Characterization of signaling pathways of P2Y and P2U purinoceptors in bovine pulmonary artery endothelial cells.

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摘要

Abstract

The actions of ATP on the endothelium are mediated by P2 purinoceptors. We have shown that P2Y and P2U purinoceptors coexist in bovine pulmonary artery endothelial cells (CPAE), where they induce phosphoinositide (PI) turnover and Ca2+ mobilization. The relative order of potency (based on the threshold concentration) of nucleotide analogues (1-100 microM) in stimulating the accumulation of inositol phosphate (IP) was 2-methylthio-ATP (2MeSATP) = 2-methylthio-ADP (2MeSADP) > or = 2ClATP > UTP = ATP = ADP. alpha, beta-methylene ATP, beta, gamma-methylene ATP, UDP, adenosine-5'-tetraphospho-5'-adenosine, and adenosine-5'-pentaphospho-5'-adenosine had no effect at concentrations as high as 100 microM. At maximal concentrations, the IP responses to 2MeSATP and UTP were additive, whereas those to ATP and either 2MeSATP or UTP were not. Moreover, the maximal response to 2MeSADP was additive to that to UTP but not to that of 2MeSATP. Pretreatment with pertussis toxin slightly inhibited 2MeSATP- and UTP-stimulated IP generation by 15%. Under Ca(2+)-free conditions, UTP-induced IP formation was inhibited more markedly than that induced by 2MeSATP. Short-term treatment of the cells with phorbol 12-myristate-13-acetate (PMA) resulted in a dose-dependent inhibition of 2MeSATP-induced IP formation greater and more sensitive than that induced by UTP; similar results were obtained for the sensitivity of inhibition by suramin and reactive blue. Stimulation of the cells with either 2MeSATP or UTP induced a rapid increase in intracellular Ca2+ level, followed by a slow decrease to basal levels, followed by Ca2+ level oscillation. In the absence of extracellular Ca2+, [Ca2+]i responses were quantitatively less and did not show the slow phase and oscillation. Together these results suggest that both P2Y and P2U purinoceptors are expressed in bovine pulmonary artery endothelial cells and are coupled to phospholipase C (PLC) activation and Ca2+ mobilization through pertussis

toxininsensitive G proteins.