

NJCSCR 2014



NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Annual Report State Fiscal Year 2014



Chris Christie, Governor
Kim Guadagno, Lt. Governor



Mary E. O'Dowd, MPH
Commissioner

**NEW JERSEY COMMISSION ON
SPINAL CORD RESEARCH**



2014 ANNUAL REPORT

JANUARY 30, 2015



January 30, 2015

The Honorable Chris Christie, Governor
Office of the Governor
State House – P.O. 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 2014, pursuant to N.J.S.A. 52:9E-4(f).

In 2014, the NJCSCR awarded nearly \$3 million in spinal cord research grant funding. This included four Individual Research Grants totaling \$2,000,635, three Exploratory Research Grants totaling \$593,410, and two Fellowship Grants totaling \$210,000. These spinal cord research projects were carefully selected by a panel of independent scientific experts from 29 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 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,

A handwritten signature in black ink that reads "Susan P. Howley". The signature is written in a cursive, flowing style.

Susan P. Howley
Chairperson



TABLE OF CONTENTS

Members of the New Jersey Commission on Spinal Cord Research - 2014	4
Acknowledgements	4
Administrative Staff	4
Executive Summary	5
Introduction	6
2001-2014 NJCSCR Summary and Performance Record	14
2014 NJCSCR Year In Review	17
Grants Program for FY 2015	18
New Jersey Spinal Cord Injury Registry	19
Financial Statement	21
2014 NJCSCR Research Grant Awards	22



2014 COMMISSION MEMBERS

Susan P. Howley, Chairperson

Cathleen Bennett

Peter W. Carmel, M.D.

John D. Del Colle

James McCormack

Michael J. Rhode

Loran C. Vocaturo, Ed.D.

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's Center for Health Statistics for the spinal cord injury surveillance statistics.

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 2014.

ADMINISTRATIVE STAFF

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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 \$41 million has been awarded to individual scientists at academic and research institutions.**
 - *185 separate scientific research projects have been awarded; 156 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 three grant programs in Fiscal Year 2014:**
 - *Individual Research Grants*
 - *Exploratory Research Grants*
 - *Postdoctoral and Graduate Fellowship Grants*

- ❖ **NJCSCR 2014 Achievements:**
 - *Twenty-nine applications requesting a total of \$10 million were submitted.*
 - *Nine awards were made in 2014 totaling \$2,804,045.*
 - *Four Individual Research Grants totaling \$2,000,635, three Exploratory Research Grants totaling \$593,410, and two Fellowship Grants totaling \$210,000 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 far more vital and productive lives. More recently, breakthroughs in research and new horizons in the life sciences are moving us closer towards 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 established and maintained by the New Jersey Department of Health.

Now in its 15th year of operation, the NJCSCR has funded 185 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 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.

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

- *The Commissioner of the NJDHSS, 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. Two-thirds of 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 are currently offered including Individual Research Grants, Fellowship Grants, and Exploratory Research 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.

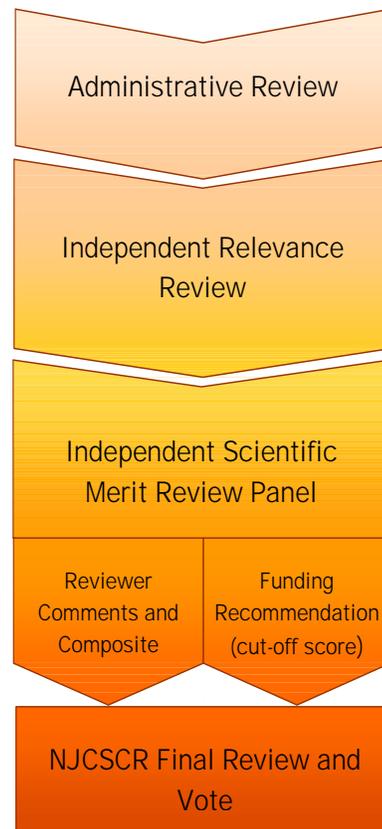
Relevance to the overall goals of the NJCSCR is assessed by an expert panel that also recommends and assigns scientific reviewers for each grant application from a pool of over 100 highly qualified scientists.

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.

