

25 INCREASED INNATE IMMUNE RESPONSES BY INTERLEUKIN-22 CONTRIBUTES TO THE INFLAMMATORY PROCESS IN RHEUMATOID ARTHRITIS

Renoud J Marijnissen,¹ Marije I Koenders,¹ Cheryl Nickerson-Nutter,² Shahla Abdollahi-Roodsaz,¹ Annemieke M H Boots,³ Leo A B Joosten,⁴ Wim B van den Berg¹ ¹Radboud University Nijmegen Medical Centre, Rheumatology Research and Advanced Therapeutics, Nijmegen, The Netherlands; ²Pfizer Inc, Cambridge, Massachusetts, USA; ³University Medical Center Groningen, Department of Rheumatology and Clinical Immunology, Groningen, The Netherlands; ⁴Department of Medicine (N4i), Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

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Background and objectives IL-22 is a mediator in antimicrobial responses and inflammatory autoimmune diseases. It can be produced by innate and adaptive haematopoietic immune cells, but the expression of the receptor (IL-22R) seems to be restricted to non-haematopoietic tissue cells. Although both IL-22 and the IL-22R have been identified in the synovium of RA patients, the contribution to disease pathogenicity remains to be established.

Materials and methods The authors first investigated the expression and origin of IL-22 and the IL-22R in the inflamed joints of IL-1Ra^{-/-} mice. Furthermore, the mice were treated with neutralising anti-IL-22 antibodies. Subsequently, the authors analysed the IL-22R expressing cells in human RA synovium by immunohistochemistry (IHC) and flow cytometry. Eventually, the authors stimulated RA synovial biopsies, RA human fibroblast-like cells (RAFLS) and endothelial (HUVEC) cells with IL-22 and analysed the production of inflammatory mediators.

Results In the arthritic joints of IL-1Ra^{-/-} mice, IL-22 is mainly produced by T cells that co-expressed IL-17. Anti-IL-22 treatment of IL-1Ra^{-/-} mice significantly reduced inflammation and bone erosion, suggesting an important role of IL-22 in joint destruction. The authors subsequently analysed the effects of IL-22 on human RA synovium. Exposure to IL-22 increased the expression of TNF α , IL-6 and IL-8. Compared to IL-17, stimulation with IL-22 induced higher levels of IL-8, and combination of the two cytokines resulted in an additional response. IHC identified endothelial cells and synovial fibroblast-like cells as the main IL-22 receptor expressing

cells. Surprisingly, stimulation of RA human fibroblast-like cells and endothelial (HUVEC) cells did not result in a clear increase in the innate immune response. This in contrast to the synovial tissue, which is heavily infiltrated with inflammatory cells.

Conclusions Our data support the dual role of IL-22 in pathological inflammation, showing that the functional importance of IL-22 is context dependent. Current SCID studies with neutralising IL-22 antibodies will have to prove the therapeutic potential of IL-22 in RA.