quantification in polarized macrophages showed that miR-326 is mainly expressed by the M2-type macrophages, and MEFV by the M1-type macrophages. Loss-of-function studies showed that neutralization of miR-326 in M2 macrophages induced the expression of MEFV and CXCL10 while reducing MRC1 expression level. Furthermore, enforced expression of miR-326 in M1 macrophages significantly repressed MEFV expression and induced the production of IL-10.

**Conclusions** A miR-326/MEFV axis seems to be implicated in macrophage polarization and might explain the observed monocyte versatility in FMF.

**Disclosure of Interest** None declared.
that is partially TNFα-mediated. This suggests that the timing of exposure to S100A8/A9 is an important determinant for monocyte-to-osteoclast differentiation.

Disclosure of Interest None declared.

P075  TARGETING NF-κB SIGNALLING IN B CELLS: A POTENTIAL NEW TREATMENT MODALITY FOR ANCA-ASSOCIATED VASCULITIS

JC van der Burg, SM van der Burg, C A. van Bree, J.H. Kuijper. 1Amsterdam Rheumatology and Immunology Center, Department of Experimental Immunology, 2Infectious Diseases, Emma Children’s Hospital, Department of Experimental Immunology, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands; 3Respiratory, Inflammation and Autoimmunity IMED Biotech Unit, AstraZeneca, Gothenburg, Sweden; 4Amsterdam Rheumatology and Immunology Center, Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands.

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

Introduction The pivotal role of B cells in the pathogenesis of autoimmune diseases such as ANCA-associated vasculitis (AAV) is well-established and further substantiated by beneficial therapeutic effects of rituximab (anti-CD20 B cell targeted therapy). However, this results in prolonged B cell depletion while long-lived plasma cells are not targeted. Thus, there is a need for novel therapeutics targeting the B-cell lineage in AAV. NF-κB signalling pathways that act downstream of various B cell surface receptors, including the B cell receptor, CD40, BAFFR and TLRs, are crucially involved in B cell responses and may be suitable as novel targets.

Objectives To identify whether inhibition of NF-κB signalling by novel pharmacological inhibitors is effective in targeting B cell responses in general and more specifically blocks (auto) antibody production and plasmablast differentiation in B cells from AAV patients.

Methods PBMC and sorted B cells from AAV patients and healthy donors were cultured with T cell-dependent (anti-IgM + anti CD40+IL-21) and T cell-independent (CpG+IL-2) stimuli. NF-κB signalling was targeted in these cultures by small molecule inhibitors of NF-κB inducing kinase (NIK, non-canonical NF-κB signalling) and Inhibitor of κB kinase β (IKKβ), canonical NF-κB signalling. Downstream NF-κB signalling and nuclear NF-κB translocation was determined by Western blot and confocal imaging. Effects on B cell proliferation and differentiation were determined by CFSE dilution assays and flow cytometric analysis of B cell markers. (Auto)antibody production was measured by ELISA.

Results In B cells of AAV patients and healthy donors, targeting of NIK and IKKβ effectively inhibited downstream non-canonical or canonical NF-κB signalling, respectively. In a B cell stimulation assay, NIK and IKKβ inhibition significantly reduced T cell-dependent (anti-IgM+anti-CD40+IL-21) and T cell-independent (CpG+IL-2) B cell proliferation. In addition, B cell differentiation towards plasmablasts (CD27++/CD38+) and functional antibody production was attenuated by both NIK and IKKβ inhibitors. Interestingly, the effects of NIK inhibition appeared to be cell-specific as T cell proliferation was largely unaffected.

Conclusions These data demonstrate that inhibition of NF-κB signalling in AAV B cells results in the modulation of various B cell responses. Ongoing studies will indicate whether targeting of NF-κB signalling in B cells may be an effective novel treatment modality for AAV.

Disclosure of Interest None declared.

P076  SYNOVIAL TISSUE FROM RHEUMATOID ARTHRITIS PATIENTS SHED THEIR ANTI-INFLAMMATORY – AND EFFECROCYTIC RECEPTOR MER

J Vullings, C Waterborg, M Koenders, P van der Kraan, F van de Loo*. Experimental Rheumatology, Radboud university medical centre, Nijmegen, Netherlands

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

Introduction We recently showed that the tyrosine-protein kinase MER, a member of the TAM (TYRO, AXL, MER) receptor family plays a protective role in mouse models of rheumatoid arthritis (RA).1 2 In both humans and mice, MER can be proteolytically cleaved and this soluble MER (sMER) acts as a decoy receptor for the TAM receptor ligands Growth Arrest-Specific 6 (GAS6) and Protein S. A recent study showed that sMER correlates with disease activity and bone destruction in RA patients.3 In this study, we measured whether sMER was also increased in the circulation of arthritic mice and in synovial fluid and conditioned medium of synovium explants from RA patients.

Methods KRN serum transfer arthritis was induced and mice were sacrificed at day 7 of full blown arthritis. Ankle joints were immunostained for MER and sMER, whereas the amount of MER+ synovial cells was unaltered. In synovial fluid and conditioned medium of synovium explants from RA patients.

Results Serum sMER levels were increased in arthritic mice whereas the amount of MER+ synovial cells was unaltered. In human RA synovium, numerous MER+ macrophages were present in the lining and sublining. We found significantly enhanced sMER and GAS6 in the synovium culture media (p=0.0045 and 0.0177) and synovial fluid (p=0.0001 and 0.0189) of RA patients compared to OA patients. Soluble AXL levels in synovial fluid of RA and OA patients was high but did not differ (p=0.5256). In synovial fluid of RA patients, sMER and GAS6 did not correlate with TNFα (Pearson r=0.5587) or IL-1β (Pearson r=−0.1667), and negatively correlated with IL-6 (Pearson r=−0.9608).

Conclusions Systemic sMER levels are enhanced in experimental arthritis, in line with the observation of Xu et al in RA patients. Synovial shedding of MER was higher in RA– than in OA patients, but this was not reflected by differences in MER positive synovial cells. As sMER acts as a decoy