serological variables and reflected the uptake of opsonized SNEC by neutrophils in the blood.

Conclusion: SNEC ELISA allows for the sensitive detection of pathologically relevant autoantibodies in the serum of patients with SLE. The clearance of nuclear remnants by neutrophils enhances inflammatory responses supporting the role of clearance deficiency in the etiopathogenesis of SLE.

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SP0175 POST-TRANSLATIONAL MODIFICATIONS OF ANTIBODIES: WHERE THERE'S SMOKE THERE'S FIRE

Rene Toes. *Leiden University Medical Center, Rheumatology, Leiden, Netherlands*

Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. One of the most prominent examples of such autoantibodies are anti-citrullinated protein antibodies (ACPA), which are directed against a wide-array of citrullinated proteins. The immune response to citrullinated antigens is a dynamic response that expands before the onset of disease and generates antibodies that are extensively glycosylated in the variable domain. This feature of ACPAs is remarkable and might be involved in the breach of tolerance to citrullinated proteins as well as function as an additional biomarker to predict disease onset in subjects at risk.

Next to ACPA, it has become clear that the autoantibody response in RA extends towards several other modified proteins, such as proteins modified by carbamylation or acetylation. Carbamylation leads to the formation of homocitrulline. Structurally, homocitrulline greatly resembles citrulline but is one methylene group longer. In contrast, acetylation is mediated by intracellular acetyltransferases and is structurally less related to citrulline or homo-citrulline. Although the presence of autoantibodies against these post-translationally modified proteins (Anti-Modified Protein Antibodies; AMPA) hallmark RA, at present, there is no conceptual framework explaining the concordant presence of different AMPA-responses in RA. In the context of this presentation, the latest insights into the development of humoral response against citrullinated-, carbamylated and acetylated proteins in relation to their role as biomarkers to predict the development of RA will be discussed.

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SP0176 PATHOGENIC ANTIBODIES IN PHOSPHOLIPID SYNDROM

Sasa Cucnik. *University Medical Center Ljubljana, Department of Rheumatology, Immunology Laboratory, Ljubljana, Slovenia*

Antiphospholipid syndrome (APS) is prothrombotic systemic autoimmune disorder characterized with multisystem manifestation, most commonly venous and arterial thromboembolism and/or recurrent pregnancy loss. The varying clinical phenotype is associated with heterogeneity in the pathogenic antiphospholipid antibodies (aPL) that are central to the diagnosis of APS. According to the international consensus statement on classification criteria, APS is classified when persistently elevated levels of specific aPL, such as lupus anticoagulant (LA), anticardiolipin (aCL) and anti- β 2 glycoprotein I (anti- β 2GPI) antibodies, are confirmed in addition to clinical manifestations (1, 2). The exact pathogenesis of APS is unknown, but aPL have been described to activate monocytes, neutrophils, dendritic cells and placental tissue (3). Despite the fact that many different proteins have been identified as being involved in the pathogenesis of APS, accumulating evidence from in vitro experiments as well as animal studies has revealed that β 2GPI is the main target for aPL. It was also shown that triple aPL positivity, defined by detection LA, high titres of aCL and anti- β 2GPI antibodies, correlates better with both thrombosis and pregnancy morbidity than any other aPL profile (4).

Several autoantibodies outside those included in APS classification criteria could be also relevant to APS pathogenesis (5) and therefore, antibodies against other antigen targets have been investigated. Current evidence shows that some of these antibodies, particularly antibodies against domain I of β 2GPI (anti-DI- β 2GPI) and phosphatidylserine dependent anti-prothrombin antibodies (aPS/PT)

