NJCSCR 2015

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Annual Report State Fiscal Year 2015

Chris Christie, Governor
Kim Guadagno, Lt. Governor

NJ Health
New Jersey Department of Health

Cathleen D. Bennett
Acting Commissioner

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

2015 ANNUAL REPORT

JANUARY 30, 2016

January 29, 2016

The Honorable Chris Christie, Governor
Office of the Governor
State House – P.0. Box 001
Trenton, New Jersey 08625

Dear Governor Christie:

On behalf of the New Jersey Commission on Spinal Cord Research (NJCSCR), its members, staff and the spinal cord injured citizens of New Jersey, it is my privilege to present the Annual Report for Fiscal Year 2015, pursuant to N.J.S.A. 52:9E-4(f).

In 2015, the NJCSCR awarded nearly $3.6 million in spinal cord research grant funding. This included five Individual Research Grants totaling $2,916,162, three Exploratory Research Grants totaling $597,794, and one Fellowship Grant totaling $60,000. These spinal cord research projects were carefully selected by a panel of independent scientific experts from 28 applications submitted by investigators at New Jersey academic institutions.

NJCSCR grants often produce the basic research findings necessary to compete successfully for larger National Institutes of Health, and National Science Foundation awards. They help attract talented scientists and students to this exciting and promising field.

Each of the funded projects has the potential to contribute significantly to the development of treatments and cures for the paralysis and secondary complications that accompany spinal cord injury.

We wish to thank you, the Department of Health, and the State of New Jersey for continued support of spinal cord injury research.

Respectfully,

Susan P. Howley

Susan P. Howley
Chairperson

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2015 COMMISSION MEMBERS

Susan P. Howley, Chairperson

Peter W. Carmel, M.D.

John D. Del Colle

James McCormack

Michael J. Rhode

Loran C. Vocaturo, Ed.D.

Anthony Welch

ACKNOWLEDGEMENTS

The NJCSCR 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.

This report is being submitted in fulfillment of the legislative mandate in the *N.J.S.A. 52:9E-4(f)*. The report describes the implementation of the Spinal Cord Research Act and evaluates the benefit of the Act as evidenced in the report of grant awards for State Fiscal Year 2015.

ADMINISTRATIVE STAFF

Christine Traynor, Administrator

Mary Ray, Fiscal Manager

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EXECUTIVE SUMMARY

The New Jersey Commission on Spinal Cord Research (NJCSCR), established in 1999, funds spinal cord injury research projects in New Jersey.

- ***Since 2001, over $45 million has been awarded to individual scientists at academic and research institutions.***
  - *194 separate scientific research projects have been awarded; 159* scientific research *projects have been completed.*
  - *Progress made by researchers has been presented in abstracts, scientific conferences, symposia, and meetings.*
  - *NJCSCR programs have enabled wider scientific interaction and numerous active research collaborations, many with out-of-state researchers.*
  - *Success in achieving NJCSCR funding has resulted in academic and career advancement for New Jersey researchers, including doctoral dissertations.*
  - *Numerous successful applications to the National Institutes of Health, the National Science Foundation and other organizations based on NJCSCR grants have been made.*

- ***NJCSCR offered four grant programs in Fiscal Year 2015:***
  - *Individual Research Grants*
  - *Exploratory Research Grants*
  - *Postdoctoral and Graduate Fellowship Grants*
  - *Spinal Cord Injury Techniques Training Travel Grants*

- ***NJCSCR 2015 Achievements:***
  - *Twenty-eight applications requesting a total of $8.7 million were submitted.*
  - *Nine awards were made in 2015 totaling $3,573,956.*
  - *Five Individual Research Grants totaling $2,916,162, three Exploratory Research Grants totaling $597,794 and one Fellowship Grant totaling $60,000 were approved.*

- ***NJ Spinal Cord Registry:***
  - *NJCSCR supports a central registry of spinal cord injured persons in New Jersey in cooperation with the New Jersey Department of Health.*

    The registry is a resource for research, evaluation and information on spinal cord injuries.

INTRODUCTION

Spinal cord injury has long been regarded as a virtually hopeless diagnosis with a grim prognosis. However, new approaches to rehabilitation and modern medicine have extended life expectancy from mere months to years and even decades.

Many people with permanent injury now look forward to vital and productive lives. More recently, breakthroughs in research and new horizons in the life sciences are moving us closer to finding cures for spinal cord injuries.

Spinal cord injury impacts individuals and families across the state and nation. Though young men remain at greatest risk, the number of women and older people suffering spinal cord injury is increasing. Falls, traffic and worksite accidents are the major causes of injuries. Black and Hispanic populations suffer disproportionately.

The economic and human cost of these injuries remains huge. Better therapies are urgently needed and the task of research is more demanding than ever. Paralysis resulting from spinal cord injury may no longer be "an ailment not to be treated," but the search for the answers remains among the greatest challenges to medical science and the healing arts.

NEW JERSEY'S COMMITMENT TO SPINAL CORD RESEARCH

The Spinal Cord Research Act (N.J.S.A. 52:9e-1 et seq.) created the New Jersey Commission on Spinal Cord Research and the New Jersey Spinal Cord Research Fund to support its activities.

New Jersey is a leader in funding research aimed at repair of the damaged spinal cord. The New Jersey Commission on Spinal Cord Research, created in 1999 under New Jersey's Spinal Cord Research Act, represents the successful culmination of years of determined effort to enlist New Jersey in the fight.

The NJCSCR offers research grant programs for both established scientists and younger researchers committed to spinal cord injury research. The Commission also supports the database of all spinal cord injured patients in New Jersey, which was established and is maintained by the New Jersey Department of Health.

Now in its 16th year of operation, the NJCSCR has funded 194 research projects and supported individual scientists at research institutions around the state. Its impartial and scientifically rigorous application and review process has helped make the NJCSCR vital to New Jersey's scientific investigators in their pursuit of the development of effective therapies for spinal cord injury.

THE NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

The NJCSCR is one of only a handful of publicly-funded organizations nationwide that, together with the National Institutes of Health, the Centers for Disease Control, the Veterans' Administration, Department of Defense and a few other entities, provide essential support for research to develop treatments for spinal cord injury and the life-threatening secondary dysfunctions that accompany it.

Created as a semi-independent public body, the NJCSCR 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 it is not a part of the Department and is not included in its budget.

The NJCSCR establishes and oversees the operations of the grant-making 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. Members serve for three-year terms. Five 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 spinal cord research.

Any qualified person wishing to be considered for appointment may submit his or her name to the Governor's Office of Appointments. Information on how to apply can be found on the following website at http://www.state.nj.us/governor/admin/bca.

