CHARACTERIZATION AND FUNCTIONAL ANALYSIS OF THE $P2Y_2R$ GENE PROMOTER

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ABSTRACT

Extracellular nucleotides can bind to the $P2Y_2R$ and modulate proliferation and migration of smooth muscle cells, which is known to be involved in intimal hyperplasia that accompanies atherosclerosis and post-angioplasty restenosis. Moreover, the $P2Y_2R$ is up-regulated in vascular smooth muscle cells and endothelial cells in response to tissue injury. These findings suggest that the $P2Y_2R$ is a potential target for the pharmacological control of progression of atherosclerosis and post-angioplasty restenosis. However, the mechanisms governing $P2Y_2R$ up-regulation remain unknown.

In this study, we have cloned a 2071 bp 5'-flanking region of the $P2Y_2R$ gene in a reporter vector and carried out a serial deletion analysis. The deletion of a 175 bp region completely abolished promoter function and results further indicate that the $P2Y_2R$ gene promoter uses an array of positive and negative response elements in the regulation of gene expression. Furthermore, other results show that the cytokine IL-1β may be involved in down-regulation of $P2Y_2R$ activity in human coronary artery endothelial cells. Further studies will potentially lead to the identification of novel pathways involved in the regulation of $P2Y_2R$ gene expression, information that might be useful to suppress neointimal hyperplasia in atherosclerosis and the restenosis of angioplasty.