitted to our hospital with neurological symptoms: headache, scotomas and vertigo. Normal MRI of the brain, led us to the conclusion that Cyclosporin A might be the incriminated agent for the current state of the patient.

***Results*:** Cyclosporine A was stopped and the patient was given methotrexate and local corticosteroids that improved the clinical condition after a few days. Next we wanted to add TNF alpha inhibitor, but it was delayed because ophthalmologist was satisfied with the uveitis stabilization and because of concomitant serious urinary tract infection.

***Conclusions*:** Using cyclosporine A for treatment of BD is associated with neurotoxicity and/or accelerated development of CNS symptoms which can be cured by using another agent like methotrexate or TNF inhibitor.

E-POSTER VIEWING 27: CLINICAL PRACTICE - THERAPY: CHECK POINT INHIBITORS AND AUTOIMMUNITY

EP221 / #626

Checkpoint Inhibitors Autoimmune Side Effects – Too Much of A Price? Case Presentation

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***Background and Aims*:** Nivolumab is highly effective, as monotherapy or in combinations (with Ipilimumab), for treatment of patients with unresectable or metastatic melanoma and many other cancers. Autoimmune side effects include systemic and organ-specific disease, from mild to life-threatening severity. Their impact on the treatment response may be important.

Methods: We present two advanced melanoma cases, male, 72/62 years old. Despite initial tolerability of Nivolumab /Ipilimumab and good response on disease progression, both developed severe autoimmune musculoskeletal side effects.

***Results*:** Case 1. Melanoma stage IV, treated with Nivolumab and Ipilimumab with good response during 6 month, presenting with progressive pain and proximal muscle weakness after discontinuation, had good initial response to GC. Inflammatory immune myopathy, polymyalgia rheumatica and sensitive neuropathy were diagnosed and efficiently controlled with GC treatment and successful oncologic course. Case 2: Metastatic melanoma. The tumor size dramatically decreased during nivolumab treatment and over the following 15 weeks. Adverse events were diagnosed by rheumatologists: monoarthritis, severe erythrodermia that promptly responded to high-dose glucocorticoids (GC) but rebounded after GC tapering, late onset, non-reversible, rapidly progressive renal failure with haemodialysis and autoimmune progressive pneumonitis with respiratory failure and death

***Conclusions*:** Development of autoimmune disease during checkpoint inhibitor treatment for neoplastic diseases may correlate with efficacy and furthermore impact survival. High-dose and long-term GCs are effective but may increase mortality. Rheumatologists may be helpful in checkpoint inhibitors autoimmune side-effects management. Careful and prolonged follow-up, developing protocols and increase patient awareness are essential to improve ouctomes.

EP222 / #588

Bullous Pemphigoid (BP) Induced by Anti-PD1 Medication

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Background and Aims: In recent years, new cancer immune checkpoint inhibitors emerged and anti-programmed cell death protein 1 (anti-PD1) treatment have raised concerns about immune-related adverse events. It has been reported that 1% of treated patients will develop iatrogenic bullous pemphigoid (BP) with atypical clinical and biological presentation.

***Methods*:** A retrospective study in the immunology laboratory department of Toulouse University Hospital was conducted on a panel of 37 patients under anti-PD1 treatment with dermatologic manifestations and BP suspicion. Autoreactivity against the basement membrane zone (BMZ) has been explored by direct immunofluorescence on skin/mucosa biopsy, and in sera with indirect immunofluorescence on monkey esophagus (Werfen) and/or on NaCl-split skin sections (EuroImmun). This was completed with IgG anti-NC16A, anti-LAD1 (cleavage product of the BP180), anti-BP230 Ab identification by ELISA (Euroimmun).

***Results*:** This study highlighted 3 subgroups among anti-PD1/PDL1 treated patients with dermatological manifestations and BP suspicion. Group 1 (BP like patients) was biologically and clinically close to classical BP patients with anti-NC16A Abs and blisters. Group 2 (atypical BP-like patients) was characterized by skin biopsy positivity in 93% of patients but anti-NC16A/BP230 Abs negativity and anti-LAD1 positivity (67%). In group 2, clinical manifestations were less specific with more pruritus and rash and less blisters. Group 3 was seronegative.

***Conclusions*:** An important number of BP patients under anti-PD1 medication are seronegative to BP180 and BP230 antibodies despite strong clinical presentation, positive direct/indirect immunofluorescence and IgG LAD1 detection may help to characterize these patients. Then, anti-LAD1 Abs testing could help physicians to distinguish non-specific dermatological irAEs from BP.

EP223 / #455

Development and Evaluation of I-Tracker Pembrolizumab and I-Tracker Anti-Pembrolizumab Kits: Fast and Innovative Chemiluminescent Assays for the Monitoring of Patients Treated with Pembrolizumab

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***Background and Aims*:** Pembrolizumab is a humanized monoclonal antibody directed against the human cell surface receptor PD-1 and blocks its interaction with PD-L1, resulting in the activation of T-cell mediated immune response against tumor cells. Pembrolizumab is used for the treatment of patients with cancers. Therapeutic Drug Monitoring is currently proposed to provide useful information to clinicians to improve the efficacy of the treatment. Theradiag has just developed the innovative i-Tracker Pembrolizumab and i-Tracker Anti-Pembrolizumab kits: fast quantification of Pembrolizumab and Anti-Pembrolizumab antibodies fully automated on the random access i-Track[10] chemiluminescent analyzer.

***Methods*:** Analytical performances were assessed in using human serum samples spiked with Pembrolizumab or Anti-Pembrolizumab antibodies. Pembrolizumab from serum sample was captured by anti-idiotypic antibody coupled magnetic microparticles and anti-Pembrolizumab polyclonal antibodies conjugated to acridinium ester were used for the detection of Pembrolizumab. Anti-Pembrolizumab antibodies were captured according to Pembrolizumab coupled magnetic microparticles and detected with the use of Pembrolizumab conjugated to acridinium ester. Light emission was linked to the quantity of Pembrolizumab, or anti-Pembrolizumab antibodies presents in the sample.

***Results*:** The dynamic ranges of the assays were 1 to 100 µg/mL for Pembrolizumab and 10 to 1000 ng/mL for anti-Pembrolizumab antibodies. Pembrolizumab measurement showed high accuracy (recovery between 80% and 120%). High precision was reached for both assays (CV < 20%) and no interference was seen with biologic agents.

***Conclusions*:** i-Tracker kits are innovative assays which exhibit fast (<40min), accurate and reproducible results for the quantification of Pembrolizumab and Anti-Pembrolizumab antibodies. I-Tracker kits are valuable tools for the monitoring of patients treated with Pembrolizumab.

EP224 / #495

Development and Evaluation of I-Tracker Nivolumab and I-Tracker Anti-Nivolumab Kits: Fast and Innovative Chemiluminescent Assays for the Monitoring of Patients Treated with Nivolumab

Georges Khater[1], Simon Daviere[1], Guillaume Noguier[2], Amandine Puig[2]
[1]Marketing, Theradiag, Croissy Beaubourg, France
[2]R&D, Theradiag, Croissy Beaubourg, France

***Background and Aims*:** Nivolumab is a humanized monoclonal antibody directed against the human cell surface receptor PD-1 and blocks its interaction with PD-L1, resulting in the activation of T-cell mediated immune response against tumor cells. Nivolumab is used for the treatment of patients with cancers. Therapeutic Drug Monitoring is currently proposed to provide useful information to clinicians to improve the efficacy of the treatment. Theradiag has just developed the innovative i-Tracker Nivolumab and i-Tracker Anti-Nivolumab kits: fast quantification of Nivolumab and Anti-Nivolumab antibodies fully automated on the random access i-Track[10] chemiluminescent analyzer.

***Methods*:** Analytical performances were assessed in using human serum samples spiked with Nivolumab or Anti-Nivolumab antibodies. Nivolumab from serum sample was captured by anti-idiotypic antibody coupled magnetic microparticles and anti-Nivolumab polyclonal antibodies conjugated to acridinium ester were used for the detection of Nivolumab. Anti-Nivolumab antibodies were captured according to Nivolumab coupled magnetic microparticles and detected with the use of Nivolumab conjugated to acridinium ester. Light emission was linked to the quantity of Nivolumab, or anti-Nivolumab antibodies presents in the sample.

***Results*:** The dynamic ranges of the assays were 2 to 150 µg/mL for Nivolumab and 10 to 1000 ng/mL for anti-Nivolumab antibodies. Nivolumab measurement showed high accuracy (recovery between 80% and 120%). High precision was reached for both assays (CV were<20%) and no interference was seen with biologic agents.

***Conclusions*:** i-Tracker kits are innovative assays which exhibit fast (< 40min), accurate and reproducible results for the quantification of Nivolumab and Anti-Nivolumab antibodies. I-Tracker kits are valuable tools for the monitoring of patients treated with Nivolumab.

EP225 / #395

Comparison of Clinical Safety Between Standard Versus Extended Interval Dosing of Immune Checkpoint Inhibitors: A Real-World Retrospective Cohort Study

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***Background and Aims*:** Extended-interval dosing (ED) for immune checkpoints inhibitors (ICI) anti-PD-1 (nivolumab, pembrolizumab) or anti-PD-L1 (durvalumab) were approved based on population pharmacokinetic analyses that predicted a benefit-risk profile comparable to the standard dosing (SD) regimen. Since safety data in real-world conditions of use are lacking, the aim of this study was to compare the incidence and the risk factors of immune related adverse events (irAEs) between SD and ED regimen.

***Methods*:** We conducted a retrospective observational study across two oncology centers. The incidence of irAES in medical records of patients receiving either SD or ED regimen of ICI between January 1, 2019 and December 31, 2020 were analyzed using Cox regression model with time-dependent covariates.

***Results*:** Among 686 patients included 34.6% experienced at least one irAE of any grade and 11.4% presented at least one serious grade ≥ 3 irAE. No statistical difference was found between SD and ED regimen on the risk of grade ≥ 3 irAEs (adjusted HR 1.40, 95% CI: 0.71-2.76) but our results suggest an increased risk of any grade irAEs with ED regimen (adjusted HR 1.46, 95%CI: 1.00-2.12, $P = .048$). Pre-existing auto-immune condition was confirmed to be a risk factor of irAEs (HR 1.60; 95%CI: 1.17-2.20). Renal carcinoma was associated with grade ≥ 3 irAEs (OR 5.46; 95% CI: 1.48-20.21). However concurrent use of an immunosuppressive drug, radiotherapy or targeted therapy was not associated with an increased incidence of irAEs.

***Conclusions*:** These results suggest that ICI safety is not correlated to the dosing schedule. This has to be confirmed with ongoing clinical studies.

EP226 / #312

Immune-Mediated Adverse Effects in Lung Cancer Patients Undergoing Immunotherapy

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Background and Aims: The landscape of immunotherapy (IT) in lung cancer is rapidly expanding and immune checkpoint inhibitors (ICIs) have become crucial in the treatment of patients with metastatic and locally advanced lung cancer with remarkable improvement in overall survival. The aim of this study was to assess the incidence of immune-mediated adverse reactions (IMARs) and to characterize the patients with lung cancer undergoing IT.

***Methods*:** Retrospective analysis of patients with lung cancer undergoing IT between January 2022 and July 2023 in a district hospital.

***Results*:** N=47 patients, 17.02% female and 82.98% males, with an average age of 70.57 years old. The most common histological subtypes of lung cancer were Adenocarcinoma (ADC) (44.68%), Squamous cell carcinoma (29.79%), Small cell lung cancer (12.77%) and Small cell lung cancer / ADC (4.24%). Stage IVB was the most prevalent (36.17%), followed by stage IVA (27.66%) and stage IIIB (12.77%). The ICIs used were: Pembrolizumab (65.96%), Atezolizumab (17.01%), Nivolumab (12.77%) and Durvalumab (4.26%). 34% of patients had IMARs, being Pembrolizumab the main cause (83%). The following IMARs were identified: hyper/hypothyroidism (12.77%), hepatotoxicity (10.64%), colitis/mucositis (8.51%), rash (4.26%), nephritis (2.13%) and interstitial pneumonitis (2.13%). Regarding the severity of toxicity, 31.58% of IMARs were G1, 47.37% G2 and 21.05% G3. In the majority of cases (57.89%), the IMARs were controlled with supportive therapy. In the other 42.11%, IT was suspended, and corticosteroid was initiated. No lethal toxicities were documented.

Conclusions: IT boosts anticancer responses by stimulating the immune system. Most IMARs are modest and treatable with supportive therapies. However, as IT also has the potential to cause serious, even fatal adverse effects, early identification of toxicities is crucial in the monitoring of lung cancer patients undergoing IT.

E-POSTER VIEWING 28: CLINICAL PRACTICE - THERAPY: DIET AND AUTOIMMUNITY

EP227 / #607

Search for Correlation Between Vitamin D Levels and Positive Antinuclear Antibodies

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***Background and Aims*:** The aim of this study is to search for a correlation between vitamin D levels and immune system disorders, such as autoimmunity confirmed by the presence of positive antinuclear antibodies (ANA).

***Methods*:** The study included 261 individuals, primarily patients from the fields of hematology, nephrology, and rheumatology, as well as external patients, for one year. Vitamin D levels were measured using the 25-OH Vitamin D Reagent kit (ABBOTT) on the Alinity i analyzer using the chemiluminescence method. Depending on vitamin D levels, the participants were divided into three groups: sufficiency, relative deficiency and deficiency. ANA examination was performed using indirect immunofluorescence with HEp-2 Cells as the substrate (Antinuclear Antibody Test Zenit autoimmunity A.MENARINI diagnostics), with ANA titers >1/160 considered positive.

