for the development of ROA up to 10 years later. Future directions include developing a predictive model that incorporates multiple features.

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Different pathophysiological pathways in axial and peripheral disease: Peripheral and axial spondyloarthritis: to split or to lump?

OP0199

THE HUMAN ENTHESES HARBOURS RESIDENT ADAPTIVE CD4+ AND CD8+ T-CELLS WITH INDUCIBLE IL-17A AND TNF PROTEIN THAT IS PHARMACOLOGICALLY SUPPRESSED BY ROR γ T AND PDE4 INHIBITORS BUT NOT METHOTREXATE IN A NOVEL IN VITRO ENTHESTITIS MODEL

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Background: Animal models have demonstrated that enthesitis is the primary lesion in experimental spondyloarthritis (SpA). In mice, innate lymphocytes were suggested as the major cytokine producers at the enthesis.

Objectives: We tested the hypothesis that the human entheses harbours tissue resident conventional T-cells. We also assessed their ability to express SpA-related cytokines including TNF and IL-17A and if this could be blocked using psoriasis therapeutic agents (methotrexate (MTX), and phosphodiesterase type 4 inhibitor (PDE4i)) and experimental ROR γ T inhibitors (ROR γ Ti).

Methods: Enthesal spinous process was obtained from patients undergoing elective orthopedic procedures (n=20) and mechanically digested or processed for confocal staining and flow cytometry. CD4+ and CD8+ T-cells were sorted and RNA was isolated and analysed by qPCR. Magnetically isolated cells were stimulated using an anti-CD3/CD2/CD28 bead with and without the presence of MTX, ROR γ Ti and PDE4i. Following stimulation IL-17A and TNF were measured by ELISA and intracellular flow cytometry.

Results: CD4+ and CD8+ T-cells represent 35.7% and 23.7% of T-cells in the entheses, respectively, with topographic confirmation by anti-CD3 immunofluorescence staining. Enthesal tissue contained a higher proportion of CD4+ and CD8+ T-cells expressing a resident memory phenotype (CD69+/CD45RA-) compared to matched blood. Sorted T-cells from enthesal tissue had a gene expression profile consistent with a tissue resident phenotype and CD4+ and CD8+ T-cells showed increased expression immunomodulatory genes including IL-10 and TGF- β compared to peripheral blood T-cells (p<0.001). Following stimulation CD4+ T-cells produced more TNF than CD8+ T-cells (p<0.05), IL-17A was robustly detected in CD4+ but not CD8+ T-cells. TNF and IL-17A production from CD4+ T-cells was effectively inhibited by PDE4i (p<0.05), while ROR γ Ti only reduced IL-17 secretion (p<0.001). MTX had no significant impact on both TNF and IL-17A production in either cell population. This pattern of inhibition was mirrored in TNF secretion from CD8+ T-cells.

Conclusion: This is the first description of conventional CD4+ and CD8+ entheses resident T-cells. PDE4i was effective in abrogating induced TNF production and IL-17, whereas ROR γ Ti is highly effective for IL-17A production but not TNF. In contrast, MTX had little effect on *in vitro* enthesitis model cytokine production. These findings may have some practical implications in the treatment of subclinical enthesitis.

Figure 1. Effect of different therapeutic agents on the TNF and IL-17A production by resident enthesal T-cells and matched peripheral blood

Figure 2. Gene expression profile of enthesal T-cells (soft tissue and adjacent bone) compared to peripheral blood

Abbreviations: ST, enthesal soft tissue; PEB, peri-enthesal bone.

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OP0200

A SET OF INFLAMMATORY MARKERS ALLOWING TO DETECT SYSTEMIC INFLAMMATION IN PSORIATIC SKIN, ENTHESEAL AND JOINT DISEASE IN THE ABSENCE OF CRP AND THEIR LINK TO CLINICAL DISEASE MANIFESTATION

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Background: Psoriatic disease is composed of skin, enthesal and joint disease, which can manifest isolated or combined. Little is known about the systemic inflammation levels in psoriatic disease as a robust IL-6 signal is missing and therefore acute phase reactants such as C-reactive protein are often normal. Measuring systemic inflammation in the different manifestations of psoriatic disease is therefore a continuous unmet need.

Objectives: To better define systemic inflammation in patients with psoriatic disease limited to the skin (S), the entheses (E) or the joints (arthritis, A) or with a combination of these disease manifestations (SE, SA, EA, SEA).