A179 TNF α AND CHERIMIN CROSS-TALK IN RHEUMATOID ARTHRITIS

M Cristina Lebre,¹ M Inês Ramos,¹ Claudia L Hofstra,² Hans van Eenennaam,² Saida Aarrass,¹ Paul P Tak¹ ¹*Division of Clinical Immunology/Rheumatology, Academic Medical Center (AMC), University of Amsterdam, Amsterdam, The Netherlands;* ²*Merck Research Laboratories, Oss, The Netherlands*

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Background and objectives Rheumatoid arthritis (RA) synovium is characterised by a dense infiltrate, consisting of macrophages, T and B cells, plasma cells and dendritic cells (DC). Inflammatory chemokines present in RA synovium may contribute to the accumulation of these immune cells. The authors have recently shown that plasmacytoid DC (pDC) are enriched in RA synovial tissue (ST) compared to CD1c myeloid DC. In line with these observations, the authors have shown that chemerin (and its receptor ChemR23) expression is upregulated in RA ST compared to non-RA arthritis patients. Moreover, in RA ST ChemR23 was specifically expressed by CD68 macrophages and pDC, while chemerin expression was confined to endothelial cells (CD31 and von Willebrand factor positive). Therefore the authors aimed at investigating the regulation of chemerin expression in an ex vivo model of human RA.

Materials and methods Arthroscopic ST biopsies were obtained from patients with active RA and cultured in medium or in the presence of recombinant (r)-tumour necrosis factor α (TNF α) or r-chemerin. After 6 days, cell-free supernatants were harvested and the levels of TNF α or chemerin were analysed by Luminex or ELISA, respectively. When indicated, antichemerin or anti-ChemR23 neutralising antibodies were added to TNF α -stimulated cultures.

Results RA synovial biopsies released chemerin spontaneously. Interestingly, TNF α stimulation induced significantly higher levels of chemerin compared to medium control. In addition, RA synovial biopsies released TNF α spontaneously and addition of chemerin to the cultures strongly induced TNF α release, suggesting a vicious cycle. Of importance, spontaneous and TNF α -induced chemerin could be blocked by the addition of neutralising antibodies against chemerin. Moreover, spontaneous TNF α could also be blocked by the addition of neutralising antibodies against chemerin.

Conclusions These findings suggest that elevated levels of chemerin in RA ST might regulate local TNF α release and vice-versa in a positive feedback loop. The reciprocal interplay between chemerin and TNF α is novel and might represent an attractive candidate for future drug development by blocking the chemerin/ChemR23 system to disrupt disease perpetuation.