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Phosphorylation of EGFR, ERK 1/2 and downstream transcription factors after $P2Y_2$ receptor activation in a human submandibular gland cell line

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P2 nucleotide receptors mediate a variety of biological responses and are activated by the extracellular nucleotides adenosine triphosphate (ATP), adenosine diphosphate (ADP), uridine triphosphate (UTP), uridine diphosphate (UDP). The $P2Y_2$ nucleotide receptor is a seven transmembrane spanning domain receptor activated by the nucleotides ATP and UTP, and is up-regulated in a variety of tissues in response to injury or stress. For example, the $P2Y_2$ receptors are not normally expressed in salivary glands, but upon disruption of tissue homeostasis, the $P2Y_2$ receptors are up-regulated. Sjogren's disease is an autoimmune disorder that affects salivary and lacrimal glands resulting in a decreased ability to produce saliva and tears. Previous work by our lab has shown that the $P2Y_2$ receptor is up-regulated in submandibular glands of a Sjogren's syndrome mouse model, suggesting that it may be up-regulated in human Sjogren's syndrome. The goal of this project is to analyze the function of $P2Y_2$ receptors in salivary gland tissues. HSG cells, which endogenously express P2Y2 receptors and are derived from a human submandibular gland tumor, were utilized as a cell model to analyze downstream signaling pathways in response to UTP. Our results show that UTP, the $P2Y_2$ receptor selective agonist, causes phosphorylation of the epidermal growth factor receptor (EGFR), extracellular regulated kinases (ERK 1/2) and the downstream transcription factors p90RSK, and ELK, suggesting that $P2Y_2$ receptors may play a role in gene transcription in salivary gland tissues.