Extracellular ATP Activates Nuclear Translocation of ERK1/2 Leading to the Induction of Matrix Metalloproteinases Expression in Human Endometrial Stromal Cells

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摘要

Abstract

ATP has been shown to activate the mitogen-activated protein kinase (MAPK) signaling pathway in various systems. However, little is known about the signaling events and the effects in human endometrial stromal cells (hESCs). The present study examined the effect of ATP on activating MAPKs and its subsequent events in hESCs. This study demonstrated the expression of the P(2U)/P2Y(2) receptor in hESCs by reverse transcription-PCR (RT-PCR). A PCR product with a sequence identical to the reported 599 bp P(2U)/P2Y(2) receptor cDNA was obtained. Western blot analysis, using a monoclonal antibody against the phosphorylated forms of ERK1/2, demonstrated that ATP activated MAPK in a dose- and time-dependent manner. Confocal microscopy showed an evident nuclear translocation of phosphorylated ERKs after 10 microM ATP treatment, but this effect was blocked by PD98059. To study the gene(s) induced by exogenous ATP, mRNA was extracted from hESCs in the presence or absence of 10 microM ATP. The gene array for 96 genes associated with members of human matrix metalloproteinases (MMPs) and adhesion molecules revealed that the expression of MMP-2, -3, -10, and -24 genes was increased and the effect was attenuated by PD98059. Furthermore the effects of ATP on the expression of MMP genes were confirmed by semiquantitative RT-PCR. To our knowledge, this is the first demonstration of the ATP-induced nuclear translocation of phospho-ERK1/2 that mediates MMPs gene expression in human endometrial cells. These results support the notion that the ERK1/2 signaling pathway is involved in mediating ATP actions in the human reproductive system.