In Vitro Culture Improves the Transcriptome and Chromosome Structure of Secondary Follicles in Aging Mice.

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Abstract

In recent years, the age of first pregnancy has continued to increase. The problem is that the proportion of aneuploid metaphase II oocytes increases rapidly with the woman's age. However, the mechanisms of aging-rerated meiotic defects and aneuploidy in oocytes remain to be clarified. The interaction of oocytes with granulosa cells (GCs) and cumulus cells (CCs) during oocyte growth and maturation is essential for obtaining functional oocytes. This study explores how age-related changes in GCs and CCs may impair oocyte development. We analyzed transcriptomic alterations in these cells and oocyte chromosome structures following *in vitro* growth (IVG). Secondary and antral follicles were collected from young (8-12 weeks) and old (44-54 weeks) C57BL/6J female mice, and GCs and CCs were isolated for RNA-seq. *In vivo* grown and IVG oocytes were subjected to *in vitro* maturation, and spindle and chromosomes were evaluated. Principal component analysis revealed variation between old and young CCs but not GCs. Notably, the expression variability in *in vitro*-cultured CCs was reduced, indicating altered gene expression dynamics by culture. Aneuploidy rates were comparable in IVG and *vivo*-grown oocytes. However, IVG oocytes exhibited improved spindle morphology and reduced chromosomal irregularities, suggesting a potential benefit of *in vitro* culture on chromosomal stability. IVG significantly reduced the distance between sister chromatid kinetochores, enhancing chromosomal alignment and possibly reducing partitioning errors during meiosis. These findings support the potential of *in vitro* techniques to alleviate age-related defects in oocyte quality.