



NEW JERSEY COMMISSION ON  
BRAIN INJURY  
RESEARCH

**DIRECTORY OF GRANT AWARDS  
2010 GRANT CYCLE**

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**JUNE 2010**

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This data was compiled in compliance with the New Jersey Commission on Brain Injury Research's statutory mandate, N.J.S.A. 52:9EE-1“ ...to compile a directory of brain injury research being conducted in the State.”

The information contained within this directory is not all-inclusive. The research projects and researchers listed in this directory are all based in the State of New Jersey and have applied to and received funding during the fiscal year 2010 grant cycle. The research projects are not categorized, or listed in any particular order.

This directory is not a complete listing of all scientific research being performed within the State of New Jersey due to the proprietary nature of the research being conducted at various institutions throughout the State. In addition, institutions are not obligated to share their research information with the New Jersey Commission on Brain Injury Research.

Please feel free to contact the New Jersey Commission on Brain Injury Research at P.O. Box 360, 369 S. Warren Street, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-633-6465, by fax at 609-943-4213, or by e-mail at [NJCBIR@doh.state.nj.us](mailto:NJCBIR@doh.state.nj.us).

For information on the New Jersey Commission on Brain Injury Research's grant award process, grant applications and deadlines, please see: [www.state.nj.us/health/njcbir](http://www.state.nj.us/health/njcbir).

### **2010 MEMBERSHIP INFORMATION**

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# NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

## GRANT AWARDS

### **INDIVIDUAL RESEARCH GRANT RECIPIENTS:**

#### **David I. Shreiber, Ph.D. – Principal Investigator**

Rutgers, The State University of New Jersey

Grant Award: \$495,000

Proposal Title: *Evaluation of Genipin as a Multi-potent Therapeutic Agent Following Brain Injury*

Traumatic brain injury (TBI) begins with mechanical disruption of tissue, which triggers a cascade of secondary insults that injures neurons for days to weeks, and even months, following the initial trauma. While the mechanical trauma can only be avoided by preventing the injury, many of the devastating, long-term functional consequences of TBI may be avoided by therapies that target these secondary effects. Several scientific studies and our preliminary data indicate that genipin, which has been used for years in traditional Chinese medicine, is an anti-oxidant, is anti-inflammatory, protects against the damaging proteins that are present in Alzheimer's disease as well as TBI, and spurs axon and dendrite growth in cellular models. Together, these results suggest that genipin is an ideal candidate for treatment following TBI, but its potency in a relevant model has not been evaluated.

In this proposal, the neuroprotective effects of genipin are first evaluated in a controlled, quantitative, and physiologically relevant model of injury. Slices of brain tissue harvested from newborn rat pups are grown in culture. These 'organotypic' cultures retain the structure and neuronal connections of the tissue in vivo, and allow direct measurement of cell death and neuronal. Organotypic cultures will be injured via specific chemically-induced secondary insults, and via mechanical trauma, and the potential of genipin to protect neurons will be evaluated. Subsequent studies will preliminarily test genipin in a rat model of brain injury. As such, this research meets the funding priorities of the NJCBIR, specifically the study of strategies to promote neuronal growth and survival, encourage the formation of synapses, and improve brain function after injury; and the evaluation of the efficacy of drugs or other interventions that prevent or reduce secondary injury. Additionally, this research is a collaboration between two young scientists, Dr. Shreiber from Rutgers, who specializes in spinal cord injury biomechanics and regeneration, and Dr. Morrison, III, who has developed the novel organotypic injury model and associated technology to record electrical function. As such, the research also meets NJCBIR programmatic objectives by encouraging Dr. Shreiber to return to his roots in TBI research, by fostering collaborative approaches to brain injury research, and by bringing the organotypic model and cortical impact models to Rutgers for the proposed and future brain injury research.

