the inherent mechanism of Nec-1 inhibit neutrophil release NETs is related to it specifically promotes neutrophil apoptosis.

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Acknowledgements Thanks to the colleagues in the team of Dr Erwei Sun.

Disclosure of Interest None declared.

P047

THE PLASMA CELL BONE MARROW NICHE IN ACPA+ RA PATIENTS CONTAIN CITRULLINE SPECIFIC CELLS

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10.1136/annrheumdis-2018-EWRR2019.39

Career situation of first and presenting author Post-doctoral fellow

Introduction Anti-citrullinated antibodies (ACPA) in RA have been postulated to contribute to disease pathogenesis. This has been supported by studies of monoclonal APCA generated by cloning from single cell sorting of different B cell subsets from peripheral blood and synovial fluid. It has been debated if the bone marrow (BM) compartment of RA patients hosts long lived plasma cells producing ACPA or if ACPA are primarily coming from plasmablasts at the sites of inflammation, e.g. the synovium.

Objectives The main objectives were to study primary lymphoid tissue from RA patients, the BM plasma cell IgG repertoire and further characterize recombinantly expressed antibodies from selected sequences to explore if ACPA producing long lived plasma cells reside in this niche.

Methods For this study we collected bone marrow from proximal or distal femur of RA patients undergoing hip replacement surgery due to secondary osteoarthritis. BM samples were processed from four ACPA+RF+ and one ACPA-RF+ RA patients. Mononuclear cells were obtained by Ficoll separation and CD138+ plasma cells were single cell sorted by flow cytometry. Paired heavy and light chains were PCR amplified, sequenced and analyzed by V-Quest and IgBLAST towards the IMGT database to annotate variable gene usage. Selected sequences were cloned and expressed as IgG in Expi293 cells.

Results Overall 465 paired IgG BM plasma cell sequences were obtained, 97 from the ACPA- patient and 368 (range 20–194) from ACPA+ patients. We observed statistically significant changes in heavy chain variable gene usage with lower VH-1 and higher VH-3 frequency in the ACPA+ sequences compared to ACPA- sequences. We also found statistically significant increase in VH N-glycosylation in ACPA+ sequences (22.6% ACPA+ vs 12.4% ACPA-; $p=0.03$). There was however no difference in mutation numbers. From these, 34 clones were selected, based on mutation numbers and presence of Fab N-glycosylation sites, for subsequent mAb-expression. Among the 34 clones we found two CCP2+ and cit-peptide

positive clones and one malondialdehyde-acetaldehyde (MAA) adduct reactive clone, originating from different APCA+ patients.

Conclusions We could identify BM plasma cells producing autoantibodies to malondialdehyde-modified proteins and citrullinated peptides, isolated from RA patients. Hence, we show for the first time, that not just at the site of inflammation but also long-lived plasma cells in bone marrow do produce RA specific autoantibodies.

Acknowledgements Orthopedic staff at Karolinska University Hospital. Danika Shepis, Louise Berg and Christina Gerstner for sorting help.

Disclosure of Interest None declared

P048

PREDICTIVE VALUE OF THE DIFFERENT CAPILLAROSCOPIC PATTERNS IN EARLY RAYNAUD PHENOMENON

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10.1136/annrheumdis-2018-EWRR2019.40

Career situation of first and presenting author Assistant.

Introduction The Raynaud phenomenon (RP) affects 3%–5% of the population. Most RPs are primary. The risk of the onset of autoimmune disease associated with RP (ADRP) is around 12%, and the diagnosis is usually made within 2 years of its onset. Capillaroscopy is a innocuous and inexpensive technique that is very useful in the study of RP.

Objectives The primary goal was to evaluate the capillaroscopic findings and their different patterns in patients with RF as the only symptom and establish their relationship between the subsequent development of ADRF. We have evaluated the relationship between the presence of the antinuclear antibodies (ANA) and the association with ADRF.

Methods We conducted an observational, descriptive, cross-sectional study of 98 patients with RP as the main manifestation. Periungual capillaroscopy was performed from the 3rd to the 5th finger of both hands. Sociodemographic variables, and results of ANA were described. To assess the validity of capillaroscopy as a diagnostic test, we determined the sensitivity, specificity, and positive and negative predictive value (PPV, NPV).

Results 73.5% were women. The median time of evolution of the RP was 2.5 years. 76% were ANA negative.

The evaluation of the predictive capacity of capillaroscopy for the development of EARP yields the following Results.

sensitivity: 83,3% (62,6–95,2), specificity: 78% (66,8–86,9), PPV 34,1% (24,5–45,3), PNV 97,1% (93,3–98,8).

The capillaroscopic findings were: 62% no alterations, 21.4% no specific capillaroscopy changes, 14.3% 'scleroderma' type capillaroscopic pattern, and 2% characteristic pattern of mixed connective tissue disease (MCDT). None of the patients who did not present alterations developed autoimmune disease. Of the 21 patients who presented nonspecific changes, 5 developed limited systemic sclerosis (SSc), 3 MCTD, and 1 diffuse SSc. Of the 14 patients who presented 'scleroderma' type capillaroscopic pattern, 5 develop limited SSc, 3 diffuse SSc, 2 MCTD and 1 did not present autoimmune disease. Of the two patients with characteristic alterations of MCDT, 1 developed this disease. When analyzing the relationship between the presence of ANA and the association

with ADRF we found that it was independent ($p: 0.002$) of the result of capillaroscopy, being the risk of developing the disease in a patient with positive ANA 8.5 times higher than in an ANA negative patient.

