AB0028 ACTIVATED STROMAL CELLS INDUCE CCL20 RELEASE AND T CELL MIGRATION

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Background: Although the role of IL-23/Th17 axis in psoriatic arthritis (PsA) is well known¹, little data is available on the contribution of stromal cells to this pathway². Enthesitis is a common feature of PsA and it may represent the site of onset^{3,4}, suggesting tendon stromal cells (tenocytes) may have an initiating role in Th17 driven pathogenesis.

Objectives: To assess the ability of stromal cells to produce CCL20, a chemokine able to recruit Th17 cells, and to induce T cell migration.

Methods: Healthy tenocytes cultured from hamstring tendons and fibroblast-like synoviocytes (FLS) from PsA patients were stimulated with human recombinant IL-1 β (1 ng/ml) and IL-17A (1, 10 and 100 ng/ml). Expression of CCL20 transcript and protein were assessed by quantitative PCR and ELISA, respectively. T cell migration assays were performed with magnetically enriched CD3⁺ cells from peripheral blood of PsA patients and healthy controls using a Transwell system. Following incubation with conditioned media from stimulated stromal cells, the migrated cells were harvested and analysed via light microscopy and flow cytometry.

Results: Both tenocytes and FLS were able to produce CCL20 following stimulation with IL-1 β . Furthermore, the addition of IL-17A induced a synergistic effect with IL-1 β . Following cytokine stimulation, diseased stromal cells produced greater levels of CCL20 compared to stimulated healthy tenocytes. In addition, conditioned media from stimulated tenocytes promoted T cell migration, compared with supernatants from unstimulated tenocytes.

Conclusions: We have shown that tendon and PsA synovium stromal cells are able to produce CCL20 and induce T cell recruitment, suggesting a role in the chemotaxis of Th17 cells. The positive feedback observed with IL1 β and IL-17A suggests a close relationship between stromal cells and Th17 cells.

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AB0029 CHARACTERISTIC PATTERNS OF HLA PRESENTATION AND T CELL DIFFERENTIATION IN ADULT-ONSET STILL'S DISEASE

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Background: The role of T cells in AOSD pathogenesis remains controversial. In autoimmune and auto-inflammatory diseases, such as rheumatoid arthritis (RA) and Behçet's disease, a human leukocyte antigen (HLA)-restricted T cell response to antigen has been shown to affect disease progression, with several HLA alleles strongly associated with disease severity.

Objectives: In this study, we investigated the frequencies of cells presenting HLA-DP, DQ, and DR, as well as differentiated T cell populations including naïve and effector memory T cells in peripheral blood leukocytes (PBLs) of patients with AOSD. Frequencies of the markers were then compared based on clinical outcomes and disease activity, to better understand the role of these cell populations in the pathogenesis of AOSD.

Methods: This study enrolled 14 active AOSD patients, 20 rheumatoid arthritis (RA) patients, and 20 healthy controls (HC). The percentage of surface-stained cells presenting HLA-DP, DQ, and DR alleles, and the proportions of differentiated T cell populations in peripheral blood leukocytes (PBLs) were measured by flow cytometry.

Results: Patients with AOSD exhibited significantly higher percentages of lymphocytes presenting HLA-DP and HLA-DR, and lower percentages of cells presenting HLA-DQ, than patients with RA or HC. The proportions of CD4⁺, CD4 +CCR7⁺, CD4 +CD62L⁺, and CD8 +CD62L⁺ cells in PBLs were decreased in

patients with AOSD relative to patients with RA or HCs. In contrast, AOSD patients exhibited increased proportions of CD8 +naïve T cells in whole blood relative to patients with RA or HC. The proportions of CD4 +effector memory T cells, CD8 +naïve T cells, and CD8 +effector memory T cells in whole blood cells and CD4 +effector memory T cell in lymphocytes were significantly associated with systemic score.

Conclusions: While the frequencies of CD4⁺, CD8⁺, CCR7⁺, CD4 +CCR7⁺, CD4 +CD62L⁺, and CD8 +CD62L⁺ cells were significantly decreased in patients with AOSD, the frequency of CD8 +naïve T cells was elevated in patients with AOSD, and correlated with systemic score. Additional studies in a larger cohort of patients will be necessary to evaluate the role of these markers in the pathogenesis of AOSD.

Disclosure of Interest: None declared

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AB0030 TARGETING NF-KB SIGNALLING IN B CELLS: A POTENTIAL NEW TREATMENT MODALITY FOR ANCA-ASSOCIATED VASCULITIS

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Background: 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 the B-cell lineage in AAV. NF- κ B signalling pathways that act downstream of various B cell surface receptors, including the B cell antigen 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- κ B 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- κ B signalling was targeted in these cultures by small molecule inhibitors of NF- κ B inducing kinase (NIK, non-canonical NF- κ B signalling) and Inhibitor of κ B kinase β (IKK β , canonical NF- κ B signalling). Downstream NF- κ B signalling and nuclear NF- κ B 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 IKK β effectively inhibited downstream non-canonical or canonical NF- κ B signalling, respectively. In a B cell stimulation assay, NIK and IKK β 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 IKK β inhibitors. Interestingly, the effects of NIK inhibition appeared to be B cell-specific as T cell proliferation was largely unaffected.

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

Disclosure of Interest: None declared

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AB0031 DEEP IMMUNE-PROFILING OF CD4+ T CELLS IN BEHÇET'S DISEASE

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Background: Functionality and immune-phenotypes of the human CD4⁺ T-cell compartment in Behçet's disease (BD) are under-investigated, but several lines of evidence point to its relevance in the pathogenesis, progression and remission of the disease.