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709 - Increased IL-7 Expression Correlates with Immunopathology in Exocrine Glands of Patients with Sjögren's Syndrome and Drives Th1-associated Immune Responses

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Background In patients with primary Sjögren's syndrome (pSS) local T cell-driven inflammation can contribute to destruction of exocrine glands associated with clinical symptoms of dryness. Evidence is accumulating that IL-7 contributes to inflammation in several autoimmune diseases. Increased levels are found in diseases such as RA and JIA. IL-7 stimulates mature T cells and induces both T cell-dependent and -independent cytokine secretion by monocytes. These prominent immunoregulatory effects indicate that IL-7 might contribute to the local pro-inflammatory response seen in the salivary glands of pSS patients. The aim of our study was to examine IL-7 expression in pSS patients in relation to immunopathology and to investigate its potential immunoregulatory role in these patients.

Methods Labial salivary gland (LSG) IL-7 expression was determined by immunohistochemistry using a quantitative scoring system in 30 sicca patients; 15 with primary (pSS) and 15 with non-Sjögren's sicca syndrome (nSS). LSG IL-7 expression was correlated to local and peripheral parameters of inflammation (lymphocyte focus score [LFS], % IgA^+ plasma cells, serum IgG, ESR). IL-7(ELISA) was also measured in the saliva and serum of pSS patients compared to healthy controls. Additionally, the *in vitro* effect of IL-7 on production of proinflammatory cytokines, chemokines and T-cell cytokines by PBMCs from pSS patients was determined (Luminex assay).

Results The LSG IL-7 expression was increased in pSS patients compared to nSS patients ($p=0.003$). IL-7 was mostly found in the vicinity of lymphocytic infiltrates and was produced by endothelial cells, a minority of CD68 macrophages and by cells with fibroblast morphology. In saliva of pSS patients compared to healthy controls IL-7 levels were also significantly increased ($p<0.05$). Although serum IL-7 levels in pSS were slightly increased compared to nSS patients this was not statistically significant. In the pSS group as well as in the whole sicca patient group, LSG IL-7 scores significantly correlated (all $p<0.05$) with both local (LFS, % IgA^+ cells), and peripheral (serum IgG) inflammation parameters. IL-7 induced production of cytokines that contribute to activation of pro-inflammatory Th1 cells (IL-12 and IL-15) and induced Th1 cytokines (IFNγ) as well as chemokines that facilitate migration of Th1 cells (MIG and IP-10, all $p<0.05$). In contrast, IL-7 did not change Th2 cytokine expression (IL-4). IL-7 also significantly elevated IL-1α and TNFα, proinflammatory cytokines that can induce immunopathology by their catabolic effects on tissue cells.

Conclusions The present data suggest an active pro-inflammatory role for IL-7 in LSG of pSS patients. The correlation of LSG IL-7 expression with immunopathology indicates that IL-7 could be a pivotal player in inflammation-induced pathology in these patients.