NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

2014 Annual Report

Chris Christie, Governor
Kim Guadagno, Lt. Governor

Mary E. O'Dowd, MPH Commissioner

January 30, 2015

The Honorable Chris Christie, Governor
Office of the Governor
State House
PO Box 001
Trenton, New Jersey 08625

Dear Governor Christie:

On behalf of the New Jersey Commission on Brain Injury Research, I am pleased to present the Annual Report for Fiscal Year 2014. Once again, the Commission has had an active and productive year. We recently completed the eighth competition for research projects directed at mechanisms of neural regeneration and repair, and are confident that these efforts will make significant contributions to our knowledge of recovery from traumatic brain injury, the development of effective interventions, and ultimately to the improvement of the quality of life for people who have sustained catastrophic brain injuries.

I would like to acknowledge the efforts and enthusiasm of all of the Commissioners during the past year, as well as the New Jersey Department of Health for their valuable support and contributions.

Sincerely,

Daniel Keating, Ph.D.
Chairman

New Jersey Commission on Brain Injury Research

Members of the Commission

Daniel Keating, Ph.D., Chairman
Dennis Benigno
Cathleen Bennett
Meiling Chin, MBA
Shonola Da-Silva, M.D., MBA
Nicholas Ponzio, Ph.D.
Mark Evan Stanley, Ph.D.
Dennie Todd
Karen Tucker, M.A.

Commission Personnel

Christine Traynor, Administrator
Mary Ray, Fiscal Administrator

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ACKNOWLEDGMENTS

The New Jersey Commission on Brain Injury Research would like to express its sincere appreciation to all present and past Commission members, to Commission staff members Christine Traynor and Mary Ray for their support, and to the New Jersey Department of Health's Center for Health Statistics, for the brain injury surveillance statistics

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EXECUTIVE SUMMARY

The New Jersey Commission on Brain Injury Research, established in 2004, funds brain injury research projects in New Jersey.

- ***Since 2007, the New Jersey Commission on Brain Injury Research (NJCBIR) has awarded over $25 million to individual scientists at various academic and research institutions, and approved 62 separate scientific research projects.***
  - *Since 2007, twenty-one scientific research projects have been completed.*
  - *Progress made by researchers has been presented in abstracts, scientific conferences, symposia, and meetings.*
  - *NJCBIR programs have enabled wider scientific interaction and research collaborations, many with out-of-state researchers.*
  - *Success in achieving NJCBIR funding has resulted in academic and career advancement for New Jersey researchers.*

- ***NJCBIR offered four grant programs in Fiscal Year 2014:***
  - *Individual Research Grants*
  - *Programmatic Multi-Investigator Research Grants*
  - *Pilot Research Grants*
  - *Postdoctoral and Graduate Fellowship Grants*

- ***NJCBIR 2014 Achievements:***
  - *Fifty-two applications requesting $18.6 million were submitted.*
  - *Sixteen awards were made in 2014 totaling $3,953,347.*

    Four Individual Research grants totaling $2,113,012, five Pilot Research grants totaling $879,053, and seven Fellowship grants totaling $961,282 were approved.

INTRODUCTION

N.J.S.A. 52:9ee-1, et seq

The Brain Injury Research Act created the New Jersey Commission on Brain Injury Research and the New Jersey Brain Injury Research Fund to support its activities. It resulted from the collaborative efforts of people with brain injuries and their families, clinicians, scientists, public officials, and representatives of research, rehabilitation, and non-profit organizations.

Facts & Figures

- Approximately 175,000 New Jersey residents suffer from traumatic injuries that damage the brain.
- Approximately 12,000* new injuries occur each year that require inpatient or outpatient treatment.
- The economic consequences of the resulting physical disabilities are enormous. Medical and long term care costs to the nation's economy are estimated to be $48 billion dollars annually.
- The personal and emotional toll on individuals and families with brain injuries is incalculable.

*Based on estimates from the Centers for Disease Control and the New Jersey Department of Health Center for Health Statistics.

NEW JERSEY'S COMMITMENT TO BRAIN INJURY RESEARCH

The Brain Injury Research Act anticipates that brain injury research will lead to effective treatments and cures for brain injuries and relieve other consequences of brain injury.

