



Annual Report
State Fiscal Year 2005

January 30, 2006

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

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DEDICATION

Christopher Reeve

September 25, 1952 - October 10, 2004



January 1, 2006

The Honorable Jon Corzine
Governor
Office of the Governor
State House – P.O. Box 001
Trenton, New Jersey 08625

Dear Governor Corzine:

On behalf of the New Jersey Commission on Spinal Cord Research, its members, staff and the spinal cord injured people of New Jersey, it is my honor and privilege to present the Annual Report for Fiscal Year 2005.

In 2005, the Commission received and reviewed 65 grant applications from eight prestigious public and private New Jersey institutions. The Commission awarded more than \$5.2 million to 21 grantees engaged in spinal cord research. The Commission looks forward to advancing this work and deeply appreciates the unwavering support it receives from the state.

The Commission continues to develop its statewide registry of spinal cord injured patients. The Registry will be a source of key statistical information, and serve as a vehicle to inform spinal cord injured persons about important clinical trial opportunities.

Each year, the Commission holds a Symposium to recognize its researchers and introduce new grantees. This year's keynote was delivered by Kentucky State Senator Tim Shaughnessy, who informed and inspired as he related the story of spinal cord research in Kentucky.

Last year we paid our final respects to Christopher Reeve, whose passing in late 2004 (our FY2005) once again underscored his inestimable contribution to the issue of spinal cord injury and the opportunity and urgency to find a cure. Few causes have had such a champion and we rededicate our efforts as a continuing tribute to his bravery, good spirits and inspiration.

We wish to extend our deepest appreciation your entire administration and Commissioner Fred M. Jacobs, M.D., J.D. for your support and advocacy of the scientific research agenda that inevitably will, one day soon we hope, allow New Jersey to join the world in announcing a definitive cure for spinal cord injury.

Sincerely,

Steven M. Reich, M.D.,
Chairperson

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ACKNOWLEDGEMENTS

The NJCSCR would like to express its sincere appreciation to all present and past Commission members, the New Jersey Department of Health and Senior Services for the expertise, time, and effort, and to Gabriel B. Milton, J.D., L.L.M., Executive Director, as the principal author and editor of the present report.

The NJCSCR also wishes to thank Kathrine Hempstead, Director, Office of Injury Surveillance and Prevention, Center for Health Statistics, and Darryl Brown, Ph.D., Spinal Cord Registry Manager, also of the Center for Health Statistics for the spinal cord injury surveillance statistics, and Commission staff members Christine Traynor and Mary Ray for their input and comment.

EXECUTIVE SUMMARY

The New Jersey Commission on Spinal Cord Research (NJCSCR) is an independent, state-supported organization, established in, but not of, the Department of Health and Senior Services.

- ✍ The NJCSCR funds spinal cord injury research projects in New Jersey.
- ✍ The NJCSCR supports a central registry of spinal cord injured persons in New Jersey.
- ✍ Overall, more than \$15.5 million has been granted covering 64 research projects.
- ✍ 23 grants have been completed; final reports received from 14 researchers.

The NJCSCR currently offers four types of grant awards:

- ✍ Five-Year Named Chairs for Senior and Junior Faculty
- ✍ Individual Research Grants
- ✍ Postdoctoral and Graduate Fellowship Grants.
- ✍ One-Time Start-Up Costs Grants

NJCSCR made significant accomplishments in 2005:

- ✍ 65 applications were received from eight New Jersey research organizations, representing a total of over \$20 million in requested funding.
- ✍ 21 research proposals were funded, with awards totaling over \$5.2 million.
- ✍ Hired Gabriel B. Milton, J.D., L.L.M. as its new Executive Director.
- ✍ Initiated a strategic planning process to take place in 2006.
- ✍ Completed a major revision of draft Commission Rules.
- ✍ Initiated new outreach activities.

2005 accomplishments of the NJ Spinal Cord Registry:

- ✍ Purchase and installation of Collector trauma software in major trauma centers, enabling electronic submission of data.
- ✍ Achieved over 80% reporting compliance in non-trauma hospitals.

2005 Annual Symposium

- ✍ Held October 11, 2005 on the campus of New Jersey Institute of Technology
- ✍ Commissioner Fred M. Jacobs, M.D., J.D., delivered opening remarks.
- ✍ Keynote: Kentucky State Senator Tim Shaughnessy.
- ✍ 89 registered; actual attendance was 75.

Center for Health Statistics 2004 figures on spinal cord injury in New Jersey:

- ✍ 355 hospitalizations for SCI
- ✍ Most significant cause: Motor vehicle crashes and falls
- ✍ Average cost of all SCI cases - \$167,150.

I. INTRODUCTION AND BACKGROUND

The New Jersey Commission on Spinal Cord Research (“NJCSCR”) is an independent, state-supported organization, created by statute in 1999, and established in but not of, the Department of Health and Senior Services. NJCSCR is committed to accelerating research to develop effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. The NJCSCR uses the funds at its disposal to support scientific endeavors that will further this goal.

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

The Act was passed by the New Jersey State Legislature in September 1999 and signed into law by Governor Christine Whitman. Assembly members Nicholas Felice and Anthony Impreveduto and Senators Robert Singer and Jack Sinagra were the principal sponsors. The legislation represented the successful culmination of the efforts New Jersey citizens with spinal cord injuries and their families, clinicians, scientists, public officials, and representatives of research, rehabilitation, and nonprofit organizations throughout the State.

Approximately 6,000 New Jersey residents suffer from traumatic injuries or diseases that damage the spinal cord with 300 new cases occurring annually. The direct and indirect economic costs of spinal cord injury represent a significant burden on individuals, families and state and local resources. Identification of an effective cure would represent a major humanitarian, scientific and public health accomplishment.

This report is being submitted in fulfillment of the legislative mandate in the *N.J.S.A. 52:9E-1 et seq.* The report describes the implementation of the Spinal Cord Research Act (the Act) and evaluates the benefit of the Act as evidenced in this report of grant awards for FY2005.

NJCSCR Membership

The NJCSCR consists of eleven members appointed by the Governor with the advice and consent of the Senate. The term of office is three years or until a successor has been appointed and qualified; members may be reappointed. The members serve without compensation, but may be reimbursed for reasonable expenses. Membership is designated by statute as follows:

- ✍ The Commissioner of the NJDHSS, or designee (voting ex-officio member)
- ✍ University of Medicine and Dentistry of New Jersey
- ✍ Rutgers, The State University of New Jersey
- ✍ Federally designated Spinal Cord Injury Model System
- ✍ Christopher Reeve Paralysis Foundation
- ✍ Six public members consisting of New Jersey residents knowledgeable about spinal cord injuries, including at least one NJ physician and one person with a spinal cord injury.

II. THE NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Overview of NJCSCR

The NJCSCR promotes and funds spinal cord research projects within the State of New Jersey that focus on the development of treatments and cures for paralysis and other consequences of spinal cord injuries and disease. In addition, the NJCSCR has established and maintains, in conjunction with the New Jersey Department of Health and Senior Services (NJDHSS), a central registry of persons who sustain spinal cord injuries other than through disease.

The activities and programs of the NJCSCR are supported by the New Jersey Spinal Cord Research Fund (the 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 surcharge is collected and forwarded to the State Treasurer and deposited annually into the Fund.

Mission and Goals

The NJCSCR's mission is to ensure that the people of New Jersey receive the utmost attention and benefit in our nation's fight against spinal cord injury and disease through its promotion of research into treatments and cures. The Act anticipates that spinal cord research will lead to effective treatments and cures for paralysis and other consequences of spinal cord injury and disease.

The goal of the NJCSCR is to assume a catalytic role in the worldwide movement to develop effective interventions and cures for paralysis and other consequences of spinal cord injury and disease.

The NJCSCR encourages and supports meritorious scientific research in New Jersey in fulfillment of that goal. This will benefit the State of New Jersey in savings on medical and support costs, enhance the development of the State's public and private biomedical sector, establish leadership in the field of spinal cord repair, and most importantly, bring therapies to people with spinal cord injuries and other neurological diseases and disorders.

Program Objectives

The NJCSCR is committed to accelerating research to develop effective interventions and cures for paralysis and other consequences of spinal cord injury and disease.

The primary objectives of NJCSCR are:

- ✍ To advance the field of spinal cord repair and regeneration and the New Jersey research community by encouraging established scientists to apply their expertise to the spinal cord.
- ✍ To foster collaborative, interdisciplinary approaches to spinal cord research.

- ☞ To nurture the next generation of spinal cord researchers through support of young scientists and postdoctoral fellows.
- ☞ To prevent or treat secondary biological conditions resulting from spinal cord injury.
- ☞ To promote dissemination of the research findings generated by those scientists supported by the NJCSCR

NJCSCR awards are intended to promote innovative, groundbreaking research, not to provide long-term support.

NJCSCR Grants Program

The NJCSCR central purpose is supporting significant research in the treatment and cure of spinal cord injury and fostering interest among New Jersey's scientific community in spinal cord research.

NJCSCR accomplishes its goals by identifying and funding meritorious scientific research, new spinal cord injury research facilities, endowing senior professorships and encouraging investigation by younger researchers in spinal cord injury.

Applications for Commission grants are subjected to a four-stage review process. Applications are initially reviewed for completeness and accuracy by the NJCSCR staff. An independent relevance review is conducted by a panel of three outside expert reviewers to assure that all applications are relevant to the overall goals of the NJCSCR and to select subject matter reviewers with appropriate background and expertise.

A panel of approximately 10-20 independent scientists is thus selected from a pool of over 100 highly qualified reviewers to conduct an independent scientific review of each application. Following independent review, the Scientific Merit Review Panel convenes to discuss and score each application. The results of this review are compiled and submitted to the NJCSCR for final consideration and vote.

NJCSCR also supports the activities of the Spinal Cord Injury Registry in the development of a comprehensive database of NJ spinal cord injured individuals. Health care facilities and providers are required under the Act to report each case to the Registry, through regulations set forth by the NJCSCR.

The NJCSCR maintains several active standing committees: Research Committee, Registry Committee, Personnel and Finance Committee, Bylaws and Legislative Committee, and Public Information Committee. Each committee meets at least once a year to review the activities and expenditures related to administration of the Fund, and the operation of the NJCSCR office.

Funding Priorities

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 NJCSCR has issued Research Guidelines that provide guidance on its grant funding priorities and polices (See Appendix A) as follows:

- ✍ 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.

Relationship of NJCSCR to NJDHSS

The NJCSCR is established in, but not of, the NJDHSS. Within NJDHSS, the office of the NJCSCR is administratively assigned in the Office of the Commissioner. The NJCSCR participates in various functions within the NJDHSS and benefits from the strong support services available in the Department, including fiscal, human resources, Center for Health Statistics, regulatory aspects, and information technology services. NJDHSS provides a supportive framework in which the NJCSCR works to effectively implement its mission of service to the public.

III. AVAILABLE GRANT PROGRAMS

The NJCSCR currently offers four types of grant awards. Each of these is the subject of a separate Notice of Grant Availability each funding cycle. - Five-Year Named Chairs for Senior and Junior Faculty, One-Time Start-Up Costs Grants, Individual Research Grants, and Postdoctoral and Graduate Fellowship Grants.

Five-Year Named Chairs for Senior and Junior Faculty Grants

The NJCSCR will fund grants totaling \$1,000,000 for senior faculty and \$600,000 for junior faculty for a Five-Year Named Chair for Senior and Junior Faculty to recruit highly qualified researchers to conduct spinal cord research in New Jersey. Successful candidates will also receive \$100,000 and \$50,000 respectively in start-up costs. The successful candidate will be called the "New Jersey Professor of Spinal Cord Research."

One-Time Start-Up Costs Grants

The NJCSCR will fund start-up costs ranging from \$250,000 to \$1,000,000 to facilitate the establishment of new spinal cord injury research laboratories. The primary focus of the research must hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. These awards may be used for renovation of space, support of research personnel (maximum of one-year salary for technical support staff; after the first year no personnel costs permitted), and the purchase of equipment directly related to the research. No indirect costs permitted. The goal of this program is to enable the establishment of new laboratories and facilitate the recruitment of highly qualified researchers to conduct spinal cord research in New Jersey.

Individual Research Grants

The NJCSCR will fund one- or two-year awards with a maximum funding level up to \$200,000 per year will be made. The goals of this program are (1) to encourage promising postdoctoral fellows and young investigators to undertake research on spinal cord regeneration, recovery and rehabilitation; (2) to encourage scientists who are well-established in other areas to transfer their efforts to spinal cord research; and (3) enable researchers with novel scientific and clinical ideas to test them and develop pilot data needed to seek larger awards from the National Institutes of Health, and other funding sources.

Fellowship Grants

Postdoctoral Fellowships are two-year awards of \$50,000 per annum. They provide an annual stipend of \$36,000, a research allowance of \$13,000, and a travel budget of \$1,000. No part of the award may be used for institutional overhead or indirect costs. Institutions may supplement stipends, but not with other full-time fellowship awards, or other NJCSCR monies. Candidates of outstanding quality must hold a Ph.D., and/or M.D., or equivalent graduate degree. Appropriate degrees must be awarded prior to activation of award. Candidates must be accepted for postdoctoral training under the

supervision of an appropriate mentor at a qualifying academic research institution in New Jersey.

Graduate Student Fellowships are two-year awards of \$30,000 per annum. They provide an annual stipend of \$25,000, a research allowance of \$4,000, and a travel budget of \$1,000. No part of this award may be used for institutional overhead, or for tuition. Institutions may supplement stipends, but not with other full-time fellowship awards or other NJCSCR monies. Applicants must be full-time graduate students in residence in a proposed course of study directly related to regeneration and repair of the damaged spinal cord.

Training Grants¹

In addition to the foregoing amounts, the NJCSCR may provide reimbursement of up to \$4,000 to successful individual and fellowship applicants for training in an approved spinal cord research techniques course.

The NJCSCR grants programs that a clear focus on its mission as established in the legislation, a strong commitment to spinal cord research and the ultimate goal of a cure. and accountability for administration of the Fund.

¹ NJCSCR spinal cord research techniques training grants were not available to FY2005 grantees but will be available to FY2006 grantees.

IV. FY2005 YEAR IN REVIEW

Overview of NJCSCR Grants Program

Since its inception, the NJCSCR has received and reviewed 169 applications and has funded 65 research projects through the 2005 fiscal year, representing a total of over \$15.8 million in awards. 50 of these awards were made for individual research proposals and 13 for fellowships. Start-up grants and named professorial chairs represent two newer and larger grant types that are likely to account for a greater share of dollars in the future. (See **Table 1**.)

Table 1 NJCSCR Grants Program – Performance to Date

Type	Applications	Grants	Amount
Individual Research	142	50	\$12,857,548
Fellowship	21	13	\$940,000
5-Yr. Named Chair	4	2	\$2,100,000
One-time Start-up	2		
Grand Total	169	65	\$15,897,548

Most NJCSCR grants run for two years, which means that final reports can reasonably be expected approximately 3-4 years after the date of the initial award. So far, 23 of the NJCSCR's grants have been completed and final reports received from 14 researchers. Only two reports are significantly overdue; nonetheless, the NJCSCR is confident of eventually receiving complete formal reports on all completed research. **Table 2** provides a view of the status of all such research by institution and type.

Table 2 Status of Completed NJCSCR-funded Research

Institution	Due	Overdue	Submitted	Total
Rutgers	3		9	12
UMDNJ	3	2	3	8
KMRREC	1		2	3
Grand Total	7	2	14	23

On January 24, 2005, letters were mailed to all grantee institutions requesting a response detailing results attributable to Commission funding in terms of access to additional funds, publications, recruitment and scientific progress.

To date, full responses have been received from all but two researchers, and clarification is being sought from one institution. A draft report should be completed and distributed for comment by mid-June.

Complete responses were received from nearly all researchers, and clarification was sought in other cases. The results of this informal survey were as follows:

- ✍ As of the date of the study, the Commission had granted \$12.7 million in 55 grants.
- ✍ Grantees reported receiving \$2.5 million in grant funding generally relevant to the work funded by the Commission.
- ✍ 44 new students and researchers were reported to have been involved in spinal cord research projects funded by the Commission.
- ✍ At least 31 publications, plus poster and other presentations were made based on funded research.
- ✍ One grantee received additional outside research funding in the form of an NIH RO1 grant of \$412,000 that was directly attributable to the work done under NJCSCR funding.

NJCSCR believes the record of accomplishment compiled thus far provides ample support for the value of its program and the contribution made by the research scientists it supports.

2005 Spinal Cord Research Grants Program

In FY2005, the NJCSCR again used two grant cycles to provide interested parties an enhanced opportunity to apply for Commission funding. Notices of Grant Availability were issued in August for the 2005 Cycle and in November 2004 for the 2005A Cycle.² The NJCSCR currently offers four grant-funding programs. These include one- and two-year Individual Research Grants, Five-Year Named Chair for Senior and Junior Faculty Grants, One-Time Start-up Cost Grants, and Postdoctoral and Graduate Fellowship Grants.

In 2005, the NJCSCR received and reviewed 64 applications, 52 or 81% of which were applications for Individual Research Grants. Eight New Jersey organizations, including public and private universities, firms and foundations submitted applications. Applicants requested a total of over \$20.8 million in funding (see **Table 3**).

