DIRECTORY OF GRANT AWARDS
2014 GRANT CYCLE

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

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JUNE 2014

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

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 2014 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.

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.

2014 MEMBERSHIP INFORMATION

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NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENTS:

Wilma Friedman, Ph.D. Grant Award: $540,000
Rutgers, The State University of NJ
Life Science Center

Project Title: *Mechanisms of Neuronal Dealth Following Traumatic Brain Injury*

We will investigate the role of the p75 neurotrophin receptor, an established death receptor that is induced in neurons after injury, in mediating neuronal loss following traumatic brain injury.

Traumatic brain injury (TBI) is a leading cause of death and disability, resulting from relatively common occurrences, such as car accidents, falls, sport and work related injuries, and firearms among others. The effects are far-reaching and detrimental, often disrupting cognitive function and normal routines, and causing long-term debilitating effects in memory, reasoning, sensation, language abilities, and emotional understanding. There are currently very limited methods for improving outcomes.

Primary damage following TBI occurs in the tissue directly in the area of impact, involving mechanical damage to brain cells. However, the secondary damage in the regions surrounding the area of impact may evolve over hours and days after the initial injury, resulting in delayed loss of brain neurons, which contributes to functional impairment. These delayed changes offer a therapeutic window for intervention to minimize this neuronal loss. Therapeutic strategies to minimize neuronal loss may prevent excessive cognitive deterioration over time following an injury. Such strategies require understanding the mechanisms that govern the neuronal death that occurs following TBI.

The goal of these studies is to define mechanisms of neuronal loss and identify inhibitors that are efficacious in TBI.

Contact Information:
Wilma Friedman, Ph.D.
Rutgers, The State University of NJ
Life Science Center
225 University Avenue
Newark, NJ 07102
973-353-1160
wilmaf@andromeda.rutgers.edu

Bonnie Firestein, Ph.D.
Rutgers, The State University of NJ
Cell Biology & Neuroscience

Grant Award: $500,999

Project Title: *Targeting Cypin for Functional Recovery Following Traumatic Brain Injury*

We will target the protein cypin to promote nerve cell connectivity and neurobehavior after traumatic brain injury.

Traumatic brain injury (TBI) is the leading cause of death in people under 45 years of age in the United States and continues to have an enormous impact on public health. Although some progress has been made in reducing the annual incidence of TBI, a majority of this progress is in brain injury prevention, and there remains a tremendous need to develop therapeutics for TBI to improve outcome and lower the morbidity associated with the disease.

In this proposal, we use a coordinated approach of in vitro models of TBI, complemented with in vivo experiments, to rapidly screen potential therapeutic agents for TBI.

Here, we study the role of cypin, a protein shown to affect nerve cell survival in models of stroke and disease, in protecting function of nerve cells after TBI. We will evaluate if altering cypin protein levels both in culture and in the animal, or if administering novel cypin activators to animals keeps the neurons communicating in the same way that they did prior to injury.

Contact Information:
Bonnie Firestein, Ph.D.
Rutgers, The State University of NJ
Cell Biology & Neuroscience
Nelson Biological Laboratories
604 Allison Road
Piscataway, NJ 08854
732-445-8045
firestein@biology.rutgers.edu

Jennifer Buckman, Ph.D.
Rutgers, The State University of NJ
Center for Alcohol Studies

Grant Award: $537,095

Project Title: *Validating Heart Rate Variability as an Objective Measure of Traumatic Brain Injury Symptom Severity and Recovery to Inform Physicians Return-to-Play Decisions*

This project measures heart-brain signaling following a sports-related traumatic brain injury (TBI) to improve predictions of symptom recovery and add neurocardiac evidence to support clinical return-to-play decisions.

