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CYTOPLASM REPLACEMENT BY SPINDLE TRANSFER DEMONSTRATES ENHANCED EMBRYO DEVELOPMENT WITHOUT COMPROMISING EUPLOIDY RATES: PRE-CLINICAL STUDY WITH DONOR OOCYTES.

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OBJECTIVE: The aim of this study was to validate the Spindle Transfer (ST) technique in human donor oocytes and explore its feasibility for clinical application in the treatment of infertility associated with poor oocyte quality.

DESIGN: Experiments were licensed by the Greek National Authority of Assisted Reproduction and approved by the IRB of IASO Maternity Hospital. Informed consent was obtained from the 20 donors participating in the study. We first aimed to compare the efficiency of two fusion protocols. In a second TABLE 1. Clinical outcome comparison of the two TE biopsy protocols. TE biopsy performed with day 3 pre-hatching (protocol 1) TE biopsy performed without day 3 pre-hatching (protocol 2) P values N_ FET Cycles 835 835 N_ ET 834 834 Age 38.1_6.2 38.3 _6.6 0.46 N_ of embryos thawed 1.4_0.6 1.3_0.5 0.0003 Survival rate after thawing (SR) 95.1% 99.2% <0.001 N_ of embryos transferred 1.3_0.5 1.3_0.5 Clinical pregnancy rate (CPR) 55.1% 65.3% <0.0001 Implantation rate (IR) 46.8% 58.4% <0.0001 Abortion rate (AR) 9.6% 11.7% 0.31 TABLE 1. PGTA- Vit n¼469 Vit n¼1008 Adjusted RR (95% CI)* TBR n¼21 Adjusted RR (95% CI)* Biochemical pregnancy 39 (8.3) 107 (10.6) p¼0.17 1.3 (0.95-1.9) 3 (14.3) p¼0.41 1.6 (0.43-6.0) Clinical pregnancy 315 (67.2) 600 (59.5) p¼0.005 0.87 (0.80-0.95) 8 (38.1) p¼0.006 0.48 (0.23-0.98) Miscarriage 37 (11.7) 111 (18.5) p¼0.008 1.7 (1.2-2.5) 3 (37.5) p¼0.06 1.8 (0.31-11.0) Data presented as n(%) P values compare group PGT-A-Vit to group Vit and group TBR *Adjusted for age, number of embryos retrieved, embryo quality e88 ASRM Abstracts Vol. 110, No. 4, Supplement, September 2018 set of experiments, we evaluated an optimized protocol using donor fresh or vitrified oocytes with different morphological/developmental characteristics.

MATERIALS AND METHODS: Micromanipulation was performed on an inverted microscope (Olympus-IX73) equipped with polarized light. Karyoplastcytoplast fusion was induced by exposure of the reconstructed oocytes to either a chemical solution or an inactivated protein extract (HVJ-E). The same donor's sperm sample was used in all experiments. Embryos underwent continuous culture (Embryoscope+, Vitrolife) in singlemedium(LifeGlobal) and were biopsied for assessing aneuploidy

andmitochondrialDNA(mtDNA) carryover. Statistical significance was assessed by Students t-test or Fisher's exact test.

RESULTS: We initially compared two fusion protocols using 63 MII donor oocytes. HVJ-E-mediated fusion rates were significantly higher (98.1%) than those obtained in the chemical method (76.8%, $p<0.01$), while fertilization and blastocyst formation rates were similar ($p>0.05$) between the control (70.2%-78.7%), HVJ-E (75.5%-76.3%) and chemical-fusion (60.5%-60.2%) groups. In the second set of experiments, ST was performed in 118 donor oocytes. Overall, results varied greatly depending on the quality of the recipient cytoplasm. When spindles were transferred from in vitro matured or morphologically ''abnormal'' oocytes into good quality cytoplasts, individual cohorts showed fertilization (66.7%-71.4%) and blastocyst rates (75.0%-60.0%) significantly improved ($p<0.05$) compared to nonmanipulated controls (50.0%-33.3% and 0.0%-0.0%, respectively) or reciprocally reconstructed (25.0%-0.0% and 37.5%-33.3%, respectively) oocytes. From a total of 36 blastocysts analysed, aneuploidy rates were statistically equivalent (p¼0.53) between controls (41.2%, n¼17) and ST (52.6%, n¼19) embryos. mtDNA carryover levels were estimated to be <1%.

CONCLUSIONS: This study shows that cytoplasm replacement by ST can enhance the potential of developmentally compromised oocytes to develop up to the blastocyst stage without compromising euploidy rates. This opens up the possibility of providing new treatment options for patients with certain forms of infertility refractory to current clinical strategies. Supported by: This study was financially supported by the Institute of Life (Athens, Greece).