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REVIEW

Behaviour of cytoplasmic organelles and cytoskeleton during oocyte maturation

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Abstract Assisted reproduction technology (ART) has become an attractive option for infertility treatment and holds tremendous promise. However, at present, there is still room for improvement in its success rates. Oocyte maturation is a process by which the oocyte becomes competent for fertilization and subsequent embryo development. To better understand the mechanism underlying oocyte maturation and for the future improvement of assisted reproduction technology, this review focuses on the complex processes of cytoplasmic organelles and the dynamic alterations of the cytoskeleton that occur during oocyte maturation. Ovarian stimulation and in-vitro maturation are the major techniques used in assisted reproduction technology and their influence on the organelles of oocytes is also discussed.

KEYWORDS: assisted reproduction technology, cytoplasmic organelles, cytoskeleton, oocyte maturation, oocyte quality, fertilization

Introduction

In recent decades, assisted reproduction technologies such as in-vitro maturation (IVM), in-vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) have become attractive options for infertility treatment. However, at present, further studies are needed to improve the success rates of assisted reproduction technology. According to the 2010 assisted reproduction technology success rates report by the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention et al., 2012), 147,260 assisted cycles were performed at 443 reporting clinics in the USA during 2010, resulting in only 47,090 live births (deliveries of one or more living infants) and 61,564 infants. Therefore, a great challenge for researchers is to find ways to improve assisted reproduction technology success rates.

Previous studies have indicated that reduced oocyte developmental competence is a primary reason for the

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reduced potential of in-vitro-produced embryos (Sirard et al., 2006; Watson, 2007). One hypothesis is that the process of cytoplasmic maturation is disturbed by ovarian stimulation or oocyte maturation *in vitro*, leading to the abnormal behaviour of cell organelles (De los Reyes et al., 2011; Lee et al., 2006a; Zeng et al., 2009). Therefore, improved knowledge of the mechanism of both nuclear and cytoplasmic maturation in the oocyte is necessary for the advancement of assisted reproduction technology.

Oocyte maturation is a long process that includes both nuclear and cytoplasmic maturation. Nuclear maturation mainly involves chromosome segregation, which has been well studied. Additionally, cytoplasmic maturation involves organelles that reorganize and store the mRNA, proteins and transcription factors required for oocyte maturation, fertilization and early embryogenesis (Watson, 2007). Cytoplasmic maturation is complex, and there are still many parts of this process that remain controversial. The proper spatial and temporal dynamics of organelles and the cytoskeleton ensures that the oocyte acquires the high developmental potency required for fertilization and subsequent embryo development (Sirard et al., 2006). Proper modification of the localization, morphology and biochemical properties of organelles must occur for the oocyte to acquire high developmental potency. Due to advances in modern experimental techniques, such as electron microscopy and immunofluorescence with different fluorescent dyes, the redistribution and morphological changes of organelles have been extensively studied.

Reorganization of cytoplasmic organelles

Mitochondria

Redistribution

Cytoplasmic maturation involves a series of complex events, including protein synthesis and transcription of cytoplasmic RNA, which consume energy. The primary function of mitochondria is to synthesize ATP. Therefore, mitochondria play an extremely important role in supplying the energy that is consumed during the maturation process (Krisher and Bavister, 1998; Stojkovic et al., 2001).

The movement of mitochondria to areas of high energy consumption is crucial for oocyte maturation (**Figures 1 and 2**). In the immature mouse oocyte, mitochondria are aggregated around the germinal vesicle (GV). The mitochondria move away from the perinuclear region at germinal vesicle breakdown (GVBD) and occupy most of the egg volume in a mature meiosis-II (MII) oocyte (Dumollard et al., 2006). An additional change in the mitochondrial distribution, involving a change in the size of mitochondrial clusters, was observed in maturing mouse oocytes. Upon GVBD, only 5% of oocytes show small mitochondrial clusters, whereas most mitochondrial clusters are larger. In contrast, at 2 h and 8 h after GVBD, a large proportion of oocytes contain mitochondria that form smaller clusters throughout the cytoplasm (Yu et al., 2010).

In GV human oocytes (**Figure 1**), mitochondria are predominantly spherical to oval with dense matrices and few arch-like or transverse cristae presenting an inert appearance (Sathananthan et al., 2006). At this stage, mitochondria are usually absent from the cortical part of the cytoplasm (Familiari et al., 2006; Sathananthan and Trounson, 2000). Mitochondria in MI and MII oocytes become even more numerous and are dispersed in the ooplasm (Motta et al., 2000; Sathananthan and Trounson, 2000). Unlike other species, mitochondria of human oocytes form voluminous aggregates with smooth endoplasmic reticulum (SER) tubules and vesicles at the end of the maturation process (Familiari et al., 2006; Motta et al., 2000; Sathananthan and Trounson, 2000. These mitochondrial-SER aggregates and the mitochondrial-vesicle complexes could be involved in the production of a reservoir of substances or membranes anticipating subsequent fertilization and early embryogenesis (Motta et al., 2000).

ATP content and oocyte quality

The distribution and organization of mitochondria are dynamic during oocyte maturation, and these changes may be related to the function of mitochondria. The main function of mitochondria is to provide ATP. Therefore, many research groups are interested in the relationship between the reorganization of mitochondria and ATP concentration. Indeed, previous studies have indicated that the reorganization of mitochondria is associated with ATP content in bovine oocytes (Stojkovic et al., 2001).

Yu et al. (2010) demonstrated, for the first time as far as is known, the ATP dynamics during maturation in a living mouse oocyte, thus providing additional evidence of the relationship between mitochondrial organization and ATP concentration. The rate of mitochondrial ATP production changes during spontaneous mouse oocyte maturation. Compared with GV-arrested oocytes, there are three distinct increases in cytosolic and mitochondrial ATP concentrations during oocyte maturation, including three phases of higher ATP production and two phases of lower ATP production. The first phase of increased ATP production occurs around the time of GVBD. The second phase occurs during the longer phase of spindle migration and the third phase occurs during the meiosis I (MI) to MII transition. This study also demonstrated that the clustering pattern correlates with the timing of ATP pulses. Specifically, it appeared that the formation of large clusters of mitochondria is associated with increased ATP production. In addition, disruption of the mitochondrial clusters by cytochalasin B treatment results in an inhibition of the bursts of ATP production (Yu et al., 2010). These results suggest that the clustering pattern correlates with bursts of ATP production.

Due to the critical role of energy metabolism in oocyte maturation, ATP content has been proposed as an indicator for the developmental potential of human (Slotte et al., 1990; Van Blerkom et al., 1995) and mouse oocytes (Leese et al., 1984). ATP is extremely important for nuclear and cytoplasmic maturation events. Spindle formation and chromosome movements depend on the expression and activity of motor proteins, which use ATP as their energy source. Previous studies demonstrated that an increase in ATP concentration is necessary for both bovine and human oocyte maturation (Duran et al., 2011; Nagano et al., 2006). Oocytes with higher concentrations of ATP have significantly higher fertilization and blastocyst rates (Nagano et al., 2006; Stojkovic et al., 2001). Lower ATP concentrations of