THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

ROBERT MCCLELLON JACKSON II

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

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Room 109, BRC, OUHSC

Regulation of Adipose Differentiation and Adipose Recovery from Obesity

COMMITTEE IN CHARGE: Ann Louise Olson, Ph.D., Chair, Kenneth Humphries, Ph.D., Guangpu Li, Ph.D., Augen Pioszak, Ph.D., Leonidas Tsiokas, Ph.D.

ABSTRACT: Adipose tissue serves a critical role in nutrient management as the body fluxes between nutrient rich and nutrient poor periods that are induced by feeding and fasting, respectively. It is exquisitely sensitive to the energy needs of the body and upon proper hormonal stimulation, such insulin, this tissue readily takes up and stores any excess nutrients to restore glucose homeostasis for the body. It is also important in the provision of triacylglycerol and other lipids to other tissues to meet their energy demands when nutrients are scarce. This emphasizes the importance of gaining a better understanding of its regulation, as adipose is the most dramatically affected and dysfunctional in obesity and the related Type II Diabetes Mellitus, cardiovascular disease, metabolic syndrome, and even some cancers. In this effort, we have sought to better understand the role of nutrients, specifically glucose, in adipogenesis, a process critical to adipose expansion characteristic of obesity. We have demonstrated that not only is adipocyte differentiation a glucose-dependent process but that is coordinates different independent regulatory mechanisms that drive GLUT4 and adiponectin expression, proteins that carry out key functions for the adipose. We identified that glucose-dependent regulation of GLUT4 expression is conveyed through the LXRE region of its promotor, while adiponectin is dependent upon flux through the pentose phosphate pathway, implicating a role for PARylation in it regulation. Additionally, we investigated the effects of diet composition and its ability to rescue obesity and the resultant effects on the adipose tissue. Mice made obese and insulin-resistant after 5 weeks on a high fat diet were returned to regular chow and exhibited rapid weight loss and recovery of insulin sensitivity within 2 weeks. RNA-Seq analysis of mice 1 week post-SWAP revealed the visceral adipose has a unique transcriptomic fingerprint during obesity recovery. Interestingly, SWAP mice showed unique upregulation of the anti-inflammation *crispld2*, implicating inflammation may play a role in adipose recovery. Together these projects further our knowledge and understanding of adipose regulation, providing novel insight into the role of nutrients and their impacts on both adipocyte differentiation and recovery.