The Commission will always have one or more individuals from each of the following institutions and categories:

- *The Commissioner of the Department of Health or designee (voting ex-officio member)*
- *Rutgers, The State University of New Jersey*
- *Spinal Cord Injury Model System (Kessler Foundation Research Center)*
- *Christopher & Dana Reeve Foundation (American Paralysis Foundation)*
- *Public Members (at least one spinal cord physician and a spinal cord injured individual)*

The NJCSCR holds public meetings at least four times a year. A majority of the sitting members constitutes a quorum for all purposes. 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 NJCSCR also maintains standing committees that meet and provide an informal structure to discuss issues and proposals on an *ad hoc* basis in advance of presenting them to the full Commission.

ADMINISTRATION

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

Administrative staff schedule and facilitate all activities, manage the scientific merit review process, negotiate with outside vendors, and maintain the necessary relationships within state government.

NEW JERSEY SPINAL CORD RESEARCH FUND

The work of the NJCSCR is supported entirely by a statutory one dollar surcharge on all New Jersey traffic and motor vehicle fines or penalties. Vehicular accidents are a significant cause of spinal cord injury.

Revenue is collected by the New Jersey State Treasurer for deposit into the New Jersey Spinal Cord Research Fund. The NJCSCR funds all its grant programs and other activities entirely from this dedicated source. No part of the NJCSCR's operating budget is paid out of New Jersey's general tax revenue.

MISSION AND GOALS

The NJCSCR implements the commitment of the State of New Jersey to the international quest for cures for catastrophic spinal cord injuries. Through its grants programs and related activities, the NJCSCR reinforces New Jersey's preeminence as a center of biomedical research, and a leader in neuroscience, neurotrauma and spinal cord research.

- *The NJCSCR supports meritorious research projects that advance the understanding of spinal cord injury and explore potential therapeutic strategies.*
- *The NJCSCR supports the progression of research from bench to bedside.*
- *The NJCSCR programs enhance the reputation of New Jersey as a focus of biomedical research and increase its attractiveness to researchers and business.*

OBJECTIVES

To accelerate research that will deepen our understanding of spinal cord injury and lead to safe and effective interventions and cures for paralysis and associated conditions.

Specifically, the NJCSCR works to:

- *Advance the field of spinal cord research in New Jersey by encouraging established scientists to apply their expertise to spinal cord research.*
- *Foster collaborative, interdisciplinary approaches to spinal cord research.*
- *Nurture future generations of spinal cord researchers by supporting young scientists and postdoctoral fellows.*
- *Prevent or treat secondary biological conditions resulting from spinal cord injury.*
- *Disseminate the research findings generated by scientists supported by the NJCSCR.*

RESEARCH FUNDING PRIORITIES

The ***NJCSCR 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 NJCSCR website: www.state.nj.us/health/spinalcord.

An array of grant programs is offered including Individual Research Grants, Fellowship Grants, Exploratory Research Grants and Spinal Cord Techniques Training Travel Grants. Each of these programs is designed to support and encourage spinal cord research in New Jersey in a unique way.

The NJCSCR is continually evaluating its programs and seeking ways to improve its performance and results.

NJCSCR Research Guidelines

The New Jersey Commission on Spinal Cord Research will fund research activities that hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. The areas of research listed below highlight the focus of current NJCSCR emphasis and funding:

- *Studying strategies to promote neuronal growth and survival, encourage the formation of synapses, enhance appropriate myelination, restore axonal conduction, replace injured cells, or otherwise improve function after spinal cord 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 spinal cord injury or disease in well-defined animal models and in the human spinal cord, specifically documenting the cellular systems vulnerable to injury or disease and the functional losses which occur as a result thereof.*
- *Elucidating biological or physical mechanisms underlying approaches to improve functions compromised by spinal cord injury, e.g., bladder, bowel, and sexual function, and alleviate chronic pain, spasticity, and severe hypertension.*
- *Developing strategies to prevent or treat secondary complications arising from injury or disease to the spinal cord.*
- *Developing innovative restorative rehabilitation strategies to promote recovery of biological function.*
- *Translating basic and pre-clinical findings into clinical application.*
- *Supporting the investigation of promising new approaches.*

OTHER ACTIVITIES

The NJCSCR is engaged in activities that promote awareness of and interest in spinal cord injury and opportunities for research.

The NJCSCR supports the New Jersey Department of Health to maintain a "*Spinal Cord Injury Registry*" - a centralized repository of a standardized data set collected and submitted by treating hospitals on each new case of spinal cord injury in New Jersey.

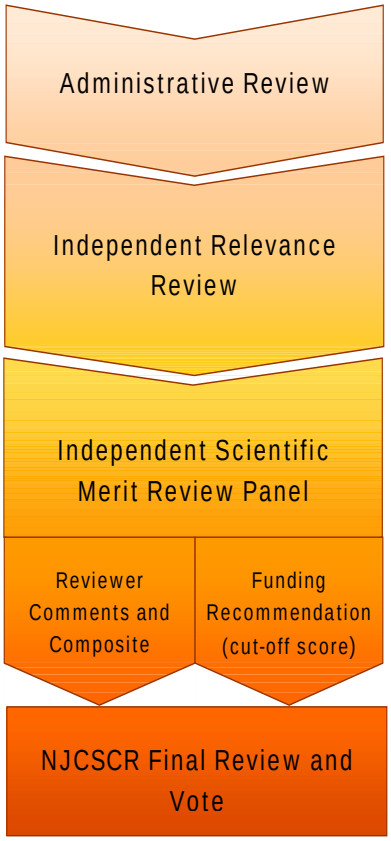
Such a registry is mandated by statute as a resource for research, evaluation, and information on spinal cord injuries.

THE NJCSCR APPLICATION AND REVIEW PROCESS

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

The NJCSCR grant application process is entirely electronic utilizing the New Jersey System for Administering Grants Electronically (SAGE) system, and is accessible through the NJCSCR website.

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



The NJCSCR administrative staff reviews all applications for completeness and accuracy, and assists applicants in correcting errors or omissions.

Relevance to the overall goals of the NJCSCR is assessed by an expert panel that also recommends and assigns scientific reviewers for each grant application from a pool of over 100 highly qualified scientists.

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

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

The NJCSCR 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

NJCSCR grant programs are designed to provide opportunities attractive to a wide range of researchers.

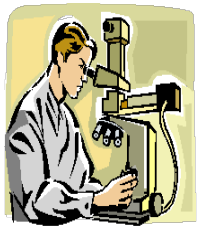
The Individual Research Grant is designed to fund senior independent researchers. Fellowship Grants offer encouragement to graduate students and postdoctoral researchers. The Exploratory Research Grant enables researchers to apply innovative ideas from other areas of science to spinal cord injury and repair in order to acquire the preliminary data needed to successfully apply for larger grants from the NJCSCR, the National Institutes of Health, and other funding agencies.

Collaborations between basic research scientists and clinicians with spinal cord injury experience are encouraged. Young investigators are encouraged to partner with established investigators to nurture their scientific growth.

All applicants are encouraged to collaborate with other New Jersey-based researchers, as well as with researchers located out-of-state, or out of the country.

Complete details on all grant programs are available on the NJCSCR website.

