spine is the worst long-term outcome of this disease, although this occurs less frequently nowadays if compared to former decades. This fact might be related either to the natural course of the disease that becomes milder over time or to a consequent anti-inflammatory treatment initiated earlier in patients with axSpA. Structural damage in the spine in axSpA is usually assessed on plain radiographs of the spine and, therefore, is frequently referred to as radiographic spinal progression. In the presentation, pathophysiology, assessment and ways of prevention and/or retardation of structural damage progression in the spine in patients with axSpA will be discussed.

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SP0081 STRUCTURAL DAMAGE PROGRESSION IN PSA

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Psoriatic arthritis is a multifaceted disease in which the arthritis tends to be less frequent than in rheumatoid arthritis. This provides a challenge to measure radiographic progression using the simple and time-honoured fashion of assessing the hands and feet. Further, radiographic progression is slower in PsA and changes over a short time period, such as the placebo controlled phase of a trial, are minimal. Newer imaging, such as ultrasound and MRI may be more sensitive and responsive but data on these techniques are limited. These challenges, and how to overcome them, will be discussed.

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THURSDAY, 13 JUNE 2019

15:30:00 – 17:00:00

Difficult to manage Sjögren's syndrome and Myositis

SP0082 SCREENING FOR MALIGNANCIES IN SJOGREN SYNDROME AND MYOSITIS

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Both myositis and Sjögren syndrome may be associated with cancer. However, there are differences between the cancer-associated myositis and cancer that appears in patients with Sjögren syndrome, and these differences make for a distinct tumor screening approach. The fact that any type of cancer -mainly of the adenocarcinoma type- can be associated with myositis -dermatomyositis, either classical or amyopathic, immune-mediated necrotizing myopathy, or polymyositis phenotypes- makes more difficult to know if an occult malignancy is present. Nevertheless, in recent years biological markers such as several autoantibodies, essentially anti-TIF1 γ , but also anti-NXP2 and to some extent anti-HMGCR, and combined techniques such as PET/CT that allow to detect structural and functional changes by means of ^{18}F -Fluorodeoxyglucose and whole CT have helped the clinician to screen for an occult cancer in patients with myositis. Alternatively, the clinical situation and screening approaches in Sjögren syndrome are more focused in the detection of lymphoproliferative disorders, mostly in salivary glands (MALT type lymphoma) but also marginal zone or diffuse large B cell lymphomas. Several approaches for detecting MALT-type lymphoma or generalized lymphomas, beyond the well-known parameters such as low complement levels, cytopenias, cryoglobulins or persistent enlargement of salivary glands, are also discussed.

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15:30:00 – 17:00:00

Anergy, exhaustion or post-activation in autoimmunity; Facts and future consequences

SP0083 MOLECULAR AND METABOLIC EVENTS WHICH UNDERWRITE T CELL PHENOTYPES IN AUTOIMMUNITY

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The distribution and function of T cell subsets in patients with systemic lupus erythematosus (SLE) is aberrant. Distinct molecular and metabolic events dictate the numbers and function of T cells. Specifically, the transcriptional repressor cyclic AMP response element modulator alpha (CREM α), which is increased in cells from patients with SLE, accounts for the decreased expression of interleukin (IL)-2 and the increased expression of IL-17 through distinct epigenetic processes. CREM α promotes Th17 cell expansion by promoting the expression of Glis1, the first enzyme in glutaminolysis and by suppressing the expression of pyruvate dehydrogenase phosphatase catalytic subunit 2 that enables entry of pyruvate into the Krebs cycle. In parallel, calcium calmodulin kinase 4 which is responsible for the increased binding of CREM α to cAMP response elements of the *IL-2* and *IL-17* loci, promotes the activity of pyruvate kinase M2 and promotes glycolysis and Th17 generation while suppressing the numbers of regulatory T cells. Understanding the exact molecular and metabolic processes that control T cell function in SLE enables therapeutic considerations.

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SP0084 POST-ACTIVATED B CELLS IN AUTOIMMUNITY

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Background: B cells are key players in autoimmune diseases such as systemic lupus erythematosus (SLE), primary Sjögren's syndrome (pSS) and rheumatoid arthritis (RA). In the past, it was believed that B cells from these patients were hyperresponsive to B cell receptor (BCR) and Toll-like receptor (TLR) signaling. New insights suggest that B cells from these patients present a post-activated *functional* phenotype.

Objectives: We aim at characterizing B cells and B cell responses of SLE, pSS and RA patients to understand which venues can be taken towards new therapies for these diseases.

Methods: B cells and B cell subsets from peripheral blood samples from SLE, pSS and RA patients and healthy donors (HD), as well as few autoimmune tissues, were analyzed for: phosphotyrosine kinase (PTK) phosphorylation kinetics, protein phosphatase activity, expression of phosphatases or of checkpoint molecules, such as *e.g.* PD-1, before and after BCR engagement, alone or together with TLR9 and CD40 stimulation, differentiation and proliferation. Expression of transcription factors, such as *e.g.* STAT1, and the effect of interferons in their expression in B cells from patients were also evaluated.

Results: B cell responses upon BCR engagement in SLE, pSS, RA patients were abnormal with diminished BCR downstream PTK phosphorylation. TLR9, but not CD40 responses were also abnormal. Part of the abnormality related to diffuse up-regulation of phosphatases that apparently counteracted PTK signaling. The abnormality was partially mimicked by repeated signaling through the BCR of HD B cells and could be overcome by CD40 engagement. Check-point molecules, such as *e.g.* PD-1, was differentially expressed in SLE naive and memory B cells. SLE naive and memory B cells expressed higher amounts of STAT1 compared to those of pSS, RA and HD.

Conclusion: Post-activated B cells are characterized by a phenotype of dysregulated expression of certain check-point molecules, such as PD-1, some transcription factors, like STAT1 and certain phosphatases (figure 1). Our data suggest that CD40 activation is involved in modulating BCR responses in post-activated B cells. This has implications for innovative therapies since blocking BCR signaling pathways and CD40 activation as well as targeting certain phosphatases may have synergistic value for treating systemic autoimmunity.