Renata S. Magalhaes
MD
WFIRM
Graduate School, PhD in Integrative Physiology and Pharmacology Program, Year-5

Preclinical pilot study using an autologous bioengineered uterine implant in female baboons: preliminary results

Renata S. Magalhaes, J. Koudy Williams, Shannon Lankford, Douglas E. Shankle, James Yoo, and Anthony Atala.

Introduction: The uterus supports complex biological functions needed for a viable live birth. Despite advancements in assisted reproductive technologies, uterine-factor infertility remains unresolved. Bioengineered functional uterine tissue would potentially benefit women with a malformed or dysfunctional uterus. Our previous studies in rabbits demonstrated that an autologous bioengineered uterine implant formed uterine tissue-like structures (endometrium with epithelial glands and two-layered myometrium) within 6 months after implantation, which supported fetal development and live birth after natural mating. In this preclinical pilot study, we tested the feasibility of bioengineering uterine tissue in NHP, aiming to translate this technology to a clinical setting. We utilized female baboons due to the relatively large size of their uterus and similar anatomy and reproductive physiology to humans.

Methods: Two adult female baboons (*Papio anubis*) were used to test the feasibility of a bioengineered autologous uterine implant for uterine tissue reconstitution applications. Animals had a 1 x 1 cm full-thickness resection of the anterior uterine wall via laparotomy for primary endometrial and myometrial cell isolation and expansion. In vitro cultured uterine cells were seeded onto a 2 x 2cm PGA/PLGA-coated scaffold and incubated for 8 days. At 4-5 weeks post uterine biopsy, an autologous cell-seeded implant was used to reconstruct a full-thickness excised portion of the anterior uterine wall.

Main Outcomes Measures: Uterine morphology and menstrual cycle patterns were assessed at baseline and followed the uterine construct implantation at different time points. Animals were monitored using ultrasound, MRI/CT, and hysterosalpingograms performed every 4 to 6 weeks. The endpoint will be 12 months after uterine reconstruction procedure.

Preliminary Results: To date, both animals recovered well from the surgical procedures. Uterine primary cells were isolated in vitro and expanded successfully. At 9 weeks after surgery, animal menstrual cycle patterns were restored. At 14 weeks after implantation, we observed radiologic evidence of complete resorption of the scaffold material, restoration of the uterine cavity lining, thinning of the uterine wall, and wedge-shaped retraction at the implantation site.

Supported by: *R&D State of North Carolina grant and NIH T32 NIBIB Grant #1T32EB014836-01A1*