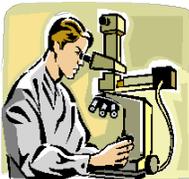
The Individual Research Grant is designed to fund senior independent researchers. Fellowship Grants offer encouragement to graduate students and post-doctoral researchers. The Exploratory Research Grant enables researchers to apply innovative ideas from other areas of science to spinal cord injury and 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.*
- *Post-doctoral 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.*





2001-2014 NJCSCR SUMMARY & PERFORMANCE RECORD

Since 2001, the New Jersey Commission on Spinal Cord Research has invested \$41,745,496.86 in New Jersey scientists. Scientific interest in the field of spinal cord injury research remains strong due to the ongoing investment of these funds.

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 584 applications from researchers, post-doctoral fellows, and graduate students from New Jersey research institutions, which cumulatively total \$161.7 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 post-doctoral 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 twelve 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 &
Veteran's Biomedical Research Institute
Stevens Institute for Technology
Drew University
JFK NJ Neuroscience Institute/JFK Health System
Progenitor Cell Therapy, LLC
Seton Hall University/School of Health &
Medical Science
Wyeth Research/Pfizer
TRIM-edicine, Inc.
Rowan University/Cooper University Hospital &
Medical School & Health System
Hackensack University Medical Center*

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.

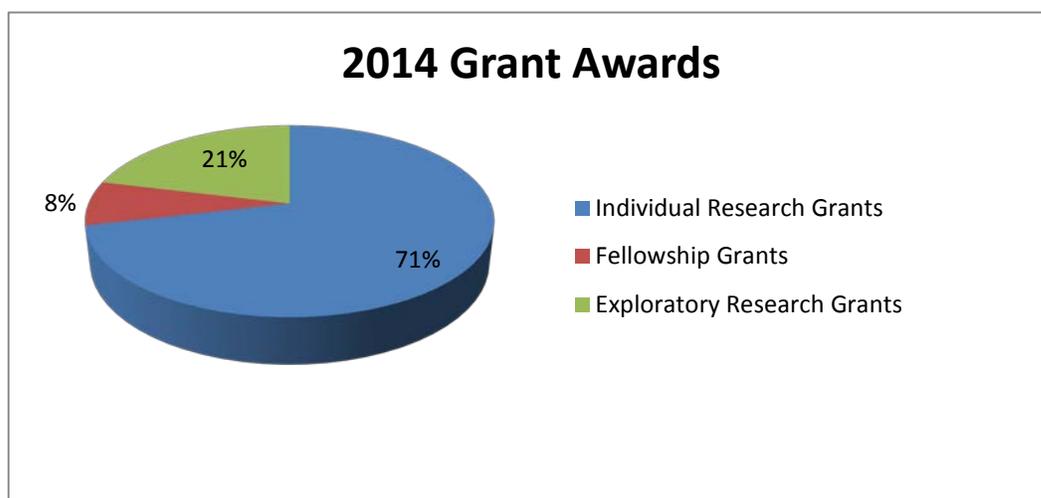


2014 NJCSCR YEAR IN REVIEW

2014 Spinal Cord Research Grants Program

Nine applicants were awarded a total of \$2,804,045 in 2014.

Four Individual Research Grants totaling \$2,000,635, three Exploratory Research Grants totaling \$593,410, and two Fellowship Grants totaling \$210,000 were funded after a careful review of the 29 applications submitted.



2014 Applications

2014 saw the New Jersey Commission on Spinal Cord Research in its 15th year of operation, and its 19th cycle of grants. Twenty-nine applications were submitted with requests for funds totaling \$10 million.

2014 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 2014, one grant cycle was offered; up to \$6 million dollars was made available for spinal cord research projects.

2014 Grant Cycle

Grant Application Deadline: December 10, 2013

Award Notification Date: May 30, 2014

Available Grant Programs:

- *Individual Research Grants*
- *Exploratory Research Grants*
- *Fellowship Grants*

GRANTS PROGRAM FOR 2015

For Fiscal Year 2015, up to \$6.5 million has been allocated for spinal cord injury research projects.

The NJCSCR authorized one grant cycle for Fiscal Year 2015 offering Individual Research Grants, Fellowship Grants, Exploratory Research Grants and Spinal Cord Injury Techniques Training Travel Grants.

