

# **2012 Annual Report**



Chris Christie, Governor Kim Guadagno, Lt. Governor



Mary E. O'Dowd, MPH Commissioner January 30, 2013

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 2012. Once again the Commission has had an active and productive year. We recently completed the sixth 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 support of the New Jersey Department of Health for their valuable support and contributions towards the work of the Commission on Brain Injury Research.

Sincerely,

Dennie Todd Acting Chairperson

## Members of the Commission

Dennie Todd, Acting Chairperson Dennis Benigno Meiling Chin, MBA Shonola Da-Silva, M.D., MBA Daniel Keating, Ph.D. Cynthia Kirchner, MPH Nicholas Ponzio, Ph.D. Mark Evan Stanley, Ph.D.

## **Commission Personnel**

Christine Traynor, Administrator Mary Ray, Fiscal Administrator

Health & Agriculture Building, Market & Warren Streets, P.O. Box 360 365 S. Warren Street, 5<sup>th</sup> Floor, Room 502, Trenton, New Jersey 08625 609-633-6465

## ACKNOWLEDGMENTS

The NJCBIR would like to express its sincere appreciation to all Commission members, and to the New Jersey Department of Health for their expertise, time, and effort that contributed to the development of this report and support of the program throughout the year.

The NJCBIR also acknowledges the contributions of the Center for Health Statistics for the brain injury surveillance statistics, and to Commission staff members Christine Traynor and Mary Ray for their contributions of substantial material as well as their review and valuable comment.

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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 \$17 million to individual scientists at various academic and research institutions, and approved 36 separate scientific research projects.

- o Since 2007, ten NJCBIR scientific research projects have been completed.
- *Progress made by NJCBIR 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 2012:

- o Individual Research Grants
- o Programmatic Multi-Investigator Research Grants
- Pilot Research Grants
- o Postdoctoral and Graduate Fellowship Grants

#### \* NJCBIR 2012 Achievements:

- o Thirty applications requesting \$12.3 million were submitted.
- Seven awards were made in 2012 totaling \$3,728,503.
  - Two Individual Research grants totaling \$1,002,103, one Pilot Research grant totaling \$180,000, one Multi-Investigator Research grant totaling \$2,034,000, and three Fellowship grants totaling \$512,400 were approved.

## NJ Brain Injury Registry:

- NJCBIR supports a central registry of brain injured persons in New Jersey in cooperation with the New Jersey Department of Health and Senior Services Center for Health Statistics.
- The database provides a resource for research, evaluation, and information on brain injuries.
- All Level 1 trauma centers now collect and submit comprehensive data electronically and soon an on-line system will allow all New Jersey acute care facilities to participate.

## 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<sup>\*</sup> 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.

<sup>\*</sup>Based on estimates from the Centers for Disease Control and the New Jersey Department of Health and Senior Services 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 the quest to develop 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, Center for Health Statistics in establishing a database of all brain injured patients in New Jersey.

Now in its eighth year of operation, the NJCBIR has funded 36 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 NJCBIR 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 NJDHSS, or designee University of Medicine and Dentistry of New Jersey Rutgers, The State University of New Jersey Eight Public Members – at least one licensed physician, a brain injured individual, a parent of a brain injured individual, 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.

The NJCBIR holds public meetings 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 NJCBIR 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. The NJCBIR funds all its grant programs and other activities entirely from this dedicated source. No part of the NJCBIR's 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 NJCBIR supports meritorious research projects that advance the understanding of traumatic brain injuries. The NJCBIR 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 NJCBIR.
- To develop and evaluate clinical interventions that lead to improved treatment and function after traumatic brain injury.

## **RESEARCH FUNDING PRIORITIES**

The NJCBIR 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 NJCBIR website: www.nj.gov/health/njcbir.

The NJCBIR currently offers an array of grant programs 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 will fund 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 NJCBIR 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.

## **<u>Clinical Studies</u>**

- 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 NJCBIR 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 NJCBIR application process is now entirely electronic utilizing the *New Jersey System for Administering Grants Electronically* (NJSAGE) grants management system, and is accessible through the NJCBIR website.

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

The NJCBIR 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 NJCBIR for final consideration and vote.

The NJCBIR 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

New Jersey Commission on Brain Injury Research grant programs are designed to provide opportunities attractive to a wide range of researchers. NJCBIR 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 NJCBIR 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 multidisciplinary 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- 2012 NJCBIR SUMMARY AND PERFORMANCE RECORD

Since 2007, the New Jersey Commission on Brain Injury Research has funded 36 separate scientific research projects to scientists at New Jersey academic and research institutions. These awards represent an investment in brain injury research of \$17 million.

