

NJCSCR 2016



NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Annual Report State Fiscal Year 2016





January 30, 2017

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 2016, pursuant to N.J.S.A. 52:9E-4(f).

In 2016, the NJCSCR awarded nearly \$3 million in spinal cord research grant funding. This included four Individual Research Grants totaling \$2,230,920, three Exploratory Research Grants totaling \$590,953, two Spinal Cord Injury Techniques Training Travel Research Grants totaling \$5,500, and one Fellowship Grant totaling \$150,000. These spinal cord research projects were carefully selected by a panel of independent scientific experts from 30 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
Chairperson

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH



2016 ANNUAL REPORT

January 30, 2017

2016 COMMISSION MEMBERS

Susan P. Howley, Chairperson
Peter W. Carmel, M.D.
John D. Del Colle
James McCormack
Carolann Murphy, PA
Michael J. Rhode
Loran C. Vocaturo, Ed.D.
Anthony Welch

ACKNOWLEDGEMENTS

The New Jersey Commission on Spinal Cord Research (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 2016.

ADMINISTRATIVE STAFF

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Mary Ray, Fiscal Manager

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



❖ **Since 2001, over \$48 million has been awarded to individual scientists at academic and research institutions.**

- o Two hundred and four separate scientific research projects have been awarded; 166 scientific research projects have been completed.
- o Progress made by researchers has been presented in abstracts, scientific conferences, symposia, and meetings.
- o NJCSCR programs have facilitated wider scientific interaction and numerous active research collaborations, along with out-of-state researchers.
- o Success in achieving NJCSCR funding has resulted in academic and career advancement for New Jersey researchers, including doctoral dissertations.
- o 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 2016:**

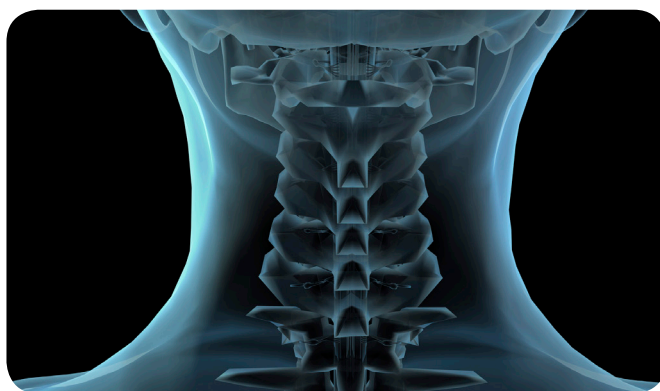
- o Individual Research Grants
- o Exploratory Research Grants
- o Postdoctoral and Graduate Fellowship Grants
- o Spinal Cord Injury Techniques Training Travel Grants

❖ **NJCSCR 2016 Achievements:**

- o Thirty applications requesting a total of \$8.9 million were submitted.
- o Ten awards were made in 2016 totaling \$2,977,373.
- o Four Individual Research Grants totaling \$2,230,920, three Exploratory Research Grants totaling \$590,953, two Spinal Cord Injury Techniques Training Travel Grants totaling \$5,500, and one Fellowship Grant totaling \$150,000 were approved.

❖ **NJ Spinal Cord Registry:**

- o NJCSCR supports a central registry of spinal cord injuries in New Jersey along 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 can now live 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

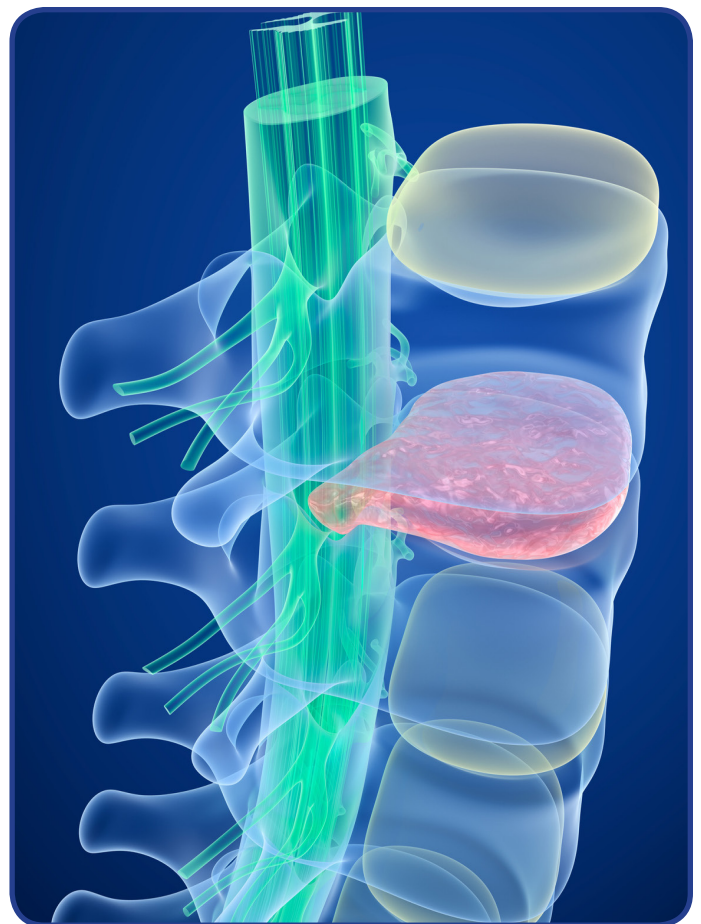
The Spinal Cord Research Act (N.J.S.A. 52:9e-1 et seq.) created the New Jersey Commission on Spinal Cord Research and the New Jersey Spinal Cord Research Fund to support its activities.

