

Department of Molecular and Cellular Biology  
**Graduate Seminar MCB\*6500**

Friday, Jan. 26, 2018 in SSC 1511 @ 12 noon

*presented by:*

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*(Advisor: M. Perreault)*

**“Profiling sex differences in neuronal network activity and drug responsiveness in the chronic unpredictable stress model of depression”**

Major depressive disorder (MDD) is an affective disorder that is two times more prevalent in women than men. However, the mechanisms responsible for this enhanced female susceptibility are unknown. Neural oscillations give rise to brain electrophysiological rhythms which are critical to neuronal communication within and between brain regions, and are dysregulated in MDD. Our recent work has shown that these oscillations can be modulated by glycogen synthase-3 (GSK-3), a protein kinase that has been implicated in the pathology of many neuropsychiatric disorders including MDD. The activity of GSK-3 can be regulated through estrogen signaling, and thus may be involved in the female susceptibility to depression. In this research proposal, we hypothesize that sex differences in oscillatory signatures predict the susceptibility to exhibit depression-like behaviours, as well as anti-depressant efficacy in the chronic unpredictable stress (CUS) model of MDD. We will therefore investigate innate and stress-induced oscillatory patterns in males and females, and correlate the normalization of these aberrant patterns with the therapeutic efficacy of anti-depressant treatments. Further, we hypothesize that sex differences in GSK-3 activity will modulate oscillatory activity and depression-like behaviours in the CUS model of MDD. The relationship between baseline and stress-induced oscillatory patterns and GSK-3 activity will first be evaluated, after which an adeno-associated viral construct containing an shRNA will be used to investigate the effect of GSK-3 suppression. This research will provide important insights into the mechanisms underlying female vulnerability to MDD, and potentially identify a biomarker of depression and novel therapeutic targets.