2015 Grant Cycle

Grant Application Deadline: December 10, 2014

Award Notification Date: May 29, 2015

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.



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 2014 <i>Projected</i>	SFY 2014 <i>Actual</i>	SFY 2015 <i>Projected</i>
Opening Fund Balance (July 1):	\$9,214,743	\$9,206,663	\$2,852,209
Revenue			
Assessments ¹	\$3,600,000	\$3,919,942	\$3,600,000
Investments Earnings - Interest ²	<u>\$15,000</u>	<u>\$14,431</u>	<u>\$15,000</u>
Total Revenue:	\$3,615,000	\$3,934,373	\$3,615,000
Total Funds Available:	\$12,829,743	\$13,141,036	\$6,467,209
Disbursements			
Spending Plan Reduction ³		\$9,000,000	
Disbursements to Grantees	<u>\$6,030,000</u>	<u>\$1,144,502</u>	<u>\$6,030,000</u>
Total Disbursements:	\$6,030,000	\$10,144,502	\$6,030,000
Expenses			
Administrative & Office Expense	\$110,000	\$114,397	\$115,000
Professional Review Panel	\$50,000	\$29,928	\$35,000
NJCSCR Registry	<u>\$0</u>	<u>\$0</u>	<u>\$0</u>
Total Expenses:	\$160,000	\$144,325	\$150,000
Total Disbursements & Expenses:	\$6,190,000	\$10,288,827	\$6,180,000
Closing Fund Balance (June 30):	\$6,639,743	\$2,852,209	\$287,209
¹ Net revenue variance.			
² Funds plus interest deposited annually in January.			
³ Funds represent 1 year of grant funding; total awarded in FY2014 was \$2,804,054.			



2014 RESEARCH GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENTS:

Mladen-Roko Rasin, M.D., Ph.D.
Rutgers, The State University of NJ

Grant Award: \$600,000

Project Title: *Semaphorin Signaling and Regeneration of Corticospinal Circuitry*

The proposed studies will identify novel roles of sema-plexin signaling in CS axon growth both during development and after SCI.

A spinal cord injury (SCI) is a trauma to the spine that destroys some or all descending corticospinal (CS) and ascending sensory axons traveling through the site of injury. SCI irreversibly damages CS axons and alters activity in the neocortical regions that receive sensory afferents. As a result, reorganization of sensorimotor cortices occurs, which sometimes contributes to functional recovery, but other times results in erroneous or maladaptive outcomes. As a consequence of SCI, approximately 1,275,000 people in the U.S. are currently living with paralysis. Because complete regeneration after SCI is uncommon, a better understanding of SCI pathogenesis and its molecular mechanisms are needed. Recently, experimental manipulations of molecular pathways in sensorimotor neocortices were found to enhance regeneration and improve functional plasticity after SCI, indicating that a greater understanding of the molecular mechanisms underlying adaptive and/or maladaptive responses to SCI may advance efforts to promote regeneration and recovery. Identification of the molecular mechanisms that regulate CS axon growth during development and after SCI is necessary for creating new therapies for SCI.

Therefore, our objectives are to examine the specific roles of semaphorin, an inhibitory axon guidance molecule, and its associated receptor Plexin in the regulation of developing CS axons in the developing and adult spinal cord with or without SCI. We found, for the first time, that a subset of CS axons is eliminated during early postnatal development in mice, and semaphorin-Plexin signaling controls the axon elimination. Furthermore, we found that defects in the axon elimination affect neural circuit formation and motor behavior. Collectively, our data revealed that semaphorin-Plexin signaling have a role in inhibition of axon growth during early postnatal development. This findings lead into a hypothesis that the same signaling pathway has a role in inhibiting axon regeneration in the adult spinal cord after SCI. Indeed, our preliminary findings show that adult depletion of Plexin receptor in mice model promotes regeneration of injured CS axons after SCI. These results suggest that semaphorin-Plexin signaling inhibits regeneration of injured CS axons after SCI in the adult spinal cord. Thus, manipulations of the semaphorin-Plexin signaling pathway should promote post-SCI regenerative efforts, which will be tested in this proposal. We anticipate that our findings will contribute to the development of advanced treatment approaches for people with devastating SCI-induced motor deficits in New Jersey and throughout the world.

Contact Information:

Mladen-Roko Rasin, M.D., Ph.D.