The NJCBIR receives approximately 35 applications annually, approving six or more new awards totaling between \$2.5 and \$3.5 million.

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

- University of Medicine & Dentistry of NJ Rutgers, State University of New Jersey Kessler Medical Rehabilitation Center Stevens Institute for Technology Princeton University Cooper University Hospital Research Institute Atlantic Health Care System Neuro. Institute St. Barnabas Medical Center The Center for Neurological & Neurodevelopment Health LLC, Clinical Research Center of NJ, & The Center for Neurological & Neurodevelopment Health II, Inc. – NeurAbilities
- Coriell Institute for Medical Research New Jersey Institute of Technology Hackensack University Medical Center International Brain Research Foundation Englewood Hospital Research JFK Neuroscience Institute Edge Therapeutics, Inc. Rowan University Morristown Medical Hospital & Medical Center St. Barnabas Medical Center

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

## 2012 NJCBIR 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 NJCBIR 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 NJCBIR 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.

NJCBIR grant programs are designed to provide opportunities attractive to a wide range of researchers. NJCBIR 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 NJCBIR has been a major factor in fostering this interest and continued involvement in brain injury research within the State of New Jersey.

## **2012 Applications**

2012 saw the New Jersey Commission on Brain Injury Research in its eighth year of operation and its sixth cycle of grants.

In 2012, 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 30 grant applications were received. Seven grants were awarded totaling \$3,728,503. The grant awards included two Individual Research grants, three Fellowship grants, one Pilot Research grant, and one Multi-Investigator Research grant.

#### **2012 Outreach and Development Efforts**

The NJCBIR 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 NJCBIR 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*.

2012 Grant Cycle Information Grant Application Deadline: October 3, 2011 Award Notification Date: April 30, 2012

**Available Grant Programs:** 

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

#### **GRANTS PROGRAM FOR 2013**

For Fiscal Year 2013, the New Jersey Commission on Brain Injury Research allocated up to \$6.5 million dollars for brain injury research projects.

2013 Grant Cycle Information Grant Application Deadline: October 3, 2012 Award Notification Date: April 30, 2013

**Available Grant Programs:** 

- Individual Research 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, directed by the Center for Health Statistics, collects brain injury data from New Jersey hospitals, and provides analysis of that data for health professionals.

#### New Jersey Traumatic Brain Injury Surveillance System

	Males		Females		Tota	
Year	Ν	Rate	Ν	Rate	Ν	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	137.3	3,942	74.2	9,707	104.7
2011	5,563	132.0	4,042	75.2	9,605	102.6

#### Hospitalizations for TBI by Gender, New Jersey, 2000 - 2011

Rates are age-adjusted using the 2000 US Standard Population, calculated per 100,000 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, 2013.

#### Age-Adjusted Traumatic Brain Injury Incidence Rates, New Jersey, 2008 - 2009

	2008		2009		Rate Difference
	Ν	Rate <sup>1</sup>	Ν	Rate	2008-2009
All Traumatic Brain Injuries	9,868	109.1	10,294	112.3	2.93%
Mechanism of Injury					
Motor Vehicle (Traffic)	2,305	26.6	2,213	25.3	-4.89%
Fall	4,760	50.7	5,194	54.5	7.50%
Assault	834	9.8	740	8.7	-11.22%
Self-injury	46	0.5	52	0.6	20.00%
Gender					
Male	5,967	144.7	6,146	148.2	2.42%
Female	3,901	75.7	4,148	78.7	3.96%
Race <sup>2</sup>					
White	6,460	104.3	6,760	107.3	2.88%
Black/African American	1,301	117.0	1,375	123.4	5.47%
Hispanic	1,218	102.5	1,339	109.6	6.93%
Fatality <sup>3</sup>					
Fatal	1,085	11.00%	1,041	10.11%	-8.03%
Non-fatal	8,783	89.00%	9,253	89.89%	0.99%

<sup>1</sup>Rates are age-adjusted using the 2000 US Standard Population, calculated per 100,000. Bridged-race estimates are used in calculations.

<sup>2</sup>Race/ethnicity information is missing for 613 (6.2%) of 2008 TBI incidents and 565 (5.5%) of 2009 TBI incidents.