New Jersey is a leader in funding research aimed at the repair of spinal cord injuries. 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 New Jersey Department of Health which maintains a database of all spinal cord injuries in New Jersey.

Now in its 17th year of operation, the NJCSCR has funded 204 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 developing 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 and Prevention, 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's budget.

The NJCSCR establishes and oversees the administrative operations of the grant-making process as well as other program activities.

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 services to 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. Auto and motorcycle accidents represent one of the leading causes of spinal cord injury in New Jersey, accounting for more than 300 new injuries each year. 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 mission is to encourage and promote scientific research projects that advance the understanding of spinal cord injury and explore potential therapeutic strategies at qualifying research institutions in New Jersey. 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
- ❖ The NJCSCR facilitates the initiatives of New Jersey scientists to obtain larger grants from sources such as the National Institutes of Health and the National Science Foundation.

OBJECTIVES

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

The NJCSCR objectives include the following:

- ❖ Develop and implement a spinal cord research grants program.
- ❖ Solicit, review, and administer grant awards in support of scientifically meritorious research projects.
- ❖ Promote development of spinal cord research projects that focus on treatments, cures, and on those that prevent or treat secondary biological conditions resulting from spinal cord injury and
- ❖ Support the progression of research from laboratory to animal and clinical applications.

More 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 at: 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 spinal cord injury case in New Jersey. This registry is mandated by statute and serves 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 the 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.

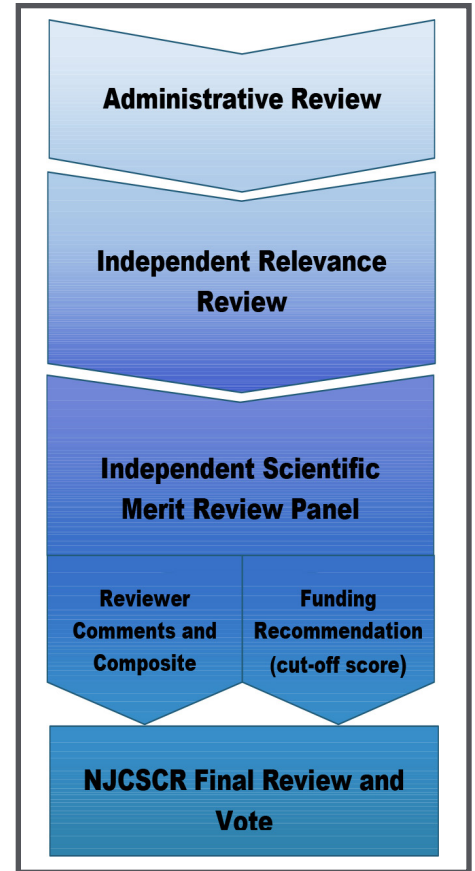
The NJCSCR administrative staff reviews all applications for completeness and accuracy, and assists applicants in correcting errors or omissions.

The overall goals of the NJCSCR are assessed by an expert panel that also recommends and assigns scientific reviewers for each grant application from a pool of over 150 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 scientific opportunities attractive to a wide range of researchers. Specifically, 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. This facilitates the need to acquire the preliminary data necessary 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 further their scientific growth.

All applicants are encouraged to collaborate with New Jersey-based researchers, as well as with other national or international scientists.

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)*
- ❖ *A 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.*
- ❖ *Allow 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 training courses on spinal cord injury techniques.*
- ❖ *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.*

2001-2016 NJCSCR SUMMARY & PERFORMANCE RECORD

Since 2001, the New Jersey Commission on Spinal Cord Research has invested \$48,296,825.86 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 642 applications from researchers, postdoctoral fellows, and graduate students from New Jersey research institutions, which cumulatively total \$179.3 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. These projects are aimed at advancing the field in significant ways and result in scientific publications as well as additional funding.

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 were 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:

- o *Rutgers, The State University of New Jersey*
- o *Kessler Foundation*
- o *Princeton University*
- o *Coriell Institute for Medical Research*

NJCSCR-DESIGNATED QUALIFIED RESEARCH INSTITUTIONS:

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

2016 NJCSCR A YEAR IN REVIEW

- *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 facilitated greater scientific interaction and research collaborations, both in New Jersey and nationally.

- ❖ 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.



2016 SPINAL CORD RESEARCH GRANTS PROGRAM

Ten applicants were awarded a total of \$2,977,373 in 2016.