***Conclusions*:** The majority of participants, regardless of the presence or absence of positive ANA, showed relative deficiency of vitamin D. Vitamin D deficiency levels do not appear to be related to the presence of positive ANA. As most of the participants belong to hematology, nephrology, and rheumatology clinics of the hospital, this may be due to the intake of vitamin D supplements by many of these patients.

Table 1.

Vitamin D levels	Deficiency (<10.0ng/mL)	Relative Deficiency (10.0-30.0ng/mL)	Sufficiency (>30.0ng/mL)
ANA(-)	29 individuals-11.1% (mean 6.5ng/mL)	97 individuals-37.2% (mean 21.4ng/mL)	53 individuals-20.3% (mean 38.7ng/mL)
ANA(+)	8 individuals-3.1% (mean 6.8ng/mL)	44 individuals-16.9% (mean 20.6ng/mL)	30 individuals-11.5% (mean 36.7ng/mL)

EP228 / #451

Vitamin D Status and Cytokine Profile in Hospitalized COVID-19 Patients with Cholecalciferol Supplementation

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***Background and Aims*:** This study is aimed to analyse vitamin D metabolites and cytokine expression levels in hospitalized COVID-19 patients with oral bolus cholecalciferol supplementation.

***Methods*:** This study was a stage of the open intervention randomized study conducted in Almazov National Medical Research Center. A total of 44 hospitalized patients comparable in demographic, clinical, laboratory and instrumental baseline characteristics with moderate/severe COVID-19 were included. All patients had similar dose of concomitant corticosteroid therapy. Twenty-two patients received 50 000 IU cholecalciferol on the 1st and the 8th days of hospitalization. Serum 25(OH)D, 1,25 $(OH)_2D$ and 28 plasma cytokines (MILLIPLEX MAP HUMAN High SENSITIVITY T Cell Magnetic Bead Panel) were estimated for each group initially and on the 9th day of hospitalization. This work was financially supported by the Ministry of Science and Higher Education of the Russian Federation (Agreement No. 075-15-2022-301).

***Results*:** initially there were no differences in 1,25$(OH)_2D$ and cytokines levels in patients with vitamin D deficiency and normal 25(OH) D. Baseline 25(OH)D level was positively associated with an anti-inflammatory IL-10 level (r = 0.36, *P* = .021). Obese patients had lower pro-inflammatory cytokines MIP-3a (15.6 & 17.9, *P* = .041) and IL-1b (2.0 & 2.45, *P* = .011) in comparison with nonobese patients. 1,25$(OH)_2D$ and cytokine expression levels were not different in groups with vitamin D supplementation and without it.

***Conclusions*:** 25(OH)D level was positively associated with an anti-inflammatory immune response, but cholecalciferol supplementation at a total dose of 100 000 IU did not affect vitamin D active form and cytokine expression levels. This fact may be explained by corticosteroid therapy impact.

EP229 / #791

Prevalence of Malnutrition in Patients with Rheumatic Diseases (RDs): A Single Center Study

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***Background and Aims*:** Patients with RDs experience clinical manifestations and nutritional challenges that pose them at higher risk of developing malnutrition. on the other hand, malnutrition is associated with more complications, augmenting morbidity and mortality rates. Hence, we aimed to determine the prevalence of malnutrition among patients with RDs and compare two screening malnutrition tools to assess their appropriateness for this population.

***Methods*:** A cross-sectional design was followed and a total of 148 inpatients and outpatients of the Department of Rheumatology and Clinical Immunology, situated at the University General Hospital of Larissa were recruited between November–July 2023. The Global Leadership initiative on Malnutrition (GLIM) criteria and the Subjective Global Assessment (SGA) were collected for all patients and Body Mass index (BMI) was calculated as an additional, crude measure of malnutrition.

***Results*:** The majority (83.1%) of the patients were malnourished according to the GLIM criteria, 11.5% were malnourished according to the SGA (*P* = .046) and 4.1% were underweight (*P* = .048) as determined by their BMI. No difference was observed between the SGA and BMI diagnoses. The GLIM and SGA agreed on malnutrition diagnosis in 11.5% of the patients and the GLIM and BMI agreed on 4.1%.

***Conclusions*:** Patients with RDs exhibit a high prevalence of malnutrition according to the GLIM criteria, while both the SGA and the BMI appear to underdiagnose malnutrition in this population.

EP230 / #771

The Influence of to the Mediterranean Diet on the Activity of Rheumatoid Arthritis

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Background and Aims: The Mediterranean diet (MD) is considered optimal for patients with RA due to its beneficial effect on joints and cardiometabolic disorders and anti-inflammatory effect. The aims of this study were to determine difference in MDSS score between patients with RA and healthy controlss matched by age and sex and to determine the association of the MDSS score with RA activity and functionality of RA patients.

***Methods*:** This cross-sectional study included 80 RA patients and 80 healthy controls. The MDSS score was calculated using MSDD questionnarie

***Results*:** There were no statistically significant difference in MDSS score between the RA group and the control group (7.57±4.11 *vs*.7.29±3.61, *P* = .661). We did not find a significant correlation of MDSS score neither with DAS28 (r=0.031, *P* = .993) and HAQ score (r=0.222, *P* = .062). Furthermore, in both groups, the mean value of the MDSS score was low, but numerically it was slightly higher in patients with RA. The mean value of the body mass index in patients with RA was 25.6±4.2, which is in concordance with low adherence to the MD. This certainly influences the RA mainly due to proinflammatory effect of obesity.

***Conclusions*:** It was shown that non-adherence to the MD can have a negative overall impact on RA activity, patient functionality, and reduced quality of life. The education of our patients about the importance of diet is necessary in order to prevent the development of unwanted events.

E-POSTER VIEWING 29: CLINICAL PRACTICE - THERAPY: IMMUNOMODULATION

EP231 / #709

Drug-Induced Lupus; A Pseudo Effect of Tocilizumab

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Background and Aims: Anti-inflammatory treatments in autoimmune and inflammatory rheumatic arthritides (AIIRD), target pro-inflammatory cytokines, are generally effective with a good safety profile. Reports exist regarding anti-TNF-related autoimmune adverse events (AE's) such as demyelinating diseases and drug-induced lupus. Our observations regarding the effects of Tocilizumab (TCZ), an IL-6 receptor antibody, on decreasing complement levels, necessitate to understand the potential risk for drug-induced lupus.

***Methods*:** We report a case-series with AIIRD effectively treated with tocilizumab, who developed low complement levels, and were suspected to have drug-induced systemic lupus erythematosus (SLE).

***Results*:** Case series, seven cases of suspected SLE in 6 patients receiving tocilizumab, mainly for rheumatoid arthritis (RA) in different treatment lines, exhibiting complement drop. Although drug-induced AE's were acknowledged, but without a definitive SLE diagnosis.

***Conclusions*:** Tocilizumab, a biological drug for rheumatic diseases, can reversibly lower complement levels with or without ANA rise. This pseudo-SLE effect appears benign, likely not due to immune complexes activation or precipitation, requiring no urgent cessation of an otherwise effective treatment, nor additional investigation or treatment for a genuine SLE.

Table 1. Case Series. Cdmard's=Conventional Disease-Modifying-Anti-Rheumatic-Drugs, +:Rf=Positive Rheumatoid Factor,++:Dual Positive Acpa=Anti-Citrullinated-Peptide-Antibodies/Rf. Ana=Anti-Nuclear-Antibodies. Gca=Giant-Cell-Arteritis. Cases 5 and 6: The Same Lady.

Case no.:AIIRD/serology/ TCZ-reatment line after c-DMARD's(no.)/TCZ-duration to hypocomplementemia(m)	Gender/Age at TCZ treatment(y)	Signs and symptoms/ ANA-titer/complement drop	Final diagnosis/ TCZ-switch
1:RA++/2/23	F/60	Elevated creatinine, proteinuria, neutropenia/low/ C3	Hypertension-related/TCZ
2:RA+/2/2	F/73	fatigue, xerostomia/high/C4	Sjogren's syndrome/TCZ
3:GCA/1/20	M/77	paresthesiae, proteinuria/negative/C3	Diabetic neuropathy-nephropathy/ TCZ
4:RA+/2/8	M/38	myalgia/negative/ C3,C4	RA relapse/Baricitinib
5:RA+/2/3	F/46	pancytopenia/ moderate/C4	TCZ-induced cytopenia after mone marrow biopsy/Adalimumab
6:RA+/7/0.5	F/56	severe neutropenia/negative/C4	TCZ-induced cytopenia/Abatacept
7:RA-/4/18	F/48	arthralgia/high/ C3,C4	Rhupus syndrome/Rituximab

EP232 / #782

A Fas-Dependent Mechanism by Which Janus Kinase Inhibitor (JAKi) Drugs Downregulate CD8+ T Cell Clonal Expansion and Alopecia Areata (AA) in Mice

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Background and Aims: We sought to understand how CD8+ T cells are inhibited by JAKi, currently in clinical use for several autoimmune disorders. The initial hypothesis was that via cytokine receptor inhibition, JAKi would directly block CD8+ T cell basal survival, growth and clonal expansion, but results did not match this expectation.

***Methods*:** In vitro, OT1 TCR transgenic T cells were stimulated with peptide ligands of varying stimulatory potency followed by flow cytometry, cell division, and viability analysis. In vivo, we used the C3H/HeJ inbred mouse model of AA, grafting non-AA skin onto full-disease alopecia universalis recipient mice, thence measuring hair loss-versus-growth on the new grafts.

***Results*:** We observed that JAKi inhibited OT1 CD8+ T cell clonal expansion as expected. However, when anti-Fas ligand (FasL) blockade was added, clonal expansion and CTL capacity were rescued. We tested whether JAKi efficacy requires Fas-mediated death in vivo using the C3H/HeJ inbred mouse model of AA. JAKi (Tofacitinib) inhibited the autoimmune reaction and favored hair regrowth in ~90% of mice; adding anti-FasL blocking antibody reduced the mouse responder frequency to this drug to ~50% at three weeks ($P < .05$, log-rank and chi-square tests). Data for later timepoints are forthcoming.

***Conclusions*:** These data suggest that JAKi drugs block CD8+ T cell responses by Fas-dependent death of dividing effector cells. An updated model suggests why JAKi treatment must be continual (some T cells being Fas-resistant) and identifies a second pathway where pharmacological targeting might be focused for improved therapeutic efficacy.

EP233 / #571

Low Blood Levels Beta-2-Glycoprotein-I Are Associated to Poor Outcome in Influenza Patients

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Background and Aims: Respiratory viral infections such as influenza or COVID-19 can be complicated by a an intense systemic inflammatory response syndrome and respiratory distress syndrome that can cause death. Beta-2-glycoprotein-I (B2GPI), is the main target of antiphospholipid syndrome. Physiologically, it is a scavenger plasma protein that removes dead cells debris, and has anticoagulant and anti-inflammatory functions. Recently, low B2GP1 levels have been associated with poor outcome in patients with sepsis and ventilatory failure in COVID-19. To identify biomarkers that allow identification of influenza patients at risk of developing hyperinflammation and serious complications of influenza and obtaining greater knowledge of the pathogenesis of these complications.

***Methods*:** A prospective observational study that included 792 influenza patients consecutively admitted to Hospital 12 de Octubre (Madrid, Spain) in the 2017/18 and 2018/19 influenza epidemics, before COVID-19 pandemics. In all of them, the markers associated with the early inflammatory response of the immune system were determined.

***Results*:** The risk factors associated with the evolution to severe forms of the disease were low levels of B2GP1 (OR: 5.43), smoking (OR: 3.41), high levels of ferritin (OR: 2.83) and CRP (OR: 2.73). In addition, low B2GP1 levels were associated to ventilatory failure (OR: 4.25). Association of severe course of antiphospholipid antibodies was not statistically significant.

***Conclusions*:** Low levels of B2GP1 behave as the main independent risk factor for complications and poor outcome, especially respiratory distress, in patients with influenza. Therefore, replacement of the deficient protein could be a new immunomodulatory therapeutic alternative in these patients.

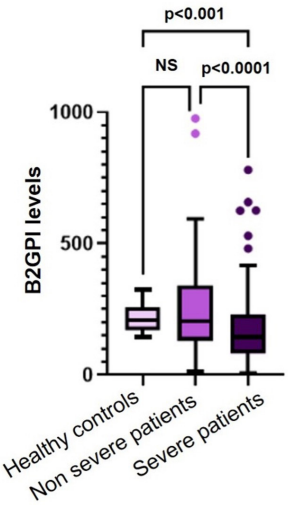

Figure 1.

EP234 / #322

Hit The Road JAK: Vascular Pathways in Autoimmunity

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Background and Aims: The Renin-Angiotensin-Aldosterone system (RAAS) has been implicated in the regulation of the cardiovascular system and linked to rheumatoid arthritis (RA). Little information has become available on the effects of Janus kinase (JAK) inhibition on RAAS. here we studied the effects of 12-month tofacitinib treatment on angiotensin converting enzyme (ACE), ACE2 production and ACE/ACE2 ratios in RA along with numerous other biomarkers.

