



**BIOMEDICAL
SCIENCES**
PhD PROGRAM

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DISSERTATION DEFENSE

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PhD Candidate

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

Friday, March 1st, 2019

9:30 a.m.

NEC Auditorium (101)

*Advisor: Keiichiro Susuki, MD, PhD
Department of Neuroscience, Cell Biology & Physiology*

**Leonid Yermakov, Biomedical Sciences PhD Program
Wright State University, 2019**

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 *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 *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.