

Determining the optimal daily gonadotropin dose to maximize the oocyte yield in elective egg freezing cycles Raoul Orvieto, Anouk Savir Kadmon, Nira Morag, Aliza Segev-Zahav, Ravit Nahum Chaim Sheba Medical Center (Tel Hashomer), Ramat Gan, Israel and Faculty of Medical and Health Science, Tel Aviv University, Tel Aviv, Israel.

Objective: Ovarian stimulation (OS) with high daily gonadotropin doses are commonly offered to patients attempting social/elective egg freezing. However, the optimal daily gonadotropin dose that would allow a higher oocyte yield in the successive IVF cycle attempt was not settled and should be determined. **Patients and Methods:** Data from all women admitted to our IVF unit for social/EEF, who underwent two consecutive IVF cycle attempts, with only those who used in the first attempt a starting daily gonadotropin dose of 300IU were analyzed. Patients characteristics and OS variables were used in an attempt to build a logistic model, helping in determining the daily gonadotropin dose that should be offered to patient during their second EEF attempt, aiming to further increase their oocyte yield. **Results:** Three hundred and thirteen consecutive women undergoing two successive IVF cycle attempts were evaluated. Using logistic regression model, two equations were developed using individual patient-level data that determine the daily

gonadotropin dose needed aiming to increase the oocyte yield in the successive cycle. (a):X=-0.514+2.87*A1+1.733*A2 - 0.194* (E2/1000) and (b): P = EXP(X) / [1+EXP(X)].

Conclusions: Using the aforementioned equations succeeded in determining the daily gonadotropin dose that might result in increasing oocyte yield, with an AUC of 0.85. Any additional oocyte retrieved to these EEF patients might get them closer to fulfil their desire to parenthood.



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| 6 | 6 The # of oocytes retrieved in the 1st IVF attempt should be placed in the red square, | | | | | | | | | | | |
| 7 | 7 while the peak E2 level in the 1st IVF cycle attempt should be placed in the blue square | | | | | | | | | | | |
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הכינוס השנתי ה-67 של **האגודה הישראלית לחקר הפוריות (איל״ה)** 12 במאי 2025, מלון דיוויד אינטרקונטיננטל, תל אביב



Impact of Aging on Gene Expression in Human Oocytes: A Comparative Analysis of Young and Older Patients- Preliminary Results. Raoul Orvieto, Omri Nayshool, Louisa Cohen, Yuval Yung, Adva Aizer, Efrat Glick Saar, Dan Dominissini.

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Background and objective: Aging affects gene expression in pathways essential for energy metabolism, DNA repair, cell cycle regulation, and antioxidant defenses, directly affecting oocyte quality and viability. Single-cell RNA deep sequencing studies of aged versus young human MII oocytes revealed many differentially expressed genes. In addition, single human oocyte transcriptome analysis at both germinal vesicle (GV) and MII stages revealed distinct stage-dependent pathways impacted by aging, with a decrease in mitochondrial-related transcripts from GV to MII oocytes, and a much greater reduction in MII oocytes with advanced age. Our aim was to investigate the age-related differences in gene expression of germinal vesicle (GV) oocytes between young and advanced age patients. Material and methods: Immature GV oocytes were donated by 6 patients, divided into two age groups: The "Young" group (ages 16-29) had three participants (mean age: 23.3 ± 6.6 years), and the "Elderly" group (ages 38-40) included three participants (mean age: 39 ± 1 year). After retrieval, oocytes were denuded and donated GV oocytes were cryopreserved at -196^{0C} until analysis. For library preparation, we used the NEBNext® Single Cell/Low Input RNA Library Prep Kit for Illumina, section 1 (cat no. E6420S, New England Biolabs (NEB), USA), strictly adhering to the manufacturer's instructions. All samples were processed in a single batch to control for technical variation. The NEBNext® RNA Library Prep Kit allows conversion of mRNA to barcoded cDNA for Illumina sequencing. RNA sequencing data underwent rigorous quality control and processing through a multi-step pipeline. Gene expression quantification was performed using feature Counts from the Subread package (v1.5.3), and comprehensive quality control reports were generated using MultiQC (v1.25.1). Results: Of top 10 significantly differently expressed genes 7 (LINC02087, POMZP3, LINC02749, MYL4, AGPAT2,

GCA, and LIMK1) were downregulated and 3 (CLEC3A, ARPP21, and CITED2) showed significant upregulation in young versus old oocytes. These genes underscore the impact of aging on critical oocyte pathways, including chromosomal stability, epigenetic regulation, mitochondrial function, immune response, structural integrity, and calcium signaling Moreover, among these genes, LINC02087 was the most downregulated (log2FC = -7.66), while CITED2 showed the strongest upregulation (log2FC = 3.43) in young versus old oocytes. **Conclusions:** Understanding the effects of aging on the oocyte transcriptome could identify biomarkers that characterize good MII oocyte quality. The different genes expressions in aged oocytes highlight their potential contributions to oocyte quality and development. Moreover, by elucidating age-related changes across diverse cellular functions, this study opens avenues for therapeutic interventions aimed at extending reproductive longevity and optimizing outcomes in assisted reproductive technologies.



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| ew_sample_name | group | LINC02087 | CLEC3A | POMZP3 | LINC02749 | MYL4 | AGPAT2 | GCA | ARPP21 | LIMK1 | CITED2 |
|----------------|--------------|-----------|--------|--------|-----------|------|--------|------|--------|-------|--------|
| Oocyte_Age_39 | Old_Oocyte | 19.2 | 9.5 | 150.9 | 189.3 | 32.4 | 23.8 | 30.0 | 0.6 | 6.0 | 1.0 |
| Oocyte_Age_38 | Old_Oocyte | 14.6 | 4.2 | 196.3 | 223.1 | 36.0 | 22.1 | 27.9 | 1.0 | 9.7 | 0.7 |
| Docyte_Age_40 | Old_Oocyte | 9.0 | 6.8 | 124.4 | 178.1 | 26.2 | 39.4 | 40.9 | 0.8 | 9.7 | 0.4 |
| Oocyte_Age_25 | Young_Oocyte | 0.0 | 35.7 | 33.7 | 51.3 | 8.1 | 10.1 | 15.1 | 2.8 | 2.2 | 9.4 |
| Ocyte_Age_29 | Young_Oocyte | 0.2 | 58.6 | 25.8 | 78.0 | 6.6 | 5.6 | 10.1 | 13.2 | 2.8 | 9.5 |
| Oocyte_Age_16 | Young_Oocyte | 0.0 | 46.0 | 55.6 | 41.7 | 1.5 | 4.6 | 10.5 | 1.9 | 2.7 | 1.4 |



Volcano plot of differential gene expression between young and old oocyte