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Pyrroloquinoline Quinone Enhances the Mitochondrial Function by Increasing Beta-Oxidation and a Balanced Mitochondrial Recycling in Mice Granulosa Cells

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Abstract : The production of competent oocytes is essential for reproductivity in mammals. Maintenance of mitochondrial efficiency is required to supply the ATP necessary for granulosa cell proliferation during the follicular development process. Treatment with Pyrroloquinoline quinone (PQQ) has been reported to increase the number of ovulated oocytes and pups per delivery in mice by maintaining healthy mitochondrial function. This study aimed to elucidate how PQQ maintains mitochondrial function during ovarian follicle growth. To do this, both in vitro and in vivo experiments were performed with granulosa cells from superovulated immature (3-week-old) mice that were pretreated with or without PQQ. The effects of PQQ on beta-oxidation, mitochondrial function, mitophagy, and mitochondrial biogenesis were examined. PQQ increased beta-oxidation-related genes and CPT1 protein content in granulosa cells and this was associated with a decreased phosphorylation of P38 signaling protein. Using the fatty acid oxidation assay on the flux analyzer, PQQ increased the reliance of beta-oxidation on the endogenous fatty acids and was associated with a mild UCP-dependant mitochondrial uncoupling, ATP production, mitophagy, and mitochondrial biogenesis. PQQ also increased the expression of endogenous antioxidant enzymes. Thus, PQQ induced beta-oxidation in growing granulosa cells relying on endogenous fatty acids. And reduced the Reactive oxygen species (ROS) production by inducing a mild mitochondrial uncoupling with keeping high mitochondrial function. Damaged mitochondria were recycled by the induced mitophagy and replaced by the increased mitochondrial biogenesis. Collectively, PQQ may enhance reproductivity by maintaining the efficiency of mitochondria to produce enough ATP required for normal folliculogenesis.

Keywords : granulosa cells, mitochondrial uncoupling, mitophagy, pyrroloquinoline quinone (PQQ), reactive oxygen species (ROS).
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