The miRNome landscape changes in human ovarian follicles in relation to aging

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MicroRNAs (miRNAs) are short non-coding RNAs involved in the control of gene expression in different species. miRNAs role has been characterized in ovarian follicles and recently Follicular Fluid (FF) exosomes have been identified. It is known that altered regulation of miRNA expression affects crucial pathways for follicle growth and oocyte maturation in reproductive diseases as PCOS and Endometriosis.

Objective. The aim of this study was to characterize the ovarian follicle miRNome to identify age-related alterations.

Methods. By using TaqMan Low Density Array technology, we analyzed the expression profile of 384 miRNAs from MII oocytes and FF exosomes and compared the profiles of women younger than 35 years and older than 38 years. The canonical comparative cycle threshold method was applied to perform relative quantification. Differentially expressed (DE) miRNAs were identified by SAM.

Patients. 30 FF samples and 12 MII oocytes were collected from healthy young and old women, who had undergone to ICSI, at an IVF Center in Catania (Italy), for male-dependent infertility.

Results. We identified 250 miRNAs in FF exosomes and 90 in MII oocytes. Among them, 70 miRNAs were detected in both samples, suggesting that at least 100 miRNAs are exclusively expressed in somatic ovary cells and released to FF as exosomal cargo. Additionally, miRNAs found in ovarian follicles are differentially regulated in women of advanced reproductive age: in particular, we detected about 50 miRNAs in FF and 10 miRNAs in oocytes, which showed highly significant differences related to aging.

Conclusions. Our data suggest that specific set of miRNAs are synthesized by somatic and germinal cells of ovarian follicles and that their level of expression is related to maternal age. Linking DE miRNAs to predicted target genes will allow to identify the pathways more affected by the aging process.