9 TH17 BUT NOT TH22 CELLS DISPLAY PATHOLOGICAL BEHAVIOUR IN ARTHRITIS

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Background Th17 cells (IL-17+IL-22+) are critically involved in the induction and progression of arthritis. Recently, Th22 cells were discovered, which were characterised by IL-22 expression in the absence of IL-17. However, it remains unclear whether IL-22 and Th22 cells, directly contribute to synovial inflammation. Therfore, the authors examined the potency of Th22 cells to activate synovial fibroblasts. In addition, it was investigated whether IL-22 is critical in Th17-mediated experimental arthritis.

Materials and methods Th17 (CD4+CD45RO+CD25-CCR6+CCR4+CCR10-) and Th22 (CD4+CD45RO+CD25-CCR6+CCR4+CCR10-) cells were analysed in peripheral blood of treatment-naïve RA patients in comparison to age and sex matched healthy controls by flow cytometry. Furthermore, synovial fluid of patients with established RA was analysed for the presence of Th17 and Th22 cells. To test the contribution of IL-22 or Th22 in synovial inflammation, co-culture experiments of RA synovial fibroblasts (RASF) with Th22 and Th17 cells were performed. The in vivo relevance of IL-22 in synovial inflammation was investigated in a T cell-mediated arthritis model using mice deficient for IL-22.

Results Both Th17 and Th22 cell populations were present in synovial fluid of patients with rheumatoid arthritis (RA) and were increased in peripheral blood of these patients compared to healthy controls. Upon interaction with RA synovial fibroblasts (RASF), Th17 cells induce activation of RASF resulting in an inflammatory feedback loop including autocrine IL-17A production. In Th17-RASF co-cultures, neutralisation of IL-22 resulted in increased RASF activation whereas the opposite was found by FICZ-induced IL-22 production. Moreover, Th17 cells were markedly more potent than Th22 cells in RASF activation. In addition, no difference in T cell-mediated experimental arthritis severity was found between IL-22 deficient mice compared to wild type mice.

Conclusion These findings show that IL-22 and Th22 cells are less potent in inducing synovial inflammation compared to Th17 cells. These data imply that targeting Th17 cells rather than Th22 cells should be the focus for the treatment of T cell mediated joint inflammation.