DISserTATION DEFENSE

LEONID YERMAKOV

PhD Candidate

“TYPE 2 DIABETES LEADS TO IMPAIRMENT OF COGNITIVE FLEXIBILITY AND DISRUPTION OF EXCITABLE AXONAL DOMAINS IN THE BRAIN”

Friday, March 1\textsuperscript{st}, 2019

9:30 a.m.

NEC Auditorium (101)

Advisor: Keiichiro Susuki, MD, PhD
Department of Neuroscience, Cell Biology & Physiology
Type 2 diabetes is a metabolic disease affecting millions of people around the world. Cognitive and mood impairments are among its many debilitating complications, but disease mechanism(s) remain elusive. Here, I present a series of behavioral tasks that demonstrate, for the first time, impairment of cognitive flexibility in \textit{db/db} mice, a commonly used type 2 diabetes model. Using immunohistochemistry, I demonstrate disruption of axon initial segments (AIS) and nodes of Ranvier, excitable axonal domains regulating neuronal output, in brain regions associated with cognitive and mood impairments. Finally, I present results of preventive exercise treatment that ameliorates AIS disruption in these animals. Establishing cognitive flexibility deficits in \textit{db/db} mice that parallel disease complications in patients with type 2 diabetes allows future research to test novel treatment strategies, while discovering disruption of excitable axonal domains fills the missing gap in our understanding of disease pathophysiology.