EXPRESSION LEVELS OF INTERLEUKIN-17A, INTERLEUKIN-17F AND THEIR RECEPTORS IN SYNOVIAL TISSUE OF PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND OSTEOARTHRITIS: A TARGET VALIDATION STUDY

L G M van Baarsen, M C Lebre, D van der Coelen, D M Gerlag, P P Tak
Division of Clinical Immunology and Rheumatology, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

Background Accumulating evidence suggests an important role for interleukin (IL)-17 in the pathogenesis of several inflammatory diseases, including rheumatoid arthritis (RA). IL-17A has been well studied in models of arthritis, but little is known about the relative expression and cellular source(s) of IL-17A, IL-17F, and their receptors in human synovial tissue.

Objective To determine the origin and expression of IL-17A, IL-17F and their receptors IL-17RA and IL-17RC in synovial tissues of patients with RA, psoriatic arthritis (PsA) and inflammatory osteoarthritis (OA).

Methods Synovial biopsy specimens were obtained by arthroscopy from patients with RA (n=13), PsA (n=15) and inflammatory OA (n=14). For comparison synovial tissues from non-inflammatory controls (n=7) were included. Immunohistological analysis was performed on frozen sections using monoclonal antibodies specific for IL-17A, IL-17F, IL-17RA and IL-17RC and evaluated by digital image analysis. Immuno-fluorescence analysis was used to determine which cells in the synovium produce IL-17A and IL-17F using antibodies specific for T cells (CD4, CD8), neutrophils (CD15), macrophages (CD68, CD163), B cells (CD19), endothelial cells (CD31, Von Willebrand Factor, FNAd), lymphatics (Lyve-1) and mast cells (mast cell tryptase). Stained sections were evaluated by confocal microscopy.

Results Levels of IL-17A, IL-17F, IL-17RA and IL-17RC were abundantly present in synovial tissues of all patient groups and highly variable between patients. Whereas IL-17RA was mostly present in the synovial sublining, IL-17RC was abundantly expressed in the intimal lining layer. Digital image analysis showed a significant increase of IL-17A but not of IL-17F, IL-17RA and IL-17RC in patients with arthritis compared to non-inflamed control tissues, while the expression of IL-17A, IL-17F and IL-17RA was similar between the different patient groups. Expression of IL-17RC in the intimal lining layer was significantly increased in PsA compared to OA patients. IL-17A was found to be expressed by CD4 and CD8 positive cells, while CD15, CD19 and mast cell tryptase (MCT) positive cells were negative. IL-17F was not expressed by CD15 positive cells and only occasionally by CD4, CD8 and MCT positive cells in the synovial tissues of arthritic patients. Interestingly, IL-17A and IL-17F staining was also observed in some macrophages as well as in endothelial cells and lymphatics.

Conclusions Increased expression of IL-17A is not restricted to synovial tissues of RA patients but also observed in other forms of inflammatory arthritis. In inflamed synovium various cell types contribute to the production of IL-17A and IL-17F.