Project: Citrate Transport in the Kidney Proximal Tubule: Effects of Calcium and pH.

Principal Investigator: Kathleen S. Hering-Smith, PhD  
Research Assistant Professor  
Departments of Medicine and Physiology, School of Medicine  
Tulane University Health Sciences Center  
Section of Nephrology and Hypertension  
khering@tulane.edu  
Office phone: (504) 988-3446; fax: (504) 988-1600

Project description:  
Kidney stones represent a major health problem, in the USA alone about 5% of American females and 12% of American males will form a kidney stone at some point in their adult life. The proposed work will aid in the understanding of kidney stone formation and prevention as well as future treatment/prevention. Urinary citrate is an important endogenous inhibitor of calcium nephrolithiasis (kidney stone formation) and is primarily determined by its fractional reabsorption in the proximal tubule. The sodium dicarboxylate transporter, NaDC1, is presumably the main mechanism of lumenal uptake of filtered citrate. Our research addresses the acute regulation of citrate transport by calcium, and the chronic regulation of citrate transport by acid-base perturbations and hypokalemia. Others have demonstrated that citrate transport is regulated both acutely and chronically, although the mechanisms are poorly understood. The most important physiologic regulator of urinary citrate excretion is acid-base status of the individual. Also, urinary citrate increases as urinary calcium increases, but the mechanism has not been established. We are investigating the acute regulation of citrate transport by calcium, and chronic regulation of citrate transport by acid-base perturbations and hypokalemia. Understanding the mechanisms of regulation of citrate transport will hopefully lead to improved diagnosis of causes of hypocitraturia and improved treatment of stone disease.

Two hypotheses are currently being examined in our laboratory: 1. Calcium acutely modulates a novel citrate transport process via a yet to be defined signal transduction mechanism present in mammalian kidney proximal tubule cells. 2. Chronic regulation of proximal tubule transport of citrate is accomplished by multiple mechanisms including changes in NaDC1 protein production and insertion of pre-existing NaDC1 protein into the apical membrane from sub-apical vesicles.

The student selected will participate in areas of these projects and will perform cell culture, preparation of DNA, RNA and/or protein extraction, biotinylation of proteins and Western blot analysis to investigate either how extracellular calcium alters the citrate transport process or the regulation of trafficking of NaDC1 into and out of the apical membrane from sub-apical vesicles under conditions of metabolic acidosis or hypokalemia.

Objectives:  
During the 10-week period, the student will gain experience with:  
• Formulating and testing scientific hypotheses;  
• Cell culture and aseptic techniques, solution preparation, DNA, RNA and protein extraction, biotinylation and Western blot techniques  
• Data analysis of experiments and organizing a poster or oral presentation

Prerequisites: The student must have successfully completed the sophomore year with a GPA of 3.00 or higher, students interested in this project should have a minimum of either introductory chemistry and/or biology including laboratories and be willing to learn new techniques.

The undergraduate student that is selected will be advised by Dr. Hering-Smith. To apply, please send application materials through LS-LAMP, including a short letter expressing your future educational, employment plans and career goals. In addition, please send or email a copy of your application to the mentor, Kathleen Hering-Smith, PhD. Tulane University Health Sciences Center, Section of Nephrology and Hypertension SL45, 1430 Tulane Avenue. New Orleans, LA 70112. Phone: (504) 988-3446; Fax: (504) 988-1600. E-mail: khering@tulane.edu.