

P2Y₂ NUCLEOTIDE RECEPTOR UP-REGULATION
AND FUNCTION IN SALIVARY GLAND EPITHELIUM

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ABSTRACT

Sjögren's syndrome (SS) is an autoimmune disease that specifically targets exocrine glands, including salivary glands, and results in an impairment of secretory function. P2Y₂ nucleotide receptors for extracellular ATP and UTP are up-regulated in response to stress or injury in a variety of tissues including submandibular glands (SMGs). Therefore, our objective was to assess whether P2Y₂ receptor expression is up-regulated in SMGs of the NOD.B10 mouse model of SS, and to determine the function of P2Y₂Rs in salivary gland tissue. Our data indicate that P2Y₂Rs are up-regulated in SMGs of the NOD.B10 mice, and this up-regulation increases as the disease progresses. Moreover, data obtained using a human submandibular gland cell line, demonstrate that P2Y₂Rs activate a signaling pathway leading to gene transcription via at least two distinct mechanisms. These findings suggest that regulation of P2Y₂Rs is likely to be an important therapeutic target for various diseases.