A178 IL-20 BLOCKADE PREVENTS THE UPREGULATION OF CCL2, CCL4, CCL5 AND CCR7 BY RA SYNOVIAL BIOPSIES

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Background and objectives Interleukin 20 (IL-20) is a pro-inflammatory cytokine member of the IL-10 family, which has been implicated in the pathogenesis of psoriasis and rheumatoid arthritis (RA). This cytokine and its receptors are present in RA synovial tissue and in synovial fibroblasts. In addition, Moreover, RA synovial fluid (SF) contains significantly higher levels of IL-20 compared to SFs from other rheumatic diseases (eg, osteoarthritis (OA) or gout). Interestingly, IL-20 induces chemokine (C-C motif) ligand 2 (CCL2)/monocyte chemotactic protein-1 (MCP-1), IL-6 and IL-8 production by RA synovial fibroblasts.

In line with these observations, the authors aimed to analyse the expression of IL-20 in RA synovial tissue and to investigate the transcriptional effects of IL-20 and its neutralisation in an ex vivo RA biopsy culture system.

Materials and methods RA synovial biopsies were obtained by knee arthroscopy. IL-20 was detected in sections of these biopsies or from commercially available tissue by immunohistochemistry using a polyclonal rabbit-anti-IL-20 antibody (2313b) and tyramide signal amplification. The specificity of 2313b was validated in sections of IL-20 transfected cells and verified by use of preimmune IgG from the same rabbit and preabsorption with IL-20. Identification of IL-20$^+$ cells with immunomarkers was performed with double-immunofluorescence. Transcriptional analysis of ex vivo stimulation of RA synovial biopsies with IL-20, 25% RA-pooled SF in the presence or in the absence anti-IL-20 (2F6) was performed with AffyMetrix genechips.

Results Immunohistochemistry revealed that IL-20 is present in RA synovial biopsies (in 26 out of 30 patients) compared with low or no immunoreactivity in normal (n=2) or OA synovium (n=9). IL-20$^+$ synoviocytes and inflammatory cells co-stained with CD1a and CD4, but not with CD3, CD8, CD31, CD68 or CD11c. Microarray analysis of ex vivo stimulated RA synovium showed that 58 genes were differentially regulated by a high concentration of IL-20 and similarly by medium containing 25% RA SF. Upregulation of CCL2/MCP-1, CCL4/MIP-1β, CCL5/RANTES and CCR7 was confirmed by quantitative reverse transcriptase PCR. Treatment of biopsies with RA SF containing an anti-IL-20 monoclonal antibody reverted the regulation observed after SF-stimulation alone.

Conclusions The expression of IL-20 by RA synovial CD1a immature DCs and its regulatory effect on several immuno-related transcripts that have been ascribed a pathogenic role in RA, suggest that IL-20 may be a therapeutic target in patients with RA and probably other inflammatory joint diseases.