25 EXPRESSION OF IL-21 RECEPTOR IN SYNOVIAL TISSUE AND BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background and objectives Cytokines regulate a broad range of inflammatory pathways in the pathogenesis of Rheumatoid Arthritis (RA), and cytokine blockade against tumour necrosis factor α and IL-6 has offered substantial advances in the treatment of articular inflammation. However, a large proportion of patients will not respond or exhibit only a partial response to treatment and new therapies are thus required. IL-21 is a member of the four-α-helix bundle family of cytokines that mediates pleiotropic effects through the IL-21 receptor (IL-21R). Since potency of IL-21 is mainly dependent on presence and abundance of its receptor on different cells types, the objective of this study was to characterise expression of IL-21R in the synovium and blood of patients with RA.

Materials and methods Immunohistochemistry for IL-21R was carried out on synovial tissue samples derived by arthroplasty from patients with RA (n=5) obtained from the Institute of Infection, Immunity and Inflammation Research Tissue Bank. Mononuclear cells were separated out from peripheral blood (PBMC) of 10 RA patients or 3 healthy controls on a density gradient using Histopaque (Sigma) and analysed by flow cytometry for IL-21R expression on T cells (CD3/CD4/CD8), B cells (CD19/CD27) and NK cells (CD16/CD56).

Results Expression of IL-21R was detected in 5/5 synovial RA tissues. The IL-21R$^+$ cells were located in the synovial intimal and sublining layers and in lymphoid aggregates. Flow cytometric analysis on blood PBMC revealed that IL-21R is highly expressed on both CD4$^+$ (73.04%, 12.58 MFI) and CD8$^+$ (50.88%, 13.69 MFI) T cells, as well as on a proportion of NK cells (73.83%, 19.15 MFI) in RA patients. On B cells, IL-21R expression was higher on the CD27$^-$ fraction of naïve B cells (95.19%, 37.02 MFI), with lower expression on the CD27$^+$ memory B cells (15.2%, 32.22 MFI).

Conclusions Our results show increased expression of IL-21R in established RA synovial tissue and peripheral blood, and indicate that targeting of the IL-21/IL-21R pathway may be a valid therapeutic strategy for the treatment of RA.