Questions and Answers with Dr. Dominic D’Agostino

Can you tell us more about your lab environment at the University of South Florida?

Our laboratory at USF Morsani College of Medicine is growing in space, personnel and research interests. Our Department of Molecular Pharmacology and Physiology has a faculty base with a broad range of expertise and backgrounds. The main focus of our laboratory is to further expand on the development and application of metabolic therapies for the treatment of seizure disorders, metabolic disorders, neurodegenerative diseases, wound healing and cancer. We now have four full time PhD students, a laboratory manager, a postdoctoral fellow and several highly motivated undergraduate and pre-medical students working in the laboratory. Each member has a primary project, but they all work as a Team to support the efforts of others by collecting data, discussing the results and presenting the information to the public. Our laboratory is equipped with a variety of equipment to assess the efficacy of metabolic therapies on neurological function, motor function and metabolism, which are all linked to clinical assessment in patients.

Collaboration is a very important and necessary part of forming a team of expertise to optimize the use of resources for scientific discovery. We maintain collaborations with a number of institutions including Boston College, Case Western University, The University of Texas Southwestern Medical Center and the University on Tampa to name a few.

How is your research funded?

Our research is funded primarily by the Office of Naval Research (ONR), which is a branch under the Department of Defense (DoD). In addition, we receive funding from private 501(c)(3) Nonprofit Foundations that are interested in the development and testing of metabolic therapies for neurological diseases and cancer. We are proud to be funded by the Glut1 Deficiency Foundation for the testing of ketone esters and other ketogenic agents for treatment of GLUT1 DS.
supplementation for seizure disorders, cancer, wound healing, amyotrophic lateral sclerosis (ALS), Alzheimer's disease and metabolic diseases associated with impaired glucose metabolism. The neuroprotective ketogenic agents being tested for specific military applications (DoD and ONR) have a broad range of therapeutic benefits associated with them, including the potential to enhance brain metabolism and improve neurological function under environmental extremes. For example, we found that metabolic treatments that produce therapeutic ketosis protect the brain from environmental extremes of high-pressure oxygen. In addition, the anticancer effects of therapeutic ketosis combined with hyperbaric oxygen have been shown to improve survival time of mice with metastatic cancer. Another ongoing project is the application of a metabolic therapy to enhance the healing process associated with ischemic wounds in elderly populations. These metabolic therapies work by virtue of their ability to enhance blood flow, oxygenation and metabolic substrate delivery to the ischemic wound tissue.

**When will the proposed Glut1 Deficiency studies begin (or when did they begin)?**

The proposed experiment to test the effects of ketone esters in a mouse model of GLUT1 DS is currently under review by the USF Animal Care and Use Committee (IACUC). This is similar to the IRB committee that reviews studies for use in humans. The IACUC committee provides oversight on all animal research. This ensures that the number of mice used in experiments is appropriate and that the experimental design and therapeutic agents will not cause unnecessary harm to the animal. We expect IACUC approval soon and plan to start experiments as early as March.
When do you expect them to be completed and the results shared?

We anticipate preliminary results on the effects of ketone esters and ketogenic agents on GLUT1 DS mice within six months of starting the pilot study. These results will describe the general behavior, bodyweight, blood glucose, ketone levels, seizure frequency and assessment of motor function in GLUT1 DS mice fed therapeutic levels of ketogenic agents.

What potential does this research have to impact the big picture for Glut1 Deficiency (and perhaps even more conditions)?

The GLUT1 DS mice are an excellent model for the “proof of concept” to demonstrate that a potent ketogenic agent can be used for the metabolic management of GLUT1 DS. Management of GLUT1 DS symptoms would likely have therapeutic effects for a broad range diseases associated with impaired brain glucose utilization, including a broad range of seizure disorders and neurodegenerative disorders.

How does this project reflect your overall approach to research and medicine?

Our laboratory believes that metabolic therapies like the ketogenic diet are grossly underutilized. This became very clear to me after talking with Jim Abrahams of the Charlie Foundation, Emma Williams of Matthew’s Friends, and meeting so many patients and families that have benefitted from the use of this nontoxic therapy. Our goals are to develop metabolic agents, including ketone supplements, which would mimic the ketogenic diet or boost the therapeutic efficacy of the diet by delivering more high energy ketone bodies to boost brain metabolism.
What can the Glut1 Deficiency community do to be helpful to you and where can we find more information?

I am always interested to hear stories from GLUT1 Deficiency families related to what has worked for them and what has not worked. This information helps guide our efforts to develop the optimal therapeutic strategy. I envision a day when potent metabolic therapies can be given in the form of great tasting drinks, meals or snacks that can reduce the need for severe dietary restriction or the need for anti-seizure drugs.

For more information:
http://ketonutrition.org/

http://health.usf.edu/medicine/mpp/profile.html?person_id=24854&Dominic&DAgostino