

Partnership for Pediatric Epilepsy Research

Fall 2008 (FY09) Roster of Awards

Jeanne Nerbonne, Ph.D.

Washington University in St. Louis

Title: Mechanisms linking SCN1B to neuronal excitability and pediatric epilepsies

Lay Summary:

Voltage-gated potassium (Kv) channels are key determinants of neuronal excitability, and dysregulation of the functioning of these channels, resulting from inherited or acquired disease, has been linked directly to epilepsy. Recent studies have revealed an unexpected interaction between one of the prominent brain Kv channel proteins (Kv4.2) and Navbeta1 (SCN1b), an accessory subunit previously shown to be the locus of mutations that cause pediatric epilepsy. Previous studies have also demonstrated that young mice lacking Navbeta1 have fatal seizures. Here, we propose that epilepsy linked to SCN1b mutations (or to loss Navbeta1) reflects the loss of Kv4.2-encoded A-type Kv channels. The studies proposed here will provide new and fundamentally important insights into the physiological roles of Navbeta subunits in the regulation of neuronal Kv channels and neuronal excitability and into how mutations in Navbeta1 lead to pediatric epilepsy.

Andrew Escayg, Ph.D.

Emory University

Title: Development of a high throughput assay to identify epilepsy mutations

Lay Summary:

Genetic mutations are known to play an important role in the etiology of idiopathic generalized epilepsy (IGE), however the identification of the specific mutations that lead to IGE has been hampered by the high cost of traditional methods of DNA sequence analysis. We propose to develop a rapid and cost-effective method to screen genes for mutations in patients with epilepsy. This study would lead to much-improved DNA sequence-based clinical testing in epilepsy patients and the development of improved therapies that are based on a clearer understanding of the mechanism of epilepsy.

Jennifer S. Haut, Ph.D.

Cleveland Clinic Foundation

Application Title: Assessing reliable cognitive change in children following epilepsy surgery

Lay Summary:

This study will develop reliable methods for assessing cognitive (i.e., intelligence, attention, memory) change in children with epilepsy. Using these methods, rates of cognitive change will be examined in pediatric patients who have undergone epilepsy surgery. This research will provide clinicians with the necessary tools to differentiate cognitive effects of epilepsy from cognitive effects of surgery. This information will help neuropsychologists inform parents and doctors about the cognitive risk associated with surgery and assist with prediction of overall learning and behavioral outcome. Furthermore, clinicians can use this information to more accurately identify cognitive and school abilities requiring intervention following surgery.