Superior athletic ability depends strongly on the coordination of body and brain signals. The heart and brain, for example, must be in continual communication to ensure that sufficient blood flow and blood pressure are available to carry out the feats of physical and mental acuity expected in elite athletic competition. An objective and quantitative measure of bidirectional heart-brain communication is heart rate variability (HRV), the variability in the time interval between heartbeats. High HRV is associated with better physical and mental health because it suggests that the heart and brain are capable of making quick and efficient changes in response to challenges, and then rapidly returning to the resting state. Substantial research demonstrated that TBI impairs heart-brain communication, but little attention has been paid to how this disruption in communication influences risk for and recovery from sports-related TBIs.

Sports-related TBI is a major public health concern based on evidence that repeated mild brain injuries can have both immediate and long-term neurocognitive and psychosocial repercussions. The proposed project addresses this important issue in NCAA Division I athletes from Rutgers, The State University of New Jersey using a non-invasive, objective, and highly sensitive 10-minute assessment of HRV prior to (n= 1000) and following (n = 200-250) a sport-related TBI.

The goal of this project is to determine whether measurement of HRV can improve TBI risk assessment, severity determination, and/or return-to-play decisions, and is an extension of an ongoing collaboration between Rutgers, Department of Sports Medicine and Cardiac Neuroscience Laboratory. The potential "translational" impact of this project is high because its results can be directly applied to real world clinical decisions that affect the lives of student athletes who suffer TBIs as well as others who suffer a TBI unrelated to sports.

Contact Information:
Jennifer Buckman, Ph.D.
Rutgers, The State University of NJ
Center for Alcohol Studies
607 Allison Road
Piscataway, NJ 08854-8001
732-445-2190
jbuckman@rutgers.edu

Vijayalakshmi Santhakumar, M.D., Ph.D.
Rutgers, The State University of NJ
Biomedical & Health Sciences
New Jersey Medical School

Grant Award: $534,918

Project Title: *Roll of Toll-Like Receptors in Post-Injury Hippocampal Microcircuit Dysfunction*

Using an animal model of brain injury, the study will examine if and how modulation of innate immune receptors, Toll-Like Receptors, alleviates hippocampal dysfunction following traumatic brain injury.

There are over 1.7 million cases of civilian brain injuries in the United States with over 12,000 annual cases in the State of New Jersey. Brain injury poses an increasingly significant health issue due to the wide spectrum of injury strengths and because even mild injuries can lead to neurological disorders such as epilepsy and memory loss several years after the precipitating trauma. Post-traumatic neurological disorders pose a particularly huge problem in injured combat veterans, since the likelihood of long-term neurological complications increases with the severity of injury.

The goal of this project is to determine how the immune response to cellular injury products contributes to the structural and functional alterations in the hippocampus after brain injury. Using a combination of anatomical and physiological experiments in an animal model of concussive brain injury, the project will examine changes in the expression of certain immune receptors (Toll-Like Receptors), known to be present in neuronal and glial subtypes, after brain injury. The study will test whether drugs modulating these receptors administered after brain injury could prevent the abnormal increases in excitability and memory dysfunction observed after brain injury.

In addition, the project will identify crucial mechanisms by which immune receptor activation affects neuronal function. It is anticipated that the proposed studies will identify the role for perturbed immune response in post-traumatic pathology and generate new treatment avenues to improve the long-term neurological outcome after traumatic brain injury. Such preventive strategies will greatly improve the quality of life of patients after brain injury and decrease the economic burden that this debilitating condition places on the state health care system.

Contact Information:
Vijayalakshmi Santhakumar, M.D., Ph.D.
Rutgers, The State University of NJ
Biomedical & Health Sciences
New Jersey Medical School
185 South Orange Avenue
Newark, NJ 07103
973-972-2421
santhavi@njms.rutgers.edu

FELLOWSHIP RESEARCH GRANT RECIPIENTS:

Matthew Long — Grant Award: $100,500
New Jersey Institute of Technology

Project Title: *Intra-Day Repetitive Sub-Concussive Injuries will Manifest in Structural Alterations and Behavioral Deficits*

This project aims at defining a model of a subconcussive insult and the effects of cumulative subconcussive insults on neuropathology and behavior. It is estimated at 1.7 million traumatic brain injuries (TBI) a year occurs in the U.S. annually, of which 80% are classified as mild traumatic brain injury (mTBI).