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**Glenn Wylie, Ph.D. - Principal Investigator**

Kessler Foundation

Grant Award: \$374,288

Proposal Title: *Examination of Cognitive Fatigue in Traumatic Brain Injury Using fMRI*

One of the chronic symptoms that affect individuals who have sustained a traumatic brain injury (TBI) is fatigue-not muscle fatigue, but cognitive fatigue, or fatigue that accompanies mental effort. In fact, cognitive fatigue has been shown to be one of the most prevalent, debilitating, and persistent sequelae of a TBI. Despite this, after over 100 years of research, the underlying causes of such fatigue remain unknown. This project seeks to shed light on this important issue by investigating changes in the brain that are associated with feelings of fatigue. By using brain imaging, we will be able to ascertain the brain mechanisms and structures that are active when participants report feeling fatigued. This work is important because it is foundational in establishing an understanding of fatigue. Once the underlying brain mechanisms have been identified, it will be possible to manipulate and study fatigue. This, in turn, will open the door to valuable advances in public health-advances that will benefit individuals who have sustained a TBI by liberating them from the constant, debilitating drain of fatigue.

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**Daniel Osherson, Ph.D. - Principal Investigator**

Princeton University

Grant Award: \$474,836

Proposal Title: *Longitudinal Assessment of Brain Structure and Function in Sports-Related Concussion.*

Researchers and clinicians at Princeton University are conducting a research study investigating the effects of sports-related concussion. Each year, a total of approximately 1.5 million Americans sustain a traumatic brain injury (TBI) and an estimated 300,000 mild traumatic brain injuries (mTBI) or concussions are sports-related, of which approximately 20% continue to suffer from long-term effects. When an individual sustains mTBI or concussion, the head trauma is usually due to contact forces or sudden acceleration, deceleration, or rotation forces acting on the brain. These forces lead to injury of small blood vessels and nerve fibers in the brain causing swelling and transport failure along the nerve fiber. Sports activities and in particular contact sports are a major cause for mTBI or concussion, but these injuries typically occur in the civilian population during falls, violence, or car accidents. In the military setting, the use of improvised explosive devices has significantly increased the number of blast-related mTBI and approximately 300,000 veterans of the wars in Iraq and Afghanistan have sustained mTBI.

So far, the effects of concussion on the structure of the brain are poorly understood. Here we propose to study long-term effects of concussion using novel neuroimaging techniques. We will first identify anatomical alterations in the brain and subsequently investigate how they affect the behavior in individuals who have suffered a concussion.

Results from this study can eventually be used for treatment strategies in individual patients with concussion, in particular in patients with sustained symptoms.

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**Jean Lengenfelder, Ph.D. - Principal Investigator**

Kessler Foundation

Grant Award: \$348,992

Proposal Title: *Examining Apathy, Depression, and Executive Functions in Individuals with TBI*

Traumatic brain injury results in a wide range of physical, cognitive, and behavioral impairments that may persist years after injury. Many researchers and clinicians examine symptoms after TBI in isolation, yet a clear understanding of interaction and influence of different symptoms on one another would enable us to focus treatment efforts and maximize improvement. The current study will do just that. That is, we will examine the presence of apathy (a common behavioral symptom; e.g. lack of motivation), depression (a common psychiatric symptom) and executive abilities (a common cognitive symptom; e.g. difficulty with organization and planning) in a sample of persons with TBI using both traditional behavioral measures (paper and pencil tests of cognitive functions) and more novel imaging techniques (fMRI: an examination of what the brain is doing while a person is completing a task). This study examines apathy, depression, and executive abilities in 90 persons, 30 persons with TBI who have apathy, 30 persons with TBI without apathy and 30 healthy participants. The study will involve two sessions of data collection. First, participants will undergo a paper-and-pencil assessment, which will examine cognitive functions such as memory, attention, planning, and problem solving, as well as some questionnaires assessing depression and apathy. Second, participants will undergo functional magnetic resonance imaging (fMRI), which allows us to examine the brain (i.e., take pictures of the brain working) while performing tasks that assess executive abilities. During the fMRI, subjects will be asked to generate a list of words, respond to different colors of words presented on the screen, and be asked to remember some letters.

