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P-530 tRNA fragments in follicle fluid can be explored in Diminished Ovarian Reserve patients as a marker of IVF outcomes

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Study question: Can tRNA fragments in follicle fluid be explored for markers that predict blastocyst formation in patients with diminished ovarian reserve?

Summary answer: tRNA-Ser-CGA-4 is up-regulated in the follicle fluid of patients with diminished ovarian reserve (DOR).

What is known already: tRNA fragments are a novel class of small non-coding RNAs that have been shown to play regulatory roles in reproductive biology.

Study design, size, duration: Non-Randomized case control study in patients presenting for IVF treatment at a University affiliated fertility clinic from September 2020- January 2021. Thirty three patients were included: 15 patients with DOR and 18 controls.

Participants/materials, setting, methods: Patients were stimulated by appropriate protocols according to their age, diagnosis and AMH.

At retrieval, non-bloody follicle fluid (FF) was retrieved for after removing the cumulus-oophorus complex. FF was centrifuged at 1600 g x 10 mins and filtered with 80 nm filter for analysis.

(1) Ultracentrifugation and negative staining to confirm the presence of exosomes
(2) Small RNA extraction using commercially available kit
(3) Next generation sequencing of 50 ng of extracted small RNA after library building

Main results and the role of chance: There were no differences between the two groups with respect to age, BMI and duration of infertility. The mean age was 35.1 years.

As anticipated, the mean AMH, antral follicle count and number of eggs retrieved were statistically lower in the DOR groups compared with controls (<0.05).

The fertilization rate was 61.2% in DOR vs 79.5% in controls

The blastocyst rate was 39.5% in DOR patients and 50.6% in controls

Total RNA yield was lower in DOR patients, as 50% of the DOR samples had undetectable levels (p < 0.001).

Samples were predominantly processed in duplicate. Input into the pipeline was paired end data which showed an overall tRNA fragment count that was higher in the DOR population. Log2FC showed an up-regulation of the tRNA fragments tRNA-Ser-CGA-4, tRNA-Cys-GCA-15, tRNA-Cys-GCA-10 and tRNA-Cys-GCA-19 in the DOR population.

Limitations, reasons for caution: Undetectable levels in follicle fluid of some of the DOR patients introduced selection bias

Larger sample size and broader applicability across various ethnic groups.
Wider implications of the findings: Follicle fluid can be explored to give insight into the signaling pathways of ovarian biology.
Non-invasive method of assessing oocyte competence
Useful in explaining the pathophysiology of DOR
Can these findings assist in the identification of therapeutic targets to delay the progression of age related/non-age related DOR?

Trial registration number: not applicable