



RESEARCH SCHOLAR PROGRAM – 2018

SUPERVISOR & PROJECT INFORMATION FORM

Please complete and return, via email only (crems.programs@utoronto.ca) by **November 3rd 2017** (forms received after this date will not be posted).

Supervisor Information

Name: Dr. Romina Mizrahi Email: romina.mizrahi@camh.ca

Degree: MD PhD SGS Appointment (IMS, IHPME, LMP etc.): IMS

Academic Rank: Full professor at Institute of Medical Science

Field of Research: Early Psychosis and Clinical High Risk, Brain Imaging

Research Institution Affiliation (if applicable): Institute of Medical Science, Department of Psychiatry, Department of Pharmacology and Toxicology, Department of Clinical Psychology at UofT Scarborough.

Allocation of student contact time (number of hours per week YOU are available to the student for any concerns or to review progress):

Available on Friday during meetings for in person meeting and over email and phone (2 hours)

Project Information

Title:

Analysis of Peripheral Endocannabinoid and Immune System Regulation in Clinical High Risk for Psychosis and First Episode Psychosis

Description (max 500 words):

It is increasingly recognized that cannabinoid signaling may play a role in psychosis. Epidemiological studies have detected a twofold increase in the incidence of SCZ with early cannabis use, identifying it as a major trigger for the disease and thus providing the first link between cannabinoids and SCZ. The most studied of endocannabinoids (eCBs), anandamide (AEA), acts on the presynaptic CB1 receptors to modulate the release of neurotransmitters. Dramatic elevations of AEA were detected in cerebrospinal fluid of patients with SCZ in the midst of a psychotic episode, which normalize after psychosis resolution. Levels of AEA in the brain are tightly regulated through hydrolysis by the fatty acid amide hydrolase (FAAH) enzyme. FAAH therefore sets the tone of the eCB system

This research will be the first exploration of changes in eCB signalling in a living brain evaluating for the first time AEA metabolism in psychosis. It may elucidate the neurochemical mechanism behind the role of cannabis in the onset of SCZ. This conceptual breakthrough would have significant impact on the field of psychosis, providing a new approach to treatment and prevention of SCZ.

Besides PET measurements and cognitive assessments blood samples are taken in order to evaluate possible changes in the peripheral endocannabinoid system. Extracted DNA will be used for methylation pattern and SNP analysis of genes related to the endocannabinoids. In addition mRNA levels of endocannabinoid related genes will be investigated. These additional analyses will further elucidate the importance of the endocannabinoid system in schizophrenia.

The endocannabinoid system also regulates and is regulated by the immune system. We are measuring peripheral markers of inflammation in blood with our collaborators with Dr. Ana Andreazza's lab. Dr. Andreazza is a Tier II Canada Research Chair in Molecular Pharmacology of Mood Disorders and holds a cross-appointment as Independent Scientist, at the CAMH and in Department of Pharmacology at University of Toronto as Associate Professor. In the periphery there is clear evidence of reciprocal endocannabinoid-cytokine regulation, however it is not known whether evidence of such a relationship would be observed in the brain. Dr. Andreazza is exploring the role of redox dysregulation (i.e. mitochondrial dysfunction and lipid oxidation) and inflammation in signaling white matter changes in major psychiatric disorders.

Significance:

We hope this study will provide novel treatment targets to treat and perhaps even delay or abort transition to schizophrenia in those at risk.

If human subjects are involved, have Ethics been obtained?

YES NO Application Submitted N/A

Do you expect this work will be published within the 20 months?

YES NO Uncertain

Student's roles and responsibilities (please be specific)

- The medical student will learn how to analyse brain images using in house CAMH RIC software ROMI in conjunction with SPM, fMOD using statistical analysis softwares (SPSS, Sigmaplot, SAS) to look for correlations, and to create graphs and figures to present findings.
- They will conduct neuroimaging research on people with clinical high risk for schizophrenia and first episode psychosis patients to gain further insight into the role of alterations in endocannabinoid metabolism in the pathogenesis of psychosis.
- They will independently read previous and current research papers to keep up to date with research relevant for our specific research topic
- They will assist in grant applications and research paper submission
Utilizing data collected from previous studies in Dr. Mizrahi's lab, specifically personality questionnaires (NEO-PI-R), cognitive behavioural batteries (Repeatable Battery for the Assessment of Neuropsychological Status) and peripheral markers in blood they will look into associations of cannabis use and psychosis

*Please indicate who will serve as the student's direct report (PI, PhD student, technician etc...) **PI***