



University of Zabol  
Graduate school  
Faculty of Basic Sciences  
Department of Biology

**The Thesis Submitted for the Degree of M.Sc (in the field of  
Genetic Science)**

**Determining the success of IVF rate in  
people with polycystic ovary syndrome  
by investigation of candidate  
microRNAs relative expression**

**Supervisors:**  
Dr. F. Haddadi  
Dr. S. M. Kalantar

**Advisors:**  
Dr. F. Montazeri  
Dr. H. amaladini

**BY:**  
**M. Jafari**

**February 2023**

### **Determining the success of IVF rate in people with polycystic ovary syndrome by investigation of candidate microRNAs relative expression**

Cumulus cells (CC) surrounding the developing oocytes support their maturation by bidirectional interactions. Transcriptome of CC has the potential to help as significant non-invasive biomarkers for oocyte capability and quality. The present study aimed at finding most important genes and pathways involved in oocyte maturation in different maturity stages germinal vesicle (GV) and MII by assessing the transcriptomic signatures of their neighboring CC. GSE145467 and GSE108886 gene expression profiles were obtained from the Gene Expression Omnibus (GEO) database. The differentially expressed genes (DEGs) between 6 GV- CC and 6 matched MII- CC were identified using the CLC software. Common DEGs in the datasets were selected by the VennDiagram package. For the functional annotation of common DEGs, DAVID v.6.8 was used to perform Gene Ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. In accordance with data collected from the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database, a protein-protein interaction (PPI) network was constructed by Cytoscape. Cytohubba in Cytoscape was used to screen the hub genes. Finally, potential micro RNAs (miRNAs) of hub genes were predicted by miRWalk 3.0 and miRDB. After comparing differential expressed genes (DEGs) between 6 GV- CC and 6 matched MII- CC we reached 1400 genes, among them we selected 422 down-regulated genes in CC encapsulating mature oocytes (MII- CC). Then, the most important pathways including candidate genes which involved in oocyte maturation were considered. The first five highlighted paths include nuclear maturation, chromatin remodeling & DNA replication initiation, apoptosis and inflammation, extracellular matrix components and remodeling and steroid metabolism and processing. Finally, we selected 4 miRNAs that were most related to hallmark pathways and also targeted the mentioned genes include *PKMYT1*, *CycB*, *E2F1*, *CHEK1*, *MYBL2* and *CCNA2*. In this study we review our findings and compare with previous literature refer to the oocyte transcriptome during different maturation stages. Our findings were in line with the available reports and enrich it with several genes and pathways, which have not been previously involved in human oocyte development. This study lays the ground for future functional studies that can enhance our understanding of human oocyte maturation. The hub genes of the bidirectional network in the cumulus-oocyte complex played a fundamental role in oocyte maturation; though, these findings need supplementary investigation.

**Keywords:** Cumulus cells (CC), differentially expressed genes (DEGs), Gene expression, Oocyte maturation, Assisted reproductive Technology (ART)