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Effects of pro-inflammatory cytokines on polarized rat parotid Par-C10 monolayers

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Sjögren's syndrome (SS), an autoimmune disorder, is distinguished by inflammation and salivary gland cell death, leading to xerostomia (dry mouth). The G protein-coupled P2Y2 receptor (P2Y2R) is up-regulated in response to damage or stress in salivary epithelium. Pro-inflammatory cytokines associated with SS can be produced by infiltrating lymphocytes or salivary epithelium. Correlations have been found between lymphocytic infiltration and increased production of pro-inflammatory cytokines such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), tumor necrosis factor- α (TNF α) and interferon- γ (IFN γ) and decreased function of exocrine glands in SS. Recent data has shown that P2Y2R activation enhances the activity of metalloproteases that release TNF α . OBJECTIVES: To study the effects of cytokines on polarized salivary epithelium. METHODS: Polarized rat parotid (Par-C10) monolayers were used to perform these studies. Cytokines released by UTP-induced P2Y2R activation were identified by ELISA. To evaluate the role of cytokines associated with SS on epithelial integrity, epithelial resistance was determined and correlated with the expression and distribution of tight junction (TJ) proteins by immunofluorescence and Western analysis, respectively. RESULTS: Activation of P2Y2Rs in Par-C10 monolayers induced the release of TNF α . The cytokines TNF α and IFN γ , but not IL-6 or IL1 β , decreased the resistance of Par-C10 cells. However, the expression/distribution of the TJ protein ZO-1 was unaffected. CONCLUSIONS: The data support a hypothesis that P2Y2R expression and activation in salivary gland cells contribute to epithelial dysfunction in SS by generating pro-inflammatory cytokines that regulate ion transport and epithelial integrity in salivary glands. Future studies will determine the role of cytokines on the expression and distribution of other TJ molecules including occludin, claudins and junctional adhesion molecules. These studies may lead to better therapeutic strategies for minimizing autoimmune-associated dysfunction of salivary gland that contributes to xerostomia in SS patient.