analysis (PCA) was applied on the BioQC enrichment scores to (i) identify potential clusters of samples and to (ii) identify the gene signatures responsible for the clustering. In addition, associations between cadherin 11 gene expression and gene signatures were tested.

Results In both studies, cadherin 11 was higher expressed in RA patients compared to healthy controls. PCA performed on gene enrichment scores showed RA patients clustered apart from the healthy controls. Moreover, fibroblast, macrophage, lymphocyte and osteoclast gene signatures were significantly enriched in the RA patients compared to healthy controls in both studies. Unexpectedly, an adipokine-related signature was significantly enriched in RA patients from one transcriptomics dataset (GSE77298), while only showing a trend in the second set (GSE7037). In addition, in both studies Cadherin 11 was associated positively with fibroblast and lymphocyte signatures and negatively with adipokines-related signature.

Conclusions The identified cadherin 11 related gene signatures expand our knowledge on cadherin 11 biology in human RA and may serve as potential biomarkers for RA studies in the future.

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P042 TARGETING NF-KB SIGNALLING IN B CELLS: A POTENTIAL NEW TREATMENT MODALITY FOR ANTIBODY MEDIATED AUTOIMMUNE DISEASES

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Introduction The pivotal role of B cells in the pathogenesis 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 cells in the B-cell lineage in AAV. Novel targets might be encountered in the NF-κB signalling pathway, which acts downstream of various B cell surface receptors, including the B cell antigen receptor, CD40, BAFFR and TLRs, and is crucially involved in B cell responses.

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 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, targeting of NIK and IKKβ effectively inhibited 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, plasmablast differentiation (CD27++/CD38+), and antibody production. The effects of NIK inhibition appeared to be B cell-specific as T cell proliferation was largely unaffected. Currently, studies are ongoing to investigate the effect of IKKβ inhibition on B cell responses and to explore the effects of targeting NF-κB signalling in AAV B cells.

Conclusions These data demonstrate that inhibition of NF-κB signalling in 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

P043 INVESTIGATING IL-6 INTRACELLULAR SIGNALLING IN PERIPHERAL BLOOD CELL SUBSETS IN PATIENTS AT EARLY AND LATER STAGES OF RHEUMATOID ARTHRITIS (RA)

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Introduction Rheumatoid arthritis (RA) is a chronic, inflammatory arthritis that evolves along an immunological and inflammatory disease continuum. The era of targeted biological therapies has been transformative; however, a significant unmet need is the effective tailoring of therapy to deliver optimal treatment responses. In addition, the concept of a window of opportunity is well-recognised whereby early commencement of treatment confers improved outcomes compared to delayed treatment. The importance of pro-inflammatory cytokines TNF and IL-6 in particular, is well recognised; but high, homogeneous response in early RA (ERA) compared to later RA remains unexplained.

Objectives The present project focuses on measuring the phosphorylation of STAT3 (p-STAT3) levels as an indication of the activation of IL-6/JAK-STAT signalling pathway at different disease stages (early and established/later). The main aim is to evaluate the variation in cell-subset IL-6 signalling and its association with response to treatment which included IL-6 targeted therapy (Tocilizumab-TCZ) as well as other bDMARD.

Methods Phosphorylation of IL-6/JAK-STAT key transcription factor STAT3 (p-STAT3) was measured using multiparameter phosphoflow cytometry (phosflow) in T-, B- cells and monocytes isolated from peripheral blood of RA patients. Patients cohorts represented groups at different stages of RA: Treatment-naïve Early RA (ERA group) n=20. Later RA group