Postdoctoral Research & Training Fellowship

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Dorian Aur, Ph.D.
Postdoctoral fellow
Stanford University
Stanford, CA, United States

Application Title:
Identification of Features for a Robust Detection of Preictal Phases

General Audience Summary:
Seizures prediction is a critical problem for patients. However, at this time there is no reliable seizure prediction system ready to be used in clinical application. In this project I will use artificial intelligence techniques, a machine learning framework, to analyze and select specific features from neural recorded data in order to improve the robustness detection of preictal states as a step toward the prediction of spontaneous epileptic seizures.

Xiaoxiao Bai, Ph.D.
Associate Research Scientist
Yale University
New Haven, CT, United States

Application Title:
Neuroimaging Biomarkers of Network Dysfunction in Childhood Absence Epileps

General Audience Summary:
We recently found evidence based on functional magnetic resonance imaging resting connectivity, and diffusion tensor imaging that spike-wave seizures give rise to chronic functional and structural changes in both animal models and in human patients. These findings raise the hope that with improved genetic knowledge, early treatment may soon become feasible in human childhood absence epilepsy patients, aimed at preventing chronic brain dysfunction.

Paul Benjamin Bernard, Ph.D.
Post Doctoral Fellow
University of Colorado Denver
Aurora, CO, United States

Application Title:
Impact of Early Life Seizures on the Mechanisms of LTD

General Audience Summary:
Previous research in our lab has indicated that a single episode of early life seizures leads to learning disabilities later in life. These learning disabilities may be the result of changes in learning and memory related mechanisms. Further insight into the magnitude and mechanisms surrounding the changes in long-term depression (a mechanism underlying learning and memory) may provide a basis for effective clinical intervention. The goal of this research is to prevent learning and memory deficits that are observed following early life seizures in children.

William John Brackenbury, Ph.D.
Research Fellow
The Regents of the University of Michigan
Ann Arbor, MI, United States

Application Title:
Regulation of migration by the voltage-gated sodium channel Beta1 subunit

General Audience Summary:
The target of study is the voltage-gated sodium channel (VGSC). VGSCs consist of one large pore-forming protein, the ‘alpha subunit’, together with one or more smaller ‘beta subunits’. The beta-1 subunit functions as a cell adhesion molecule and regulates cell-cell adhesion, outgrowth of neurites, and cellular migration in the developing cerebellum of young mice. Mice lacking beta-1 have epileptic seizures from 14 days after birth. In this study, the candidate will investigate whether migration errors occur in hippocampal neurons from mice lacking beta-1. This will provide important information on the role of beta-1 in relation to epilepsy.

Jerome Clasadonte, Ph.D.
Tufts University
Boston, MA, United States

Application Title:
Suppression of gliotransmission reduces epileptic seizures

General Audience Summary:
In the past decade, our pioneering research conducted in the Haydon Lab has shown that the glial cells, astrocytes, in the brain play a major role in the control of neuronal activity. Consequently, we wonder what would happen if the function of astrocytes was disrupted? Could this affect epileptic seizures? We have genetically modified mice to disrupt selectively the gliotransmission, the process used by astrocytes to communicate with neurons. Interestingly, our preliminary data shows that chemically-induced epileptic seizures in living brain slices obtained from these mice are significantly reduced. This identifies astrocytes as a novel therapeutic target for epilepsy.

Ashish Dhir, Ph.D.
Postdoctoral Scholar
University of California- Davis
Sacramento, CA, United States

Application Title:
Intrapulmonary aqueous propofol prodrugs in acute treatment of seizures

General Audience Summary:
This project lays the groundwork for the development of an inhaler device, like that employed for rescue treatment in asthma, to abort an impending seizure in a person with epilepsy who experiences seizure warning signs. I will obtain information on the ability of new series of water soluble prodrugs of propofol (a powerful anticonvulsant substance) to safely prevent seizures when delivered into the lung. The information to be obtained in this project is intended to form the basis for clinical trials of an inhaler that may eventually allow persons with epilepsy to control their seizures.

David Matthew Feliciano, Ph.D.
Postdoctoral Fellow
Yale University
New Haven, CT, United States

Application Title:
Electrophysiological analysis of a malformation of cortical development

General Audience Summary:
Malformations of cortical development (MCDs) are associated with pharmacologically refractory seizures. MCDs are characterized by abnormal cortical architecture and hypertrophic cells which are present outside of the normal location. The aberrantly

localized cells, referred to as ectopic neurons, may be responsible for epileptogenesis. Tuberous sclerosis complex (TSC) is a representative MCD for which inactivating mutations in two genes, Tsc1 and Tsc2 have been identified as the cause. Using a novel model of TSC I propose to determine the morphology and to measure the electrophysiological properties and map the network circuitry of ectopic neurons. This study will determine the contribution of ectopic neurons to epileptogenesis.

