



**DIRECTORY OF GRANT AWARDS
2007 B GRANT CYCLE**

**NEW JERSEY COMMISSION ON
SPINAL CORD RESEARCH**

2007 B CYCLE

**DIRECTORY OF GRANT AWARDS
FOR SPINAL CORD INJURY AND
DISEASE RESEARCH**

DECEMBER 2006

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

This data was compiled in compliance with the New Jersey Commission on Spinal Cord Research's statutory mandate, N.J.S.A. 52:9E-1, "...to compile a directory of spinal cord research being conducted in the State."

The information contained within this directory is not all-inclusive. The research projects and researchers listed in this directory are all based in the State of New Jersey, and have applied to and received funding during the fiscal year 2007 B grant cycle. The research projects are not categorized, or listed in any particular order.

This directory is not a complete listing of all scientific research being performed within the State of New Jersey due to the proprietary nature of the research being conducted at various institutions throughout the State. In addition, institutions are not obligated to share their research information with the New Jersey Commission on Spinal Cord Research.

Please feel free to contact the New Jersey Commission on Spinal Cord Research at PO Box 360, Health & Agriculture Building, Market and Warren Streets, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-292-4055, by fax at 609-943-4213, or by e-mail at NJCSCR@doh.state.nj.us.

For information on the New Jersey Commission on Spinal Cord Research's grant award process, grant applications, and deadlines, please see: www.state.nj.us/health/spinalcord/

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH GRANT AWARDS

INDIVIDUAL RESEARCH GRANT RECIPIENTS:

PRINCIPAL INVESTIGATOR – Tracy D. Parker & Moriah I. Szpara

Princeton University
Basic Science Proposal
Grant Award: - \$362,313

Proposal Title: **Elucidating Alpha-Herpesvirus Interactions with Host Neurons**

Spinal cord injury (SCI) has a devastating medical prognosis, with potential for paralysis, neuropathic pain, and limited functional recovery. Gene therapy is a promising strategy to deliver both regeneration-promoting molecules and pain relief to damaged spinal cord tissue. Herpesviruses, in particular herpes simplex virus 1 (HSV-1), have features that recommend them for this purpose. Herpesviruses are particularly useful for gene therapy because these viruses naturally infect neurons, cause life-long infections, and are able to move to neurons in the spinal cord from distant sites in the body. In these gene therapy systems, herpesviruses are made safe by gene deletions that limit their infectious potential and made therapeutic by insertion of genes that promote growth and survival of neurons following traumatic spinal cord injuries. In addition, herpesviral vectors can be used to deliver pain relieving agents directly to neurons.

Herpesviral gene therapy vector systems have undergone extensive pre-clinical studies in animal models of SCI, but their use is still complicated by occurrences of inflammation and toxicity early in infection. One way to approach these issues is to uncover what is going on in neurons during these early stages of infection. By understanding this, we may be able to circumvent immune system triggers or other cues that lead to these inflammatory side effects. Our research will address how neurons respond to herpesviral infection, as well as how these changes in neuronal host proteins in turn affect the viral life cycle.

We will first examine the changes in cellular gene levels in neurons during infection with two different herpesviruses. We plan to identify changes that are common to both infections, which may indicate a mechanism of general importance to herpesvirus infection. We will also use the viral protein gE, which is important for viral transport in neurons, as a lure to detect neuronal proteins that are also important for this movement. For cellular proteins that are changed during infection, or that are shown to interact with viral gE, we will then experimentally block their function in neurons and test the effects of this blockade on subsequent viral infection. In this way we can separate bystander effects of viral infection on neurons, from those effects that serve a purpose in facilitating viral replication or transport.

This research will tell us how neurons respond to herpesviruses under normal circumstances, and which of these effects are utilized by the virus for its own purposes. This information will allow for the design of improved herpesviral vectors for gene therapy, in that new vectors can be checked for their ability to preserve those neuronal responses that are key to viral gene expression or movement within neurons, but eliminate those neuronal responses that are not crucial to the virus and many instead be responsible for inflammatory or undesirable secondary effects.

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PRINCIPAL INVESTIGATOR – William G. Wadsworth, Ph.D.

