

# **ATP activates mitogen-activated protein kinase in human granulosa-luteal cells.**

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摘要

## **Abstract**

ATP has been shown to activate the phospholipase C/diacylglycerol/protein kinase C (PKC) pathway. However, little is known about the downstream signaling events. The present study was designed to examine the effect of ATP on activation of the mitogen-activated protein kinase (MAPK) signaling pathway and its physiological role in human granulosa-luteal cells. Western blot analysis, using a monoclonal antibody that detected the phosphorylated forms of extracellular signal-regulated kinase-1 and -2 (p42mapk and p44 mapk, respectively), demonstrated that ATP activated MAPK in a dose- and time-dependent manner. Treatment of the cells with suramin (a P2 purinoceptor antagonist), neomycin (a phospholipase C inhibitor), staurosporin (a PKC inhibitor), or PD98059 (an MAPK/ERK kinase inhibitor) significantly attenuated the ATP-induced activation of MAPK. In contrast, ATP-induced MAPK activation was not significantly affected by pertussis toxin (a Gi inhibitor). To examine the role of Gs protein, the intracellular cAMP level was determined after treatment with ATP or hCG. No significant elevation of intracellular cAMP was noted after ATP treatment. To determine the role of MAPK in steroidogenesis, human granulosa-luteal cells were treated with ATP, hCG, or ATP plus hCG in the presence or absence of PD98059. RIA revealed that ATP alone did not significantly affect the basal progesterone concentration. However, hCG-induced progesterone production was reduced by ATP treatment. PD98059 reversed the inhibitory effect of ATP on hCG-induced progesterone production. To our knowledge, this is the first demonstration of ATP-induced activation of the MAPK signaling pathway in the human ovary. These results support the idea that the MAPK signaling pathway is involved in mediating ATP actions in the human ovary