



Comprehensive Research Experience for Medical Students
Summer Research Program 2019

Supervisor/Project Information Form

Due February 20 2019 by email to crems.programs@utoronto.ca

Supervisor Name:
Dr. Ellen Greenblatt

Project Title:
Blastocyst mitochondrial DNA copy number as marker for reproductive outcome\

Hospital/Research Institution:
Mount Sinai Hospital

Email:
Ellen.Greenblatt@sinaihealthsystem.ca

Field of Research (2 keywords):
Reproduction
Embryology

Department:
Obstetrics and Gynecology

School of Graduate Studies Appointment (IMS, LMP, IHPME etc)? Yes/No:No If
YES, please name:

Project Title: Blastocyst mMitochondrial DNA copy number as marker for reproductive
outcome

Brief Project Description (<300 words):

The field of assisted reproductive technologies (ART) has been in continuous evolution
for decades. Assisted reproduction has undergone continuous evolution since the 1978
birth of Louise Brown, the first IVF conceived liveborn infant. Despite ongoing research,

the chance of a single embryo resulting in a viable infant has not exceeded 60%. ~~One~~ A particular research focus has been on predictors of pregnancy and of treatment success identifying which embryo from several produced in a single IVF cycle is most likely to lead to a livebirth. One recent development is the application of pre-implantation genetic testing for aneuploidy (PGT-A) which has demonstrated that many embryos that look morphologically normal are aneuploid with limited potential to continue to birth. Although PGT identifies embryos most likely to implant, transfer of a PGT screened euploid embryo still only achieves success in 60-70% of cycles.

~~One particular focus has been on predictors of pregnancy and of treatment success.~~ Embryo mitochondrial DNA (mtDNA) content has been identified as one possible biomarker ~~of success and~~ of embryo competence that may be a reflection of embryo energy supply. ~~Still, limited knowledge of this exists and there~~ Despite several publications, is quite a bit of controversy in the controversy persists regarding the association between blastocyst mtDNA copy number, methods of measurement and reproductive outcomes.

~~In this research project~~ With this project, we ~~are seeking to~~ will evaluate the association ~~of between blastocyst~~ mtDNA content ~~with and~~ reproductive success by ~~by~~ using ~~studying~~ embryos previously biopsied for ~~preimplantation genetic testing (PGT).~~ PGT-A We ~~will also look~~ will to examine how reproducible is the ~~our~~ assessment of mtDNA content really is using our current methodologies ~~by~~ repeating performing ~~repeat biopsies biopsy in of abnormal, previously PGT-A screened donated human research~~ embryos donated for research.

The study will be conducted in conjunction with ~~the~~ Mount Sinai Fertility and Mount Sinai's Division of Diagnostic Medical Genetics.

Part one will involve ~~an examination of a retrospective analysis data from of data from~~ chromosomally normal (euploid) embryos that have already undergone PGT A and been transferred to the patient. ~~The measure of mitochondrial~~ Mitochondrial DNA (Mitoscore) was previously determined for each ~~such~~ embryo but not reported or used clinically. ~~Subsequent to testing, only normal (euploid) embryos were transferred back into the uterus. These are the cases being considered for this part of the study.~~ All Mitoscores will be extracted, from the database and matched ~~up~~ to the specific embryo and corresponding patient IVF ~~cycle details, reproductive outcomes, and corresponding embryological data~~ cycle outcomes. This data will then be analyzed to ~~gauge evaluate~~ the association between Mitoscore and reproductive success within our own clinic.

Part two will involve confirming the reproducibility and validity of the mitochondrial DNA quantity assessment. We will do this by repeating multiple biopsies on abnormal (aneuploidy) embryos, donated for research, by thawing and re-biopsying these embryos ~~at from~~ several different cell sites.

If ~~a true connection is noted between~~ a significant connection is found between mtDNA content and reproductive outcomes, that is shown to be stable across multiple biopsies, ~~we will~~ this will help optimize embryo selection-prioritization techniques in ART for transfer in ART, potentially improve pregnancy rates in the infertility patient, and gain further insight into the importance of mtDNA overall in the context of reproductive biology.