comparisons across outcomes, these were standardised (difference between the individual score and the mean of all scores divided by the standard deviation, per reader, wave and time-point) before running the models. The high (95%) standardised coefficient the more change in inflammation/damage is captured.

Results: In total, 345 patients were included (mean SD) symptom duration: 1.6 (0.9) years; 53% males; 89% HLA-B27 positive). Inflammation on MRI-SIJ (according to both the ASAS definition of sacroilitis and the continuous SPARCC score) was more sensitive to change as compared to inflammation on the spine that remained essentially unchanged regardless of the outcome (table 1). Structural damage on the SIJ was found to increase over time, but with a higher standardised yearly rate of change on MRI-SIJ (range: 0.015–0.274) as compared to X-SIJ (range: 0.043–0.126). Notably, >3 fatty lesions on MRI-SIJ was the structural outcome in the SIJ with highest sensitive to change (0.274), while >3 erosions was the least sensitive (0.015). Spine structural damage slowly progressed over time but, in contrast to SIJ, radiographic outcomes (i.e. >1 syndesmophytes and mSASSS) were more sensitive to change than MRI structural outcomes.

Conclusions: Our data adds to the body of evidence showing that structural damage assessed in pelvic radiographs only has low sensitivity to change. MRI-SIJ is a promising alternative (especially fatty lesions) capturing more structural changes. In contrast, in detecting structural change in early axSpA radiographic outcomes outperform MRI outcomes.

Disclosure of Interest: None declared


FRIO166

CHARACTERISATION OF PHOSPHODIESTERASE 4 (PDE4) BLOCKADE IN THE SYNOVIAL OF PSORIATIC ARTHRITIS PATIENTS: A FOCUS ON SYNOVIAL INVASIVENESS AND T-CELL POLYFUNCTIONALITY


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Background: Owing to the multi-faceted nature of the pathogenesis of psoriatic arthritis (PsA), the development of multi-targeted agents has been an area of intensive research. Such agents include the phosphodiesterase 4 (PDE4) inhibitors, Rolipram and Apremilast, which elevate intracellular cAMP levels to modulate a number of anti-inflammatory mechanisms. However, the effect of PDE4 blockade within the complex inflammatory environment of the inflamed synovial remains to be elucidated.

Objectives: To characterise the effect of PDE4 blockade in PsA using ex vivo synovial whole tissue explants and synovial single cell suspensions reflective of the complex synovial micro-environment.

Methods: Ex-vivo PsA whole tissue synovial explants were cultured in the presence of PDE4 inhibitor, Rolipram, for 24 hour. The expression of pro-inflammatory mediators were quantified by ELISA and MSD multiplex. A 21 day synovial explant matrigel model was utilised to examine synovial fibroblast (SFC) invasiveness to allow for a long-term assessment. For the characterisation of synovial T-cells, synovial explants were digested and cultured in the presence of Rolipram for 8 hours, stimulated and stained for surface and intracellular T-cell markers. Cell surface expression of CD161 was used to identify Th17 lineage (CD161+CD4+ T cells) and Th22 lineage (CD4+ CD161+ T cells). SPICE analysis was utilised to determine the proportions of mono- and polyfunctional T-cells, which were correlated with disease activity scores.

Results: Rolipram treatment inhibited the spontaneous secretion of inflammatory mediators IL-6, IL-8, MCP-1 and MMP-1 (all p<0.05), with a parallel increase in IL-10 expression. Under DMSO control conditions, a significant increase in SFC outgrowths from PsA explants (indicative of SFC invasiveness) was observed from day 8–21 (all p<0.05), effects of which were significantly decreased in the presence of Rolipram (all p<0.05). A comparative analysis of T cells in PsA using ex vivo synovial explants revealed an enrichment of Th1 (p<0.05), Th17 (p=0.06) and Th22 (p<0.05) cells in PsA synovial tissue, which displayed distinct polyfunctional cytokine profiles, in particular Th17 cells, as compared to matched PBMC. The frequency of polyfunctional triple positive GM-CSF/TNF/IL-17 and or IFNy producing Th1 (n=0.8, p<0.05), Th17 (n=0.8, p<0.05) and Th22 (n=0.9, p<0.05) cells positively correlated with PsA disease activity, suggesting an important role of T-cell polyfunctionality in PsA synovial pathogenesis. Analysis of synovial tissue cell suspensions and matched PBMC cultured in the presence of Rolipram showed a significant decrease in the proportion of these triple positive synovial T cells compared to DMSO (p<0.05), suggesting that PDE4 blockade can effectively targets the polyfunctional hyper-phenotypic synovial T cells in PsA, particularly polyfunctional CD8+ T cells and Th17 lineage, Th17 and exTh17 cells.

Conclusions: PDE4 blockade mediates broad anti-inflammatory mechanisms in PsA synovial tissue through the reduced expression of pro-inflammatory mediators, decreased invasiveness and reduced T cell polyfunctionality. We also demonstrate the feasibility of using ex vivo models to determine “in situ like” assessments of therapeutic agents and further our understanding of disease pathogenesis.

Disclosure of Interest: None declared


FRIO167

EXPRESSION LEVELS OF IL-17, IL-22 AND IL-23 RECEPTORS IN FOUR OSTEOBLAST MODELS AND THE EFFECTS OF IL-17, IL-22 AND IL-23 ON OSTEOBLASTS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory joint disease that chiefly affects the sacroiliac joints and the spine. Radiographs reveal erosive changes at the corners of the vertebral bodies in the early stages of disease, and outgrowth of bony spurs known as syndesmophytes in the later stages. Some data imply a pivotal role of IL-23/IL-17 axis in the regulation of bone homeostasis. However, it remains unknown whether IL-17, IL-22 or IL-23 has any direct effects on osteoblasts or new bone formation in AS.

Objectives: To examine the expressions of IL-17, IL-22, and IL-23 receptors in four osteoblast models and the effects of IL-17, IL-22, and IL-23 on osteoblasts.

Methods: Gene expression levels of receptors, alkaline phosphatase (ALP), osteocalcin (OCN), and Runt-related transcription factor 2 (Runx-2), were