Rutgers, The State University of NJ, Biomedical & Health Sciences

675 Hoes Lane West, Piscataway, NJ 08854 - 732-235-4553

roko.rasin@rutgers.edu



Monica Driscoll, Ph.D.
Rutgers, The State University of NJ

Grant Award: \$350,000

Project Title: *Probing In vivo Mechanisms by which Exercise Enhances Regeneration of Individual Severed Neurons*

We will investigate the molecular mechanisms by which exercise promotes neuronal regeneration in vivo at the single axon level, work that should suggest novel options for reparative therapies.

In spinal cord injury axons are often sheared, causing a loss of neuronal connectivity and impaired function. The rapid regeneration of severed neurons is an obvious goal for the treatment of spinal cord injury, yet knowledge of molecular mechanisms that actively promote neuronal regrowth and reconnection in the living animal remains too limited to be applied for effective repair.

The central goal of our work is to identify the molecules that promote regeneration of injured neurons. To accomplish this, we exploit the powerful *C. elegans* model, which offers unique advantages. *C. elegans* is a simple transparent invertebrate nematode with a nervous system of only 302 neurons. We can directly visualize fluorescently labeled neurons, induce single axon breaks using a laser, and monitor regeneration of that neuron (some *C. elegans* neurons can regenerate, some cannot). We also can systematically reduce the activity of each gene to test its importance in regeneration and reconnection. Since most basic biological processes—including molecular pathways that promote regeneration—are conserved from *C. elegans* to humans, we expect that work in *C. elegans* should provide novel insight into the mechanisms regulating neuronal regeneration and repair in humans.

Exercise stimulates functional recovery in SCI, but the mechanisms mediating this response in neurons native context are essentially unknown. We recently developed a swimming exercise regimen that improves *C. elegans* physical performance—these tiny animals can train. Moreover, we have made the exciting observation that exercise training can enhance the regeneration capacity of injured neurons. We are thus uniquely poised to unleash the molecular genetic and cell biological approaches available in this system to identify the mechanisms via which molecules and cells signal to enhance regeneration consequent to exercise. We propose four experimental objectives:

1) DEFINE THE RELATIONSHIP BETWEEN EXERCISE AND REGENERATION CAPACITY FOR INDIVIDUAL INJURED NEURONS IN THEIR NATURAL CONTEXT.

We will establish the effect of exercise on the regeneration proficiency of specific sensory and motor neurons, and determine the timeframe in which exercise must occur. We will ask whether neurons that are unable to regenerate might be activated for repair by exercise, and whether exercise might delay the onset of age-dependent shutdown in regeneration capacity.

2) IDENTIFY EXERCISE PATHWAY GENES THAT MODULATE ENHANCED

REGENERATION. How conserved molecules of exercise biology influence recovery from axotomy is unknown. We will ask whether nematode orthologs of mammalian exercise genes are needed for exercise-potentiated regeneration. We hypothesize that we might identify specific sub-pathways that are particularly important for regeneration.



3) TEST DRUGS THAT INCREASE EXERCISE PERFORMANCE ACROSS PHyla FOR PROMOTION OF NEURON REGENERATION AT THE SINGLE AXON LEVEL. We will address whether two drugs that impact exercise performance can improve in vivo regeneration consequent to axotomy. Because both drugs are efficacious in mammalian models, our studies may suggest novel and specific interventions to stimulate regeneration.

4) DETERMINE WHETHER EXERCISE SIGNALING IS NEEDED DIRECTLY IN NEURONS FOR ENHANCED REGENERATION. We will manipulate exercise signaling only in specific tissues and determine impact on exercise-associated potentiation of regeneration. Distinguishing the cellular/tissue circuits by which exercise enhances regeneration is critical for full mechanistic understanding and for consideration of where to activate pathways to enhance neuronal repair.

In sum, our study will provide some of the first molecular insight into the impact of exercise on isolated injured neurons in vivo and as such might ultimately suggest novel therapeutic strategies.

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Jeanne Zanca, Ph.D.
Kessler Foundation

Grant Award: \$450,635

Project Title: *Improving Functioning in Persons with Chronic Pain Post-SCI through Virtual Classroom Delivery of a Mindfulness-Based Chronic Pain Management Program*

This project will examine the feasibility and potential benefits of a web-based Mindfulness-Based Chronic Pain Management intervention for persons with chronic pain post-SCI.

