SP0165 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.

Disclosure of Interests: Eugen Feist Grant/research support from: Pfizer, Roche, Novartis, BMS, Sanofi, Lilly, Consultant for: Pfizer, Roche, Novartis, BMS, Abbvie, Celgene, Sanofi, MSD, Lilly, Speakers bureau: Pfizer, Roche, Novartis, BMS, Abbvie, Celgene, Sanofi, Lilly

DOI: 10.1136/annrheumdis-2019-eular.8474

FRIDAY, 14 JUNE 2019

15:30:00 – 17:00:00

Ultrasound advanced II
SP0166 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 detect and 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.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8433

SP0167 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, discrimination and feasibility. Due to the thickening of interlobular septa for edema or fibrosis, US beam can interact with those structure and produce artifacts on the screen:

B-lines (BL) and pleural line irregularity (PLI). A positive correlation between BL and HRCT has been established both in systemic sclerosis patients and in other patients with ILD; more recently similar results have been published by using PLI as a finding for US assessment in patients.

BL has been recently defined by the OMERACT as a vertical hyperechoic reverberation artifact that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding, while PLI has been defined as a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular.

A low number of BLs has been described in healthy subjects but they are generally confined to the posterior and lower part of the thorax.

Up to now, many different scanning protocols have been used to assess BL or PLI in patients, providing similar results.

Conclusion: US lung evaluation is a useful and feasible imaging technique.

Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD

DOI: 10.1136/annrheumdis-2019-eular.8458

SP0168 US FOR SYNOVIAL BIOPSIES – 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 enables 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.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8479

FRIDAY, 14 JUNE 2019

17:30:00 – 19:00:00

Complement and autoimmunity – emerging therapeutic opportunities
SP0169 COMPLEMENT AND LUPUS IN THE YOUNG AND THE OLD

Marina Botto. *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 phenotype of disease varies between patients, the fact that C1q deficiency is sufficient to cause SLE in almost all humans identifies a pivotal role for this molecule. The challenge is to identify the relevant physiological activity that can explain this strong association.

On the other hand, C1q seems to play a different role in old people. The concentration of C1q rises with aging and can be modulated by exercises. Of note, increased levels of C1q have been reported in the central nervous system of old people, with the highest levels being seen in close proximity to synapses and central regions of the brain suggesting that C1q may play a role in the development of problems associated with aging. Consistent with this hypothesis aged C1q-deficient mice showed less cognitive and memory decline in hippocampus-dependent behaviour tests compared to their wild-type litter mates.

In summary, the traditional view of the role of C1q as just initiator of the classical complement pathway needs revision. Evidence is emerging that C1q has roles outside the complement system and these will be discussed.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8434

SP0170 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 classified 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:

- [1] Holers, V.M., et al. 2018. Rheumatoid arthritis and the mucosal origins hypothesis: protection turns to destruction. *Nature Reviews Rheumatology* 14:542-557. 2. Holers, V.M., and Banda, N.K. 2018. Complement in the initiation and evolution of rheumatoid arthritis. *Front. Immunol.* 9:1057.

Disclosure of Interests: V. Michael Holers Grant/research support from: Janssen, Consultant for: Janssen

DOI: 10.1136/annrheumdis-2019-eular.8502

SP0171 THE NEW COMPLEMENT THERAPEUTICS

Claire Harris. Newcastle University, School of Medicine, Newcastle-upon-Tyne, United Kingdom

Despite a wealth of knowledge in the complexities of the complement cascade, and many decades of endeavour, very few drugs have progressed to the clinic. Recently, strong genetic associations of complement with common diseases have emerged and fuelled the fire of complement drug discovery leading to an explosion in complement therapies in development; while many of these agents and others before them have failed to progress, their legacy is key to future success. Obstacles to successful drug development include target concentration and turnover rates, and ability to target to the appropriate site. The drug development landscape is littered with agents that have failed at the preclinical or early clinical stage; their modes of action and modalities are wide-ranging. It is becoming increasingly clear that an understanding of disease mechanism and matching of drug modality and mode of action to the right disease and patient population (or stratified sub-population) is critical to success. A number of drugs are now in phase 3 clinical development for a number of different diseases. In this talk, innovative approaches that are emerging to overcome obstacles blocking success will be explored, highlighting drugs in development which employ new state-of-the-art strategies. These include 'homing' drugs and a new generation of orally bioavailable molecules.

