THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

# JAMI MICHELLE GURLEY

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY

Tuesday, July 26, 2016, 10:00 a.m.
Room 109, Biomedical Research Center, OUHSC

## *Regulation of Glut4 and Glut4-dependent Glucose Uptake During Exercise and Nutrient Stress*

COMMITTEE IN CHARGE: Ann Louise Olson, Ph.D.; Kenneth Humphries, Ph.D.; Karla Rodgers, Ph.D; Franklin Hays, Ph.D.; Courtney Griffin, Ph.D.

ABSTRACT: Insulin resistance is a condition in which cells of the body fail to increase tissue glucose uptake in response to increased production and release of the hormone insulin. Glucose transporter 4 (Glut4) mediates the rate-limiting step for glucose uptake in muscle and adipose tissues in response to both insulin and contraction. Conversely, downregulation of Glut4 expression with insulin resistance results in dysregulation of metabolic balance, which can have grave effects on tissue metabolic flexibility and whole-body metabolic homeostasis. Because Glut4 function was initially discovered in the context of its prime role in insulin-mediated glucose uptake, it has long been regarded as the “insulin-responsive” glucose transporter. However, skeletal muscle Glut4 expression and function are also increased in response to muscle contraction, which utilizes an insulin-independent mechanism that remains poorly understood. Although understanding insulin-dependent Glut4 regulation remains crucial, we must shift our focus toward understanding the insulin-independent Glut4 response in muscle if we are to develop more viable treatment options for patients with insulin resistance--a condition characterized by aberrant insulin signaling. Additionally, if our target is to increase

Glut4-mediated glucose flux in skeletal muscle, we must understand the metabolic implications for doing so.

This work describes the problem of insulin resistance and affected individuals, recognizes the need for more effective treatments against insulin resistance, provides a review of the current understanding of Glut4 regulation, highlights the importance of Glut4-dependent glucose uptake in skeletal muscle, examines the impact of enhanced Glut4-mediated glucose uptake on skeletal muscle metabolism, investigates the exercise mechanism for insulin-independent upregulation of skeletal muscle Glut4 expression, and discusses a potential role for targeted exercise regimens as a therapeutic for enhancing peripheral tissue glucose uptake under conditions of insulin resistance.