# MECHANISMS OF SALIVARY GLAND CELL PROLIFERATION BY $P2Y_2R$ ACTIVATION

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## ABSTRACT

Sjögren's syndrome (SS) and the side-effects of γ-radiation therapies for head and neck cancers cause salivary gland dysfunction. Salivary gland regeneration has been considered to be a very promising approach for restoring saliva secretion. To regenerate a functional salivary gland in a clinical setting, it is first necessary to gain a better understanding of the mechanisms involved in salivary gland regeneration. This thesis focuses on the proliferative role of extracellular nucleotides via the activation of the $P2Y_2$ nucleotide receptor in salivary gland epithelial cells. Our previous studies have shown that the $P2Y_2R$ interacts with many signaling molecules to regulate multiple signaling pathways involved in cell proliferation. These studies support the overall hypothesis that expression and activation of $P2Y_2Rs$ in damaged or diseased salivary gland cells promotes cell proliferation. In this project, we demonstrate that activation of the $P2Y_2R$ increases the proliferation of human salivary gland (HSG) epithelial cells *in vitro*. Other data indicate that inhibition of Src and ERK1/2 prevents $P2Y_2R$-mediated proliferation of HSG cells. Thus, the current results suggest that activation of $P2Y_2Rs$ by extracellular nucleotides promotes proliferation of HSG cells by stimulating Src-dependent pathway and activating ERK1/2. Accordingly, the $P2Y_2R$ represents a promising target for salivary gland regeneration.