Concussion is often used as a synonym for mTBI. Immediate consequences of concussion may affect cognition or motor functions, such as dizziness, headaches, confusion, and loss of coordination, mobility and memory. Athletes and military personnel that engage in contact activities are already at an increased risk of sustaining mTBI or concussion. In addition, these activities make an individual more susceptible to repetitive subconcussive injuries. A single subconcussive insult may not produce a detectable injury to the brain or diminish brain function; however, repeated subconcussive insults may manifest into an injury.

In the lay media, reports on former football players' battles with depression, early onset of dementia and suicide at a young age, have drawn more attention to the nature of repetitive impacts, of which, these athletes sustain over their career. Understanding what a subconcussion entails and the cumulative effects are difficult to ascertain. Some important parameters of repetitive injury include the magnitude on injury, number of injuries and duration between injuries. A general definition of subconcussion is below the threshold of concussion; however, establishing what that threshold is in a clinical setting is difficult to obtain.

We have created a novel injury device for animal models, which can generate low impact magnitudes in repeatable instances. We will use this device to model what a subconcussion is based on acute behavioral and cellular biomarkers. Once we establish our definition of subconcussion, we will assess intra-day cumulative subconcussive insults to simulate what an athlete (in contact sport) experiences during a game. Using behavioral and cellular markers, we predict impaired deficits in behavior and neuropathology. This is the first step towards understanding cumulative subconcussive impacts over a season and potentially a career.

Contact Information:
Matthew Long
New Jersey Institute of Technology
University Heights
Newark, NJ 07102
mtl4@njit.edu

Vanisha Lakhina, Ph.D.
Princeton University
Lewis Sigler Institute for Integrative Genomics

Grant Award: $217,872

Project Title: *Identifying Genes that Confer Injury-Induced Regenerative Ability to Aging Neuronal Axons*

We aim to identify key genes that confer regenerative ability to older axons that do not normally regrow upon injury.

Patients with various types of traumatic brain injury (TBI) commonly suffer damage to central and peripheral nerves due to injury to their axons; long cables that conduct electrical impulses and transmit information between two neurons. Axonal peripheral neuropathy, caused by peripheral nerve damage, is a very painful condition that develops in the hands, arms, feet and legs leading to numbness, weakness and slower reflexes. Regrowing injured axons to restore function is a potential therapy that would greatly improve the lives of TBI patients, regardless of the specific type of brain injury.

When adult axons of the peripheral but not central nervous system (CNS) are injured, they readily regrow across short distances and recover function. Remarkably, young axons (including CNS axons) regenerate efficiently, whereas old axons do not. This is due to an age-dependent loss of the axon's intrinsic regenerative ability. The variables that determine a axon's intrinsic regrowth capacity remain poorly defined at a molecular level. Harnessing the inner regenerative potential of axons to make them regrow upon injury would be a ground-breaking therapy which could potentially help about 1.7 million people in the United States, and about 12,000 in New Jersey, who are annually affected by TBI.

The nematode C. elegans has been used extensively in axonal regeneration studies for various reasons. The basic biology of axon regenerative growth is conserved between C. elegans and vertebrates. Every neuron in C. elegans can be consistently identified, thus researchers can specifically injure the same axon across different animals, which reduces experimental variability. Identifying the same neuron in different animals is impossible to do in higher organisms. Researchers can conduct large-scale genetic and chemical screens for factors affecting axonal regrowth upon injury in C. elegans. Such large scale screens are expensive and difficult to do in higher organisms.

Interestingly, when the gene encoding a specific protein called Dual Leucine zipper Kinase 1 (DLK-1) is expressed in middle aged neurons, their ability to regenerate axons upon injury is restored. This provides the proof-of-principle that it is possible for older axons to regenerate, when provided with the right molecular cocktail. We aim to identify key regeneration-associated genes such as the previously discovered DLK-1 that mediate the regrowth of young axons upon injury, and whose expression can restore regenerative capacity in older axons that do not normally regenerate. In the future, these genes will be tested for a role in the regrowth of vertebrate axons, for the ultimate goal of creating novel axonal regeneration based therapies for TBI patients.