New Jersey is a leader in supporting research aimed at developing effective interventions and cures for the disabilities associated with traumatic brain injury.

The New Jersey Commission on Brain Injury Research provides research grant programs for both established scientists and younger researchers committed to the goals of brain injury research. The commission also supports the New Jersey Department of Health, in establishing a database of all brain injured patients in New Jersey.

Now in its tenth year of operation, the NJCBIR has funded 62 scientific research projects and supported individual scientists at institutions around the state. Its impartial and scientifically rigorous application and review process has helped make the commission vital to New Jersey's best researchers in their pursuit of answers and cures.

NEW JERSEY COMMISSION ON BRAIN INJURY RESEARCH

Created as a semi-independent public body, the New Jersey Commission on Brain Injury Research is "…allocated in, but not of…" the New Jersey Department of Health. It is subject to all the administrative rules and procedures of the Department, but is not a part of the Department, and is not included in its budget.

The New Jersey Commission on Brain Injury Research establishes and oversees the operations of the grants process and other activities that are implemented by its administrative staff. Eleven uncompensated commissioners are appointed by the Governor with the advice and consent of the Senate, and serve for three-year terms.

Two commission seats are designated by statute to represent the state's major academic research institutions and stakeholders. Public members provide a diversity of backgrounds and interests united by a shared commitment to the cause of brain injury research. The Commission will always have one or more individuals from each of the following institutions and categories:

The Commissioner of the NJ Department of Health, or designee

Rutgers, The State University of New Jersey

Eight Public Members – at least one licensed physician, an individual with a brain injury, a parent of an individual with a brain injury, one public member appointed by the President of the Senate, one public member appointed by the Speaker of the Assembly

All public members shall be residents of the state, or otherwise associated with the state, and shall be known for their knowledge, competence, experience or interest in brain injury medical research. Any qualified person wishing to be considered for appointment may submit his or her name to the Governor's Office of Appointments.

Public meetings are held at least four times a year. Members are recused from discussing or voting on matters in which they may have a potential conflict. A Chair and Vice-Chairperson are elected annually and preside over all formal proceedings.

The NJCBIR also maintains standing committees that meet and provide an informal structure to discuss issues on an *ad hoc* basis in advance of presenting them to the full commission.

ADMINISTRATION

The New Jersey Commission on Brain Injury Research's administrative office provides the vital linkages and machinery that implement its programs and ensure the integrity of its operations. The office staff manages the day-to-day operations, including program administration, interaction with applicants and grantees, contract administration, budgeting and financial matters, record-keeping and reporting.

The office staff schedule and facilitate all activities, manages the scientific merit review process, negotiates with outside vendors, and maintains the necessary relationships within state government.

NEW JERSEY BRAIN INJURY RESEARCH FUND

The work of the New Jersey Commission on Brain Injury Research is supported entirely by a statutory one dollar surcharge on all traffic and motor vehicle fines or penalties. Similar sources of funding have been implemented successfully by several other jurisdictions – vehicular accidents are a significant cause of brain injuries.

Revenue is collected by the State Treasurer for deposit into the New Jersey Brain Injury Research Fund. All grant programs and other activities are funded entirely from this dedicated source. No part of the operating budget is paid for out of New Jersey's general tax revenue.

MISSION AND GOALS

The New Jersey Commission on Brain Injury Research's mission is to encourage and promote innovative brain injury research projects in New Jersey through the funding of approved research projects at qualifying research institutions in the State of New Jersey.

The New Jersey Commission on Brain Injury Research supports meritorious research projects that advance the understanding of traumatic brain injuries, and is committed to accelerating research to develop effective interventions and cures for the disabilities associated with traumatic brain injury.

Simply stated, the commission's goals are:

- To advance and accelerate brain injury research,
- To promote collaboration among brain injury researchers in New Jersey,
- To promote the development of brain injury researchers and their research capabilities in order that they may seek federal and other external funding, and
- To encourage innovative research.