might be relevant in the better recognition of APS patients. These antibodies are commonly referred as non-criteria aPL (6) because they have not been yet accepted as laboratory criterion for the diagnosis of APS. The DI of β 2GPI has been identified as the most relevant antigenic target involved in β 2GPI/anti- β 2GPI antibody binding. Anti-DI- β 2GPI antibodies were found to be strongly related to thrombosis and pregnancy complication and are more frequently detected in patients with APS than in asymptomatic aPL carriers (7). High titres of anti-DI- β 2GPI are also frequently present in triple aPL positive patients. Nevertheless, it is far too soon to recommend replacement of anti- β 2GPI testing with an anti-DI- β 2GPI antibody assay because it was shown that about 30% of patients with anti- β 2GPI antibodies are negative for anti-DI- β 2GPI antibodies (8). The clinical significance of autoantibodies reacting with epitopes other than DI was also investigated in multicenter study (9). The results showed a diverse clinical association with reactivity to different epitopes on β 2GPI, suggesting all domains were relevant. Therefore, more detailed profiling of domain specificity and avidity of anti- β 2GPI antibodies may be useful as risk stratification for clinical events.

aPS/PT antibodies also represent strong risk factor for thrombosis. Results of multicenter study demonstrated that IgG aPS/PT detection might contribute to a better and more reliable identification of APS patients (10).

Due to the heterogeneity of aPL (criteria and non-criteria) the interpretation of aPL results is huge challenge in daily routine practice and should always be related to clinical symptoms and therefore, interaction between the laboratory and clinician is essential.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Lessons learned from checkpoint inhibitors

SP0177 IMPACT OF CHECKPOINT INHIBITORS ON B CELLS

David Pisetsky. *Duke University Medical Center, Medicine/Immunology, Durham, North Carolina, United States of America*

Immune checkpoint inhibitors (ICI) are a new class of biological agents that has revolutionized the treatment of cancer. Unlike conventional cytotoxic agents that

are designed to kill cells, ICI block interactions that regulate the T cell response to cancer. At present, two classes of ICI are available to treat a wide variety of malignancies: antibodies to cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and antibodies directed to the programmed death-1 (PD-1) and PD-1 ligand (PD-L1) axis, either to PD-1 or PD-L1. While both anti-CTLA-4 and antibodies to PD-1/PD-L1 are effective, these systems differ in the T cell populations affected, the location of these cells and the downstream signaling pathways involved. ICI can be used alone or in combination. Despite differences in mechanism of action, treatment with both types of ICI is associated with severe side effects that have been termed immune-related adverse reactions (irAE). irAE include, among other manifestations, dermatitis, colitis, pneumonitis, endocrinopathy (hypothyroidism, hypophysitis, adrenal insufficiency) and arthritis and related conditions. Because of the goal of ICI therapy is the induction or stimulation of cytotoxic T cells, the effect of these agents on B cells has received much less attention. In general, effects of ICI on tumors are considered the action of T cells. irAE, however, may result from B cell effects and the induction of autoantibodies. Thus, autoantibodies to thyroid antigens may lead to thyroiditis and subsequent hypothyroidism. Similarly, ICI can lead to the production of antibodies to islet antigens as well as glutamic acid decarboxylase 65 and induction of diabetes. On the other hand, while arthritis can be an irAE, affected patients usually do not show antibodies to citrullinated proteins (ACPA). Importantly, functional and phenotypic properties of B cells following ICI may help predict the emergence of irAE. Much of the data on this issue comes from a detailed analysis of patients with melanoma treated with anti-CTLA-4, anti-PD-1 or the combination. With this combination, B cells of treated patients showed characteristic changes that include a decrease in the number of circulating B cells in conjunction with an increase in plasmablasts and a population of B cells characterized by low expression of CD21. Furthermore, in treated patients, the CD21^{lo} B cells population showed greater clonality as well as a higher frequency of clones in comparison to the CD21^{hi} population. These changes, which may resemble those seen in patients haploinsufficient for CTLA-4, may predict the development of irAE. The CD21^{lo} B cell population may have a particular role in the development of irAE since these cells appear to be recent emigrants from germinal centers and may undergo rapid activation. The effects of ICI on B cell populations is also relevant for ICI use in the setting of pre-existent inflammatory or autoimmune disease marked by autoantibody production. While ICI, either alone or in combination, can lead to the exacerbation of these conditions, the effect on autoantibody production has not yet been well studied. These exacerbations, however, can respond to agents such as glucocorticoids or TNF blockers whose B cell effects are not clear. Since B cells can express PD-1 as well as PD-L1, the effects of ICI may direct actions or the indirect effects on other cell populations. Future studies are needed to delineate more precisely the contribution of B cells to the response of cancer to ICI as well as the development of irAE.

