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CUMULUS CELLS HAVE LONGER TELOMERES THAN LEUKOCYTES IN REPRODUCTIVE AGE WOMEN.

E. E. Lara Molina,^a J. M. Franasiak,^b D. Marin,^c X. Tao,^d P. Diaz-Gimeno,^e M. Florensa,^a M. Martin,^a E. Seli,^{f,g} A. Pellicer.^h ^aIVI RMA, Barcelona, Spain; ^bIVI RMA New Jersey, Basking Ridge, NJ; ^cResearch, IVI RMA New Jersey, Basking Ridge, NJ; ^dThe Foundation for Embryonic Competence, Basking Ridge, NJ; ^eIVI RMA Fundaci_ on IVI, Valencia, Spain; ^fYale School of Medicine, New Haven, CT; ^gIVI RMA New Jersey, Basking Road, NJ; ^hIVI RMA, Rome, Italy.

OBJECTIVE: Given that progressive shortening of telomeres has been linked with reproductive aging, we aimed to determine if telomere length (TL) in granulosa cells (GC) and cumulus cells (CC) are correlated with TL in leukocytes (L), so that TL measurements in blood could become useful indicators of follicular biology. **DESIGN:** Prospective, non-interventional study.

MATERIALS AND METHODS: Thirty-five egg donors were included in the study. Following controlled ovarian hyperstimulation using an antagonist protocol with standard doses of subcutaneous FSH, oocytes retrieval was done 36 hours after a bolus of GnRH agonist. CC were obtained after oocyte stripping, and GC were isolated from the pooled follicular fluid using a density gradient method. Genomic DNA (gDNA) from L, CC and GC from all donors was isolated for TL measurements. Relative TL was obtained using a SYBR green quantitative real-time PCR protocol. A Taqman assay for the multicopy gene Alu was used for normalization of measurements. Association between TL in L, CC and GC was primarily investigated and paired comparisons were performed. Age, smoking, confirmed fertility, anti-Müllerian hormone (AMH), antral follicular count (AFC) and number of mature oocytes were also analyzed against TL data. Paired t-tests and Pearson correlation coefficients were computed for TL comparisons and to determine associations between the TL and the aforementioned variables, respectively.

RESULTS: Mean age of subjects was 25.43_4.57 years, AMH levels were 1.90_0.92 ng/ml, AFC 23.29_5.11 and number of mature oocytes 23.29_9.13. No significant association between these variables, or confirmed fertility, and TL of GC, CC, or L was found. In addition, no correlation was observed between TL measurements of L vs CC ($p=0.924$), L vs GC ($p=0.154$) or between CC vs GC ($p=0.512$). Interestingly, TL of CC was significantly higher compared to L (1.54 fold, $p<0.0001$), while no significant differences were found between TL of GC vs CC ($p=0.120$), or GC vs L ($p=0.114$).

CONCLUSIONS: Cumulus cells from mature follicles have significantly longer telomeres than leukocytes, suggesting that the follicular environment could possess different and perhaps more effective mechanisms to cope against telomere shortening and therefore cellular aging than other somatic tissues. Further, these data do not support the utility of

telomere DNA measuring in blood to estimate TL in follicular cells as an indicator of ovarian aging. Supported by: IVI RMA Fundaci_ on IVI.