Conclusions Capillaroscopy in patients with RP has a high PNV, which allows us to estimate, with high reliability, the association of this phenomenon with autoimmune disease in patients with normal capillaroscopic patterns.

Disclosure of Interest None declared.

P049

AGE-ASSOCIATED B CELLS IN EARLY DRUG-NAÏVE RHEUMATOID ARTHRITIS PATIENTS

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10.1136/annrheumdis-2018-EWRR2019.41

Career situation of first and presenting author Student for a master or a PhD.

Introduction Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by joint inflammation and bone destruction. The presence of autoantibodies, years before the clinical onset of disease, and the efficacy of Rituximab, a B-cell depleting therapy, highlight a pathogenic role for B cells. Different groups have recently identified a novel subset of B cells named age-associated B cells (ABCs). Studies in mice autoimmune models and patients suffering from autoimmune diseases described these cells as CD19^{high} CD21⁻ CD11c⁺. Moreover, a subset of synovial fluid B cells with low levels of CD21, expresses FcRL4 and produces the cytokine RANKL, which stimulates the differentiation and activation of osteoclasts. The ABCs found in peripheral blood could therefore be the precursors of this FcRL4 positive subset found in synovia.

Objectives We aimed to investigate the proportion and phenotype of peripheral blood ABCs in patients suffering from early drug naïve RA.

Methods Newly presenting patients, naïve to immunomodulatory treatment, were recruited from the Newcastle Early Arthritis Clinic, and followed until diagnoses were confirmed. B-cell subsets in peripheral blood were detected and phenotyped using flow cytometry. NanoString nCounter Immunology v2 Panel (NanoString Technologies) was used to detect mRNA from cell lysates of sorted ABCs, naïve, memory and CD5⁺ B cells from RA patients, age-matched healthy controls and disease controls (Psoriatic Arthritis patients).

Results Our work showed that there are no significant differences in the frequency of ABCs between RA patients, disease controls and age-matched healthy controls. There is a possible trend for increased frequencies of ABCs with age as well as those who have a high disease activity. Our results also show that ABCs resemble a memory B cells phenotype with regard to class-switch immunoglobulins expression, with a significant percentage of them being positive for IgG and IgA. Interestingly, the FcRL4⁺, the proliferating Ki67⁺ and the T-bet expressing B cells were enriched in the ABC population compared to the other B cell subsets. Furthermore, ABCs expressed high levels of MHC class II and co-stimulatory molecules, as well as the activation marker, CD69. In addition, gene expression analysis using NanoString showed differentially expressed genes between ABCs and memory B cells.

Conclusions These data supports an activated phenotype of the ABCs, which supports the idea that ABCs have a pathogenic role in RA, potentially via autoantibody and T cell stimulatory ability. However, further characterisation of this subset and functional studies are needed.

Disclosure of Interest None declared.

P050

JAN GÖSTA WALDENSTRÖM AND RHEUMATOLOGY

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10.1136/annrheumdis-2018-EWRR2019.42

Career situation of first and presenting author Post-doctoral fellow.

Introduction On 2. September 1943 Jan Waldenström (1906–1996) successfully submitted a paper to Acta Medica Scandinavica describing two patients with a new disease. The discovery was to make him world famous.¹ This year marks the 75th anniversary of macroglobulinemia and it coincided with the 10th biennial international workshop of Waldenström's macroglobulinemia, discussing advances in the genetic basis, pathogenesis and treatments of the disease.² Jan Waldenström 7[MO1] (JW) would have enjoyed this workshop immensely, sharing the information that over 95% of the patients had somatic mutations affecting the MYD88 gene on the 2nd chromosome as well as the impressive advances in treatment. Attending this excellent meeting brought back memories of my time as Waldenström's PhD student and triggers me to compose this vignette, focusing on connections between the interests of my mentor and rheumatology. For a more comprehensive account of Jan Waldenström's legacy I recommend Robert Kyle's superb obituary, published in Blood, a journal JW was attached to from its start.³

After the successful defence of his landmark PhD Thesis on acute intermittent porphyria⁴ Waldenström's interest focused on haematology. He worked in Uppsala, a university where the study of proteins had prominence. There The Svedberg had developed the ultracentrifuge and Arne Tiselius the free electrophoresis and Robin Fåhrus the ESR. Conditions with elevated sedimentation rate (ESR) caught his special attention. An early witness is a paper from 1937, analysing 5 cases diagnosed with uveoparotitis, a rare condition most prevalent in women and considered by many to be a form of tuberculosis. He noticed the several multiorgan manifestations, the similarities with von Mikulits' disease and Boeck's sarcoid, the presence of high ESR, unspecific Wasserman reaction, absence of proof of tuberculosis, presence of xerostomia, and frequent CNS manifestations.⁵ Today the diagnosis could have been IgG4 related disease in several of these patients. This early paper also shows a keen interest in inflammatory systemic conditions.

In the early 1940s JW collected serum from some 100 patients with longstanding ESR exceeding 120 mm, and had it analysed by the new technique of free boundary electrophoresis by K.O. Pedersen in the Department of Physical Chemistry. In 1943 he described 3 cases from this population characterised by repeated bouts of declive purpura, leaving spots of brown discoloration, mild anaemia, and on the whole, good general health. Two of the 3 women also had dry eye problems and one had dry mouth and swollen parotid glands. He named the condition 'purpura