

Public Abstract

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Ph.D.

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Title: P2Y₂ nucleotide receptor up-regulation and function in submandibular gland epithelium.

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Sjögren's Syndrome (SS) is an autoimmune disease that specifically targets exocrine glands, including salivary glands, and results in an impairment of secretory function. Clinical symptoms of SS include dry mouth and the development of cavities due to salivary gland dysfunction. The P2Y₂ receptor (P2Y₂R) is a cell surface protein activated by extracellular nucleotides such as ATP and UTP. Previous data have shown that P2Y₂R expression increases (up-regulates) in response to stress or injury in a variety of tissues, including salivary gland. Therefore, it was determined whether up-regulation of P2Y₂R expression also occurs in a mouse model of SS. The data obtained indicate that P2Y₂Rs are up-regulated in salivary gland from the NOD mouse model of SS as compared to normal, control mice. Furthermore, results demonstrate that P2Y₂Rs are up-regulated further as the disease progresses, indicating that P2Y₂Rs may play a role in the pathology of SS. Other data presented in this dissertation demonstrate the function of the P2Y₂R in the activation of cell signaling proteins (for example: EGFR, ERK1/2, ELK, and P90RSK) that control gene expression. Moreover, activation of signaling proteins by the P2Y₂R was found to occur by rapid and slow pathways and the different mechanisms involved were delineated. Thus, findings in this dissertation support the conclusion that P2Y₂Rs are up-regulated in salivary gland disease such as SS, and novel signaling pathways for P2Y₂Rs that were identified may offer important therapeutic targets in a variety of diseases where tissue stress or damage occurs.