by IL21 and/or IL6 in the additional presence of transforming growth factor- β . In addition, CD4 IL21 could be detected in RA ST that do not co-localise with either IL17 or IL22.

Conclusions IL21 and IL21-blocking therapy is now being tested in a number of diseases. The results of this study enhance the rationale for a trial of IL21 blockade in RA where it may provide a useful adjunct in those patients refractory to or unable to tolerate anti-TNF therapy.

A171 EXPANSIONS OF INTERLEUKIN 21-SECRETING CD4 T HELPER CELLS IN INFLAMMATORY ARTHRITIDES

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10.1136/ard.2010.129668h

Background and Objectives Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting synovial tissue in multiple joints. The inflammatory process in RA is regulated by several cytokines, especially tumour necrosis factor (TNF), which is produced not only by macrophages and dendritic cells but also by activated antigen-specific CD4 T helper (Th) cells. An increasing number of inflammatory molecules are being identified that may contribute to RA pathology. Therefore the authors investigated the expression of interleukin 17A (IL17A), IL21 and IL22 in RA, psoriatic arthritis (PsA) and undifferentiated arthritis (UA). In addition, the authors dissected the in vitro requirements for the differentiation of human IL21-secreting CD4 T helper (Th) cells.

Methods Expression of surface markers and cytokine production at the single cell level in peripheral blood (PB) and matched synovial fluid (SF) from RA, PsA and UA compared to PB of healthy control subjects was evaluated by flow cytometry following polyclonal stimulation ex vivo. IL17A and IL21 concentrations were assessed by ELISA in cell-free SF samples of RA, PsA and UA patients. Immunofluorescence analysis of RA synovial tissue (ST) was performed using specific antibodies against CD4, IL21, IL22 and IL17.

Results Neither IL17-secreting CD4 Th (Th17) cells nor Th22 cells were expanded in the inflamed joint. In contrast, the authors observed significant expansions of IL21-secreting cells, which represented up to 47% of total CD4 Th cells in SF. IL21, an inflammatory cytokine that belongs to the common γ -chain receptor binding family, is secreted by several cell types including Th17 and T follicular helper cells (TFh). Synovial IL21-secreting cells did not phenotypically fit the TFh cell paradigm in that they did not express the chemokine receptor and differed in some respects to in vitro-generated IL21-secreting cells. In humans, differentiation of naive CD4 T cells into IL21-secreting cells in vitro was preferentially driven