

DIRECTORY OF GRANT AWARDS 2025 GRANT CYCLE

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DIRECTORY OF GRANT AWARDS FOR SPINAL CORD INJURY AND DISEASE RESEARCH

DECEMBER 2024

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 2024 grant cycle. The research projects are not categorized or listed in any 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 P.O. Box 360, 25 S. Stockton Street, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-913-5005, or by e-mail at <u>NJCSCR@doh.nj.gov</u>.

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

2024 MEMBERSHIP INFORMATION

Carolann Murphy, PA, Chairperson Carolyn Daniels, D.H.Sc., M.Ed.

COMMISSION PERSONNEL

Mary Ray, Administrator Tunisia Sye, Fiscal Manager

EXPLORATORY RESEARCH GRANT RECIPIENT:

Peter Barrance, Ph.D. Kessler Foundation CSCR25ERG003 \$199,973

Using muscle functional MRI to better evaluate muscle activation patterns in neurorehabilitation following spinal cord injury

This study will investigate the information provided by muscle functional MRI - an imaging technique that can measure the spatial activation of muscles during exercise - in people with spinal cord injury, particularly in the assessment of changes accompanying transcutaneous spinal stimulation and activity based therapy for neurorehabilitation.

Several types of treatment and therapy have been shown to promote improvements in movement and other health gains in people with spinal cord injury (SCI). Researchers use many different methods to measure these gains- for instance they measure their ability to stand and walk and use scanning technologies to measure bone loss and recovery. They also often use a technique known as electromyography (EMG), which detects electrical signals coming from muscles, to measure how well the muscles are being activated. While EMG has many advantages, it also has some important limitations. For instance, it is difficult to gather information from muscles below the surface, and the results can change significantly if the sensing electrodes are moved only slightly, making it harder to measure differences across different testing sessions.

In this project, we will use another technique to study muscle activations in people with SCI. This technique, known as muscle functional MRI (mfMRI), uses MRI scanning to measure the activation of muscles. One of the signals that MRI imaging uses has been found to change with exercise; this change is understood to be related to a buildup of chemicals in the water inside the muscle. MRI scanning has many variable settings, or parameters, that can be changed to pick up specific signals, and our team has developed a set of settings (also known as an MRI sequence) that is specially adapted to measure the mfMRI signal. Although other groups have used mfMRI to study muscle activation in other groups of people and other activities, we do not believe there have been any previous studies in people with SCI. Participants in our study will lie on their back with their knee raised on a bolster and raise the lower part of their leg to straighten the knee, for several repetitions. They will do this in a room outside the MRI scanner, on a table that can be attached to the scanner for imaging. After they finish exercising, they will be moved into the MRI scan room for mfMRI scanning of the muscles of the thigh. The four muscles of the quadriceps that straighten the knee will be studied, with specialized data processing used to measure the overall activation of each of the muscles.

This project will use this method in two studies, each involving people with SCI. In the first study, we will compare mfMRI values between people with SCI and a control group of able bodied people. These people will have motor incomplete SCI, meaning that they still have some

ability to move their body in regions below the injury. In the second study, we will use the same experimental methods in two groups of people with SCI- those with motor complete and those with motor incomplete injuries – but all without the ability to straighten the knee. We will study both groups before and after they participate in an existing therapy program designed to help them restore muscle function and movement. This program uses an advanced method known as spinal cord transcutaneous ('through the skin') stimulation, as well as standing and walking training, to promote regeneration of neural pathways that were disrupted by the injury. In this second study, the same transcutaneous stimulation will also be used to assist the muscle activation and movement before the mfMRI scanning. We expect that the scanning will detect increases and changes in the patterns of activation related to the stimulation and training. By completing this study, we will provide new information on spatial muscle activation patterns, and we expect that this will lead the way to more widespread application of the technique in the future.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

Einat Haber, Ph.D. Kessler Foundation CSCR25ERG009 \$199,926

Assessing Cardiovascular Effects: Is There a Time Too Early for Spinal Stimulation in Acute SCI? A Year-Long Evaluation of Autonomic Function Following Injury

This exploratory study seeks to evaluate the blood pressure response to transcutaneous spinal stimulation in five individuals recently affected by SCI, spanning a year from the injury's onset. Our goal is to discern whether there is a time that is too early for stimulation and to study the underlying processes governing the BP response to spinal stimulation and their relation to autonomic system activation.

Traumatic spinal cord injury (SCI) is a devastating condition that affects not only mobility and sensation but also significantly disrupts cardiovascular function, especially in those with severe injuries. These individuals often face blood pressure irregularities, experiencing dangerously low or high levels, which can emerge shortly after the injury and hinder rehabilitation efforts, and also persist indefinitely, diminishing quality of life and increasing the risk of cardiovascular complications.

