THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Blake R. Hopiavuori

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE

GRADUATE COLLEGE

Department of Neuroscience

26, April, 2017, 2:00 p.m.
Location: BRC-109

A NOVEL ROLE FOR VERY LONG-CHAIN FATTY ACIDS IN BRAIN FUNCTION

COMMITTEE IN CHARGE: Robert E. Anderson,MD, PhD (chair), Nicolas G. Bazan, MD, PhD, David M. Sherry,PhD, Ferenc Deák, MD, PhD, Scott Plafker, PhD, and William E.Sonntag, PhD

ABSTRACT: Lipids serve a multitude of roles in the brain, from synaptic stabilization and signaling to DNA regulation and neuroprotection. ELOVL4 catalyzes the rate-limiting step in the biosynthesis of very long chain fatty acids (VLC-FAs; ≥28 carbons). Homozygous mutant Elovl4 mice die at birth from dehydration, but can be kept alive by expressing Elovl4 in their skin. These mice develop severe seizures at P18-P20 and die by P21, similar to homozygous inheritance of mutant ELOVL4 in humans. Electrophysiology confirmed aberrant epileptogenic hippocampal activity in homozygous mutant mice. FM1-43 dye imaging studies revealed a loss of slow-releasing synapses in homozygous mutant hippocampal neurons, signifying loss of a novel physiological braking system. We rescued this defect in synaptic release by exogenous neuronal supplementation of the VLC-FAs 28:0 and 30:0. The described studies provide the first evidence of a neuron-specific role for VLC-FA in the regulation of pre-synaptic function by impacting synaptic vesicle membrane properties and release dynamics.