Individual Research Grants



- *Individual Research Grants support senior scientists to explore meritorious novel scientific and clinical ideas.*
- *Up to $600,000 for up to three years ($200,000 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 spinal cord research.*
- *All fellowships include an annual stipend, research allowance and travel budget.*
- *Postdoctoral Fellowships run for three years with a total award of $150,000; ($50,000 per annum)*
- *Graduate Fellowships run for two years with a total award of $60,000 ($30,000 per annum)*

Exploratory Research Grants

- *Enable independent investigators to apply their specific expertise to spinal cord research.*
- *Develop preliminary data needed to justify higher levels of funding.*
- *Apply innovative ideas from other areas to spinal cord research.*
- *Encourage inter-institutional and/or inter-state collaborations.*
- *Up to $200,000 for a two-year non-renewable grant.*

Spinal Cord Injury Techniques Training Travel Grants

- *Offers applicants the ability to participate in a spinal cord injury techniques training course.*
- *Applicants may select from a course of their own choosing, or choose to attend a course located at either Rutgers, The State University of New Jersey or at the Spinal Cord Injury Research Training Program held at the Ohio State University.*
- *A one-time per applicant non-renewable award of up to $4,000 is provided.*

2001-2015 NJCSCR SUMMARY & PERFORMANCE RECORD

Since 2001, the New Jersey Commission on Spinal Cord Research has invested $45,319,452.86 in New Jersey scientists. Scientific interest in the field of spinal cord injury research remains strong due to the ongoing investment of these funds.

Typically the NJCSCR receives approximately 30 applications annually, approving 10 or more new awards, totaling between $2-$3 million.

Grant Applications

To date, the NJCSCR has received 612 applications from researchers, postdoctoral fellows, and graduate students from New Jersey research institutions, which cumulatively total $170.4 million in grant funding requests.

The NJCSCR has explored a range of grant programs that provide opportunities for both very senior and younger researchers, and larger programs for establishing new spinal cord research facilities and support for professorships.

Applications for Individual Research grants typically account for about two-thirds of the total. Interest in both the Fellowship and Individual Research grant programs is historically strong. Fellowships offer the advantage of engaging the greatest number of scientists in spinal cord research for the least cost.

Grant Funding

Individual Research grants awarded to established investigators are the mainstay of spinal cord research in New Jersey. These projects aim at advancing the field in significant ways and are most productive as measured by publications and applications for additional funding.

The Fellowship program is the NJCSCR's most cost-effective initiative, as measured by the number of researchers supported per grant dollar. The NJCSCR is committed to bringing new researchers and promising students into the field. Its programs of graduate and postdoctoral Fellowships have been a success, in both numbers and the quality of applicants.

Qualified Research Institutions

The NJCSCR requires that the organization or institution of a grant applicant be approved as a qualified research institution prior to the submission of a grant application. NJCSCR funds may only go to researchers affiliated with qualified research institutions.

Five institutions are named in the Spinal Cord Research Act, and fourteen others have been designated by the NJCSCR. These organizations provide a continuing source of interest and applications for NJCSCR funds.

Statutory Qualified Research Institutions:

Rutgers, The State University of New Jersey
University of Medicine and Dentistry of NJ
Kessler Foundation
Princeton University
Coriell Institute for Medical Research

NJCSCR-Designated Qualified Research Institutions:

New Jersey Institute of Technology
VA New Jersey Health Care System & Veterans Biomedical Research Institute
Stevens Institute for Technology
Drew University
JFK NJ Neuroscience Institute/JFK Health System
Progenitor Cell Therapy, LLC
Seton Hall University/Seton Hall School of Health & Medical Science
Wyeth Research/Pfizer
TRIM-edicine, Inc.
Rowan University
Cooper University Hospital & Cooper University Medical School & Health System
Hackensack University Medical Center
Celvive, Inc.
Montclair State University

Results and Achievements

Although a cure for spinal cord injury remains elusive, the investment of millions of dollars by the NJCSCR and other organizations has led to a wealth of new knowledge and insights that hold promise for effective therapies and cures.

NJCSCR grantees and their institutions have capitalized on the opportunities afforded by the availability of Commission funding. Scientific knowledge and careers have been advanced and institutional revenue and scientific achievements have been increased.

The NJCSCR has been a major factor in fostering the interest and continued involvement in spinal cord research within the State of New Jersey.

The NJCSCR continues to pursue its mission, encouraging and supporting spinal cord research in New Jersey. Many of its researchers can point to significant accomplishments.

- *Numerous scientific articles reporting on work funded by NJCSCR have appeared in peer-reviewed scientific publications, and additional articles are in preparation.*
- *Progress made by NJCSCR researchers has been presented in numerous abstracts, scientific conferences, symposia, and meetings.*
- *NJCSCR programs have enabled wider scientific interaction and research collaborations, many with out-of-state researchers.*
- *Success in achieving NJCSCR funding has resulted in academic and career advancement for New Jersey researchers, including doctoral dissertations.*
- *Applications to the National Institutes of Health, the National Science Foundation, and other organizations have been submitted, based in part on work funded by NJCSCR grants.*

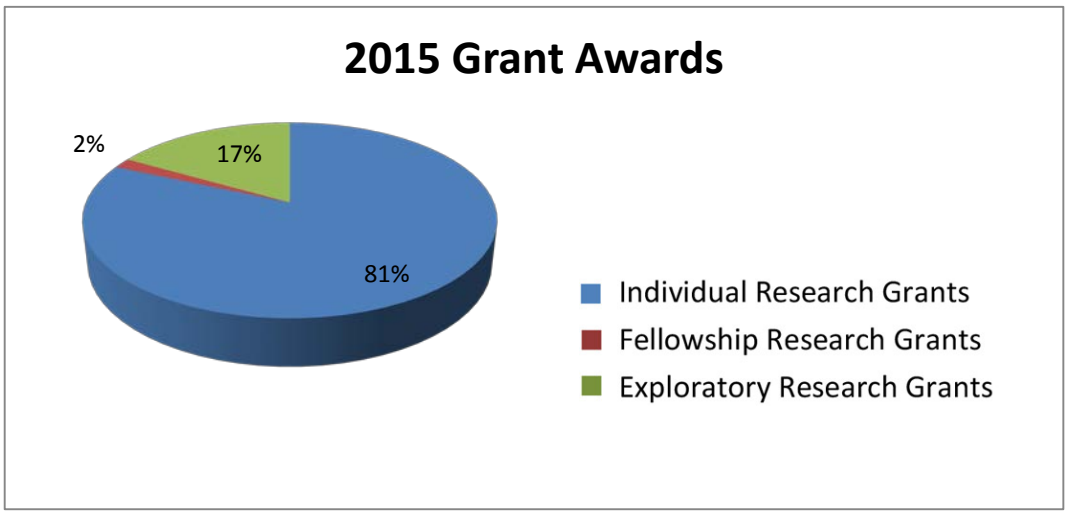
The NJCSCR is committed to broadening its portfolio of institutional grantees and increasing the size and diversity of its funding activities. Through outreach activities, the NJCSCR encourages participation by all research organizations with an interest in spinal cord research.