Table 3 2005 Applications

Type	Applications	% of #	Amount	% of \$
Individual Research	52	81.3%	\$17,453,773	83.6%
5-Yr. Named Chair	2	3.1%	\$2,025,112	9.7%
One-time Start-up	1	1.6%	\$830,000	4.0%
Fellowship	9	14.1%	\$580,000	2.8%
Grand Total	64	100.0%	\$20,888,885	100.0%

The NJCSCR awarded over \$5.2 million dollars to 22 grantees in FY2005, funding 32% of all applications. 14 grants went to individual researchers and 7 to graduate and post-doctoral fellows. Research institutions receiving grants included Rutgers, the State University of New Jersey of New Jersey, University of Medicine and Dentistry of New Jersey, and Princeton University (see **Table 4**).

² For historical reasons, the first Grant Cycle of Fiscal Year is designated as the B Cycle and the second as the A Cycle.

Table 4 2005 Funded Grants

Grant Type	Grants	% of #	Amount	% of \$
Individual Research	15	68.2%	\$4,774,758	91.2%
Fellowship	7	31.8%	\$460,000	8.8%
One-time Start-up		0.0%		0.0%
5-Yr. Named Chair		0.0%		0.0%
Grand Total	22	100.0%	\$5,234,758	100.0%

Twelve grant recipients were eligible to seek second-year continuation funding during State Fiscal Year 2005. Their continuation applications were submitted in February 2005 and were evaluated by their 2004 independent scientific merit reviewers for appropriate progress. All twelve applications were favorably reviewed and recommended to the NJCSCR for continued second-year support. Notification of continuation funding was made by May 30, 2005. **Table 5** lists the 2005 grant awards by cycle. Lay summaries of all 21 2005 research projects may be perused in **Appendix E** below.

Table 5 2005 NJCSCR Grant Awards

Cycle	PI	Title	Institution	Grant
2005B	Mengqing Xiang, Ph.D.	Role of Foxn4 in Spinal Cord Development and Regeneration	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$400,000
2005B	Michael Matisse, Ph.D.	Molecular Control of Spinal Cord Neuronal Progenitor Differentiation	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$400,000
2005B	Renping Zhou, Ph.D.	Roles of Ephrin-A5 in Spinal Cord Development	Rutgers, The State University of New Jersey Chemical Biology	\$397,888
2005B	Wise Young, Ph.D., M.D.	OEG Remyelination of Axons after Spinal Cord Injury	Rutgers, The State University of New Jersey, W.M. Keck Ctr for Collaborative Neuroscience	\$391,704
2005B	William Wadsworth, Ph.D.	Molecular Mechanisms of Axon Guidance	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$315,204
2005B	Martin L. Yarmush, Ph.D.	Microfabrication of a Bioreactor System to Characterize Neuronal Stem Cell Differentiation	Rutgers, The State University of New Jersey, Biomedical Engineering	\$221,130
2005B	Christopher Rongo, Ph.D.	The Role of Notch/LIN-12 in Glutamate Receptor Signaling and Excitotoxic Neuronal Damage	Rutgers, The State University of New Jersey, Waksman Institute	\$191,712
2005B	Noshir Langrana, Ph.D.	Bifunctional Biomaterial Design for Spinal Cord Regeneration	Rutgers, The State University of New Jersey, Biomedical Engineering	\$150,000
2005B	Margaret Julias	A Novel Micromechanical Method for Controlling Microstructure in Nerve Grafts	Rutgers, The State University of New Jersey, Biomedical Engineering	\$60,000
2005B	Christopher L. Gaughan	Fabrication of a Tunable Hydrogel for Spinal Cord	Rutgers, The State University of New Jersey, Biomedical Engineering	\$60,000

Cycle	PI	Title	Institution	Grant
		Regeneration		
2005B	Gary Monteiro	3D Microreactors for Stem Cell Differentiation	Rutgers, The State University of New Jersey, Biomedical Engineering	\$60,000
2005B	Yu-Wen Chang	Combination of Radial Glial Transplantation with Anti-Inflammatory Treatment in Rat Spinal Cord Injury	Rutgers, The State University of New Jersey W.M. Keck Ctr for Collaborative Neuroscience	\$60,000
2005B	Ron Weiss, Ph.D.	Programmed Tissue Engineering for Spinal Cord Regeneration	Princeton University	\$391,189
2005A	Yasuhiro Maeda, M.D.	Effect of Erythropoietin Therapy on Acute Traumatic Spinal Cord Injury and Mechanism of Action	Veterans' Administration Medical Center - E. Orange	\$393,800
2005A	Hosea F. S. Huang, Ph.D.	Preservation of Sperm Functions after Spinal Cord Injury	University of Medicine and Dentistry of New Jersey, NJ Medical School	\$392,155
2005A	Randall D. McKinnon, Ph.D	Netrin Directed Glial Migration	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$360,690
2005A	Melitta Schachner, Ph.D.	Genes Involved in Spinal Cord Regeneration in Zebrafish	Rutgers, The State University of New Jersey, W.M. Keck Center for Collaborative Neuroscience	\$317,768
2005A	Frank V. Castello, M.D.	The Effect of FES on Children with Spinal Cord Dysfunction	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$267,498
2005A	Ronald P. Hart, Ph.D.	Differentiation of Therapeutic Stem Cells Using Micro RNAs	Rutgers, The State University of New Jersey, W.M. Keck Ctr for Collaborative Neuroscience	\$185,573
2005A	Hyuk Wan Ko	The Role of Ciliogenesis and Cell Cycle Phase in Hedgehog Signaling During Embryonic Stem Cell Differentiation	Princeton University	\$100,000
2005A	Ahryon Cho	The Role of FK506-Binding Protein 8 in Mammalian Neural Patterning and Axon Guidance	Princeton University	\$60,000
2005A	Tanya Borsuk	QTL Mapping and Phenotypic Analysis of Dreher Suppressing Modifying Loci	University of Medicine and Dentistry of New Jersey, Robt. Wood Johnson Medical School	\$60,000

In 2005, NJCSCR completed preparations for transitioning the grants submission process to an electronic format. NJCSCR has retained RamsCompany to provide access through its proposal management system, [proposalCENTRAL](#). Applicants will now only have to submit four copies plus the signed original in addition to completing the on-line application. Beginning in FY2006, the NJCSCR will be fully automated for all new grant applications. This will represent a significant reduction in paper work and handling both for applicants and the NJCSCR office staff. Previously, applicants were required to submit 25 copies plus exhibits of each application. The process is also expected to expedite and ease the process of distribution and review of applications by the Scientific Merit Review Panel.

Office of the NJCSCR

In January 2005, Robert Recine resigned as Executive Director to pursue other interests. Mr. Recine made a significant contribution to the Commission during his tenure and his resignation was accepted with regret.

In March 2005, Gabriel B. Milton, J.D., L.L.M. joined the staff of the NJCSCR as its new Executive Director. Mr. Milton brings extensive experience in law, health care, technology assessment and management in addition to degrees in law and economics.

Meetings were held with each Commissioner individually to acquire their individual perspectives on the opportunities and challenges facing the NJCSCR as well as their expectations. Additional meetings were held with individuals whose activities and responsibilities are important to or impact the affairs of the Commission. These included Rita Strmensky, Executive Director, Executive Commission on Ethical Standards, and Kathrine Hempstead, Director, Office of Injury Surveillance and Prevention, Center for Health Statistics.

Several new initiatives and projects were completed that provided NJCSCR a perspective on its operations and which may serve as a basis for developing a longer-term vision and plans.

- ✍️ Compilation of a database that for the first time will contain all significant historical information on grant applications received by the NJCSCR.
- ✍️ Provide a comprehensive report to the NJCSCR reviewing and summarizing its performance over the five years of its existence.
- ✍️ Completion of a project undertaken at the direction of NJCSCR by the outgoing Executive Director, purporting to examine the “return on investment” for the NJCSCR.
- ✍️ Create a dossier of completed and closed grants, providing a brief summary of goals, challenges, results, successes and future plans.

Completion of the foregoing activities will provide a foundation for a comprehensive review of the achievements and horizons of NJCSCR. A more formal strategic planning process is projected for FY2006.

Outreach Efforts

Achieving greater participation in the NJCSCR grants program is a primary aim. A range of activities and initiatives are undertaken to create greater awareness and stimulate broader interest in spinal cord research.

Publication of information regarding each grant cycle is essential. As in past years, Notices of Grant Availability were published in the *New Jersey Register*, and in the New Jersey Department of Health and Senior Services’ *Directory of Grant Programs*. Grant advertisements were also placed in a number of scientific journals including *Nature*, *Journal of Neuroscience*, *Community of Science* (on-line), and through the American Association for Advancement of Science – Science America.

NJCSCR seeks out and develops meaningful contacts with the State's universities, colleges, and public and private research institutions. The aim of these activities is to increase the number of scientists in New Jersey who specialize in spinal cord research as well as increase the number and quality of grant applications being submitted. In 2005, the NJCSCR added New Jersey Institute of Technology as a qualified research organization and received a major grant application from that institution for the 2006B cycle.

Outreach efforts in 2005 employed mass mailings and e-mail contacts to reach the private sector. Response to over 200 letters and emails resulted in one private firm submitting an application. Future outreach activities will seek more direct and targeted contacts.

The NJCSCR continues to promote its grant opportunities through the internet at its web site, www.state.nj.us/health/spinalcord, and through the distribution of its brochures which are continuously updated to reflect the most recent award information.

NJCSCR Rules

The NJCSCR is required by statute to promulgate Rules governing its operation. Draft rules have been in preparation for a considerable time. Significant progress was achieved in the latter part of FY2005 with a major revision streamlining the proposed rules and allowing finalization of a draft. The rules with minor changes are now in readiness for internal review by NJDHSS and the Attorney General's office prior to submission, for publication and comment prior to promulgation.

2005 Research Symposium

The 2005 Annual Symposium was held on October 11 at the campus of NJIT. Official registration for the event was 89 persons of which 23 were students. Actual attendance was 75, including 22 walk-ins (20 students). 53 or about 47% of those originally registered attended.

Following a welcome by Chairman Steven M. Reich, M.D., Commissioner Fred M. Jacobs, M.D., J.D. provided introductory remarks, highlighting New Jersey's commitment to biomedical and stem cell research. The keynote address was delivered by Kentucky State Senator Tim Shaughnessy. Senator Shaughnessy was instrumental in establishing his state's spinal and head injury research center and proved to be an engaging and inspirational speaker.

Presentations were made by 2003 grant recipients (three grantees were absent due to conflicts or other circumstances.) Following the lunch break, Drs. Melitta Schachner and Richard Nowakowski, New Jersey Commission on Spinal Cord Research designated New Jersey Professors of Spinal Cord Research, led an interactive presentation and panel discussion. Introduction of the 2005 grant recipients concluded the meeting.

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. This registry will provide a database indicating the incidence and prevalence of spinal cord injuries and will serve as a resource for research, evaluation, and information on spinal cord injuries.

The New Jersey Commission on Spinal Cord Research operates in part under a Memorandum of Agreement (MOA) with the New Jersey DHSS' Center for Health Statistics (CHS) to provide for the collection and analysis of spinal cord injury data. The NJCSCR employs Darryl Brown, Ph.D., as Registry Manager to manage all aspects of the Spinal Cord Registry. The Registry Manager's responsibilities include the collection of all spinal cord injury data from New Jersey hospitals, provide analysis of that data for health professionals and research scientists, and provide the data in a format to be useful in proposed clinical trials. A Spinal Cord Injury Self-Reporting Enrollment form is used to capture information on individuals who were injured prior to implementation of the Registry. The form is distributed through associations, advocacy groups, and public departments that serve the spinal cord injury population, and is also available on the NJCSCR web site. The program is fully HIPAA-compliant.

In 2005, nearly 80% compliance was achieved in the collection of traumatic spinal cord injury data items from New Jersey's acute care hospitals. Work was also begun to standardize the submission of these data from New Jersey trauma centers. In addition, the trauma centers submitted the National Trauma Data Bank reports that are prepared for the American College of Surgeons to the NJDHSS. A SAS program was developed to read and report to the trauma centers on the completeness of these reports. NJCSCR installed Collector trauma software (purchased by NJDHS and NJDHSS) and installed it in major trauma centers, enabling the electronic reporting of central nervous system injury.

Three registered nurses were funded to abstract medical records for approximately 25 non-trauma hospitals, because they did not have adequate staff to complete SCI data collection requirements. Other non-trauma hospitals that treated spinal cord injured patients submitted their data electronically (16 hospitals), or performed their own chart abstraction and mailed the hardcopies to CHS (17 hospitals).

V. GRANTS PROGRAM FOR FY2006

The NJCSCR intends to fully fund scientifically meritorious and relevant research awards for a total of up to six million dollars during State Fiscal Year 2006. The NJCSCR will again offer two funding cycles in FY2006. All four grant types are eligible for each cycle. The grant funding cycle will be: Cycle A – Grant Application Deadline: December 8, 2005, with an award notification date of May 28, 2006; and Cycle B – Grant Application Deadline: June 8, 2006, with an award notification date of November 30, 2006.

VI. SPINAL CORD INJURY (SCI) SURVEILLANCE - NEW JERSEY: 2005

SCI Case Definition and Methodology

Potential spinal cord injury cases have been identified from the UB-92 data file using the ICD-9-CM codes 806 and 952:

806.0-806.9: Fracture of a vertebral column with a spinal cord lesion

952.0-952.9: A spinal cord lesion without evidence of spinal bone injury

The following report provides an enumeration of all New Jersey spinal cord injury hospitalizations for 2002-2004. Also provided is a set of analyses specific to New Jersey residents for 2004. These analyses exclude pre-hospital mortality information; out-of-state hospitalizations to New Jersey residents; and out-of-state residents hospitalized in acute care facilities in New Jersey.

SCI-Related Hospitalizations in New Jersey, 2004

In 2004, New Jersey hospitals reported 355 hospitalizations for spinal cord injury. Of this total, 8 percent or 27 cases involved out-of-state residents. The overall increase in cases was seen among men, particularly in the 25-44 age cohort (**Table 6**).

Spinal cord injuries among men account for two-thirds of all hospitalized cases. In 2004, the ratio of male to female spinal cord cases for persons aged 15 and 44 was nearly 4:1, with males comprising 80 percent of cases. Increased numbers of female spinal cord injury hospitalizations were seen among women aged 65 and over.

Among all hospitalized spinal cord injury cases, less than ten percent of SCIs requiring hospitalization are fatal, although these figures exclude those who die before hospitalization (for whom spinal cord injury is rarely a cause of death). Approximately 50 percent of non-fatal spinal cord injury cases are transferred from the hospital to a rehabilitation facility.

Table 6 New Jersey Hospitals: Total Inpatient Spinal Cord Injury Cases by Age and Sex

	2004			2003			2002		
	Female	Male	Total	Female	Male	Total	Female	Male	Total
Under 5	0	1	1	1	0	1	1	0	1
(%)	0.0%	100.0%	100.0%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
5-15	6	8	14	4	10	14	3	3	6
(%)	42.9%	57.1%	100.0%	28.6%	71.4%	100.0%	50.0%	50.0%	100.0%
15-24	8	42	50	12	31	43	11	51	62
(%)	16.0%	84.0%	100.0%	27.9%	72.1%	100.0%	17.7%	82.3%	100.0%
25-44	15	87	102	27	77	104	16	64	80
(%)	14.7%	85.3%	100.0%	26.0%	74.0%	100.0%	20.0%	80.0%	100.0%
45-64	26	61	87	22	70	92	31	50	81
(%)	29.9%	70.1%	100.0%	23.9%	76.1%	100.0%	38.3%	61.7%	100.0%
65-74	17	22	39	13	7	20	17	12	29
(%)	43.6%	56.4%	100.0%	65.0%	35.0%	100.0%	58.6%	41.4%	100.0%
75-84	17	16	33	22	18	40	18	23	41
(%)	51.5%	48.5%	100.0%	55.0%	45.0%	100.0%	43.9%	56.1%	100.0%
85+	16	13	29	13	9	22	13	10	23
(%)	55.2%	44.8%	100.0%	59.1%	40.9%	100.0%	56.5%	43.5%	100.0%
TOTAL	105	250	355	114	222	336	110	213	323
(%)	29.6%	70.4%	100.0%	33.9%	66.1%	100.0%	34.1%	65.9%	100.0%

New Jersey resident figures for selected causes of spinal cord injury (**Table 7**) show a relationship to age. Assaults are most important for adolescents and young adults (ages 15 to 24 years). Motor vehicle crashes are most important as a share of all injuries among adults aged 25 to 64 years. Notably, hospitalization for SCI as a result of motor vehicle crashes was more likely to occur among adults aged 25 to 44. For persons aged 65 and over, falls are by far the most important cause of spinal cord injury.

Table 7 Spinal Cord Injury Hospitalizations Among New Jersey Residents by Selected Cause and Age: 2004

Cause	AGE					
	<15	15-24	25-44	45-64	65+	All
Motor Vehicles	2	11	37	20	14	84
(%)	2.4%	13.1%	44.0%	23.8%	16.7%	25.6%
Falls	4	11	30	39	62	146
(%)	2.7%	7.5%	20.5%	26.7%	42.5%	44.5%
Assault	0	8	9	2	2	21
(%)	0.0%	38.1%	42.9%	9.5%	9.5%	6.4%
Other/Unknown	9	15	20	15	18	77
(%)	11.7%	19.5%	26.0%	19.5%	23.4%	23.5%
Total	15	45	96	76	96	328
(%)	4.6%	13.7%	29.3%	23.2%	29.3%	100.0%

The two primary causes of spinal cord injury for men and women are falls and motor vehicle crashes (**Table 8**). Among females, these two causes account for 76 percent of SCI hospitalizations. Among males, injuries due to falls and motor vehicle crashes comprise

nearly 70 percent of all SCI-related hospitalizations. Hospitalizations for SCI due to assault were six times more likely to occur among men than women.