Four Individual Research Grants totaling \$2,230,920, three Exploratory Research Grants totaling \$590,953, two Spinal Cord Techniques Training Travel Grants totaling \$5,500, and one Fellowship Grant totaling \$150,000 were funded.

2016 APPLICATIONS

2016 saw the New Jersey Commission on Spinal Cord Research in its 17th year of operation, and its 21st cycle of grants. Thirty applications were submitted with requests for funds totaling \$8.9 million.

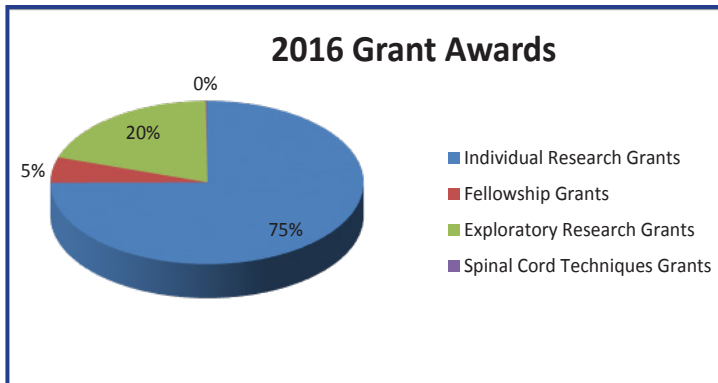
2016 Outreach and Development Efforts

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 2016, one grant cycle was offered; resulting in the availability of upto \$6.5 million for spinal cord research projects.



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

GRANTS PROGRAM FOR 2017

For Fiscal Year 2017, up to \$6.5 million has been allocated for spinal cord injury research projects.

The NJCSCR authorized one grant cycle for Fiscal Year 2017 offering Individual Research Grants, Fellowship Grants, Exploratory Research Grants and Spinal Cord Injury Techniques Training Travel Grants.

2017 GRANT CYCLE

Grant Application Deadline: December 12, 2016

Award Notification Date: June 30, 2017

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

Groups	2003			2004			2005			2006			2007			2008		
	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

Groups	2009			2010			2011			2012			2013			2014		
	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

NEW JERSEY SPINAL CORD INJURY REGISTRY

ALL SPINAL CORD INJURY INPATIENT HOSPITALIZATIONS FATAL AND NON-FATAL, NEW JERSEY RESIDENTS, 2015

Groups	2015		
	Trauma	Acute	Total
Males	239	63	302
Females	97	58	155
Under 15 years	7	0	7
15-24 years	31	0	31
25-34 years	39	2	41
35-44 years	38	7	45
45-54 years	55	13	68
55-64 years	56	31	87
65-74 years	50	28	78
75-84 years	35	26	61
85 years and older	25	14	39
White non-Hispanic	183	79	262
Black non-Hispanic	75	17	92
Native American	1	0	1
Asian/Pacific Islander	8	8	16
Hispanic	44	12	56
Other or Unknown	25	5	30
Total	336	121	457

MECHANISM OF SPINAL CORD INJURY, NEW JERSEY RESIDENTS, 2013-1015

Mechanism	Discharged Alive		Discharged Dead		Ratio	Total Discharges	
	N	%	N	%	Alive:Dead	N	%
Motor vehicle occupants	171	12.9	10	9.3	17.1	181	12.6
Pedestrian (traffic and other)	28	2.1	4	**	7.0	32	2.2
Pedal cyclists (traffic and other)	31	2.3	1	**	31.0	32	2.2
Motorcyclists	20	1.5	1	**	20.0	21	1.5
Unspecified MV position	10	0.8	3	**	3.3	13	0.9
Other transport vehicles	18	1.4	1	**	18.0	19	1.3
Falls	679	51.1	61	56.5	11.1	740	51.5
Struck by/against	43	3.2	0	-	-	43	3.0
All other unintentional injuries	90	6.8	9	8.3	10.0	99	6.9
Assault/homicide	64	4.8	4	**	16.0	68	4.7
Self-inflicted/suicide	3	**	1	**	3.0	4	**
Undetermined intent	7	0.5	2	**	3.5	9	0.6
All other/unspecified injuries	165	12.4	11	10.2	15.0	176	12.2
Total	1,329	100	108	100	12.3	1,437	100

NEW JERSEY SPINAL CORD INJURY REGISTRY

SPINAL CORD INJURY HOSPITALIZATIONS BY AGE AND GENDER, NON-FATAL, NEW JERSEY RESIDENTS, 2013-2015

Age Groups	Males		Females		Total	
	N	Rate	N	Rate	N	Rate
Under 15	15	**	9	**	24	0.5
15-24 years	82	4.6	23	1.4	105	3.0
25-34 years	98	5.6	16	**	114	3.3
35-44 years	104	6.0	26	1.5	130	3.7
45-54 years	190	9.7	44	2.1	234	5.8
55-64 years	147	8.9	71	3.9	218	6.3
65-74 years	120	12.0	82	6.9	202	9.3
75-84 years	77	15.8	95	13.8	172	14.6
85 and older	51	26.6	79	20.2	130	22.3
Total	884	6.5	445	2.7	1,329	4.5