UMDNJ-Robert Wood Johnson Medical School
Basic Science Proposal
Grant Award – \$331,112

Proposal Title: Molecular Mechanisms of UNC-6/Netrin Axon Branching

Following injury, regenerating axons must be guided back to their targets in order for the proper connections of the nervous system to be reestablished. Several of the molecules that are involved in axon guidance were first discovered in the nematode *C. elegans*, a model organism that is extensively used for genetic analyses. Although the nervous system of this organism is relatively simple, the same molecules that function to ensure proper nervous system connections in the nematode also function to guide the building of more complex circuits in the human nervous system. It is known that these molecules are present at the sites of spinal cord injury and that they may 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*, further molecules required for axon guidance and branching are being discovered through genetic screens. Knowledge of these molecules and a better understanding of the mechanisms by which they function could lead to better treatments to regenerate normal neural connections following injury.

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PRINCIPAL INVESTIGATOR – Gail Forrest, Ph.D.

Kessler Medical Rehabilitation & Education Corporation
Clinical Science Proposal
Grant Award - \$388,309

Proposal Title: **Stand Retraining and FES for SCI**

Functional mobility for individuals after spinal cord injury often plateaus before recovering the ability to walk. Lack of strength or coordination in the legs results in the individual relying on a wheelchair for moving around, which results in less loading on bones and muscles. This immobilization causes a rapid loss of muscle and bone in lower limbs, which can lead to high risk of fractures and long term associated medical risks, and attendant costs. Standing and walking on a treadmill equipped with an overhead harness to support body weight allows for the individual to learn how to stand and walk again. With enough body weight support (BWS) treadmill training there is independence in stepping and walking. In addition, there are studies involving cycling and resistance training that have shown that with Functional Electrical stimulation (FES) of lower limbs and intense training there are increases in muscle strength and bone density. The aim of this study is to expand on our current and ongoing research to understand what happens to the muscle and bone after four months of training using stand retraining (with BWS) and FES. Specifically, researchers will investigate neural, muscle and bone changes in the lower limbs in response to stand retraining (using BWS) and FES compared to standing alone and FES alone. We suggest that FES will produce leg muscle contractions while standing and this pulling on bone will be sufficient to promote more of an increase in bone and muscle. With neural, bone and muscle adaptations we predict an increase in functional ability to stand independently without assistance.

This project will be completed at two sites: Kessler Medical Rehabilitation Research and Education Corporation (KMRREC), (the grant PI site) and Frazier Rehabilitation Institute, University of Louisville, Louisville, Kentucky. Participants (n=36) who had an incomplete spinal cord injury and whose duration since time of injury is 6 months to 2 years will be randomly assigned to either FES alone, stand retraining alone, stand retraining (using BWS) and FES. All participants will complete twenty weeks (1.25 hour training or therapy, 3 sessions / week) of intervention training. Leg muscle activity, muscle volume as determined from MRI's, bone density, markers for bone formation and resorption and the impact on function and quality of life will be collected and analyzed before and after the intervention.

It is significant that KMRREC will be one of the few sites nationally researching the effect of BWS walking in Incomplete SCI. This study about multi – modality approaches may establish clinical guidelines for BWSTT and launch future multi center studies that combine pharmacological interventions, functional electrical stimulation and BWS treadmill training to further enhance the recovery of walking.

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PRINCIPAL INVESTIGATOR – Noshir A. Langrana, Ph.D.

Rutgers, The State of New Jersey
Basic Science Proposal
Grant Award - \$388,627

Proposal Title: **Bifunctional DNA Hydrogel to Promote Spinal Cord Regeneration**

As described in the NJCSCR guidelines, approximately 6,000 New Jersey residents suffer from traumatic injuries or diseases that damage the spinal cord and approximately 300 new injuries occur each year. These injuries come with devastating economic and personal consequences. It is our hope that, through multidisciplinary efforts such as those described herein, we at Rutgers, and specifically the Department of Biomedical Engineering, can contribute to the quest for a cure for the effects of spinal cord injury. Biomedical Engineering represents the interface between engineering and medicine. The biomedical industry thrives in New Jersey, and we believe it is crucial that the BME department at Rutgers thrive as well, to infuse the industry with a topnotch, educated, homegrown workforce. The success of the program is linked to the success of its faculty. Based on NJCSCR proposal funding on axon regeneration investigation, we accomplished specific aims of the force-actuating potential of DNA-crosslinked hydrogels by introducing more crosslinks into the gel and functionalize DNA-crosslinked hydrogels for axon attachment and growth.