WHY IS THIS STUDY BEING DONE? Chronic pain is common among people with SCI, is often severe, and can interfere significantly with daily life. Medications are the most common method for treating chronic pain in people with SCI, but these provide only partial relief from pain and can produce side effects like constipation or sleepiness that reduce quality of life. Other pain treatments include surgery, physical therapy, massage, and others, but none of these has been found to be consistently effective in reducing pain. Because current treatments (used alone or in combination) do not eliminate pain for most individuals, it is important for us to identify ways to reduce the negative effects of pain on daily life and well-being, so that people with pain can live happy, healthy, and productive lives, even if some pain still remains after other treatments are used.

WHAT WILL THE STUDY TEACH US? The proposed study will examine how well we can implement a web-based treatment program known as Mindfulness-Based Chronic Pain Management in persons with chronic pain after SCI. It will also assess what benefits this treatment has for them. Mindfulness-Based Chronic Pain Management aims to use the connections between the mind and body to affect how pain is experienced and reduce the suffering associated with pain. It is a 10 week program that includes weekly classes of approximately 1.5 hours each as well as daily homework assignments. Participants in the class are taught to think about their pain in a way that separates the sensation of pain (awareness of something that hurts) from the thoughts and feelings that pain creates (such as thoughts that it will never end, or feelings of sadness or anxiety). Interventions that are based on the concept of mindfulness have been found to improve pain coping, increase ability to do daily activities, and promote greater mental health in people who are dealing with chronic pain, but do not have SCI. Prior studies have also shown that the Mindfulness-Based Chronic Pain Management program has benefits for persons with chronic pain whether delivered face-to-face or delivered through live web-based video and sound. We want to see if a web-based Mindfulness-Based Chronic Pain Management program is feasible to deliver, and acceptable to persons with SCI, and assess the amount of improvement that program participants experience relative to those who participate in a web-based education program about health and functioning that does not include content related to mindfulness or pain.

WHAT WILL HAPPEN IN THE STUDY? In this study, we will enroll 80 participants who have had spinal cord injury for at least 1 year and pain of moderate or greater intensity for three months or more. After collecting information about their spinal cord injury, pain, and functioning, we will randomly select (like the flip of a coin) one half of these participants to participate in the web-based Mindfulness-Based Chronic Pain Management program. The other half of the participants will participate in the health and functioning web-based education series.



Participants will complete questionnaires about pain, functioning, well-being and other topics before and after they complete the courses so we can examine changes over time.

HOW WILL THIS STUDY BENEFIT PERSONS WITH SCI? The proposed study will help identify a low-cost, low-risk treatment option that can be combined with other treatments (such as medications) to maximize functioning and quality of life in people with chronic pain after SCI. It will do this by providing the information that researchers need to design the larger-scale, multi-site studies that will provide evidence to clinicians, consumers, and insurers to support the use of Mindfulness-Based Chronic Pain Management to improve functioning and well-being in people with chronic pain after SCI.

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Bonnie Firestein, Ph.D.
Rutgers, The State University of NJ

Grant Award: \$600,000

Project Title: *Spinal Cord Motor Neuron-Based Biodegradable Neural Interface Design*

Our goal is to devise a prosthetic that uses biocompatible, biodegradable nanofibers that release protective compounds to align muscle cells and spare neurons from secondary injury due to SCI.

A major issue for patients who have suffered a SCI is loss of motor control and function. Manufacturing a device that would improve communication between neurons and muscle cells or artificial limbs would significantly improve quality of life.

Using previous funding from the NJCSCR, we have devised a prosthesis that uses cultured neurons and muscle cells to study how we can improve connections between the two. In this new proposal, we improve upon and extend this prosthetic to use a biocompatible, biodegradable material platform to not only increase connectivity between neurons and muscle cells, but also to release protective compounds so that the neurons will survive injury due to SCI.

At this stage, our work is performed on cells, but as we improve upon our design, we anticipate a prosthetic that can be implanted into the injured patient. The optimization of our device will improve motor function, allowing injured patients to perform activities that they were previously incapable of performing.