***Methods*:** Thirty RA patients were treated with tofacitinib in this prospective study. Serum ACE concentrations were assessed by ELISA. ACE2 activity was determined by a specific quenched fluorescent substrate. ACE/ACE2 ratios were calculated. We also determined common carotid intima-media thickness (ccIMT), brachial artery flow-mediated vasodilation (FMD) and carotid-femoral pulse-wave velocity (cfPWV) by ultrasound. C-reactive protein (CRP), rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) were also determined. All measurements were performed at baseline, as well as after 6 and 12 months of tofacitinib treatment.

***Results*:** After the dropout of 4 patients, 26 completed the study. Tofacitinib treatment increased ACE levels after 6 and 12 months, while ACE2 activity only transiently increased at 6 months. The ACE/ACE2 ratio increased after one year of therapy ($P < .05$). Logistic regression analyses identified correlations between ACE, ACE2 or ACE/ACE2 ratios and RF at various time points. Baseline disease duration also correlated with erythrocyte sedimentation rate (ESR) ($P < .05$). one-year changes of ACE or ACE2 were determined by tofacitinib treatment plus ACPA or RF, respectively ($P < .05$).

***Conclusions*:** The effect of tofacitinib on RAAS provides a plausible explanation for the cardiovascular effects of JAK inhibition in RA.

EP235 / #491

Is It Metabolism That Stands Behind the Dysfunction of T-Regulatory Cells in Autoimmunity?

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***Background and Aims*:** A lowered number or dysfunction in regulatory T-cells is a component of numerous autoimmune diseases. The current approaches focus on how to adjust the cell machinery and use it in the treatment of autoimmune diseases. The study aims to assess whether metabolic activity in T-cells may vary in health and autoimmunity and whether it is connected with cell function.

***Methods*:** We used flow-sorted T-regulatory and T-effector cells from type 1 diabetic patients (n=14) and healthy blood donors (n=14). Cells were cultured for 11 days under GMP conditions. on day 11 cells were harvested, washed, and suspended in PBS. The second research stage involved the modification of culture conditions to imitate hypo-, hiper- and normogly-

cemic conditions. Here, we cultured cells only from healthy donors (n=7). The preparation process was performed in accordance with the first-step protocol. Cells were analyzed using spectrophotometry to determine the activities of hexokinase, glucose-6-phosphate dehydrogenase, isocitrate dehydrogenase, lactate dehydrogenase, aconitase, and fatty acid synthase. Cell purity and phenotype were assessed using flow cytometry.

***Results*:** There were differences in the activity of isocitrate dehydrogenase and fatty acid synthase of T-regulatory and T-effector cells from type 1 diabetic patients. Additionally, T-regulatory cells cultured in conditions with a limited concentration of glucose are characterized by the lowered activity of isocitrate dehydrogenase.

***Conclusions*:** Differences in enzymatic activity may indicate that Tregs use different energy sources than Teffs to fuel their activity and support function. Moreover, these results may point out pathological mechanisms underlying autoimmunity which will help to design innovative treatment methods in the future.

EP236 / #398

T-Cell Immunomodulation via Peptides Targeting the BTLA-HVEM Complex

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Background and Aims: The BTLA-HVEM complex, an inhibitory immune checkpoint, has recently gained much attention as one of the pathways vital for T cell responsiveness to various stimuli. Based on our previous studies on peptides targeting the BTLA-HVEM complex, we selected the most promising compounds. Here, we report the immunomodulatory potential of five peptides, named Pep(1)-Pep(4) targeting HVEM and Pep(5) targeting BTLA, on the activity of T cells.

***Methods*:** Isolated T cells from healthy individuals were exposed to the examined peptides alone or in combination with a TCR stimulus for 3-5 days. Then flow cytometry analysis was performed. We evaluated the expression of T-cell activation markers and changes within the T-cell memory compartment. with the DCT method, we evaluated the impact of the examined compound on T-cell proliferation. Finally, we assessed T cell apoptosis with the annexin V and 7-AAD staining.

***Results*:** Our results showed the immunomodulatory potential of the examined compounds when applied simultaneously with the CD3/CD28 mAb. The peptides exposure led to an increased percentage of CD4+ and CD8+ T cells expressing CD69 and CD25, accompanied by changes in cell proliferation rate and shifts in the T cell memory compartment.

***Conclusions*:** Based on the obtained results, we hypothesize that the immunomodulatory properties of the examined compounds may differ depending on the T cell activation state. We showed that Pep(2) and Pep(5) were the most promising compounds, displaying a putative immune-restoring function.

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E-POSTER VIEWING 30: CLINICAL PRACTICE - THERAPY: IVIG AND NATURAL AUTOANTIBODIES

EP237 / #809

Regulatory Role of Natural Autoantibodies in Hashimoto's Thyroiditis and Pregnancy

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***Background and Aims*:** In autoimmune diseases, the regulatory role of natural autoantibodies (nAAb) in tolerance induction is well known, but their effect on the development of fetal tolerance during pregnancy is not yet clear. The aim of the present study was to identify IgM and IgG nAAbs against mitochondrial citrate synthase (CS), heat shock proteins (Hsp60 and Hsp70) and IgG nAAbs against cytokines important during pregnancy.

***Methods*:** Serum samples from normal and Hashimoto's thyroiditis (HT) pregnant women in the first and third trimesters were compared with samples from healthy control and HT women. Measurements were performed using in-house developed ELISA kits and MILLIPLEX anti-cytokine autoantibody kit.

***Results*:** Our results show that IgM nAAb against CS are elevated, while against Hsp60 and Hsp70 are lower in healthy pregnant women than in HC. Anti-Hsp60 and Hsp70 IgG nAAb levels are elevated in HT patients compared to HC, but diminished during their pregnancy. A regulatory, scavenging role of IgM nAAbs against Hsp60 and Hsp70 is hypothesized in pregnancies. The opposite changes in the levels of natural IgG autoantibodies against Th1 and inflammatory cytokines and BAFF, responsible for B-cell activation during pregnancy also support a regulatory role of these autoantibodies on cytokine availability and activity.

***Conclusions*:** We hypothesize that upon a prompt immunological trigger like pregnancy, the physiological nAAbs exhibit a moderate plasticity and inducibility to recent antigenic triggers to regulate immune response and tolerance. Supported by RRF-2.31-21-2022-00012 "National Laboratory on Human Reproduction."

EP238 / #350

Low-Dose Intravenous Immunoglobulin in Ocular Myositis

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***Background and Aims*:** Ocular Myositis (OM) is an inflammation of the orbital region that predominantly affects the extra-ocular muscles (EOM). It represents about 8% of idiopathic orbital inflammatory (IOM) diseases, diagnosed through clinical, radiological, and sometimes histopathological assessments. Corticosteroids are the mainstay of treatment, but some patients do not respond adequately or suffer from steroid-related side effects. Recurrences are managed using high-dose steroids, immunosuppressive drugs, biological agents, or intravenous immunoglobulins (IVIg)

***Methods*:** In 2014, a 62-year-old woman developed left exophthalmos without other significant symptoms. Initial tests ruled out thyroid orbitopathy, while an MRI revealed abnormal thickening and enhancement in the left EOM.

Additionally, there was enhancement in retro-orbital fat and periorbital soft tissue structures. Further laboratory analyses were conducted to exclude lymphoproliferative disorders, sarcoidosis, or IgG4-related diseases. Although serum protein electrophoresis was normal, low levels of serum immunoglobulin were detected, along with a deficiency in the IgG2 subclass. The patient had already undergone high-dose corticosteroid therapy elsewhere, which provided partial relief from ocular muscle inflammation.

***Results*:** Given her persistent IgG2 subclass deficiency, she was subsequently treated with low-dose IVIg (20 g), which not only stabilized serum immunoglobulin levels but also achieved lasting remission from OM.

***Conclusions*:** While literature on the use of IVIg in OM is limited, low-dose IVIg has shown promise in various autoimmune diseases. A previous case treated with low-dose subcutaneous immunoglobulin (0.2 g/kg/week) has also been reported. In this instance, low-dose IVIg effectively controlled the disease, highlighting its potential as a treatment option for OM.

EP239 / #368

Effectiveness of Intravenous Immunoglobulin Treatment for Refractory Chronic Spontaneous Urticaria in Two Patients with Common Variable Immunodeficiency

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***Background and Aims*:** Common Variable Immunodeficiency (CVID) is a complex syndrome marked by recurrent infections often leading to diagnostic challenges and potential misidentification. This report focuses on a peculiar case where CVID initially presented itself as chronic spontaneous urticaria.

***Methods*:** A 48-year-old woman presented to our clinic with diffuse urticaria and angioedema episodes that started in 2017, with exacerbations occurring during the perimenstrual period and following infectious episodes and vaccinations. These symptoms were poorly responsive to steroid and antihistamine therapies. Over the years, we attempted various therapeutic strategies, including a one-year course of omalizumab and subsequently six months of cyclosporine A, both of which provided no relief. Additionally, the patient reported recurrent infectious episodes, particularly affecting the urinary tract. Laboratory test showed elevated inflammation markers and hypogammaglobulinemia with deficits in all IgG subclasses. Further laboratory investigations were carried out: screenings for HIV, HBV, HCV, CMV, EBV, HHV8, Mantoux, anti-Bartonella, anti-Borrelia antibodies, parasitological stool exam and coproculture. All results returned negative. Anti-tetanus antibody levels at baseline and four weeks after a booster showed non-protective levels. Lymphocyte typing indicated defective B lymphocyte maturation.

***Results*:** According to the ESID criteria, a diagnosis of CVID associated with chronic urticaria was established. It was also important to exclude the association with autoimmune diseases, which often overlap with chronic urticaria and CVID.

***Conclusions*:** Treatment with intravenous immunoglobulin (IVIg) at a monthly dosage of 20 g was effective in reducing both the frequency of urticarial exacerbations and the occurrences of infectious episodes.

EP240 / #878

Refractory Dysphagia in a Patient with Inflammatory Myopathy

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Background and Aims: inflammatory myopathies (IM) are a heterogeneous group of autoimmune disorders with chronic muscle inflammation and severe manifestations, including interstitial Lung Disease (ILD) and dysphagia, which must be treated rapidly to diminish morbidity. The aim is to report a patient with refractory dysphagia to different treatments.

Methods: Case report on a patient with refractory dysphagia.

***Results*:** A 43-year-old female started in 2010 with hair loss, Raynaud, arthralgias, and skin thickening; she received hydroxychloroquine and prednisone with limited improvement. In 2015, she developed "puffy fingers," muscle weakness, Gottron and Holster signs, and elevated creatine kinase (CK), positive antinuclear antibodies with negative myopathy-associated antibodies. Methotrexate, cyclosporine, and Rituximab provided limited relief. Due to progressive dysphagia, she started intravenous immunoglobulin (IVIg) therapy in 2017. Despite treatment, her condition has not improved.

Discussion: The treatment of IM in refractory cases includes IVIg or biological therapy (rituximab, abatacept, etc), nevertheless, our patient has not responded. Schrey *et al.*found that injection of botulinum toxin (BT) in the cricopharyngeus muscle (CM) alleviates dysphagia in 100% after 12 months, which is supported by the results of Witting *et al., 13* patients with dystrophy and myositis were included and injected with BT; 50% of patients improved after four months. Our patient has not received this treatment but will be given the option.

***Conclusions*:** Refractory dysphagia can be difficult to treat even after IVIg or biological therapy. Injection with botulin toxin can be a good option since previous studies have shown positive results.

Table 1. Control Laboratories.

Test	Result	Normal value
Chemistry panel		
Glucose (mg/dL)	97	70 - 100
Urea (mg/dL)	94	15 - 45
Creatinine (mg/dL)	1.66	0.51 - 0.95
Uric Acid (mg/dL)	9.7	2.6 - 6.0
Sodium (mEq/L)	137.0	136 - 148
Potassium (mEq/L)	4.6	3.5 - 5.2
Proteins (g/dL)	7.4	6.5 - 8.2
Albumin (g/dL)	4.0	3.6 - 5.5
Bilirubin total (mg/dL)	0.42	0.1 - 1.1
AST (U/L)	97	7 - 40
ALT (U/L)	61	7 - 45
Transferrin (mg/dL)	187	200 - 360
CK total (U/L)	10230	<10 - 170
CK-MB(U/L)	152	<10 - 25
Vitamin D (25-OH) ng/mL	31.7	30 - 100
Hematic biometry		
White Blood Count (K/ µL)	4.73	4.0 - 10.8
Lymphocytes (K/uL)	1.46	1.0 - 4.8
Hemoglobin (g/dL)	8.57	11.7 - 15.7
Red Blood Count (M/µL)	2.91	3.8 - 5.2
Platelets (K/ µL)	313	130 - 440

AST: Aspartate transaminase. ALT: Alanine transaminase. CK: Creatine Kinase.

E-POSTER VIEWING 31: CLINICAL PRACTICE - THERAPY: GASTRO INTESTINAL, LIVER AND AUTOIMMUNITY

EP241 / #1088

Crohn's Disease and Hypnosis : A Focus on Lymphocyte Subsets

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Background and Aims: Crohn's disease (CD) is an autoimmune disease, caracterised by bowel inflammation, with periods of relapse and periods of remission. Local inflammation is mediated by proinflammatory cytokines and immune cells. Hypnosis could be an effective complementary approach for the treatment of CD ; since the vagus nerve regulates inflammation, hypnosis could help in modulating inflammatory factors and thus maintaining remission. The objective of this study was to explore lymphocyte subsets in CD affected patients treated by classical treatments and hypnosis.

