**A183 CCR6 TH17 BUT NOT CCR6 TH1 CELLS COOPERATE WITH
SYNOVIAL FIBROBLASTS IN A PROINFLAMMATORY
FEEDBACK LOOP IN EARLY RHEUMATOID ARTHRITIS**

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Th17 cells are implicated in human autoimmune diseases such as rheumatoid arthritis (RA) and in experimental autoimmune models. Consistently, Th17 cell activity in early RA is strongly suggested by elevated levels of interleukin (IL)17A and tumour necrosis factor (TNF) α . However, the pathogenic role of Th17 cells in driving persistent arthritis has not been established. In peripheral blood of patients with treatment-naïve early RA, the authors found increased numbers of IL17A/TNF α -producing CCR6 CD45RO memory CD4 T cells. Functional co-culture experiments with early RA synovial fibroblasts (RASf) revealed that these Th17-enriched CCR6 memory T cells, but not Th1-enriched CCR6 memory T cells, were potent inducers of IL6, IL8 and matrix metalloproteinases (MMPs) in RASf. Conversely, IL17A production by CCR6 T cells was markedly increased through this Th17-RASf interaction. Since blocking TNF α did not fully reduce IL17 activity in the Th17-RASf co-cultures, neutralising IL17A was needed to further downregulate Th17 activity. The authors conclude that RASf and Th17 cells cooperate in a proinflammatory feedback loop, revealing a potential mechanism of Th17 cells driving persistent arthritis. Furthermore, targeting IL17A may be beneficial to current anti-TNF therapies in neutralising Th17 activity in early RA and potentially other Th17-mediated disorders.