A ROLE FOR IL-4 AND IL-13 IN MODULATING THE IL-23/IL-17 AXIS IN ENTHESIS

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Background: IL-4 and IL-13 are related Th2 cytokines, with documented roles in allergic inflammation such as atopic dermatitis (AD). Psoriatic Arthritis (PsA) is typically thought to be a result of Th1/Th17 driven response, and blockade of this pathway (IL-23, IL-17 and TNF) has proven successful. Despite this, there is a strong genetic risk association for IL-13 and PsA, however, the precise role this pathway (IL-23, IL-17 and TNF) has proven successful. Despite this, there is a strong genetic risk association for IL-13 and PsA(1), however, the precise role of IL-13 in PsA is presently unknown. The enthesis is the region where tendons or ligaments attach to bone, and inflammation of this site (enthesisis) is thought to be the cardinal lesion of PsA, whereas as Rheumatoid Arthritis inflammation is more synovial centric. Dupilumab is a monoclonal antibody that works by blocking the common receptor chain (IL-4 and IL-13 to ascertain whether this modulated entheseal cytokine production.

Results: Both IL-23 and IL-17 were readily induced from enthesis samples with IL-23 coming predominately from entheseal myeloid cells (Fig 1B) and IL-17A from T-cells (Fig 1C). Pre-treatment of entheseal digested material with either IL-4 or IL-13 attenuated IL-23 secretion (Fig 1D). Neither IL-4 nor IL-13 was able to significantly attenuate IL-17 secretion from enthesis T-cells, however IL-13 trended downwards and IL-4 surprisingly trended upwards (Fig 1E).

Conclusion: Our clinical and vitro data point towards a previously unknown role for IL-4 and IL-13 having a protective role in entheseal induction of IL-23/17 axis cytokines. These findings point towards a novel explanation for IL-13 pathway SNPs in PsA and also a molecular explanation for why anti-IL4/13 therapy may induce entheseal pathology.

References: