Biomedical Research & Therapy

ISSN: 2198-4093
www.bmrat.org

POSTER

The antidepressant fluoxetine inhibits adenylate cyclase stimulation by FSH or Forskolin in the COV434 human ovarian granulosa tumor cell line

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Competing interests: The authors declare that no competing interests exist.

Received: 2017-03-06
Accepted: 2017-06-28
Published: 2017-09-05

Abstract

Fluoxetine (Prozac), a selective Serotonin Reuptake Inhibitor antidepressant, exhibits other mechanisms of action in various cell types and has been shown to induce cell death in cancer cells, paving the way for its potential use in cancer therapy. The ovary is a complex endocrine organ responsible for steroidogenesis and folliculogenesis, and human granulosa cells are essential for scientific research to improve the understanding of these two processes. However, little is known about fundamental signaling pathways in human granulosa cells. In this study, we investigated the dynamics of intracellular cyclic adenosine monophosphate AMP, a conserved signaling messenger that can regulate virtually every physiological process. We show that incubating COV434 human ovarian granulosa cells with fluoxetine induces a decrease in intracellular cAMP response to Follicle-stimulating hormone (FSH) and forskolin (FSK). In order to study the intracellular cAMP kinetic responses of COV434 cells to FSH or FSK, we used COV434 cells transiently expressing a chimeric cAMP-responsive luciferase so that real-time variations of intracellular cAMP concentration could be monitored, by using oxiluciferin luminescence produced from catalyzed luciferin oxidation. Our data show that fluoxetine induces an increase in the extracellular Ca2+ entry and reduces ATP concentration as well as cell viability. Targeting these signaling pathways with fluoxetine could permit to get better knowledge in the molecular mechanisms involved in ovarian follicular development.

Keywords

Fluoxetine, adenylate cyclase, human ovarian granulosa, COV434

Funding

References

DOI 10.15419/bmrat.v4iS.315