Journal of Fertilization: In Vitro - IVF-Worldwide, Reproductive Medicine, Genetics & Stem Cell Biology

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Short Communication

Intercellular Mitochondrial Transfer between Granulosa Cells and Oocytes and its Influence on Oocyte Bioenergetic Competence in Assisted Reproduction

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DESCRIPTION

Oocyte developmental competence is strongly dependent on adequate mitochondrial function, as mitochondria provide the energy required for meiotic maturation, fertilization, and early embryonic cleavage. In assisted reproductive cycles, variability in oocyte quality is often observed even among follicles stimulated under similar hormonal conditions [1]. One emerging concept in reproductive biology that may explain this variability is intercellular mitochondrial transfer between granulosa cells and the oocyte, a process that contributes to oocyte bioenergetic support and developmental potential.

Granulosa cells form a tightly connected layer surrounding the oocyte within the ovarian follicle. These cells are metabolically active and play an essential role in supporting oocyte growth and maturation. Communication between granulosa cells and the oocyte occurs through gap junctions, paracrine signaling, and metabolic coupling. Recent evidence suggests that this interaction may extend beyond metabolite exchange to include the transfer of mitochondria or mitochondrial components under specific physiological conditions [2].

Mitochondrial transfer refers to the movement of intact mitochondria or mitochondrial-derived vesicles from one cell to another. In the ovarian follicle, this process may provide the oocyte with additional functional mitochondria during critical stages of maturation. Since oocytes rely heavily on maternally derived mitochondria, any supplementation from surrounding granulosa cells may enhance bioenergetic capacity and improve developmental outcomes.

During follicular growth, granulosa cells undergo metabolic adaptation characterized by increased glycolysis and mitochondrial activity [3]. These cells generate metabolic substrates such as pyruvate and lactate, which are transported to the oocyte through intercellular connections. In addition to metabolite transfer, experimental evidence suggests that tunneling nanotube-like structures or extracellular vesicles may facilitate the movement of mitochondrial material between cells.

Oocyte maturation involves a significant increase in energy demand, particularly during meiotic spindle formation and chromosomal segregation. Adequate adenosine triphosphate production is essential for maintaining spindle integrity and preventing chromosomal misalignment. If mitochondrial content or function within the oocyte is insufficient, errors in meiotic division may occur, potentially leading to aneuploidy or developmental arrest after fertilization [4].

Granulosa cell mitochondrial quality may therefore indirectly influence oocyte competence. Cells with higher mitochondrial membrane potential and lower oxidative damage may be more capable of contributing functional mitochondrial components to the oocyte. Conversely, granulosa cells exposed to oxidative stress, metabolic dysfunction, or inflammatory conditions may provide impaired mitochondrial support, negatively affecting oocyte quality [5].

Age-related decline in reproductive function is associated with mitochondrial dysfunction in both oocytes and surrounding granulosa cells. With advancing maternal age, mitochondrial DNA mutations accumulate, and oxidative phosphorylation efficiency decreases. This dual decline may reduce the effectiveness of intercellular mitochondrial support, contributing to reduced fertility and increased embryo developmental variability in assisted reproductive treatment.

Controlled ovarian stimulation protocols may also influence mitochondrial dynamics within the follicular environment. Hormonal stimulation alters granulosa cell proliferation and metabolic activity, which may affect mitochondrial biogenesis and transfer capacity [6]. Variations in stimulation response among patients may therefore be partially explained by differences in follicular mitochondrial interactions.

Follicular fluid provides a medium for metabolic exchange and contains extracellular vesicles that may carry mitochondrial components or regulatory molecules. These vesicles can influence gene expression, metabolic activity, and stress response pathways within the oocyte. The presence of mitochondrial-derived vesicles in follicular fluid has been proposed as a

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Received: 02-Jun-2026, Manuscript No. JFIV-26-41863;**Editor assigned:** 04-Jun-2026, PreQC No. JFIV-26-41863 (PQ); **Reviewed:** 18-Jun-2026, QC No. JFIV-26-41863; **Revised:** 24-Jun-2026, Manuscript No. JFIV-26-41863 (R);**Published:** 02-Jul-2026, DOI: 10.35841/2329-9495.26.14.410

Citation: Hernández A (2026). Intercellular Mitochondrial Transfer between Granulosa Cells and Oocytes and its Influence on Oocyte Bioenergetic Competence in Assisted Reproduction. J Fertil *In Vitro* IVF World w Reprod Med Gent Stem Cell Biol. 14:410.

potential indicator of follicular health and oocyte developmental potential [7,8].

Reactive oxygen species play a dual role in mitochondrial transfer processes. At physiological levels, they act as signaling molecules regulating mitochondrial biogenesis and intercellular communication. However, excessive oxidative stress can damage mitochondrial Deoxyribonucleic Acid (DNA) and impair transfer efficiency [9]. Antioxidant systems within the follicle help maintain redox balance, but this system may become less effective in conditions such as polycystic ovarian syndrome or endometriosis.

Assisted reproductive technologies provide a unique opportunity to study mitochondrial dynamics under controlled conditionsm [10]. Although mitochondrial transfer cannot be directly observed in standard clinical practice, indirect markers such as Adenosine Triphosphate (ATP) content, mitochondrial DNA copy number, and spindle morphology are used to assess oocyte quality. Advances in imaging and molecular techniques may allow more direct evaluation of mitochondrial exchange in the future.

CONCLUSION

Current evidence indicates that intercellular mitochondrial transfer between granulosa cells and oocytes may contribute significantly to oocyte bioenergetic competence. This process, along with metabolic coupling and oxidative regulation, plays an important role in determining developmental outcomes in assisted reproductive cycles. Continued research integrating reproductive cell biology, bioenergetics, and clinical embryology may enhance understanding of follicular function and improve fertility treatment strategies.

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