Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 9, 2018 in SSC 1511 @ 12 noon

presented by:

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(Advisor: M. Perreault)

"Therapeutic effects of ketamine and regulation of neuronal oscillatory activity in an animal model of treatment resistant depression"

Ketamine has shown strong antidepressant effects in both animal models and patients with treatment-resistant depression. Unfortunately, its harsh side effects diminish its clinical value. The purpose of this research is to delineate ketamine's antidepressant mechanism of action from those of a traditional antidepressant. Pivotal research has indicated that ketamine, in comparison to standard serotonin based antidepressants, exhibits unique effects in the nucleus accumbens (NAc) region of the brain, which will be the primary target of this study. Alterations to biochemical targets glycogen synthase kinase 3 (GSK3) and the transcription factor ΔFosB in the NAc have been shown to exert antidepressant-like effects in animal models. These effects may be brought about through the regulation of neuronal oscillatory activity, the dysregulation of which has been linked to depression. An animal model of treatment-resistant depression (WKY) will be used to determine if ketamine regulates these proteins in the NAc. WKY and Wistar control rats will undergo electrode implantation to gather neuronal oscillatory data, and the open field test and forced swim test will be used to determine the efficacy of ketamine, a serotonin based antidepressant (8-OH-DPAT), and control (saline). After chronic treatment (21 days) brains will be extracted and expression/activity levels of the proteins will be determined using immunohistochemistry. Additionally, the phenotype of the dopamine receptors in which alterations occur will be determined with antibodies to dopamine D1 and D2 receptors, known to be predominantly segregated in this region. Ultimately, this information will be correlated to the normalization of oscillatory activity as a result of treatment. Positive findings in this research will provide unique insight into ketamine's mechanism of action in the NAc, while generating oscillatory signatures that could be used as a therapeutic index for the development of novel treatments.