A novel FSH-induced Gαh/PLC-δ1 signaling pathway mediating rat Sertoli cell Ca2+-influx

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摘要

Abstract

Follicle-stimulating hormone (FSH) is known to activate Gs/cAMP signaling pathway in Sertoli cells (SCs) to support spermatogenesis. However, the molecular mechanism of FSH-induced Gs/cAMP-independent Ca2+-influx in SCs is not clear. In this study, FSH indeed induced an immediate and dose-dependent intracellular Ca2+-elevation in rat SCs. In the presence of EDTA (2.5 mM) or in the absence of extracellular Ca2+, the FSH-induced intracellular Ca2+-elevation was abolished. The Confocal microscopic observation of Ca2+ image revealed that the SC cellular Ca2+ level was gradually increased after 50 seconds of FSH treatment. Dantrolene, a blocker of intracellular Ca2+-release, did not affect this FSH-induced intracellular Ca2+-elevation. The pretreatment of rat SCs with PI-PLC specific inhibitor, U73122 (3 and 10 μM) dose-dependently inhibited the FSH-induced Ca2+-influx, but not with Gs specific inhibitor, NF449 (0.1 and 0.3 μM). On the other hand, the activation of Gαh was immediately induced by FSH in the rat SCs within 5 seconds of treatment. The translocation of PLC-δ1 from cytosol to cell membrane and the formation of Gαh/PLC-δ1 complexes occurred within 5 and 10 seconds, respectively, of FSH exposure. The intracellular IP3 production was also detected after 30 seconds of FSH treatment. The synthetic peptide of PLC-δ1 (TIPWNSLKQGYRHVHLL), not Gs inhibitor, predominantly inhibited the FSH-induced PLC-δ1 translocation, formation of Gαh/PLC-δ1 complex, intracellular IP3 production, and Ca2+-influx. In contrast, the peptide did not interfere with FSH-induced 4 intracellular cAMP accumulation. In conclusion, the FSH-induced immediate Ca2+-influx is unambiguously mediated by an alternative Gαh/PLC-δ1/IP3 pathway that is distinct from Gs/cAMP pathway in rat SCs.