DIFFERENTIALLY EXPRESSED MIRNAS IN PREMATURE OVARIAN AGING (POA) PATIENTS AND THE INFLUENCE OF MIR-106A ON THE PROLIFERATION AND APOPTOSIS OF HUMAN GRANULOSA CELLS

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Objective: To detect the differentially expressed miRNAs in the serum and ovarian granulosa cells of premature ovarian aging (POA) patients and normal cycling women, and explore the influence of mir-106a miRNA on the proliferation and apoptosis of human granulosa cells.

Methods: An oligonucleotide microarray chip and bioinformatic methods were used to profile miRNA expressions in the serum and granulosa cells of POA patients and normal cycling women who undergoing in vitro fertilization-embryo transfer (IVF-ET). Quantitative real-time PCR was used to verify the differentially expressed miRNAs. The effect of mir-106a on granulosa cell proliferation and apoptosis was studied by Western blot, MTT assay and Hoechst 33258 staining.

Results: The microarray chip results demonstrated that 3 miRNAs (miR-3613-3p, let-7g and miR-222) were significantly upregulated and 5 miRNAs (miR-30e, miR-299-5p, miR-665, miR-365 and miR-106a) were downregulated in granulosa cells of POA patients; 11 miRNAs (miR-576-5p, miR-664, miR-2964a-5p, miR-4275, miR-520e, miR-3914, miR-636, miR-615-3p, miR-654-5p, miR-181d and miR-3184) were significantly upregulated and 11 miRNAs (miR-381, miR-129-3p, miR-3168, miR-106a, miR-330-5p, miR-20a, miR-4298, miR-483-5p, miR-206, miR-383 and miR-625) were downregulated in the serum of POA patients compared with normal cycling women. Mir-106a, which downregulated expression both in the serum and granulosa cells of POA patients compared to normal cycling women, was next confirmed by real-time RT-PCR. Both Gene Ontology analysis and pathway analysis suggested that many signaling pathways, including protein kinase B signaling cascade, mitogen-activated protein kinases signaling pathway, and others, were regulated by this group of differentially expressed miRNAs. Mir-106a inhibitor decreased proliferation of granulosa cells as compared to the control group. Phospho-ASK1 was significantly upregulated and PCNA was significantly downregulated in the granulosa cells of miR-106a inhibitor group as compared to the negative control group (p<0.05)

Conclusions: Mir-106a was differentially expressed in the serum and granulosa cells of POA patients compared to normal cycling women. This miRNAs may play an important role in regulating the proliferation of ovarian granulosa cells, and it may be associated with ovarian aging.