SPINAL CORD INJURY HOSPITALIZATIONS BY AGE AND GENDER, NON-FATAL, NEW JERSEY RESIDENTS, 2015

Age Groups	Males		Females		Total	
	N	Rate	N	Rate	N	Rate
Under 15	5	**	2	**	7	**
15-24 years	22	3.7	7	**	29	2.5
25-34 years	34	5.8	7	**	41	3.5
35-44 years	32	5.6	12	**	44	3.8
45-54 years	52	8.0	14	**	66	5.0
55-64 years	55	9.7	29	4.7	84	7.1
65-74 years	45	13.1	30	7.3	75	10.0
75-84 years	21	12.8	32	13.9	53	13.5
85 and older	14	**	15	**	29	14.7
Total	280	6.0	148	2.7	428	4.3

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 of the 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; National Center for Health Statistics bridged-race population estimates.

Source All Tables: New Jersey Central Nervous System Injury Surveillance Data, 2003-2015
 Center for Health Statistics and Informatics
 Population Health Division
 New Jersey Department of Health
 December 19, 2016

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 2016 <i>Projected</i>	SFY 2016 <i>Actual</i>	SFY 2017 <i>Projected</i>
Opening Fund Balance (July 1):	\$3,775,475	\$4,689,428	\$366,097
Revenue			
Assessments ¹	\$3,600,000	\$3,646,488	\$3,600,000
Investments Earnings - Interest ²	<u>\$10,000</u>	<u>\$30,481</u>	<u>\$15,000</u>
Total Revenue:	\$3,610,000	\$3,676,969	\$3,615,000
Total Funds Available:	\$7,385,475	\$8,366,397	\$3,981,097
Disbursements			
Spending Plan Reduction		\$3,500,000	
Disbursements to Grantees ³	<u>\$6,030,000</u>	<u>\$4,184,771</u>	<u>\$3,600,000</u>
Total Disbursements:	\$6,030,000	\$7,684,771	\$3,600,000
Expenses			
Administrative & Office Expense	\$275,000	\$293,668	\$275,000
Professional Review Panel	\$35,000	\$21,861	\$35,000
NJCSCR Registry	<u>\$0</u>	<u>\$0</u>	<u>\$0</u>
Total Expenses:	\$310,000	\$315,529	\$310,000
Total Disbursements & Expenses:	\$6,340,000	\$8,000,300	\$3,910,000
Closing Fund Balance (June 30):	\$1,045,475	\$366,097	\$71,097
¹ Net revenue variance.			
² Funds plus interest deposited annually in January.			
³ Funds for Multi-Year Grants.			

2016 RESEARCH GRANT AWARDS - INDIVIDUAL RESEARCH GRANTS

Below is a summary of the individual research grant applications

CSCR16IRG005

Kamana Misra, Ph.D.

Celvive, Inc.

\$452,149

Project Title: Mechanisms Underlying Bone Marrow Transplant Driven Activation of Endogenous Stem Cells for Spinal Cord Injury Repair

Decipher mechanisms underlying the therapeutic effect of autologous, adult bone marrow derived stem cells on spinal cord injuries. Spinal cord injury (SCI) results in drastic life style alterations for the patients and their family members.

Therapeutic interventions require regeneration of multiple types of neurons to recreate lost neurons. Research advances using cell therapies have ushered in an era of new hope and the field is witnessing a surge in clinical studies using cellular transplantation for treating SCI. Progression into main line therapies is however impeded largely due to ambiguity about A) variability in cell derivation protocols, B) fate of the transplanted cells, and C) mechanisms underlying the therapeutic benefit.

Our earlier work has demonstrated that patients own unexpanded, minimally manipulated adherent bone marrow cells (ABMCs) can effectively induce repair at spinal cord injury

site. The scope of the current grant proposal is to address deficiencies in the field mentioned above by using transgenic mouse models and sophisticated in vivo imaging techniques to understand the interactions between the transplanted bone marrow stem cells and the endogenous neural stem cells that lie quiescent in the adult spinal cord.

We plan to study these interactions in real time. Such real time monitoring of in vivo transplanted cells and resulting mobilization of endogenous cell populations can help validate the full potential of cell-based therapy. Additionally, identification of potential impediments can help in designing improved cell transplantation strategies.

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2016 RESEARCH GRANT AWARDS - INDIVIDUAL RESEARCH GRANTS

Below is a summary of the individual research grant applications

CSCR16IRG007

Jeffrey Zahn, Ph.D.

Rutgers University

Biomedical Engineering

\$593,792

Project Title: Multi-Layer Implantable Cortical Microelectrodes to Improve Recording Potential for Spinal Cord Injury Treatment

We will create neural microprobes minimizing tissue damage while maximizing the number of recording electrodes using a multilayer fabrication approach for use in rehabilitative applications in SCI.

