

THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER
ANNOUNCES THE FINAL EXAMINATION OF

Dustin Raymond Masser

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE

Graduate College
Department of Physiology
Tuesday, April 18, 2017, 2:00 pm | Biomedical Research Center, Room 109 |

METABOLIC MEMORY OF NEURONAL MORPHOLOGY, FUNCTION, AND DNA METHYLATION IN AN EXPERIMENTAL MODEL OF DIABETIC RETINOPATHY



Committee in Charge: Willard M. Freeman, PhD, Chair, Michael H. Elliott, PhD, William Sonntag, PhD, Raju Rajala, PhD, Patrick Gaffney, MD.

Diabetic retinopathy is the most common progressive secondary complication of systemic hyperglycemia, and is the leading cause of adult blindness. Empirical evidence suggests that the initiation of vision loss is neuronal and precedes the clinical diagnostic symptoms of retinal vascular abnormalities. There are no preventative treatment options for diabetic patients, however glycemic control is a critical factor in halting diabetic retinopathy progression. In an experimental rat model of diabetic retinopathy, insulin treatment was used to determine if retinal synapse loss, retinal function, DNA methylation, and mitochondrial function and genomic maintenance demonstrate metabolic memory, or persistent hyperglycemic complications after restoration of euglycemia, in the neural retina. State of the art quantitative molecular tools were developed and applied to test the proposed hypotheses. Retinal synapse loss and DNA methylation were found to follow the metabolic memory phenotype. Mitochondrial homeostasis as a potential contributor to the mechanism of synapse loss was found not to be disturbed. These data demonstrate that early neuronal changes in the retina with hyperglycemia occur on the cellular and molecular level, and that restoration of euglycemia is critical to mitigate a portion of these neuronal changes. These studies bring novel tools to the field of diabetic retinopathy research and extend previous findings solidifying the importance of identifying neuronal cellular and molecular mechanisms of diabetic retinopathy in order to develop preventative therapeutic options to ameliorate vision loss in diabetic patients.