<sup>3</sup> "Fatal TBI" includes out of hospital deaths and inpatient deaths with TBI listed in the multiple cause of death fields, and

hospitalized deaths of patients with "severe" TBI who have no TBI listed specifically in the cause of death fields. "Non-fatal TBI" are inpatients who may have died, but had only mild or moderate severity TBI, or inpatients who were discharged from the hospital "alive".

Incidence data are from the New Jersey Central Nervous System Injury Surveillance, 2013, and includes all New Jersey resident hospitalizations in New Jersey hospitals and deaths of New Jersey residents regardless of state of death.

## 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.

Fund Balance Statement:			
	SFY 2012	SFY 2012	SFY 2013
	Projected	Actual	Projected
Opening Fund Balance: (July 1)	\$5,289,270	\$5,275,659	\$5,509,431
Revenues			
Assessments <sup>1</sup>	\$3,600,000	\$4,067,022	\$3,600,000
Investments Earnings - Interest <sup>2</sup>	\$35,000	\$22,927	\$20,000
Total Revenue:	\$3,635,000	\$4,089,949	\$3,620,000
Total Funds Available:	\$8,924,270	\$9,365,608	\$9,129,431
Disbursements and Expenses			
Disbursements to Grantees	\$6,532,500	\$3,728,503	\$6,532,500
Total Disbursements:	\$6,532,000	\$3,728,503	\$6,532,500
Expenses			
Administrative & Office Expense	\$187,478	\$100,306	\$60,750
Professional Review Panel	\$60,000	\$25,368	\$50,000
NJCBIR Registry	\$50,000	\$2,000	\$0
Total Expenses:	\$297,478	\$127,674	\$110,750
Total Disbursements and Expenses:	\$6,829,978	\$3,856,177	\$6,643,250
•			
Closing Fund Balance: (June 30)	\$2,094,292	\$5,509,431	\$2,486,181

## State Fiscal Year 2012

<sup>1</sup>Net revenue variance

<sup>2</sup>Funds plus interest deposited annually in

January

## 2012 RESEARCH GRANT AWARDS

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

Helen Genova, Ph.D.

Grant Award: \$462,103

Kessler Foundation

#### Project Title: The Longitudinal Examination of the Relationship between White Matter Pathology & Cognitive Impairment in Traumatic Brain Injury using Diffusion Tensor Imaging

The current proposal will examine the relationship between reduced white matter integrity, assessed by Diffusion Tensor Imaging, and cognitive decline in chronic TBI. 5.3 million people in the United States experience long-term disability due to a Traumatic Brain Injury (TBI). While some individuals may recover cognitively from TBI, many individuals experience long-term cognitive impairment which can negatively impact quality of life and the ability to maintain relationships and careers. An understanding of why some individuals with TBI show improved cognitive outcome, while others decline is critical to the prescription of early interventions, such as cognitive rehabilitation. However, researchers have consistently failed to find appropriate predictors of cognitive outcome. Pathology assessed by conventional MRI following TBI does not appear to be strongly associated with cognitive measures, mainly due to the fact that traditional MRI methods cannot detect microscopic damage.

A newly emerging neuroimaging technique, Diffusion Tensor Imaging (DTI) has been shown to be sensitive to microscopic damage, such as Diffuse Axonal Injury (DAI) and damage to white matter, which is strongly correlated with cognitive impairment following TBI. However, no one to our knowledge has examined the relationship between changes in white matter integrity over time (using DTI) and changes in cognition over time in a chronic sample of TBI (more than 2 years post-injury).

The goal of the proposed study is to examine changes in both white matter integrity and cognition over time and assess their relationship with one another. Additionally, the predictive value of DTI will be investigated by examining white matter integrity at time point 1 and determining if it predicts cognitive impairment at time point 2. If DTI proves to be a useful biomarker of cognition in TBI, it will have critical value to both scientists and clinicians to determine which individuals should be targeted for specific interventions to improve white matter integrity. Further, targeting of "at risk" individuals will enable us to utilize interventions aimed at halting cognitive decline.

Grant Award: \$540,000

Martin Yarmush, Ph.D. Department of Biomedical Engineering Rutgers, The State University of NJ

## Project Title: Evaluation of Encapsulated Mesenchymal Stromal Cells as a Therapeutic for Traumatic Brain Injury Treatment

Traumatic brain injury (TBI) begins with mechanical disruption of tissue, which triggers a cascade of secondary insults that injures neurons for weeks, and even months, following the initial trauma.