Complement biomarkers that can decipher disease mechanism and be applied for patient stratification will be discussed. It is clear that a range of different drugs, or combination of drugs, will be needed for effective management of the many and diverse complement-mediated diseases.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8492

SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Lights at both ends of the tunnel? Advances in GI Involvement in SSC

SP0172 CASE 2 PRESENTER: ALWAYS AT THE EDGE: SEVERE GI COMPLICATIONS

Kristina Clark. University College London, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom

The clinical impact of lower gastrointestinal tract involvement in systemic sclerosis will be illustrated through a case presentation. This will describe the challenges of managing patients with systemic sclerosis presenting with pseudo-obstruction, severe malnutrition, and electrolyte imbalance and how these were managed to optimise patient care.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8447

SP0173 CASE 2 DISCUSSANT: IMMUNOSUPPRESSION OR ANTIBIOTICS – WHEN TO CHOOSE WHAT?

Christopher Denton. Royal Free Campus, x, x, United Kingdom

Gastrointestinal tract involvement is almost universal in systemic sclerosis but in most patients is relatively mild with symptoms of gastro-oesophageal dysmotility and reflux or lower bowel symptoms of constipation. A minority of cases have severe involvement, and this can be life-threatening. The key issues related to severe disease are attacks of pseudo-obstruction with complications such as pneumatosis coli and perforation of infection. Additional issues include malnutrition and intestinal failure that may require long term home parenteral supplementation. Finally, the most severe lower tract involvement can result in intractable diarrhoea, persistent anorectal incompetence and complications of severe chronic constipation such as sigmoid volvulus. Management is challenging and requires interaction with gastroenterology and nutritional expert colleagues. Some newer approaches that have been beneficial include long term intravenous immunoglobulin therapy although in general response to immunosuppression are relatively modest. This discussion will focus on treatment with immunomodulation and use of antibiotic therapy to treat small intestinal bacterial overgrowth and also to manage other infective problems and the potential impact on intestinal dysbiosis.

Disclosure of Interests: Christopher Denton Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant for: Roche-Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer

DOI: 10.1136/annrheumdis-2019-eular.8459

SATURDAY, 15 JUNE 2019

09:00:00 – 10:30:00

Novel autoantibodies in RMD: a neverending quest?

SP0174 ADVANCES IN THE DETECTION OF PATHOGENIC AUTOANTIBODIES IN SLE

Luis Munoz. Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Internal Medicine 3, Erlangen, Germany

Background: The accumulation of late apoptotic or so-called Secondary Necrotic Cells (SNEC) in germinal centers challenges B and T cell tolerance and leads to the development of autoimmunity and the production of autoantibodies.

Objectives: Determine the test performance of immobilized SNEC autoantigens for the diagnosis of Systemic Lupus Erythematosus.

Methods: SNEC ELISA of sera from patients with SLE and test performance statistics were deployed to evaluate the diagnostic potential SNEC-derived autoantigens. Functional assays confirmed its pathophysiological relevance.

Results: SNEC contains nuclear autoantigens bearing apoptosis-associated modifications such as histone H3 K27me3, histone H2A/H4AcK8,12,16, and histone H2B-AcK12. The SNEC ELISA clearly discriminated patients with SLE from patients with Rheumatoid Arthritis (RA), Primary Anti-Phospholipid Syndrome (PAPS), Spondyloarthritis (SpA), Psoriatic Arthritis (PsA), and Systemic Sclerosis (SSc). A positive test result in SNEC ELISA significantly correlated with