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FELLOWSHIP GRANT RECIPIENTS:

Siliang Wu

Grant Award: \$60,000

New Jersey Institute of Technology

Project Title: *An Electroactive Scaffold for Schwann Cell-Induced Spinal Cord Repair*

Develop a novel Schwann cell supported piezoelectric conduit for spinal cord repair.

In the United States alone, there are close to 1 million persons with damaged spinal cords. Spinal cord injury (SCI) is a devastating condition for which there is no cure. Bioengineering efforts have been focused on developing biomaterials that promote the regeneration of axons across lesions. Although these materials show promise, directing axons from the biomaterial conduit back into the spinal cord to connect with host synaptic pathways remains to be achieved.

Recent efforts, therefore, have been exploring combination strategies using conduits with cells and/or neurotrophic or neuroprotective factors. Using a tissue engineering strategy, our goal is to improve axon regeneration across a Schwann cell (SC)-laden conduit/bridge and into the spinal parenchyma caudal to the injury site to improve functional recovery. Our overall hypothesis is that axonal regeneration and functional recovery are improved by utilizing an appropriate conduit with SCs that provides both physical and neurotropic cues in combination with neurotrophin release caudal to the injury. The conduit will be piezoelectric, which means it has intrinsic electrical properties, and will release neurotrophins to support axonal regeneration. A combination of cells and effective neurotrophin delivery within a piezoelectric conduit is a novel and translatable approach. Aim 1 will fabricate and characterize the piezoelectric scaffold and evaluate neurotrophin release. Aim 2 will evaluate axonal growth using the piezoelectric scaffold with or without neurotrophin release in vitro. The goal here is to establish that biomaterials can be an effective method for the controlled release of neurotrophins and will improve axonal growth. Aim 3 will evaluate axonal growth and functional recovery using the combination approach in vitro in a complete transection model. The goal is promote axon growth throughout the conduit and extend into the caudal spinal parenchyma following the controlled release of neurotrophins. This study proposes a novel tissue engineering strategy utilizing piezoelectric conduits, neurotrophins and SCs to promote axonal regeneration into, through and out of the SC bridge to improve functional recovery.

Currently, there are approximately 6,000 New Jersey residents suffering from traumatic injuries or diseases that damage the spinal cord. Our research work provides potential therapies that could improve their quality of life.

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Hui Wang, Ph.D.

Grant Award: \$150,000



Rutgers, The State University of NJ

Project Title: *Cooperation of Shh and Fgf signaling for generating oligodendrocytes during development and following SCI*

My experiments will define the role of FGF and Shh signaling in the specification and differentiation of embryonic and adult spinal cord OPCs under normal and post-injury conditions, respectively. Successful functional recovery following spinal cord injury (SCI) involves the production of specialized glial cells that are involved in controlling neurotransmission. Among these cells are the myelin-producing oligodendrocytes (OLs) that are generated from progenitor cells (OPCs) that are located in the adult spinal cord. It has been shown that two important cell signaling pathways are involved in this process. These are the Sonic Hedgehog (Shh) and Fibroblast Growth Factor (FGF) pathways, which are up-regulated in the spinal cord following SCI. Because these pathways have been shown to play important roles in generating glial cells in development and in some previous experiments on SCI, we believe they are likely to contribute to functional recovery. Notably, there is evidence from studies using the forebrain that both pathways cooperate to induce OLs after injury, but so far prior investigation has failed to establish this relationship in the spinal cord. Specifically, the role of FGF signaling in the production of spinal cord OLs is not thought to be as important as it is in the brain.

I have now obtained preliminary data that reveals a similar, broad requirement for FGF signaling in generating OLs in the spinal cord. In addition, prior published work from our lab has provided evidence that FGF pathway genes in the ventral spinal cord are regulated Shh signaling, suggesting a possible mechanism for pathway interactions. Together, these data provide the first evidence that the Shh and FGF pathways cooperate to generate the majority of OLs in the spinal cord. The fact that both pathways are also involved in producing OLs in adults after SCI raises the likely possibility for a similar link in adult OL stem cells.

