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Opinion Article

Expression of Noncoding RNAs in Cumulus Cells and their Relationship with Oocyte Maturation during Assisted Reproduction

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DESCRIPTION

Oocyte maturation represents one of the most important biological events in human reproduction because developmental competence acquired during this stage influences fertilization, embryo formation, and implantation success. In assisted reproductive treatment, the quality of retrieved oocytes varies considerably even among patients receiving similar ovarian stimulation protocols. While hormonal measurements and follicular morphology provide indirect information regarding ovarian response, researchers continue searching for molecular indicators capable of predicting oocyte competence more accurately. During recent years, noncoding Ribonucleic Acids (RNAs) expressed within cumulus cells have emerged as important regulators of follicular development and meiotic progression.

Cumulus cells surround the oocyte within the ovarian follicle and maintain continuous bidirectional communication through gap junctions and paracrine signaling. These cells support nutrient transport, steroid metabolism, and protection against oxidative stress during follicular maturation. Since cumulus cells remain closely associated with the oocyte until retrieval, their molecular activity reflects conditions within the follicular microenvironment. Analysis of cumulus cell gene expression has therefore become an important area of reproductive biology research.

Noncoding RNAs are RNA molecules that do not encode proteins but instead regulate gene expression through multiple cellular mechanisms. These molecules include microRNAs, long noncoding RNAs, small interfering RNAs, and circular RNAs. Within ovarian follicles, noncoding RNAs influence granulosa cell proliferation, apoptosis, hormone signaling, and meiotic control. Altered expression patterns may contribute to impaired oocyte maturation, diminished ovarian reserve, and infertility-related disorders.

MicroRNAs are among the most extensively studied noncoding RNAs in reproductive medicine. These short RNA molecules regulate messenger RNA translation and degradation, thereby influencing protein synthesis within target cells. Numerous microRNAs have been identified in cumulus cells collected during intracytoplasmic sperm injection procedures. Certain microRNA profiles appear associated with mature metaphase II oocytes and improved embryo development after fertilization.

MicroRNA-21 has attracted particular attention due to its involvement in apoptosis regulation and cellular survival pathways. Elevated expression of this molecule within cumulus cells has been associated in some studies with improved oocyte maturity and blastocyst formation. Conversely, abnormal expression patterns involving microRNA-320 and microRNA-93 have been linked to impaired follicular development and reduced fertilization rates. These findings suggest that specific noncoding RNA signatures may reflect follicular health before embryo culture begins.

Long noncoding RNAs also participate in ovarian physiology through chromatin modification, transcriptional regulation, and interaction with microRNAs. Some long noncoding RNAs influence granulosa cell sensitivity to follicle stimulating hormone and luteinizing hormone during controlled ovarian stimulation. Altered expression of these molecules has been reported in women with polycystic ovarian syndrome, endometriosis, and premature ovarian insufficiency. Since these disorders frequently affect oocyte competence, researchers continue examining how noncoding RNA regulation contributes to reproductive dysfunction.

Meiotic progression within the oocyte depends on coordinated signaling between cumulus cells and the oocyte itself. Cyclic adenosine monophosphate and cyclic guanosine monophosphate maintain meiotic arrest during follicular growth. The luteinizing hormone surge subsequently initiates meiotic resumption through complex intracellular signaling pathways. Noncoding RNAs appear capable of regulating enzymes and transcription factors involved in this process. Disruption of these regulatory networks may impair spindle formation, chromosome segregation, and cytoplasmic maturation.

Mitochondrial activity within cumulus cells represents another important factor linked to noncoding RNA expression. Oocytes

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require substantial energy reserves during maturation and fertilization, though they possess limited glycolytic capacity. Cumulus cells therefore provide metabolic substrates including pyruvate and lactate that support mitochondrial function. Oxidative stress affecting cumulus cell mitochondria may alter noncoding RNA profiles and compromise oocyte quality. Several investigations have identified associations between antioxidant-related microRNAs and successful embryo development following assisted reproduction.

Endometriosis has similarly been associated with abnormal noncoding RNA regulation within the follicular environment. Chronic inflammatory activity and oxidative stress characteristic of this condition may influence granulosa cell function and meiotic regulation. Researchers have identified several microRNAs linked to inflammatory cytokine pathways in cumulus cells from women with endometriosis undergoing IVF treatment. These molecular changes may partly explain reduced fertilization and implantation rates observed in some patients. Advances in sequencing technology have expanded opportunities for noncoding RNA analysis in reproductive medicine. High-throughput sequencing platforms now permit comprehensive profiling of RNA expression within small cell populations collected during oocyte retrieval. Artificial intelligence methods are increasingly being used to analyze complex RNA datasets and identify molecular patterns associated with successful fertilization and embryo development.

CONCLUSION

Current evidence indicates that noncoding RNAs expressed within cumulus cells participate actively in the regulation of oocyte maturation during assisted reproduction. These molecules influence apoptosis, mitochondrial activity, hormone signaling, meiotic progression, and inflammatory regulation within the follicular environment. Although clinical implementation remains under development, noncoding RNA analysis offers significant potential for improving understanding of oocyte competence and reproductive biology. Continued collaboration among molecular geneticists, embryologists, and reproductive endocrinologists will remain important for translating these discoveries into practical fertility treatment applications.