The creation of precedent setting guidelines for the groundbreaking commission research agenda and the cutting edge and innovative science needed to accomplish commission goals is a tedious process that often requires unique and challenging solutions. Cutting edge and innovative science is urgently needed, and the task of research is more demanding than ever. Through its grants programs, the commission implements the commitment of the State of New Jersey to the international quest for treatments and cures for brain injuries and their effects.

The State of New Jersey benefits in savings on medical and support costs, enhancements to and further development of the state's public and private biomedical sectors,

establishes leadership in the field of brain injury treatments and cures, and improves the lives of those living with brain injuries and their effects.

OBJECTIVES

The New Jersey Commission on Brain Injury Research is committed to accelerating research to develop effective interventions and cures for the disabilities associated with traumatic brain injury. Its primary objectives are:

- *To advance the field of brain cell repair and regeneration in the New Jersey research community by encouraging established scientists to apply their expertise to the brain.*
- *To foster collaborative, interdisciplinary approaches to brain injury research.*
- *To develop models of neural repair and regeneration that establishes a basis for additional scientific investigation.*
- *To develop models of neural repair and regeneration after brain injury that can lead to clinical interventions.*
- *To stimulate epidemiological analysis of the New Jersey Traumatic Brain Injury Registry data in order to improve injury prevention, develop treatment guidelines and enhance patient outcomes.*
- *To promote dissemination of the research findings generated by those scientists supported by the New Jersey Commission on Brain Injury Research.*
- *To develop and evaluate clinical interventions that lead to improved treatment and function after traumatic brain injury.*

RESEARCH FUNDING PRIORITIES

The New Jersey Commission on Brain Injury Research's Research Guidelines set forth the commission's scientific agenda, research criteria and areas of particular interest. They offer applicants detailed guidance and instruction on funding criteria and policies. The full text appears on the website at: www.nj.gov/health/njcbir.

Currently, an array of grant programs is offered including Individual Research Grants, Fellowships, Pilot Research Grants and Programmatic Multi-Investigator Research Grants. Each of these programs is designed to support and encourage brain injury research in New Jersey in a unique way.

The NJCBIR funds research activities that hold promise of developing effective interventions and cures for the disabilities associated with traumatic brain injury. The areas of research listed below highlight the focus of current emphasis and funding:

Basic Studies

- Studying strategies to promote neuronal growth and survival, encourage the formation of synapses, enhance appropriate myelination, restore axonal conduction, replace or regenerate injured brain cells, or otherwise improve function after brain injury.
- Evaluating efficacy of drugs and other interventions that prevent or reduce secondary neuronal injury or providing insight into the mechanisms causing progressive damage.
- Defining anatomical characteristics of brain injury in well-defined animal models and in the human brain, specifically documenting the cellular systems vulnerable to injury and the functional losses which occur as a result thereof.
- Translational research on the mechanism and interventions that promote recovery of function after brain injury.

Clinical Studies

- Demonstrating the efficacy of innovative rehabilitation strategies based on basic research that offer promise to promote recovery of function (e.g., physiologic function, cognitive impairment, activity limitation, social participation, quality of life) through their clinical application.
- Demonstrating the putative mechanisms of action of rehabilitation intervention based on changes in brain activity (e.g., functional imaging), neurocognitive function, or psychosocial factors (e.g., resilience).
- Comparative effectiveness research to evaluate the relative risks and benefits of alternative rehabilitation interventions intended to promote recovery of function.
- Epidemiological studies of the New Jersey Traumatic Brain Injury Registry data, to identify contributions of demographic and risk factors, patient transport, rehabilitation and physical therapy, and medical/surgical interventions to population treatment and outcomes.

THE NJCBIR APPLICATION AND REVIEW PROCESS

The grants review process was designed to emulate National Institutes of Health standards and procedures to provide an impartial and rigorous review. This effort has been largely successful and has earned respect from grantees and applicants.

The application process is now entirely electronic utilizing the New Jersey System for Administering Grants Electronically grants management system, and is accessible through the website.

The on-line process ensures broad access, convenience and flexibility, and greatly reduces administrative workloads for applicants, the commission office, and the Scientific Merit Review Panel.

The Commission's administrative staff reviews all applications for completeness and accuracy and assists applicants in correcting errors or omissions.

