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Bench to Bedside: Oncofertility Advances in Males and Females

Welcome to the 8th Annual Meeting

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Poster 32

Androgens Promote the Development of Nonhuman Primate Preantral Follicles Cultured Individually in a Three-Dimensional (3D) Matrix

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Objectives: To evaluate the role of androgens in the development of secondary follicles of nonhuman primates (*Macaca mulatta*) in a 3D matrix.

Methods: The ovarian cortex (n=8 adult females) was cut into 1mmx1mmx1mm cubes, secondary follicles were isolated and cultured for 5 weeks in 0.25% (w/v) alginate. Experiment 1: Testosterone replacement. Follicles (n=4 animals) were divided into groups: Control (vehicle), TRL (3β-hydroxysteroid dehydrogenase inhibitor), T Low (TRL + 20 ng/mL testosterone), T High (TRL + 50 ng/mL testosterone); Experiment 2: Dihydrotestosterone (DHT) replacement. Follicles (n=4 animals) were divided into groups: Control (vehicle), TRL, DHT (50 ng/mL), TRL + DHT. Endpoints analyzed: follicle survival, growth, antrum formation, steroid hormone production, and oocyte maturation and viability.

Results: The percentage of survival, growth (diameters at week 5 of culture) and antrum formation were lower in the presence of TRL in both experiments, compared with controls. Estradiol and progesterone levels were higher in controls than TRL. Replacement with T and DHT in the presence of TRL, restored follicle survival, growth and antrum formation rates. Estradiol and progesterone had levels comparable to controls in T Low group. However in T High group, estradiol levels were higher than control and T Low groups, and progesterone levels were lower than controls, indicating a dose-dependent increase in estradiol and decrease in progesterone levels by T. DHT groups had lower levels of estradiol than control. DHT alone group had higher levels of progesterone than control and DHT + TRL groups. Both T and DHT replacement reduced AMH levels. Oocyte viability was improved with T and DHT treatment alone and with TRL. Mature oocytes were obtained only in the T High, DHT + TRL and control groups.

Conclusions: This study provides *in vitro* evidence of a role for androgens in preantral follicular development in primates. Due to the dose-dependent effect on estradiol levels by T, we cannot rule out that T actions were partially due to its conversion to estrogen. However, the effects of T exposure appear due primarily to androgen action because both T and DHT restored follicle survival, growth, antrum formation, and oocyte viability, plus reduced AMH production, of preantral follicles cultured in a steroid-depleted milieu and 3D alginate matrix. Continuing studies on the requirements of steroid hormones for preantral follicular development in primates, should lead to further improvements in this *in vitro* technique that can be used as an alternative for female cancer patients who wish to preserve their fertility. Supported by The Oncofertility Consortium (UL1DE019587, RL1HD058294, PL1EB008542), the SCCPIR (U54HD071836), BIRCWH (2K12HDO43488) and ONPRC (P51OD011092).