We will first characterize the relationship between neuronal age and the ability of its axon to regenerate upon injury. To do this, we will test the regenerative capacity of mutant animals that display reduced or accelerated aging. We predict that mutants whose neurons age slower than

normal can regenerate axons well into old age, while mutants whose neurons age faster have reduced regrowth ability, even at larval stages. Next, we will use a technique developed in our laboratory to identify genes whose expression is correlated with increased regenerative capacity. We will test the ability of these genes to confer regenerative capacity to older axons. We will also examine whether conferring regenerative capacity on older axons alters their rate of aging, which is relevant from a therapeutic perspective.

This project will be the first to directly assess how modulating neuronal age affects the ability of its axon to regenerate upon injury. We will also be the first to systematically define the essential molecular machinery required to induce the regenerative program in axons that do not normally regrow upon injury. Our data will provide novel targets for future studies of vertebrate axonal regeneration.

Contact Information:
Vanisha Lakhina, Ph.D.
Princeton University
Lewis Sigler Institute for Integrative Genomics
148 Carl Icahn Laboratory
Washington Road
Princeton, NJ 08544
609-258-9396
vanisha@princeton.edu

Julia Coyne, Ph.D. Grant Award: $240,910
Kessler Foundation

Project Title: *Applying Cogmed to Improve Working Memory Abilities in Children and Adolescents after Traumatic Brain Injury*

The proposal will examine the efficacy of Cogmed, an application created to improve working memory (WM) in children with TBI as measured by neurological tests of WM and other measures of functioning.

Following TBI in children and adolescents, damage to the brain results in significant impairment in attention, working memory (WM), processing speed, and executive functions. WM impairment is one of the most commonly reported difficulties experienced by children and adolescents post-TBI, contributing to long-term deficits in academic growth and negatively impacting quality of life. In children and adolescents post-TBI, impairments in WM are by far the most common and disabling outcomes of brain injury and such deficits have been shown to have a negative impact on academic and social functioning.

Cogmed is a commercially available, computer-based training program designed to improve working memory. Though Cogmed has substantial data demonstrating its effectiveness in adult and pediatric populations, it has yet to be studied in pediatric TBI. The current study will do so by examining changes in objective cognitive functioning from pre- to post- Cogmed treatment, as well as changes in everyday life functioning as a result of treatment in a randomized clinical trial (RCT).

In this study, 40 children and adolescents with a documented history of TBI and memory impairment will be included. They will be randomly assigned to either a treatment group or a wait list control group. The treatment group will receive the Cogmed WM training program 30-40 minutes per day, 5 days a week for 5 weeks for a total training time of approximately 15 hours. The wait list control group will have no contact for 5 weeks, and then will begin treatment with Cogmed. All participants will complete the same battery of tests following Cogmed training after the 7th week), and again after the 13th week of study participation to examine post treatment changes in working memory and the stability of these changes over time.

This study will have a significant impact on the clinical care of children with TBI by demonstrating the effectiveness of a treatment program used in other populations to improve WM. Such research is at the heart of the NJCBIR priorities and will serve to improve the overall quality of life and intellectual advancement of children with TBI.

Contact Information:
Julia Coyne, Ph.D.
Kessler Foundation
300 Executive Drive, Suite 70
West Orange, NJ 07052
973-324-8455
jcoyne@kesslerfoundation.org

Pelin Avcu
Rutgers, The State University of NJ
Biomedical & Health Sciences
New Jersey Medical School

Grant Award: $100,500

Project Title: *Understanding Maladaptive Coping after Mild Traumatic Brain Injury in Rats*

The goal of this project is to identify maladaptive stress coping after mild traumatic brain injury (mTBI) and determine whether these changes are responsible for persistent emotional sequelae.

