Small RNAs: new candidates for the regulation of the human cumulus-oocyte complex crosstalk

Abstract

Objective

To identify and quantify small RNAs, including microRNAs, in human cumulus cells (CCs) and mature MII oocytes and to characterize the biological relationships between miRNAs and the messenger RNA expression profiles of MII oocytes and CCs.

Design

Mature MII oocytes and CCs were collected from women who underwent IVF/ICSI under COS.

Materials and Methods

Using Illumina/deep-sequencing technology, we dissected the small RNAome of pooled mature MII oocytes and CCs (n=24 and n=20 respectively). The correlation between these microRNAs and their corresponding validated mRNA targets was investigated using in silico prediction algorithms. Using oligonucleotide microarrays, genome-wide gene expression was studied in mature MII oocytes or CCs. TaqMan miRNA assays were used to confirm the sequencing results. The functional roles of microRNAs, were validated in an in vitro system of primary cultures of human CCs.

Results

Deep sequencing of small RNAs yielded more than one million raw reads. We identified known microRNAs that were abundant in MII oocytes (MIR100 and MIR10A) or CCs (MIR29a, MIR30d, and the LET7 family). Predicted target genes of the oocyte miRNAs were associated with regulation of transcription

and cell cycle, whereas, genes targeted by CC miRNAs were involved in extracellular matrix and apoptosis. Comparison of the predicted miRNA target genes and mRNA microarray data resulted in a list of 224 target genes that were differentially expressed in MII oocytes and CCs, including CTGF (fold: 38, $p<0.0001$) and BMPR1B (fold: 15.4, $p<0.0001$) that are important for cumulus-oocyte communication.

Conclusion

This study provides the first characterization of the microRNA profile in human CCs and mature MII oocytes.. These results might help improving our understanding of the roles of miRNAs in oocyte maturation. Moreover, many of the identified miRNAs might be used as a tools to monitor the oocyte health, viability and competence and consequently to improve IVF/ICSI outcome.