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TITLE

IDENTIFICATION OF MICRORNAS RELATED TO HUMAN MII OOCYTE IN REPRODUCTIVE AGING

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ABSTRACT

Context. Maternal RNAs represent an important store that oocytes accumulate during their growth, determine oocyte quality, and establish embryo features. In spite of the basic role of microRNAs (miRNAs) in the regulation of gene expression, few studies have analyzed their role in human oocytes and, to date, little is known on miRNA expression profile during reproductive aging.

Objective. To identify human oocyte miRNAs and demonstrate their altered regulation in aging: a condition reducing oocyte quality.

Methods. By using TaqMan Low Density Array technology, we explored the expression profile of 384 miRNAs from MII oocytes of women younger than 35 yr and older than 38 yr. Finally, we identified evolutionarily conserved miRNAs between humans and mice and their shared mRNA targets. We compared their expression profiles in old and young mice assessing, at the same time, the expression of miRNAs and mRNAs.

Patients. Oocytes were collected from healthy women who had undergone ICSI at the IVF Center in Cannizzaro Hospital, Catania, Italy, for male dependent primary infertility.

Results. We identified 128 miRNAs in human MII oocytes. Among them, 12 miRNAs displayed significant expression differences related to aging. Specifically, we found 3 miRNAs strongly downregulated, and 9 miRNAs upregulated in oocytes from older women. Linking 12 differentially expressed miRNAs to target genes and performing GO and pathway analysis, we demonstrated miRNA role in oocyte aging. Finally, we found the upregulation of miR-29a-3p, miR-203a-3p, and miR-494-3p, evolutionarily conserved miRNAs, also in aged mouse oocytes, and demonstrated that their overexpression is antithetically correlated with the downregulation of Dnmt3a, Dnmt3b, Pten and Tfam.

Conclusions. Altered regulation of human oocyte miRNAs may contribute to low oocyte quality in reproductive aging.

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