development and bone homeostasis. It has recently been demonstrated that RANK-activated astrocytes release CCL20 and attract T cells to the central nervous system in a model of Multiple Sclerosis and that transgenic RANK expression in the skin promotes aberrant epithelial cell proliferation and is sufficient to induce ectopic formation of tertiary lymphoid structures (TLS). Ductal epithelial cells (SGEs) have been implicated in Sjögren's Syndrome (SS) pathogenesis where they mediate immune recruitment by expression of pro-inflammatory chemokines and support the formation of pre-malignant myoepithelial lesions.

Objectives To address the role of RANK-RANKL interaction in primary (p) SS.

Methods A combination of human and mouse studies were used to explore the RANK-RANKL interaction in pSS. Salivary glands (SGs) and saliva samples from patients recruited in the OASIS cohort (University of Birmingham) were studied to evaluate this pathway in human disease. Consecutive stimulated saliva samples (n=69) were analysed using Proseek Multiplex $INF^{96 \times 96}$, covering 92 unique inflammation-related protein biomarkers. Taking advantage of a viral induced model of pSS we studied the effect of this pathway with a RANKL blocking antibody and by inducing gain of function with direct cannulation in the salivary glands of recombinant RANKL. Murine SGs were studied by immunofluorescence, flow cytometry and qPCR on total tissue and sorted cells.

Results Fourteen proteins in saliva were significantly separated between pSS and sicca controls, and elevated levels of just two proteins, RANKL and TNFβ, could classify pSS or sicca with 75% accuracy. Levels of salivary RANKL and CCL20 were strongly correlated ($r=0.6$; $p<0.01$). We demonstrated that both human and murine inflamed SGEs upregulate both RANK and CCL20, a chemokine known to recruit pathogenic T cells. Upregulation of RANKL was found in human Th2 cells, classically associated with humoral responses and germinal centre (GC) formation. SGs from mice treated with anti-RANKL antibody showed decreased epithelial proliferation, reduced T cell infiltration and defective TLS establishment. On the contrary, viral infected SGs treated with recombinant RANKL showed increased T cell infiltration, CCL20 expression and enhanced differentiation of GC B cells.

Conclusions *In vivo* RANK/RANKL interaction mediates recruitment of activated T cells that are skewed toward a Th2 phenotype. These, in turn, will favour the establishment of TLS in the SG. Those data were confirmed in human pSS, where expression of RANK is found in inflamed epithelium and RANKL detection in saliva is able to differentiate patients with pSS from sicca controls, thus candidates this pathway both for drug targeting and patient stratification.

Disclosure of interest None declared

P018 PROTEASE ACTIVATED RECEPTOR 2 (PAR2) EXPRESSION IN THE MYELOID COMPARTMENT IMPACTS OSTEOCLASTOGENESIS

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Introduction Protease activated receptor 2 (PAR2) is a G protein coupled receptor responsive to serine proteases, which plays a key role in inflammation and pain reception. Rheumatoid arthritis (RA) patients have up-regulated surface expression of PAR2 in circulating monocytes which correlates with disease activity. We have previously demonstrated that *Par2*$^{-/-}$ mice are protected from inflammation, bone erosion, and cartilage destruction in a Freund's Complete Adjuvant (FCA) induced arthritis model. However, it is unclear how PAR2 affects the composition of the myeloid compartment and osteoclastogenesis.

Objectives The aim of this study was to evaluate the impact of loss of PAR2 on the myeloid compartment and osteoclastogenesis.

Methods Bone marrow (BM) from 6–10 week old *Par2*$^{-/-}$ and control C57BL/6 mice was cultured in pro-osteoclastogenic media for 5 days and the generated mature osteoclasts, tartrate-resistant acid phosphatase positive (TRAP) multinucleated cells, were counted. The resorption potential of these cells was assessed using osteolysis plates and the total osteo-resorption quantified after 7–14 days of culture. BM was also collected for flow cytometric analysis of the haematopoietic cellular composition (with the following markers: CD3, B220, CD11b, Ly6C, Ly6G, CD115, and CD117) and assessed for osteoclast precursors.

Results *In vitro* osteoclastogenesis revealed an increase in numbers of mature osteoclasts from *Par2*$^{-/-}$ BM compared to WT, corresponding with increased levels of resorption. Flow cytometry of BM from both WT and *Par2*$^{-/-}$ mice showed 3 distinct monocyte populations defined by the cell surface expression levels of CD11b and Ly6C. The overall ratio of these populations was not altered in *Par2*$^{-/-}$ animals.

Conclusions BM from *Par2*$^{-/-}$ mice has increased osteoclastogenic potential and overall resorptive activity. We propose that this is not due to differences in bone marrow residing osteoclast pre-cursor numbers. This study indicates a potential role for PAR2 in osteoclast differentiation and bone remodelling.

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P019 ULTRASOUND DETECTED TENOSYNOVITIS AS A MARKER OF SUBCLINICAL INFLAMMATION PRIOR TO ARTHRITIS ONSET

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Introduction Prospective studies of individuals at increased risk of developing rheumatoid arthritis (RA) will further improve the understanding of disease development. Ultrasound emerges clinically useful in detecting subtle inflammatory changes in rheumatic diseases.

Objectives To investigate ultrasound (US) detected changes as markers for future arthritis development.

Methods Patients presenting with musculoskeletal complaints and a positive Anti-Citrullinated Protein Antibody (ACPA) test at primary care, were referred to Karolinska rheumatology clinic for further rheumatic joint disease assessments. Those lacking arthritis by clinical and US examination (defined as synovial hypertrophy with Doppler activity) were recruited