Table 8 Spinal Cord Injury Hospitalizations Among New Jersey Residents by Selected Cause and Sex: 2004

Cause	Female	Male	Total
Motor Vehicles	22	62	84
(%)	26.2%	73.8%	25.6%
Falls	54	92	116
(%)	46.6%	79.3%	35.4%
Assault	3	18	21
(%)	14.3%	85.7%	6.4%
Other/Unknown	21	56	77
(%)	27.3%	72.7%	23.5%
Total	100	228	328
(%)	30.5%	69.5%	100.0%

Figures for spinal cord injury hospitalizations by selected cause and race (**Table 9**) reveal some notable racial differences. The share of SCI resulting from falls and motor vehicle crashes is far greater among Whites than it is among minorities. At the same time, assaults comprise a far higher share of all spinal cord injuries among Blacks when compared with Whites. Levels for Hispanics are generally lower than those of Blacks and Whites, and the number of spinal cord injuries among Asians is too low to analyze.

Table 9 Spinal Cord Injury Hospitalizations Among New Jersey Residents by Selected Cause and Race: 2004

Cause	White ¹	Black ¹	Hispanic ²	Asian	All Other	Total
Motor Vehicles	48	16	7	2	11	84.0
(%)	57.1%	19.0%	8.3%	2.4%	13.1%	25.6%
Falls	90	12	14	2	28	146.0
(%)	61.6%	8.2%	9.6%	1.4%	19.2%	44.5%
Assault	5	9	3	0	4	21.0
(%)	23.8%	42.9%	14.3%	0.0%	19.0%	6.4%
Other/Unknown	35	16	9	0	17	77.0
(%)	45.5%	20.8%	11.7%	0.0%	22.1%	23.5%
Total	178	53	33	4	60	328.0
(%)	54.3%	16.2%	10.1%	1.2%	18.3%	100.0%

¹No Hispanic ethnicity; ²Hispanic ethnicity – all Races

Spinal cord injuries result in relatively lengthy hospital stays. As seen in **Table 10**, more than 50 percent of injuries result in stays of a week or longer.

Table 10 Spinal Cord Injury Hospitalizations Among New Jersey Residents by Selected Cause and Length Of Stay: 2004

Cause	< 2 Days	2 - 6 Days	> 6 Days	All Stays
Motor Vehicles	8	26	50	84
(%)	9.5%	31.0%	59.5%	25.6%
Falls	12	57	77	146
(%)	8.2%	39.0%	52.7%	44.5%
Assault	0	4	17	21
(%)	0.0%	19.0%	81.0%	6.4%
Other/Unknown	14	26	37	77
(%)	18.2%	33.8%	48.1%	23.5%
Total	34	113	181	328
(%)	10.4%	34.5%	55.2%	100.0%

The impact of longer stays is highlighted by **Table 11**. These data indicate that additional inpatient care was required for 33 SCI cases. The death rate was 8.4 per hundred, or a total of twenty-eight deaths in 2004.

Table 11 Hospital Discharge Disposition of Spinal Cord Injury Cases Among New Jersey Residents by Selected Cause: 2004

Cause	Home ¹	Extended Inpatient Care ²	Rehabilitation ³	Died	All Cases
Motor Vehicles	27	7	44	6	84
(%)	32.1%	8.3%	52.4%	7.1%	25.6%
Falls	56	12	62	16	146
(%)	38.4%	8.2%	42.5%	11.0%	44.5%
Assault	7	4	10	0	21
(%)	33.3%	19.0%	47.6%	0.0%	6.4%
Other/Unknown	32	10	29	6	77
(%)	41.6%	13.0%	37.7%	7.8%	23.5%
Total	122	33	145	28	328
(%)	37.2%	10.1%	44.2%	8.5%	100.0%

¹Includes: Discharges/transfers to home and/or home care and patients who left against medical advice

²Includes: Discharges/transfers to other private or Federal general hospitals, and long-term acute care

³Includes: Discharges/transfers to hospital-based or freestanding inpatient rehabilitation and specialty nursing facilities

Hospital charges for spinal cord injury differ by cause. As indicated in **Table 12**, the average or mean cost of all SCI cases was \$167,150 in 2004. Transportation-related SCI generates a higher level of charges per case, with maximum cost exceeding \$1.3 million and an average cost \$227,298.

The variability of mean charges is indicated by the standard deviation, the variation in charges per individual case is lower for self-inflicted/assault spinal cord injuries as compared to transportation-related SCI.

Table 12 Average Hospital Charges for Spinal Cord Injury Cases Among New Jersey Residents by Selected Cause: 2004

	Total SCI Cases	Mean	Min	Max	St. Dev
All Transportation	92	\$227,298	\$8,260	\$1,321,143	\$294,879
Falls	146	\$145,315	\$8,110	\$1,330,329	\$224,145
Intentional	21	\$201,186	\$20,384	\$867,836	\$219,498
All Other	69	\$122,795	\$243	\$949,561	\$168,791
Total SCI Cases	328	\$167,150	\$243	\$1,330,329	\$238,888

VII. FINANCIAL STATEMENTS

The activities and programs of the NJCSCR are supported by the New Jersey Spinal Cord Research Fund (the 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 surcharge is collected and forwarded to the State Treasurer and deposited annually into the Fund.

In 2005, the Fund received revenues of \$4.04 million, in line with expectations. Funds on hand at the end of FY2004 in the amount of \$7.29 million, plus investment interest, brought the sum of funds available for FY2005 to \$11.63 million.

The NJCSCR projected awarding grants during FY2005 of over \$7 million. As a result of the careful review process, it was determined that an insufficient number of proposals met the rigorous standards required to meet this goal. In consequence, total expenditures to grant recipients totaled \$5.42 million, \$1.62 million less than projected.

The NJCSCR reduced office expenditures by \$90,000 in FY2005 as a result of smaller outlays for equipment, salaries, software utilization, reviewer fees, registry costs and other projected expenses. In all, overhead and office expenses were \$450,000, representing a savings of \$170,000 vs., the projected budget.

Net reduction in actual versus projected expenditures for FY2005 totaled \$1.19 million. As a result, the fund balance at the end of the year was \$5.76 million. The NJCSCR is committed to making sufficient grants each year to keep the year-to-year fund balance at or below this level. This commitment ensures the majority of funds are disbursed to worthy grantees each year, while retaining the ability to meet expenses.

Projected revenues for FY2006 of \$4.30 million will afford the NJCSCR anticipated funds totaling \$10.06 million. The NJCSCR plans to disburse \$6.02 million in grants in 2006 and spend another \$650,000 in administrative costs. While actual expenditures and disbursements may vary substantially, the fund balance as of June 30, 2006 is projected to be \$3.39 million. See **Table 13** below.

Table 13 NJCSCR Fund Balance Summary

	SFY 2005 <i>Projected</i>	SFY 2005 <i>Actual</i>	SFY 2006 <i>Projected</i>
Opening Fund Balance (July 1)	\$7,290,000	\$7,290,000	\$5,760,000
Revenues			
Assessments ¹	\$4,000,000	\$4,040,000	\$4,000,000
Investments Earnings - Interest ²	\$120,000	\$300,000	\$300,000
Total Revenue:	\$4,120,000	\$4,340,000	\$4,300,000
Total Funds Available	\$11,410,000	\$11,630,000	\$10,060,000
Disbursements and Expenses			
Disbursements to Grantees	\$7,040,000	\$5,420,000	\$6,020,000
Total disbursements	\$7,040,000	\$5,420,000	\$6,020,000
Expenses			
Administrative & Office expense	\$440,000	\$350,000	\$470,000
Professional Review Panel	\$80,000	\$40,000	\$80,000
NJCSCR Registry	\$100,000	\$60,000	\$100,000
Total expenses	\$620,000	\$450,000	\$650,000
Total Disbursements and Expenses	\$7,660,000	\$5,870,000	\$6,670,000
Closing Fund Balance (June 30)	\$3,750,000	\$5,760,000	\$3,390,000

¹Net revenue variance

²Funds plus interest deposited annually in Jan.

APPENDIX

Appendix A NJCSCR FY2005 Membership Information

Member, Residence and Affiliation	Term Expires:
John D. Del Colle, Chairman Franklin Lakes, New Jersey Public Member	December 18, 2002
Scott A. Whitman, Vice Chairperson Milltown, New Jersey Public Member	May 25, 2004
Peter W. Carmel, M.D. New York Representing the University of Dentistry and Medicine of New Jersey	March 27, 2003
Susan P. Howley Short Hills, New Jersey Representing the Christopher Reeve Paralysis Foundation	June 26, 2005
Cynthia Kirchner, M.P.H. Ex-Officio Representing the Commissioner of the New Jersey Department of Health & Senior Services	N/A
Henry R. Liss, M.D. Summit, New Jersey Physician Member	June 26, 2003
Patricia Morton, Ph.D. North Brunswick, New Jersey Public Member	March 23, 2003
Mark L. Pollard Princeton, New Jersey Representing the Spinal Cord Model System	May 25, 2005
Steven M. Reich, M.D. East Brunswick, New Jersey Public Member	May 25, 2004
Public Member (vacant)	March 27, 2004
Public Member (vacant)	March 27, 2004

Appendix B FY2006A Research Program Guidelines

INTRODUCTION

Approximately 6,000 New Jersey residents suffer from traumatic injuries or diseases that damage the spinal cord. Approximately 300 new injuries occur each year. The economic consequences of the resulting physical disabilities are enormous. The personal toll on individuals and families with spinal cord injuries and their communities is incalculable.

Therefore, in September 1999, Governor Christine Todd Whitman signed legislation creating the New Jersey Commission on Spinal Cord Research (NJCSCR), allocating funding to the New Jersey Spinal Cord Research Fund.

The charge to the NJCSCR is:

The NJCSCR will solicit and approve support of research projects, administer the awards through research grants, and promote development of spinal cord research projects within the State of New Jersey that focus on treatments and cures. The NJCSCR will compile a research directory of all spinal cord research projects being conducted within the State, and provide the Governor and the Legislature with an annual report by January 30th of each year describing the status of the NJCSCR's activities and the results of its funded research projects.

PROGRAM OBJECTIVES

The NJCSCR is committed to accelerating research to develop effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. Its primary objectives are:

- ✍ To advance the field of spinal cord repair and regeneration and the New Jersey research community by encouraging established scientists to apply their expertise to the spinal cord.
- ✍ To foster collaborative, interdisciplinary approaches to spinal cord research.
- ✍ To nurture the next generation of spinal cord researchers through support of young scientists and postdoctoral fellows.
- ✍ To prevent or treat secondary biological conditions resulting from spinal cord injury.
- ✍ To promote dissemination of the research findings generated by those scientists supported by the NJCSCR.

NJCSCR awards are intended to promote innovative, groundbreaking research, not to provide long-term support. Grantees are eligible to apply for funding for additional research projects, but all applications will be reviewed competitively.

FUNDING PRIORITIES

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.

ELIGIBILITY

The following researchers are eligible to submit proposals to the NJCSCR for research grant awards. All applicants, organizations/institutions must be located within the State of New Jersey.

- ✍ Ph.D., M.D., or other such professionals.
- ✍ Independent investigators at any stage of professional development.
- ✍ Postdoctoral fellows, Graduate fellows.
- ✍ Established investigators new to the field of spinal cord injury research.
- ✍ Young Investigators (five years post-completion of formal training)

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 including s and organizations/institutions are encouraged to collaborate with other New Jersey-based researchers as well as with researchers located out-of-state, or out of the country. Senior scientists, young investigators, postdoctoral and graduate fellows may serve as Principal Investigator. If the applicant is a fellow, he/she must submit a letter of support from the laboratory's senior scientist, as well as two other appropriate letters of reference.

PROTECTION OF HUMAN SUBJECT, ANIMAL WELFARE, AND RECOMBINANT DNA

Compliance with National Institutes of Health regulations for the protection of human subjects, animal welfare, recombinant DNA, and inclusion of women and minorities in clinical trials is required for all grants.

It is the responsibility of the applicant as a potential recipient of a NJCSCR grant to assure that the rights and welfare of all human subjects used in any NJCSCR sponsored research are protected. Any applications involving human subjects must be reviewed and approved by the appropriate institutional review board.

It is the responsibility of the applicant as a potential recipient of a NJCSCR grant to assure proper care and treatment of all laboratory animals used in any NJCSCR sponsored research. Any applications involving laboratory animals must be reviewed and approved by the appropriate institutional review committee.

It is the responsibility of the applicant as a potential recipient of a NJCSCR grant to assure that the physical and biological containment needed for research involving any recombinant DNA molecules is within policies set out in the current "National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules." Any applications involving recombinant DNA molecules must be reviewed and approved by the appropriate institutional review board.

RESEARCH GRANTS AVAILABLE

The NJCSCR offers four types of grants - Five-Year Named Chairs for Senior and Junior Faculty, One-Time Start-Up Costs Grants, Individual Research Grants, and Postdoctoral and Graduate Fellowship Grants.

Qualifying Institutions: For the purpose of all NJCSCR grants, a qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with a demonstrated capability to conduct grant funded research, and specifically approved by the vote of the NJCSCR, but in no case can an individual be a qualifying research institution.

The NJCSCR reserves the right to distribute funds among the grants in all its grant programs. The NJCSCR reserves the right not to fund any grant in any of its grant programs to the maximum amount, or not to fund any grant in any grant program at all. Grant awards to all four programs will not exceed \$3,000,000 as published in the *New Jersey Register*.

Five-Year Named Chair for Senior and Junior Faculty Grant

The NJCSCR will fund grants totaling \$1,000,000 for senior faculty and \$600,000 for junior faculty for a Five-Year Named Chair for Senior and Junior Faculty to recruit highly qualified researchers to conduct spinal cord

research in New Jersey. All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of support such as appropriate laboratory facilities and the commitment of financial support necessary to sustain the research for a minimum of five years. A qualifying research institution may not apply for both a "One-Time Start-Up Costs" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year.

Grants will total \$1,000,000 for senior faculty and \$600,000 for junior faculty (including direct and indirect costs; a maximum of 10% may be applied to indirect costs). Successful candidates also will receive \$100,000 and \$50,000 respectively in start-up costs. The person holding this position will be called "New Jersey Professor of Spinal Cord Research."

A senior faculty candidate will have a Ph.D. and/or M.D., an outstanding record of excellence and achievement in areas relevant to spinal cord injury research, high quality publications, a national/international reputation, demonstrated leadership capabilities, evidence of sustained success in competitive science funding, and a commitment to the development of practical therapies. Experienced researchers in other fields moving to spinal cord research also will be considered.

A junior faculty candidate will have a Ph.D. and/or M.D., appropriate postdoctoral experience in a well-established research facility, and confidential recommendations from the director and senior leaders of his/her present research setting. Outside references will enhance the application.

Applications are evaluated based upon evidence provided by the qualifying institution that the proposed candidate has accepted a position and that appropriate research facilities are available or will be provided by the start date of this award.

Awards will begin on or about June 15, 2006. Money granted must be held in a separate account by the institution with all accrued interest being maintained in the account. Any change in either awardee or the research focus will result in the revocation of the award and the return of all funds on a prorated basis. Annual funding within the five-year period will be contingent upon the availability of funds and the submission of an annual Narrative Report that is favorably reviewed by an independent scientific merit review panel. The panel's continuation recommendations will be made to the NJCSCR for funding approval. Project periods may not exceed five years. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of a Five-Year Named Chair grant. All forms are available at www.state.nj.us/health/spinalcord/.

One-Time Start-Up Costs Grant

The NJCSCR will fund start-up costs ranging from \$250,000 to \$1,000,000 to facilitate the establishment of new spinal cord injury research laboratories. The primary focus of the research must hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease.

All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of qualified research leadership for the new laboratory and the commitment of financial support necessary to sustain the research for a minimum of five years. A qualifying research institution may not apply for both a "One-Time Start-Up Costs" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year.

Grants ranging from \$250,000 to \$1,000,000 will be available from the New Jersey Spinal Cord Research Fund to support the initiation of new research programs in spinal cord injury. These awards may be used for the renovation of space, support of research personnel (maximum of one year salary for technical support staff; after the first year, no personnel costs are permitted), and the purchase of equipment directly related to the research. No indirect costs are permitted. The goal of this program is to enable the establishment of new laboratories and facilitate the recruitment of highly qualified researchers to conduct spinal cord research in New Jersey.

Proposals are evaluated based upon evidence provided by the qualifying institution that a new research laboratory will be established upon receipt of these funds. Such evidence should include, but is not limited to, range of construction, detailed equipment listing, evidence of other support from the institution, evidence that the institution is providing space to be renovated, information on a newly recruited faculty or staff member, or evidence that an experienced researcher in a related field will establish a new laboratory dedicated to spinal cord injury research.

Awards will begin on or about June 15, 2006. Money granted must be held in a separate account with all accrued interest being maintained in the account. Each grant award will be contingent upon the availability of funds. Any change in the research focus will result in the revocation of the award and the return of funds on a prorated basis. This is a one-year grant award with a progress-reporting period of five years during which time an annual Narrative Report must be submitted to the NJCSCR office. Evidence of the necessary organizational/institutional financial support to sustain the research must be included as part of the report. All forms are available at www.state.nj.us/health/spinalcord/.

Individual Research Grant

The NJCSCR will fund Individual Research Grants. Applicants are encouraged to apply for a one-year or two-year award. Maximum funding is up to \$200,000 per year including direct and indirect costs, (10% maximum for the latter).

