



NEW JERSEY COMMISSION ON  
BRAIN INJURY  
RESEARCH

**DIRECTORY OF GRANT AWARDS  
2011 GRANT CYCLE**

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**JUNE 2011**

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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 2011 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).

### **2011 MEMBERSHIP INFORMATION**

Dennis Benigno  
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Christine Traynor, Administrator  
Mary Ray, Fiscal Manager

# NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

## GRANT AWARDS

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

**Haesun Kim, Ph.D.**

**Rutgers, The State University of New Jersey**

**\$540,000**

Project Title: *The Effects of Diffused Axonal Injury on Myelin and Myelinated Axons*

Traumatic brain injury (TBI) is one of the most common and devastating conditions in our society. An important and frequent component of TBI is diffuse axonal injury (DAI), which mostly affects myelinated axons in the white matter. Previous studies have attempted to elucidate the mechanism of DAI and its effects on the axons, however, not much is known about the DAI effects on myelin. It is also unknown how the presence of myelin affects the progression of axon pathology after DAI. Myelin plays a crucial role in maintenance of brain homeostasis and is vital for neuronal survival. Therefore, damages to the myelin, or progressive demyelination following DAI could result in long-term axonal loss.

The long-term objective of the present study is to investigate the pathologies of myelinated axons and myelin after DAI. We hypothesize that myelin alters the axonal response to DAI by modulating axon elasticity, ionic influx and survival, thus the overall progression of the axonal damage. To test this hypothesis, the study will focus on two specific aims; 1) to investigate the effects of DAI on myelinated axons and 2) to investigate the effect of DAI on myelin and oligodendrocytes. We will also investigate whether the injured surviving axons after DAI can support oligodendrocyte differentiation and remyelination.

A key to our study plan is an in vitro axonal stretch injury model that closely reproduces many of the morphological and ultra-structural changes on axons following DAI in vivo, combined with an in vitro oligodendrocyte myelinating culture system. This innovative system allows us to generate DAI on myelinated axons, thus mimicking the white matter damage in vivo. Injury responses of the myelinated axons and the oligodendrocytes will be determined using morphological, biochemical and immunocytochemical analyses. Results from the study are likely to provide in depth insights into understanding TBI-associated progression of the white matter damage and the development of therapeutic strategies for white matter repair.

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**Denise Krch, Ph.D.**  
**Kessler Foundation**  
**\$378,917**

Project Title: *Cognitive Reserve in Traumatic Brain Injury*

Cognitive impairment is the leading cause of disability following Traumatic Brain Injury (TBI), with impairments in memory and executive function as the most common cognitive deficits. Such deficits exert substantial negative impact on occupational and social functioning. To date, however, etiological factors are weakly associated with neuropsychological outcomes. The theory of Cognitive Reserve (CR) may serve to explain this disconnect. According to CR theory, life experiences, such as educational attainment, result in greater capacity and efficiency of neural networks. When cognition is challenged by neurologic disease or injury, individuals with greater CR are able to withstand greater neuropathology/disease severity before incurring cognitive deficits. CR theory has been supported in other neurologic populations (e.g., Alzheimer's disease, multiple sclerosis), but its relevance in TBI is unclear. If the mechanisms responsible for different outcomes in cognitive function following TBI are to be determined, the impact of CR on the neuropathology-cognition relationship must be understood. This proposal represents an important step in assessing this relationship.

Therefore, the goal of the proposed study is to determine whether higher cognitive reserve provides protection against the negative consequences of TBI pathology in regard to cognitive functioning. To achieve this goal, 65 individuals with TBI will undergo a neuropsychological assessment of cognitive reserve, memory, and executive function, and a magnetic resonance imaging scan, from which cerebral atrophy and white matter integrity measures will be collected. An analysis of the relationship between these variables will clarify whether persons with higher intellectual enrichment are less vulnerable to the negative cognitive effects of TBI. This knowledge will facilitate future research investigating whether intellectual enrichment following a TBI can be used to build reserve.

