A36 SENSITISATION OF THE IFNγ-STAT1-SIGNALLING-PATHWAY IN RHEUMATOID ARTHRITIS MONOCYTES

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Background Both, type I interferons (IFNα, IFNβ) and the type II IFN IFNγ signal via phosphorylating Stat1. Immunohistochemistry and gene expression signatures of synovial tissues suggest an activated IFN-Stat1-signalling-pathway in rheumatoid arthritis (RA). This study was performed to determine the activity of the IFN-Stat1-signalling-pathway in RA peripheral blood monocytes.

Methods Flourocytometry or qPCR was used to measure the expression of Stat1, phospho-Stat1 (pStat1) and IFN-inducible genes, such as IP-10 and OAS in RA and healthy (HC) peripheral blood monocytes. To examine the significance of Stat1 and of the IFNγ-inducible chemokine MIG (monokine induced by IFNγ) were measured using fluorocytometry.

Results Levels of Stat1 and pStat1 protein expression were significantly increased in RA monocytes when compared to HC (mfi 14.7±8.1 vs 8.0±3.9, p=0.0002; mfi 5.1±1.3 vs 3.2±0.7, p<0.0001, respectively). Stat1 mfi in RA monocytes correlated with RA disease activity such as DAS28 (Disease Activity Score; r=0.47, p<0.008) or CDAI (Clinical Disease Activity Index; r=0.51, p<0.003). Further, Stat1 mRNA expression in RA monocytes correlated with the expression of other IFN target genes, such as IP-10 or OAS.

RA monocytes demonstrated a considerably higher increase in pStat1 and MIG levels upon IFNγ stimulation when compared to monocytes from HC (pStat1: +2.8±1.8 vs +1.5±1.1, p<0.03; MIG: +565±351 vs +303±253, p<0.05), indicating that RA monocytes are more sensitive to IFNγ stimulation.

Conclusions Consistent with a systemic proinflammatory activity of RA monocytes, these studies suggest activation of the IFNγ-Stat1-signalling pathway in RA.