The goals of this program are (1) to encourage promising postdoctoral fellows and young investigators to undertake research on spinal cord regeneration, recovery and rehabilitation; (2) to encourage scientists who are well-established in other areas to transfer their efforts to spinal cord research; and (3) enable researchers with novel scientific and clinical ideas to test them and develop pilot data needed to seek larger awards from the National Institutes of Health, and other funding sources.

s must be affiliated with a New Jersey State academic institution, research organization, public or private agency or other entity with demonstrated capability to conduct research responsibly. Senior scientists, young investigators, and postdoctoral fellows may serve as Principal Investigator. If the applicant is a fellow, s/he must submit a letter of support from the laboratory's senior scientist, as well as two other appropriate letters of reference. Unaffiliated individuals will not be funded. Individuals of any nationality or citizenship status may apply, provided they are employed by or affiliated with a qualified New Jersey State organization/institution. Awards will begin on or about June 15, 2006. All qualifying institutions in the State of New Jersey may apply. Two-year awards are made through one-year contracts. Each funding award within the two-year period will be contingent upon the availability of funds. Second-year support for all Individual Research grants is contingent upon submission of a Grant Continuation Application. The Grant Continuation Application must be favorably reviewed by an independent scientific merit review panel and recommended to the NJCSCR for continued funding. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of an Individual Research grant. All forms are available at www.state.nj.us/health/spinalcord/.

Postdoctoral and Graduate Student Fellowship Grants

Postdoctoral Fellowships are two-year awards of \$50,000 per annum. They provide an annual stipend of \$36,000, a research allowance of \$13,000, and a travel budget of \$1,000. No part of the award may be used for institutional overhead or indirect costs. Institutions may supplement stipends, but not with other full-time fellowship awards, or other NJCSCR monies. Candidates of outstanding quality must hold a Ph.D., and/or M.D., or equivalent graduate degree. Appropriate degrees must be awarded prior to activation of award. Candidates must be accepted for postdoctoral training under the supervision of an appropriate mentor at a qualifying academic research institution in New Jersey. A candidate may not apply for a NJCSCR Postdoctoral Fellowship and a NJCSCR Individual Research grant in the same grant cycle. If a first-year fellow applies for and is awarded a NJCSCR Individual Research Grant, funding will be contingent upon cancellation of the second year of the fellowship. Non-research activities, such as teaching, may not occupy more than 10% of the fellow's time.

Graduate Student Fellowships are two-year awards of \$30,000 per annum. They provide an annual stipend of \$25,000, a research allowance of \$4,000, and a travel budget of \$1,000. No part of this award may be used for institutional overhead, or for tuition. Institutions may supplement stipends, but not with other full-time fellowship awards or other NJCSCR monies. Applicants must be full-time graduate students in residence in a proposed course of study directly related to regeneration and repair of the damaged spinal cord. Students must begin study in the semester following activation unless special permission is received prior to activation date. The NJCSCR prefers to support graduate student candidates who have completed the first year of graduate study and are concentrating on research projects at least 80% of their time. Applicants may serve as teaching assistants while holding a NJCSCR Graduate Student Fellowship without special permission.

Postdoctoral and Graduate Student Fellowship awards will begin on or about June 15, 2006. Each funding award within the two-year period will be contingent upon the availability of funds. All Postdoctoral and Graduate Student Fellows must submit a first-year Progress Report accompanied by a letter of support from the fellow's mentor. Second-year fellowship funding is contingent upon the successful review of the first-year Progress Report and a recommendation from the mentor. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of the Fellowship grant. All forms are available at www.state.nj.us/health/spinalcord.

REVIEW PROCESS

All research proposals will be reviewed for scientific merit, technical merit, research significance, and relevance to the NJCSCR priorities by an independent scientific merit review panel. The independent scientific merit review panel will forward its recommendations to the NJCSCR for final review and action. Scientists supported by the NJCSCR are expected to fully report the results of their research to the NJCSCR, and may be asked to report on their results, or work in progress, at a symposium organized by the NJCSCR. Grantees also are expected to acknowledge the support of the New Jersey Commission on Spinal Cord Research in all presentations and publications.

All grant applications must be submitted following the guidelines below. Grant applications that do not adhere to these guidelines will be returned to the applicant without further consideration. Grant applications sent by fax or e-mail will **NOT** be accepted.

The deadline for all grant applications to be received at the NJCSCR office is 5:00PM on DECEMBER 8, 2005. **No exceptions will be made.**

All necessary and required grant application forms, grant continuation application forms, progress reports, narrative reports, final narrative reports, policies, research guidelines, and other additional information can be viewed and downloaded from the NJCSCR website at: www.state.nj.us/health/spinalcord/

Documents can also be obtained by sending a written request to the NJCSCR office at:

New Jersey Commission on Spinal Cord Research
P.O. Box 360
Market and Warren Streets
Trenton, New Jersey 08625

LETTER OF INTENT

A one-page letter of intent is highly recommended for the "Five-Year Named Chair for Senior and Junior Faculty" grant and for the "One-Time Start-Up Costs" grant. The remaining grant categories do not require a letter of intent.

PROPOSAL SUBMISSION

For all grant categories, one original (signed), and 25 additional copies of grant applications, including all reprints, appendices, and any attachments, must be sent to and received by the NJCSCR office no later than 5:00PM, December 8, 2005. **No grant applications will be accepted past this stated deadline.**

Please use this address for all overnight mail deliveries (FedEx, UPS, USPS, Express Mail, etc.):

New Jersey Commission on Spinal Cord Research
Health and Agriculture Building
Warren & Market Streets
4th Floor, Room 404
Trenton, New Jersey 08625

Please use this address for all regular U.S. mail deliveries:

New Jersey Commission on Spinal Cord Research
P.O. Box 360
Health & Agriculture Building
Warren and Market Streets
Trenton, New Jersey 08625

GRANT REVIEW PROCESS

For all grant categories, the determination of grant awards will be made through a three-step review process:

1. Administrative Review (NJCSCR office):

Upon receipt, all grant applications will be reviewed by the NJCSCR office for compliance with all applicable New Jersey State statutes and regulations, and to ensure completeness, and accuracy. In the event a grant application needs correction due to a budgetary issue, the applicant will be contacted to provide a revised budget.

2. Independent Relevance Review (Appointed Panel):

Independent relevance review will be conducted by a three-person panel appointed by the NJCSCR; members will have varied expertise. The panel will determine the relevance of all applications to the NJCSCR Research Guidelines and assign scientific reviewers for each proposal.

The decision to forward an application for independent scientific merit review is based only on relevance to the NJCSCR mission, priorities, and research guidelines, and does not guarantee that an award will be made.

3. Scientific Merit Review (Independent Scientific Merit Review Panel):

Members of the independent scientific merit review panel will convene to evaluate all grant applications, applying the criteria described below. This panel will assign scores to each application and make funding recommendations to the NJCSCR.

If it is determined that *ad hoc* expertise is needed, additional scientific referees may be used.

The Independent Scientific Merit Review Panel will forward its recommendations to the NJCSCR for final review and action. The authority to authorize or not authorize grants is fully vested in the NJCSCR according to New Jersey statute N.J.S.A. 52:9E-1-10.

CRITERIA FOR INDEPENDENT SCIENTIFIC REVIEW

Grant applications will be judged on scientific and technical merit, relevance to the NJCSCR's mission and priorities, clinical relevance, and interdisciplinary collaborations.

The independent scientific reviewers will perform two levels of review:

1. Each panel member will peer review his/her assigned proposals for scientific and technical merit and significance, and determine an initial score for each proposal.

The panel will then convene for group discussion, final scoring, and ranking of all proposals; the panel will also recommend a cut-off point for funding.

The following topics will be addressed during the review process:

- ✍ Is the research proposal of significance to the field of spinal cord injury research?
- ✍ Is the proposed research innovative, including novel concepts, approaches, and/or methods?
- ✍ Is the research proposal relevant to NJCSCR priorities?
- ✍ Is the research proposal original in theory and application?
- ✍ Does prior research and theory provide a rational basis for the proposed research?
- ✍ Is the proposed project adequate in terms of experimental design and analyses, anticipation of potential problems, and consideration of alternative approaches?
- ✍ Does the researcher have access to appropriate facilities, equipment, expertise, and research environment either in-house and/or with collaborators or consultants?
- ✍ Does the design include interdisciplinary collaborations, and if so, is the proposed combination of disciplines both novel and likely to generate meaningful results?
- ✍ Are the qualifications, productivity, and time commitments of and key staff commensurate with the proposed project?

- ☞ If a human model is proposed, is the availability of subjects adequate and system of education and protection of subjects appropriate?
- ☞ Is there evidence of compliance with National Institutes of Health regulations for the protection of animal welfare?
- ☞ Is the justification for procedures assessing the effects of interventions on recovery recognized, standardized, and generally accepted?
- ☞ Is the budget reasonable and justified for the project proposed? Is there evidence of institutional commitment and/or cost sharing in the proposal?
- ☞ Are there other factors both pro and con that may affect the ability of the applicant to successfully complete the research goals?
- ☞ Will the project make an original and important contribution to the field of spinal cord research and more specifically, to the mission of the NJCSCR?

RESULTS NOTIFICATION

All applicants including s and organizations/institutions will be formally notified of the outcome of his/her application at the conclusion of the selection process anticipated to be no later than May 30, 2006. At that time, formal notification will be made to the institutions of successful applicants and contracts will be initiated shortly thereafter.

Blinded reviews will be provided to both funded and non-funded applicants; no further information shall be provided.

Non-funded applicants also will be notified. There is no appeal process. All non-funded applicants in any given grant cycle are eligible to reapply through the reapplication process. Non-funded applicants have a 30-day period of time to revise and resubmit their grant application as a new competing proposal in the next grant cycle. One original and 25 additional copies must be submitted.

ANTICIPATED RESULTS

The goal of the NJCSCR is to assume a catalytic role in the worldwide movement to develop effective interventions and cures for paralysis and other consequences of spinal cord injury and disease.

Through the judicious use of funds raised through violations under Title 39 of the Revised Statute, or any other motor vehicle, or traffic violation in the State of New Jersey, the NJCSCR will encourage and support meritorious scientific research in the State of New Jersey in fulfillment of that goal. This will benefit the State of New Jersey in savings on medical and support costs, enhance the development of the State's public and private biomedical sector, establish leadership in the field of spinal cord repair, and most importantly, help develop effective interventions for paralysis and other consequences of spinal cord injury and disease.

Appendix C 2005B Notices of Grant Availability

NOTICE OF GRANT AVAILABILITY

NEW JERSEY COMMISSION ON SPINAL CORD
RESEARCH

NAME OF GRANT PROGRAM: Five-Year Named Chair for
Senior & Junior Faculty

GRANT PROGRAM NO. 05-SCR-4

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L.
1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Cost-Reimbursement
Grants

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS
WILL BE USED:

The NJCSCR will fund grants totaling \$1,000,000 for senior faculty and \$600,000 for junior faculty for a Five-Year Named Chair for Senior and Junior Faculty grant to recruit highly qualified researchers to conduct spinal cord research in New Jersey. All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of support such as appropriate laboratory facilities and the commitment of financial support necessary to sustain the research for a minimum of five years. A qualifying research institution may not apply for both a "One-Time Start-Up Cost" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year. A person holding one of these positions will be called "New Jersey Professor of Spinal Cord Research."

AMOUNT OF MONEY IN THE GRANT PROGRAM:

Grants will total \$1,000,000 for senior faculty and \$600,000 for junior faculty (includes direct and indirect costs, a maximum of 10% may be applied to indirect costs). Successful candidates also will receive \$100,000 and \$50,000 respectively in start-up costs. Awards will begin on or about December 15, 2004. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-4 as well as among the NJCSCR's other grant programs 05-SCR-1, 05-SCR-3, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-4 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$4,000,000. Any change either in awardee or the research focus on spinal cord injury will result in the revocation of the award and the return of all funds on a prorated basis. Annual funding within the five-year period will be contingent upon the availability of funds and the submission of an annual Narrative Report that is favorably reviewed by an independent scientific merit review panel. The panel's continuation recommendations will be made to the NJCSCR for funding approval. Project periods may not exceed five years. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of a Five-Year Named Chair grant.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE
FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants
2. General and specific Grant Compliance requirements issued by the Granting Agency.
3. Applicable Federal Cost Principles relating to the Applicant

GROUP OR ENTITIES WHICH MAY APPLY FOR THE
GRANT PROGRAM:

All qualifying institutions in the State of New Jersey may apply for Five-Year Named Chair for Senior and Junior Faculty grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the Commission, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE
CONSIDERED FOR A GRANT:

A Senior Faculty candidate will have a Ph.D. and/or M.D., an outstanding record of excellence and achievement in areas relevant to spinal cord injury research, high quality publications, a national/international reputation, demonstrated leadership capabilities, evidence of sustained success in competitive science funding, and a commitment to the development of practical therapies. Experienced researchers in other fields moving to spinal cord research also will be considered.

A Junior Faculty candidate will have a Ph.D. and/or M.D., appropriate postdoctoral experience in a well-established research facility, and confidential recommendations from the director and senior leaders of their present research setting.

Outside references will enhance the application. Applications are evaluated based upon evidence provided by the qualifying institution that the proposed candidate has accepted a position and that appropriate research facilities are available or will be provided by the start date of this award.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a year.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research

Department of Health and Senior Services

PO Box 360 Trenton, New Jersey 08625-0360

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE
SUBMITTED:

Letter of Intent – May 3, 2004

Applications must be received in the NJCSCR office by June 8, 2004, between the hours of 8AM and 5PM.

(NO EXCEPTIONS WILL BE MADE)

DATE BY WHICH APPLICANT SHALL BE NOTIFIED
WHETHER THEY WILL RECEIVE FUNDS:

Notification – November 30, 2004

NOTICE OF GRANT AVAILABILITY

New Jersey Commission on Spinal Cord Research

NAME OF GRANT PROGRAM: One-Time Start-Up Costs Grant

GRANT PROGRAM NO. 05-SCR-5

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L. 1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Cost Reimbursement Grants

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS WILL BE USED:

The NJCSCR will fund start-up costs to facilitate the establishment of new spinal cord injury research laboratories. The primary focus of the research must hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of qualified research leadership for the new laboratory and the commitment of financial support necessary to sustain the research for a minimum of five years. These awards may be used for the renovation of space, support of research personnel (maximum of one year salary for technical support staff; after the first year, no personnel costs are permitted), and the purchase of equipment directly related to the research. No indirect costs are permitted. The goal of this program is to enable the establishment of new laboratories and facilitate the recruitment of highly qualified researchers to conduct spinal cord research in New Jersey. A qualifying research institution may not apply for both a "One-Time Start-Up Costs" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year.

AMOUNT OF MONEY IN THE GRANT PROGRAM:

The NJCSCR will fund start-up costs ranging from \$250,000 to \$1,000,000 to facilitate the establishment of new spinal cord injury research laboratories. Awards will begin on or about December 15, 2004. Money granted must be held in a separate account with all accrued interest being maintained in the account. Each grant award will be contingent upon the availability of funds. Any change in the research focus will result in the revocation of the award and the return of funds on a prorated basis. This is a one-year grant award with a progress reporting period of five years during which time an annual Narrative report must be submitted to the NJCSCR office. Evidence of the necessary organizational/institutional financial support to sustain the research must be included as part of the report. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-5 as well as among the NJCSCR's other grant programs 05-SCR-1, 05-SCR-3, 05-SCR-4. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-5 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$4,000,000.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants
2. General and specific Grant Compliance requirements issued by the Granting Agency.
3. Applicable Federal Cost Principles relating to the Applicant

GROUP OR ENTITIES WHICH MAY APPLY FOR THE GRANT PROGRAM:

All qualifying institutions in the State of New Jersey may apply for One-Time Start-Up Costs grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the Commission, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE CONSIDERED FOR A GRANT:

Proposals are evaluated based upon evidence provided by the qualifying institution that a new research laboratory will be established upon receipt of these funds. Such evidence should include, but is not limited to, range of construction, detailed equipment listing, evidence of other support from the institution, evidence that the institution is providing space to be renovated, information on a newly recruited faculty or staff member, or evidence that an experienced researcher in a related field will establish a new laboratory dedicated to spinal cord injury research.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a year.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research
Department of Health and Senior Services
PO Box 360

Trenton, New Jersey 08625-0360

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE SUBMITTED:

Letter of Intent – May 3, 2004

Applications must be received in the NJCSCR Office by June 8, 2004, between the hours of 8AM and 5PM.

(NO EXCEPTIONS WILL BE MADE)

DATE BY WHICH APPLICANT SHALL BE NOTIFIED WHETHER THEY WILL RECEIVE FUNDS:

Notification – November 30, 2004

NOTICE OF GRANT AVAILABILITY

New Jersey Commission on Spinal Cord Research

NAME OF GRANT PROGRAM: Individual Research Grant

GRANT PROGRAM NO. 05-SCR-1

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L.
1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Cost-Reimbursement
Grants

**PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS
WILL BE USED:**

The NJCSCR will fund research activities that hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. All qualifying institutions in the State of New Jersey may apply. The goals of this program are (1) to encourage promising postdoctoral fellows and young investigators to undertake research on spinal cord regeneration, recovery and rehabilitation; (2) to encourage scientists who are well-established in other areas to transfer their efforts to spinal cord research; and (3) enable researchers with novel scientific and clinical ideas to test them and develop pilot data needed to seek larger awards from the National Institutes of Health, and other funding sources.