Relevance to the overall goals of the NJCBIR is assessed by an expert panel who also recommend reviewers for each grant from a pool of over 100 highly qualified scientists.

Each application is reviewed and scored independently by two or three peers prior to discussion at the Scientific Merit Review Panel meeting; "triaged" applications are not discussed or scored.

The remaining applications are fully discussed and scored by the entire panel and given a composite score. The panel also suggests a cut-off point for funding. The scores, comments and funding recommendations are delivered to the Commission for final consideration and vote.

The Commission makes the final decision whether to fund each application by majority vote. The commissioners pay close attention to the results of the independent scientific merit review, but retain discretion to take other factors into consideration in judging the merit of each application. Any application that was scored and not funded may be resubmitted with appropriate changes in the next grant cycle.

All applicants, regardless of the decision, receive "blinded" reviewer comments. These are often valuable and may help a researcher rethink a project or reframe a future application.

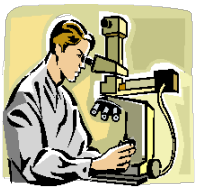
CURRENT GRANT PROGRAMS

Grant programs are designed to provide opportunities attractive to a wide range of researchers. Awards are intended to promote collaboration among brain injury researchers in New Jersey and encourage innovative research, not to provide long-term support. It is expected that this initial support will lead investigators to acquire necessary levels of preliminary data so that they may compete successfully for federal grant support.

The Individual Research grant is designed to fund senior independent researchers, while the Fellowship grant offers encouragement to graduate students and post-doctoral researchers, the Multi-Investigator grant supports collaborative research from at least three investigators from different laboratories, and the Pilot Research grant enables researchers to pursue a new direction in brain injury research, or encourages new investigators who want to gather preliminary data for larger research projects.

Inter-institutional and/or inter-state collaboration is strongly encouraged. Complete details on all grant programs are available on-line.

Individual Research Grants



Individual Research Grants support senior scientists to explore meritorious novel scientific and clinical ideas.

Up to $540,000 for up to three years ($180,000 per year)

Key goal is to enable established researchers to test and develop pilot data needed for future funding.

Fellowship Grants

Postdoctoral and Graduate Student Fellowships engage promising young investigators in brain injury research.

All fellowships include an annual stipend, research allowance and travel budget.

Post-doctoral Fellowships are three year awards based on years of relevant research experience since obtaining a doctoral degree and range from $64,550 to $83,376 a year.

Graduate Fellowships are three year awards with a total award of $33,500 per year.

Pilot Research Grants

Enable independent investigators to pursue a new direction in brain injury research, or new investigators who want to gather preliminary data for larger research projects.

Up to $180,000 for a two year award ($90,000 per year)

Programmatic Multi-Investigator Research Grants

Support collaborative research from at least three investigators from different laboratories.

Preference is given to proposals that demonstrate complementary approaches to addressing a research question through multi-disciplinary investigations.

Collaborations are encouraged among independent laboratories within the same institution or among laboratories from different institutions.

Up to $720,000 per year for up to three years, maximum of up to $2.1 million.

2007- 2014 NJCBIR SUMMARY AND PERFORMANCE RECORD

Since 2007, the New Jersey Commission on Brain Injury Research has funded 62 separate scientific research projects to scientists at New Jersey academic and research institutions. These awards represent an investment in brain injury research of over $25 million.

Approximately 48 grant applications are received annually; approval of ten or more new grant awards totaling between $2.5 and $3.5 million are made.

Due to its continued investment in brain injury research, the number of New Jersey researchers interested in the field is growing.

NEW JERSEY QUALIFIED RESEARCH INSTITUTIONS

Under the Brain Injury Research Act, funds may only go to researchers affiliated with "New Jersey Qualified Research Institutions". The following organizations have been designated by the New Jersey Commission on Brain Injury Research. They provide a continuing source of interest and applications for funds.