2015 NJCSCR YEAR IN REVIEW

2015 Spinal Cord Research Grants Program

Nine applicants were awarded a total of $3,573,956 in 2015.

Five Individual Research Grants totaling $2,916,162, three Exploratory Research Grants totaling $597,794, and one Fellowship Grant totaling $60,000 were funded after a careful review of the 28 applications submitted.



2015 Applications

2015 saw the New Jersey Commission on Spinal Cord Research in its 16th year of operation, and its 20th cycle of grants. Twenty-eight applications were submitted with requests for funds totaling $8.7 million.

2015 Outreach and Development Efforts

The NJCSCR maintains an ongoing interest in expanding spinal cord injury research in New Jersey. Direct contacts, attendance at events and meetings, plus its website and publications are some of the resources used to publicize NJCSCR grant opportunities throughout the state.

Publication of Grant Programs

Official Notices of Grant Availability advise interested parties of the grant programs. These were published in the *New Jersey Register* and in the New Jersey Department of Health's *Directory of Grant Programs*.

In Fiscal Year 2015, one grant cycle was offered; up to $6 million was made available for spinal cord research projects.

2015 Grant Cycle
Grant Application Deadline: December 10, 2014
Award Notification Date: May 30, 2015
Available Grant Programs:

- *Individual Research Grants*
- *Exploratory Research Grants*
- *Fellowship Grants*
- *Spinal Cord Injury Techniques Training Travel Grants*

GRANTS PROGRAM FOR 2016

For Fiscal Year 2016, up to $6.5 million has been allocated for spinal cord injury research projects.

The NJCSCR authorized one grant cycle for Fiscal Year 2016 offering Individual Research Grants, Fellowship Grants, Exploratory Research Grants and Spinal Cord Injury Techniques Training Travel Grants.

2016 Grant Cycle
Grant Application Deadline: December 10, 2015
Award Notification Date: June 29, 2016
Available Grant Programs:

- *Individual Research Grants*
- *Exploratory Research Grants*
- *Fellowship Grants*
- *Spinal Cord Injury Techniques Training Travel Grants*

NEW JERSEY SPINAL CORD INJURY REGISTRY

The Spinal Cord Research Act mandates the establishment and maintenance of a central registry of persons who sustain spinal cord injuries throughout the State. The NJCSCR has been supporting the work of the Department of Health to create the mechanism for the collection and analysis of spinal cord injury data.

The registry is a resource for research, evaluation, and information on spinal cord injuries. The Department of Health Center for Health Statistics publishes an annual report providing data on spinal cord and brain injuries in New Jersey.

The following tables summarize data collected on spinal cord injury in New Jersey.

All Spinal Cord Injury Inpatient Hospitalizations Fatal and Non-Fatal, New Jersey Residents, 2003-2014

	2003			2004			2005			2006			2007			2008		
Groups	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*
Males	148	48	**196**	173	55	**228**	201	62	**263**	187	57	**244**	203	64	**267**	204	80	**284**
Females	59	44	**103**	50	48	**98**	62	50	**112**	81	57	**138**	71	57	**128**	67	63	**130**
Under 15 years	12	0	**12**	13	2	**15**	20	0	**20**	8	1	**9**	11	2	**13**	3	0	**3**
15-24 years	36	1	**37**	41	3	**44**	58	7	**65**	40	1	**41**	69	4	**73**	51	6	**57**
25-34 years	29	7	**36**	39	2	**41**	42	6	**48**	35	6	**41**	18	8	**26**	30	8	**38**
35-44 years	37	15	**52**	40	14	**54**	41	13	**54**	34	12	**46**	33	9	**42**	44	15	**59**
45-54 years	34	13	**47**	21	15	**36**	33	13	**46**	40	11	**51**	46	16	**62**	40	22	**62**
55-64 years	18	18	**36**	28	12	**40**	25	15	**40**	35	18	**53**	42	18	**60**	37	15	**52**
65-74 years	12	7	**19**	18	19	**37**	22	14	**36**	27	13	**40**	25	23	**48**	26	19	**45**
75-84 years	21	18	**39**	12	18	**30**	18	23	**41**	36	30	**66**	21	21	**42**	25	32	**57**
85 years and older	8	13	**21**	11	18	**29**	4	21	**25**	13	22	**35**	9	20	**29**	15	26	**41**
White non-Hispanic	108	69	**177**	121	74	**195**	147	82	**229**	137	74	**211**	135	92	**227**	137	104	**241**
Black non-Hispanic	52	6	**58**	48	11	**59**	56	17	**73**	71	22	**93**	58	14	**72**	53	23	**76**
Native American	0	1	**1**	1	1	**2**	1	0	**1**	0	0	**0**	0	0	**0**	1	0	**1**
Asian/Pacific Islander	3	2	**5**	3	1	**4**	4	3	**7**	8	4	**12**	10	3	**13**	8	2	**10**
Hispanic	24	7	**31**	34	10	**44**	29	7	**36**	32	8	**40**	41	9	**50**	4	6	**10**
Other or Unknown	20	7	**27**	16	6	**22**	26	3	**29**	20	6	**26**	30	3	**33**	28	8	**36**
Total	**207**	**92**	**299**	**223**	**103**	**326**	**263**	**112**	**375**	**268**	**114**	**382**	**274**	**121**	**395**	**271**	**143**	**414**

	2009			2010			2011			2012			2013			2014		
Groups	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*	*Trauma*	*Acute*	*Total*
Males	227	93	**320**	218	96	**314**	266	83	**349**	239	70	**309**	235	98	**333**	227	104	**331**
Females	81	54	**135**	89	57	**146**	92	59	**151**	92	59	**151**	88	69	**157**	99	60	**159**
Under 15 years	6	0	**6**	5	2	**7**	10	1	**11**	9	1	**10**	10	0	**10**	7	2	**9**
15-24 years	58	6	**64**	37	5	**42**	58	2	**60**	39	1	**40**	30	4	**34**	41	3	**44**
25-34 years	32	9	**41**	43	8	**51**	53	8	**61**	39	4	**43**	38	5	**43**	32	5	**37**
35-44 years	30	10	**40**	40	9	**49**	41	16	**57**	24	10	**34**	36	10	**46**	32	13	**45**
45-54 years	57	21	**78**	50	30	**80**	38	7	**45**	53	14	**67**	58	37	**95**	53	25	**78**
55-64 years	40	23	**63**	38	25	**63**	56	26	**82**	61	29	**90**	41	23	**64**	50	30	**80**
65-74 years	35	25	**60**	43	25	**68**	41	24	**65**	47	27	**74**	38	25	**63**	44	28	**72**
75-84 years	36	24	**60**	32	27	**59**	39	31	**70**	35	31	**66**	33	37	**70**	35	27	**62**
85 years and older	14	29	**43**	19	22	**41**	22	27	**49**	24	12	**36**	39	26	**65**	32	31	**63**
White non-Hispanic	174	110	**284**	173	120	**293**	193	98	**291**	191	85	**276**	196	125	**321**	190	120	**310**
Black non-Hispanic	58	26	**84**	62	21	**83**	79	21	**100**	70	23	**93**	64	22	**86**	66	18	**84**
Native American	0	0	**0**	0	0	**0**	0	1	**1**	0	0	**0**	1	0	**1**	0	0	**0**
Asian/Pacific Islander	11	3	**14**	11	5	**16**	11	9	**20**	6	5	**11**	7	7	**14**	9	6	**15**
Hispanic	45	4	**49**	41	4	**45**	44	10	**54**	38	7	**45**	38	9	**47**	38	10	**48**
Other or Unknown	20	4	**24**	20	3	**23**	31	3	**34**	26	9	**35**	17	4	**21**	23	10	**33**
Total	**308**	**147**	**455**	**307**	**153**	**460**	**358**	**142**	**500**	**331**	**129**	**460**	**323**	**167**	**490**	**326**	**164**	**490**

