MicroRNAs: new candidates for the regulation of the human cumulus–oocyte complex

Abstract

STUDY QUESTION:

What is the expression pattern of microRNAs (miRNAs) in human cumulus–oocyte complexes (COCs)?

SUMMARY ANSWER:

Several miRNAs are enriched in cumulus cells (CCs) or oocytes, and are predicted to target genes involved in biological functions of the COC.

WHAT IS KNOWN ALREADY:

The transcriptional profiles of human MII oocytes and the surrounding CCs are known. However, very limited data are available about post-transcriptional regulators, such as miRNAs. This is the first study focussing on the identification and quantification of small RNAs, including miRNAs, in human oocytes and CCs using a deep-sequencing approach.

STUDY DESIGN, SIZE, DURATION:

MII oocytes and CCs were collected from women who underwent IVF.

PARTICIPANTS/MATERIALS, SETTING, METHODS:

Using the Illumina/deep-sequencing technology, we analyzed the small RNAome of pooled MII oocytes (n = 24) and CC samples (n = 20). The mRNA targets of CC and MII oocyte miRNAs were identified using *in silico* prediction algorithms. Using oligonucleotide microarrays, genome-wide gene expression was studied in oocytes (10 pools of 19 ± 3 oocytes/each) and 10 individual CC samples. TaqMan miRNA assays were used to

confirm the sequencing results in independent pools of MII oocytes (3 pools of 8 ± 3 oocytes/each) and CC samples (3 pools of 7 ± 3 CCs/each). The functional role of one miRNA, *MIR23a*, was assessed in primary cultures of human CCs.

MAIN RESULTS AND THE ROLE OF CHANCE:

Deep sequencing of small RNAs yielded more than 1 million raw reads. By mapping reads with a single location to the human genome, known miRNAs that were abundant in MII oocytes (*MIR184*, *MIR100* and *MIR10A*) or CCs (*MIR29a*, *MIR30d*, *MIR21*, *MIR93*, *MIR320a*, *MIR125a* and the *LET7* family) were identified. Predicted target genes of the oocyte miRNAs were associated with the 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 *PTGS2*, *CTGF* and *BMPR1B* that are important for cumulus–oocyte communication. Functional analysis using primary CC cultures revealed that *BCL2* and *CYP19A1* mRNA levels were decreased upon *MIR23a* overexpression.

LIMITATIONS, REASONS FOR CAUTION:

Only known miRNAs were investigated in the present study on COCs. Moreover, the source of the material is MII oocytes that failed to fertilize.

WIDER IMPLICATIONS OF THE FINDINGS:

The present findings suggest that miRNA could play a role in the regulation of the oocyte and CC crosstalk.

STUDY FUNDING/COMPETING INTEREST(S):

This work was partially supported by a grant from Ferring Pharmaceuticals. The authors of the study have no conflict of interest to report.

TRIAL REGISTRATION NUMBER:

Not applicable.