Two aims of this proposal will address this issue. First, I will define the requirement of embryonic FGF signaling to produce ventral spinal cord OLs by extending my preliminary analysis. These studies will provide important mechanistic insights into Shh/FGF pathway cooperation that will be directly applicable to my adult SCI studies due to the conserved reactivation of developmental signaling pathways following CNS injury. Second, I will determine whether FGF signaling is required downstream of Shh adult glial progenitor cells following SCI. The overall goal of these experiments is to test whether FGF signaling is required in reactive cells to generate glial progeny (oligodendrocytes and astrocytes) downstream of Shh after SCI. Thus, these experiments will establish a definitive role for FGF signaling in the specification and differentiation of embryonic and adult spinal cord OPCs under normal and lesioned conditions, respectively. Results from my studies will provide important information on the molecular sequence of events that occurs in OL progenitors following SCI that could be used to improve treatment and recovery from this devastating problem.

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EXPLORATORY RESEARCH GRANT RECIPIENTS:

Rakesh Pilar, Ph.D.
Kessler Foundation

Grant Award: \$194,976

Project Title: *Development of Signal Processing Toolbox for Assessing Neuromuscular Response during Electrical Stimulation*

We propose to develop a novel robust algorithm to extract artifact-free EMG signal during electrical stimulation to study the neuromuscular response of the stimulated muscle.

Traditionally, electrical stimulation (ES) has been used in SCI patients as one of the rehabilitation paradigms to assist or restore neuromuscular function in paralyzed muscles. Functional Electrical Stimulation (FES) operates on a basic principle that the application of electrical current to a muscle nerve or muscle itself can activate contraction in paralyzed muscles. When muscle contraction made either voluntarily or by ES, action potentials (APs) are generated in each muscle cell (fiber) and these APs from activated fibers can be recorded invasively using surface electrodes as electromyography (EMG). The EMG recording tells intensity or activation level of muscle contraction, patterns of AP generation which are important for understanding the neuromuscular and physiological effects created by ES. However collection of high quality EMG during ES has been difficult to achieve because of the presence of stimulus artifact. The overlap between the stimulus artifact and EMG signals obstructs the use of conventional signal filtering techniques to extract the true EMG signals from the artifact-contaminated recordings. The goal of this study is to develop a robust signal processing algorithm to extract EMG during ES and study the physiological significance of ES on neuromuscular properties of the stimulated muscle.

First aim of this study is to develop a robust signal processing algorithm for the removal of stimulus artifact from contaminated surface EMG signals during ES. Our preliminary results show that Empirical Mode Decomposition (EMD) based algorithm to extract ES artifact from stimulated EMG has a lot of potential. Although the algorithm was able to extract the major portion of the EMG, some data was lost in discarded artifact components indicating EMD alone is not sufficient to successfully isolate EMG signal. We propose to use another decomposition technique, Independent Component Analysis (ICA) to further separate the EMG. Overall, we will develop a toolbox that combines the merits of both EMD and ICA to optimize the performance and further minimize the EMG signal loss.

Second aim is to establish the validity of EMD-ICA algorithm by assessing the quality of the separated EMG before interpreting and assigning it any kind of physiological meaning. We will use a test signal consisting of sequence of only EMG (voluntary muscle activation) and electrical stimulated EMG. The algorithm will be applied 'EMG+ES' sequence and artifact-free EMG will be extracted. The various properties of this extracted EMG will be compared with voluntary 'EMG only' sequences to calculate the validation measure.

Once we establish the validity, as our third aim, we will optimize the ES parameters by analyzing changes in the filtered EMG due to varying patterns of ES for this study. Numerous tests would be required to find the optimum ES training pattern (frequency, pulse width) for each patient and for each functional task. Currently, not many mathematical models or theoretical foundations exist which will successfully identify the relationships between the patterns of ES and optimum



neuromuscular responses. We will bridge this gap by analyzing artifact-free EMG collected during ES contractions and observing the changes in it occurring due to change in ES pattern. The properties of EMG collected during varied patterns of ES will enable us to know the effect of certain frequencies, amplitude, pulse width of ES on motor recruitment patterns and muscle fatigue. We will be the first to assess these changes by studying the pure, artifact-free EMG during stimulated contractions.

The outcomes of the study will help in understanding the direct effects of ES on muscles by getting access to high quality EMG during ES and help the clinician or researcher to modify and optimize FES training paradigms based on the target muscle response. This could have a major impact on the field of spinal cord injury research and rehabilitation.