Spinal Cord Injury Hospitalizations by Age and Gender
Non-Fatal New Jersey Residents, 2012-2014

	Males		Females		Total	
Age Groups	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*
Under 15	15	**	12	**	27	0.5
15-24 years	91	5.1	22	1.3	113	3.3
25-34 years	97	5.6	17	**	114	3.3
35-44 years	97	5.5	21	1.2	118	3.3
45-54 years	184	9.3	47	2.3	231	5.7
55-64 years	143	8.8	75	4.2	218	6.4
65-74 years	116	12.1	81	7.1	197	9.4
75-84 years	87	18.0	90	13.1	177	15.1
85 and older	51	27.2	77	19.8	128	22.2
Total	881	6.5	442	2.6	1,323	4.5

Spinal Cord Injury Hospitalizations by Age and Gender
Non-Fatal New Jersey Residents, 2014

	Males		Females		Total	
Age Groups	*N*	*Rate*	*N*	*Rate*	*N*	*Rate*
Under 15	5	**	2	**	7	**
15-24 years	32	5.4	10	**	42	3.6
25-34 years	29	5.0	6	**	35	3.0
35-44 years	34	5.9	7	**	41	3.5
45-54 years	64	10.0	14	**	78	5.8
55-64 years	53	9.6	20	3.3	73	6.3
65-74 years	40	12.0	28	7.1	68	9.4
75-84 years	28	17.3	30	13.1	58	14.8
85 and older	15	**	33	25.2	48	24.6
Total	300	6.6	150	2.6	450	4.6

Notes For All Tables:
Inpatient hospitalizations for spinal cord injuries for New Jersey residents selected according to bill type in the NJ Hospital Discharge Data System. Rates are calculated per 100,000 population and are either age-specific or age-adjusted using the 2000 US Standard Population. Rates are not calculated for fewer than 20 observations, percent's not calculated for fewer than 5 observations, denoted by **.
Races are as reported. Hispanics can be of any race.

Data Sources: New Jersey Central Nervous System Injury Surveillance Data; NCHS Bridged Race Estimates for Population.

Source All Tables: New Jersey Central Nervous System Injury Surveillance Data, 2003-2014
Center for Health Statistics and Informatics
Office of the Commissioner, New Jersey Department of Health
December 29, 2015

FINANCIAL STATEMENTS

The activities and programs of the NJCSCR are supported by the New Jersey Spinal Cord Research Fund as established by the Act. A one dollar ($1.00) surcharge is imposed on all fines or penalties levied under the provisions of Title 39 of the Revised Statutes or any other motor vehicle or traffic violation. The revenue surcharge is collected and forwarded to the New Jersey State Treasurer and deposited annually in an interest-bearing account designated as the New Jersey Spinal Cord Research Fund.

FUND BALANCE STATEMENT:	**SFY 2015** *Projected*	**SFY 2015** Actual	**SFY 2016** *Projected*
Opening Fund Balance (July 1):	***$2,852,209***	**$2,640,374**	**$3,775,475**
Revenue			
Assessments[1]	*$3,600,000*	*$3,784,353*	*$3,600,000*
Investments Earnings - Interest[2]	*$15,000*	*$10,217*	*$10,000*
Total Revenue:	*$3,615,000*	*$3,794,570*	*$3,610,000*
Total Funds Available:	***$6,467,209***	***$6,434,944***	***$7,385,475***
Disbursements			
Spending Plan Reduction			
Disbursements to Grantees[3]	*$6,030,000*	*$2,373,956*	*$6,030,000*
Total Disbursements:	***$6,030,000***	***$2,373,956***	***$6,030,000***
Expenses			
Administrative & Office Expense	*$115,000*	*$269,763*	*$275,000*
Professional Review Panel	*$35,000*	*$15,750*	*$35,000*
NJCSCR Registry	*$0*	*$0*	*$0*
Total Expenses:	***$150,000***	***$285,513***	***$310,000***
Total Disbursements & Expenses:	***$6,180,000***	***$2,659,469***	***$6,340,000***
Closing Fund Balance (June 30):	***$287,209***	***$3,775,475***	***$1,045,475***

[1]Net revenue variance.

[2]Funds plus interest deposited annually in January.

[3]Funds for one year of grant funding.

2015 RESEARCH GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENTS:

Jean Schwarzbauer, Ph.D. **Grant Award: $548,914**
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Project Title: ***A Cell-Assembled Matrix Template to Guide Nerve Regeneration in the Spinal Cord***

With nature as our guide, we will develop a biomaterial that is composed of a natural aligned extracellular matrix to direct axon growth across an implantable polymer scaffold for spinal cord repair. A spinal cord injury (SCI) is a trauma to the spine that damages nerve pathways and disrupts function leading to sensory and motor loss. SCIs occur at a rate of 30 per day in the United States with almost half resulting in complete loss of function below the level of injury. The initial injury is further compounded by wound healing responses in the spinal cord that involve bleeding, inflammation, and scarring at the site of injury. Regeneration of the nerve pathways is greatly restricted because of scarring and inhibitory factors, so it is highly uncommon for an injured person to gain complete restoration of function. Currently, the treatment of SCI is limited beyond stabilizing the injury and rehabilitation to maintain existing function. Clearly, new therapies for SCIs are greatly needed to promote full recoveries; these must overcome problems of the inhibitory microenvironment at the injury site and the failure of nerves to regenerate across it.

In order to bridge the injury site and promote nerve regeneration, we propose a new, double-pronged tissue-engineering strategy based on concepts of natural nerve development that integrates a spinal cord-mimicking hydrogel scaffold with native cell-assembled extracellular matrix (ECM) for neuron guidance. The two primary aims for this proposal are: (1) developing an optimal regenerative microenvironment combining ECM and growth factors for neurons; (2) constructing hydrogel scaffolds functionalized with these optimized ECM conditions to implant into SCI sites. The great novelty of this program lies in its uniting micropatterned hydrogel materials with a natural, cell-instructive ECM in order to develop successful therapies to restore function after SCIs.

