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Title: *$P2Y_2$ Receptor as Therapeutic Target in a Sjögren's Syndrome Mouse Model*

Research Description:
Sjögren's syndrome is a chronic autoimmune disease of the salivary and lacrimal glands that causes dry eye and dry mouth in affected patients. The chronic inflammation characteristic of this disease can lead to more severe systemic effects such as secondary autoimmune conditions and lymphoma. Our lab studies nucleotide receptors that respond to nucleotides released by damaged cells, in turn mounting an inflammatory response. In this proposal, we aim to understand the role of G-protein coupled P2Y2 receptors (P2Y2Rs), and how it works to promote chronic inflammation in the salivary gland when expressed on infiltrating B cells. Our goal is to evaluate P2Y2Rs as a target for future therapy for the treatment of Sjögren's syndrome, specifically as a way to diminish the chronic inflammatory response that leads to systemic effects.

Scientific Abstract:
Sjögren's syndrome (SS) is a chronic autoimmune exocrinopathy characterized by lymphocytic infiltration of the salivary and lacrimal glands. Chronic inflammation leads to salivary gland dysfunction and systemic effects including fibrosis, secondary autoimmune diseases, and lymphoma development. Using the NOD.H-2h4,IFNγ-/-,CD28-/- mouse model of SS, we explore the contributions of P2Y2R-mediated inflammation to the SS phenotype. Our preliminary findings demonstrate that P2Y2R antagonism improves salivation and diminishes inflammation in the submandibular gland (SMG). Additionally, functional P2Y2R is expressed in SMG B cells. Through the nucleotide activation of P2Y2R on infiltrating SMG B cells and subsequent chemokine and cytokine release, we hypothesize that P2Y2R might facilitate the recruitment of peripheral lymphocytes leading to salivary gland destruction, hyposalivation, and chronic inflammation. It is the goal of this proposal to elucidate the role P2Y2R plays in infiltrating SMG B cell function and evaluate P2Y2R as a novel therapeutic target for the treatment of SS.