University of Medicine & Dentistry of NJ
Rutgers, State University of New Jersey
Kessler Foundation
Stevens Institute for Technology
Princeton University
Cooper University Hospital/Health System
Atlantic Health Systems Hospital Corporation
St. Barnabas Medical Center
Edge Therapeutics, Inc.
The Center for Neurological & Neurodevelopment Health LLC, Clinical Research Center of NJ, & The Center for Neurological & Neurodevelopment Health II, Inc. – NeurAbilities
Centra State Medical Center
Coriell Institute for Medical Research
New Jersey Institute of Technology
Hackensack University Medical Center
International Brain Research Foundation
Englewood Hospital Research
JFK Neuroscience Institute, JFK Health System & Seton Hall University School Health Medical Science
Rowan University
Morristown Medical Hospital & Medical Center
VA NJ Health Care System & Veterans Biomedical Research Institute

The Commission is committed to broadening its portfolio of institutional grantees and increasing the size and diversity of its funding activities. Through outreach activities, the Commission encourages participation by all research organizations with an interest in brain injury research.

2014 YEAR IN REVIEW

The New Jersey Commission on Brain Injury Research developed policy guidelines to accommodate what promises to be an exciting research agenda for the New Jersey science community. The Commission is providing the opportunity for New Jersey to become a leader in traumatic brain injury research, as our program was the first of its kind in the nation.

As we move forward, it is our belief that the Commission will set the example for other states to follow as the search for treatments and cures begins to play a major role in medical research initiatives. Indeed, our early recognition of unmet needs in traumatic brain injury research is paving the way to develop methods of regeneration and repair.

Grant programs are designed to provide opportunities attractive to a wide range of researchers. Awarded grantees and grantee institutions have capitalized on the opportunities afforded by the availability of commission funding through advancement of individual careers, increased institutional investment, and applying for additional outside funding.

The Commission has been a major factor in fostering this interest and continued involvement in brain injury research within the State of New Jersey.

2014 Applications

2014 saw the New Jersey Commission on Brain Injury Research in its tenth year of operation and its eighth cycle of grants.

In 2014, four types of grant programs were offered. They included Individual Research grants, Fellowship grants, Programmatic Multi-Investigator Research grants, and Pilot Research grants. The NJCBIR allocated up to $6.5 million for brain injury research projects, but it is not required to award any, or all of that amount.

A total of 52 grant applications were received. Sixteen grants were awarded totaling $3,953,347. The grant awards included four Individual Research grants, seven Fellowship grants, and five Pilot Research grants.

2014 Outreach and Development Efforts

The Commission maintains an ongoing interest in expanding brain injury research in New Jersey. Direct contacts, attendance at events and meetings, plus website and publication resources are some of the ways used to publicize grant opportunities throughout the state.

Publication of Grant Programs

Official Notices of Grant Availability advise interested parties of the New Jersey Commission on Brain Injury Research grant programs. These notices are published annually on the Commission's website and in the New Jersey Department of Health's *Directory of Grant Programs*.

2014 Grant Cycle Information
Grant Application Deadline: October 3, 2013
Award Notification Date: April 30, 2014

Available Grant Programs:

- Individual Research Grants
- Programmatic Multi-Investigator Research Grants
- Fellowship Grants
- Pilot Research Grants

GRANTS PROGRAM FOR 2015

For Fiscal Year 2015, the New Jersey Commission on Brain Injury Research allocated up to $6.5 million dollars for brain injury research projects.

In 2015, five types of grant programs were offered. They included Individual Research grants, Fellowship grants, Programmatic Multi-Investigator Research grants, Pilot Research grants and Brain Injury Core Facilities grants. The NJCBIR allocated up to $6.5 million for brain injury research projects, but it is not required to award any, or all of that amount.

New Grant Program Offered
New for 2015 was the creation of a new grant program, the Brain Injury Core Facilities Grant with start-up costs of up to $1,500,000 to provide researchers with an opportunity to facilitate the establishment of new Brain Injury Core Facilities.

The goals of the new Brain Injury Core Facilities Grant program are:

- To make research more efficient and convenient by providing services and technologies that cannot be readily reproduced in individual laboratories in an efficient, cost-effective manner.

- To support basic or translational research of the highest caliber that will significantly impact and advance the field of traumatic brain injury. Studies involving either experimental models or clinical projects will be considered.

