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THE TELOMERE LENGTH OF LEUKOCYTES AND CUMULUS CELLS ARE NOT DIFFERENT BETWEEN POOR RESPONDERS AND GOOD RESPONDERS TO CONTROLLED OVARIAN HYPERSTIMULATION FOR IVF.

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OBJECTIVE: Decreasing telomere length (TL) has been proposed as a mechanism to explain reproductive aging. Indeed, leukocyte telomere length (LTL) has been correlated with the duration of the reproductive lifespan from menarche to menopause. Furthermore, cumulus cell telomere length (CCTL) has been proposed as a biomarker for oocyte and embryo quality in ART cycles. However, there are no current studies that analyze the relationship between TL and response to controlled ovarian stimulation in an IVF cycle. In this study, we aimed to determine: 1) whether patients with abnormal response to stimulation exhibited different LTL or CCTL compared to patients with age appropriate response, and 2) whether TL differed between leukocytes and cumulus cells from the same patient.

DESIGN: Prospective Cohort

MATERIALS AND METHODS: Patients in one of the following four categories were recruited for inclusion: Group A) <35 yo with good response (>15 follicles measuring 15mm [mature foll] on day of trigger), Group B) <35 yo with poor response (<5 mature foll), Group C) >40 yo with poor response (<4 mature foll), and Group D) >40 yo with good response (>12 mature foll). Blood and CC were collected at time of oocyte retrieval and genomic DNA was isolated and stored at -80 C. Telomere DNA quantity was measured by a quantitative real time PCR method. The AluYa5 gene was targeted as endogenous control in all samples. CCTL and LTL comparisons were made between good and poor responders in each age group (Group A vs. B and C vs. D, respectively). CCTL was also compared to LTL in all age groups. Analysis was performed via T-tests and Wilcoxon- Mann-Whitney tests where appropriate.

RESULTS: A total of 77 patients enrolled in the study. All patients had sufficient quantities of leukocyte DNA for analysis. Fourteen of the pooled cumulus samples were unable to be analyzed due to poor DNA yield. The CCTL and LTL were no different between patients with good response to stimulation and patients with poor response to stimulation in both the <35 year old group (CC Fold Change: 0.86 +/- 0.35, p ¼ 0.22, L Fold Change: 0.88, +/- 0.3 p ¼ 0.14) and >40 year old group (CC Fold Change: 1.03 +/- 0.21, p ¼ 0.1385, L Fold Change: 1.01 +/- 0.32, p ¼ 0.94). In the 66 patients with evaluable samples in each sample type, telomeres were significantly longer in CC than leukocytes in white blood cells, with a mean 2.16 fold change (+/-0.2, p < 0.0001).

CONCLUSIONS: Neither CC or leukocyte telomere length is correlated with response to ovarian stimulation. While telomeres may play a role in the reproductive aging process, CCTL and TL do not appear to influence the pool of gonadotropin responsive follicles in an ART cycle. Interestingly, CC appear to feature longer telomeres than leukocytes. This is consistent with findings from prior findings by our group that the methylation profile of CC is younger than chronologic age would predict in other somatic cells. References: 1. Cheng EH, Chen SU et al. Evaluation of telomere length in cumulus cells as a potential biomarker of oocyte and embryo quality. Hum Reprod 2013; 28(4):929-936. Supported by: Foundation for Embryonic Competence FERTILITY & STERILITY_ e327 OVARIAN STIMULATION