Adenosine 5'-triphosphate activates nuclear translocation of mitogen-activated protein kinases leading to the induction of early growth response 1 and raf expression in human granulosa-luteal cells.

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摘要

Abstract

With the stimulation of many types of cell surface receptors, MAPKs are activated. We have previously demonstrated an effect of extracellular ATP on ERKs and gonadotropin- induced progesterone secretion, implicating the significance of ATP in the regulation of ovarian function. However, little is known about the specific role of ATP in the subsequent MAPK-induced signaling cascade in human granulosa-luteal cells (hGLCs). The present study was designed to examine the effect of ATP on the activation of the MAPK signaling pathway, including nuclear translocation and the expression of the immediate early genes in hGLCs. Western blot analysis, using a monoclonal antibody, which detected the total and phosphorylated forms of ERK1 and ERK2 (p42(mapk) and p44 (mapk), respectively), demonstrated that exogenous ATP evoked ERKs in a dose- and time-dependent manner. In contrast, p38 and JNK were not significantly activated after ATP treatment. To examine the translocation of activated ERKs, fluorescein isothiocyanate-conjugated secondary antibody was used to detect the distribution of total and phosphorylated ERKs. Immunofluorescent staining revealed that phosphorylated ERKs were translocated from cytoplasm into nucleus subsequent to 10 渭m ATP treatment. To study the gene(s) induced by exogenous ATP, mRNA was extracted from hGLCs in the presence or absence of 10 渭m ATP. 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 and c-raf-1 was increased. To our

knowledge, this is the first demonstration of the ATP-induced nuclear translocation of MAPKs in the human ovary. These results suggest that the MAPK signaling pathway plays a role in mediating ATP actions in the human ovary.