***Methods*:** 35 patients affected by CD in remission phase were included in Grenoble Alpes University Hospital: 18 patients treated with anti-TNFα monoclonal antibodies or other immunosuppressive drugs, and 17 patients treated with the same classical CD treatments and, in addition, participating to eight hypnosis sessions. A deep analysis of lymphocyte subsets was performed by flow cytometry, and different T, B, NK and NKT subsets have been compared by ANOVA test between the two groups of patients during the follow-up at 3 and 6 months.

***Results*:** Between the two groups of patients with or without hypnosis no statistically significant difference was observed concerning lymphocyte subsets. The overall assessment of patients' stress and quality of life is currently ongoing, as well as the quantification of cytokines in the sera of the patients.

***Conclusions*:** Hypnosis could be an interesting complementary approach for the treatment of CD ; further studies are needed, focusing in the exploration of immune cells and cytokines in blood and local tissues in a larger cohort of patients.

EP242 / #855

Primary Biliary Cirrhosis Associated with Sjogren Syndrome: A Case Report

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Background and Aims: Primary biliary cirrhosis (PBC) is a rare slowly progressive autoimmune disease of the liver that primarily affects women aged between 40 and 60. PBC often manifests with extrahepatic conditions as is the case with Sjogren syndrome (SS).

***Methods*:** We report a case of a 60-year-old female with a diagnosed primary biliary cirrhosis treated with UDCA (ursodeoxycholic acid a250mg twice daily). After the diagnosis of PBC was made the patient had a consult with a rheumatologist for elevated ANA levels, but at the time there was no need for prescribing additional medication. 6 years after the beginning of the disease the patient had an onset of sicca symptoms dry mouth, eyes and joint pain. Her ANA and AMA results from the immunological tests are positive after all this time. A treatment with bisphosphonates was started for a diagnosis of osteoporosis confirmed with a dexa scan. Hydroxychloroquine and topical pilocarpine was started as a standard therapy for SS. Other than this the patient was started with a low dose of azathioprine (50 mg/daily) and oral corticosteroid prednisolone.

***Results*:** The transaminase levels during the whole period of the disease were slightly elevated but the alkaline phosphatase had a drop in the levels.

***Conclusions*:** The triple combination of UDCA, azathioprine and prednisolone is superior in relation to the monotherapy with UDCA for slowing her progression of the disease, but more studies are needed for monitoring the effect it has over the biochemical and clinical sign of the patient with PBC associated with SS.

E-POSTER VIEWING 32: CLINICAL PRACTICE - THERAPY: NOVEL THERAPIES – CHECKPOINT INHIBITORS, BIOSIMILARS, CANNABIS, MUSIC

EP243 / #656

Immune Checkpoint Inhibitors and Autoimmunity – More Than Side Effects

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Background and Aims: Immune checkpoint inhibitors (ICIs) have improved dramatically the prognosis of many formerly fatal malignancies such as melanoma. Through blocking signals of tumor cells, ICIs inhibit the process of cell activation and as result causing malignant cells growth retardation. The cytotoxic T-lymphocyte antigen number 4 (CTLA-4) inhibitor was the first molecule to be discovered. The invention was followed by the introduction of anti-PD-1 (pembrolizumab and nivolumab) and anti-PD-L1 antibodies (atezolizumab, durvalumab, avelumab), approved for the treatment of various malignancies. Secondary to their direct action on the immune system and key immune cells, the immune related side effects of ICIs, known as immune-related adverse events (irAEs) have been extensively documented and studied. Among others, hepatitis, colitis, abnormal thyroid function, and central nervous system (CNS) manifestations were described in medical literature.

***Methods*:** Recently, the concerned irAEs were shown to represent more than merely an immune-related side effects of ICIs treatment. Interestingly, patients diagnosed with autoimmune diseases were excluded from clinical trials investigating ICIs or enrolled with caution in come studies.

***Results*:** Subsequently, autoimmune diseases developing secondary to ICIs drugs have been reported. For instance, GI tract inflammatory conditions, hepatitis, cutaneous manifestations, all requiring and subsiding after systemic corticosteroid treatment are common following ICIs administration.

***Conclusions*:** Navigating through the immune-autoimmune reactions triggered by ICIs, we aimed to shed light on the mechanisms related to the emergence of autoimmune diseases following ICIs therapy.

EP244 / #427

Switching from Original to Biosimilar Etanercept SB4 in Rheumatoid Arthritis and Axial Spondyloarthritis: The Experience from 2 Romanian Academic Centers

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Background and Aims: The biological therapy in rheumatology field has achieved an extreme broadening during the last years, especially after the biosimilar development. To analyze the maintenance of remission and low disease activity in patients switched from etanercept original to its biosimilar SB4

***Methods*:** Patients diagnosed with rheumatoid arthritis (RA) and axial spondylarthritis (axSpA) (non-radiographic and radiographic axSpA) initially receiving "reference" etanercept for their active disease according to the local recommendations underwent non-medical switch to the same etanercept biosimilar SB4. Data were collected from patients' files at switch and every six months (disease activity, therapeutic response, safety); patients were followed in two academic rheumatology department.

***Results*:** 15 axpA (out of 45) and 13 RA (out of 35) under original etanercept were switched to SB4 since persistent remission or low disease activity were achieved, as recommended by local legislation; the assessment performed at 6 months after switching showed that all patients maintained the same level of disease activity (ASDAS-CRP and DAS28-ESR, respectively) and response to treatment under SB4. No significant statistically significant differences were reported in patient reported outcomes, inflammatory parameters and function (BASFI and HAQ-DI respectively). No safety signal were registered.

***Conclusions*:** Switching to etanercept biosimilar SB4 is feasible in patients with axSpA and RA achieving treatment target (remission and low disease activity) after longstanding reference etanercept management. Long-term follow-up is required to fully demonstrate that switching between original etanercept and its biosimilar SB4 is a valid option and result in persistent treatment outcomes in axSpA and RA.

EP245 / #985

Effectiveness and Safety of Biosimilars in Pediatric Non-Infectious Uveitis: Real-Life Data from the International AIDA Network Uveitis Registry

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Background and Aims: Biosimilar drugs (BIOs) are achieving greater visibility in the treatment of non-infectious uveitis (NIU), but there is still no comprehensive view in terms of efficacy and safety in pediatric age.

***Methods*:** This retro-prospective observational study was aimed at describing a multi-centre cohort of patients from the Autoinflammatory Disease Alliance (AIDA) international Registries with pediatric-onset uveitis treated with BIOs, examining their response to treatment and the overall drug retention rate (DRR); moreover, the safety profile was evaluated.

***Results*:** 47 patients (77 eyes) were enrolled. The BIOs employed were adalimumab (89.4%), etanercept (5.3%), and infliximab (5.3%). The number of relapses 12 months prior to BIOs and at last follow-up was 282.14 and 52.43 per 100 patients/year. The relative risk (RR) of developing ocular flares before BIOs introduction compared to the period following the start of BIOs was 4.49 (95%, CI 3.38-5.98, $P = .004$). The number needed to treat (NNT) for ocular flares was 3.53. Median BCVA was maintained during the whole BIOs treatment ($P = .92$). A significant GCs-sparing effect was observed throughout the treatment period ($P = .002$). The estimated DRR at 12-, 24-, and 36-month follow-up were 92.7, 83.3, and 70.8%, respectively. The risk rate for developing structural ocular complications was 89.9/100 patients/year before starting BIOs and 12.7/100 patients/year during BIOs treatment, with a RR of new ocular complications without BIOs of 7.1 (CI 3.4-14.9, $P = .0003$). Three minor AEs were reported.

***Conclusions*:** TNF inhibitors BIOs are effective in reducing the number of ocular uveitis relapses, preserving visual acuity, allowing a significant GCs-sparing effect, and preventing structural ocular complications.

E-POSTER VIEWING 33: CLINICAL PRACTICE - THERAPY: PREGNANCY, SEX HORMONES AND AUTOIMMUNITY

EP246 / #827

Successful Prevention of Recurrent Idiopathic Hydrops Fetalis with Anti-Platelets/ Anti-Coagulant Therapy; Is It Linked to Maternal Undetected Thrombophilia or Anti-Phospholipid Syndrome (APS)?

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***Background and Aims*:** Hydrops fetalis (HF) involves abnormal fetal fluid accumulation with placental thickening, often due to non-immune causes (85%). About 70% of non-immune cases result from cardiovascular, chromosomal, or infectious factors. The rest are idiopathic non-immune (i-NIHF). Pathogenesis involves tissue hypoxia, and recurrence may suggest heritable conditions. Despite advanced in-utero therapy, mortality is high (50-95%) for most non-immune cases, with idiopathic cases having the worst prognosis. Implementing a preventive treatment protocol for fetal loss is the utmost important approach to enhance fetal vitality and improve pregnancy outcomes.

***Methods*:** Presenting a case series of women with recurrent miscarriages, some attributed to i-NIHF, treated with standard APS-prophylaxis protocol, used for prevention of fetal loss, including low-dose aspirin and/or daily subcutaneous heparin.

***Conclusions*:** Idiopathic non-immune hydrops fetalis (i-NIHF) is a serious condition with high mortality and limited effective therapy, emphasizing the importance of prevention. It may co-occur with other pregnancy morbidities reported in antiphospholipid syndrome (APS) and may recur. A prophylactic regimen for APS, involving anti-platelets and anti-coagulant therapy during pregnancy, shows promising effects.

Table 1. Case-Series; 5 Women, Normal Thrombophilia Tests, No Definitive Aps Diagnosis, *Mild Hf, Born, Healthy Male. Iufd=intra-Uterine-Fetal-Death. In Five Women, with Significant Obstetrical Morbidity; Multiple Spontaneous Early Abortions and a Total of Eight Pregnancies with i-Nihf, Were Followed by 12 Successful Pregnancies with Uneventful Delivery of Healthy Babies After Treatment.

	total	i-NIHF (age:w)	preterm (age:w)	IUFD (age:w)	apontaneous-abortion (<10 weeks)	normal live-birth
no. of pregnancies before APS prophylaxis; outcome	23	8(22-30)	1(30)	2(21,31)	11	1
no. of pregnancies on APS prophylaxis; outcome	12	1(30*)				11

EP247 / #763

The Effects of Prednisolone on Pregnancy Outcomes in Women Undergoing in Vitro Fertilization

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Background and Aims: The role of autoimmunity in vitro fertilization (IFV) is very complex and immunomodulatory therapy may be considered in some patients. The aim of this study was to evaluate the effects of prednisolone in implantation and pregnancy rate in women undergoing IFV or embryo transfer (ET).

***Methods*:** 38 women starting IFV/ET were treated with prednisolone and were examined for the presence of antinuclear antibody (ANA) and autoimmune disease. The implantation and pregnancy outcome were recorded, and the correlation between ANA and the pregnancy outcome was examined.

***Results*:** The mean age was 39.13 years (28-49). ANA was noted in 89.5% women antiphospholipid antibodies were present in 2.6%; 10.5% had confirmed diagnosis of systemic autoimmune disease and 10.5% had sicca syndrome. Other notable comorbidities were insulin resistance (86.8%), vitamin D deficiency (68.4%), PCOS (13.2%), Hashimoto thyroiditis (21.1%), celiac disease (5.3%). 82.4% of women had IVF before, with 38.7% success implementation and 8.3%live birth rate. Out of 38 patients, only one didn't get pregnant, while 10.8% naturally got pregnant before the IFV. The pregnancy outcome data were available for 23 women receiving prednisolone: 87% had a successful live birth and 13% had spontaneous abortion. ANA positivity, systemic autoimmune disease did not show correlation with the pregnancy outcome. Age of the patient was not associated with implementation, or the pregnancy outcome ($P > .05$). Previous positive implantation outcome was associated with the successful implantation rate ($P < .05$).

***Conclusions*:** In women going IFV/ET corticosteroid administration may improve pregnancy outcome. The previous positive implantation may indicate successful implantation rate.

EP248 / #568

Intravenous Immunoglobulin Therapy for Recurrent Pregnancy Loss in Women with High DFS70 Autoantibodies: A Case Report

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***Background and Aims*:** Anti-DFS70 antibodies are frequently detected in healthy individuals. Their clinical significance in recurrent pregnancy loss (RPL) is still under investigation. We present two sisters with secondary infertility due to RPL. The first sister had a blighted ovum in 2019 followed by a missed abortion at 9 w.g. in 2020. The second sister had two blighted ovum pregnancies in 2017 and a missed abortion in 2020. Their grandmother also had three abortions. Chromosomal karyotypes of the spouses were normal, and there was no evidence of urogenital infection, hydrosalpinx, uterine malformations, or abnormal ovarian function. However, ANA screening test and blotting assay showed high levels of anti-DFS70 autoantibodies in both sisters.

***Methods*:** Anti-DFS70 autoantibodies in both sisters were measured by indirect immunofluorescence on HEp-2 cells and by immunoblot method.

***Results*:** Administration of intravenous immunoglobulin (IVIG, 150 mg/kg, twice) after visualization of the fetal sac in the two sisters with recurrent pregnancy losses resulted in successful pregnancies and healthy newborns.