- To provide state-of-the-art equipment and highly skilled staffing to support researchers.
- To make use of sophisticated technologies and equipment, in order to provide researchers with access to centralized expertise and service.
- To provide education and training opportunities for aspiring researchers.
- To provide useful and appropriate services to researchers located within the State of New Jersey and their collaborators at other in-state or out-of-state institutions.

2015 Grant Cycle Information

Grant Application Deadline: October 3, 2014
Award Notification Date: April 30, 2015

Available Grant Programs:

- Individual Research Grants
- Brain Injury Core Facility Grants
- Programmatic Multi-Investigator Research Grants
- Fellowship Grants
- Pilot Research Grants

NEW JERSEY BRAIN INJURY REGISTRY

The "Brain Injury Research Act" mandated the establishment of a central registry of people who sustain brain injuries throughout the state. This registry will provide a database indicating the incidence and prevalence of brain injuries and will serve as a resource for research, evaluation, and information on brain injuries.

The Registry, collects brain injury data from New Jersey hospitals, and provides analysis of that data for health professionals.

New Jersey Traumatic Brain Injury Surveillance System

Hospitalizations for TBI by Gender, New Jersey, 2000-2013

	Males		Females		Total	
Year	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*
2000	4,934	126.7	3,070	65.3	8,004	94.8
2001	4,733	120.3	2,884	61.2	7,617	89.7
2002	4,783	120.9	2,904	60.7	7,687	89.5
2003	5,006	125.5	3,173	64.8	8,179	94.1
2004	4,986	124.8	3,219	64.9	8,205	93.8
2005	5,109	126.7	3,256	65.4	8,365	95.1
2006	5,510	135.4	3,524	70.2	9,034	102.0
2007	5,526	135.3	3,659	71.8	9,185	102.6
2008	5,556	135.0	3,786	73.3	9,342	103.3
2009	5,816	140.4	4,072	77.1	9,888	107.7
2010	5,765	137.6	3,942	74.3	9,707	104.9
2011	5,563	131.9	4,042	75.1	9,605	102.4
2012	5,893	137.8	3,963	72.6	9,856	103.8
2013	5,609	129.8	3,995	71.7	9,604	99.6

Rates are age-adjusted using the 2000 US Standard Population, calculated per 100,000 population. Bridged-race estimates are used in calculations. Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2014.

Hospitalizations for TBI by Age Group, New Jersey, 2000-2013

	Under 15		15-24		25-44		45-64		65+		Total	
Year	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*	*N*	*AARate*
2000	1,010	57.4	1,236	122.4	1,932	73.7	1,345	69.8	2,481	222.6	8,004	94.8
2001	904	51.2	1,287	125.3	1,782	68.5	1,300	65.6	2,344	210.3	7,617	89.7
2002	865	48.8	1,240	118.9	1,708	66.2	1,368	67.1	2,506	224.6	7,687	89.5
2003	925	52.2	1,209	113.9	1,727	67.6	1,469	70.1	2,849	254.7	8,179	94.1
2004	821	46.5	1,211	112.3	1,664	66.0	1,548	72.0	2,961	264.5	8,205	93.8
2005	828	47.4	1,245	113.5	1,713	68.9	1,568	71.1	3,011	268.7	8,365	95.1
2006	843	48.9	1,347	121.2	1,817	74.3	1,779	78.9	3,248	288.8	9,034	102.0
2007	804	47.1	1,318	117.6	1,652	68.4	1,862	81.0	3,549	312.5	9,185	102.6
2008	827	48.7	1,167	103.5	1,717	71.9	1,923	82.3	3,708	320.2	9,342	103.3
2009	812	47.9	1,139	100.4	1,609	68.1	2,074	86.9	4,254	362.5	9,888	107.7
2010	805	47.5	1,125	98.7	1,580	67.3	2,117	87.3	4,080	344.0	9,707	104.9
2011	695	41.3	999	87.3	1,527	65.4	2,081	84.4	4,303	356.1	9,605	102.4
2012	678	40.5	1,006	87.9	1,557	66.9	2,230	90.3	4,385	350.7	9,856	103.8
2013	626	37.6	822	71.6	1,431	61.6	2,176	87.7	4,549	354.4	9,604	99.6

Except where noted, rates are CRUDE RATES directly calculated using the NJ age-specific population, calculated per 100,000. Bridged-race estimates are used in calculations. Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2014.