The purpose of this proposal is to improve neural recordings for use in brain computer interfaces (BCI). BCI is a method which records thoughts in the form of electrical activity from the brain and then processes and decodes these signals which can be used in different ways such to control a wheelchair or computer. There has been a rising interest in using BCI to assist people who suffer from spinal cord injury (SCI) by replacing the lost sensory and motor functions with external neural prosthetic devices so that patients can regain a level of independence and improve their quality of life.

One of the essential components of a functional BCI is the ability to record a strong lasting signal from the brain. One way of recording

nerve signals is by using implanted microelectrodes, also called neuroprobes. Unfortunately, when these probes are implanted in the brain a process of tissue scarring, called gliosis, degrades the probe's recording potential within a few months. To address this issue we have created ultraminiaturized recording probes from flexible biocompatible plastic materials. Because these probes are so small and flexible once they are implanted in the brain this tissue scarring response is not seen. However, one challenge in creating these probes is that only a single recording electrode can be defined on such a small probe. Multielectrode recordings of distributed neurons improve recording fidelity due to activation of an area of the brain during task volition allowing better decoding of motor intent. So, in order to have the highest recording potential while limiting tissue scarring we will design and fabricate cortical recording neuroprobes which maximize the number of recording electrodes on a single miniaturized microprobe so that multiple neighboring neurons can be recorded simultaneously. To accomplish this task, we will use a novel multilayer fabrication process allowing vertical definition of recording sites. Each layer will consist of recording traces insulated by a thin polymer layer electrically isolating the traces from their neighbors. This will maximize the number of probe recording sites along the length of the probe while minimizing the overall probe dimensions. To our knowledge no other research group has investigated such a multilayered design. Once we have fabricated this device we will implant the probes in a mouse model to

stimulate and record from nearby neurons to assess the probe function over a 24-week period. We will also use the animals as a model of brain plasticity relevant to SCI by training the animal in motor tasks and recording motor volition using our microprobes.

Completing our goals, we will have demonstrated the ability to maximize recording potential using the novel flexible microprobes while minimizing the device dimensions. Neural recording from these probes implanted for long-periods of time holds great promise for development of rehabilitation strategies following SCI, and improving the effectiveness of microelectrodes currently limited by gliosis around the probe. Importantly, the new electrodes can be immediately integrated with the advanced approaches under development for the other three essential elements of a BCI, which currently utilize EEG- or ECoG-generated signals. Moreover, our approach for insertion can be used for microelectrodes developed in other laboratories.

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2016 RESEARCH GRANT AWARDS - INDIVIDUAL RESEARCH GRANTS

Below is a summary of the individual research grant applications

CSCR16IRG010

Nancy Chiaravalloti, Ph.D.

Kessler Foundation

\$585,303

Project Title: A Longitudinal Examination of Aging with a Spinal Cord Injury: Cardiovascular, Cerebrovascular and Cognitive Consequences

The goals of this proposal are to determine if cardiovascular and cerebrovascular dysfunction contribute to cognitive deficits in older and aging individuals with SCI.

The population is getting older; it is reported that the number of individuals in the United States older than 65 increased 10 times over the past 100 years. Likewise, individuals with spinal cord injury (SCI) are also aging and more than 80% are older than 50 years. However, as the general population is getting older, they are living longer; this is not the case in people with SCI. In fact, people with cervical SCI (neck injury) can expect to live 34 years less than an individual of the same age who is not injured. The reasons for reduce life expectancy in the SCI population are not clear, but cardiovascular and cerebrovascular diseases were the leading causes of death from 1952-2001.

Similar to the non-injured population, as people with SCI get older, they are faced with the

increased likelihood of developing age-associated diseases like cardiovascular disease and stroke (cerebrovascular disease). In fact, people with SCI are 5-times more likely to have had a stroke than people without SCI, which may be due to the secondary complications of the SCI, such as the inability to control heart rate and blood pressure.

Furthermore, because of damage to the nervous system it is often more difficult to prevent and treat diseases and illness in the SCI population, which may worsen disease progression and reduce life expectancy. In addition to cardiovascular and cerebrovascular disease, people with SCI are reported to have impaired thinking (cognitive) abilities at a relatively young age, and as many as 60% of individuals with SCI have functional deficits in memory, information processing and executive function. In the general population there is an association between aging and the development of cognitive deficits that may be related to cardiovascular and cerebrovascular dysfunction. We do not know the effects of aging with SCI on cardiovascular, cerebrovascular or cognitive function, but we do know that the SCI population is getting older.

It is likely that the impact of worsening disease progression and the inability to adequately address these complications, coupled with advancing cognitive impairments would be expected to not only reduce life expectancy, but could significantly detract from independence, social interaction and quality of life. Improving our under-

standing of the cardiovascular, cerebrovascular and cognitive profiles in older individuals with SCI compared to older non-injured controls will help to define differences among these aging populations and inform clinical treatment algorithms for those with SCI. Further, getting a glimpse of how cardiovascular, cerebrovascular and cognitive function change over time in relatively young individuals with SCI compared to age-matched controls, will aid in the development of timely intervention strategies to prevent or ameliorate the pronounced functional deficits reported in the SCI population.

