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. Katarzyna Jerzak

Project Title: Exploring novel therapeutic targets for patients with breast cancer brain metastases: A retrospective cohort study

Hospital/Research Institution: Sunnybrook Research Institute

Email: Katarzyna.jerzak@sunnybrook.ca

Field of Research (2 keywords): Breast cancer; retrospective database

Department: Medicine

School of Graduate Studies Appointment (IMS, LMP, IHPME etc)? Yes/No:
If YES, please name: I have applied to be an Associate Member of the IMS; my application will be reviewed in May 2019.

Project Title: Exploring novel therapeutic targets for patients with breast cancer brain metastases: A retrospective cohort study

Brief Project Description (<300 words):

The survival of women with metastatic breast cancer has increased over time, largely due to the development of more effective systemic therapies; unfortunately, most systemic therapies do not penetrate the central nervous system (CNS) and women are now living longer to experience the spread of their cancer to the brain. Despite the availability of various local therapies, including surgery and radiotherapy, the prognosis of women with breast cancer brain metastases remains very poor. Novel systemic therapies that can cross the blood brain barrier, and ideally target proteins that are over-expressed in brain metastases tissue are urgently required.

The main goal of this study is to identify potentially "targetable" proteins and genomic markers that are expressed in the tissue of patients' brain metastases. A retrospective cohort of patients (n=334) who required surgical resection of breast cancer brain metastases at Sunnybrook Health Sciences between January 2010 and December 2018 will be used for this purpose. Protein markers of interest will be evaluated via immunohistochemistry, including the PD-L1 receptor (a

marker of response to immunotherapy) and the androgen receptor (AR) because both immunotherapy and anti-androgen therapies are known be active in the CNS. In addition, whole exome sequencing of both the brain metastases and matched primary breast tumors will be performed in collaboration with Dr. Priscilla Brastianos at Harvard University to explore potential pathways that may lead to the development of brain metastases.

The proportion of patients whose breast cancer brain metastases express PD-L1 (as defined using a validated biomarker of response to Atezolizumab) and the AR (Allred score 1+) will be described. In addition, results of whole exome sequencing will be analyzed and compared to the primary breast tumor as per previously published methods. REB approval for this study has already been obtained at the Sunnybrook Research Institute.