A comparison of patterns of activation on the different tasks in individuals with TBI with and without apathy to the activation seen in the healthy volunteers will allow us to identify the source of the apathy seen in TBI and whether or not having apathy affects executive abilities. The results of the present study will provide an in-depth understanding of the changes in the way the brain works in the presence of multiple clinical symptoms (apathy and depression) common in individuals with TBI and the relationship of these symptoms to executive abilities. This knowledge will provide the tools needed for developing and improving treatments that will alleviate these symptoms and thus improve everyday functioning and overall quality of life for persons with TBI.

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## **PILOT RESEARCH GRANT RECIPIENTS:**

**Jean Lengenfelder, Ph.D. – Principal Investigator**

Kessler Foundation

Grant Award: \$148,275

Proposal Title: *Aging in Traumatic Brain Injury: A Pilot Study of Cognitive and Cerebral Profiles*

Traumatic brain injury can result in long; lasting cognitive problems. One area of research that is significantly lacking is an accurate understanding of what happens to individuals who have already sustained a TBI as they age, and researchers have found that certain cognitive abilities such as working memory, processing speed and higher level executive abilities like planning, reasoning, and judgment are sensitive to age-related changes. The current pilot study will begin to fill the void in the research by using both traditional behavioral measures (paper and pencil tests of cognitive functions) and more novel imaging techniques (fMRI: an examination of what the brain is doing while a person is completing a task) to examine the effects of aging in TBI in three cognitive areas known to be susceptible to age-related changes; working memory, processing speed, and executive abilities, using paradigms that have been established in healthy older individuals.

This pilot study will evaluate 15 older individuals with TBI, 15 younger individuals with TBI, and 15 older healthy participants. The study will involve two sessions of data collection. First, participants will undergo a paper-and-pencil assessment, which will examine cognitive functions such as memory, attention, planning, and problem solving. Second, participants will undergo a functional magnetic resonance imaging (fMRI), which allows us to examine the brain (ie., take pictures of the brain working) while performing particular cognitive tasks that assess executive abilities. During the fMRI, subjects will be asked to respond to different pictures on a screen, respond to different colors of words presented on the screen, and be asked to remember some letters.

A comparison of patterns of activation on the different tasks in the older individuals with TBI to the activation seen both in the younger individuals with TBI and the older healthy volunteers will allow us to identify whether the impact of age in TBI has different patterns of activation and performance. The results of the present study will provide an in-depth understanding of the changes in the way the brain works as people age with a TBI. This knowledge will provide a better understanding of whether interventions or treatments would affect younger and older persons with TBI differently with the ultimate goal of improving everyday functioning and overall quality of life for persons with TBI.

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**Anthony Lequerica, Ph.D. - Principal Investigator**

Kessler Foundation

Grant Award: \$97,206

Proposal Title: Pilot Study: *The Effect of Rozerem on Sleep Disturbance After Traumatic Brain Injury*

Sleep disturbance is a large problem among many individuals who have sustained a traumatic brain injury (TBI). In addition, individuals with TBI tend to report higher levels of daytime sleepiness, fatigue, anxiety, and depression, all of which have been associated with poor occupational outcomes.

Most of the current sleep aids commonly prescribed by physicians have side effects likely to worsen many of the symptoms individuals typically report after TBI, such as problems with attention, memory, and fatigue. In addition, common sleep medications can easily lead to addiction because of the way they affect the brain. Rozerem is a medication that acts on the brain's natural sleep/wake center to affect sleep. It avoids many side effects that other drugs can cause and is indicated for the long term treatment of insomnia with little risk for abuse or dependence. To date, there are no studies that have examined the effect of Rozerem on sleep disturbance among individuals with TBI. This study proposes to see how Rozerem can improve the sleep of individuals with post-TBI sleep difficulties compared with a sugar pill. To remove bias, the participant will not be told whether they are taking the drug or a sugar pill. To measure the rest/activity cycle and sleep quality, an actigraph (sensitive motion detector) will be used. The effect of treatment on the participant will be measured using questionnaires about mood, fatigue, and sleepiness. A battery of tests to look at forgetfulness, attention span, and speed of thinking and responding will look at how the participant's mind is working during the daytime.