Therefore, the objectives of this project are to compare cardiovascular, cerebrovascular and cognitive function among older individuals with SCI (50-75 years) compared to older age-matched non-injured controls and to determine 3-5-year change in cardiovascular, cerebrovascular and cognitive function in relatively young individuals with SCI (28-45 years) compared to age-matched controls. The results will help guide interventional studies aimed at improving health, longevity and quality of life in the aging SCI population.

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2016 RESEARCH GRANT AWARDS - INDIVIDUAL RESEARCH GRANTS

Below is a summary of the individual research grant applications

CSCR16IRG013

Tracy Tran, Ph.D.

Rutgers University

Chemistry & Chemical Biology

\$599,716

Project Title: Novel Cell Autonomous and Non-Cell Autonomous Mechanisms of Semaphorin-Neuropilin/Plexin Signaling Regulate Spinal Commissural Axon Pathfinding in the Mammalian CNS

This project aims to understand how spinal cord projection axons use intermediate target structures and environmental cues to navigate long-distances to find their functional targets in the brain.

Spinal cord injuries often lead to severing of nerve fiber tracts, made up of individual axons (thin processes extended by neurons) carrying important sensory and motor information, that leads to paralysis and other debilitating conditions. During development growing axons are capable of navigating over long distances and between a series of intermediate targets to find their proper functional targets via the instructional (attractive or repulsive) signals given by molecular cues present in their environments. Therefore, it is critical to identify the molecular mechanisms underlying axon guidance in order to establish a foundation to devise suitable treatments for promoting the regeneration of axons damaged by spinal cord injury.

Previous studies have shown that commissural neurons, which extend axons from one side of the spinal cord to the other, across the midline, and then project to the brain, represent components of important ascending axon tracts, which convey external sensory information (touch, pain and body position) to higher brain centers. However, the precise paths followed by different subsets of spinal commissural axons as they extend to the appropriate target cells in the brain are not known. Moreover, very little is known about the molecules that guide the specific subsets of axons to their appropriate targets.

Therefore, we propose to trace the trajectories of multiple classes of ascending spinal commissural axons in mouse embryos, and to identify the molecules and understand the guidance mechanisms that these axons use to navigate through their intermediate target, the floor plate, at the midline, and ultimately find their targets. In order to establish a “roadmap” for ascending commissural axons to find their targets, it is essential to first visualize the long-range trajectories of these spinal axons as they initially develop in the embryo.

The proposed studies will be carried out in whole mouse embryos using molecular genetic techniques to permanently label particular subsets of spinal commissural neurons and their axonal projections to their target sites. In addition, we will use mouse genetic techniques to specific delete genes encoding molecular cue

receptors in the Semaphorin protein family that were previously shown to play important roles in guiding commissural axons to cross the midline and sort their trajectories on the contralateral side of the spinal cord. Curiously, members of the Semaphorin protein family and their receptors are also present in the adult nervous system.

Accumulating evidence indicates that the levels of these molecules are dramatically altered after spinal cord injury, which could underlie the inability of the spinal cord to regenerate following injury. Therefore, studying the mechanisms of how these guidance molecules function will not only give a better understanding of how they control axon navigation during development, but also will be critical for designing strategies to modulate their expression levels and function in the injured spinal cord. Thus, our proposed studies on how commissural axons are guided, by Semaphorins and their receptors, to their functional targets during normal development will significantly contribute to our understanding of the molecular mechanisms governing the formation of specific neuronal connections from the spinal cord to the brain. Collectively, our anticipated results will also provide the biological basis to spur new approaches for the design of therapeutic strategies aimed at regenerating the injured spinal cord.

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2016 RESEARCH GRANT AWARDS - FELLOWSHIP GRANT RECIPIENTS

Below is a summary of the fellowship grant recipient

CSCR16FEL008

Jyothi Shilpa Akella, Ph.D.

Rutgers University

Human Genetics Institute

\$150,000

Project Title: Identifying Mechanisms that Regulate Stress-Induced Neuronal Restructuring using Caenorhabditis Elegans

This proposal aims to identify the mechanisms that contribute to stress-induced neuronal restructuring and recovery using the powerful model system *Caenorhabditis elegans*.

Every year 12,500 Americans experience a Spinal Cord Injury (SCI). One of the immediate effects of SCI is lowering of extracellular pH (acidosis), an event that triggers processes affecting neuronal survival, pain and recovery. Acid Sensing Ion Channels (ASICs) are cation selective channels that get activated at low pH and play a role in acidosis-induced remodeling of dendritic spines- structures involved in learning, memory and pain. In rodent models of injury, inhibiting ASIC activity is neuroprotective and lowers pain. However, the role of ASICs in acidosis-induced neuronal remodeling in vivo and the contribution of neuronal remodeling to recovery of function remains a mystery. Since it is difficult in humans to study the connection between SCI, stress, acidosis, neuronal restructuring, and recovery of function, alternative experimental systems are

necessary. The simple animal model *C. elegans* is excellent for studying the effects of stress and acidosis on neuron morphology, function and activity.