Based on our basic biomedical engineering research on DNA-hydrogel behavior and its potential ability to guide neuronal growth, we are proposing further investigation that will ultimately enable us to implement both strategies of spinal cord regeneration in vivo. The specific Aims of this proposal are (1) to design a DNA crosslinked bifunctional construct and quantify the force created by the actuating functionalized gels to control axon growth by introducing additional crosslinking DNA strands based on our current study, and (2) to assess neuronal survival and neurite outgrowth in spinal cord neurons grown on the DNA crosslinked bifunctional construct. 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.

Dr. Noshir Langrana, PI on this proposal has an international reputation and more than 25 years of research experience in spinal biomechanics. He has published extensively and he serves on the editorial boards of two international spine journals and one Biomedical journal. In past three years his research has been focused on design of active reversible DNA crosslinked hydrogels, and he has transitioned into spinal cord injury with a one-year initial grant. NJCSCR funding has made it possible to create an interdisciplinary research team of young and experienced investigators, from both engineering and biology, and from different institutions.

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PRINCIPAL INVESTIGATOR – John K. Li, Ph.D.

Rutgers, The State of New Jersey
Basic Science Proposal
Grant Award - \$159,500

Proposal Title: **Rapid Noninvasive Oxygen Monitoring in Cerebrospinal Injury**

Mechanisms of stroke and spinal cord injury have eluded researchers and clinicians for decades. Brain and spinal cord tissues are most sensitive to variations in oxygenation and blood flow. Noninvasive quantitative assessment and continuous monitoring of oxygenation during cerebrospinal injury are very limited.

This project proposes to establish a noninvasive method for the continuous assessment of global and regional brain oxygen metabolism and perfusion during reduction of cerebral blood flow (ischemia) and oxygenation (hypoxia) with a novel design of a near infrared spectroscopy (NIRS) system that is coupled with measurements of brainstem auditory evoked potentials (BAEP). The novel fast electro-optical NIRS device will be developed that utilizes low power laser diodes and photo-detectors in the NIR wavelengths range for monitoring oxygenation. This rapid oxygenation monitoring device will be evaluated in in-vivo animal experiments to examine how brain circulation and oxygenation alter during hypoxia and transient ischemic attacks and how re-oxygenation can improve the outcome of cerebrospinal injury.

The result of the proposed research can significantly improve our current understanding of the interplay of oxygenation and perfusion during cerebrospinal ischemia and hypoxia, with a closer step to understanding the mechanism of the role of reduced oxygenation during transient ischemia attacks, stroke and spinal cord injury.

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FELLOWSHIP GRANT RECIPIENT:

PRINCIPAL INVESTIGATOR – Cynthia Camarillo, Ph.D.

Rutgers, The State University of New Jersey
Grant Award - \$100,000

Proposal Title: **Pre-Differentiation of Therapeutic Stem Cells Using Micro RNAs**

The transplant of stem cells is a promising therapy for restoring function following spinal cord injury. However, before stem cells can be transplanted, the mechanism that controls the fate of those stem cells to become tissue appropriate for recovery of spinal cord function needs to be identified and understood. A new class of genes, micro RNAs, have been identified that code for small RNA molecules that regulate cellular proteins. A set of these micro RNAs has been identified that are expressed during central nervous system (CNS) development and in cultured stem cells. Research studies have shown that controlling a single micro RNA directs the fate of that stem cell into a specific cell type. Based on these studies, we hypothesize that controlling specific micro RNA promotes the differentiation of neural stem cells to a glial cell type, the support cells of the CNS. Thus, selecting the population of cells that myelinate axons, the oligodendrocytes, will be augmented prior to transplantation to save spared axon fibers to promote spinal cord repair. This novel approach is designed to increase the effectiveness of stem cell therapies by “programming” the stem cell prior to transplant.

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