Calcium stimulates mitochondrial biogenesis in human granulosa cells

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Abstract

ABSTRACT: Ovarian granulosa cells are known to play a key role in regulating ovarian physiology. Age increases apoptosis in follicular granulosa cells and subsequently decreases ovarian fecundity. The aging ovary also contains fewer follicles that possess fewer granulosa cells. The viability of follicular granulosa cells may be essential for development of the oocyte. Calcium ion plays an im-portant role in a variety of biological processes, including gene expression, cell cycle regulation, and cell death. To study the ability of mitochondrial biogene-sis in human granulosa cells, we determined the mitochondrial marker pro-teins, including the nuclear-encoded NADH-ubiquinone oxidoreductase alpha subunit 9 (NDUFA9) and mitochondrial-encoded COX I, after treatment of the cells with the calcium ionophore A23187. We showed that the expression of these mitochondrial marker proteins in human granulosa cells increased with changes in cytosolic Ca2+ using the ionophore A23187. Treatment of granulosa cells with 0.5 &#1;M of A23187 for 120 h increased the levels of NDUFA 9 and COX I subunit by up to 2.6- and 2.4-fold, respectively. Raising Ca2+ by exposing granulosa cells to 1 &#1;M of A23187 for 48 h significantly increased mitochon-drial transcription factor (mtTFA) gene expression by up to 2.9-fold. Our re-sults indicate that the adaptive responses of granulosa cells to increased Ca2+ may include upregulation of mitochondrial proteins and that mtTFA may be involved in such a mitochondrial biogenesis pathway.