Proteomic Approaches to Identify Age-Specific Biomarkers in Oocyte

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The increase in pregnancy at advanced maternal age (AMA, age ≥35) can be attributed to various factors such as socioeconomic changes and advancements in medical technology. Furthermore, despite the decline in the birth rate, the birth rate among AMA mothers has shown an increasing trend for a few decades. However, pregnancy at AMA has gradually been recognized to increase several risks, including miscarriage, stillbirth, and obstetric complications. Additionally, pregnancy at AMA can act as a risk factor for the structure and functions of oocytes, subsequently contributing to subfertility. Therefore, this study was designed to profile correlated changes during aging that can be used as age-specific biomarkers in mouse oocytes. The age-specific mouse groups were categorized into three in accordance with the reproductive age of mice equivalent to humans. The age of human sexual maturity, AMA, and menopause were used as criteria. MII stage oocytes were collected from each age-specific group and used to evaluate the differences in age-related physiological and proteomic biomarkers. Initially, nonlethal factors (e.g. tail length and body weight) and the number of ovulated oocytes per mouse showed age-dependent changes. Moreover, increased morphological abnormality of the uterus, ovary, and oocyte in the older mice group was confirmed. Additionally, the evaluation of comprehensive oocyte function (e.g. mitochondrial activity and ROS level) revealed abnormal changes in older oocytes. Proteomic research identified 14 differentially up- and down-regulated (> 3-fold) proteins between each group. These proteins are closely related to component and function of oocytes, including kinetochore, nucleus, macromolecular complex, ubiquitin-dependent process, and nucleotide binding. Consequently, in vitro fertilization assay confirmed the significantly decreased cleavage and blastocyst formation rates. Taken together, our results implicate the cellular and molecular changes between younger and older oocytes. Therefore, continued efforts are needed to evaluate how aging affects oocytes and the intermolecular process of fertilization.

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