

A175 TH17 CELLS IN AUTOIMMUNE ARTHRITIS

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Background The role of Th17 cells in the pathogenesis of human autoimmune diseases is elusive. To gain insights into the role of Th17 cells in human autoimmune diseases, the authors analysed Th17 cells in patients with prototypic autoimmune diseases such as rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

Methods and Results Th17 cells were analysed in well-defined homogeneous cohorts of patients: treatment-naïve patients with active early RA (n=6; disease duration 2.8 months; disease activity score 28 (DAS28) 5.0) and PsA (n=9; disease duration 2.3 months), and patients with established RA responding or not responding to therapy with methotrexate/adalimumab (n=1; mean disease duration 68 months). Healthy individuals and patients with osteoarthritis were used as control cohorts. Th17 cell frequencies and IL17 production strongly correlated with systemic disease activity at both the onset and the progression of the diseases. They were reduced to control levels in response to clinically effective treatment. Th17 cells were enriched in the joints, and increased frequencies of synovial Th17 cells expressed CCR4 and CCR6, indicative of selective migration of Th17 cells to the joints. The intrinsically elevated expression of the master transcription factor for Th17 cells, RORC, accompanied by biased Th17 cell development and a resistance of Th17 cells from the patients to natural

antagonists of their development (for example, interleukin 4 and interferon γ) are suggestive of the underlying molecular mechanisms of uncontrolled Th17 activity in patients with autoimmune arthritides.

Conclusions These data offer intriguing insights into the mechanisms of autoimmune inflammation, identify Th17 cells as a central effector T cell in the pathophysiology of autoimmune arthritides and provide the scientific basis for targeting Th17 cell functions in the treatment of RA and PsA.