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Characterizing Glucose Metabolism and Insulin Resistance in Adult LEW.1WR1. Rats

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A proposal for the Research and Creative Experience for Undergraduates Program Summer 2018

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Project Summary:

Diabetes prevention is a large topic of research that is focused on nutritional and exercised based interventions with some genetic predisposition based interventions. According to a recent report by the Centers for Disease Control, "Although the risk of developing chronic diseases increases as a person ages, the root causes of many of these diseases often begin early in life." [1] Two-thirds of older American's have multiple chronic conditions.[2] These diseases may potentially steep from organ-specific responses from a common pathophysiological change occurring in several different organs.

FAT10 is a ubiquitin-like protein and Type 1 Diabetes (T1D) susceptibility gene. FAT10 knock out (KO) mice appeared to have smaller islets and increased beta-oxidation and insulin sensitivity. However, FAT10 KO mice were also shown to be protected from insulin resistance but not obesity in response to a high-fat diet. However, the T1D susceptible, LEW.1WR1 rat, has been shown to overexpress FAT10 and have higher fasting concentrations of blood insulin and triglyceride. The LEW rat has a susceptibility window of 21-40 days for T1D induction that has been shown to be related to the genetic regulation of FAT10. It is unclear how the over expression of FAT10 effects insulin sensitivity. What is unclear is the initial insulin sensitivity of this animal model and if this plays a role in this disease susceptibility. This project will analyze the effect high fat diet has on insulin resistance and glucose and lipid metabolism in insulin-sensitive tissues of an animal model shown to overexpress FAT10.

Student Prerequisites:

Students should have completed general chemistry, introduction to biology, and organic chemistry. An understanding of biochemistry prior the beginning of the summer project would be advantageous to the data analysis. Would prefer a junior level chemistry or biology major with at least a 3.0 GPA.

Student Duties:

- The student will play an active role in the handling, and care of LEW.1WR1 rats.
- Student will also be responsible for the isolation and processing of samples from rats.
- Students will be responsible for running quantitative real-time polymerase chain reaction analysis of genes related to lipid metabolism and insulin sensitivity in isolated samples.
- Student will be responsible for the assisting a graduate student/research mentor in performing glucose and insulin tolerance tests.
- Students will be responsible for assisting in ELISAs analyzing specific blood-based markers of metabolism.

Mentor Supervision and Interaction:

Student duties will be monitored by Dr. Love-Rutledge and graduate student. Analysis of data, preparation of poster, manuscript, and any oral presentations will be supervised by Dr. Love-Rutledge. Student will participate in group meetings and will be expected to present at least one peer-reviewed article in a journal club style presentation prepared with the assistance of Dr. Love-Rutledge. The student has access to the supervisor as needed.

1(https://www.cdc.gov/aging/pdf/State-Aging-Health-in-America-2013.pdf)

2 (US Department of Health and Human Services. Multiple Chronic Conditions: A Strategic Framework— Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions. Washington, DC: US Dept of Health and Human Services; 2010. http://www.hhs.gov/ash/initiatives/mcc/mcc_framework.pdf.)