Heidi Louise Grabenstatter, Ph.D
Postdoctoral Fellow
University of Colorado Denver, AMC and DC
Denver, CO, United States

Application Title:
Inhibition of the JAK/STAT pathway: effects on chronic epilepsy

General Audience Summary:
One molecular mechanism potentially responsible for spontaneous seizures that define chronic temporal lobe epilepsy (TLE) will be quantitatively studied by examining Janus Kinase and Signal Transducer and Activator of Transcription (JAK/STAT) protein and mRNA levels in the dentate gyrus of pilocarpine-treated rats. JAK/ STAT signaling will be inhibited in epileptic rats in the pilocarpine model of TLE; and chronic video-electroencephalography (EEG) in correlation with biochemical measurements will be used to determine whether (1) downstream effects of the pathway are altered and (2) progression of TLE and number of spontaneous seizures are reduced.

Daniel Jones, Ph.D.
Postdoctoral Scholar
Duke University Medical Center
Durham, NC, United States

Application Title:
Using remote control of neural activity to explore inhibition and epilepsy

General Audience Summary:
The study of inhibitory brain cells is of vital importance to understanding epilepsy. I propose to study the role of inhibitory systems in the regulation of seizures using “remote control” of neural activity. Using this technique, I will selectively activate specific populations of inhibitory cells, examining the consequences of inhibitory cell activation on seizures and on the function of brain circuits. These experiments will answer long-standing questions in the epilepsy field about the role of inhibitory brain cells in epilepsy.

Kyle Patrick Lillis, Ph.D.
Research Fellow
Massachusetts General Hospital
Charlestown, MA, United States

Application Title:
Functional imaging of post-traumatic epileptogenesis in vitro

General Audience Summary:
In this proposal, we describe a set of experiments in which we use a new model of post-traumatic epilepsy to study how brain circuits are re-wired following injury. Our unique combination of recording techniques and experimental preparations will allow us to image activity in the brain tissue as it becomes epileptic. This strategy will give us insight into both the process of epileptogenesis and the nature of fully formed seizures. Ultimately, we hope to gain information that will be useful in developing treatment strategies that will prevent the onset of epilepsy following brain injury.

Jeanne Tamar Paz, Ph.D.
Postdoctoral Fellow
Stanford University
Stanford, CA, United States

Application Title:
The role of thalamus in epileptogenesis following cortical stroke.

General Audience Summary:
Thalamus is involved in generation of both generalized and focal epileptic seizures in both animal models of epilepsy and in men. Over the past decade most of the emphasis has been made on the role of thalamus in generalized epilepsies. Much less is known about the role of thalamus in the partial epilepsies. This proposal will lead to the first complete study of intra-thalamic anatomical reorganization and synaptic and/or intrinsic plasticity that occur following cortical injuries, leading to a better understanding of the underestimated role of thalamus in post-lesional epileptogenesis.

Timothy Petros, Ph.D.
Postoctoral Associate
Joan & Sanford I. Weill Medical College of Cornell University
New York, NY, United States

Application Title:
Developing a cell based therapy for intractable cortical seizures

General Audience Summary:
Approximately 30% of patients with epilepsy do not respond to current medication, necessitating the search for new therapeutic approaches. In this proposal, we plan to develop a cell-based therapy to treat epilepsy by deriving interneurons from genetically

engineered stem cells that inducibly express the anticonvulsant agent neuropeptide Y (NPY). These NPY-expressing interneurons can then be transplanted into epileptic foci. This approach combines the endogenous inhibitory action of interneurons with the ability to control the temporal and spatial expression of seizure suppression agents, a potentially powerful mechanism for the treatment of epilepsy.

Eduardo Sequerra, Ph.D.
Postdoctoral Scholar
University of California Davis
Sacramento, CA, United States

Application Title:
Neural Tube Defects and Epilepsy: Role of Neurotransmitter Signaling

General Audience Summary:
Antiepileptic drugs (AED) control harmful episodes of electrical activity in the brain of epileptic patients. However, these drugs are capable of crossing the placental barrier. Clinical studies have shown that administration of AEDs to epileptic pregnant women increases the incidence of neural tube defects in their offspring. Neural tube defects consist of failure of neural tissue to fold and form a tube. Our hypothesis is that AEDs impair neural tube formation by interfering with electrical activity of developing fetuses. The information gained from this study may help devising appropriate therapies for epileptic pregnant women and their offspring.

Jamie Joseph Van Gompel, M.D.
Resident Doctor
Mayo Clinic College of Medicine
Rochester, MN, United States

Application Title:
Novel Neurochemical Monitoring for Seizure Detection

General Audience Summary:
Here we propose utilizing advanced electroencephalography with a novel detection technique for neurochemicals named WINCS, which is capable of detecting dopamine and other neurochemicals for the detection and prediction of seizures. In the field of epilepsy, it has been shown that dopamine is elevated during seizures, however its exact temporal relationship is not known. Here we propose the integration of these two technologies to test the hypothesis that dopamine increases prior to the onset of electrographic seizures, and this increase is coincident with high frequency oscillations.