THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Ashley Martin

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
Department of Physiology

May 28, 2020, 9 am
https://us02web.zoom.us/j/85410465378?pwd=TXlmeFY0d1F5Q25sNEtwdGFseE1qQT09
Meeting ID: 854 1046 5378
Password: 064978

Maternal Adiposity Alters Transcriptomic and Epigenomic Neurodevelopmental Landscapes in the Fetal Hippocampus

COMMITTEE IN CHARGE:
Dean A. Myers, PhD; Willard M. Freeman, PhD
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David M. Sherry, PhD

ABSTRACT:

Maternal obesity is a prevalent issue in the U.S. with approximately ½ of the pregnant population being overweight or obese at time of conception. Offspring from obese pregnancies display increased fetal adiposity, metabolic disturbances and obesity that persist into adulthood. These offspring also demonstrate increased risk for early and late-onset neurodevelopmental diseases (NDDs), suggesting that maternal obesity during pregnancy can have organizational impacts on the developing brain as well as long-lasting, activational effects on neuronal function. A potential mechanism for the persistent effects of intrauterine environment is the epigenetic program that occurs during CNS development. Our own work, and that of others, clearly demonstrates that early life epigenetic changes can have long lasting effects through altering cellular neurodevelopment and by epigenomic patterns persisting into adulthood. These findings provide a causal mechanism for Barker's Developmental Origins of Health and Disease (DOHaD) hypothesis. Using a naturalistic model of obesity/adiposity during pregnancy, we have found: dysregulation of the fetal hippocampal developmental transcriptome in neuronal development and neurotransmission pathways as well as differential expression of NDD associated genes with high maternal leptin; increased ten-eleven translocase 3 (TET3) expression with higher maternal leptin levels; and a genome-wide hypo-methylation and hyper-hydroxymethylation phenotype. These altered DNA modification profiles were also found to be correlated to the altered gene expression, suggesting possible programming potential for the deposition of these long-lasting mark in the fetal epigenome as well as a potential target, TET3, for therapeutic interventions.