***Conclusions*:** This case report suggests that anti-DFS70 autoantibodies may be a risk factor in RPL and IVIG treatment could be a beneficial option for women with this condition. The presence of anti-DFS70 autoantibodies in both sisters suggests a possible genetic association. Further research is needed to confirm these findings and to investigate the underlying genetic mechanisms.

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EP249 / #578

Pregnancy Outcomes in Patients Exposed to Certolizumab Pegol: Multicentric Study in Croatia

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***Background and Aims*:** Several studies have shown that the use of certolizumab pegol (CZP) in pregnancy is not associated with poor pregnancy outcomes. The aim of our study was to determine the outcomes of pregnancies in patients treated with CZP in Croatia.

***Methods*:** The medical records of patients of reproductive age who were exposed to CZP were reviewed. Patients who were pregnant during exposure to CZP for at least 12 weeks were included in the further analysis. Data on the duration of CZP administration during pregnancy, pregnancy outcome including mode of delivery, birth weight, premature births and fetal malformations were recorded.

***Results*:** 19 pregnant women with an average age of 31.7 years (range 23-40) were exposed to CZP for more than 12 weeks. 9/19 patients had rheumatoid arthritis, 3/19 psoriatic arthritis, 5/19 spondyloarthritis and 2/19 juvenile arthritis. The mean exposure to CZP was 27.1 weeks (range 12-39). The duration of pregnancy was 39 weeks (range 37-41). from 19 pregnancies, 20 newborns were born (one twin pregnancy). All newborns had a birth weight above 2500g, although intrauterine growth retardation was recorded in 3 (15%) fetuses (fetuses from a twin pregnancy and one from a singleton pregnancy). There were no premature births, fetal malformations, miscarriages or stillbirths. 10 (52.6%) deliveries ended vaginally and 9 (47.4) by caesarean section. All pregnancies except twins were conceived naturally.

***Conclusions*:** CZP exposure during pregnancy had no significant effect on pregnancy outcome. No malformations of newborns were recorded. Birth weight was normal. No deviations were observed in the length of pregnancy and the time of delivery.

E-POSTER VIEWING 34: CLINICAL PRACTICE - THERAPY: PULMONARY ARTERIAL HYPERTENSION AND SYSTEMIC SCLEROSIS

EP250 / #445

Case of Systemic Sclerosis After Stemcell Transplantation

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Background and Aims: This case report describes a patient with persisting clinical features of limited Systemic Sclerosis (lSSc) after autologous stemcell transplantation (AST) and with subsequent negative ANA IIF.

***Methods*:** In March 2019 a female patient (age 70) was diagnosed with AL amyloidosis of the stomach (25% plasmacells on bone marrow biopsy and elevated free light Kappa chains in serum (450 mg/L) and urine) and concomitant lSSc (Raynaud's phenomenon, diffuse muscle uptake on PET scan and centromere (AC-3) pattern titer 1/1280 on ANA IIF with confirmed anti-CENPB antibodies). After chemotherapy she was treated with AST in July 2019 and responded well for the AL amyloidosis. within 6 months ANA IIF became negative (<1/80). In follow-up gastric biopsy continued to show amyloid and PET scans showed persistent FDG avid lymph nodes. Biopsy revealed no malignancy, but reactive lymph nodes. In August 2023 the patient was referred to the rheumatology department with persisting[SS1] clinical features of lSSc: puffy hands, tight skin on the feet, and the typical facial signs, as well as petechiae. However ANA IIF remained negative (<1/80). Staging for pulmonary hypertension is ongoing. CT scan of the lungs shows no pulmonary fibrosis. Long function showed a lsightly decreased diffusion. Capillaroscopy showed few megalocapillary vessels.

***Results*:** As the patient has already received maximal therapy for lSSc (AST and chemotherapy including cyclophosphamide) immunosuppressive therapy was not initiated, but a 'watchful waiting' strategy was adopted.

***Conclusions*:** Persisting systemic sclerosis clinically, normalisation of ANA after AST.

EP251 / #750

BiP (GRP78) as Potential Blood and Tissue Biomarker in Systemic Sclerosis

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Background and Aims: Systemic sclerosis (SSc) is a rare autoimmune disease belonging to the group of connective tissue disorders. Studies unveiled involvement of ER-stress in white blood cells and muscle tissue, which lead to activation of the unfolded protein response (UPR). BiP, a chaperone, is a major player that binds nascent polypeptides as they translocate into the ER and misfolded/aberrant proteins destined for degradation. Since therapy in SSc is currently oriented towards individual symptoms rather than the causes of the disease, a deeper understanding of the pathophysiology is invaluable to provide improved therapies. Therefore, UPR modulation represents an attractive target, as it is therapeutically addressable by e.g. small molecules. Hence, we investigated the potential involvement of BiP in the etiology of SSc.

***Methods*:** We analyzed muscle tissue from patients with SSc by immune histochemistry, unbiased proteomic profiling, and sera by ELISA.

***Results*:** Proteomic profiling revealed clear increase of BiP in skeletal muscle from SSc patients. Immunostaining also revealed an increase of BiP. Interestingly, BiP-deposits were not identified within the muscle fibers, but rather within the extracellular space. Notably, previous studies have shown that extracellular BiP-localization impacts immune cell function and thus immune response. Furthermore, BiP-measurement in serum also showed a significant increase, supporting the concept of cellular BiP-release and thus the interesting finding obtained in muscle.

***Conclusions*:** Our combined results unravel BiP as a tissue and blood biomarker with potential impact on immune responses in SSc. Further functional studies are crucial to address a potential therapeutic impact of this finding.

E-POSTER VIEWING 35: CLINICAL PRACTICE - THERAPY: RITUXIMAB AND B-CELL DEPLETION THERAPY

EP252 / #448

Synthetic Peptide Analogues as Targeting and Endosomal Guiding Reagents for Gene Therapy of Autoimmune Diseases

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Background and Aims: RNA interference (RNAi) is a powerful gene therapy technique that utilizes small interfering RNA (siRNA) for gene silencing and knockdown of pathogenic proteins. However, despite the immense therapeutic potential, clinical application of siRNA is limited due to the lack of efficient delivery systems. by conjugating siRNA to peptides, targeted delivery to specific cells or tissues becomes possible, increasing the effectiveness and possibly reducing off-target effects. Peptide-siRNA conjugates hold great potential for advancing RNA-based therapies and overcoming delivery limitations associated with siRNA alone. In this regard, we aim to explore peptide-siRNA as a novel targeted gene therapy strategy for knockdown of pathogenic autoantibodies associated with two autoimmune diseases, Graves' Disease and Type 1 Diabetes.

***Methods*:** We develop large libraries of peptides from native autoantigens, and use these for epitope mapping. Identified peptide epitopes are investigated for interactions with immune cells. Conjugates of these peptides to siRNA are investigated for the ability to knockdown specific anitbodies.

***Results*:** We have identified peptide sequences, based on the sequence of preproinsulin, that selectively binds antibodies of paitents with Type 1 Diabetes, compared to healthy controls. Furthermore, we have identified sequences, based on the sequence of TSHR, that selectively binds antibodies of paitents with Graves' Disease.

***Conclusions*:** Through screening and epitope mapping of peptide libraries derived from native autoantigens, we have identified specific peptide sequences that show selectivity towards antibodies of patients with autoimmune diseases. These peptides hold the potential as targeting reagents for gene therapy of autoantibody producing cells.

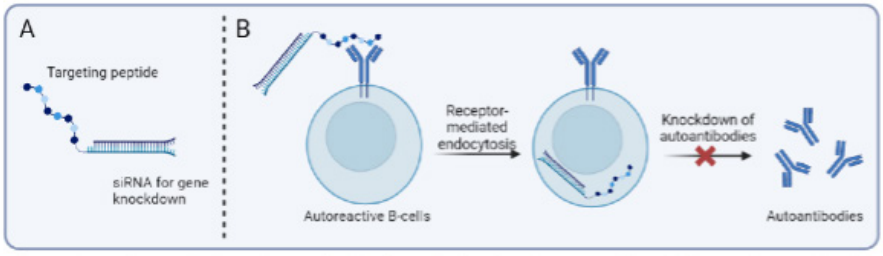

Figure 1. A) Conjugate Design. B) Hypothesis of Mode of Action For Targeted Knockdown of Autoantibodies.

EP253 / #540

Rituximab as an Effective Treatment Option for Refractory Thrombocytopenia in a Patient with Mixed Connective Tissue Disease

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***Background and Aims*:** Mixed connective tissue disease (MCTD) is a disease that has overlapping features of systemic sclerosis, poly/dermatomyositis and systemic lupus erythematosus. The main laboratory finding in patients with MCTD is the elevated titer of anti-U1 ribonucleoprotein (U1-RNP) antibodies. Immune thrombocytopenia associated with MCTD is considered rare. Rituximab is a monoclonal antibody directed against CD20 membrane glycoprotein expressed on the surface of B cells. As the blockage of CD20 leads to fast and reversible B-cell depletion, rituximab has become a common choice in the treatment of autoimmune diseases that have B-cell activity as the main pathogenic mechanism.

***Methods*:** We present a case of a patient with refractory thrombocytopenia associated with MCTD that was successfully treated with rituximab.

***Results*:** A 49-year-old female patient was diagnosed with MCTD based on the following clinical and laboratory features: thrombocytopenia with hemorrhagic syndrome (Plt 3x10^9/L), polyarthralgia, syndroma Raynaud, pulmonary involvement, presence of anti-nuclear (ANA Hep2 1:320) and anti-U1-RNP antibodies. She was initially treated with high-dose intravenous corticosteroids, followed by the administration of intravenous immunoglobulins (2g/kg BW). Due to the lack of response to this therapy, the treatment was continued with rituximab. The partial platelet recovery (Plt 44x10^9/L) was achieved. The treatment was well tolerated, without adverse events. Subsequently, mycophenolate mofetil (2g/kg BW) was given as a maintenance therapy. During the follow-up, six months after rituximab was given, the patient is doing well, with a stable platelet number.

***Conclusions*:** Rituximab is an effective and safe option for treating refractory thrombocytopenia in patients with MCTD.

EP254 / #501

Rituximab as Success Biological After a Mandatory Switching of Tocilizumab in Patients with Rheumatoid Arthritis - A Registry of Real-Life

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***Background and Aims*:** Rheumatoid Arthritis (RA) is a chronic inflammatory disease with treatment using conventional and biological DMARDs. one of the most used biologicals is Tocilizumab (TCZ). At the end of 2021 in Colombia, a TCZ shortage situation occurred, which led to the mandatory need to change treatment with TCZ to other biologicals in RA patients. The objective was to assess the therapeutic success rate after mandatory switching from TCZ to other drugs.

***Methods*:** A retrospective cohort study from September/2021 to October/2022 was performed. A descriptive statistics of TCZ switching to other biologicals, and which were the most effective medications in real life. Treatment failure was defined as those patients who did not achieve low disease activity/remission, or in whom there was no good EULAR response.

***Results*:** 135 RA patients using TCZ were switched to other biologicals; 97% women. The characteristics of switching to the first biological and which were most effective are described; in addition, switching to a second biological or resumption of the TCZ due to failure to the first switching. It was found that Rituximab with 78.5% and Golimumab with 58.8% effectiveness were the most successful biologics in real life when switching post-TCZ; between 6.7% and 29.4% of non-responders returned to TCZ. When analyzing the DAS28, no statistically significant differences were found between patient's groups.

***Conclusions*:** This study shows that the most effective biological in real-life after the TCZ change is apparently Rituximab. A third of patients return to treatment with TCZ due to failure to switch to the first biologic post-TCZ.

EP255 / #790

Rituximab in Cryoglobulinemic Vasculitis Related to Primary Sjögren's Syndrome: Long-Term Follow-Up from a Reference Italian Centre

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***Background and Aims*:** Cryoglobulinemic vasculitis related to primary Sjögren's syndrome (CV-pSS) is a rare condition, with high disease activity and risk of lymphoma (NHL) in pSS. Herein we describe a single-center cohort of CV-pSS patients treated with rituximab (RTX).

***Methods*:** Data from CV-pSS patients admitted to the Rheumatology Unit of Udine from 2008 to 2021 and treated with RTX were retrospectively collected.

***Results*:** We reported 9 patients (7 females, 2 males) with a mean age of 62±9.5 years at the onset of CV. 7/9 patients received RTX for skin, joint, or peripheral nervous system involvement, while 2/9 received RTX for NHL before CV. In the group treated for CV, 4/7 patients received early treatment within 12 months of disease onset, followed by maintenance therapy with RTX every 6 or 12 months. The remaining 3/7 patients received RTX later and without maintenance. Two patients developed NHL after CV, with one case each occurring in the former and one in the latter treatment group. RTX was effective in all patients on glandular, cutaneous, articular, and nervous involvement. Excluding the 2 patients who developed NHL, the ESSDAI score clearly decreased at the last follow-up (mean follow-up duration: 6.7±4.7 years). Notably, no adverse effects were observed (hypogammaglobulinemia, infections, or infusion reactions).

***Conclusions*:** Early and maintenance therapy with RTX is effective and safe in CV-pSS, in the long term, while it cannot prevent NHL development.