Approximately 12,000-15,000 New Jersey residents sustain traumatic brain injury each year due to motor vehicle crashes, falls, assaults, and self-inflicted injuries. Mild traumatic brain injuries account for 75-90% of traumatic brain injuries each year. Soft signs such as headaches, dizziness, tinnitus, nausea and/or vomiting occur immediately after sustaining mTBI, but are generally resolved within a short time frame. To date, most research has focused on long-term consequences of moderate to severe injuries. Yet, recent studies have shown that a significant minority of mTBI patients continue to experience physical, cognitive, and emotional symptoms such as difficulties in attention, concentration and memory, as well as sleep disturbances, depression and anxiety. This broad constellation of persistent symptoms is collectively termed post-concussive syndrome (PCS), and can develop over a course of years.

Medical decisions for 'return to work', 'return to play' or 'return to duty' have been made based on mTBI patients' self-report of symptoms and neurocognitive testing. However, mTBI may also produce symptoms that manifest below the level of an individual's self-awareness. An example of such a symptom can be maladaptive coping.

Coping with stressors is crucial to maintain a good quality of life. Research reported that poor stress coping in mTBI populations is associated with the development of impaired cognitive functioning and emotional complains. To date, the effectiveness of coping strategies and its role in stress regulation have not been studied in mTBI populations. The proposed studies will determine whether mTBI reduces the ability to predict and avoid stress in rats. The results will help inform strategies for therapeutic interventions aimed at improving the chronic emotional sequelae that may develop after mTBI.

Contact Information:
Pelin Avcu
Rutgers, The State University of NJ
Biomedical & Health Sciences
New Jersey Medical School
Medical Science Building
185 South Orange Avenue, H 506
Newark, NJ 07101
973-972-5208
avcupe@njms.rutgers.edu

Charu Garg
Rutgers, The State University of NJ
Biomedical & Health Sciences
Pharmacology & Physiology

Grant Award: $100,500

Project Title: *Pannexin Hemichannels as Regulators of Inflammation after Traumatic Brain Injury*

We aim to reveal the role of pannexin1 hemichannels in neuroinflammation elicited by traumatic brain injury.

Traumatic brain injury (TBI) is one of the leading causes of morbidity, mortality and cognitive impairments worldwide. It results in long lasting consequences on the cognitive ability of patients due to neuronal loss. Following the primary damage to the brain by mechanical trauma, secondary events in the lesion penumbra include prolonged release of inflammatory response that exacerbates neuronal damage. One of the major inflammatory components followed by traumatic impact is the migration, proliferation, and activation of microglial cells; the resident immune cells of the brain. The sustained activation of microglia post TBI is recognized as one of the detrimental causes for damaging the brain tissue, predisposing individual to various neurodegenerative disorders such as Alzheimer's disease, and Amyotrophic Lateral Sclerosis.

Recently, pannexin proteins have been involved in facilitating and coordination of the inflammatory responses in macrophages and astrocytes. Although it is well known that microglia expresses functional pannexin; the contribution of pannexin in activated microglial cells promoting neuroinflammation is not fully understood.

In this proposal we seek to understand the role of pannexin in neuroinflammation using a mice model of controlled cortical impact, so that therapeutic approaches targeting these proteins can be designed to treat pathologies followed by TBI. Specifically, we expect to reveal that an increase in the activity of pannexin in activated microglia enhances the neuroinflammatory response elicited by TBI. Suppression of the ongoing microglial activation in the brain by specifically targeting pannexin activity may significantly help to reduce neuroinflammation and improve the outcome of patients that suffered TBI.

Contact Information:
Charu Garg
Rutgers, The State University of NJ
Biomedical & Health Sciences
New Jersey Medical School
Pharmacology & Physiology
185 South Orange Avenue, MSB I-641
Newark, NJ 07103
973-972-1350
gargc1@njms.rutgers.edu

Victoria DiBona
Rutgers, The State University of NJ
Biomedical & Health Sciences
Cell Biology & Neuroscience

Grant Award: $100,500

Project Title: *Modulating Neuroinflammation for Treatment of Traumatic Brain Injury*

We aim to understand how neuroinflammation is regulated and to test a novel treatment option to modulate the inflammatory response following TBI.