Discharge Disposition of the Major Causes of Traumatic Brain Injuries, 2013

	Home, Routine		Extended Inpatient Care[1]		Home, With Services[2]		LTC, Nursing, Hospice[3]		Rehab		Left AMA		Discharge/ Transfer w Planned Readmission[4]		Died		Total
Cause of Injury	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*	*%*	*N*
Motor Vehicle	1,297	**67.4**	190	**9.9**	79	**4.1**	15	**0.8**	244	**12.7**	16	**0.8**	1	**	83	**4.3**	**1,925**
Falls	2,380	**42.0**	1,618	**28.5**	422	**7.4**	161	**2.8**	676	**11.9**	51	**0.9**	1	**	361	**6.4**	**5,670**
Assault	569	**82.5**	30	**4.3**	7	**1.0**	2	**	30	**4.3**	23	**3.3**	0	-	29	**4.2**	**690**
Self-Inflicted	16	**35.6**	14	**31.1**	0	-	2	**	2	**	0	-	0	-	11	**24.4**	**45**
Other and Unknown	**770**	**60.4**	**200**	**15.7**	**80**	**6.3**	**12**	**0.9**	**117**	**9.2**	**22**	**1.7**	**0**	-	**73**	**5.7**	**1,274**
Total	5,032	**52.4**	2,052	**21.4**	588	**6.1**	192	**2.0**	1,069	**11.1**	112	**1.2**	2	**	557	**5.8**	**9,604**

Hospitalization data are from the New Jersey Central Nervous System Injury Surveillance, 2013; percentages are based on New Jersey residents admitted to New Jersey hospitals, all outcomes.
** Percentages not calculated for under 5 observations.

Notes:
[1]Includes: Discharges/transfers to other short term general care hospitals, skilled nursing and intermediate care facilities, federal hospitals,
[2]Includes: Discharges/transfers to home withi either a home health service provider or IV therapy
[3]Includes: Discharges/transfers to long-term care facilities, Medicaid certified nursing facilities, and hospice
[4]Includes: Discharges/transfers to home/self care, short term general hospitals, skilled nursing and intermediate care facilities, custodial or supportive care facilities, cancer centers or children's hospitals, home with services, law enforcement, federal hospitals, Medicare swing-bed facilities, rehab facilities, long-term care, Medicaid-certified nursing facilities, psych hospitals, critical access hospitals, and others not elsewhere classified; with planned inpatient readmission to an acute care hospital. (New for 2013)

FINANCIAL STATEMENT

The activities and programs of the New Jersey Commission on Brain Injury Research are supported by the New Jersey Brain Injury Research Fund as established by the Brain Injury Research Act.

A $1.00 surcharge was added to the amount of each fine and penalty imposed and collected under authority of any law for any violation of the provisions of Title 39 or any other motor vehicle or traffic violation in the State of New Jersey. This revenue surcharge is collected and forwarded to the State Treasurer and deposited into the New Jersey Brain Injury Research Fund. Interest earned on the money collected, through the Division of Investments, New Jersey State Department of Treasury, is credited to the Fund.

The NJCBIR is committed to granting a substantial majority of the Fund each year to support as much meritorious research as possible, while retaining the ability to meet expenses.

State Fiscal Year 2014
Fund Balance Statement:

	SFY 2014 *Projected*	SFY 2014 Actual	SFY 2015 *Projected*
Opening Fund Balance: (July 1)	*$1,366,413*	*$1,566,420*	*$1,420,825*
Revenues			
Assessments[1]	*$3,600,000*	*$3,992,947*	*$3,600,000*
Investments Earnings - Interest[2]	*$20,000*	*$18,974*	*$20,000*
Total Revenue:	*$3,620,000*	*$4,011,921*	*$3,620,000*
Total Funds Available:	*$4,986,413*	*$5,578,341*	*$5,040,825*
Disbursements and Expenses			
Spending Plan Reduction		*$2,547,000*	
Disbursements to Grantees[3]	*$4,200,000*	*$1,458,066*	*$3,500,000*
Total Disbursements:	*$4,200,000*	*$4,005,066*	*$3,500,000*
Expenses			
Administrative & Office Expense	*$70,000*	*$108,407*	*$110,000*
Professional Review Panel	*$50,000*	*$44,043*	*$50,000*
NJCBIR Registry	*$0*	*$0*	*$0*
Total Expenses:	*$120,000*	*$152,450*	*$160,000*
Total Disbursements and Expenses:	*$4,320,000*	*$4,157,516*	*$3,660,000*
Closing Fund Balance: (June 30)	*$666,413*	*$1,420,825*	*$1,380,825*

[1]Net revenue variance.
[2]Funds plus interest deposited annually in January.
[3]Funds represent 1 year of grant funding; total awarded in FY2014 was $3,953,347.

2014 RESEARCH GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENTS:

Wilma Friedman, Ph.D.
Rutgers, The State University of NJ
Life Science Center

Grant Award: $540,000

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.

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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.

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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.

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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.

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FELLOWSHIP RESEARCH GRANT RECIPIENTS:

Christopher Lowe
Rutgers, The State University of NJ
Biomedical Engineering

Grant Award: $100,500

Project Title: *Immobilized BDNF fragment peptide-grafted collagen hydrogels to promote neural survival and regeneration after TBI*

A novel collagen scaffold which incorporates recently developed neuroactive peptides is evaluated for its ability to promote recovery and regeneration of neurons after simulated TBI. Traumatic brain injury (TBI) affects more than a million new people in the United States every year, caused most commonly by vehicle crashes, falls, violence, and sports related injuries. TBI often results in debilitating loss of brain function, severely reducing the quality of life of those afflicted. Loss of brain function is caused by the damage or death of neurons, the cells responsible for signaling and communication within the nervous system, including the brain. The damage or death of neurons is caused either by the initial physical head trauma or by the toxic response in the brain which follows a severe head trauma.

The brain cannot heal itself from severe injuries which cause death and damage to neurons and no treatment currently exists to repair this type of damage. Brain derived neurotrophic factor (BDNF) has been shown to promote the survival of neurons following TBI, but soluble BDNF is cleared too quickly from the injury site to have the desired effect. Neural stem cells (NSCs) have been injected into the injured brain to replace dying neurons, but many of the cells do not survive transplantation into the injured brain, due to the toxic environment. Our project combines these two strategies with a collagen hydrogel as a potential therapeutic for TBI. Small peptide mimics of BDNF will be grafted to collagen so that they remain localized to the injected site. NSCs will be loaded into this collagen prior to injection to protect them from the toxic environment in the injured brain. We hypothesize that this hydrogel system will help to heal damaged neurons and the NSCs will be a source of replacement neurons to repopulate the injury site.

We will evaluate the effect of our proposed hydrogel system on the viability and development of both primary neurons and NSCs in cell culture using antibody staining and will evaluate the neuron function through calcium imaging to observe the firing of neurons. Later, we will use an in vitro model to simulate the effects of TBI on primary neurons. Following the simulated injury we will deliver our NSC containing BDNF-mimic hydrogel and evaluate its efficacy in promoting survival of injured neurons and development of the NSCs into new neurons. The development of the proposed hydrogel system represents a combined therapeutic which will improve future strategies in treatment of TBI.

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Matthew Long
New Jersey Institute of Technology

Grant Award: $100,500

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.

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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.

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Julia Coyne, Ph.D.
Kessler Foundation

Grant Award: $240,910

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.

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Pelin Avcu
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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.

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Charu Garg
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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.

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New Jersey Commission on Brain Injury Research

Victoria DiBona
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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.

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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.

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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.

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Denise Krch, Ph.D.
Kessler Foundation

Grant Award: $176,606

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.

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New Jersey Commission on Brain Injury Research

Anthony Lequerica, Ph.D.
Kessler Foundation

Grant Award: $163,760

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.

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New Jersey Commission on Brain Injury Research

Anna M. Barrett, M.D.
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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.

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