In Aim 1, hydrogels will be micropatterned in order to create an aligned, cell-assembled ECM that can spatially guide nerve regeneration along the original nerve pathways. We will use this template to develop an optimized, regenerative ECM using nerve-specific cells and factors that facilitate enhanced nerve outgrowth. In Aim 2, to examine the efficacy of our engineered scaffolds and ECM, we will implant our scaffolds into a transected spinal cord

model to assess restoration of function and nerve guidance in the longer term. Together, these studies will enable us to better understand how to create optimal regenerative microenvironments for nerve growth and how to use this information for the design of bioactive hydrogel scaffolds to facilitate recovery in SCI victims.

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Grant Award: $600,000

Project Title: ***Role of Gsx1 in Activation of Neural Stem Cells and Neurogenesis after Spinal Cord Injury***

This project is to determine the functional role and molecular mechanism of Gsx1 in the activation of the neural stem/progenitor cells and neurogenesis after spinal cord injury.

The goal of this project is to elucidate the molecular mechanism underlying the activation (proliferation and differentiation) of neural stem/progenitor cells (NSPCs) after spinal cord injury (SCI). NSPCs persist in the adult mammalian central nervous system (CNS), and they function as a potential source of nerve cells for repair and regeneration after injury. Studies have shown that injury induces activation and proliferation of NSPCs in the adult mammalian CNS. However, the mechanism underlying injury-induced NSPC activation remains to be elucidated. In addition, the regenerative capacity of injury-induced neurogenesis is limited possibly due to the low efficiency. Thus, the potential uses of endogenous NSPCs in SCI to provide "self-repair" and regeneration cannot be fully realized.

Studies have established that the homeobox genes Gsx1 and Gsx2 play essential roles in the development of the mammalian spinal cord. Gsx2 is expressed in a subset of NSPCs and can be ectopically induced in injured brains, indicating a critical role of Gsx2 in injury-induced regenerative response. However, the role of Gsx1 in injury-induced neurogenesis is not well characterized. We have previously identified a NSPCs-specific cis-element, derived from the second intron of the Notch1 gene (Notch1CR2), can control reporter gene expressions in NSPCs. Using a Notch1CR2-GFP transgenic mouse line in which GFP expression correlates with endogenous Notch1 expression and is rarely visible in the adult CNS, we show that SCI induces a marked increase in the number of GFP+ NSPCs at the injury site. Sequence analysis shows that Notch1CR2 contains a Gsx1 binding site and we have showed that in the developing chick CNS, Gsx1 regulates Notch1CR2 function in NSPCs. Our preliminary studies further demonstrate that Gsx1 can control Notch1CR2 function in spinal cord NSPCs during embryonic development. It is known that Notch1 actively functions in the post-injury neural regeneration by regulating spontaneous cell proliferation, gliogenesis, synapse formation and axon remyelination. It is possible that Gsx1 can activate Notch signaling and/or other NSPCs-specific signaling pathways by interacting to its binding sites found in cis-elements. We hypothesize that the transcription factor Gsx1 is a key regulator of NSPC activation upon injury. We will determine the role of Gsx1 in injury-induced NSPC proliferation and differentiation; and the mechanism of Gsx1 in regulating NSPC-specific gene activation after injury.

Successful completion of this project will not only advance our understanding of the molecular mechanism of NSPC regulation during development and regeneration after injury, but also provide a basis for the future development of clinical interventions for millions of people who suffer from injury. Thus, our comprehensive studies will have a significant impact on both the basic stem cell biology and clinical translation.

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Grant Award: $599,482

Project Title: ***Spinal Cord Protection: Understanding the Ischemic Insult to the Spinal Artery***

The development and testing of novel translational approaches to avoid ischemic spinal cord injury with endovascular approaches to thoracoabdominal aortic aneurysm repair.

The aorta is the largest blood vessel in the human body and is responsible for transporting oxygenated blood pumped from the left ventricle of the heart to all parts of the body through the systemic circulation. In some people, the wall of the aorta may become weak and enlarge, a disorder known as an aortic aneurysm. Though the risk for these localized bulges in the wall of the aorta are higher in some families due to genetic abnormalities in the connective tissues that make up the vessel wall, there are a wide range of factors that put people at an increased risk for acquiring this disorder, from uncontrolled high blood pressure to increasing age. The most common form of aortic aneurysm involves the part of the aorta that extends between the upper chest, or thorax, and the abdominal cavity. These types of aneurysms are called thoracoabdominal aortic aneurysms or TAAAs. Though many people have TAAAs without experiencing any symptoms, in some cases - particularly when the aorta dilates to greater than 1.5 times its normal size – individuals may experience back pain that is considered a sign that the vessel might burst. If TAAAs rupture, massive internal bleeding can occur and, unless treated quickly, can rapidly lead to shock and death.

In recent years, many advances have occurred in the surgical options available for the treatment and repair of TAAAs. Among these are minimally invasive options that take advantage of large vessels in the body that can be easily accessed through small cuts to the groin, also known as endovascular access. These approaches avoid the need to open the chest wall to gain access to the diseased portion of the aorta and allow for synthetic tubes (made of fabric-coated metal mesh), or stents, to be placed in the vessel to stabilize it and insure that it does not rupture.

Although endovascular techniques have been found to have a lower rate of mortality than open surgical methods, when properly placed, stents block a large number of the vessels that serve the tissues surrounding the aorta, including the spinal cord. This surgery, therefore, carries a high risk for spinal cord injury and paraplegia. Paraplegia is the severe or complete loss of the ability to move or feel the lower body. Symptoms of paraplegia may include an inability to walk or to control one's bladder and/or bowels.

The Cardiothoracic Research Group of Hackensack University Medical Center is trying to better understand the injury response of the vessels that service both the spinal cord, and the

structures around it. They are looking at new ways to protect the spinal cord to reduce the large risk for paraplegia that comes with current methods to repair aneurysms. Though their ideas are gained through actual experiences with humans, new methods are tested using pigs since their anatomy is very similar to humans. This insures that any new findings can to be tested for their safety and effectiveness before they are offered to patients.

To this end, the research group is refining a new surgical strategy where endovascular procedures are done in two steps, the first of which is used to stimulate the growth of new and bigger vessels that will assure the spinal cord continues to get the blood it needs, even after a stent blocks those channels. After the two-stage procedure, samples collected from the pigs are used to look at mediators of inflammation and healing that are supported by this new method. Based on previous successes that have led to better outcomes in humans, the group is confident that their experiments will offer new insight that will help prevent the possible catastrophic consequences of this surgery for people in New Jersey and across the globe.

