

VIP / VPAC system involved in the interaction of primary Sjögren Syndrome immune cells and a human salivary gland epithelial cell line

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Primary Sjögren's syndrome (pSS) is a chronic inflammatory and systemic autoimmune disease with a prevalence of 0.3–0.5%. The clinical hallmark of pSS is a progressive oral and ocular dryness that poorly correlates with the extent of inflammatory infiltrates of exocrine glands. Evidence of aberrant expression of inflammatory mediators and apoptosis of glandular epithelial cells has been proposed as early events in pSS pathogenesis. Vasoactive Intestinal Peptide (VIP) is a pleiotropic secretory and vasodilator neuropeptide with potent immunomodulatory effects in various animal models of chronic inflammation. Also, we have recently proposed an anti-apoptotic effect of VIP on murine acinar epithelial cells through VPAC1 subtype of VIP receptors. The aim of this work was to study the role of VIP / VPAC system in the interaction of monocytes from pSS patients with a human salivary gland epithelial cell line. Monocytes were isolated from peripheral blood of women with pSS (Vitali C et al., 2002) (n=26) and age-matched healthy women as the control group (n=10). Mononuclear cells were analyzed by flow cytometry and reverse transcription-quantitative polymerase chain reaction (RT-qPCR) for cytokines, chemokines and VIP receptors before and after activation with lipopolysaccharide (LPS) and also after co-cultures with salivary epithelial cells (HSG cell line) in the presence or absence of 100 nM VIP. We found an increased expression of VPAC2 subtype of VIP receptors on pSS monocytes compared with healthy control patients (P<0.05, Student) that was differentially modulated by LPS and VIP. CD14 positive cells from pSS but not from control subjects showed increased expression of IL-12 after co-culture with epithelial cells which was partially reversed by VIP. Moreover, only pSS cells induced the expression of inflammatory and migration markers on epithelial cells after co-cultures with a 2.2 fold increase of Toll like receptor 4 TLR4 (P<0.05 vs. basal expression) and Monocyte chemoattractant protein-1 (MCP-1) among other molecules. These observations support that salivary gland epithelial cells could be actively involved in the priming of peripheral monocytes of pSS patients and that VIP / VPAC system might have a role in this interaction.

Key words: Sjögren Syndrome, VIP, monocytes, salivary epithelial cells