

Public Abstract

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Graduation Term:SS 2008

Department:Biochemistry

Degree:MS

Title:PHENOTYPIC MODULATION OF VASCULAR SMOOTH MUSCLE CELLS: EVIDENCE FOR A ROLE OF THE G PROTEIN-COUPLED P2Y2 RECEPTOR

G protein-coupled receptors regulate two major functions of vascular smooth muscle cells (SMCs) - the vasomotor contractile response and the proliferative response. The contractile phenotype of SMCs has mainly been studied in situ within intact blood vessels, whereas the synthetic or proliferative SMC phenotypes can be studied in culture and represent a model of the SMC phenotype seen in vascular proliferative diseases. G protein-coupled P2Y receptors for extracellular nucleotides are known to regulate vascular SMC functions, although there is little information on P2Y receptor expression, distribution or function in SMCs of different phenotypes. Previous studies indicate that the P2Y2 receptor subtype for ATP or UTP regulates SMC proliferation and migration, and we postulate that its expression may be up-regulated in the proliferative phenotype of SMCs.

To investigate the distribution of the P2Y2 receptor subtype in SMCs of different phenotypes in culture, SMC cultures were established from rat aorta that displayed different morphological and biological features. We analyzed the expression of P2Y2 receptor mRNA in SMC cultures having contractile or synthetic phenotypes using real-time PCR and characterized receptor activity by monitoring agonist-induced intracellular calcium mobilization. Our data indicate a selective dominance in the distribution of P2Y2 receptors in the contractile SMC phenotype, consistent with its role in the regulation of SMC growth in culture. These data suggest that up-regulation of the P2Y2 receptor subtype in SMCs may contribute to increased cell proliferation and migration associated with the development of atherosclerotic lesions.