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Anita Singh, Ph.D.
Rowan University

Grant Award: \$198,437

Project Title: *Using Bioengineered Scaffold Loaded with Neurotrophins to Enhance Functional Recovery after Locomotor Training in SCI Animals*

To investigate the efficacy of a combinatorial bioengineering treatment strategy using scaffold loaded with neurotrophins and treadmill training in a clinically relevant spinal cord injury animal model.

Spinal cord injury (SCI) is a devastating and debilitating condition that affects an estimated 227,080 to 300,938 persons in the United States with approximately 12,000 new cases occurring each year. Current treatment strategies include activity based rehabilitation therapies, such as body weight supported treadmill training (BWSTT) that utilizes the uninjured descending pathways in incomplete SCI patients and spinal circuits below the level of injury in complete SCI patients. If the descending inputs are minimal or absent, recovery in walking over-ground is never observed in SCI patients. Since the amount of spared descending input strongly regulates the extent of recovery after BWSTT, combining transplantation treatment strategies that increase the number of descending inputs by inducing neuroprotective and regenerative environment around the injured spinal cord holds most promise to further enhance the functional recovery after BWSTT. Transplantation strategies using cells genetically engineered to deliver neurotrophins, which is a neuroprotective and neuroregenerative agent, limit spinal tissue loss, promote regeneration/sprouting of injured axons, bridge the site of injury and result in some functional recovery in animal SCI models. Clinical translation of these techniques poses several problems, including rejection and issues with regulation of release, requiring more invasive approaches with additional problems associated with potential rejection and regulation of release of bioactive compounds. To overcome these limitations, we propose using bioengineered scaffold poly N-(isopropylacrylamide) – poly (ethylene glycol) (PNIPAAm-PEG), which has shown to be highly biocompatible and when functionalized to secrete a neurotropic factor can promote regeneration and functional recovery in a surgically induced SCI animal model. In the proposed study, we aim to further investigate the efficacy of this bioengineered scaffold secreting neurotrophins as an alternative to cellular transplants in a clinically relevant contusion SCI animal model. Furthermore by incorporating BWSTT in these animals, our collaborative group will for the first time report the combinatorial effect of scaffold+neurotrophins+BWSTT in a clinically relevant contusion SCI model. Successful findings from this study will help develop a unique tissue-engineering approach with promising clinical application in incomplete SCI patients. By adding other growth promoting agents to this bioengineered scaffold, future studies can explore the beneficial effects of the proposed combinatorial treatment strategy in complete SCI animal model.

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Gal Haspel, Ph.D.
New Jersey Institute of Technology

Grant Award: \$199,997

Project Title: *A Minimal Locomotion Circuit to Investigate Neuronal Regeneration*

In this exploratory grant, I propose to develop a new, compact and modular preparation in a live animal to study neuronal circuit parameters that can support recovery from spinal cord injury.

A spinal cord injury is complex. It involves processes at many levels from molecules through cells, neuronal circuits and organs to the whole animal or patient. While we have very fruitful and established experimental models at the molecular, cellular and whole animal levels, it has been difficult to isolate factors that rise from the level of the neuronal circuit and its activity: Are neuronal regeneration and plasticity affected by the circuit activity? Does it matter if the activity is similar to the naturally occurring one and if so, how similar does it need to be? How does a circuit, dedicated to locomotion deal with a lesion of a connection and with the reconnection?

My research on the neurobiology of locomotion of this animal has led me to identify a small circuit that is composed of two neurons and two opposing muscle cells that they control. In the new preparation, I combine several cutting edge technologies to enable recording and separately controlling the activity of each neuron and muscle and to perform a very precise lesion in one or the other axons of the neurons with a focused laser beam. The activity of the circuit can be recorded before, during and after the lesion as neuronal regeneration or plasticity occurs. Results, ideas and principals that will arise from these studies will be evaluated through my collaboration with a laboratory that studies a vertebrate model of spinal cord injury. The preparation will allow us to test existing hypotheses, develop new ones and contribute to our understanding of the effects of circuit activity on recovery from spinal cord injury.

When concluded, I expect this experimental preparation of a minimal locomotion circuit to be a springboard to the study of neuronal recovery from injury at the circuit and cellular levels and lead to therapeutic breakthroughs.

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