Adenosine triphosphate-evoked cytosolic calcium oscillations in human granulosa-luteal cells: role of protein kinase C

戴承杰

Tai CJ;Kang SK;Leung PC

摘要

Abstract

ATP has been shown to modulate progesterone production in human granulosa-luteal cells (hGLCs) in vitro. After binding to a G protein-coupled P2 purinergic receptor, ATP stimulates phospholipase C. The resultant production of diacylglycerol and inositol triphosphate activates protein kinase C (PKC) and intracellular calcium [Ca2+]i mobilization, respectively. In the present study, we examined the potential cross-talk between the PKC and Ca2+ pathway in ATP signal transduction. Specifically, the effect of PKC on regulating ATP-evoked [Ca2+]i oscillations were examined in hGLCs. Using microspectrofluorimetry, [Ca2+]i oscillations were detected in Fura-2 loaded hGLCs in primary culture. The amplitudes of the ATP-triggered [Ca2+]i oscillations were reduced in a dose-dependent manner by pretreating the cells with various concentrations (1 nM to 10 μM) of the PKC activator, phorbol-12-myristate-13-acetate (PMA). A 10 μM concentration of PMA completely suppressed 10 μM ATP-induced oscillations. The inhibitory effect occurred even when PMA was given during the plateau phase of ATP evoked [Ca2+]i oscillations, suggesting that extracellular calcium influx was inhibited. The role of PKC was further substantiated by the observation that, in the presence of a PKC inhibitor, bisindolylmaleimide I, ATP-induced [Ca2+]i oscillations were not completely suppressed by PMA. Furthermore, homologous desensitization of ATP-induced calcium oscillations was partially reversed by bisindolylmaleimide I, suggesting that activated PKC may be involved in the mechanism of desensitization. These results demonstrate that PKC negatively regulates the ATP-evoked [Ca2+]i mobilization from both intracellular stores and extracellular influx in hGLCs and further support a modulatory role of ATP and P2 purinoceptor in ovarian steroidogenesis.