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## **MULTI-INVESTIGATOR RESEARCH GRANT RECIPIENT:**

**Bryan Pfister, Ph.D.**  
**New Jersey Institute of Technology**  
**\$1,639,522**

Overall Project Title:

*Investigation of Physiological Dysfunction from Repetitive Mild Head Injury*

An estimated 2 million traumatic brain injuries (TBI) occur each a year. Many of these people do not seek medical attention as only 500,000 are hospitalized or their case is deemed too mild to prescribe treatment. Among all types of injuries, TBI is the most likely to result in permanent disability affecting a person cognitively, physically and emotionally that greatly impacts their everyday life. Mild TBI does not cause damage that can be revealed by neurological imaging so diagnoses are often missed or uncertain. However, mild injuries do inflict unknown changes to brain function. More importantly, serious consequences can arise when repetitive mild head injuries occur, as the initial insult makes the individual more vulnerable to subsequent injuries. The duration of the vulnerability period is particularly important when evaluating return to play decisions in a sport or active military duty. We believe that pervasive deficits associated with mild injuries result from injured and dysfunctional neurons that negatively impact overall brain function. Unfortunately, compared to severe forms of TBI, little is known about the consequences of mild and repetitive TBI on brain function and behavior.

This proposal will take a multi-faceted approach to analyzing changes in neuronal signaling and behavioral due to single and repetitive mild head injuries. The three investigators in this proposal bring a complement of expertise in TBI modeling, anatomical evaluation, neural engineering, neurophysiology and behavior. Our joint efforts will test our hypothesis that mild and repetitive TBI causes physiological changes in neurons and neural circuits without clear loss of brain cells. These physiological changes will be linked to behavioral impairments, in particular learning, memory and motor function. The studies of this proposal will provide a comprehensive analysis of the effect of mild and repetitive TBI from individual neurons to the complex behavioral level.

Sub-Project 1: Investigation of Persistent Electrophysiological Dysfunction of Mild and Repetitively Stretch-Injured Axons. **Bryan Pfister, Ph.D., New Jersey Institute of Technology**

Implement an animal and tissue culture model to describe the anatomical and physiological effects of mild and repetitive head injury. We will focus on three endpoints: a single percussion that produces detectable histopathology, a single percussion that is just below the threshold to produce detectable histopathology (sub-threshold), and repetitive sub-threshold exposure.

Sub-Project 2: Effect of Mild, High Rate & Repetitive Brain Injury on Hippocampal Circuits.  
**Vijayalakshmi Santhakumar, Ph.D., University of Medicine & Dentistry of New Jersey –  
New Jersey Medical School**

Investigate *in vitro* and *in vivo* electrophysiological alterations in the neural circuits following single mild TBI at increasing rates and repetitive sub-threshold exposure to concussive pressures. Using different approaches, we will investigate the alterations in the biophysical and synaptic characteristics of neurons that survive a single or repetitive sub-threshold injuries and their effect on neuronal circuit function.

**Sub-Project 3: *Repetitive Mild Traumatic Brain Injury: Effects on Brain Rhythms, Learning & Memory.* Kevin Pang, Ph.D., New Jersey Institute of Technology**

Describe network and behavioral changes resulting from single and repetitive mild head injuries. We hypothesize that a major effect of repetitive mild head injuries is to impair the function of long axons pathways. Using electrophysiological recordings from animals performing learning and memory tasks, we will evaluate critical parameters of mild TBI that alter synchronization of neural networks, learning and memory.

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## **FELLOWSHIP RESEARCH GRANT RECIPIENTS:**

**Akshay Gupta, M.D., Ph.D.**

**University of Medicine and Dentistry of New Jersey**

**New Jersey Medical School**

**\$209,808**

Project Title: *Role of Semilunar Granule Cells in Post-Traumatic Hyperexcitability*

The incidence of traumatic brain injury (TBI) from falls, traffic accidents, assault, combat injuries, and sports is constantly on the rise. Recent reports estimate over 1.7 million TBI cases in the U.S. each year resulting in an annual economic burden beyond \$60 billion. TBI is a major risk factor for several chronic disorders such as temporal lobe epilepsy and memory and cognitive dysfunction. Earlier studies have suggested that increases in excitability of the hippocampal dentate gyrus after brain injury could underlie post-traumatic epilepsy. However, the mechanisms contributing to dentate network hyperexcitability after TBI remain obscure.

