FALL FY07 AWARDS ROSTER
POST-DOCTORAL RESEARCH TRAINING FELLOWSHIPS

$40,000 awards for one year

Name: Mark Peke Beenhakker, Ph.D.
Institution: Stanford University
Project: Regulation of Inhibitory Transmission in a Model of Absence Epilepsy
Preceptor: John R. Huguenard, Ph.D.
Lay Summary: Brain cells primarily communicate by using neurochemicals that either stimulate or inhibit neighboring cells. Epilepsy often results when the balance of these signals is disturbed. To develop drug therapies that can restore balance, it is critical to identify factors that control the actions of neurochemicals. This proposal aims to understand how factors that increase signaling by inhibitory neurochemicals may contribute to a childhood form of epilepsy.

Name: Julia Annette Brill, Ph.D.
Institution: Stanford University
Project: Altered AMPA receptor mediated excitability in the microgyric rat cortex
Preceptor: John R. Huguenard, Ph.D.
Lay Summary: Epileptic seizures are the result of hyperexcitability with the brain. This project addresses changes in the cerebral cortex that occur as a result of an injury early in life. It focuses on identifying changes in the number of connections between neurons and the nature of these connections, i.e. whether individual connections are strong, weaker, or mediated by different molecular components. A better understanding of these mechanisms may lead to new therapeutic approaches.

Name: Cynthia L. Fuller, Ph.D.
Institution: The Regents of the University of Michigan
Project: Influence of Adult Hippocampal Neurogenesis in Intact and Epileptic Mice
Preceptor: Jack M. Parent, M.D.
Lay Summary: The purpose of this research plan is to examine the contribution of adult-born nerve cells to epilepsy development and associated learning impairments. The investigator will genetically eliminate production of new neurons and determine if these adult-born cells contribute to seizure development and learning deficits in a model of temporal lobe epilepsy.

Name: Boris Shamilevich Gafurov, Ph.D.
Institution: Uniformed Services University of the Health Sciences
Project: Activity patterns and propagation in temporal lobe epilepsy
Preceptor: Suzanne Barbara Bausch, Ph.D.
Lay Summary: This project will use a technique that will allow studying entire hippocampal electricity in all different parts at the same time and monitor relationship between them. Each electrical impulse in each part of the hippocampus will be observed separately on its own and in the entire hippocampus. The experiments will use epileptic and normal rats to make a comparison and find out which hippocampal part or feature malfunctions. Therefore, the investigators will be able to see the spread of electricity in the brain of normal rats and how it changes epileptic rats. This will lead to better understanding of the role and relationship between all parts of hippocampus involved in epilepsy and it can provide a basis for treatment of epilepsy.

Name: Jonathan Dean Hommel, Ph.D.
Institution: Duke University Medical Center
Project: The role of arc in epileptogenesis
Preceptor: James O. McNamara, Ph.D.
Lay Summary: It is clear that certain genes are required for the development of epilepsy. There is evidence that the gene named Arc may be one of those critical genes. This idea will be tested by blocking Arc in cultured neurons and determining if those neurons can become ”epileptic.”

Name: Stuart Gordon Jarrett, Ph.D.
Institution: University of Colorado Health Sciences Center
Project: Mechanisms of Redox Regulation of the Ketogenic diet
Preceptor: Manisha Patel, Ph.D.
Lay Summary: Epilepsy is a recent addition to the diverse array of neurological disorders in which mitochondrial dysfunction has been implicated as a major factor. The ketogenic diet is an important treatment that benefits children by alleviating epileptic seizures. At present, its beneficial effects are not fully understood. The goal of this proposal is to determine the mechanism by which the ketogenic diet improves mitochondrial function. This study will help us to identify new therapeutic interventions for the treatment of childhood epilepsy.

Name: Xiaoming Jin, Ph.D.
Institution: Stanford University School of Medicine
Project: Inhibitory Synaptic Connectivity in Post-Traumatic Epileptogenesis
Preceptor: David A. Prince, M.D.
Lay Summary: Traumatic brain injury often results in epileptic seizures by causing excessive excitatory electrical activity and insufficient inhibitory activity in neurons of the brain. This research proposal will focus on studying inhibitory electrical activities in the brain. Results will contribute to a further understanding of how epilepsy occurs and provide insights for the treatment of epileptic seizures after the brain trauma.

