Erin N. Frey
PhD Candidate

“ACID-SENSING ION CHANNELS: TARGETS FOR NEUROPEPTIDE MODULATION AND NEURONAL DAMAGE”

April 9th, 2013
Biomedical Research Institute, Rm 105
9:00 AM
VITA

October 5th, 1985..........................Born in Springfield, Ohio

June 2004 ..................................Shawnee High School

May 2008 ....................................B.A.
Biochemistry/Neuroscience,
Ohio Wesleyan University

2008 to present .........................Graduate Research Associate,
Department of Neuroscience,
The Ohio State University

AWARDS AND HONORS

7/1/08 – 6/30/09
First Year Graduate Student Fellowship from The Ohio State University, Columbus, Ohio

7/1/09 – 6/30/10
Systems Integrative Biology Training Grant T32 GM068412

7/1/10 – 6/30/11
Fellowship from The College of Medicine at The Ohio State University, Columbus, Ohio

FUTURE PLANS

I plan to pursue a postdoctoral fellowship focusing on mechanisms of neuronal damage and/or dysfunction in neurological disorders.

COMMITTEE MEMBERS

Professor Candice Askwith, Advisor
Professor Georgia Bishop
Professor Dana McTigue
Professor Robert Stephens
ABSTRACT

Acid-sensing ion channels (ASICs) are proton-gated channels expressed in neurons in the central and peripheral nervous systems. These ion channels are sensors for extracellular pH and contribute to a variety of normal functions including learning and memory, seizure termination, fear, anxiety, and pain. Additionally, ASICs mediate neuron death and axon degeneration during pathological conditions such as ischemic stroke, inflammation, and traumatic injury.

My thesis work began focused on ASICs in the peripheral nervous system. In rodent sensory neurons ASICs contribute to sensory transduction and pain. However, little was known about human ASIC channels in sensory neurons. In an effort to address this disparity, I cloned and characterized a novel human ASIC1 transcript variant (human ASIC1b). I discovered that this variant forms functional channels and is expressed in dorsal root ganglia. Furthermore, I discovered that, unlike its rodent homolog, human ASIC1b displays a non-inactivating sustained current and is permeable to calcium. These experiments are the first report of a human ASIC channel homologous to rodent ASIC1b and identify critical characteristics of the channel that may be vital for the function of ASIC1b in humans, particularly in pain.

Due to the role of ASIC in neuronal damage in the central nervous system, I became interested in understanding how ASIC modulated damage in the peripheral nervous system, a question that has been largely overlooked. Therefore, I set out to determine how prolonged acidosis and ASICs affected peripheral neurons. I discovered that prolonged acidosis results in decreased axonal complexity that is dependent on both ASIC1 and ASIC2. For the first time, this work established that ASICs may contribute to peripheral axon morphology. Furthermore, this has implications for many peripheral nervous system diseases where ischemia and inflammation are present and contribute to acidosis.

In addition to my work on peripheral ASICs, I also studied mechanisms of ASIC1a neuropeptide modulation. Modulation of
ASIC can either potentiate or inhibit its activity and therefore may affect physiological and pathological roles of ASIC. Yet, the mechanism of peptide modulation of ASIC is unknown. In my studies I have discovered a potential binding site and effector site that contribute to peptide modulation. These discoveries suggest a novel model for peptide modulation of ASIC and provide essential information for targeted drug design.

Taken together, my work has addressed important gaps in our knowledge of ASICs in two major areas. First, my work has identified a human homolog of ASIC1b that displays unique channel characteristics. These characteristics are likely critical for ASIC1b function in humans and must be considered, especially since studies in animal models will overlook their role. Furthermore, I have shown that peripheral ASICs are capable of altering axon morphology of sensory neurons following prolonged acidosis, and this may relate to a variety of peripheral nervous system diseases. Finally, I have identified a binding site and potential mechanism for peptide modulation of ASIC channels. This work has furthered our understanding of peptide modulation of ASIC activity and establishes a foundation essential for drug-design to target ASIC activity and reduce acid-induced neuronal damage in the central and peripheral nervous systems.

**NATIONAL MEETING ABSTRACTS AND INVITED TALKS**


E.N. Frey* and C.C. Askwith. Role of L280C in ASIC1a Desensitization and Peptide Modulation. (2011) 41st Annual Meeting of the Society for Neuroscience; Washington, DC. *(poster presentation)*


E.N. Frey* and C.C. Askwith. How Do Acid Sensing Ion Channels Mediate Neuronal Damage in the Peripheral Nervous System. Annual Retreat for the Biomedical Sciences Graduate Program; The Ohio State University Medical Center, Columbus, Ohio. December 2, 2011. *(invited talk)*