A147 IL-7-ACTIVATED T CELLS AND MONOCYTES DRIVE B CELL ACTIVATION IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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10.1136/ard.2010.149005.14

In primary Sjögren's syndrome (pSS) patients local T and B cell-driven inflammation can contribute to destruction of exocrine glands associated with clinical symptoms of dryness. Recently we documented increased interleukin 7 (IL-7) and IL7R expression in labial salivary glands of pSS patients. We have shown that IL-7 causes T cell-dependent monocyte activation. Although there are indications that IL-7 affects the activity of developing human B cells, the effect of IL-7 on mature B cell activation in human autoimmune diseases has not been reported. Because B cell activation plays a pivotal role in pSS pathology we investigated the capacity of IL-7 to induce T cell-dependent B cell activation.

Peripheral blood mononuclear cells (PBMCs) from pSS patients (n=6) were cultured with and without IL-7. Furthermore, isolated CD4 T and CD19 B cells were co-cultured with and without IL-7 as well, and in the presence or absence of CD14 monocytes/macrophages (n=6). Proliferation was measured using ³H-thymidine incorporation and by Ki67 expression (FACS analysis). Ex vivo IL-7R expression and activation marker expression (HLA-DR, CD25) on CD4 T and B cells were measured by FACS analysis.

Nearly all CD4 T cells express the IL-7R (93.6 ±1.4%), while B cells and monocytes do not. IL-7 increased proliferation of PBMC pSS (from 2000 to 13000 cpm, p≤0.001), which was associated with significant increases in Ki67+CD4 T cells (from 2.7 ±0.4% to 13.8 ±4.0%) and Ki67+B cells (from 1.5 ±0.2% to 3.4 ±0.5%). Additionally, IL-7 up regulated markers of activation on CD4 T cells (CD25+ CD4 T cells from 28.8 ±4.0% to 79.8 ±2.4%, p≤0.001; HLA-DR+ T cells from 7.1 ±0.4% to 8.9 ±0.7%, p≤0.05), and on B cells (HLA-DR MFI from 317 ±109 to 421 ±129, p<0.01; mean increase 33%). In CD4 T and B cell co-cultures, IL-7 activated T cells, but caused minimal B cell activation (MFI HLA-DR from 214 ±32 to 233 ±30, p≤0.05; mean increase 8.8%). As it has been shown that monocytes are able to support B cell activation and can be stimulated by IL7-activated CD4 T cells, the capacity of monocytes to facilitate IL-7-induced B cell activation was examined. We report that indeed IL-7-induced T cell activation of B cells is significantly enhanced by monocytes (MFI HLA-DR on B cells from 210 ±32 to 284 ±53, p≤0.05; mean increase 35%).

Our results show that IL-7 activates B cells in a T cell-dependent manner which is facilitated by monocytes. Since increased IL-7 levels and monocyte/macrophage numbers are associated with increased immunopathology in pSS this suggests that IL-7-driven B cell activation might contribute to inflammation and tissue-destruction in pSS.

Funding This study was financially supported by the Dutch Arthritis Association ('het Nationaal Reumafonds').