

**A110 FMS-LIKE TYROSINE KINASE 3 LIGAND (FLT3L) LEVELS ARE ELEVATED IN RA SYNOVIAL FLUID**

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**Introduction** Fms-like tyrosine kinase 3 ligand (Flt3L) is a potent endogenous growth factor for myeloid (m)DC and plasmacytoid (p)DC. Its administration to mice and human leads to dramatic increases of various DC subsets while Flt3L<sup>-/-</sup> mice show reduced DC numbers. Flt3L and its receptor have been poorly studied in the setting of autoimmune diseases in general and in experimental arthritis in particular. The highly differentiated cellular pattern in rheumatoid arthritis (RA)

synovium led to the hypothesis that Flt3L, with its ability to induce proliferation and differentiation, might be important in induction and/or progression of arthritis. Since in RA, circulating blood DC subsets numbers are reduced and enriched in synovial fluid (SF) and synovial tissue (ST) we investigated whether Flt3L contribute to local generation of DC in these compartments.

**Methods** Healthy donors and patients with active RA or gout were included in this study. Flt3L levels in SF and serum were determined using a commercially available ELISA and expression of Flt3L and its receptor (CD135) in peripheral blood mononuclear cells and SFMC was assessed by FACS. Immunohistochemistry stainings for Flt3L and CD135 were performed in synovium RA frozen sections.

**Results** The levels of Flt3L in RA and gout SF were significantly higher compared to paired serum. Interestingly, the levels of Flt3L in RA SF were significantly higher compared to gout SF. Moreover, we observed that anticitrullinated protein antigen (ACPA) positive RA patients showed higher levels of synovial Flt3L compared to ACPA negative RA patients. In RA peripheral blood monocytes, B cells and mDC the expression of Flt3L was higher compared these cells in healthy donors. The expression of CD135 was confined to monocytes and mDC (MFI  $\pm 20$ ) and the levels are higher in RA SF (MFI  $\pm 30$ ). Immunohistochemistry data confirmed the presence of Flt3L-expressing cells and its receptor CD135 in RA ST.

**Conclusion** Monocyte-, B- and mDC-derived Flt3L might be important for the local generation of synovial DC. Achieving a detailed understanding of Flt3L function(s) in RA may unravel novel immunotherapies in autoimmune diseases.