Extracellular ATP activates the PLC/PKC/ERK signaling pathway through the P2Y2 purinergic receptor leading to the induction of early growth response 1 expression and the inhibition of viability in human endometrial stromal cells.

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摘要

Abstract

ATP is an extracellular signaling molecule that activates specific G protein-coupled P2Y receptors in most cell types to mediate diverse biological effects. ATP has been shown to activate the phospholipase C (PLC)/diacylglycerol/proteiri kinase C (PKC) pathway in various systems. However, little is known about the signaling events in human endometrial Stromal cells (hESCs). The objective of this study was to examine the presence of the P2Y2 receptor and the effects of exogenous ATP on the intracellular mitogen-activated protein kinases (MAPKs) signaling pathway, immediate early genes expression, and cell viability in hESCs. Western blot analysis, gene array analysis, and MTT assay for cell viability were performed. The current study demonstrated the existence of the P2Y2 purinergic receptor in hESCs. UTP and ATP activated MAPK in a dose- and time-dependent manner. Suramin (a P2-purinoceptor antagonist), neomycin (a PLC inhibitor), staurosporin (a PKC inhibitor), and PD98059 (a MEK inhibitor) significantly attenuated the ATP-induced activation of MAPK. ATP activated ERK1/2 and induced translocation of activated ERK1/2 to the nucleus. The gene array for 23 genes associated with members of the mitogenic pathway cascade and immediate early genes revealed that the expression of early growth response 1 was increased. In addition, MTT assay revealed an inhibition effect of ATP on cell viability. ATP activated MAPKs through the P2Y2 purinoceptOF/PLC/PKC/ERK

signaling pathway and induced translocation of ERK1/2 into the nucleus. Further, ATP induced the expression of early growth response 1 and inhibited cell viability in hESCs.