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.

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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

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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

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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.

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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