

## **Research Grants**

### **Meritorious Research 2010 – each \$50,000**

**Chad Edward Carlson, M.D.**  
**Assistant Professor of Neurology**  
**New York University School of Medicine**  
**New York, NY, United States**

**Application Title:**

Detection of epileptogenic malformations with surface-based MRI morphometry

**General Audience Summary:**

Despite the development of new medications to treat epilepsy, around one third of patients continue to have seizures despite treatment. For these patients, epilepsy surgery may be an option for achieving seizure freedom. This study aims to utilize computational techniques to analyze MRI data to identify potential regions associated with seizures. We expect this study will enhance the traditional visual diagnostic approach to patients with epilepsy. This will allow for improved identification of the focus from which seizures begin and, ultimately, increase the likelihood of achieving seizure freedom following epilepsy surgery.

**Bernard S. Chang, MD**  
**Assistant Professor of Neurology, Staff Physician**  
**Beth Israel Deaconess Medical Center**  
**Boston, MA, United States**

**Application Title:**

Abnormal Brain Connectivity in Gray Matter Heterotopia with Epilepsy

**General Audience Summary:**

Medically uncontrolled epilepsy affects 675,000 Americans, and is commonly caused by developmental brain malformations. Periventricular nodular heterotopia (PNH) is a malformation with nodules of misplaced gray matter deep in the brain. Unfortunately, treatments for epilepsy in PNH have been disappointing. There is growing evidence that connections between regions of gray matter are important in brain function, and epilepsy may be a disorder of abnormal connections. We will use advanced neuroimaging methods to study structural and functional connectivity in PNH. Our results will shed light on the mechanisms of how seizures develop and suggest novel treatment strategies for patients with epilepsy.

**Timothy Ellmore, Ph.D.**  
**Instructor**  
**The University of Texas Health Science Center at Houston**  
**Houston, TX, United States**

**Application Title:**

Diffusion imaging for seizure focus localization

**General Audience Summary:**

Surgical approaches represent a viable option for curing epilepsy, but success depends on identifying the location in the brain where the seizures start. When this cannot be determined from a routine structural MRI, implantation of electrodes followed by days of monitoring in the hospital are required. This research seeks to develop a non-invasive imaging method for localizing the seizure focus. Diffusion imaging, a type of MRI that allows one to see how different brain areas are connected, will be used to determine whether the seizure focus is characterized by differences in the number of connections with other brain areas.

**Todd A. Fiacco, Ph.D.**  
**Assistant Professor**  
**University of California, Riverside**  
**Riverside, CA, United States**

**Application Title:**

Astrocyte role in epilepsy via swelling-induced release of glutamate

**General Audience Summary:**

Astrocytes are star-shaped cells in the brain that are important regulators of neuronal excitability. Astrocytes take up both extracellular potassium ions as well as glutamate, the primary excitatory neurotransmitter in the brain, released by neurons. Under certain conditions, astrocytes are also capable of releasing glutamate themselves that can cause local increases in neuronal firing rates in key brain regions known to be susceptible to seizure initiation. Despite their importance in regulating brain excitability, astrocytes have received little attention in their possible involvement in epilepsy. Therefore, we are proposing to study the involvement of astrocytes in the initiation of epileptic seizures.

**John Joshua Lawrence, Ph.D.**  
**Assistant Professor of Neurophysiology**  
**The University of Montana**  
**Missoula, MT, United States**

**Application Title:**

The Impact of Kv7 Channel Openers on GABAergic Networks

**General Audience Summary:**

Seizure activity results when excitation spreads out of control and overcomes inhibition in the brain. Antiepileptic agents help bring excitation and inhibition back into balance. One class of anticonvulsants, called Kv7 channel activators, holds tremendous promise, but their effects on inhibition have not been well understood due to secondary effects at GABAergic receptors. However, ICA-27243, an exciting new compound that is highly selective for Kv7 channels, allows us to examine the effects of Kv7 activators on inhibitory networks. These studies will help evaluate the therapeutic potential for this

particular class of anticonvulsive agents.

**Vijayalakshmi Santhakumar, Ph.D**  
**Assistant Professor**  
**UMDNJ-New Jersey Medical School**  
**Newark, NJ, United States**

**Application Title:**

Proton Modulation of Perisomatic Interneurons in Epilepsy

**General Audience Summary:**

How seizures begin and terminate are both questions of fundamental importance in epilepsy. While recent studies have shown that intrinsic properties of neurons can be modified during development of epilepsy, our understanding of mechanisms of seizure termination is shaped largely by studies in acute seizure models. Using a model of chronic epilepsy, this proposal will test the hypothesis that specific changes in inhibitory neurons which occur as a long-term consequence of status epilepticus undermine a crucial mechanism of seizure termination in epilepsy.

**Kristina Simeone, PhD**  
**Resident Professor**  
**Creighton University**  
**Omaha, NE, United States**

**Application Title:**

Mitochondrial Impairment During Epileptogenesis

**General Audience Summary:**

Seizures induce neuronal death, which may contribute to the pathogenesis of epilepsy. Mitochondria have an interesting role in epilepsy. Not only are mitochondria critically involved in initiating cell death signaling cascades, but they are the target for damage under high energy demands, such as during seizures. Epilepsy is associated with impairment of mitochondrial function, which will reduce the cell's energy supply (ATP), increase injurious reactive oxygen species and disrupt calcium homeostasis. These conditions in turn make the cell more susceptible to cell death and can potentially exacerbate epileptic pathology. Whether mitochondrial dysfunction contributes to the generation of the epilepsy and its associated pathology or is a consequence of the disease remains unknown and will be the focus of this grant. Targeting mitochondria may attenuate or postpone epileptic pathology and potentially seizure genesis.