Many of the devastating, long-term functional consequences of TBI may be avoided by therapies that target secondary inflammatory effects. Although current anti-inflammatory treatment approaches have been only minimally effective, an expanding body of evidence suggests that transplanted Mesenchymal Stromal Cells (MSC) can improve functional traumatic nervous system outcomes via secretion of cytokines and neurotrophic factors. However, current MSC infusion strategies are inefficient and lack the necessary control features needed for clinical translation.

Therefore, one of the objectives of our proposed studies is improve upon current TBI therapeutics by determining whether the anti-inflammatory and neurotrophic benefits of MSC can be harnessed and optimized by encapsulating MSC within an alginate matrix. The encapsulation approach allows the MSC to sense soluble factors in the environment without directly interacting with tissue. We have shown that this strategy improves the anti-inflammatory capabilities of MSC, and that this approach improves outcomes after spinal cord injury. However, we have yet to test the system in models of brain injury. As such, this research meets the funding priorities of the NJCBIR, specifically the study of strategies to promote neuronal growth and survival, and improve brain function after injury; and the evaluation of the efficacy of interventions that prevent or reduce secondary injury.

Additionally, this research is a collaboration between two scientists, Dr. Shreiber from Rutgers, who specializes in spinal cord injury biomechanics and regeneration, and Dr. Yarmush who has a wealth of experience in evaluating MSC encapsulation and therapeutic approaches in a number of injury models.

## MULTI-INVESTIGATOR RESEARCH GRANT RECIPIENT:

**Gabriella D'Arcangelo, Ph.D.** Department of Cell Biology & Neuroscience Rutgers, The State University of NJ Grant Award: \$2,034,000

## Overall Project Title: The Role of mTOR Signaling in Recovery after Traumatic Brain Injury

This project investigates the role of Akt/mTOR signaling in recovery after traumatic brain injury and other types of neuronal injury. Traumatic brain injury (TBI) is no longer a silent epidemic. On track to become the third leading cause of death and disability worldwide by 2020, the recent public awareness surrounding TBI only increases the need to find an effective treatment for this disease.

In this proposal, we study one central signaling pathway (mTOR/Akt) as a possible approach for developing new treatment approaches for TBI. This specific signaling pathway may be important in repairing the brain after TBI because it plays a significant part in shaping the function of neural circuits. We evaluate if this signaling pathway is activated in both in vivo and in vitro models of TBI, test if controlling parts of this pathway will improve recovery in the wiring and function of neural circuits after injury, and examine if controlling this pathway with drug treatment will improve outcome in a preclinical model of TBI. Our ambitious scope is made possible through the coordinated activities of investigators across three distinct projects, and will provide a strong foundation that can progress into federal support beyond the timetable of the proposed research plan.

## <u>Sub-Project #1 Title</u>: Analysis of the Akt/mTOR Signaling Pathway after Pten Deletion, Traumatic Brain Injury or Neuronal Injury

Gabriella D'Arcangelo, Ph.D., Department of Cell Biology & Neuroscience Rutgers University

In this project, we will generate genetically modified mouse lines in which the Akt/mTOR signaling pathway is upregulated in distinct neuronal populations, and determine whether in vivo TBI or in vitro neuronal injury modulates this pathway. We examine the progression of Akt/mTOR activation over time following injury. Biochemical assays measure the levels of signaling activity, and confocal fluorescence microscopy techniques identify cell types in which these events take place. Our major hypotheses are that Akt/mTOR activation alters neuronal growth, differentiation and function in Pten mutant mice, and that this signaling pathway also occurs in response to TBI/mechanical injury. Here we determine if the activation persists for a prolonged period of time after injury, and if it is influenced by the severity of the injury.

## <u>Sub-Project #2 Title</u>: *Effects of PTEN Loss on Functional Recovery after Traumatic Brain Injury*

**Bonnie Firestein, Ph.D.**, Department of Cell Biology & Neuroscience Rutgers University

This study utilizes a genetic approach to examine the effect of mTOR activation by PTEN deletion after TBI using both in vivo and in vitro models. With a systematic analysis of the mTOR activation pathway after mechanical trauma in vitro and in vivo (Sub-Project 1) and a goal of testing therapeutic options in this pathway in vivo (Sub-Project 3), this project uses genetic tools from Subproject 1 to test how the mTOR pathway contributes to the structure and function of neural circuits after mechanical injury. We test the general hypothesis that neuronal damage and loss of functionality is decreased when PTEN is deleted, and as a result, mTOR activity is increased. Imaging, electrophysiological, and neurobehavioral assays will be used to compare recovery in normal and mutant mice and cultures from these mice.