AMOUNT OF MONEY IN THE GRANT PROGRAM:

Applicants are encouraged to apply for a one-year or two-year award. Maximum funding is up to \$200,000 per year including direct and indirect costs, (10% maximum for the latter). Two-year awards are made through one-year contracts. Each funding award within the two-year period will be contingent upon the availability of funds. Second-year support for all Individual Research grants is contingent upon submission of a Grant Continuation Application. The Grant Continuation Application must be favorably reviewed by an independent scientific merit review panel and recommended to the NJCSCR for continued funding. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of an Individual Research grant. Awards will begin on or about December 15, 2004. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-1 as well as among the NJCSCR's other grant programs 05-SCR-3, 05-SCR-4, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 04-SCR-1 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$4,000,000.

**ELIGIBLE APPLICANTS MUST COMPLY WITH THE
FOLLOWING REQUIREMENTS:**

1. Terms and Conditions for the Administration of Grants
2. General and specific Grant Compliance requirements issued by the Granting Agency.

3. Applicable Federal Cost Principles relating to the Applicant
**GROUP OR ENTITIES WHICH MAY APPLY FOR THE
GRANT PROGRAM:**

All qualifying institutions in the State of New Jersey may apply for Individual Research grants under this program. A qualifying research institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with a demonstrated capability to conduct grant funded research, and specifically approved by the vote of the Commission, but in no case can an individual be a qualifying research institution.

**QUALIFICATIONS NEEDED BY APPLICANT TO BE
CONSIDERED FOR A GRANT:**

Principal investigators must be affiliated with a New Jersey State academic institution, research organization, public or private agency or other entity with demonstrated capability to conduct research responsibly. Senior scientists, young investigators, and postdoctoral fellows may serve as principal investigator. If the applicant is a fellow, s/he must submit a letter of support from the laboratory's senior scientist, as well as two other appropriate letters of reference. Unaffiliated individuals will not be funded. Individuals of any nationality or citizenship status may apply, provided they are employed by or affiliated with a qualified New Jersey State organization/institution.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a year.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research

Department of Health and Senior Services

PO Box 360

Trenton, New Jersey 08625-0360

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

**DEADLINE BY WHICH APPLICATIONS MUST BE
SUBMITTED:**

Applications must be received in the NJCSCR Office by June 8, 2004, between the hours of 8AM and 5PM.

(NO EXCEPTIONS WILL BE MADE)

**DATE BY WHICH APPLICANT SHALL BE NOTIFIED
WHETHER THEY WILL RECEIVE FUNDS:**

Notification - November 30, 2004

NOTICE OF GRANT AVAILABILITY

**NEW JERSEY COMMISSION ON SPINAL CORD
RESEARCH**

NAME OF GRANT PROGRAM: Postdoctoral & Graduate
Student Fellowship Grant

GRANT PROGRAM NO. 05-SCR-3

STATUTORY AUTHORITY:

NJCSCR Fund Chapter 201 P.L. 1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Letter of Agreement

**PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS
WILL BE USED:**

The NJCSCR will fund Postdoctoral and Graduate Student Fellowship grants to attract and retain in New Jersey's qualifying academic research institutions talented young scientists who wish to pursue a career in spinal cord regeneration and repair research. All awards will be made to the research institution in the name of the fellow. All proposals are reviewed by a panel of independent scientific experts who are appointed by the NJCSCR. The panel will evaluate candidates on academic qualifications, the scientific merit of the proposed research project and its relevance to the research priorities of the NJCSCR, the qualifications of the candidate's mentor, the adequacy of facilities, and institutional support.

AMOUNT OF MONEY IN THE GRANT PROGRAM:

Postdoctoral Fellowships are two-year awards of \$50,000 per annum. They provide an annual stipend of \$36,000, a research allowance of \$13,000, and a travel budget of \$1,000. No part of the award may be used for institutional overhead or indirect costs. Institutions may supplement stipends, but not with other full-time fellowship awards, or other NJCSCR monies. A candidate may not apply for a NJCSCR Postdoctoral Fellowship and a NJCSCR Individual Research grant in the same grant cycle. If a first-year fellow applies for and is awarded a NJCSCR Individual Research grant, funding will be contingent upon cancellation of the second year of the fellowship. Non-research activities, such as teaching, may not occupy more than 10% of the fellow's time.

Graduate Student Fellowships are two-year awards of \$30,000 per annum. They provide an annual stipend of \$25,000, a research allowance of \$4,000, and a travel budget of \$1,000. No part of this award may be used for

institutional overhead, or for tuition. Institutions may supplement stipends, but not with other full-time fellowship awards or other NJCSCR monies. Applicants may serve as teaching assistants while holding a NJCSCR Graduate Student Fellowship without special permission.

Awards will begin on or about December 15, 2004. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-3 as well as among the NJCSCR's other grant programs 05-SCR1, 05-SCR-4, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-3 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$4,000,000. Each funding award within the two-year period will be contingent upon the availability of funds. All Postdoctoral and Graduate Student Fellows must submit a first-year Progress Report accompanied by a letter of support from the fellow's mentor. Second-year fellowship funding is contingent upon the successful review of the first-year Progress Report and a

recommendation from the mentor. Any change in relationship between the fellow and the mentor, or between the fellow and the host institution will require the submission of a new, competing application by the fellow as opposed to a Progress Report. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of the Fellowship grant.

**ELIGIBLE APPLICANTS MUST COMPLY WITH THE
FOLLOWING REQUIREMENTS:**

1. Terms and Conditions for the Administration of Grants
 2. General and specific Grant Compliance requirements issued by the Granting Agency.
 3. Applicable Federal Cost Principles relating to the Applicant
- GROUP OR ENTITIES WHICH MAY APPLY FOR THE GRANT PROGRAM:**

All qualifying institutions in the State of New Jersey may apply for Fellowship grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the Commission, but in no case can an individual be a qualifying research institution.

**QUALIFICATIONS NEEDED BY APPLICANT TO BE
CONSIDERED FOR A GRANT:**

Postdoctoral Fellowship Specifications - Candidates of outstanding quality must hold a Ph.D., and/or M.D., or equivalent graduate degree. Appropriate degrees must be awarded prior to activation of award. Candidates must be accepted for postdoctoral training under the supervision of an appropriate mentor at a qualifying academic research institution in New Jersey. The NJCSCR reserves the right to limit the number of fellowships awarded under the supervision of an individual mentor.

Graduate Student Fellowship Specifications - Candidates must be full-time graduate students in residence in a proposed course of study directly related to regeneration and repair of the damaged spinal cord. Students must begin study in the semester following activation unless special permission is received prior to activation date. The NJCSCR prefers to support graduate student candidates who have completed the first year of graduate study and are concentrating on research projects at least 80% of their time.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a year.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research
Department of Health and Senior Services
PO Box 360

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

**DEADLINE BY WHICH APPLICATIONS MUST BE
SUBMITTED:**

Applications must be received in the NJCSCR Office by June 8, 2004, between the hours of 8AM and 5PM..

(NO EXCEPTIONS WILL BE MADE)

**DATE BY WHICH APPLICANT SHALL BE NOTIFIED
WHETHER THEY WILL RECEIVE FUNDS:**

Notification - November 30, 2004

Appendix D 2005A Notices of Grant Availability

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

NOTICE OF AVAILABILITY OF GRANT FUNDS

Take notice that, in compliance with NJSA 52:14-34.4 et seq. (L. 1987, c.7), the New Jersey Commission on Spinal Cord Research hereby publishes notice of grant availability of the following grant program:

NAME OF GRANT PROGRAM: New Jersey Commission on Spinal Cord Research

Five-Year Named Chair for Senior and Junior Faculty Grant

GRANT PROGRAM NO. 05-SCR-4

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L. 1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Cost-Reimbursement Grants

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS WILL BE USED:

The NJCSCR will fund grants totaling \$1,000,000 for senior faculty and \$600,000 for junior faculty for a Five-Year Named Chair for Senior and Junior Faculty grant to recruit highly qualified researchers to conduct spinal cord research in New Jersey. All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of support such as appropriate laboratory facilities and the commitment of financial support necessary to sustain the research for a minimum of five years. A qualifying research institution may not apply for both a "One-Time Start-Up Cost" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year. A person holding one of these positions will be called "New Jersey Professor of Spinal Cord Research."

AMOUNT OF FUNDS IN THE GRANT PROGRAM:

Grants will total \$1,000,000 for senior faculty and \$600,000 for junior faculty (includes direct and indirect costs, a maximum of 10% may be applied to indirect costs). Successful candidates also will receive \$100,000 and \$50,000 respectively in start-up costs. Awards will begin on or about June 15, 2005. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-4 as well as among the NJCSCR's other grant programs 05-SCR-1, 05-SCR-3, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-4 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$3,000,000. Any change either in awardee or the research focus on spinal cord injury will

result in the revocation of the award and the return of all funds on a prorated basis. Annual funding within the five-year period will be contingent upon the availability of funds and the submission of an annual Narrative Report that is favorably reviewed by an independent scientific merit review panel. The panel's continuation recommendations will be made to the NJCSCR for funding approval. Project periods may not exceed five years. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of a Five-Year Named Chair grant.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants
2. General and Specific Grant Compliance requirements issued by the Granting Agency.
3. Applicable Federal Cost Principles relating to the Applicant GROUP OR ENTITIES WHICH MAY APPLY FOR THE GRANT PROGRAM:

All qualifying institutions in the State of New Jersey may apply for Five-Year Named Chair for Senior and Junior Faculty grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the NJCSCR, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE CONSIDERED FOR A GRANT:

A Senior Faculty candidate will have a Ph.D. and/or M.D., an outstanding record of excellence and achievement in areas relevant to spinal cord injury research, high quality publications, a national/international reputation, demonstrated leadership capabilities, evidence of sustained success in competitive science funding, and a commitment to the development of practical therapies. Experienced researchers in other fields moving to spinal cord research also will be considered.

A Junior Faculty candidate will have a Ph.D. and/or M.D., appropriate postdoctoral experience in a well-established research facility, and confidential recommendations from the director and senior leaders of their present research setting. Outside references will enhance the application. Applications are evaluated based upon evidence provided by the qualifying institution that the proposed candidate has accepted a position and that appropriate research facilities are available or will be provided by the start date of this award.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a cycle.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research

TELEPHONE: 609-292-4055

PO Box 360

FAX: 609-943-4213

Trenton, New Jersey 08625

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE SUBMITTED:

Letter of Intent - November 3, 2004

Applications - December 8, 2004

DATE BY WHICH APPLICANT SHALL BE NOTIFIED WHETHER THEY WILL RECEIVE FUNDS:

Notification - May 30, 2005

NEW JERSEY COMMISSION ON SPINAL CORD
RESEARCH

NOTICE OF AVAILABILITY OF GRANT FUNDS

Take notice that, in compliance with NJSA 52:14-34.4 et seq. (L. 1987, c.7), the New Jersey Commission on Spinal Cord Research hereby publishes notice of grant availability of the following grant program:

NAME OF GRANT PROGRAM: New Jersey Commission on Spinal Cord Research

One-Time Start-Up Costs Grant

GRANT PROGRAM NO. 05-SCR-5

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L. 1999 NJSA 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Cost Reimbursement Grants

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS
WILL BE USED:

The NJCSCR will fund start-up costs to facilitate the establishment of new spinal cord injury research laboratories. The primary focus of the research must hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. All qualifying institutions in the State of New Jersey may apply. The qualifying institution must provide evidence of qualified research leadership for the new laboratory and the commitment of financial support necessary to sustain the research for a minimum of five years. These awards may be used for the renovation of space, support of research personnel (maximum of one year salary for technical support staff; after the first year, no personnel costs are permitted), and the purchase of equipment directly related to the research. No indirect costs are permitted. The goal of this program is to enable the establishment of new laboratories and facilitate the recruitment of highly qualified researchers to conduct spinal cord research in New Jersey. A qualifying research institution may not apply for both a "One-Time Start-Up Costs" grant and a "Five-Year Named Chair for Senior and Junior Faculty" grant using the same faculty member in the same grant year.

AMOUNT OF FUNDS IN THE GRANT PROGRAM:

The NJCSCR will fund start-up costs ranging from \$250,000 to \$1,000,000 to facilitate the establishment of new spinal cord injury research laboratories. Awards will begin on or about June 15, 2005. Money granted must be held in a separate account with all accrued interest being maintained in the account. Each grant award will be contingent upon the availability of funds. Any change in the research focus will result in the revocation of the award and the return of funds on a prorated basis. This is a one-year grant award with a progress-reporting period of five years during which time an annual Narrative report must be submitted to the NJCSCR office. Evidence of the necessary organizational/institutional financial support to sustain the research must be included as part of the report. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-5 as well as among the NJCSCR's other grant programs 05-SCR-1, 05-SCR-3, 05-SCR-4. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-5 to the maximum amount, or not to

fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$3,000,000.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE
FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants
 2. General and specific Grant Compliance requirements issued by the Granting Agency.
 3. Applicable Federal Cost Principles relating to the Applicant
- GROUP OR ENTITIES WHICH MAY APPLY FOR THE GRANT PROGRAM:

All qualifying institutions in the State of New Jersey may apply for One-Time Start-Up Costs grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the NJCSCR, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE
CONSIDERED FOR A GRANT:

Proposals are evaluated based upon evidence provided by the qualifying institution that a new research laboratory will be established upon receipt of these funds. Such evidence should include, but is not limited to, range of construction, detailed equipment listing, evidence of other support from the institution, evidence that the institution is providing space to be renovated, information on a newly recruited faculty or staff member, or evidence that an experienced researcher in a related field will establish a new laboratory dedicated to spinal cord injury research.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a cycle.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research
PO Box 360

Trenton, New Jersey 08625

FAX: 609-943-4213

TELEPHONE: 609-292-4055

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE
SUBMITTED:

Letter of Intent - November 3, 2004

Applications - December 8, 2004

DATE BY WHICH APPLICANT SHALL BE NOTIFIED
WHETHER THEY WILL RECEIVE FUNDS:

Notification - May 30, 2005

NEW JERSEY COMMISSION ON SPINAL CORD
RESEARCH

NOTICE OF AVAILABILITY OF GRANT FUNDS

NAME OF GRANT PROGRAM: New Jersey Commission on
Spinal Cord Research

Individual Research Grant

GRANT PROGRAM NO. 05-SCR-1

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L.
1999 NJSA 52:9E-1

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS
WILL BE USED:

The NJCSCR will fund research activities that hold promise of developing effective interventions and cures for paralysis and other consequences of spinal cord injury and disease. All qualifying institutions in the State of New Jersey may apply. The goals of this program are (1) to encourage promising postdoctoral fellows and young investigators to undertake research on spinal cord regeneration, recovery and rehabilitation; (2) to encourage scientists who are well-established in other areas to transfer their efforts to spinal cord research; and (3) enable researchers with novel scientific and clinical ideas to test them and develop pilot data needed to seek larger awards from the National Institutes of Health, and other funding sources.

AMOUNT OF FUNDS IN THE GRANT PROGRAM:

Applicants are encouraged to apply for a one-year or two-year award. Maximum funding is up to \$200,000 per year including direct and indirect costs, (10% maximum for the latter). Two-year awards are made through one-year contracts. Each funding award within the two-year period will be contingent upon the availability of funds. Second-year support for all Individual Research grants is contingent upon submission of a Grant Continuation Application. The Grant Continuation Application must be favorably reviewed by an independent scientific merit review panel and recommended to the NJCSCR for continued funding. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of an Individual Research grant. Awards will begin on or about June 15, 2005. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-1 as well as among the NJCSCR's other grant programs 05-SCR-3, 05-SCR-4, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-1 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$3,000,000.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE
FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants

2. General and specific Grant Compliance requirements issued by the Granting Agency.

3. Applicable Federal Cost Principles relating to the Applicant
GROUP OR ENTITIES WHICH MAY APPLY FOR THE
GRANT PROGRAM:

All qualifying institutions in the State of New Jersey may apply for Individual Research grants under this program. A qualifying research institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with a demonstrated capability to conduct grant funded research, and specifically approved by the vote of the NJCSCR, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE
CONSIDERED FOR A GRANT:

s must be affiliated with a New Jersey State academic institution, research organization, public or private agency or other entity with demonstrated capability to conduct research responsibly. Senior scientists, young investigators, and postdoctoral fellows may serve as Principal Investigator. If the applicant is a fellow, s/he must submit a letter of support from the laboratory's senior scientist, as well as two other appropriate letters of reference. Unaffiliated individuals will not be funded. Individuals of any nationality or citizenship status may apply, provided they are employed by or affiliated with a qualified New Jersey State organization/institution.

APPLICATION PROCEDURES:

Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a cycle.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research

PO Box 360

Trenton, New Jersey 08625

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE
SUBMITTED:

Applications - December 8, 2004

DATE BY WHICH APPLICANT SHALL BE NOTIFIED
WHETHER THEY WILL RECEIVE FUNDS:

Notification - May 30, 2005

NEW JERSEY COMMISSION ON SPINAL CORD
RESEARCH

NOTICE OF AVAILABILITY OF GRANT FUNDS

Take notice that, in compliance with NJS A 52:14-34.4 et seq. (L. 1987, c.7), the New Jersey Commission on Spinal Cord Research hereby publishes notice of grant availability of the following grant program:

NAME OF GRANT PROGRAM: Postdoctoral and Graduate Student Fellowship Grant

GRANT PROGRAM NO. 05-SCR-3

STATUTORY AUTHORITY: NJCSCR Fund Chapter 201 P.L. 1999 NJS A 52:9E-1

TYPE OF AWARDS TO BE ISSUED: Letter of Agreement

PURPOSE FOR WHICH THE GRANT PROGRAM FUNDS WILL BE USED:

The NJCSCR will fund Postdoctoral and Graduate Student Fellowship grants to attract and retain in New Jersey's qualifying academic research institutions talented young scientists who wish to pursue a career in spinal cord regeneration and repair research. All awards will be made to the research institution in the name of the fellow. All proposals are reviewed by a panel of independent scientific experts who are appointed by the NJCSCR. The panel will evaluate candidates on academic qualifications, the scientific merit of the proposed research project and its relevance to the research priorities of the NJCSCR, the qualifications of the candidate's mentor, the adequacy of facilities, and institutional support.