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Grant Award: $567,766

Project Title: ***Nanoparticle-Based Treatment of Pressure Sores in Spinal Cord Injury Patients***

This project develops nanoparticles carrying bioactive peptides that speed up the healing of pressure sores. There are approximately 400 new patients per year who suffer from spinal cord injury in New Jersey. A major secondary complication in spinal cord injury patients is the development of pressure ulcers, which are open wounds that occur as a result of injury to skin and muscle from prolonged sitting or lying. These wounds can take a long time to heal, which can prevent the patient from performing daily activities. Open wounds are also highly susceptible to infection, which can lead to amputation or severe septicemia.

Pressure sores can be difficult to treat, especially in patients who have co-morbidities, such as diabetes. In order to speed up the wound healing process, we propose to develop a nanoparticle technology that can release bioactive peptides when placed topically to the wound area and help accelerate wound healing. Although bioactive peptides, such as growth factors, have been proposed to improve wound healing, this strategy by itself does not work because the wound environment contains high levels of proteases that quickly degrade these factors.

The nanoparticle technology that we propose will protect the bioactive peptides from degradation and allow long-term release to the wound environment, so that they persist in the wound environment much longer. This nanoparticle technology also has several advantages from the standpoint of product manufacturing. First, the components can be made by genetic engineering bacteria to produce large amounts of the raw material. Second, the raw material spontaneously self-assembles into nanoparticles, which are very easily purified, unlike typical peptide growth factors that require slow and expensive purification methods. Third, the nanoparticles are very small, which makes them easy to incorporate into existing wound treatment strategies, such as bandages, skin substitutes, creams, and so on. Finally, the nanoparticle platform can be used with a variety of bioactive peptides that target different cellular components of the skin.

In this particular proposal, we plan to generate nanoparticles that target three different aspects of skin wound healing. We hypothesize that these nanoparticles will significantly enhance the performance of existing skin substitutes and wound dressings.

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Grant Award: $600,000

Project Title: ***Enhancement of Cytoskeletal Dynamics and Motor Transport By Manipulation of Post-Translational Microtubule Glutamylation To Maximize Neuroregeneration***

We will manipulate post-translational glutamylation of microtubules to promote cytoskeletal dynamics and intracellular transport to maximize neuroregeneration after injury. Spinal cord injury (SCI) leads to devastating neurological defects and disability. Although neurons in our central nervous system (CNS) possess an intrinsic ability to regenerate, this ability is often insufficient to restore function after SCI. For functional regrowth, injured neurons must dramatically reorganize their microtubule (MT) networks. MTs act as both structural components of the cytoskeleton and "cellular highways" for intracellular transport. If MTs are the highways, molecular motors are the trucks that transport essential cargos to the far reaches of the neuron—especially the growing tips of axons where they are most needed after neuronal injury. Therapies that target the process of MT reorganization and motor trafficking might promote regrowth of injured neurons. But first, we need to understand how MTs and transport are regulated.

The dynamic cytoskeletal changes in injured neurons occur microscopically, so they cannot be visualized in human patients or in living vertebrate experimental model systems. Therefore, our lab studies these processes in Caenorhabditis elegans, a powerful experimental animal model. Major assets of C. elegans include a transparent body that allows us to directly observe neuronal remodeling after physical or genetic injury. Because most basic biological processes, including axon development and neuronal transport, are conserved between C. elegans and humans, we can apply the fundamental principles we discover in C. elegans to higher organisms. By using cutting edge technologies to visualize MT dynamics and transport in living C. elegans animals, we can identify molecules that enhance intrinsic regenerative capacity of a neuron.

Using these techniques, our lab has identified genes that regulate a MT modification, called polyglutamylation that acts as a signpost along the MT highways. Mutations that affect polyglutamylation cause fundamental defects in the MT highways, resulting in traffic jams of motors. Such traffic jams might mean that needed cargos cannot reach their destinations, and in some cases can result in neuronal degeneration. For example, MT glutamylation can act as "speed limit" sign to restrict the velocity of particular motors and cargos inside neurons. Additionally, we found that MT modifications act as "under construction" signs that specify the preservation, construction, or demolition of particular MT highways. Our discoveries suggest MT signposts are essential regulators of neuronal regrowth and survival, a notion that

we will test in rodent models of SCI. The overall goal of this project is determine how MT signposts that regulate the MT highways in neurons can be used to improve regeneration after injury by controlling motor transport and MT dynamics. Outcomes of this research should have groundbreaking impact for understanding the most fundamental elements of neuronal degeneration and regeneration, and possibly provide new therapeutic avenues for SCI.

FELLOWSHIP GRANT RECIPIENT:

Keerthana Deepti Karunakaran **Grant Award: $60,000**
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Project Title: ***Understanding Cortical Reorganization in Spinal Cord Injury Using Resting State fMRI***

A spinal cord injury (SCI), often a result of blunt or sharp force trauma, is a devastating event that results in paralysis to lower limbs and in more severe cases to both lower and upper limbs. A major goal of SCI is to reduce the neurological damage and reestablish functionality by utilizing the plastic property of the brain. Although it is known that rewiring occurs in the brain in order to compensate for the loss, secondary complications such as phantom sensations, neuropathic pains etc. are very common. Despite the occurrence of non-desirable outcomes first described a century ago, lack of non-invasive tools to study the dynamic properties of the brain has limited our understanding of the underlying mechanisms.

Functional magnetic resonance imaging (fMRI) is a noninvasive imaging technique that allows us to study the baseline activity of the brain at resting condition. This provides an advantage to the SCI community, as it does not require the subject to perform any tasks, but allows us to study the brain reliably.

Our goal is to study large-scale changes in brain function in SCI subjects during the first 3 months of SCI onset and later at 9 months of SCI onset, such that changes in brain activity during recovery can be analyzed. This research could provide a reliable marker that could be used to predict the likelihood of a patient responding positively to a treatment and monitor the efficiency of a particular rehabilitative approach.

EXPLORATORY RESEARCH GRANT RECIPIENTS:

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Project Title: ***The Role of Hv1 Proton Channel in Secondary Spinal Damage and Central Neuropathic Pain after Spinal Cord Injury***

We test the hypothesis that the Hv1 proton channel contributes to spinal cord inflammation, secondary spinal damage, and central neuropathic pain following experimental spinal cord compression injury. Spinal cord injury refers to any injury to the spinal cord that is caused by trauma, typically associated with major trauma from motor vehicle accidents, falls, sports injuries, and violence. Depending on where the spinal cord is damaged, the symptoms can vary widely, from pain to paralysis to incontinence. According to the National SCI Statistical Center, the number of people in the United States who were alive in 2012, and who had spinal cord injury was estimated to be approximately 270,000 persons, with a range of 236,000 to 327,000 persons. Treatment of spinal cord injuries can vary widely depending on the location and extent of the injury, but usually starts with restraining the spine and controlling inflammation to prevent further damage. In general, we are interested in how inflammation causes the secondary damage and central neuropathic pain after spinal cord injury. Specifically, we are studying inflammatory cells, such as microglia, macrophage, and neutrophil, and their functions in spinal cord injury. Microglia/macrophages are immune cells that circulate in the brain to detect and control or kill invading bacteria. Their primary weapons are reactive oxygen species (ROS) and inflammatory mediators, and damage proteins and lipids in the bacteria, thus killing or hindering them. Unfortunately, ROS not only damage invading bacteria, but can also damage normal brain tissue and the vessels that supply blood to the brain under disease conditions, such as stroke and spinal cord injury.