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SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Orthotic treatment: is it in or out?

SP0178 LOWER LIMB ORTHOSES

Martin van der Esch. *Amsterdam Rehabilitation Research Center | Reade, Rehabilitation, Amsterdam, Netherlands*

Background: Osteoarthritis (OA) is the most common rheumatic disease of the musculoskeletal system, with the knee as the most affected joint. The number of people with OA of the knee is likely to increase due to the ageing society and the obesity epidemic. The predominant clinical symptom of knee OA is pain, which is described as worsening by activity and relieving by rest. Knee instability has been recognized as an important clinical feature in persons with knee OA. Pain and knee instability are associated with limitations in performing daily activities. Non-pharmacological options in the management of knee OA consist of education, weight loss, exercise, braces and physical therapy. Knee bracing has been recommended by the Osteoarthritis Research Society International (OARSI). Valgus knee braces designed to decrease loads on the medial compartment of the knee for patients with varus alignment are the most common. It has been shown however, that valgus bracing may have little or no effect on pain and physical functioning, and adherence to this treatment in patients with knee OA is low.

Because of ease of use and access, lack of complications and low cost, soft knee braces are commonly used in persons with knee OA. However, the evidence for efficacy of soft knee bracing on pain and activity limitations in knee OA is limited. Therefore, it is important to strengthen the evidence of using a soft brace to reduce pain and activity limitations as well as to evaluate the efficacy of soft knee bracing on knee instability in persons with knee OA. There is also debate about the

effectiveness of soft braces in other affected joints of the lower extremity and in conditions other than OA such as rheumatoid arthritis.

Objectives: The aim of the study will be to evaluate the effect of wearing a soft brace on dynamic knee instability in patients with OA of the knee.

Methods: Persons with knee OA and self-reported knee instability from the Amsterdam Osteoarthritis cohort participated in a single-session lab-experimental study. A within-subject design was used, comparing no brace versus brace, and comparing a non-tight versus a tight brace (standard fit). The primary outcome measure was dynamic knee instability, expressed by the Perturbation Response (PR), i.e., a biomechanics based measure reflecting deviation in the mean knee varus-valgus angle after a controlled mechanical perturbation, standardized to the mean (SD) varus-valgus angle during level walking. Linear mixed-effect model analysis was used to evaluate the effect of a brace on dynamic knee instability.

Results: The wearing of a soft brace reduced the knee instability significantly during perturbed walking. Results will also be presented from the literature search and from the lab-experimental study.

Conclusion: Wearing a soft brace reduces dynamic knee instability in patients with knee OA. However, longitudinal studies are needed to evaluate the clinical implications of wearing a soft brace.

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SP0179 ORTHOSES AND ASSISTIVE DEVICES FOR THE HAND

Nina Osteras. *Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway*

This presentation will summarize the scientific evidence for the effects of orthoses and assistive devices for the hand. The main focus will be on hand osteoarthritis. The presentation will shed light on how orthoses and assistive devices may facilitate participation.

Disclosure of Interests: None declared

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SP0180 FOOT ORTHOSES IN RA

Jim Woodburn. *Glasgow Caledonian University, School of Health and Life Sciences, Glasgow, United Kingdom*

In this presentation I will: (1) Provide a general overview of the indications and use of foot orthoses in rheumatoid arthritis (RA) ¹, (2) Explore mechanisms of action with respect to preserving, maintaining and restoring foot biomechanics ², (3) Summarise current evidence on the use of foot orthoses for managing foot pain, disability, deformity and quality of life by drawing on recently published systematic reviews and meta-analyses³. Further I will direct delegates to national, European and International evidence-based clinical guidelines where they exist^{1,4}, and (4) Introduce new technology advances with regards to materials and digital design and manufacturing concepts².

I will conclude the presentation by setting out future directions and priorities for both clinical practice and research and innovation.

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