Comprehensive Research Experience for Medical Students
Summer Research Program 2021
Supervisor/Project Information Form

Due February 24, 2021 by email to crems.programs@utoronto.ca

Supervisor Name:
Dr. Clifford Librach and Dr. Mahmoud Aarabi (Co-Supervisors)

Project Title:
Functional Characterization of the Variants of Uncertain Significance in Patients Undergoing Cancer Genomic Testing

Hospital/Research Institution:
Dr. Librach: CReATe Fertility Centre
Dr. Aarabi: North York General Hospital

Email:
Dr. Librach: drlibrach@createivf.com
Dr. Aarabi: Mahmoud.Aarabi@utoronto.ca

Field of Research (2 keywords):
Cancer Genetics; RNA Sequencing

Department:
Dr. Librach: Obstetrics and Gynecology, University of Toronto
Dr. Aarabi: Laboratory Medicine and Pathobiology, University of Toronto

School of Graduate Studies Appointment (IMS, LMP, IHPME etc)?
Dr. Librach: Department of Physiology and Institute of Medical Sciences (IMS)
Dr. Aarabi: No
Brief Project Description (<300 words):

Rapid development of next generation sequencing (NGS) has revolutionized the diagnosis of hereditary cancer syndromes. Patients with clinically-actionable mutations are followed up by a personalized clinical surveillance program, and their at-risk family members get tested for early detection and prevention. However, individuals carrying variants of uncertain clinical significance (VUS) may not qualify for such procedures due to the absence of sufficient functional and population data. As a result, a large group of individuals with VUS finding (30-40% of all tested) may not benefit from cancer genomic testing. This study aims to address this issue by investigating the functional impact of genetic variants detected in cancer patients.

In this collaborative study, we aim to assess the genetic variants of uncertain significance (VUS) detected in patients tested by the hereditary breast/ovarian cancer NGS panel at the North York General Hospital. We will particularly focus on a selected group of variants that are predicted by in silico tools (computer-based) to affect the normal splicing of mRNA, the product of genomic DNA. RNA-Seq will be performed on the peripheral blood samples to quantify the mRNA levels of specific genes affected in each patient. An initial Research Ethics Board approval has been obtained and the final approval is expected very soon. The functional data provided by this study is required, along with the population and segregation data, for a possible change of classification and, thus, for a personalized surveillance of cancer patients and their at-risk families. The impact of this study extends beyond the individual patients and helps cancer patients with similar variants everywhere. Selected students will work with a multidisciplinary group of clinicians, laboratory geneticists and genetic counsellors. They will be involved in data analysis and manuscript preparation, as well as in the laboratory procedures if permitted based on the pandemic situation.