## Sub-Project #3 Title: Role of mTOR in Recovery from Traumatic Brain Injury

**David F. Meaney, Ph.D.**, Department Chair, Department of Bioengineering University of Pennsylvania, Philadelphia, PA

This project uses pharmacological approaches to modulate the activity of mTOR in vivo and in vitro, examining the consequence of these manipulations on recovery from TBI. Our general hypothesis is twofold: (a) mild mechanical injury leads to an enhancement in mTOR activation that causes an increase in neural network function without a change in dendritic morphology, and (b) more severe mechanical injury will trigger an increase in mTOR activation that causes a change in dendritic morphology, an impairment in network function, and a vulnerability to secondary chemical injury. We test the possible neuroprotective role of mTOR/Akt activation/inhibition on neuronal survival and improvement in neural circuit function and neurobehavior, and we examine if the role of mTOR/Akt changes across the severity of TBI.

Our major hypotheses include: Mechanical injury activates mTOR/Akt across the injury severity spectrum in vivo and in vitro. Mild mechanical injury leads to an enhanced network activity, sustained at least in part by mTORC1 assembly. Moderate mechanical injury in vitro and in vivo leads to a change in dendritic morphology that reduces the functional connectivity of local microcircuits. Alterations in dendritic morphology are mediated by the neuronal cytoskeleton, and can be influenced by mTORC2. Protecting against this loss in the physical wiring of neural microcircuits mediated by mTOR/Akt triggered cytoskeletal reorganization - will help promote the recovery of neural circuits after traumatic injury. To test these hypotheses, we use information on the timing and activation of specific mTOR/Akt pathway components after mild and moderate TBI in vivo (Sub-Project #1) to plan our pharmacological approaches. In addition, we integrate our studies with Subproject #2 that concentrates on how TBI in causes dendritic varicosities and circuit malfunction both in vitro and in vivo. Based on these data, we test if these morphological changes are influenced through the mTOR/Akt pathway.

## FELLOWSHIP RESEARCH GRANT RECIPIENTS:

#### Nolan Skop

Grant Award: \$86,700

UMDNJ - Department of Neuroscience

## Project Title: Delivery of Neural Stem Cells Using a Multifunctional Microsphere Scaffold for Traumatic Brain Injury Repair

This project aims at regenerating the brain after severe injury using neural stem cells transplanted within a novel, multifunctional tissue engineered scaffold.

Traumatic brain injury (TBI) affects approximately 1.7 million Americans each year. Injuries in people over the age of 65 years can be attributed largely to falls, whereas hits to the head, motor vehicle accidents or casualties of war are often the reasons for TBI in younger adults and children. Immediate consequences may affect cognitive or motor functions including the loss of mobility, coordination, memory, reasoning, sensations, emotions, ability to communicate and process information. Other effects may take a while to appear such as an increased risk for developing epilepsy, Alzheimer's disease, Parkinson's disease, or other neurological disorders. Medical expenses from hospital bills and rehabilitation services can exacerbate the problem, costing a person with TBI up to four million dollars in a lifetime.

Usually after a person sustains an injury the medical team will do what is necessary to minimize secondary damage to the brain as a result of the inflammatory response. Doctors try to maximize blood flow (which allows for oxygen and nutrients to supply the brain) while minimizing the swelling caused by intracranial pressure that may damage more cells. The central nervous system does not have the same regenerative capability as other organs of the body and there are currently no approved strategies to regenerate brain cells after TBI.

Stem cells have emerged for their therapeutic potential as an attractive cell source for neural regeneration. Despite significant progress in stem cell transplantation after brain injury, success has been limited. Cells are being transplanted into a lesion lacking a substrate and necessary nutrients to promote their growth and survival. We have created a novel biomaterial scaffold to be used with stem cells to promote neural regeneration after severe brain injury. In this application we are requesting funds to take our studies out of the tissue culture dish into an animal model of TBI to see whether by combining our scaffold with neural stem cells that new neurons and glial cells can be produced to heal the injured cerebral cortex.

**Starla Weaver, Ph.D.** Kessler Foundation Grant Award: \$199,764

## Project Title: The Effects of Task Switching Training on Traumatic Brain Injury

The proposed research will use a task switching training to improve executive functioning and examine the neuroplasticity in patients with TBI.

