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Comparing Insulin Sensitivity in the LEW.1WR1 and Wistar Furth Rat

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Project Title: Comparing Insulin Sensitivity in the LEW.1WR1 and Wistar Furth rat

Faculty Mentor: Sharifa T Love-Rutledge, Ph.D. Assistant Professor. Chemistry; Bernhard Vogler, Ph.D. Associate Professor. Chemistry

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Proposal Identifier: RCEU19-CHE-SLR-01

Project Description: 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 that is upregulated in several chronic conditions like kidney disease, several cancers, and Type 1 Diabetes (T1D). FAT10 knock out (KO) mice appeared to have increased beta-oxidation and insulin sensitivity. However, FAT10 KO mice were also protected from insulin resistance but not obesity in response to a high-fat diet. The T1D susceptible, LEW.1WR1 rat, has been shown to overexpress FAT10 and have higher fasting concentrations of blood insulin and triglyceride from an early age. It is unclear how the overexpression of FAT10 effects insulin sensitivity as we age. It is also unclear if the initial insulin sensitivity of the 1WR1 model plays a role in this disease susceptibility. This model has a RT1^u haplotype with a missing regulatory element for FAT10. This project will analyze the effect aging has on insulin sensitivity of an animal model shown to overexpress FAT10.

Using LEW.1WR1 and a haplotype control rat, the Wistar Furth rat, we will probe the insulin sensitivity using insulin tolerance test at strategic time points in the life span of the rats. The rats will be maintained on a control (less than 1% sucrose) or increased sucrose (7% sucrose) diet to observe age related changes in insulin sensitivity. We have observed that the LEW.1WR1 rat may have reduced insulin sensitivity and we hope to further probe this phenomenon.

Student Duties and Contributions: The student will play an active role in the handling, and care of LEW.1WR1 rats; The student will be responsible for the maintenance of equipment used in experiments; The student will play a critical role in sample collection; The student will be responsible for assisting a graduate student/research mentor in performing insulin tolerance tests; Students will be responsible for assisting in ELISAs analyzing specific blood-based markers of metabolism; The students will be responsible for recording, organizing and graphing data from twice weekly weighing, feeding and insulin tolerance tests; The 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.

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.)

Student Outcomes:

- The student will gain experience with developing and presenting an oral scientific presentation on peer reviewed literature.
- The student will gain animal handling experience.
- The student will be exposed to classical biomedical research skills like pipetting, making sterile solutions, performing ELISAs, etc.
- The student will learn skills in effective communication and collaboration.
- The student will learn the value of time management.
- The student will learn organizational skills as well as project management skills.
- The student will learn the value of accuracy, proper use and maintenance of lab equipment.
- The student will also sharpen solution making skills in a laboratory environment.

Student Prerequisites:

Students should have a good background in foundational chemistry and biology courses (CH121 & BYS119 required). An understanding of biochemistry, anatomy & physiology, and/or cell biology before the beginning of the summer project would be advantageous to the data analysis and is preferred. Student must at least be a sophomore by the beginning of the summer. This project is a continuation of RCEU projects from 2018.

Mentor Supervision and Interaction:

Student duties will be monitored by Dr. Love-Rutledge and two graduate students. Students will interact with Dr. Love-Rutledge at least weekly, and daily during the early training stages. Analysis of data, preparation of poster, manuscript, and any oral presentations will be supervised by Dr. Love-Rutledge. The students will be trained in necessary techniques by Dr. Love-Rutledge. The students will regularly interact with the graduate students in their final year of their thesis during the duration of the project. The student has access to the supervisor as needed. Dr. Vogler is an adjunct mentor for this project as the students will be helping with collection of samples needed to support studies in his laboratory.

Prior Awardees

Award Year and Project Title: 2018 Characterizing production changes in INS-1 exosomes from after exposure to an immune-stimulating trigger

Tangible Contributions: The student was able to develop a technique for culturing islets during a secretion study, the student also worked out the logistics of performing Insulin ELISAs in the lab. The student learned how to analyze data, and prepare a poster.

Specific Outcomes provided to the student: The student learned sterile technique, animal handling, islet isolation, glucose stimulated insulin secretion assays, ELISAs, preparation of Journal Club presentation, time management, handpicking, cell culturing, the preparation of sterile media, use of a well plate reader, and the physiology of islets of Langerhans.