Our laboratory recently discovered that the protein responsible for proton secretion is an ion channel we call Hv1. In order to test the function of Hv1, we have generated mice lacking Hv1. Using these mice, we have found that Hv1 is coupled with immune response including ROS and cytokine production. Under disease conditions such as ischemic stroke, Hv1 contributes to brain damage. Also, we have some preliminary results that show the Hv1 proton channel is important for neuropathic pain after peripheral nerve injury. In the current proposal, we will determine whether Hv1 is needed for the spinal cord inflammation, tissue damage, and central neuropathic pain after spinal cord contusion injury. If this is the case, drugs may be developed that inhibit Hv1 and can prevent the generation of harmful effects following spinal cord injury. Therefore, our study will provide a potential therapeutic target for treatment of spinal cord injury. In summary, our proposal will be the first attempt to

investigate Hv1's function in secondary damage and central neuropathic pain in spinal cord injury, with the aim of evaluating Hv1 as a potential new therapeutic target for its treatment.

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Grant Award: $197,794

Project Title: ***Assessing Spinal Cord Structure Changes using Diffusion Tensor Imaging in Patients with Incomplete Traumatic Spinal Cord Injury***

This project proposes to use a special MRI technology to assess nerve fiber structural changes in spinal cord in acute incomplete spinal cord injury patients (some abilities to move their limbs).

Each year in the United States there are 12,000 new cases of spinal cord injury (SCI). Not only does SCI cause considerable physical damage and disability to the individuals, it imposes a significant economic and emotional burden on them and their families. Average lifetime costs can be in the millions for a given SCI patient.

There has been mounting evidence of movement function recovery and changes occurring in the spinal cord following SCI, especially after rehabilitation therapy. To evaluate the functional outcome of recovery, clinicians often rely on questionnaire-based neurological tests to score the motor and sensory functions. These tests are subject to short comings including inability to measure recovery below injury level and inherent variability across examiners.

To overcome these shortcomings, we propose to use advanced and non-invasive diffusion tensor imaging (DTI), a special MRI technology that measures distribution of water elements in nerve fibers, to detect nerve fiber structural changes above and below the injury level in SCI. A group of patients with incomplete SCI (iSCI) will be enrolled into the study and treated by standard rehabilitative therapies. Before, 1 month, 2 month, 4 month and 6 month after the treatment program, the DTI measurements will be taken and statistically analyzed. It is expected that the DTI measurement of nerve fiber structure in SCI will be worse in patients than that of healthy people, and the integrity or quality of the fiber structure in patients will improve as a result of combined repair effect from rehabilitation and spontaneous recovery, indicating SCI recovery. It is also expected that the improvement of spinal cord nerve fiber quality will be associated with gains in movement ability of the patients. This association will potentially allow us to use the DTI measurement to predict SCI patients' motor recovery and vice versa. Thus, the MRI DTI measurement may potentially serve as an objective tool to aid clinicians for more accurate SCI diagnosis.

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Grant Award: $200,000

Project Title: ***SCI-Induced Denervation of the Diaphragm: Regulation by MHCI Immune Proteins***

We will attempt to enhance the body's own neuroprotective mechanisms as a new therapeutic approach to preserve or restore normal breathing after paralyzing spinal cord injury.

After spinal cord injury (SCI), one of the most common and devastating complications is breathing paralysis. More than half of all SCI cases affect the cervical spine, which contains the neurons that control the diaphragm, an essential breathing muscle. Injury to the cervical spine is common in car accidents and in sports and recreational injuries, which affect thousands of New Jersey residents every year. The resulting breathing problems require intensive management, and increase the risk of complications, including pneumonia. Thus identifying ways to improve respiratory function is a high priority for treating patients with SCI. The goal of this proposal is to explore a new therapeutic approach to preserve or restore normal breathing after a paralyzing spinal cord injury.

Remarkably, not all damage to breathing circuitry with SCI occurs at the time of the accident. After the initial physical trauma, damaged cells release chemicals that cause prolonged, insidious secondary damage. In particular, the neurotransmitter glutamate is released in excessive amounts after SCI, over-activating a class of glutamate receptors called AMPARs, and causing excitotoxic damage. This secondary excitotoxic damage significantly expands the tissue damage and loss of muscle control after SCI. Because secondary excitotoxicity is still occurring weeks after spinal cord injury, there may be an opportunity to stop this damage before it happens, and help protect breathing in patients with SCI. Drugs that block excitotoxicity often have serious side-effects, because they block both the harmful and essential functions of glutamate. A different approach is needed to reduce excitotoxicity while leaving essential AMPAR function intact.

The hypothesis guiding the current proposal is that enhancing the body’s own neuroprotective mechanisms can reduce secondary damage after SCI, while minimizing harmful side-effects. The proposed experiments build on recent, ground-breaking findings that specific immune proteins, members of the major histocompatibility complex class I (MHCI), inhibit the AMPARs that mediate excitotoxicity. These results suggest that MHCI might have the ability to reduce AMPAR-mediated excitotoxicity after cervical SCI. Promisingly, mice that have been genetically engineered to make more

MHCI show significantly improved leg movements after injury to the thoracic spinal cord. These results show that in animal models, MHCI can promote recovery from damage to parts of the spinal cord that control the legs. However, it is unknown if MHCI can help preserve breathing after damage to the cervical spine.

This proposal will test if enhancing MHCI function can help preserve diaphragm innervation and breathing following cervical SCI. The proposed studies will build a new collaboration between scientists at Princeton and Thomas Jefferson Universities. The combined expertise of the two groups is uniquely suited to answer these questions: The Boulanger Lab first identified MHCI's ability to inhibit glutamate receptors, and the Lepore Lab has developed and tested an animal model of cervical SCI that reproduces denervation of the diaphragm.

The proposed studies will evaluate the effects of MHCI on histological and functional outcomes associated with most human cervical SCI, including phrenic MN loss, diaphragm denervation, and respiratory dysfunction. The cervical SCI model developed in the Lepore Lab is ideal to study the role of MHCI in secondary damage and recovery after SCI. In these studies, cervical SCI will be induced in mice in which MHCI levels have been genetically reduced or enhanced, and the effects on diaphragm innervation and breathing determined. The ways in which MHCI levels change after SCI will also be determined. Together, the proposed research could help identify an unexpected approach to prevent respiratory compromise and reduce morbidity and mortality following cervical SCI.