Figure 1. Response to RTX treatment in PSS-Related CV Cohort

Treatment with RTX	Reason for treatment	Dosage RTX for CV	Age at CV onset, gender	Glandular domain ESSDAI		Cutaneous domain ESSDAI		SNP domain ESSDAI		Articular domain ESSDAI		Lymphadenopathy / Lymphoma domain ESSDAI		Total ESSDAI		Adverse effects (Hypogammaglobulinemia and/or infectious)
				Before RTX	After RTX	Before RTX	After RTX	Before RTX	After RTX	Before RTX	After RTX	Before RTX	After RTX	Before RTX	After RTX	
Early and maintenance treatment	CV	375 mg/m2 weekly for 4 weeks	50y, male	2	0	2	0	0	0	1	0	1	0	23	4	0
	CV	250 mg/m2 weekly for 2 weeks	65y, female	0	0	2	0	2	0	2	0	0	0	22	4	0
	CV	250 mg/m2 weekly for 2 weeks	60y, male	0	0	2	0	1	0	0	0	0	0	17	6	0
	CV	375 mg/m2 weekly for 4 weeks	69y, female	1	0	2	0	2	0	1	0	0	3	22	26	0
Non-early and non-maintenance treatment	CV	250 mg/m2 weekly for 2 weeks	65y, female	1	0	2	0	0	0	0	0	0	3	12	22	0
	CV	1000 mg 2 weeks apart	71y, female	1	0	2	0	2	0	1	0	0	0	29	2	0
	CV	375 mg/m2 weekly for 4 weeks	47y, female	0	0	2	0	2	2	1	0	0	0	20	12	0
	NHL	NA	75y, female[a]	1	2	2	0	0	0	0	0	3	3[b]	22	20	0
	NHL	NA	56y, female[a]	2	2	2	0	2	0	0	0	3	3[b]	34	19	0

[a]onset of NHL before CV
[b]recurrence of NHL

EP256 / #819

Comparing Longitudinal Changes in IgG and IgM Profiles in MS Patients Undergoing B-Cell Depleting Therapy: A Retrospective Analysis

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Background and Aims: There is a lack of direct comparison of Immunoglobulin G and M (IgG/IgM) profiles across different B-cell depleting therapies (BCDTs) in MS patients, representing a knowledge gap of associated infection risks. We compared IgG and IgM levels between MS patients on Ocrevus, Kesimpta, and Rituximab and its derivatives.

***Methods*:** Data was retrospectively collected from the time of patient enrolment until April 1,2023. The number of years between the start of BCDT and the date of the first recorded abnormal IgG and IgM levels among different BCDTs and MS types was measured using Chi-squared tests.

***Results*:** 140 (64%) were female, 18 (8.2%; average time of treatment 1.4 years) were on Kesimpta, 78 (35.8%; 3.9 years) on Ocrevus and 122 (55.9%;1.1 years) on Rituximab. 21 (9.6%) had primary progressive MS (PPMS, average time on BCDTs 3.8 years), 185 (85%) had relapsing remitting MS (RRMS;1.5 years) and 12 (5.5%) had secondary progressive MS (SPMS; 1.6 years). More Ocrevus patients (IgG:17%, IgM: 28%) had abnormal IgM and IgG levels (IgG: $P = .07$, IgM: $P = .04$). More SPMS patients (IgG: 42%, IgM: 58%) had abnormal IgG and IgM (IgG: $P = .03$, IgM: $P = .01$). It took longer to observe abnormal levels of IgG/M in patients on Ocrevus (IgG:1.4, IgM:1.5) and longer time periods to observe abnormal levels of IgG/M in PPMS patients (IgG:1.8, IgM:1.0).

***Conclusions*:** Findings reveal immunological differences between patients on different BCDTs, and the impact of treatment duration on IgG and IgM levels. Longitudinal monitoring of IgG and IgM may be a valuable tool to assess the safety of BCDTs.

E-POSTER VIEWING 36: CLINICAL PRACTICE - THERAPY: SLE, ANTI PHOSPOLID SYNDROME, SJÖGREN'S DISEASE AND RELATED CONDITIONS

EP257 / #858

Delayed Onset of Cyclophosphamide-induced Male Infertility After Treatment for Lupus Nephritis

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Background and Aims: Systemic Lupus Erythematosus (SLE) is a classical autoimmune disease with manifestations in multiple organs. Urgent immune-modulation and immunosuppressive therapy, particularly with cyclophosphamide, are essential in cases of diffuse vasculitis or involvement of critical organs like the central nervous system or kidneys, aiming to control the disease and improve outcomes. However, due to significant side effects, particularly on fertility, alternative regimens such as mycophenolate mofetil have been explored, especially in cases of lupus nephritis. In male SLE patients, routine semen collection is done before initiating any cyclophosphamide therapy to ensure future fertility options if chemotherapy-related infertility becomes a concern.

***Methods*:** Presenting a case series of four young, single patients (ages 20-25) who underwent the high-dose cyclophosphamide induction regimen (NIH protocol) for active lupus nephritis. Follow-up records include information on specimen tests, pregnancies and whether they occurred naturally or with the use of frozen semen samples.

***Results*:** All patients exhibited normal fertility status, and their wives conceived and gave birth without complications for the initial 3-4 years post-cyclophosphamide therapy. Unexpectedly, azoospermia and continuous infertility emerged subsequently, requiring the use of frozen semen specimens for in-vitro fertilization.

***Conclusions*:** SLE-related nephritis requires urgent induction therapy, with cyclophosphamide being a cornerstone, despite concerns about gonadal failure and infertility. A presented case series suggests a more reassuring perspective: the onset of clinical infertility and findings of oligo/azospermia after cyclophosphamide treatment may occur several years later, providing a natural window for normal fertilization and family planning. The underlying explanation for this phenomenon requires further investigation.

EP258 / #31

Low Muscle Strength Impacts on Quality of Life of Indonesian Women with Systemic Lupus Erythematosus

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***Background and Aims*:** Recent advancement in diagnosis and therapies for SLE improves life expectancy and prognosis. Unfortunately, quality of life is still lacking for affected patients. We aim to evaluate the impact of muscle strength on Sarcopenia related Quality of Life (SarQoL) in indonesian women with SLE.

***Methods*:** 61 female with SLE was recruited as a volunteer; we measured muscle function with a Jamar hand-held dynamometer, 6 minutes walk test, and quality of life using the SarQoL questionnaire that has recently been validated for the indonesian population. Statistical analysis was done with a t-test for mean difference and linear regression to adjust for confounders by using the Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA).

***Results*:** Our volunteers consist primarily of younger Lupus patients, mean age of 32.66 (SE 10.13), mostly below 40 years old (73.8% vs. 26.2%). Nevertheless, we found a higher proportion of volunteers with low muscle strength

(55.7 vs. 44.3%), low physical performance (90.2 vs. 9.8%), and low weekly physical activity (75.4 vs. 24.6%). Low muscle strength was found to be correlated with lower total SarQoL (P = .009), physical and mental (P = .049), locomotion (P = .046), functionality (P = .015), and independence domain (P = <.001). The correlation between low muscle strength and lower total SarQoL score was still statistically significant after multivariate adjustments with protein intake and exercise activity (P = .022).

***Conclusions*:** Low muscle strength independently correlated with lower quality of life in indonesian women with systemic lupus erythematosus, especially in the independence and functionality domain.

EP259 / #462

Impact of Imlifidase Treatment on Immunoglobulins After Kidney Transplantation in an HLA-Hypersensitized SLE Patient with Anti-SSA/SSB Antibodies

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Background and Aims: The cysteine protease imlifidase can be used in rare IgG-mediated autoimmune conditions and to prevent humoral transplant rejection in highly sensitized recipients with donor specific antibodies (DSA).

***Methods*:** The selected case report describes a 51-year-old woman with lupus nephritis at end stage kidney disease (ESKD-LN) who presented three preformed DSA (HLA-A*25, -B*35, and -B*51) together with anti-SSA/SSB autoantibodies (Abs).

***Results*:** Following a second kidney transplantation in the presence of imlifidase, immunoglobulin longitudinal monitoring revealed at the time of initiation (6 hours and 24-72 hours), an IgG selective effect on total and subclasses IgG together with negative assays for DSA, lymphocytotoxicity by cross-match, IgG anti-SSA/SSB Abs as well as IgG anti-vaccine Abs. At rebound (30-60 days), total and subclasses IgG levels as well as anti-SSA/SSB and anti-vaccine Abs were partially restored. In contrast, the 3 preformed DSA did not reach the pathogenic threshold (mean fluorescence intensity>1000) at 30 and 60 days post-imlifidase infusion although detectable at low level.

***Conclusions*:** The dichotomy in alloreactive Abs and autoreactive Abs rebound may be explained in part through the effect of imlifidase combined with IVIG (day 7) and rituximab (day 9) on memory B cell to prevent short-lived plasma cells differentiation. In other words, DSA production appeared to be dynamic and related to memory B cells and short-lived plasmacells.

EP260 / #513

Interferon-A in Juvenile and Adult Systemic Lupus Erythematosus (SLE)

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***Background and Aims*:** Data of the level and role of interferon (INF)-α in SLE with juvenile (jSLE) and adult (aSLE) onset are limited. The aim of the study was to evaluate the level of IFN-α and its interrelations with the course of the disease in adult patients with the jSLE and aSLE.

***Methods*:** Totally 46 jSLE and 50 aSLE patients were involved. The level of serum IFN-α was determined by ELISA.

***Results*:** The age of jSLE and aSLE patients was 30.9±8.21 and 37.7±7.43 years, disease duration 4 [1;25] and 2 [1;21] years (P < .05), SLEDAI-2K 4.76±3.53 and 4.7±4.24, respectively (P ≥ .05 for all). INF-α in aSLE was 7.63 [2.82; 75.6] pg/ml and in jSLE 4.27 [2.08; 38.5] pg/ml, P = .0004. No differences in SLE manifestations and no interrelations with INF-α were found in jSLE and aSLE (P ≥ .05 for all). The daily dosages of glucocorticoids in jSLE and aSLE were 12.1 ± 7.73 and 14.4 ± 12.4 mg respectively (P = .049), other therapy was equal for both groups (P ≥ .05). The number of exacerbations of SLE (per year) in jSLE exceeded the number of aSLE's exacerbations (3.3±2.05 and 2.38±1.29 respectively, P = .035). An interrelation was established between the number of exacerbations of SLE and the level of INF-α, r=-0.58, P < .05.

***Conclusions*:** In patients with the aSLE the level of the INF-α is higher than in jSLE. Serum level of INF-α is associated with a smaller number of exacerbations and a greater need for glucocorticoids in each exacerbation of aSLE.

EP261 / #918

Volumetric Analysis of Brain Structures and Evaluation of Neurological Symptoms of Patients with Sjögren's Syndrome: Anatomical, Radiological and Neurological Study

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Background and Aims: Sjögren's syndrome (SS) is an autoimmune disease that is more common in women, especially affecting the salivary and tear glands. In this study, the volumes of many anatomical structures in the brain of female patients diagnosed with SS were measured and their neurological symptoms were evaluated.

***Methods*:** In our study, brain magnetic resonance images (MRI) of 21 female patients with SS and 34 healthy women were evaluated and the volumes of some anatomical structures were measured.

***Results*:** It was determined that the total temporal lobe, right temporal lobe and 4th ventricle volumes of patients with SS were significantly smaller compared to the control group. In SS patients, the volume of the right corpus amygdaloideum was found to be significantly smaller than the left side. Volume measurements of other anatomical structures, except vermis volume, were smaller than those in the control group but statistically insignificant. When patients with primary and secondary SS were compared: left corpus amygdaloideum, left insular cortex, total corpus amygdaloideum and total insular cortex volumes were found to be significantly smaller in secondary SS patients. Our study shows that structures related to the limbic lobe are more affected in patients with secondary SS. The most common neurological symptoms in patients are vertigo, headache and forgetfulness. Headache symptom correlates with nucleus accumbens and third ventricle volume.

***Conclusions*:** SS can cause neurological symptoms in patients and affect the anatomical structures of the brain, even if their neurological examinations are normal. We recommend early diagnosis and treatment of the disease and regular neurological check-ups.

EP262 / #19

Complications During Pregnancy in Patients with Systemic Lupus Erythematosus

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***Background and Aims*:** Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that mainly affects women of childbearing age, during pregnancy it has alternate patterns of remission and flare-ups; many pregnant patients tend to worsen with poor obstetric outcomes, such as increased risk of spontaneous abortion, prematurity, intrauterine growth retardation, preeclampsia, and neonatal lupus.

***Methods*:** Descriptive, observational, retrospective. Records were reviewed between January 2018-December 2022. Inclusion criteria: >18 years, SLE according to ACR/EULAR 2019 classification, pregnancy confirmed by ultrasound and test of bHCG, minimum of 3 visits per year. Activity assessed by SLEDAI 2K: Inactive (≤3), mild/moderate (4-11), severe (≥12), SLEPDAI: Inactive (0), mild/moderate (1-5), severe (≥6). Descriptive analysis was done by using The Statistical Package for Social Sciences version 23.0 software (IBM Corp.; Armonk, NY, USA).

