A179 TNFα AND CHEMERIN CROSS-TALK IN RHEUMATOID ARTHRITIS

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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 (TNFα) or r-chemerin. After 6 days, cell-free supernatants were harvested and the levels of TNFα or chemerin were analysed by Luminex or ELISA, respectively. When indicated, antichemerin or anti-ChemR23 neutralising antibodies were added to TNFα-stimulated cultures.

Results RA synovial biopsies released chemerin spontaneously. Interestingly, TNFα stimulation induced significantly higher levels of chemerin compared to medium control. In addition, RA synovial biopsies released TNFα spontaneously and addition of chemerin to the cultures strongly induced TNFα release, suggesting a vicious cycle. Of importance, spontaneous and TNFα-induced chemerin could be blocked by the addition of neutralising antibodies against chemerin. Moreover, spontaneous TNFα 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 TNFα release and vice-versa in a positive feedback loop. The reciprocal interplay between chemerin and TNFα is novel and might represent an attractive candidate for future drug development by blocking the chemerin/ChemR23 system to disrupt disease perpetuation.