Our lab identified six neurons of *C. elegans* that undergo reversible stress-induced neuronal restructuring. In non-stressful conditions, these IL2 neurons display a simple bipolar architecture with a single dendrite and single axon. When stressed, the dendrites and axons of the IL2 neurons extend branches. Upon removal of stress, neuronal branches are retracted and regain the simple bipolar neuronal features. These remodeling events are similar to the stress-induced changes in neuron structure observed in rodent models of SCI and upon acidosis injury. To identify genes that may play important roles in stress-induced neuronal remodeling and recovery, we defined the cell-specific transcriptome (parts list) of the IL2 neurons. We found two ASIC encoding genes *asic-2* and *egas-1* exclusively expressed in the IL2 neurons, but their functions remain unknown. We will determine the function of these ASICs in IL2 neuron restructuring (Aim 1). We will create mutations that will enhance or reduce the ASIC channel activity and then measure their ability to induce dendritic remodeling in living animals. This will establish *C. elegans* as an in vivo model to study the effects of acidosis-induced neuronal remodeling. Changes in dendrite morphology associated with alterations in neuronal activity contribute to pain. We will determine whether IL2 neuronal activity changes during stress-in-

duced neuronal remodeling (Aim 2). Our work will reveal conserved molecules and mechanisms that modulate neuronal restructuring and activity and contribute to pain after SCI.

Extracellular vesicles (EVs) are submicron sized particles released by many cells in the nervous system and function in intercellular communication. EVs are found in body fluids including cerebrospinal fluid. The content and nature of the EVs is changes in health and neurodegeneration, and the factors that regulate the properties of EVs in disease or stress remain unknown. The *C. elegans* IL2 neurons in addition to dynamic remodeling ability, also release EVs. Since stress affects EV dynamics in vitro and since IL2 neurons also respond to stress by remodeling, we will use the IL2 neurons to examine the effects of stress on EVs and a role for EVs in stress-induced neuronal restructuring (Aim 3). Our studies will provide insight to mechanisms controlling stress-induced neuronal restructuring and EV dynamics. This knowledge will help design therapies that may promote formation of beneficial EVs that encourage recovery and neuroregeneration while blocking the formation of pathological EVs that promote neurodegeneration.

Our studies in a simple animal model for stress-induced neuronal restructuring and recovery may pave to way to therapies that promote neuron survival, recovery of function and pain reduction after SCI.

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2016 RESEARCH GRANT AWARDS - EXPLORATORY RESEARCH GRANT RECIPIENTS

Below is a summary of the exploratory research grant recipients

CSCR16ERG019

KiBum Lee, Ph.D.

**Rutgers, Chemistry & Chemical
Biology**

\$200,000

Project Title: Promoting Axonal Regeneration in the CNS Using NanoScript (Nanoparticle-Based Transcription Factor)—Based Repression of PTEN

A novel treatment method using nanoparticle based synthetic transcription factor, NanoScript, to genetically induce axon regeneration to effectively promote functional recovery in spinal cord injury.

Spinal cord injury (SCI) is one of the most common causes of disability in young adults, affecting approximately 12,000 people in the United States every year. SCI results in a number of cellular and molecular changes in and around the injury site, leading to a host of debilitating symptoms that result in increasing loss-of-function. Given the complex damage caused by SCI and the intrinsically limited regenerative potential of the mammalian CNS, there is a strong clinical need for effective strategies to: 1) alleviate the inhibitory environment, 2) regenerate the destroyed neural cells, and 3) re-establish the damaged neuronal circuitry in the injury site. To this end, gene therapy has shown great promise in treating SCI. Recent studies indicate that the phos-

phatase and tensin homolog (PTEN) gene regulates mTOR pathways, which stimulate axon growth and regeneration. Remarkably, it allows corticospinal tract regeneration in mice, despite the presence of growth inhibitory factors in the spinal cord and injury site. However, previous approaches required viral vectors to deliver siRNA to silence or Cre to knock out PTEN. Such viral approaches have significant safety obstacles to overcome, including the potential oncogenic effects of PTEN deletion. Addressing the aforementioned challenges in gene therapy, our group (KBLEE group) has previously developed a nanoparticle-based synthetic transcription factor platform that emulates the fundamental functions of transcription factors, thereby allowing for regulating transcriptional activity (e.g. activation or repression) and targeted gene expression (e.g. PTEN) in both an effective and selective manner. In addition to transiently regulating genes in both non-viral and efficient manner, we designed the NanoScript platform to be interchangeable, and hence applicable for almost any cellular application, especially stem cell differentiation and cellular reprogramming applications. Moreover, NanoScript, can be synergistically combined with epigenetic modulators (e.g. SAHA and CTB) and has been demonstrated to both effectively activate or deactivate specific endogenous genes in stem cells, which could lead to myogenesis, chondrogenesis, and neurogenesis. However, to facilitate the translation of our nanoparticle-based STF platform to the effective treatment of SCI, several critical parameters must be further investigated and im-

proved, including: 1) the specificity of NanoScript-PTEN modulating the PTEN/mTOR pathways without off-target effects, 2) the functionality of our nanoparticle-based STF platform – by replacing the gold nanoparticle with a multifunctional nanoparticle we can bestow our platform with significantly more functionality, and 3) we need to determine its in vivo biocompatibility and efficacy.

