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Metabolomics to Quantify Changes in the TCA Cycle Relevant to Diabetes Using a Rat Model

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METABOLOMICS to Quantify Changes in the TCA Cycle Relevant to Diabetes Using a Rat Model. (TCA-Metabolomics-Vogler-RCEU-2019)

A Proposal for the Research and Creative Experience for Undergraduates (RCEU) Program, Summer 2019

Faculty Sponsors: Bernhard Vogler, PhD, Chemistry, Sharifa T Love Rutledge, PhD

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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. Diabetes is also one of the diseases observed in the older population, however, might be triggered in early life.

Research Plan:

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. We will collect rat urine, and tissue samples and will analyze samples over the course of the 10 weeks. We have already collected NMR data (HSQC) to identify individual components, subsequently we developed quantitative protocols based on MS data that now should be applied to the chemicals involved in the relevant biochemical pathway.

Student Duties:

Run NMR and MS samples; identify components and monitor concentration differences between different samples.

Tentative plan for the 10 week schedule:

- week 1/2: familiarization with, LC-MS and NMR.
- week 3/4: building of reference data files, establishing concentration curves
- week 5/6: familiarization with VNMRJ, MestreNova (NMR), and Tracefinder (MS) for data analysis.
- week 7/8: analysis of data sets.
- week 9/10: refine measurements.

Manuscript preparation:

Dr. Vogler encourages all undergraduate student researchers to write up their results in the form of a manuscript for publication. The RCEU participant, under the supervision of Dr. Vogler, will help prepare the manuscript(s), which may include data from other undergraduate or graduate students.

Expected Student Background :

Students should have good background in General Chemistry, knowledge of Organic Chemistry is advantageous, so typically students with a major in Biology, Chemistry, and or Chemical Engineering should be ok. Previous exposure to analytical instrumentation is a clear benefit. This is a continuation of RCEU projects from 2018.

Expected results and deliverables:

The student will be exposed to important instrumental techniques such as mass spectrometric analysis, NMR analysis, preparation of samples in smallest concentrations, error analysis, literature studies. Exposure to state of the art instrumental techniques will greatly enhance any students' career chances in chemistry or related disciplines. Instrumental skills are highly regarded.

Faculty Supervision and Mentoring:

NMR and LC-MS measurements will be supervised by Dr. Vogler and James Wolfsberger, my graduate student. Manuscript preparation will be supervised by Dr. Vogler. We will hold regular group meetings weekly.

The student will be part of a group of three graduate students, two undergraduate students and will have access to the instructor at least once a day.