Student Statement:

I'm Marissa Moore and I am currently a senior double majoring in Spanish and Biology. I wish to go to graduate school for a neuroscience program, and continue research after completion. I'm extremely interested in behavioral and cognitive neuroscience research and plan to focus in one of these areas in my future career. I'm currently taking the first section of anatomy and physiology with Dr. MacGregor and have gained even more interest in pursuing disease states of the nervous system. I really enjoy reading new neuroscience journal articles as well as books to learn about new research methods and breakthroughs in research. I am currently in preparation for research that I am doing this upcoming December with Dr. MacGregor about the same theme as the proposal. We will be assessing possible short term memory impairments associated with tyrosinemia and its treatment. I have prepared the protocol as well as the tests for short term memory that will be used for this research, and I believe I would excel in creating new tests for this proposal next summer. I also just began my employment at UAH as an animal room worker in which I take care of the mice that will be involved in the experiments two days each week. I am also working with another animal room worker to handle the mice every day in order to decrease their anxiety as well as get them accustomed to being handled for the experiments. I believe my daily presence with the mice as well as my upcoming research and animal room job would be more than enough experience required to excel in this research proposal.

I really wish to participate in this research program to gain experience for graduate school as well as continue investigating the memory impairments associated with tyrosinemia. I've really enjoyed working with the mice and planning my upcoming research in December, and I wish to improve upon the experiments as well as utilize different tests for memory. I also hope to gain experience analyzing neurotransmitters and would greatly enjoy participating in this proposal to gain more experience in DNA extraction and PCR. My research this December will give me the experience of not only creating my own experiment, but also experience with the camera equipment as well as the software that will be used. By next summer I will have experience collecting the data from the software, analyzing it, and writing a paper on my findings that we plan to present to the Alabama Academy of Science meeting in February. I also plan to become involved with the upcoming UAH research journal, in which I hope to become editor in chief or associate editor. This position would allow me to be involved and write about the amazing research at UAH as well as further aid me with my writing skills. I believe my prerequisites as well as my research opportunity in December would greatly aid me in this research proposal for Dr. MacGregor, and I hope I will be able to continue working on the memory impairment with tyrosinemia to make advances in its treatment.

Title

Learning, Memory and Cognitive Studies in a Mouse Model of Tyrosinemia Type I

Faculty and Research Mentor

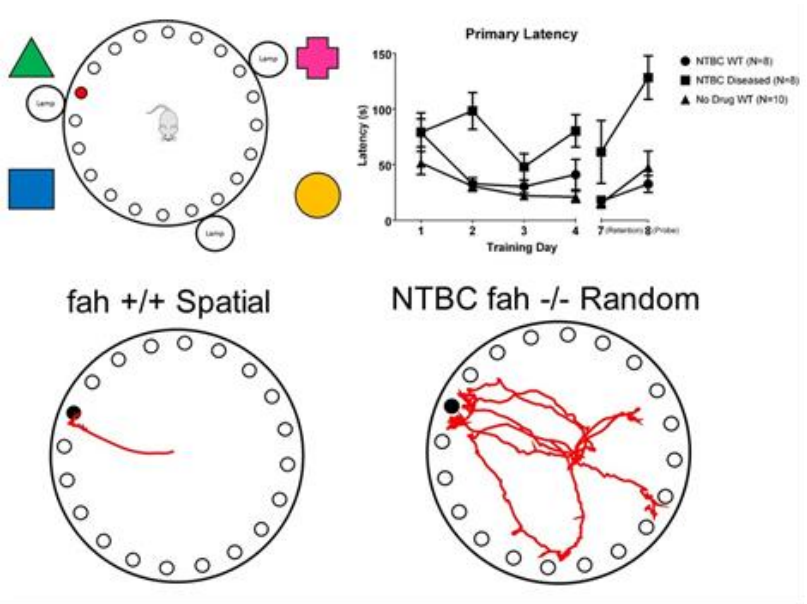
Mentor: Gordon MacGregor PhD

E-mail: gordon.macgregor@uah.edu **Phone:** 256-824-4925

Contact: Dept. of Biological Sciences, 301 Sparkman Drive, SST 361, Huntsville, AL, 35899

Project Summary

Tyrosinemia Type 1 (TT1) is an autosomal recessive disorder that is caused by a deficiency of the FAH enzyme that serves as the terminal enzyme in the tyrosine catabolic pathway. This deficiency results in the buildup of toxic metabolites that can eventually cause death without treatment. The only pharmacologic treatment currently available for those with TT1 is Nitisinone (NTBC), which blocks the tyrosine catabolic pathway above the enzyme deficiency. This drug saves the lives of children with TT1, yet has recently been associated with neurocognitive changes and learning deficits. Based on this association, we are using mice as a model to unravel to contribution of the disease itself or the treatment, NTBC, to these alterations in cognitive function. We will use classic models to study mouse learning, memory and anxiety, such as elevated plus maze, Barne's maze, open field maze, hole-board and social interaction analysis. We will also quantify any differences in neurotransmitter levels in mouse urine and plasma.



Tyrosinemia type I mice have altered spatial learning and memory in the Barnes maze model of testing.

Student Duties

The student is critical to this project as firstly, they will learn correct animal handling skills. The mice need to be comfortable with the person who usually works with them, so that they are not excessively stressed when it is time to be tested. The mice should react solely to the maze and not to the stress invoked by unfamiliar handling. One of their daily duties is to check on the mice, confirm their well-being, and have them be familiar with handling. Secondly, the student will genotype the knock-out mice litters. This will involve DNA extraction, PCR, agarose gel electrophoresis, and restriction nuclease fragment analysis. The third and largest part of the students duties will be for them to develop their own protocols for the testing of mouse cognitive abilities, anxiety and memory, using several mouse tests and mazes and to develop tests of mouse gait and neuro-motor skills. The tyrosinemia mouse, and NTBC treated mouse have not been studied in this way before so all data will be novel. As well as developing the testing protocols, the student will analyze their own data, determine its significance and present it correctly for publication.

The student will learn to use state of the art Noldus Ethovision animal tracking and analysis software. The student will be provided with an individual copy of GraphPad Prizm software for data plotting and analysis. The student will perform ELISA quantifications for neurotransmitters in mouse plasma and urine and use 96 well fluorescence and absorption spectrophotometer plate readers.

Mentor Supervision and Interaction

My goal is to allow the student independence enough to develop, perform and analyze their own experiments. I will guide them, and point them in the correct direction and solve problems that they can't resolve on their own. I will be in the lab fulltime on a daily basis for interaction and bouncing ideas off. I aim to introduce the students to research methodology, correctly performed data analysis, and techniques for correct amalgamation of their data for presentation in the form of a poster or oral presentation for use at a conference.

This project will require full time presence in the lab for 32-40 hours per week, for 10-12 weeks.