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide, with around 15,000 New Jersey residents suffering from an event each year. As treatment and recovery options are limited, life for those stricken can be debilitating. A main hurdle in treating TBI patients is controlling an over-activated neuroinflammatory response, which causes additional insults to injury. This chronic neuroinflammation can last up to decades, and causes progressive damage throughout the brain. The main culprit for this chronic inflammation is microglia, the resident immune cells of the brain. Microglia naturally provide a protective function to the brain. However, following injury, microglia become persistently over-activated, which is toxic to the neurons. Unfortunately, much research is still unexplored in understanding how and why microglia are chronically activated following TBI.

Our preliminary studies show that the serine/threonine kinase Par1 is involved in microglia activation following TBI. Loss of Par1 facilitates the activation of microglia. In this project, we aim to examine whether TBI causes a decrease in Par1 activity in microglia, which leads to the hyperactivated inflammatory response. We will then explore strategies to stimulate Par1 activity to reduce microglia activation following TBI. Interestingly, metformin, a drug that has been used for decades to treat diabetes, can activate Par1. We will test whether metformin can improve the outcome of TBI by using mouse models. If successful, our studies can directly lead to a novel treatment approach for TBI, as the safety of metformin has already been tested.

Contact Information:
Victoria DiBona
Rutgers, The State University of NJ
Biomedical & Health Sciences
Cell Biology & Neuroscience
675 Hoes Lane West
RT-304
Piscataway, NJ 08854-8021
732-235-2820
dibonavl@rwjms.rutgers.edu

PILOT RESEARCH GRANT RECIPIENTS:

Nada Boustany, Ph.D.
Rutgers, The State University of NJ
Biomedical Engineering

Grant Award: $180,000

Project Title: *Quantifying the Structure-Function Relationship of Neurons Following Mechanical Injury*

We propose to use a novel method to study structural defects and dynamic structural changes in mechanically-injured neurons to give insight into the mechanisms causing neuronal damage following injury.

The branching structure of neurons is essential to their function and their communication with other cells. During mechanical trauma, which occurs in traumatic brain injury, this branching structure is damaged resulting in loss of synaptic function and latent cell injury or cell death secondary to the initial mechanical injury. The mechanisms of neuronal damage following mechanical injury are still poorly understood and without this knowledge it is difficult to devise strategies to mitigate neuronal damage and enhance recovery.

Here we hypothesize that a detailed and objective measurement of neuronal structure can help provide insight into the mechanisms leading to loss of neuronal function following mechanical injury. Our rationale stems from the recent finding that proteins traditionally involved in synaptic function, were found to control dendrite morphology and branching. These studies point to the significance of understanding structural remodeling in neurons following injury and therefore the need to enhance methodologies to measure neuronal structure.

We therefore propose to apply an optical method we recently developed to provide novel objective and quantitative measurements of neuronal structure following mechanical injury. We will demonstrate that structural changes measured with this method can report on neuronal function, and investigate how these structural changes can report on the extent of injury or predict functional recovery. As part of these studies, we will use the structural markers to evaluate the efficacy of treatments and interventions aimed at encouraging branching and synapse formation and preventing cell death. Together these studies will result in a novel method to assess structural defects in neurons and will shed light on how structural defects dictate neuronal function. This understanding could guide the design of treatments aimed directly at controlling neuronal structure as a means to improve neuronal function after injury.

Contact Information:
Nada Boustany, Ph.D.
Rutgers, The State University of NJ
Biomedical Engineering
599 Taylor Road
Piscataway, NJ 08854
nboustan@rci.rutgers.edu

Radek Dobrowolski, Ph.D.
Rutgers, The State University of NJ
Biological Sciences

Grant Award: $180,000

Project Title: *Functional Analysis & Modulation of mTOR & Wnt Signaling during Regeneration after Traumatic Brain Injury*

We will further characterize and restore molecular signaling pathways involved in neural regeneration by transplanting engineered stem cells into the injured mouse brain.

