INVESTIGATION OF IGA IMMUNE COMPLEX CAPTURE BY FCLR4+ B CELLS IN PERIPHERAL BLOOD AND SYNOVIAL FLUID

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Introduction Increasing evidence points to a mucosal origin of the autoimmune process in the development of rheumatoid arthritis. A B cell subset identified by surface expression of Fc receptor-like 4 (FcRL4) associates with inflammation in the mucosa associated lymphoid tissue. Our group identified these cells in the synovium of RA patients. They express high levels of RANKL and participate in the autoimmune response to citrullinated proteins. Recent in vitro work suggested that FcRL4 may be a low-affinity receptor for aggregated IgA. FcRL4 +B cells in RA SF express low levels of CD21 and high levels of CD11c, a phenotype they share with Age-Associated B cells (ABC). Very low numbers of ABC are found in blood of healthy individuals but their frequency increases with age however their exact role in RA is not yet understood.

Objectives 1) Investigate the binding activity of IgA immune complexes to FcRL4+ B cells in tonsil, RA synovial fluid, and the peripheral blood of healthy individuals and RA patients.
2) Determine if FcRL4 can specifically capture IgA from the RA SF.
3) Examine the specificity of FcRL4 for secreted and serum IgA and for different IgA isotypes.

Methods SF, peripheral blood and tonsil mononuclear cells were labelled for FcRL4, IgA, IgG, and CD19 (PBMCs were also labelled for CD21 and CD11c) and analysed by flow cytometry. Cells pre-treated with a pH3 buffer to remove receptor-bound immunoglobulins were compared with untreated cells to distinguish IgA B cell receptor expression from receptor-bound IgA Immune complexes. An FcRL4 expressing cell line was incubated with RA synovial fluid and purified human IgA to assess FcRL4s specificity.

Results Receptor-bound IgA Immune complexes were observed on ex vivo RA SF and tonsil FcRL4+ B cells but not on FcRL4- B cells (p=0.001). Intriguingly, this IgA capture was not observed in peripheral blood FcRL4 +ABC from HC or RA patients. Furthermore, the proportion of B cells with IgA BCRs was increased in tonsil and SF FcRL4 +B cells but not in peripheral FcRL4+ B cells, compared to FcRL4- B cells. Using a cell line, we show that FcRL4 specifically binds IgA immune complexes from SF and shows a preference for IgA1 over IgA2 (p=0.02).

Conclusions FcRL4 is a receptor for IgA immune complexes in RA joints. RA SF and tonsil FcRL4+ B cells RA SF differ from peripheral blood FcRL4 +ABC in their in vivo capture of IgA immune complexes and in their frequency of IgA BCRs, suggesting distinct function and origin of these cells.

Disclosure of Interest None declared.

REFERENCES