Name: Young-Min Lim, M.D.
Institution: National Institutes of Health - National Institute of Neurological Disorders and Stroke
Project: Imaging serotonergic neurotransmission in epilepsy
Preceptor: William H. Theodore, M.D.
Lay Summary: Depression is more frequent in patients with epilepsy than with any other chronic disorders, and may be highest in temporal lobe epilepsy. Serotonin, a kind of neurotransmitter, has numerous functions in the human brain, affecting mood control, sleep, and appetite. Several drugs modulating serotonin are currently prescribed for the treatment of depression. The serotonergic system may be involved in the development of epilepsy. Studying the role of serotonin may be very important for understanding why people with epilepsy develop depression, and developing new treatment modalities. Positron emission tomography (PET) is an imaging tool that has the unique ability to measure brain neurotransmitter function. In this study, PET will be used to measure the binding of serotonin to brain receptors that seem to be involved in regulation of mood, and also nerve cell excitability. The investigator will also measure transport of serotonin in and out of nerve cells after it has been released, and when it has taken up again. These studies will be performed in patients with epilepsy with and without depression as well as healthy volunteers. Each of the patients will receive an evaluation of their mood. Since some previous studies have found that patients with a genetic variant in serotonin transport may be more likely to become depressed, patients will be tested for their transporter variant. Brain glucose metabolism with PET will also be measured. This is a standard test to study brain function and help localize seizure foci in people with epilepsy. Brain MRI will be performed in all participants. It is hoped that this study will help understand the cause of depression in people with epilepsy, as well as the role of serotonin.

Name: Joaquin N. Lugo, Ph.D.
Institution: Baylor College of Medicine
Project: Neuroprotective Role for Potassium Channels in Early-Life Status Epilepticus
Preceptor: Anne E. Anderson, M.D.
Lay Summary: Status epilepticus (uncontrollable continuous seizures) is one of the most common diagnoses for children transported to the Pediatric Intensive Care Units at a number of major children's hospitals and is associated with serious long-term consequences. This study is anticipated to provide insight into the mechanism involved in regulating seizure susceptibility and status epilepticus in the developing brain and thereby may identify novel candidate targets for therapeutics in childhood epilepsy.

Name: Sumon Kumar Pal, Ph.D.
Institution: Harvard University
Project: Subtype specific modifications of GABAergic synapses induced by chronic hyperactivity
Preceptor: Venkatesh N. Murthy, Ph.D.
Lay Summary: A decline or loss of inhibitory systems is a widely proposed candidate mechanism in epilepsy. Changes in inhibitory synaptic strength and number will have a large role in regulating the excitability of a circuit, as well as in shaping network oscillations. Although, it has been widely accepted that there is a loss of GABAergic interneurons in both human and animal studies of epilepsy, the consequence of this to remaining GABAergic systems remains unclear. Delineating and mechanisms that govern plasticity in GABAergic synapses is critical for understanding activity-dependant changes in the network as a whole. Both increases and decreases in inhibition have been reported in human and experimental models of epilepsy. Due to the heterogeneity of GABAergic interneurons it is possible that there are subtype specific alterations in inhibitory synapses as a result of hyperactivity. This project will use organotypic slice cultures of hippocampus, which preserve the native organization, and yet allow greater accessibility than in vivo models, to test specific hypotheses. These hypotheses will focus on mechanisms underlying changes in GABAergic synaptic transmission after increased network activity. The investigators will first test if different GABAergic synapses responses respond in distinct ways to chronic changes in activity. Finally, the investigators will investigate potential presynaptic mechanisms underlying modifications in GABAergic synaptic transmission.

Name: Waldemar Swiercz, Ph.D.
Institution: University of Colorado at Denver and Health Sciences Center
Project: CA3 burst initiation and termination hypothesis verification using artificial neural network with releasable glutamate
Preceptor: Kevin Staley, M.D.
Lay Summary: The investigator plans to develop and test using experimental data, a computer model of an area of the brain that is frequently involved in seizure initiation. Using this model, questions will be able to be asked regarding the initiation, spread, and termination of seizures that currently can't be addressed experimentally. It is hoped that with these insights new experiments and possible new treatments for epilepsy will be devised.

Name: Philip Andrew Williams, DVM, Ph.D.
Institution: Case Western Reserve University School of Medicine
Project: Network functions of inner molecular layer neurons
Preceptor: Ben W. Sturbridge, Ph.D.
Lay Summary: Temporal lobe epilepsy is the most common form of epilepsy in adults. The proposed project will investigate the basic network function of currently unstudied neurons in an area in the brain (the inner molecular layer if the hippocampal dentate gyrus) that is actively involved in temporal lobe epilepsy.

Name: Wei Zhang, Ph.D.
Institution: Stanford University
Project: Do somatostatin-immunoreactive interneurons inhibit perforant path excitory input to granule cells in dentate gyrus?
Preceptor: Paul Buckmaster, Ph.D.
Lay Summary: Loss of hilar somatostatin-immunoreactive interneurons (SS+ interneurons) in the dentate gyrus is commonly found in temporal lobe epilepsy. The purpose of this study is to test whether SS+ interneurons control the excitatory input to dentate gyrus. If so, the loss of SS+ interneurons may contribute to the hyperexcitation of granule cells and temporal lobe epileptogenesis.