Traumatic brain injury (TBI) is one of the most frequent causes of disability in the United States. There is presently no treatment for the thousands of New Jersey residents who have incurred TBIs from traffic accidents, falls, assault, and sports affects. TBI frequently leads to impairment of overall cognitive and motor functions; these permanent consequences are due to neuronal loss. Neuronal death is observed immediate and long after injury. Interestingly, these long-term consequences mostly reconstitute the pathophysiology of Alzheimer's disease and develop most of its molecular hallmarks, like the neurotoxic phosphoTau (pTau) proteins.

One of the central molecular pathways in neuroregeneration, neuronal stem cells (NSCs) maintenance, and regulation of Tau phosphorylation is Wnt signaling. Our data suggest that Wnt signaling is inhibited by autophagy after neuronal injury. Autophagy is a cellular "self-eating" process which is induced after cellular stress and needed for removal of dysfunctional cellular organelles. Autophagy inhibits canonical Wnt signaling stalling regeneration and stem cell maintenance after injury.

Restoration of Wnt signal transduction and expression of its target genes which are crucial for regeneration of neurons, constitutes a promising approach for TBI treatment. This hypothesis will be evaluated by transplantation of genetically modified NSCs into mouse brains following TBI. We propose to engineer NSCs capable of secreting factors modulating autophagy and reactivating Wnt signaling to promote neuronal protection and regeneration in the brain. Expression and secretion of these regenerative factors by our modified NSCs is tightly regulated and can be turn-off if no longer needed.

The proposed study will determine the efficacy of the autophagy and Wnt pathway integration after TBI, and will test a novel and feasible therapeutic strategy facilitating state-of-the-art transplantation techniques of engineered NSCs into injured brains.

Contact Information:
Radek Dobrowolski, Ph.D.
Rutgers, The State University of NJ
Biological Sciences
225 University Avenue
Life Science Center, Rm 401c
Newark, NJ 07102
973-353-5536
R.Dobrowolski@rutgers.edu

Denise Krch, Ph.D. Grant Award: $176,606
Kessler Foundation

Project Title: *Improving Emotional Adjustment and Quality of Life in Patients with Traumatic Brain Injury and their Caregivers*

The pilot will evaluate the effectiveness of a support intervention for decreasing burden, and improving emotional functioning and quality of life in caregivers of persons with traumatic brain injury.

The number of individuals in New Jersey who survive traumatic brain injury (TBI) is growing. Individuals with TBI suffer from behavioral, cognitive, and physical problems, which negatively impact their ability to perform daily or routine activities. The lasting effects of the brain injury result in life-long challenges not just for the individual with TBI, but also for the family members who care for them.

The role of caregiving comes with considerable physical and emotional burden and decreased quality of life. Further, the physical and mental state of the caregiver often determine whether the caregiver will be able to provide an environment for their loved one that is optimal for improved function. A great deal depends upon the health of the caregiver, highlighting the need for increased attention to develop treatments for TBI caregivers. Unfortunately, limited research has been conducted in this area to date. The current study will address this healthcare gap by examining the impact of a support intervention for caregivers of persons with TBI.

The design of the proposed treatment was shaped by the direct feedback from caregivers. The treatment provides three kinds of support services: 1) monthly support groups, 2) weekly support phone calls, and 3) sharing of educational materials and resources. Participants will be randomly assigned to either a treatment group or a control group. Both groups will complete questionnaires that evaluate emotional and physical functioning, quality of life, self-confidence, and perceived burden. This design will allow us to evaluate the preliminary effectiveness of a support treatment for caregivers, the knowledge of which will set the stage for future research investigating the effectiveness of the treatment on a larger scale.