AMOUNT OF FUNDS IN THE GRANT PROGRAM:

Postdoctoral Fellowships are two-year awards of \$50,000 per annum. They provide an annual stipend of \$36,000, a research allowance of \$13,000, and a travel budget of \$1,000. No part of the award may be used for institutional overhead or indirect costs. Institutions may supplement stipends, but not with other full-time fellowship awards, or other NJCSCR monies. A candidate may not apply for a NJCSCR Postdoctoral Fellowship and a NJCSCR Individual Research grant in the same grant cycle. If a first-year fellow applies for and is awarded a NJCSCR Individual Research grant, funding will be contingent upon cancellation of the second year of the fellowship. Non-research activities, such as teaching, may not occupy more than 10% of the fellow's time.

Graduate Student Fellowships are two-year awards of \$30,000 per annum. They provide an annual stipend of \$25,000, a research allowance of \$4,000, and a travel budget of \$1,000. No part of this award may be used for institutional overhead, or for tuition. Institutions may supplement stipends, but not with other full-time fellowship awards or other NJCSCR monies. Applicants may serve as teaching assistants while holding a NJCSCR Graduate Student Fellowship without special permission.

Awards will begin on or about June 15, 2005. The NJCSCR reserves the right to distribute funds among the grants in this program 05-SCR-3 as well as among the NJCSCR's other grant programs 05-SCR1, 05-SCR-4, 05-SCR-5. The NJCSCR reserves the right not to fund any grants in this program 05-SCR-3 to the maximum amount, or not to fund any grant in this program at all. Grant awards to all four programs (05-SCR-1, 05-SCR-3, 05-SCR-4, 05-SCR-5) will not exceed \$3,000,000. Each funding award within the two-year period will be

contingent upon the availability of funds. All Postdoctoral and Graduate Student Fellows must submit a first-year Progress Report accompanied by a letter of support from the fellow's mentor. Second-year fellowship funding is contingent upon the successful review of the first-year Progress Report and a recommendation from the mentor.

Any change in relationship between the fellow and the mentor, or between the fellow and the host institution will require the submission of a new, competing application by the fellow as opposed to a Progress Report. An Evaluation Form must be submitted to the NJCSCR office each year for two years following termination of the Fellowship grant.

ELIGIBLE APPLICANTS MUST COMPLY WITH THE FOLLOWING REQUIREMENTS:

1. Terms and Conditions for the Administration of Grants
 2. General and specific Grant Compliance requirements issued by the Granting Agency.
 3. Applicable Federal Cost Principles relating to the Applicant
- GROUP OR ENTITIES WHICH MAY APPLY FOR THE GRANT PROGRAM:** All qualifying institutions in the State of New Jersey may apply for Fellowship grants under this program. A qualifying institution is defined as any academic institution, research organization, public or private institution or other entity, located in the State of New Jersey, with demonstrated capability to conduct grant funded research, and specifically approved by the vote of the NJCSCR, but in no case can an individual be a qualifying research institution.

QUALIFICATIONS NEEDED BY APPLICANT TO BE CONSIDERED FOR A GRANT:

Postdoctoral Fellowship Specifications - Candidates of outstanding quality must hold a Ph.D., and/or M.D., or equivalent graduate degree. Appropriate degrees must be awarded prior to activation of award. Candidates must be accepted for postdoctoral training under the supervision of an appropriate mentor at a qualifying academic research institution in New Jersey. The NJCSCR reserves the right to limit the number of fellowships awarded under the supervision of an individual mentor.

Graduate Student Fellowship Specifications - Candidates must be full-time graduate students in residence in a proposed course of study directly related to regeneration and repair of the damaged spinal cord. Students must begin study in the semester following activation unless special permission is received prior to activation date. The NJCSCR prefers to support graduate student candidates who have completed the first year of graduate study and are concentrating on research projects at least 80% of their time.

APPLICATION PROCEDURES: Applications and NJCSCR Research Guidelines governing grants are available from the NJCSCR office, or can be downloaded from the website at www.state.nj.us/health/spinalcord/. Review and the awarding of grants will occur once a cycle.

FOR INFORMATION CONTACT:

New Jersey Commission on Spinal Cord Research
PO Box 360

Trenton, New Jersey 08625

TELEPHONE: 609-292-4055

FAX: 609-943-4213

E-MAIL: NJCSCR@doh.state.nj.us

DEADLINE BY WHICH APPLICATIONS MUST BE SUBMITTED & AWARD NOTIFICATION DATE:

Applications - December 8, 2004

Award Notification Date - May 30, 2005

Appendix E 2005 Grant Award Recipients

Appendix E-1 2005 Individual Research Grant Recipients

The Role of Notch I Lin-12 in Glutamate Receptor Signaling and Excitotoxic Neuronal Damage

Christopher Rongo, Ph.D.

Waksman Institute of Microbiology

Department of Genetics

Rutgers, The State University of New Jersey of New Jersey

\$191,712

The goal of this proposal is to test whether Notch/UN-12 signaling molecules play a role in glutamate-mediated neuronal death. Spinal cord injury is a distressing illness that results in the loss of sensory and motor function. Affected individuals often experience, with varying degrees, the loss of mobility, sensation and autonomic function, and often experience chronic neuropathic pain. The key cells that are damaged by spinal cord injury are neurons, and this damage can result from mechanical damage (e.g., traumatic injury) or ischemia (oxygen deprivation) caused by breakdowns or obstructions in the blood vessels that supply the spinal neurons. The initial events of the spinal cord injury are often restricted to a small region of neurons in the spinal cord. However, this early damage event results in the release of large quantities of the neurotransmitter glutamate at the initial damage site. This massive release of glutamate leads to a build up of glutamate in the secondary tissues that surround the initial injury site. Whereas low levels of glutamate are used by neurons as chemical signals that shuttle back and forth between neurons, high levels of glutamate caused by injury instead over activate glutamate receptors on secondary site neurons, resulting in the excessive depolarization of these cells, calcium influx, and subsequent death of the neurons. Dying secondary neurons often release their own stores of glutamate, leading to yet more glutamate accumulation and waves of dying neurons spreading out from injury site.

The identification of drugs that block or delay glutamate receptor activation would significantly limit receptor-induced damage that results from spinal cord injury. One of the primary ways by which neurons regulate glutamate receptor activity is by regulating the amount of these receptors that reach the surface of neurons. This proposal aims to identify important proteins that regulate the movement of glutamate receptors to the surface of neurons using a genetic approach in the nematode *C. elegans*. *C. elegans* use glutamate receptors in the sensory circuits that are strikingly similar to the sensory circuits that are found in the spinal cord. My lab previously showed that these receptors are localized to the surface of the neuron, and we have been identifying *C. elegans* genes that regulate the movement of these receptors. The over activation of these same glutamate receptors in *C. elegans* leads to excitotoxic neural death. Our preliminary results suggest that a protein called LIN-12 regulates the movement of glutamate receptors to the neuron surface. This proposal contains three aims for understanding the role of LIN-12 signaling in this process. First, we will determine what other proteins help LIN-12 regulate the movement of glutamate receptors. Second, we will determine whether LIN-12 works in neurons or in the cells that support neuron function. Finally, we will test whether mutants in LIN-12 or other proteins that we discover can decrease neuronal death in an existing model of glutamate-mediated neuronal death in *C. elegans* that is similar to the glutamate-mediated toxicity that follows an initial spinal cord injury. We hypothesize that LIN-12 and its partner proteins help facilitate the glutamate-mediated toxicity observed during the critical period that follows an initial spinal cord injury. By identifying and characterizing these proteins, this work should identify key targets for new therapeutic interventions that limit neuronal damage following spinal cord injury. Researchers have previously used *C. elegans* as the foundation for understanding the process of cell death, extrapolating their findings to the corresponding human genes; indeed, the Nobel Prize in Physiology & Medicine for 2002 celebrated these achievements. Of the five genes that my lab has discovered to be playing a role in glutamate receptor biology so far, all five have human equivalent genes playing a similar or identical role, suggesting that our findings in *C. elegans* are likely to be applicable to human health.

Role of Foxn4 in Spinal Cord Development and Regeneration

Mengqing Xiang, Associate Professor

Center for Advanced Biotechnology & Medicine UMDNJ-Robert Wood Johnson Medical School

\$400,000

Spinal cord injury, currently without any effective treatment, presents an enormous medical, public health and economic problem. Thanks to recent advances in the study of neural stem cells, the previously inconceivable regeneration of the damaged spinal cord is within the reach of reality. Stem cell-based therapy aims to restore functional sensory and motor circuits and axon connections in the damaged spinal cord through stem cell transplantation or by activation of spared endogenous stem cells. Such an approach has been successfully applied in rodent models of spinal cord injury to achieve some neural regeneration which restores limited sensory and motor functions. To improve further on this exceptionally promising approach to develop it as a viable therapy, however, it is a prerequisite to understand the development and genetic programs that direct the proliferation, specification and differentiation of stem cells. Since the differentiation of stem cells normally recapitulates the events that occur during embryogenesis, the study of the molecular basis governing spinal cord development is important for the future success of stem cell mediated regeneration.

The goal of this proposal is to understand the molecular events that control the specification and differentiation of sensory and motor neurons during development and regeneration of the spinal cord. This application will focus on the role of an important transcription factor, which displays several salient features implicating it as a putative regulator for fate specification and/or early differentiation of a distinct spinal sensory neuron subtype. The proposed experiments are designed to test this hypothesis using

Molecular genetic approaches in the mouse and chicken model systems as well as to test the feasibility to achieve controlled regeneration of desired sensory neurons in the chick system. The knowledge gained from these studies may help to identify novel molecular targets that can be used to promote functional reconstruction of neuronal circuits in the injured spinal cord.

Molecular Control of Spinal Cord Neuronal Progenitor Differentiation

Michael P. Matisse, Ph.D., Assistant Professor

Department of Neuroscience & Cell Biology

University of Medicine and Dentistry of New Jersey

Robert Wood Johnson Medical School

\$400,000

The long-term goal of this proposal is to improve the success of stem cell replacement therapies to treating spinal cord injury (SCI) by characterizing the activity of an important regulator of neurogenesis in the embryonic spinal cord. Some of the most exciting strategies for restoring function following SCI involve therapies that seek to employ immature "stem cells" to replace the function of cells that are lost as a consequence of the trauma. Much attention has been focused on isolating and characterizing stem cells that can, when transplanted into the CNS, develop into fully functioning neurons. While promising, to date the success of these approaches has been limited, perhaps due to the fact that the adult spinal cord does not present a conducive environment for the formation of neurons from immature cells. Furthermore, most current studies focus primarily on the ability of transplanted cells to adopt a "generic" neuronal identity. However, the mature spinal cord is composed of hundreds of distinct neuronal cell classes that are generated exclusively during embryonic development. Therefore, in order to restore even partial function, transplanted stem cells must do much more than simply differentiate into a neuron with an unspecified identity, but rather must generate at a minimum the types of neurons that comprise the circuitry controlling movement and sensation.

Neuronal stem cells possess the potential to generate the wide array of cell types that normally exist in the adult spinal cord. These cells are essentially specialized versions of normal spinal cord progenitor cells found in the developing embryo. Their utility as a therapeutic tool depends on preserving their full potential in vivo in adult injury sites, and understanding the steps that normal progenitor cells must undergo to generate neurons is critical to the success of this approach. The cell-cycle regulators being investigated in this proposal play a central role in regulating the transition of multi-potent progenitors into newly-born neurons with distinct phenotypic properties in the developing spinal cord, and are likely to be critically involved in this success of such SCI treatment strategies.

In the experiments described in this grant proposal, we will investigate the function of a key regulator of neurogenesis. We believe this factor, p57kip2, plays a central role in controlling the generation of neurons from multi-potent neuronal stem cells by regulating two important steps in this transition. Our experiments will make use of well-established vertebrate animal model systems for studying spinal cord development. These systems permit us to perform a variety of experimental manipulations that will allow us to define the function of p57 protein in the spinal cord.

We expect that it will be feasible to extend our basic work in the near future to studies that will directly examine the role of cell-cycle/neurogenesis regulators in controlling the formation of functional neurons from experimental stem cells in vitro and in vivo.

Bifunctional Biomaterial Design for Spinal Cord Regeneration

Noshir A. Langrana, Ph.D., Professor

Department of Mechanical & Aerospace Engineering & Biomedical Engineering

Rutgers, The State University of New Jersey of New Jersey

\$150,000 - One Year Grant

This proposed research addresses fundamental issues in enhancing axon regeneration following spinal cord trauma, which is the first listed objective in the NJCSCR guidelines. The broad, long-term objective of this research is to develop biomaterials that spur regeneration of the spinal cord. Two general tissue-engineering strategies have been employed in attempts to restore spinal cord function following trauma. The first and most prevalent is the development of biomaterials that serve as scaffolds to stimulate axons to regenerate and grow through the injury site. The second strategy is to employ mechanical force, or traction, to axons at very slow rates and physically force the nerves to grow, just as the spinal cord lengthens as we mature from infants to adults. The second technique has been used in vitro to generate neural tissue in hope to ultimately "splice" together the spinal cord. We have developed a novel biomaterial that will ultimately enable us to apply both strategies of spinal cord regeneration in vivo. The biomaterial is a polyacrylamide hydrogel that can be reversibly crosslinked with DNA strands to change its stiffness and apply force. When crosslinks are introduced, the hydrogel shrinks, and, if attached to an object, exert force on that object. Moreover, the biomaterial backbone can also be functionalized with extracellular matrix molecules to support axon attachment and growth. Thus, we believe that our DNA-crosslinked gels will induce spinal cord regeneration via two important mechanisms. To our knowledge, this dual modality has not been tried.

The goal of this proposal is to optimize the characteristics of the biomaterial and DNA delivery to induce axon regeneration through the hydrogel scaffold and physically stretch and reconnect the spinal cord. The specific aims of this proposal are: (1) To identify the force-actuating potential of DNA-crosslinked hydrogels; (2) To functionalize DNA-crosslinked hydrogels for axon growth in vitro. Following completion of these aims, we will have demonstrated the capacity of our novel hydro gels to stimulate axon regeneration by the two distinct mechanisms. We plan to proceed to animal studies to evaluate the efficacy of the hydro gels in vivo, and to investigate modifying other acryl-based polymers, such as poly-methyl methacrylate to enhance our biomaterial library for spinal cord regeneration.

Roles of Ephrin-A5 in Spinal Cord Development

Renping Zhou, Ph.D., Professor

Department of Chemical Biology

Ernest Mario School of Pharmacy, Rutgers, The State University of New Jersey of New Jersey

\$397,888

Spinal cord injury is a major cause of disability. Extensive clinical and experimental studies showed that traumatic spinal cord injury results in loss of neurons and nerve pathways, which lead to partial disability or complete paralysis. Recent advances in the research of stem cells, a type of cells capable of producing different types of tissues, hold the promise that one day, replacement of lost spinal cord neurons with stem cells may lead to complete recovery of spinal cord injuries. However, a major challenge of stem cell therapy will be the rewiring of the transplanted neurons, connecting them into functional spinal neural circuits. Although considerable advances have been made in the understanding of the molecular signals that help to guide the nerve fibers, in general using invertebrate model systems such as fruit flies and nematodes, much remains unknown about how the vertebrate spinal cord neural circuits are constructed and what are the molecules that regulate this process. Our long-term objective is to identify molecules that contribute to the construction of functional spinal cord neural circuits, in the hope that this information will be used in future cell replacement therapies for spinal cord injuries.

The preliminary studies conducted in our laboratories showed that two molecules, named ephrinA5 and EphA5, might play important roles in the construction of spinal cord neural circuits. These two molecules are located on the membranes that wrap around the cells and they talk to each other by physically forming a complex, eliciting biochemical changes within the cells. It has been shown in our previous analysis that ephrin-A5; a known repulsive signal for nerve fibers is localized in spinal cord regions where the spinal cord nerve fibers avoid. It is hypothesized that ephrin-A5 functions to prevent spinal cord nerves from traveling to this region, and thus playing critical roles in organizing the spinal nerves. To test this hypothesis, experiments are proposed to study localization of ephrin-A5 and its receptor EphA5 proteins during development of spinal cord neural circuits, using techniques that will reveal the presence of these proteins. Since the spinal cord is made of many different cell types, it will be determined in which cell types they are located. The functions of ephrin-A5 and EphA5 will be further studied using a well-established spinal cord tissue culture method in an incubator. Artificially generated mutant molecules that block the functions will be added to the cultured spinal cord tissues to examine effects on the organization of spinal cord nerve pathways. Finally, mice deficient for ephrin-A5 and EphA5 genes, alone or in combination, will be examined using techniques that trace nerve fibers to identify defects in spinal cord organizations. These studies together will provide a critical assessment of roles of this molecular pair in the development of spinal cord.

Understanding how the spinal cord nerve fibers are organized will help to design interventions to properly reconnect spinal cord nerve fibers in future stem cell therapy or other regenerative therapies. Spinal cord injury patients in New Jersey and elsewhere will all benefit from these therapeutic advances.

