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Mito-Q promotes porcine oocytes maturation by maintaining mitochondrial thermogenesis via UCP2 downregulation

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ABSTRACT

Mitochondrial thermogenesis is an adaptive response of cells to their surrounding stress. Oxidative stress is one of the common stresses during *in vitro* maturation (IVM) of oocytes, which leads to mitochondrial dysfunction. This study aimed to probe the effects of the mitochondria-targeted antioxidant Mito-Q on oocyte development and unravel the role of Mito-Q in mitochondrial ATP production and thermogenesis regulation. Our results showed that Mito-Q had a positive effect on porcine oocytes maturation and subsequent embryo development. During oocytes IVM, Mito-Q could reduce ATP levels and ROS, increase lipid droplets accumulation, induce autophagy, and maintain mitochondrial temperature stability. Moreover, in metaphase II (MII) oocytes, Mito-Q would induce mitochondrial uncoupling manifested by decreased ATP, attenuated mitochondrial membrane potential (MMP), and increased mitochondrial thermogenesis. Notably, the expression of mitochondrial uncoupling protein (UCP2) was significantly reduced in oocytes treated with Mito-Q. Further study indicated that specific depletion of UCP2 in oocytes also resulted in increased thermogenesis, decreased ATP and declined MMP, suggesting that UCP2 downregulation may participate in Mito-Q-induced mitochondrial uncoupling. In summary, our data demonstrate that Mito-Q promotes oocyte maturation *in vitro* and maintains the stability of mitochondrial thermogenesis by inhibiting UCP2 expression.

1. Introduction

Oocyte *in vitro* maturation (IVM) provides sufficient eggs for embryo biotechnologies such as cloning and transgenesis. Although being widely used in assisted reproductive technology (ART), IVM oocytes are still confronted with poor maturation quality and low embryonic development potential, which would inevitably limit the development of embryonic biotechnology [1].

Mitochondria are the powerhouse in the cell, and accumulating studies have shown that mitochondrial dysfunction can lead to the impaired developmental potential of oocytes during *in vitro* maturation [2–4]. Mito-Q is a mitochondria-targeted antioxidant composed of cationic triphenylphosphine (TPP) and the ubiquinone portion of coenzyme Q, which directly targets mitochondria to remove excess reactive oxygen species (ROS) [5]. Since 2000, Mito-Q has been used in the treatment of various oxidative stress-related events, including organ and tissue cryopreservation [6], obesity, insulin resistance, and cardiovascular diseases [7–9]. In oocytes, Mito-

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