Each year, 12,000 to 15,000 people sustain a TBI and there are approximately 175,000 people in New Jersey currently living with disabilities and/or other consequences related to their TBI. This pilot study will provide information that can potentially lead to improved measurement and treatment of sleep disturbance commonly seen after TBI. Successful treatment of sleep disturbance is likely to result in improved mood and performance during the day which could lead to improved subjective well-being and health-related quality of life for individuals who have a traumatic brain injury.

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## **FELLOWSHIP GRANT RECIPIENTS:**

### **Yi Pan, Ph.D. - Principal Investigator**

Rutgers, The State University of New Jersey

Grant Award: \$192,324

Proposal Title: *A FEM Kinematic Model for Brain White Matter*

A novel model, which accounts for the interacting between the axon and the surrounding matter, is proposed to capture the mechanical response of brain tissue at microscale level. This model enables evaluation of the injury state (e.g., partial recovery of the neurological functions or irreversible damage) of the patient and provides accurate insight into a spatial location of the injury for medical treatment. The brain white matter, that consists mostly of fiber-like axons, and random fiber composites share common features, from the perspective of mechanics. So the former is treated as a "composite material", in which the undulated, reinforcing axon fibers are embedded within a supportive tissue matrix comprised primarily of glia. To determine the mechanical properties of the brain tissue, we will adopt the well developed composite mechanics and micromechanics as well as the finite element method to the microstructure interacting model.

First, a representation of the brain white matter will be generated using a random sequential adsorption method, which randomly adds axon fiber into a fixed volume according to the geometry and orientation of the axon fiber. The geometric description of the axon and the surrounding tissue matrix is obtained from the neurofilament images. Second, the kinematics of the axon that describes the interacting of the axon and the surrounding matter under different stretch will be embedded into this model. The nodal kinematic coupling of axon fibers will be dynamically modulated to the surrounding matrix within representative volume elements using stochastic models.

Third, hyperelastic material constitutive models, which depict the material response to external loading, will be applied to describe the behaviors of the axon and surrounding matrix, respectively.

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**Carolyn M. Tyler, Ph.D. – Principal Investigator**

Princeton University

Grant Award: \$192,324

Proposal Title: *Investigating the Role of MHC Class I Proteins in Traumatic Brain Injury*

Traumatic brain injury (TBI) afflicts roughly 1.4 million US citizens each year and can cause long-term functional changes to the brain that disrupt normal thinking, perception, and emotions. Despite the fact that approximately 2% of the US population has long-term effects of TBI severe enough to prevent normal daily functioning, TBI is poorly understood and there are very few treatments to prevent or reduce the functional deficits observed in TBI patients. The primary injury in TBI is a blow to the head or penetrating injury to the brain which damages the cells of the brain required for normal information processing (neurons). However, following the initial injury, there is a second prolonged phase of injury in which increased release of brain chemicals causes damaging overstimulation of the neurons around the injury site. This process compounds the severity of the initial injury and results in increased functional deficits following TBI.

Therefore researching this secondary phase of injury could lead to the development of therapeutic strategies that could be applied after the initial injury to decrease neuronal damage and lead to better functional recovery. Recently, a family of genes that normally play a role in the immune system have been shown to unexpectedly regulate specific brain receptors that mediate the secondary injury in TBI. Since these immune genes limit activation of these receptors it is possible they are a natural neuroprotective agent against damaging overstimulation of neurons. However, it is currently unknown if these immune genes regulate TBI-induced receptor overactivation, or the subsequent neuronal damage. This proposal seeks to understand the role of this immune gene family in the pathophysiology of TBI and its utility in the development of therapeutic strategies for treating TBI.

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