Molecular Mechanisms of Axon Guidance

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University of Medicine and Dentistry of New Jersey

Robert Wood Johnson Medical School

\$315,204

This proposal intends to research genetic study to explore the molecular mechanisms that guide axons back to their targets following injury. Following injury, regenerating axons must be guided back to their targets in order for the proper connections to be reestablished. Several of the molecules that are involved in axon guidance were first discovered in the model organism *C. elegans*, a nematode. The same molecules that function to guide axons in the simple nematode nervous system also guide axons in the complex human nervous system. They are present in the adult nervous system and recent studies indicate that their expression changes during injury, which could have a profound influence on the ability of regenerating neurons to find their proper targets and form functional circuits. Using the powerful genetic techniques available in *C. elegans*, other molecules that interact with the guidance molecules and that are required for their function are being sought.

The discovery of new molecules involved in axon guidance and a better understanding of the molecular mechanisms of axon guidance could lead to new therapies aimed at directing regenerating axons towards their proper targets

Programmed Tissue Engineering for Spinal Cord Regeneration

Ron Weiss, Ph.D.

Department of Electrical Engineering

Princeton University

\$391,189

This project will focus on building synthetic gene networks that precisely control stem cell differentiation. Spinal cord injury is a major cause of paralytic disabilities. Currently, there are no effective therapies that result in significant alleviation of such disabilities. The therapies that are in use are generally limited to preventing more extensive accumulation of tissue damage. No effective therapies can reverse spinal damage through the regeneration, or re-growth of new cells. Several experimental studies suggest that transplantation of undamaged cells into the site of injury may eventually be an effective avenue for therapeutic intervention. While encouraging, such therapies are inherently limited by a lack of suitable transplantable material that will fully regenerate the spinal cord without complications

such as tissue rejection. Recently, it has been suggested that stem cell populations, whether from embryonic or adult tissue sources, may represent a source of transplantable material for therapeutic tissue repair. Stem cells are cells that can generate many types of mature cell populations for lifelong time periods. The major barrier to realizing the potential of stem cells is to devise ways to direct these cells toward different pathways of mature tissue or cell production. That is, for spinal cord repair it is necessary to ensure the production of the nerve and associated cells that are normally found in this tissue. It will also be necessary to ensure that the mature cells are produced in the proper amounts and in an appropriate three-dimensional tissue structure. The mechanisms that control the production of mature cells from stem cells in normal fetal or adult physiological contexts are poorly understood. Nevertheless, a number of molecules that function as genetic "master switches" in stem cells to direct the production of different cell types have been identified.

We propose to harness these "master switches" by implementing them in artificially controlled regulatory circuits constructed inside stem cells by genetic engineering. In this way, it will be possible to trigger the controlled production of different mature cell populations after transplantation of the genetically modified stem cells into the site of tissue injury. In addition, it will eventually be possible to produce these cells in a correct spatial and temporal tissue organization. Precedents for the successful construction of artificial genetic circuits have been reported. In general, these have been limited to simpler cells such as bacteria or yeast; however, we have ample preliminary results that demonstrate the successful construction of such circuits in mammalian cells. Thus, there is no insurmountable barrier to extending our results to stem cells. One of the laboratories (Weiss) in this proposal has pioneered the design and implementation of artificially controlled genetic circuits. The second laboratory (Lemischka) has been a leader in stem cell research for many years. Our joint expertise should facilitate the rapid progress of the studies in this proposal. We will begin by developing a number of "proof-of-principal" genetic circuits in mouse embryonic stem (ES) cells. We will take advantage of then known "master switch" molecules, and ask if we can build, circuits where these "master switches" can be artificially controlled by small pharmaceutical agents used to treat the stem cells that have been genetically modified to contain the artificial circuits. We will address how effectively the stem cells can be triggered to produce alternate types of mature cells in response to controlled stimuli. These relatively simple circuits will also produce a wealth of necessary information regarding the dynamics and overall behavioral properties of artificial circuits in stem cells. Finally, we will take advantage of new results from the Lemischka laboratory that have begun to identify the naturally occurring regulatory components, pathways and networks that control biological functions of stem cells. We anticipate that the successful completion of the studies in this proposal will lay a broad and rigorous framework that will have broad applications in stem cell mediated repair of damaged tissues including the spinal cord.

Microfabrication of a Bioreactor System for Differentiation of Stem Cells into Neural Lineages

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\$221,130

Incorporation of stem cell differentiation strategies into clinically relevant research endeavors, offers promising new approaches to therapeutic intervention. This is especially evident in the treatment of central nervous system injury and disease where mature neuronal cell implantation has met with both success and further challenges. In the case of spinal cord injury, the success of cell implantation protocols are limited by the non-permissive tissue environment, composed of both scar tissue and inhibitory molecules, secreted at the site of injury. In addition, the lack of readily available and renewable sources of mature nerve cells certainly limits the efficacy of cell implantation strategies. Clearly, the addition of stem cell research into this field offers the promise of readily available and renewable cell source. However, incorporation of stem cell research into spinal cord repair has two barriers to overcome. First, ethical issues have limited the potential of this endeavor. In addition, many differentiation protocols have been developed, which independently investigate the effect of a large number of variables on both the induction and maturation stages of neuronal differentiation. In essence, the tremendous effort extended in elucidating neural stem cell progenitor regulation by so many investigators and in so many different culture systems, has actually complicated extension of the basic research into clinical relevance. Therefore, developing an approach to systematically investigate the positive and negative variables, which regulate stem cell differentiation on a micro-scale, is critical in furthering the clinical adaptation of cell implantation following spinal cord injury. The additional benefit of this approach is that it reduces the number of stem cells needed for evaluation and testing of multiple parameters.

The proposed studies will develop a micro-scale differentiation environment. This microfabricated chamber will be used to optimize stem cell and adult neural cell culture approaches for the development of implantation protocols following spinal cord injury. This approach, using the most current microfabrication techniques, will be developed by an interdisciplinary team at Rutgers. The PI, Dr. Martin Yarmush, is a world-renowned tissue engineer and has a proven track record in design and development of microfluidically-controlled devices and in hepatic stem cell bioengineering. He now wishes to transfer these skills to area of spinal cord research. His expertise will be complimented by a team of co-investigators, skilled in neural and stem cell culture, and spinal cord injury models.

OEG Remyelination of Axons after Spinal Cord Injury

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\$391,704

Olfactory ensheathing glia (OEG) cells normally reside in nasal mucosa, olfactory nerves and bulbs. These cells migrate alongside growing axons, secrete growth-promoting molecules, and may be why olfactory nerves regenerate in adult mammals. Several investigators have reported that OEG cells stimulate regeneration and remyelination when transplanted into cut spinal cords. However, when we transplanted OEG cells into rat spinal cords after contusion injury, which is more like most human spinal cord injuries, the cells did not survive or consistently improve functional recovery. Further studies showed that the environment of the acutely contused spinal cord is toxic to OEG cells and that the immune system rapidly rejected the cells. By transplanting OEG cells into the spinal cord surrounding the injury site, and suppressing the immune system with high-dose cyclosporin A (CyA), we showed that OEG cells not only survived for months, but migrated

extensively into the injury site and surrounding cord and remyelinated many axons. Methylprednisolone (MP), a drug that is used to treat people with acute spinal cord injury, markedly enhanced survival of OEG transplants.

Dr. Hongyun Huang, a neurosurgeon who worked on some of these OEG experiments, went back to China and used a similar approach to transplant human fetal OEG cells into over 300 patients with spinal cord injury. The preliminary results of the trial revealed a surprising early recovery of motor and sensory function close to the injury site within several weeks, too rapid to be due to regeneration or remyelination. Although long-term data is not yet available from the trial, this early recovery is so striking that we propose a two-year study to investigate mechanisms of DEG-induced early recovery in rats, and to assess methods to enhance the beneficial effects of OEG transplants in spinal cord injury.

In the first year, we will determine whether OEG transplants stimulate sprouting and reconnection of axons close to the injury site in rats, whether OEG remyelination improves functional recovery, and whether CyA or MP affects regenerative sprouting after OEG transplants. In the second year, we will combine OEG transplants with a growth factor that may enhance the regenerative effects of OEG transplants: glial-derived neurotrophic factor (GDNF). We will assess the effects of using this combination therapy to enhance the regenerative effects of OEG transplants. These experiments are crucial for understanding what is happening after OEG transplants to the spinal cord, and to find ways to enhance the beneficial effects of this promising therapy for people with spinal cord injury.

Effect of Erythropoietin Therapy on Acute Traumatic Spinal Cord Injury and Mechanism of Action

Yasuhiro Maeda, M.D.

Veterans Biomedical Research Institute, Inc. University of Medicine & Dentistry of New Jersey-NJMS

\$393,800

We plan to study the effect of erythropoietin (EPO) on traumatic spinal cord injury. We believe EPO may be an effective form of therapy that mediates its effect through downmodulating immune reactions within the injury site in the spinal cord. To test this possibility, we will first measure the effect of therapeutic intervention with erythropoietin on wild type mice using untreated spinal cord injured wild type mice as a control. As a second measure of therapeutic effectiveness, we will measure the histopathologic alterations at the site of injury in treated and untreated control cord injured animals. We predict that erythropoietin will limit the area of pathology to much smaller dimensions. The findings from these first experiments will then be compared to a second series of experiments in which immunodeficient RAG 1 -1- mice are subjected to spinal cord injury and the clinical and neuropathological alterations in them compared to those observed in the cord injured wild type mice. We predict that the lesions in the immunodeficient mice will be far smaller and the animals will manifest less elements of paralysis. In the next step, we will again determine if therapy with erythropoietin will further block the smaller lesion characteristic of the immunodeficient mouse, and also protect the immunodeficient animals from severe paralysis.

In the final series of experiments, we will determine if activated T cells called in from the blood stream contribute to the severity of the injury at the site of trauma. To test this hypothesis, we will obtain naive T cell lymphocytes from the spleen of normal unharmed wild mice. The naive cells will be rapidly purified and injected by IV into the immunodeficient RAG 1 -1- mice. The animals will be rested for 24 hours and then an acute spinal cord injury will be induced. We predict that injured RAG 1 -1- animals that have received wild type T cell lymphocytes will demonstrate much more paralytic illness, and a much larger zone of spinal cord injury. Selected groups of RAG 1 -1- mice that have received the wild type T cells will be treated with erythropoietin and the effect of erythropoietin, therapy on traumatic spinal cord injury in this adoptive transfer experiment will be quantified.

In addition to measuring the effect of erythropoietin on clinical paralysis and histopathology of the injured spinal cord, we will employ high resolution novel MR imaging techniques using labeled immune cells, (T lymphocytes) and intravenous gadolinium on living animals to further assess by MRI the mechanism of tissue injury and the effectiveness of the test therapy on traumatic spinal cord injury.

The Effect of FES on Children with Spinal Cord Dysfunction

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Robert Wood Johnson Medical School

\$267,498

Loss of the ability to walk due to spinal cord dysfunction has profound effects on patients, both physically and psychologically. Physical complications include a significant loss of muscle mass due to lack of use and a significant reduction in bone mineral density resulting in severe osteoporosis, especially of the long bones of the legs. The psychological impact can be quite profound and result in a significant negative impact on sense of well-being and sense of control over one's life. One promising method found to reverse some of the complications associated with the loss of the ability to walk is Functional Electrical Stimulation (FES) of the lower extremities. Patients with lower extremity paralysis are placed on a stationary bicycle. Electrodes are placed on the thighs, hamstrings, calves, and other appropriate muscle groups and attached to a signal generator that systematically stimulates muscle contraction so that pedaling the cycle is achieved. While patients have no voluntary control of their legs, studies in adults indicate increases in muscle mass and bone mineral density, as well as in cardiovascular endurance. However, no studies have been done in children to examine these effects. We propose to examine the effects of regular exercise using FES in children who have lost the ability to walk due to spinal cord dysfunction on cardiorespiratory function, muscle mass, bone mineral density, and psychological well-being. It is believed that a regular program of FES exercise will improve cardiorespiratory function, and increase muscle mass and bone mineral density, making children less susceptible to fractures. Resultant decreased muscle atrophy is hypothesized to improve physical appearance and sense of control, leading to improved psychological well-being.

An initial medical evaluation, including baseline measures of cardiorespiratory function, muscle mass, and bone mineral density, will be done in order to assess the appropriateness of participation in the program. Twenty-four children will undergo 9 months of FES cycling using the ERGYS 2 system at Children's Specialized Hospital, 12 children during year 1 (Group 1) and 12 children during year 2 (Group 2). A time-lag design will be used, such that all 24 children will be recruited and given initial medical evaluations in year 1. During year 1, Group 2 children will be given the physiological and psychological measures at the same time as Group 1 children. This will provide a control group with which to compare the effectiveness of the treatment in the Group 1 participants. Children will be monitored for blood pressure, heart rate, and complaints of fatigue while cycling. Subsequent measures of cardiorespiratory function, muscle mass, and bone mineral density will be measured every 3 months during participation in the study and at the end of the 9 months. Both child and parent reports of child psychological wellbeing related to emotional functioning, social functioning, and school functioning will be collected on the same schedule as the measures of cardiorespiratory function, muscle mass, and bone mineral density. Data analysis will investigate the change in cardiorespiratory function, muscle mass, bone mineral density, and psychological wellbeing given time (baseline, 3, 6, and 9 months) and age. Also considered will be the child's weight and year's post onset of injury or disease, the number of sessions, and the maximum workload achieved during exercise. Data analysis also will compare changes in these measures in the control group compared to the initial treatment group. If there are differences such that the initial treatment group is significantly better than the control group, we will have evidence of the effectiveness of the intervention. We then will be able to combine Groups 1 and 2 in a pre- vs. post-treatment comparison, increasing the number of subjects.

Differentiation of Therapeutic Stem Cells Using Micro RNAs

Ronald P. Hart, Ph.D.

W. M. Keck Center for Collaborative Neuroscience

Rutgers, The State University of New Jersey of New Jersey

\$185,573

Stem cell transplants represent a new and promising therapy for curing chronic spinal cord injury. However, little is known about what may control the fate of these transplanted cells. Without control of cell fate, stem cell transplant may produce tissues that are inappropriate for the environment of the spinal cord at worst or non-functional in spinal cord recovery at best. A new class of genes, micro RNAs, has been identified in the past few years. These genes produce very small RNA molecules that control the production of specific proteins in the cell. Others and we have found that there are stem cell-specific populations of micro RNAs, and that these populations change during differentiation. Others have demonstrated that artificially changing a single micro RNA restricts the differentiation of precursors into adipocytes. Based on this observation, we believe that specific changes in micro RNAs will restrict differentiation of transplanted stem cells into selected cell types. If this is true, stem cells may be "programmed" prior to transplant in order to produce the most effective cell type, such as oligodendrocytes to enhance remyelination.

Towards this goal, we will characterize the micro RNA expression patterns in stem cells that have been effective in promoting spinal regeneration. Once we have identified micro RNAs that change during differentiation, we will test if these micro RNAs can restrict differentiation in culture. This is a novel approach to the use of transplanted stem cells as therapies for chronic spinal cord injury since it may allow the "programming" of cells prior to transplant.

Preservation of Sperm Functions after Spinal Cord Injury

Hosea F. S. Huang, Ph.D.

University of Medicine & Dentistry of New Jersey New Jersey Medical School

\$390,602

Over 80% of the individuals who survive spinal cord injury from all causes are men in the prime of their reproductive years. These men usually become infertile because they can no longer produce normal spermatozoa, perhaps due to abnormalities in their testicles. We have demonstrated that there are multiple causes which are responsible for these defects. With the support of the New Jersey Commission for Spinal Cord Research, we have investigated the relationship between the extent of cord injury and sperm function by using rats whose spinal cords were injured by surgical cutting or dropping of a rod from different heights directly onto the spinal cord. The results of these experiments demonstrated that sperm production persisted in these rats, but their sperm cannot move normally. The changes in sperm function appeared to be related to the degree of cord injury. This result is similar to that in SCI men in that they usually continue to produce sperm, but the sperm cannot move normally. We will continue to use these animal models to investigate the causes of abnormal sperm function after spinal cord injury, and test different treatments to improve sperm functions. Results of our previous experiments indicate that a series of biochemical processes that depend on a chemical called cAMP, referred to as "cAMP signaling cascade", in the testes and sperm became abnormal after spinal cord injury. We postulate that this is one of the major reasons that sperm of spinal cord injured men can no longer be fertile. In this new project, we will perform multiple experiments to determine the steps in this "cAMP signaling cascade" that are affected by spinal cord injury, and how these changes affect sperm functions.

We also will test the possibility of using antioxidants, vitamin E and selenium, to prevent the effects of spinal cord injury on sperm function. The results of these experiments will tell us the major reasons for abnormal sperm function after men have suffered spinal cord injury. We will then be able to develop a method to treat these men so that they can produce normal spermatozoa and become fertile again. If successful, such treatments will offer a simple and inexpensive therapeutic option to restore or preserve sperm functions after spinal cord injury, and will provide a low cost alternative to costly in vitro fertility technologies to restore reproductive capability of SCI men.

Netrin Directed Glial Migration

Randall D. McKinnon, Ph.D.

