thereby mimicking RA-related conditions. Cytokine/chemokine secretion of IL-6, IL-10, IL-12, IL-8 and CXCL13 was measured using ELISA. Changes of inflammatory pathways including JAK/STAT were evaluated by Western Blot.

Results TLR4-stimulation of M2-macrophages results in suppression of miR-221-3p, while *in vivo* expression in synovial tissue and fluids is significantly increased in RA versus OA or OIA. M2-macrophages with high levels of miR-221-3p lose their anti-inflammatory response and support a M1-like profile. miR-221-3p in combination with miR-155-5p leads to the secretion of M1-specific IL-12 and lowered IL-10. miR-221-3p is affecting the JAK/STAT pathway in M2-macrophages by downregulating JAK3 protein leading to decreased STAT3 activation. Treatment of M2-macrophages using JAK3 inhibitors display the same shift in cytokine/chemokine pattern as increased miR-221-expression.

Conclusions TLR4-activated M2-macrophages exposed to elevated miR-221-3p expression diminished anti-inflammatory response partly by suppressing JAK3/STAT3 pathway. Thus, miR-221-3p is a homeostatic regulator of M2-M1 inflammatory function, which is dysregulated in RA condition.

Acknowledgements Tissue RNA from RA and OA patients was kindly provided by Caroline Ospelt, University of Zurich, Center of Experimental Rheumatology, Switzerland.

Disclosure of Interest None declared.

P071/O13

RNA SEQUENCING DETECTION OF GENE DYSREGULATION IN B CELLS SORTED FROM SALIVARY GLAND TISSUE AND FROM PERIPHERAL BLOOD REVEALS NEW PATHWAYS INVOLVED IN PRIMARY SJÖGREN'S SYNDROME PATHOPHYSIOLOGY

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10.1136/annrheumdis-2018-EWRR2019.60

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

Introduction Primary Sjögren's syndrome (pSS) is a chronic auto-immune disorder characterized by lymphocytic infiltrates and destruction of the salivary glands (SG). Chronic B cell activation, the secretion of autoantibodies and the critical role of BAFF have been demonstrated. However, mechanisms leading to B cells dysregulation remain partially understood.

Objectives To establish transcriptomic maps of the B cells sorted from the SG and from blood in pSS patients and controls using RNASeq.

Methods Patients had pSS according to 2016 EULAR/ACR criteria and controls had sicca symptoms without any antibodies and with normal SG biopsy. B cells were sorted from SG biopsies and from blood using a FACS ARIA. RNASeq profiling was performed using MiSeq. Statistical analysis identified differentially expressed genes between pSS and controls in B cells sorted from SG (9 pSS, 4 controls), from blood (16 pSS, 7 controls); and between B cells sorted from SG and blood in the same patients (4 pSS patients). Functional enrichment analysis used Ingenuity Pathway Analysis.

Results The pSS vs controls comparison in B cells sorted from SG identified up-regulated genes involved in activation of B cells including CD48, CD22 and CD40. TLR10, which

is involved in innate immunity was also up-regulated in pSS.

In blood B cells, TLR7 and the downstream signaling molecule IRF7 were up-regulated in pSS. Additionally, IL-6 which is involved in B cells growth was up-regulated. Enrichment analysis highlighted EIF2 signaling pathway, interferon (IFN) signaling pathway and role of JAK in IFN signaling.

The paired comparison between B cells from SG and from blood identified up-regulated genes including CD138, a plasma cell marker, IL-6, TLR5 and IFN induced genes.

The confirmation by qPCR of these results is ongoing.

Conclusions This study allowed to explore the mechanisms that support B cell activation in pSS focusing on tissue resident and circulating cells. Data confirmed B cell activation and differentiation through several markers and highlighted the role of innate immunity and key pathways including IFN and JAK signaling. Precise understanding of these dysregulations should offer development of new targeted therapeutic perspectives.

Disclosure of Interest None declared.

P072

MEFV/MIR-326 AXIS INVOLVEMENT IN HUMAN MACROPHAGE POLARIZATION

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10.1136/annrheumdis-2018-EWRR2019.61

Career situation of first and presenting author Young investigator.

Introduction Familial Mediterranean fever (FMF) is an inherited autoinflammatory disease, characterized by acute self-resolving attacks of fever and serositis, which mainly prevails in populations around the Mediterranean sea. It is caused by mutations in the *MEFV* gene, which encodes the pyrin protein. The alteration of *MEFV* mRNA expression in monocytes is related to both genotype and phenotype of the disease, suggesting that the pathophysiology of FMF can be regulated on a quantitative defect of *MEFV* mRNA.

Objectives Since microRNAs (miRNAs) are implicated in a number of diseases including FMF, the present study aimed at identifying miRNA regulators of *MEFV* expression involved in monocyte inflammatory response.

Methods MiRWalk2.0 database was used to identify putative miRNA target sequences within the 3'-UTR mRNA of *MEFV*. Human primary CD14⁺ monocytes were sorted from peripheral blood of healthy donors using magnetic microbeads and differentiated into M1 or M2 macrophages following IFN γ /LPS or IL4/IL13 stimulation, respectively. Using RT-qPCR, M1/M2 polarization was validated by measuring the expression of prototypic M1 and M2 markers: the chemokine *CXCL10* and the macrophage mannose receptor 1 (*MRC1* also known as CD206), respectively, as well as the *MEFV* mRNA. We used loss-of-function method to evaluate the effect of candidate miRNA on CD14⁺ monocytes, i.e. its role on macrophages classical versus alternative polarization. IL-10 expression was quantified using ELISA.

Results *In silico* analyses revealed that miR-326 targets putatively the 3'UTR mRNA of *MEFV*. miRNAs and mRNAs