Contact Information:
Denise Krch, Ph.D.
Kessler Foundation
1199 Pleasant Valley Way
West Orange, NJ 07052
973-324-3559
dkrch@kesslerfoundation.org

Anthony Lequerica, Ph.D. Grant Award: $163,760
Kessler Foundation

Project Title: *Sleep, Procedural Learning and Therapeutic Engagement Among Inpatients with Traumatic Brain Injury in an Acute Rehabilitation Hospital*

This study uses principles of sleep-dependent neuroplasticity and learning demonstrated in research on healthy individuals and applies it to an intervention to maximize gains in TBI rehabilitation.

Studies show that if you train healthy adults on a motor learning task where they must learn a skilled sequence of movements, they improve to a certain point with practice. After the practice period, participants who were given a brief nap after training showed improvement in their performance on the task beyond where they left off after training. In other words, their performance increased during the span of time spent napping even though there was no additional practice after the one training session. This leap in performance was not found when individuals were given the same span of time spent awake and relaxing. This effect, shown in healthy individuals, has never been shown in individuals with TBI in acute rehabilitation. This boost in performance in learning a motor skill can be useful in this setting where individuals with TBI re-learn activities of daily living to maximize independence.

This study will look at the effect of a daytime nap after training on a motor skill compared with the same amount of time after training spent awake and resting. If a simple nap after therapies can promote the learning of tasks worked on in physical and occupational therapies, it can potentially increase the effectiveness of rehabilitation, enhance progress toward greater independence, and lessen burden of care after discharge.

This study will also use a state-of-the-art instrument to determine how two different sleep stages contribute to motor learning and patient engagement in rehabilitation. Because different sleep stages can be affected by medications prescribed on the inpatient rehabilitation unit, it is important for doctors to be aware of potential impact this can have on recovery. By looking at the effect of a daytime nap and the distribution of sleep stages, this study will be the first to attempt to utilize sleep research findings gained from healthy individuals to create an intervention to maximize gains in rehabilitation after TBI.

Contact Information:
Anthony Lequerica, Ph.D.
Kessler Foundation
1199 Pleasant Valley Way
West Orange, NJ 07052
973-324-3551
alequerica@kesslerfoundation.org

Anna M. Barrett, M.D.
Kessler Foundation

Grant Award: $178,697

Project Title: *Medication Self-Management after Traumatic Brain Injury*

We will demonstrate a feasible, objective medication self-administration (MSA) assessment; identify TBI patients making errors, and measure impact on post-discharge needs.

After a traumatic brain injury, self-administering medication is a daily activity that provides a foundation for recovery, health and function. Medication self-administration (MSA) errors affect competence and dignity, but we found MSA errors also strongly predict the amount of skilled help a person with brain injury will need after hospital discharge.

In this application, our interdisciplinary research group proposes to extend our research on methods to identify and predict MSA errors in a two-year pilot project exploring the needs of people with TBI. To optimize successful return to the community after TBI, we need to predict when MSA errors might occur. Objective indicators of MSA errors are particularly needed, because, as our group reported, many people in neurorehabilitation are completely unaware when they cannot perform MSA. Their claims of excellent MSA ability seem to be more than a social white lie—overestimating MSA ability occurs in people with memory loss. Thus, the people with TBI who need the most help with medication adherence, and may be at the highest risk of falls, re-hospitalizations, and infection, may be the least likely to ask for assistance.

We will examine whether MSA errors predict the need for post-hospital skilled assistance, and we will ensure that these errors really predict medication performance with computer tracking of how people take their medications after discharge. Lastly, we will try to predict when the most MSA errors occur by looking at the reasons why people with TBI take medications and the types of TBI and TBI-associated symptoms they may experience. We hope our project will increase public knowledge of the significant obstacle that MSA errors can present to health in people with TBI. This then may build strong interest in care pathways to manage and treat MSA errors during rehabilitation, to obtain best results of future TBI medication treatments.

Contact Information:
Anna M. Barrett, M.D.
Kessler Foundation
1199 Pleasant Valley Way
West Orange, NJ 07052
973-324-3563
abarrett@kesslerfoundation.org