**NEW TRENDS IN BIOMARKERS IN INFLAMMATORY JOINT DISEASE**

Eugen Feist, Charité Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany

This lecture provides an overview on new developments in biomarker research and standardization in inflammatory joint diseases. The presentation includes an introduction of established and new biomarkers in serum and synovial fluid as well as methods for their detection. Furthermore, an overview on different modifications of auto-antigens (including citrullinated, carbamylated and acetylated isoforms) and their role in immune response and pathogenesis of disease will be given. The diagnostic performance of new and established biomarkers will be discussed including antibodies against modified antigens also illustrated by difficult to diagnose cases. In this context, special attention will be attributed to the predictive value of biomarkers for diagnosis of disease and treatment response.

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**SPEAKER:** Speakers bureau: Pfizer, Roche, Novartis, BMS, Abbvie, Celgene, Sanofi, Lilly

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**US FOR SYNOVIAL BIOPSY – CLINICAL RELEVANCE AND SAFETY + DEMO**

Andrew Filer, University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom

**Background:** The introduction of ultrasound guidance to access synovial tissue samples has facilitated a rapid growth in tissue-related research. Ultrasound guidance allows operators to use less invasive approaches compared to a gold standard direct vision arthroscopy procedure while maintaining the quality of samples obtained. Patients find the procedures easy to tolerate and are willing to undergo repeat biopsy, facilitating the analysis of tissue samples in clinical trials and experimental medicine studies. Advanced analytic techniques including single cell analytics are now being used to exploit the tissue samples obtained in order to provide dramatic leaps in understanding of synovial pathology.

**Objectives:** In this session the key aspects of the dominant techniques in use will be presented, including safety, patient tolerability and quality of output. The research and clinical utility of synovial biopsy will be discussed. Sonographic approaches to the major techniques will then be illustrated through video demonstrations, and competencies required to undertake training will be discussed alongside current EULAR initiatives for training. Finally, examples of research outputs generated through synovial biopsy will be explored alongside the logistics required to deliver such clinical studies.

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**ULTRASOUND OF THE HAMSTRING MUSCLE COMPLEX-CLINICAL APPLICATION + DEMO**

David Andrew Bong, Instituto Poal de Reumatologia, Universitat de Barcelona, Rheumatology; Anatomy, Barcelona, Spain

The hamstring muscle complex (HMC) are the “brakes” of human bipedal ambulation and are susceptible to injury during concentric contraction. Although common in sports medicine practice, a recent systematic review of severe hamstring injuries (grade II-III) suggests that greater than 10% of these severe injuries are non-sports related and disproportionately affect older women. Musculoskeletal ultrasound (MSKUS) is one of the basic imaging techniques utilized to define these injuries and eliminate other potential causes of posterior thigh pain. This presentation will discuss the clinical application of MSKUS of the HMC in rheumatology/musculoskeletal medicine and offer a systematic anatomically-based method of examining this important non-articular region.

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**US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO**

Andrea Delle Sedie, University of Pisa, Rheumatology Unit, Pisa, Italy

**Background:** Evaluation of interstitial lung disease (ILD) is always difficult (low sensitivity for X-ray and pulmonary function tests or high level of radiation for HRCT): ultrasound (US) has recently shown interesting results on truth, discrimina-

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**COMPLEMENT AND LUPUS IN THE YOUNG AND THE OLD**

Marina Botti, Imperial College London, Centre for Inflammatory Disease/Immunology and Inflammation, London, United Kingdom

Complement component C1q is known to play an important recognition role in adaptive and innate immunity. More recently evidence has emerged that C1q may have roles outside the complement system and the relevance of these functions may change with ageing. Homozygous deficiency of the first component of the complement system, C1q, is one of the most powerful susceptibility genetic factors for the development of systemic lupus erythematosus (SLE). The vast majority of patients with C1q deficiency develop a syndrome closely related to SLE. The disease is typically of early onset and is often very severe. Although the pheno-

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**IS COMPLEMENT A CRITICAL INGREDIENT IN THE DEVELOPMENT OF RA?**

V. Michael Holers, University of Colorado Denver, Rheumatology, Aurora, CO, United States of America

**Background:** Prior studies of patients with classilied rheumatoid arthritis (RA) have demonstrated in synovial fluid, on cartilage surfaces and in the synovium the presence of pro-inflammatory complement activation fragments C3a and C5a, the membrane attack complex (MAC), and C3 fragment-bound immune complexes. Ex vivo studies of RA-related autoantibodies have shown the capacity to activate complement pathways, and also demonstrated the presence of disease-
associated changes in antibody glycosylation that promote engagement of the complement system. In contrast, clinical trials in patients with classified RA utilizing inhibitors of complement C5 have demonstrated minimal improvement. Nevertheless, recent translational research studies of patients during the natural history of RA have opened up new avenues for therapeutic intervention. Specifically, there exists in seropositive RA a prolonged asymptomatic preclinical stage wherein mucosal autoantibody production in the lung is associated with NETosis, elevated cytokines and evidence of activated innate immunity, with the capacity of each to interact and promote localized inflammation. Beyond this, murine studies have strongly suggested that complement C3d generation promotes autoimmunity and therapeutic pathway inhibitory strategies should encompass all of the effector mechanisms and not just those at C5 and beyond.

**Objectives**: The presentation objective is to explore the evidence for involvement of the complement system in the preclinical development of RA, and what mechanisms may be involved to promote autoimmunity and ultimate joint damage.

**Methods**: The presentation will review studies of the natural history of human RA, with an emphasis on the potential roles for complement in multiple stages of disease. In addition, the results of informative murine studies which have explored the mechanisms by which the complement system can modulate the development of experimental autoimmune arthritis will be summarized.

**Results**: Studies of preclinical RA in subjects have suggested the potential for complement and NETs to interact and promote localized mucosal inflammation in the lung. In addition, murine studies of the roles of complement have supported that all components of the pathway, including C3d linked to antigens, the anaphylatoxins C5a and C3a, as well as the MAC, are centrally involved in promoting arthritis.

**Conclusion**: Complement likely plays a role in multiple phases of RA development, including: 1) mucosal inflammation and the break in systemic tolerance to citrullinated antigens, 2) initial inflammation following targeting of ACPA to the synovium in early RA, and 3) regulation of RA-related autoantibody production. In addition, it is likely that inhibition of C3 and C5 convertases in tandem will be necessary to see major clinical effects in patients with active synovitis. Finally, the use of a complement inhibitor or modulator in the pre-clinical, transitioning and/or early RA populations are all intriguing approaches.

**REFERENCE:**

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