***Results*:** 22 met inclusion criteria. Mean age 33±7 years, mean time of diagnosis 7.1 years, arterial hypertension 41% (9), nephritis 18.2% (4), dyslipidemia 13.6% (3), diabetes mellitus 13.6% (3). Nulliparous 45.5% (10), multiparous 54.5% (12). Hydroxychloroquine 100%, glucocorticoids 63.6% (14), mycophenolate mofetil 18.2% (4), azathioprine 13.6% (3), rituximab 9.1% (2), anti-Ro52+ 27.3% (6), SLEDAI 2K/SLEPDAS 1st trimester: no flare 54.5% (12), mild 41% (9), moderate 4.5% (1). SLEDAI 2K/SLEPDAS 2nd trimester: no flare 63.6% (14), mild 36.4% (8). SLEDAI 2K/SLEPDAS 3rd trimester: no flare 68.2% (15), mild 31.8% (7). Complications during pregnancy 27.3% (6): polyhydramnios 50%(3), preeclampsia 33.3% (2), anemia 16.7% (1). Gestational outcome: full term 86.4% (19), preterm 4.5% (2). Delivery: vaginal 63.3% (14), cesarean section 36.4% (8). Anti-Ro52/compromise correlation: polyhydramnios 33.3% (2).

***Conclusions*:** Polyhydramnios was the most frequent complication, followed by preeclampsia. Most of them had a full-term pregnancy. More than half of the deliveries were eutocic. Most of the patients had no flares during pregnancy. There was a direct association between anti-Ro52 and polyhydramnios.

EP263 / #784

Discovery and Characterization of Mimotopes for Anti-C1q Antibodies in Systemic Lupus Erythematosus

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Background and Aims: Systemic Lupus Erythematosus (SLE) is a complex autoimmune disease, which can develop into severe forms. Essential tolerance mechanisms are increasingly affected during worsening of the disease and anti-double-stranded (ds) DNA antibodies are accused to be involved in the pathologies. They react with nucleic acids but are not strictly specific to it. Via recognizing non-DNA antigens such as the complement component 1q (C1q), inflammatory responses, apoptosis and tissue fibrosis can be triggered. Here we aimed to identify peptides that function as blocking mimotopes for anti-dsDNA autoantibodies and subsequently validate a possible harmful T-cell modulating effect of the mimotopes.

***Methods*:** To identify epitopes of autoantibodies, we designed a peptide microarray that contains non-nucleic acid targets of anti-dsDNA autoantibodies. The microarray contains 4309 linear or cyclic overlapping peptides (13 aa, overlap 10 aa), including 169 peptides of C1q subunit A and B. The microarrays were applied to map the IgG antibody response of 6 SLE patients in comparison to 6 healthy donors. Promising peptides were tested for the specific blocking of antibodies in their soluble form and validated for T-cell activation via ELISpot assays.

***Results*:** We observed a significant elevated IgG response in the serum of SLE patients against three peptide sequences in the C1q alpha and beta subunit. The soluble mimotopes blocked antibody-binding epitope-specific and showed no alarming activation of effector T-cells.

***Conclusions*:** Peptide microarrays are a powerful tool to investigate the misdirected humoral immune response in autoimmune diseases and can support the development of peptide-based therapeutic strategies.

EP264 / #798

Incomplete Systemic Lupus Erythematosus: What Medications Are Used?

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Background and Aims: Often, patients present with clinical symptoms and immunologic abnormalities suggestive of systemic lupus erythematosus (SLE), while not meeting classification criteria yet. This is referred to as incomplete SLE (iSLE). Timely treatment, however, is important to limit disease progression, and prevent organ damage and mortality. The aim of the study was to evaluate the therapy administered to patients with iSLE.

***Methods*:** iSLE (n=60) was defined by rheumatologists as clinical diagnosis, not fulfilling ACR or SLICCcriteria and had no classification or specific symptoms of other rheumatic diseases. The majority of the iSLE patients were female (97%), aged 38 [26-47] years. The median age of iSLE diagnosis was 33 [25-42] years, disease duration was 12 [2-39] months, 12 (20%) pts had a disease duration of ≥ 5 years. The median SLEDAI-2K was 2 [1-5] score, SDI–0 [0-0] score

***Results*:** A large proportion of iSLE patients (57%) were prescribed hydroxychloroquine at a dose of 200 mg/day and oral corticosteroids (42%), the maximum dose of prednisolone was 15 [6-40] mg/day. 5 (8%) patients with iSLE were taking immunosuppressants: sulfasalazine-2 (3%), methotrexate-1 (2%), azathioprine-1(2%), and cyclophosphamide-1(2%). 6 (10%) iSLE patients were taking biology: rituximab -1(2%), IL-6 inhibitor–1(2%), intravenous human immunoglobulin - 4(7%). Other medicines: NSAIDs–28%, vitamin D–27%, course of antibiotics–18%, low dose aspirin–17%, anticoagulants–10%, antipsychotics–5%, eltrombopag and antihistamines–2% each of patients

***Conclusions*:** Although iSLE is sometimes considered a mild form of lupus, the clinical man-

ifestations of iSLE can be significant. This may explain why many iSLE patients are treated with immunomodulatory medications.

EP265 / #820

Systemic Lupus Erythematosus Induced by Treatment with a Combination of Monoclonal Antibodies Against the SARS-COV2 Surface S-Protein

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***Background and Aims*:** To present the case of Systemic lupus erythematosus (SLE) that developed after therapy with a combination of monoclonal antibodies against the SARS-CoV2 surface S-protein.

***Methods*:** A case report.

***Results*:** Patient, 60 years old. In 2018, symmetrical non-erosive arthritis of the hand joints appeared. ACCP,RF-normal, ANA-negative. Seronegative rheumatoid arthritis (DAS28 4,7) was diagnosed and methotrexate (MT) 22.5 mg/week was prescribed with a positive effect. Due to arthritis recurrence two years later, methylprednisolone (MP) 4mg/day and hydroxychloroquine (HCQ) 200mg/day were added. In January 2022, the patient had mild COVID-19 confirmed by RT-PCR, CT scan of the lungs without pathology. On 23.01.2022, she was treated with combination of monoclonal antibodies against SARS-CoV-2 surface S-protein(Bamlanivimab 700mg+Etesivimab 1400mg). In March 2022, examination revealed arthritis, urtic rash, CRP 6.2mg/L (0-5), ANA 1/320, anti-dsDNA 200IU/ml (0-25), anti-C1q 24.4IU/ml (0-10), C3 0.83g/L (0.9-1.4). Given the chronological relationship with the administration of monoclonal antibodies, the late age of onset and the absence of visceral organ involvement, drug-induced lupus (DIL) with skin involvement (anti-C1q vasculitis) was initially diagnosed. Therapy:MP IV 1500mg, oral MP 8mg/day, HCQ 400mg/day, MT 20mg/week with positive effect: Reduction of arthritis and skin elements. However, considering the persistence of serological abnormalities (anti-dsDNA 800 IU/ml, anti-C1q 27.9 IU/ml, C3 0.76 g/L) by November 2022, the diagnosis is revised in favor of SLE, SELENA-SLEDAI 4 without clinical manifestation. Last visit in October 2023, no clinical manifestations, previous serological abnormalities remain, therapy-MP 4mg/day, HCQ 200mg/day, MT 15mg/week.

***Conclusions*:** There are known cases of the development of DIL/SLE on therapy with monoclonal antibodies, mainly TNF-α inhibitors. However, SLE after therapy with Bamlanivimab and Etesivimab has not been previously described.

EP266 / #32

Metformin Improves FOXP3 and Interleukin-17 Balance in Pristane-Induced Murine Lupus

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Background and Aims: Recent studies in women with low disease activity lupus have shown metformin's ability to reduce flares comparable to low-dose prednisolone, with the added benefit of lower infection rates. This study aims to study one of the potential mechanisms of this result.

***Methods*:** 31 female BALB/C mice, aged six weeks, were intraperitoneally injected with 0.5 ml of pristane (2,6,10,14-tetramethylpentadecane). After the induction period (120 days), the mice were given the following treatments for 60 days: oral 100 MCL normal saline, oral 100 mg/kgBW metformin, or intraperitoneal 100 mg/kgBW metformin. Levels of FOXP3 mRNA expression (DNA Genotek, Qiagen) and IL-17 (Abcam) were determined according to the manufacturer's instructions. Statistical analysis was done with multiple ANOVA to determine the mean difference between groups by using the Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA).

***Results*:** Post induction with pristane compared with control; there is an increase in IL-17 levels (64.20 vs. 52.3; mean difference 11.87 pg/ml; 95% CI 8.93-14.81; $P < .001$) and a decrease in FOXP3 mRNA expression (8.80 vs. 7.17 fold change; mean difference -1.63; 95% CI -2.17 –(-1.09); $P < .001$). Post-treatment with metformin there is a reduction of IL-17 levels (64.62 vs. 60.30 vs. 55.04; $P = .004$), an increase in FOXP3 mRNA expression (6.9 vs. 7.79 vs. 9.02 fold change, $P < .001$), and improvement in FOXP3 mRNA/IL-17 ratio (0.010 vs. 0.012 vs. 0.016; $P < .001$), results are for normal saline, oral and intraperitoneal metformin respectively.

***Conclusions*:** Metformin therapy improved FOXP3 mRNA expression, IL-17 levels, and its ratio in pristane-induced murine lupus.

E-POSTER VIEWING 37: CLINICAL PRACTICE - THERAPY: VASCULITIDES, HORMONES AND AUTOIMMUNITY

EP267 / #835

Clinical Significance of Antiphospholipid Antibodies in Patients with Takayasu Arteritis

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Background and Aims: Takayasu arteritis (TA) is an idiopathic systemic vasculitis, affecting predominantly females below the age of 40. Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by recurrent thrombosis and pregnancy morbidity in the presence of antiphospholipid antibodies (aPLs)**.**

***Methods*:** This study included 28 consecutive (27 female) TA patients. We investigated the presence of anticardiolipin (aCL), antibodies against β2 glycoprotein 1 (β2GPI), and lupus anticoagulant (LA) in treatment-naive TA patients and their relationship with thrombotic and/or obstetric complications during the disease course.

Results: At least one persistently positive (measured 12 weeks apart) aPLs was detected in 16/28 (57.1%): LA in 11/28 (39.3%), aCL in 8/28 (28.6%) and anti β2GPI in 2/33 (6.1%) patients with TA. Diagnosis of APS was established in 6/28 (21.4%) TA patients. There were 21/27 (77.8%) successful pregnancies, significantly more often ($P = .026$) in aPL-positive (15/16, 93.8%) compared to -negative (6/11, 23.5). Pregnancy losses were statistically more often detected in aPL-positive (12/16, 75%) than in -negative (7/11, 63.6%) patients. No statistical difference in the occurrence of an acute coronary syndrome (ACS) in aPL-positive (5/28, 31.3%) and -negative (4/28, 23.5%), ischemic cerebrovascular events in aPL-positive (1/28, 6.3%) and -negative (2/28, 11.8%) was detected ($P = .622$, $P = 1.000$ respectively).

Conclusions: Pregnancy occurrence and losses were affected by the presence of aPLs. No difference in the frequency of thrombotic ischaemic events between aPL positive and -negative patients. Testing for the presence of

the aPLs is of significant clinical importance allowing complications prevention by the timely initiation of primary or secondary thromboprophylaxis in selected patients.

EP268 / #807

Human Immunoglobulin Therapy in a Patient with Necrotizing Vasculitis

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***Background and Aims*:** It concerns a 66-year-old patient with first symptoms from February 2022. The first complaints included spontaneous onset of lower extremity pain, paresthesias, and the appearance of a petechial rash distal to the knee joints with a rapidly progressive course and confluence of rash units. A consultation with a vascular surgeon and a dermatologist was carried out and outpatient therapy with Methylprednisolone, Rupatadine and Rutozid trihydrat was started. For about a week, the rash progressed, an inflammatory and edematous syndrome appeared in small joints of the hands and feet with evidence of inflammatory activity - CRP outpatient 17 mg/l.

***Methods*:** Clinical examination, blood tests, X-Ray examination, capilliaroscopy, consultations.

***Results*:** As a result of three months of therapy with human immunoglobulin, methylprednisolone and vasotonic agents, the patient is with significant improvement of local status and no recurrence of vasculitis at present. The pathological skin lesions paramalleolar and on the back of the feet are expressed in erythematous macules, in places with a light infiltrate papules. on upper limbs, torso and both lower legs - hyperpigmented macules.

***Conclusions*:** Intravenous immunoglobulins are used as a replacement treatment for immunodeficiency conditions occurring with humoral or combined immune deficiency, as well as as an immunomodulatory therapy for various autoimmune and inflammatory diseases. The present clinical case is an example of a good effect with the administration of human immunoglobulin in three consecutive months at a dose of 200 mg/kg.

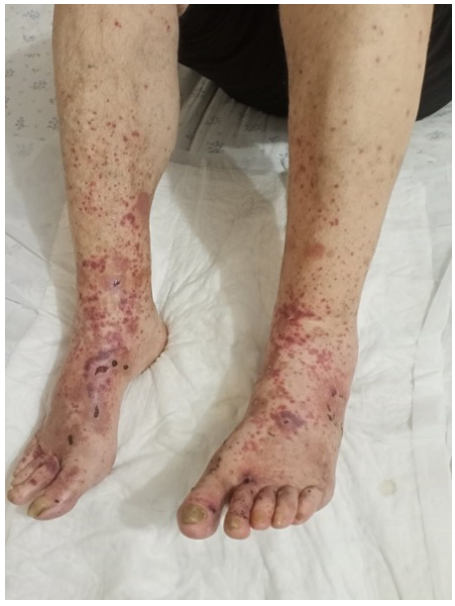

Figure 1.