Our unique NanoScript system is designed to induce axon regeneration to effectively promote functional recovery. In this proposal, we combine our expertise in nanomedicine (Lee lab) and spinal cord injury repair (Young lab) to develop a new nanomaterial-based treatment strategy to SCI. Given the complexities caused by the injury, we believe our novel NanoScript platform can serve as a multifunctional tool for developing future therapies for CNS-related diseases and injuries.

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2016 RESEARCH GRANT AWARDS - EXPLORATORY RESEARCH GRANT RECIPIENTS

Below is a summary of the exploratory research grant recipients

CSCR16ERG018

Kathy Chiou, Ph.D.

Kessler Foundation

\$190,953

Project Title: Investigation of Structural White Matter Substrates Underlying Cognitive Impairment After SCI

This study utilizes diffusion tensor imaging/neuropsychological testing to examine and document the relationship between cerebral white matter integrity and cognitive performance in adults with SCI. Advances in neuroimaging techniques have allowed scientists to expand their knowledge of the neural mechanisms underlying traumatic spinal cord injury (SCI). Diffusion tensor imaging (DTI), is a non-invasive neuroimaging technique that yields information about the movement of water molecules in the intercellular architecture of the central nervous system. Measurements of the magnitude and direction of water diffusion (or movement) allows for inferences to be made about the integrity of white matter tissue in the central nervous system. Through DTI, researchers have discovered that traumatic SCI not only affects the white matter tracts of the spinal cord, but also negatively impacts white matter tissue in the brain. Specifically, persons with SCI have been found to have reduced white matter integrity in the cerebral cortex compared to healthy peers. Importantly, disruption of cerebral white matter integrity has

been shown to be associated with poor cognitive function in other populations. While impairments in cognitive functioning have, in fact, been well-documented after SCI, the influence of cerebral white matter integrity on such cognitive deficits remains unknown.

This study utilizes DTI and neuropsychological evaluation to document the association between cerebral white matter integrity and cognitive functioning in adults with SCI. Measures of the magnitude (mean diffusivity) and direction (fractional anisotropy) of water diffusion in the brain will serve as measures of cerebral white matter integrity. These measures will be correlated with scores from neuropsychological testing to document the relationship between cerebral white matter integrity and cognitive functioning.

This project will expand the field of SCI research by simultaneously investigating two important, but understudied areas in spinal cord research: cerebral integrity and cognitive functioning. Importantly, the documentation of the relationship between cerebral white matter integrity and cognitive functioning in SCI will provide a clearer understanding of the neural mechanisms underlying cognitive functioning after injury. Through this knowledge, predictive biomarkers of cognitive functioning can be identified. These biomarkers may have significant clinical applicability as they may facilitate easier and faster detection of cognitive deficits after SCI. Improving the detection of these deficits would

assist individuals with SCI in gaining access to services that could ultimately improve their functional outcome.

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2016 RESEARCH GRANT AWARDS - EXPLORATORY RESEARCH GRANT RECIPIENTS

Below is a summary of the exploratory research grant recipients

CSCR16ERG014

Treena Livingston Arinzeh, Ph.D.
New Jersey Institute of Technology
\$200,000

Project Title: Schwann Cell GAG Mimetic Combination Strategy for Spinal Cord Repair

This study will evaluate the use of glycosaminoglycan (GAG) mimetics in combination with Schwann Cells for spinal cord repair

In the United States alone, there are approximately 300,000 persons with damaged spinal cords with 12,000 new cases added annually. Spinal cord injury (SCI) is a devastating condition for which there is no effective treatment at the present time.

Neural tissue engineering strategies using scaffolds that more closely mimic the native extracellular matrix (ECM) during neural development may be a promising strategy to promote axonal growth. During neural development, glycosaminoglycans (GAGs) have been known to play an important role in axonal guidance and growth. Depending upon the degree and pattern of sulfation, GAGs can provide a permissive environment for cellular and axonal growth. We have developed GAG mimetics derived from cellulose that have chemical structures similar to native GAGs but can be tailored to have different chemistries. The GAG mimetic, sodium cellulose sulfate (Na-

CeS), can be synthesized to vary in the degree and pattern of sulfation, which makes it attractive over native GAGs because it can be tailored. In preliminary studies, neurite extension was greatest on scaffolds containing NaCeS in comparison to naturally-occurring GAGs and controls. In the proposed studies, we will combine NaCeS containing scaffolds with Schwann cells (SCs) to promote axonal growth.

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SPINAL CORD TECHNIQUES TRAINING TRAVEL RESEARCH GRANTS

Spinal Cord Techniques Training Travel Research Grants

CSCR16TTT02 - \$4,000

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CSCR16TTT3 - \$1,500

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