Recently, a novel class of hippocampal dentate excitatory neurons, the Semilunar Granule Cells (SGCs), have been identified and suggested to play a crucial role in hippocampal memory formation and circuit function. SGCs share several structural features with granule cells (GCs), the dentate projection neurons. Additionally, their critical location in the dentate input pathway, connectivity to inhibitory neurons, and persistent firing properties make them key players in prolonged dentate inhibition. I hypothesize that brain injury leads to changes in excitability and synaptic connectivity of SGCs and that these alterations contribute to post-injury dentate dysfunction. The proposed study will determine the changes in the structure, and physiological behavior of SGCs after moderate concussive brain injury and examine if these changes contribute to dentate network hyperexcitability after brain injury. My experiments will reveal whether a novel class of excitatory neurons could be targeted to prevent post-injury seizures and memory related disorders which contribute to long-term morbidity and major socioeconomic burden not only on the caregivers, but whole New Jersey.

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## **PILOT RESEARCH GRANT RECIPIENTS:**

**Mark Pinsk, Ph.D.**  
**Princeton University**  
**\$179,994**

Project Title: *Cortical Lesion Effects on White Matter Connectivity: DTI of the Macaque*

Two significant challenges in neuroscience are to understand (1) how exactly different brain areas are connected to convey information, and (2) how these connections change as a result of injury and rehabilitation. In the past decade, a brain scanning technique known as diffusion tensor imaging (or DTI) has been developed that allows researchers and clinicians to visualize the interconnections of the human brain in a safe and non-invasive manner. This is a valuable new technology that can be used to look at changes of brain organization following an injury; however, the results from DTI are often difficult to interpret because we know very little about the detailed anatomical organization of the human brain. Furthermore, researchers who wish to study patients with brain injuries have additional difficulties in interpreting the data because they do not have images of the patients' brains before the injury has occurred, and the size and location of a brain injury varies from patient to patient, making generalizations of the data difficult.

To advance our understanding of how the brain changes after it is injured, we propose a line of research that uses an animal model (i.e. macaque monkey) to study brain injury. Animal models are advantageous because we have very detailed knowledge of their anatomical brain organization. With an animal model, we can circumvent the above problems researchers encounter with human patients, and study the same brain systematically both before and after injury. Such studies will provide an unprecedented bird's eye view of the brain as it recovers from injury, and provide valuable insights on how the brain reorganizes its networks. In the end, this knowledge will help researchers and clinicians develop better models of recovery from brain injury due to trauma or stroke.

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**Chi Kwan Tsang, Ph.D.**  
**University of Medicine & Dentistry of New Jersey**  
**Robert Wood Johnson Medical School**  
**\$180,000**

Project Title: *Regulation of Neuronal Regeneration and Survival by mTOR*

Traumatic brain injury (TBI) is caused by motor vehicle accidents, falls, assaults, stroke, self-inflicted injuries. Each year, approximately 12,000 New Jersey residents are afflicted with TBI, which cannot only result in death but also have devastating long-term effects on those who survive. TBI causes significant mechanical damage to neurons (brain cells) at the site of injury. This primary mechanical damage is typically followed by a secondary phase of slow progressive cell death. It was thought that the neurons in the adult central nervous system cannot regenerate after injury because of the presence of extrinsic inhibitory factors inside the adult brain.

However, exciting recent findings from animal models have shown that the activation of a protein called “mammalian target of rapamycin (mTOR)” inside the neurons can promote their regeneration and survival after brain injury. Recent scientific evidence also revealed that mTOR plays a crucial role in regulation of neuronal cell size, formation of new neuronal branches and various forms of synaptic connections. These encouraging results clearly demonstrate that mTOR plays an essential role in promoting brain cell repair and regeneration after TBI. However, how mTOR regulates these important processes in injured brain cells remains unclear. Preliminary data in our laboratory have suggested that mTOR promotes neuronal regeneration by transcription (the first important step leading to gene expression) and we also identified a major protein target of mTOR for its function. In this project, we will elucidate the molecular mechanism by which mTOR promotes neuronal regeneration and survival after TBI. More importantly, we will identify the effective molecular and gene targets for promoting neuronal regeneration and survival after TBI. Completion of this pilot research will be important for developing effective interventions to stimulate neuronal regeneration and restore brain functions after traumatic brain injury.

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