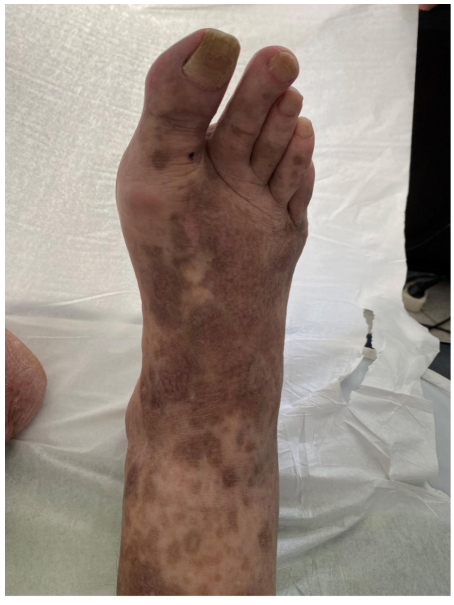

Figure 2.

E-POSTER VIEWING 38: CLINICAL PRACTICE - THERAPY: OTHER

EP269 / #330

Scleromyositis: More Than a Simple Overlap

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***Background and Aims*:** 'Scleromyositis' (SM) is a distinct emerging entity within the diffuse systemic sclerosis (dSSc) and autoimmune inflammatory myopathies (AIM) spectrum. Compared with other subsets of SSc and AIM, SM patients have poorer prognosis due to multisystemic involvement and extra-muscular complications, and no consensual treatment is accepted for SM.

***Methods*:** 20-year-old woman, with history of infections (SARS-CoV-2, Herpes Zoster) during the last year, was admitted for myalgias over 4 months. Physical examination revealed: scapular and pelvic girdle muscle weakness; sclerodactyly. Laboratory testing showed: creatine kinase 13 000 U/L, aldolase 15.6 U/L, lactate dehydrogenase 1481 U/L and myoglobin 4400 ng/mL; positive for antinuclear antibodies (1/640), anti-PM/Scl 75 and 100 and anti-CENP-B. Magnetic resonance imaging revealed hyperintensity of pelvic girdle muscles compatible with acute/subacute myositis. Distal and proximal myopathy was documented on electromyography. Muscle biopsy showed extensive necrosis without significant inflammatory infiltrate (isolated CD20 infiltration). Nailfold capillaroscopy was compatible with a late pattern of scleroderma. Computed tomography and spirometry documented interstitial mildly restrictive lung disease.

***Results*:** Induction therapy was made with intravenous immunoglobulin, mycophenolate mofetil (MMF) and prednisolone (15 milligrams/day), followed by maintenance with MMF and Rituximab (RTX) every 6 months. Progressive recovery of muscle strength and normalization of muscle enzymes, after 6 months of treatment.

***Conclusions*:** It is necessary to stratify patients prior to carrying out a therapeutic approach. Our case shows the need of an induction and maintenance protocol, given the patient's extensive activity.

EP270 / #765

EGPA and IL-5 Blockade Therapy: Not Only an Eosinophils' Driven Disease

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***Background and Aims*:** We report the case of a 52-years-old man with a history of hypogammaglobulinemia and EGPA, presenting with asthma, nasal polyposis, paranasal sinusitis, transient pulmonary nodules (honey-combing pattern peri-hilar nodules at the HRCT, with contrast enhancement at the CT-PET), mononeuritis multiplex (hearing and visual loss, acoustic muffling, dizziness), slight peripheral eosinophilia.

***Methods*:** Patient was treated initially with DMARDs (azathioprine, MMF) with unsatisfactory response and severe gastrointestinal side effects. Therefore, IgEV at immunomodulatory doses and Rituximab were started, with initial good control of the symptoms. Due to recrudescence of the disease, an IL5-inhibitor (Mepolizumab) was started. However, the patient developed severe nausea, fever and intense arthralgia of the elbows and shoulders within 6-hours from the injection requiring switch to an IL5-R-inhibitor (Benralizumab). The patient developed intense arthritis of the elbows within 36-hours from the administration, requiring a prompt suspension of the treatment.

***Results*:** Finally, another cycle of Rituximab and steroid was initiated, with clinical remission and without developing side effects.

***Conclusions*:** Evidence suggests that IL-5 pathway inhibition may lead to the suppression of Th2 immunity and hyperactivation of Th-1 and Th-17 pathway promoting neutrophile induced inflammation RA-like.

EP271 / #420

Challenging Case of Rheumatoid Arthritis: The Future Looks Bright

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Background and Aims: Recent data focus on the emerging role of oral Janus kinase (JAK) inhibitors in the management of rheumatoid arthritis (RA). To discuss a challenging case of long-history of active rheumatoid arthritis achieving remission under baricitinib.

***Methods*:** Review of patient's file since the diagnosis.

***Results*:** We describe the case of a 51-year woman diagnosed with RA at 30 years old; she also had cardiovascular comorbidities (hypertension, ischemic heart disease) and lung fibrosis and has undergo 9 months tuberculosis chemoprophylaxis before starting JAK inhibitors. After inadequate response to different conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), she developed toxic hepatitis while on maximal sulfasalazine doses combined with hydroxychloroquine; her autoimmune hepatic evaluation was negative and the gastro-enterologist suggested hepatic toxicity due to csDMARDs. Taking into account high RA activity (DAS28-ESR of 6.73) and the hepatic issue, baricitinib monotherapy was initiated, leading to rapid decline in pain after only 3 weeks and significant reduction in local as well systemic inflammation after only 1 month; remission was achieved as soon as 3 months (DAS28-ESR=1.25) and maintained throughout last monitoring (DAS28-ESR=2.4)

***Conclusions*:** We reported a problematic RA case with csDMARDs toxicity, who achieved a rapid and significant response to oral Janus kinase inhibitors; remission was obtained as soon as one month of baricitinib and persisted for more than 4 years of treatment.

EP272 / #906

The Association Between Psoriasis and Fibromyalgia Syndrome: Effects on Treatment from a Large Population-Based Study

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Background and Aims: Psoriasis (PsO) is a widespread chronic inflammatory disease often accompanied by Psoriatic Arthritis (PsA), frequently necessitating biologics. The co-occurrence of Fibromyalgia Syndrome (FMS) in inflammatory conditions and its impact on PsO/PsA are poorly understood. This study investigates the association between PsO/PsA and FMS, exploring the risk of FMS in individuals with pre-existing PsO and its influence on biological therapy drug survival.

***Methods*:** A retrospective-cohort study involved 61 003 PsO patients and 244 012 matched-controls (2000-2020). The risk of FMS was compared using survival analysis and multivariable Cox-regression, adjusting for confounding factors. The relationship between FMS and mean duration of therapy on each biological line among patients with PsO/PsA was assessed using multivariable linear-regression analysis.

***Results*:** FMS prevalence was higher in PsO patients (3.3% vs. 2.3%, OR=1.45, 95%CI:1.38-1.53; $P < .001$). Among PsO patients with FMS (n=2037), 81% were female, and 33.6% had PsA. The incidence of FMS was higher in PsO patients treated with biologics (HR=3.17, 95%CI:2.28-4.42, $P < .001$) than those with phototherapy, though adjustment rendered this effect insignificant (adjusted HR=1.16, 95%CI:0.79-1.71, $P = .44$). Patients with FMS and PsA were more likely to receive multiple biological therapy lines (42.1% vs. 30.6%, OR=1.65, 95%CI:1.19-2.28, $P = .003$). FMS was associated with shorter treatment durations (3.0±3.1 years vs. 4.2±3.6 years, $P = .001$). Linear regression showed a negative association between FMS and mean duration of each biological therapy (B=-0.97, β=-0.1, $P = .001$).

***Conclusions*:** This study highlights a heightened FMS prevalence in PsO patients, revealing increased likelihood of therapy switching and shorter treatment durations. It underscores the importance of comprehensive management strategies addressing both PsO and FMS, optimizing treatment adherence for improved patient outcomes.

EP273 / #409

Comprehensive Description of Adult-onset Still's Disease After COVID-19 Vaccination

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***Background and Aims*:** Cases of adult-onset Still's disease (AOSD) have been reported after COVID-19 vaccination. Here we provide a comprehensive description and analysis of all cases of AOSD reported in the literature and in pharmacovigilance databases through April 2022.

***Methods*:** We collected all cases of AOSD after COVID-19 vaccination reported in the World

Health Organization's pharmacovigilance database or published in the literature until June 2022. Disproportionality analyses of pharmacovigilance data were performed in order to further explore the association between vaccination and AOSD.

***Results*:** We included 159 patients, 144 from the World Health Organization pharmacovigilance database and 15 from the literature. Detailed clinical characteristics were described for the cases from the literature and from the French pharmacovigilance database (n=9). The cases of AOSD after COVID-19 vaccination concerned women in 52.2% of cases. The median age was 43.4 years. More than 80% of AOSD reports occurred during the first three weeks and concerned mostly the BNT162b2 mRNA vaccine. We identified 14.5% of disease flare with a median time-to-onset of AOSD flare-up significantly shorter than for the new onset form. More than 90% patients received steroids. Although all cases were considered serious and required hospitalization, most cases presented a favorable outcome (67.1%) with a good response to corticosteroid therapy with a mean time to recovery of 7.2 days. Disproportionality analyses suggested that AOSD was associated with COVID-19 vaccines as well as other vaccines. AOSD was nearly five times more frequently reported with COVID-19 vaccines than with all other drugs (ROR=4.96; 95%CI: 4.11–5.99).

***Conclusions*:** Our results suggest an association between COVID-19 vaccination and new onset or flare of AOSD. Clinicians should be informed about this potential risk and the importance of its early detection to optimize its management.

EP274 / #799

Influence of Rheumatoid Factor Titers on Serum Drug Levels of TNF Inhibitors with Different Molecular Structures in Rheumatoid Arthritis

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Background and Aims: Certolizumab pegol (CZP), an Fc-free antibody fragment, has shown stable serum levels and steady efficacy in the treatment of RA patients, irrespective of RF levels at baseline. Here, we examine, in clinical practice, the effect of baseline RF levels on serum drug levels of IFX, ADL and CZP an Fc-free antibody fragment.

***Methods*:** In this retrospective study we assessed 170 patients with RA: 90 (53%) received IFX, 48 (28%) ADL and 32 (19%) CZP. Demographic and clinical variables and RF levels were obtained at the baseline visit (T0), and patients were stratified based on negative, low, medium, or high levels. After 6 months (T6) serum drug levels and anti-drug antibodies (ADAb) were computed.

***Results*:** While CZP serum levels did not differ across RF groups at T6, high baseline RF was linked to lower serum drug levels compared to RF negative status in treatment with IFX and ADL. No differences in disease activity measured by DAS28 at baseline were observed across RF quartiles in patients treated with IFX or ADL. ADAb was observed in 26 patients with IFX, 3 with ADL and 1 with CZP, following 6 months of treatment. Patients with high baseline RF levels dropped out more frequently by secondary inefficacy in IFX or ADL than CZP (80% vs 75% vs 33%, $P = .002$).

***Conclusions*:** CZP serum levels were independent of RF levels in patients, however patients with high baseline RF levels who obtained IFX or ADL had lower serum drug levels at T6 than baseline RF-negative patients.

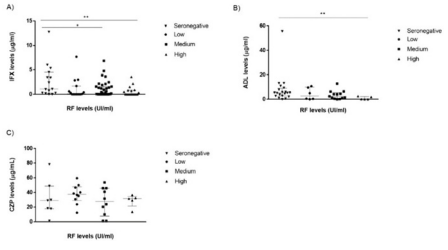

Figure 1.

EP275 / #352

The Effects of Pilates Exercise Training Combined with Walking on Cardiorespiratory Fitness, Functional Capacity and Disease Ac-Tivity in Patients with Non-Radiologically Confirmed Axial Spondylitis

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***Background and Aims*:** The objective of the study was to examine the effects of pilates exercise training combined with walking on cardiorespiratory fitness, functional capacity and disease activity in patients with non-radiologically confirmed axial spondylitis (nr-axSpA).

***Methods*:** 30 patients with nr-axSpA [27 women (90%), with a mean age of 46.07±10.48 years old and C-reactive protein (CRP) 2.26±2.14 mg/l] were randomly divided into two groups: A (n_1=15 patients) and B (n_2=15 patients). Group A followed a 6-month home-based pilates exercise training program, while group B remained untrained until the end of the study. CPET, TUG, 5xSTS, SR, BSR and BSL, BASDAI and ASDAS, were applied to all patients, both at the begin and at the end of the study.

***Results*:** After 6 months, group A showed higher values in exercise time by 37.41% (P = .001), VO_2peak by 25.41% (P = .01, VO_2/HRmax by 14.83% (P = .04) and SR by 18.70% (P = .007), while lower values were observed in TUG by 24.32% (P = .001), 5xSTS by 12.13% (P =.001), BASDAI by 20.00% (P = .04) and ASDAS score by 23.41% (P = .03), compared to group B. Linear regression analysis showed a positive correlation in group A between BASDAI and 5xSTS (r=0.584, P = .02), BASDAI and TUG (r=0.538, P = .03), and ASDAS and 5xSTS (r=0.538, P =.03), while a negative correlation was found between BASDAI and VO_2peak (r=-0.782, P < .001), ASDAS and SR (r=-0.548, P = .03) and ASDAS and VO_2peak (r=-0.659, P = .008).

***Conclusions*:** To sum up, cardiorespiratory fitness, functional capacity and disease activity improved after a long-term pilates exercise training program in patients with nr-axSpA.