More than three million Americans are estimated to be living with a lifelong disability as a result of TBI. Rehabilitation programs that are able to target and improve executive functioning are critical to reducing disability among patients. Task switching ability has been found to be the best predictor of performance on real-world abilities necessary for independent living. In task switching subjects switch between the performance of two simple tasks. A number of studies have demonstrated the potential for task switching training to improve performance, particularly among populations who show impairments in executive function.

The proposed research will use task switching training to improving executive function among patients with TBI. An initial behavioral experiment will be used to compare the effects of tasks switching training on patients with TBI, with the effects of task switching training on healthy controls, and the effect of a non-task switching, single task training on patients with TBI. A second experiment will examine the neural correlates of improvements in executive function that result from task switching training. fMRI will be used to compare activation patterns of TBI patients with poor or good outcomes following task switching training. Task switching training is hypothesized to lead to generalizable improvements of executive function that result in lasting benefits for patients with TBI. Andrea Giovannucci, Ph.D. Princeton University Department of Molecular Biology Grant Award: \$225,936

Project Title: Optical Imaging and Computational Modeling of Cerebellar Injury

This project will use optical functional imaging data from cerebellar circuitry to computationally model lost function and possible interventions.

Traumatic brain injury represents an enormous challenge for rehabilitation. Most therapies for TBI focus on the cerebral cortex (a.k.a. neocortex), which is a prominent site of injury. Less appreciated is the role of the cerebellum, the second-largest major division of the brain. The cerebellum and neocortex are heavily interconnected and are likely to play a tandem role in motor, social, and cognitive function. Brain circuits can change as a result of both injury and experience over time. This carries two implications for injury and rehabilitation. First, TBI can have long-term consequences in any brain structure that is connected to the site of injury. Second, neuroprosthetic interventions are potentially effective at sites that are distant to the site of injury.

This proposal takes two novel approaches to addressing long-term consequences of TBI using modern optical methods for observing and influencing brain activity. The first approach is two-photon microscopy, an advanced imaging method that allows brain circuits to be monitored for up to weeks. Two-photon microscopy will be used to monitor the consequences of TBI for cerebellar function. The second approach is computational simulation: we will adopt an understand-and-repair strategy, which can drive the design of therapeutic interventions at the cellular level. Our studies will provide a proof of concept for the rehabilitation of brain function by next-generation neuroprosthetic.

## PILOT RESEARCH GRANT RECIPIENT:

Sridhar S. Kannurpatti, Ph.D. UMDNJ – New Jersey Medical School Grant Award: \$180,000

## Project Title: Mitochondrial Function and Translational Markers of Reorganization in Traumatic Bain Injury

Functional Magnetic Resonance Imaging (fMRI) markers specific to mitochondrial function after traumatic brain injury will be developed to bridge existing gap in drug evaluation for brain injury. Humans sustain mild traumatic brain injuries under various circumstances. In survivors progressive deterioration in brain function occurs months to years after sustaining the injury. Structural markers of concussive injuries are not easily visible in anatomical clinical imaging rendering the visualization of brain lesions and subsequent healing after therapy difficult.

Functional Magnetic Resonance Imaging (fMRI) has emerged as an effective tool to study human brain function. Though expensive, it is a very powerful tool to image the brain without injecting any medication or invading the patient's body. Further, this does not involve any harmful radiation that the patient may be exposed to with other radiological imaging techniques such as PET, CT or X-ray. Due to its high speed in collecting images of the brain (several in a few seconds) they can be mathematically processed to visualize activity within the brain.

Brain circuits alter after TBI with notable changes in neuronal cells and blood vessels that support them. One of the main causes for deficient brain function after TBI is impaired mitochondrial function. Mitochondria being the energy source of cells support several brain functions including the regulation of its blood supply and functioning of its neurons. When mitochondrial function is impaired after TBI, profound deficiencies occur in neurons and their supporting blood vessels. We hypothesize that this leads to altered activation of neural circuits leading to cognitive deficiency, sensory and motor dysfunction. This study will introduce innovative fMRI methods to map brain function after TBI to track the brain reorganization after treatment with mitochondria altering drugs.

This proposal will characterize the workings of normal and injured mitochondria in the intact animal without any simplification and decipher its relationship with measurable imaging markers. Normal rats and rats that sustain a mild TBI will be imaged. Brain activation will be performed through tactile stimulation of the rat whiskers when their brain mitochondria function normally or impaired after mild TBI. The pharmacology-imaging model developed will be readily translatable to humans to better visualize therapy-induced brain reorganization during TBI rehabilitation.