Department of Neurosurgery

University of Medicine & Dentistry of New Jersey

Robert Wood Johnson Medical School

\$360,690

The failure of regeneration in injured spinal cord is due in part to inhibitory molecules in myelin, the insulating sheath that wraps around neuronal axons to enhance axonal conduction. It is only after axonal connections are established that myelin-forming cells (oligodendrocytes) populate the axonal tracts, and the normal function of these inhibitors may be to prevent axons from branching out and making new, inappropriate connections. This then may explain why the injured adult spinal cord is not competent at regeneration, as any myelin present prevents axons from regenerating. This also identifies targets for therapeutic intervention, and one approach under intense study is to block the interaction of myelin inhibitory molecules with their axonal receptors in the injured spinal cord.

An alternative strategy which we will explore is to create an environment at the wound site that more closely approximates the cellular composition of early development. Specifically, we wish to remove myelin competent oligodendrocytes while axons attempt to regrow, and then subsequently allow these cells to repopulate the repair site for remyelination. If this strategy only modestly improves axon regeneration, it will advance the current status of therapeutic intervention. Our general strategy will employ growth factors (FGF and PDGF) to promote oligodendrocyte motility, and a directional cue (netrin) to direct traffic. The specific studies outlined in this proposal focus on the efficacy of the directional cue netrin.

Genes Involved in Spinal Cord Regeneration in Zebrafish

Melitta Schachner, Ph.D.

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\$317,768

Regeneration of neurons following spinal cord injury is generally believed to be inhibited by the glial scar at the site of injury, the generally inhibitory tissue environment of the adult central nervous system, and the intrinsic inability of some neuronal cell types to regrow their processes (axons and/or dendrites) after injury. In mammals, and in particular, humans, the glial scar and the inhibitory tissue environment are major impediments to neuronal regrowth and motor and sensory recovery after trauma. However, in zebrafish, a recognized biological model system benefiting from detailed genetic studies, neurons are able to regenerate and recover function after spinal cord injury, suggesting that the inhibitory elements characteristic of the adult mammalian central nervous system do not predominate.

Our research has demonstrated that spinal cord injured zebrafish indeed regenerate specific neuronal tracts, and that this regeneration requires the neuronal expression of an adhesion protein named L 1.1 that makes cells interact in a beneficial manner to foster regeneration. We believe that other genes are required for regeneration of neurons. Since we can dissociate the intrinsic neuronal growth from inhibitory tissue cues in zebrafish, we can easily identify regeneration-associated genes in neurons. Furthermore, some neuronal tracts regenerate (such as NMLF) and some do not (Mauthner cells). We can compare individual cells collected by laser capture micro-dissection from these two brain regions to select genes associated with successful regeneration. We will use DNA microarrays to identify specific genes expressed in successfully regenerating neurons and not in non-regenerating neurons. Our past studies with L 1.1 also demonstrate that we can block putative regenerative genes by adding morpholino antisense DNA molecules to injured spinal cords. These methods will allow us to demonstrate that a gene selected for its presence in regenerating neurons participates in the regeneration process. These studies will identify new cellular processes that are necessary for regeneration. In complement with newly developed therapies to reverse inhibition in the central nervous system of mammals, the newly identified regeneration-associated genes represent attractive new targets for drug development or gene therapy in humans.

Appendix E-2 2005 Fellowship Grant Recipients

Combination of Radial Glial Transplantation with Anti-Inflammatory Treatment in Rat Spinal Cord Injury

Yu-Wen Chang

W.M. Keck Center for Collaborative Neuroscience Rutgers, The State University of New Jersey of New Jersey
\$60,000

Cell transplantation is a promising strategy for spinal cord injury (SCI) research. Recent studies suggest that delayed implantation of embryonic stem cells or olfactory, ensheathing cells promote axonal regeneration and improve behavioral performance. The rationale for delayed transplantation is to prevent implanted cells from exposure to a non-favorable environment to yield a better survival rate. In our lab, we study radial glia and have been exploring their applications in spinal cord injury. Radial glial cells play essential roles in developing brain to guide and support neuronal migration. They are also neural stem cells that have the potential to become neurons and glia. Previous studies showed that radial glia migrated extensively in white matter in the normal spinal cord. We have acutely transplanted radial glia in the contused adult rat spinal cord and have demonstrated that radial glia cells have protective effect to the injured tissue and improve behavioral recovery. In this proposed study, we will conduct nine day delayed transplantation of radial glial RG3.6 to injured spinal cord.

Spinal cord injury triggers pronounced and progressive inflammatory and immune responses. A variety of inflammatory mediators are induced quickly in response to injury, which induces further cell death and tissue damage - so called secondary injury. Anti-inflammation is the current accepted acute phase treatment for human SCI. Several anti-inflammatory drugs used in rat models have been shown to be neuroprotective reducing lesion volumes and improving locomotor function. We will reduce secondary damage by anti-inflammatory drug immediately after the injury and conduct a nine day delayed radial glial transplantation in attempts to obtain a synergistic outcome. Our goal is to create a permissive environment by combining anti-inflammatory drugs with transplantation of cells to bridge the injury, promote injured axon regeneration and further enhance behavioral recovery.

Fabrication of a Tunable Hydrogel for Nerve Regeneration

Christopher L. Gaughan

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\$60,000

The primary focus of my research is to design a hydrogel biomaterial that will provide the best combination of properties to entice spinal cord neurons to regenerate axons. In essence, this gel will serve as a pathway along which growing axons can migrate. In this proposal, I focus on optimizing the physical properties such that it maximizes this migration. It is known that neurons prefer softer, more porous materials, and inhibitory cells, such as astrocytes, prefer stiffer materials. Therefore, by modifying the physical properties, we can design a material that optimizes the likelihood of restoring neural connections. The gel is made up of four distinct protein subunits that link together and form an extensive hydrated network of fibers. By varying ratios of certain subunits used to form the gel, I hope to alter the stiffness of the fibers and thus optimize axonal migration. It is the modular nature of this design that enables such gel parameters to be controlled in this way. Furthermore, by using protein as the primary component of the gel, it is more amenable to bio-degradation. It could also be optimized for the purposes of injectability.

In this research proposal, I focus on the production of the subunits that will be used to make the gel described above. In short, four distinct protein subunits will be made using standard DNA cloning techniques. Four synthetic genes that code for each subunit will be cloned separately into small pieces of DNA that E.coli will propagate. E.coli can then serve as a type of factory wherein it can be made to produce the proteins that each of the genes encode for. Each protein produced in these E.coli has been specifically engineered such that it carries a tag that allows for its purification. After purifying each protein, I can mix them in the proper ratios that optimize the axonal growth characteristics of the gel. Furthermore, the DNA coding for two of the subunits can be modified to include ligands that specifically bind neurons and stimulate axonal growth cues, but are not permissive for astrocyte or fibroblast attachment.

The ultimate goal of this research is to fabricate a material that could be injected into a damaged or severed region of spinal cord. It is possible that once put in place; this gel could help "re-ligate" or join the ends of severed axons. In doing so, a significant step towards restoring the functionality of the cord would be taken.

A workable material such as I have described would have a significant impact on the citizens of New Jersey. Approximately 6,000 New Jersey residents suffer from traumatic injuries or diseases that damage the spinal cord. Estimates indicate that 300 new injuries occur each year in New Jersey. These injuries exact a considerable cost to the state and individuals, both monetary and emotional. Thus, any and all effective strategies that target spinal cord regeneration cannot be under-valued. I feel that my proposed biomaterial would be part of an effective strategy towards this end.

Optimization of Stem Cell Differentiation with Microfluidics

Gary A. Monteiro

Department of Biomedical Engineering

Rutgers, The State University of New Jersey of New Jersey

\$60,000

The objective of this research is to quantify the mechanical and adhesive forces that govern stem cell differentiation into neurons. The derivation of in vitro differentiated stem cells into neuron cells has two-fold value. It helps us learn more about the early stages of neurogenesis as well as provide an unlimited source of neural transplantable donor cells for spinal cord disorders.

During embryonic development, there are mechanical, chemical and adhesive cues in the extra cellular matrix that direct stem cell growth. These signals change dynamically throughout development to orchestrate cell and tissue differentiation and organization. While much has been learned concerning stem cell fate, the interactions among cues are far from understood, especially in 3D environments, in which the cells reside in vivo. We believe in addition to chemical factors, mechanical forces as well as adhesion properties plays a role in the proliferation and differentiation of stem cells. Using microfluidics, we propose to fabricate microenvironments of varying stiffness and adhesion properties to study the differentiation of stem cells into nerve cells in a combinatorial fashion.

Following completion of these aims, we will have defined a parameter space for the design of biomaterial scaffolds with optimum mechanical and adhesive properties for stem cell differentiation into nerve cells. Further, this research may be used as a basis to optimize the differentiation of stem cells into various other cell types.

QTL Mapping and Phenotypic Analysis of Dreher Suppressing Modifying Loci

Tanya E. Borsuk

Center for Advanced Biotechnology & Medicine

University of Medicine & Dentistry of New Jersey

\$60,000

Our research focuses on the production of neurons in the spinal cord. Specifically, we are interested in a structure called the roof plate, which forms in the spinal cord upon neural tube closure, and is responsible for secreting a multitude of signaling molecules that control the proper production of neurons in the dorsal spinal cord. By studying a mouse called dreher, a spontaneous mouse mutant that lacks completely a roof plate, we can gain a better understanding of how and when neurons are generated in the spinal cord. We have previously shown that the loss of the roof plate in the central nervous system has profound effects on the dreher mouse, including a disruption in both the pattern and generation of neurons in the spinal cord, as well as behavioral abnormalities in dazed adults, including hyperactivity and motor uncoordination. The use of the dreher mouse thus provides us with an important genetic tool to study the role that the roof plate plays in neuronal production in the spinal cord, and the development of the central nervous system.

We have recently identified a type of dreher mouse that displays less severe effects in the adult (less hyperactive, loss of ataxia). This phenomenon can be attributed to areas in this mouse's genome that are somehow suppressing the mutation. Through the identification of these genetic areas, we hope to gain further knowledge into the pathways that lead to the production of the roof plate and its secreted factors, and how they control the generation of neurons in the spinal cord. For spinal cord regeneration research to advance, more knowledge needs to be obtained on exactly how neurons are generated, and how to instruct stem cells to a spinal cord lineage so that they can differentiate into functional neurons. Exposure of stem cells to developmentally important signaling molecules has led to partial recovery, and these results suggest that exposing stem cells to additional developmental factors could result in even greater functional recovery.

Further research on the mechanisms behind the suppression of the dreher mutation will benefit spinal cord research in two ways. First, it will increase our existing knowledge on how the roof plate and its secreted signaling molecules control the production of neurons in the spinal cord. Second, the identification of new pathways or signaling molecules involved in the production of neurons in the spinal cord can result in knowledge necessary to develop new techniques in the fields of stem cell based therapies seeking to regenerate missing or damaged spinal cord neurons following disruption or trauma.

The Role of FK506-Binding Protein 8 in Mammalian Neural Patterning and Axon Guidance

Ahryon Cho

Department of Molecular Biology

Princeton University

\$60,000

The mammalian central nervous system consists of the brain and spinal cord. One important function of the brain is to process outside information from the rest of the body and to control the actions of the body. As the spinal cord mediates communication between the brain and the rest of the body, damage to the spinal cord disrupts the connection, which most often results in some form of paralysis. Spinal cord injury (SCI) was thought to be irreversible because the distinct neuronal subtypes are spatially organized with respect to their functions during early development of the spinal cord. Those cell types and their functional connectivity are not normally regenerated in the adult. However, novel therapeutic approaches are currently being developed, holding great promise for the functional recovery from SCI. One example is transplantation of specialized neural cells grown in the laboratory into the damaged spinal cords of SCI patients. The grafted neural cells can repopulate the injured spinal cord and restore functional neural circuits.

For the purpose of tissue engineering, it is important to find ways to produce large numbers of particular neuronal cell types from embryonic stem cells (ESCs), which have the capacity of becoming many different cell types. Recent studies showed that ESCs in the culture dish become specific cell types of the spinal cord under the same instructive cues used during developmental processes in the body. Sonic hedgehog (Shh) is one such cue in mammals: in early development, cells in the spinal cord determine their fates or subtypes in Shh concentration-dependent manner. However, tight control of the Shh-mediated neuronal differentiation is required for generating large, homogeneous populations of particular neuronal cell types that can be used for transplantation. Despite the potential usefulness of Shh for such therapies, the way it acts is not well understood. Thus, in order to get a better idea about how we can control Shh signaling with precision, we must uncover its mode of action.

For this reason, I will investigate the role of FK506-binding protein 8 (FKBP8), a novel component of Shh pathway. Our preliminary data show that FKBP8 acts like a brake on the Shh signaling machine; when FKBP8 functions, cells will respond only when they are exposed to Shh, but when FKBP8 function is disrupted, cells will respond whether or not Shh is present. Based on these findings, I will explore the role of FKBP8 in the spinal cord under this fellowship. First, I will continue and extend my ongoing genetic analysis of FKBP8 to better place it within the Shh pathway and determine the roles for FKBP8 in late neural development. Second, I will investigate the biochemical mechanism by which FKBP8 works as a negative regulator of the Shh pathway. Finally, I will test the role of FKBP8 in guiding embryonic stem cells to adopt the fate of specific neurons in the spinal cord. I hope that my research will help optimize transplantation therapies for SCI.

A Novel Micromechanical Method for Controlling Microstructure in Nerve Grafts

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Schwann cells are cells found in the peripheral nervous system that enhance spinal cord regeneration when incorporated into nerve grafts, also called guidance channels, implanted at the site of spinal cord injury. Until very recently, the therapeutic potential of this approach was limited by the fact that regenerating neurites entered the graft, but had difficulty exiting it to complete the regeneration process beyond the injury site. However, in 2004, Dr. Mary Bunge's group at the University of Miami published a new protocol that successfully enhances regeneration beyond the Schwann cell graft. With this major advance, it is timely to focus

on optimizing the environment within the graft to maximize regeneration. Guidance channels are filled with a scaffold material, typically containing extracellular matrix components, through which the regenerating neurites grow. Several studies have shown that appropriate microstructural features of this scaffold enhance neurite outgrowth. One successful approach has involved the use of extracellular matrix gels whose fibers are oriented parallel to the axis of the guidance channel. It is believed that the effects of this fiber orientation are further amplified by the alignment of Schwann cells with the fibers, providing a clear path for the neurites to grow along through the channel. If this is true, then straightforward protocols for orienting the scaffold material will be an advantage in further optimizing Schwann cell nerve grafts. However, the method previously used to orient extracellular matrix gels, exposure to a high-strength magnetic field, involves a specialized facility that is not widely available to others who might wish to pursue this approach.

This proposal seeks to establish an alternative method based on the use of very fine gauge needles, with diameters on the order of 100nm. Studies have shown that connective tissue fibrils attach to and orient around acupuncture needles of this size, thus creating a field of tissue alignment along the needle axis. If a similar phenomenon occurs in extracellular matrix gels, which have a similar composition to the extracellular matrix component of connective tissue, this would provide a simple, accessible means of orienting the gel. To test this hypothesis, we will first establish a methodology for the use of micro mechanical needling to orient two different gel systems, collagen and fibrin, both of which are used in guidance channel construction. The oriented gel configurations produced in this way will then be tested for their ability to guide Schwann cells into an oriented arrangement within the guidance channel. These pre-oriented Schwann cell grafts will be tested in future work for their ability to enhance neurite regeneration, both in vitro and in animal studies. This project matches the first item listed in the NJCSCR funding priorities, "studying strategies to promote neuronal growth and survival."

The role of Ciliogenesis and Cell Cycle Phase in Hedgehog Signaling During Embryonic Stem Cell Differentiation

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Recent studies showed that transplantation of embryonic stem cells may restore the loss of neurons and glial cells in a model of spinal cord injury. Because ES cells can be easily maintained, propagated, and genetically manipulated, they hold great promise as a source of specialized cell types for therapeutic approaches in treating and curing spinal cord injury. However, less than 10% of an entire population of transplanted embryonic stem cells differentiate into neurons. Therefore, one of the major challenges in cell therapy is to develop reliable protocols for differentiation of embryonic stem cells into specific types of neurons and glia in culture prior to transplantation.

In this proposal, I investigate the mechanism by which embryonic stem cells differentially respond to cell fate-inducing signals to become specialized types of spinal cord cells. Our laboratory is using mouse genetics and cell biology to approach issues such as this. Recently, our lab and another group identified a novel mechanism required for controlling cell fate during spinal cord development. This mechanism, called intraflagellar transport, is intimately tied to the way cells respond to a signal called "Hedgehog", which controls neural cell fate.

Most mammalian cells use the intraflagellar transport mechanism to produce a highly specialized structure at the cell surface called the primary cilium. The role of primary cilia in most cell types has remained mysterious, although recent data suggest they may play a role in cell-cell signaling. Indeed, various mutations that alter intraflagellar transport activity affect the ability of cells to produce primary cilia, but also change the way they interpret and respond to Hedgehog signals. While most cell types generate a primary cilium, they do so only during certain phases of cell cycle, suggesting that response to Hedgehog signals may also be tied to the phase of the cell cycle.

I will carry out experiments to investigate the role of primary cilia and the cell cycle in the way embryonic stem cells respond to Hedgehog signals as they differentiate into various neural cell types. I will use different mutant strains of mice that are defective in the formation of primary cilia to test the function of these structures in embryonic stem cell differentiation. I will also test the hypothesis that developing cells might respond differently to Hedgehog signals in different phases of cell cycle. I will approach these issues using a combination of genetic, molecular and cell biological techniques. From this study, we can better understand how embryonic stem cells interpret positional cues with respect to their cellular context to tightly regulate the types of neurons produced from these cells. This work should help us to design efficient protocols for tissue engineering that would be required for successful transplantation therapies in the treatment of spinal cord injury.