The period immediately following an SCI is crucial for intervention due to heightened neural plasticity (that is, the brain/spinal cord ability to reorganize). Spinal stimulation has emerged as a promising treatment for individuals with chronic SCI, showing benefits in cardiovascular regulation by increasing blood pressure in those with low blood pressure and reducing it in cases of high pressure. However, its effectiveness shortly after injury is not well understood. Transcutaneous spinal cord stimulation, a non-invasive method using skin-attached electrodes, is particularly of interest for its flexibility and potential benefits.

Despite the scientific community's advocacy for early post-injury intervention, including stimulation to improve BP control, the optimal timing for such interventions after SCI remains uncertain. Existing literature suggests there may be an initial phase post-injury when the autonomic nervous system—the regulator of cardiovascular functions—is least responsive, rendering stimulation less effective in controlling blood pressure. An ongoing study at our institute, a pioneering investigation focusing on individuals recently injured (within 50 days), corroborates this observation, as we have noted minimal blood pressure response to stimulation. These findings contrast with other observations from our lab, where individuals with chronic SCI (> 6 months) exhibit a significant increase in blood pressure with stimulation, often leading to the resolution of low blood pressure symptoms.

Based on these insights, we have formulated the current proposal to further investigate this line of research. Our aim is to monitor the cardiovascular response to stimulation over a year, starting

early after injury, with assessments conducted every three months. Five individuals with high injury level (above thoracic level T6) and severity (AIS A/B), who were recently admitted to our inpatient rehabilitation program, will be enrolled. Through a series of tests, including stimulation at various positions, questionnaires, and 24-hour blood pressure monitoring, we will evaluate the activity of the autonomic nervous system and assess blood pressure changes. Our hypothesis suggests that initially, the autonomic nervous system may be less responsive, but it is expected to become more responsive over time.

This research aims to identify the most beneficial timing for initiating stimulation therapy and to elucidate the relationship between stimulation, blood pressure responses, and autonomic system activity. Understanding the intricacies of stimulation timing and effectiveness could pave the way for enhanced treatment strategies, ultimately improving cardiovascular health and overall outcomes for individuals with SCI.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

Francois Berthiaume, Ph.D. Rutgers, The State University of New Jersey CSCR25IRG008 \$600,000

Dynamic Sensing of Pressure Wounds in Spinal Cord Injury

The purpose of this project is to develop a smart bandage for pressure skin wounds that contains sensors that report on the wound status.

Pressure wounds on the skin are a common occurrence in spinal cord injured patients who are confined to a wheelchair or bed. These wounds may take weeks to heal and typically require weekly medical visits for ongoing evaluation and treatment until fully healed. The multiple medical visits create a significant burden for patients with limited mobility and are costly to the healthcare system.

Pressure wound diagnosis and care are largely based on subjective and qualitative criteria, and there is much trial and error in making therapeutic decisions. Valuable time may be lost before an effective therapeutic regimen is found. We seek to develop a "smart" bandage that has embedded sensors within it, that can report on an almost continuous basis, the physical and biochemical state of the wound. The information may be transmitted wirelessly on a frequent basis to the healthcare personnel, thus helping to make more informed and timely decisions about wound care.

The technology will be further developed to simultaneously measure multiple biomarkers in wounds in situ. We will use this information to stage experimentally induced pressure skin wounds in both healthy and spinal cord injured (SCI) mice (the latter of which exhibit delayed healing), in order to optimize the timing of therapies.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

Peter Galie, Ph.D. Rowan University CSCR25IRG011 \$599,994

Evaluating the therapeutic potential of altered hemodynamics to treat spinal cord injury

These studies will interrogate the effects of drag-reducing polymers on spinal cord vasculature using both in vitro and in vivo approaches.

Altered blood flow and vascular function at the site of spinal cord injury are major contributors to the secondary injury processes that exacerbate the initial insult and are thus potential therapeutic targets to mitigate the effects of injury. Recent developments in ultrasound imaging by our collaborators at the University of Washington, Drs. Khaing and Bruce, reveal acute, localized hypoperfusion at the site of injury, and indicate that the extent of hypoperfusion correlates to the severity of functional deficits.

Although previous studies have attempted to increase spinal cord perfusion by raising the mean arterial pressure with norepinephrine, this approach leads to mixed results due to the complexity of the spinal cord vasculature and the damage associated with spinal cord injury. In contrast, this proposal focuses on using drag-reducing polymers to decrease the pressure drop locally across the spinal cord vasculature, which ultrasound imaging by our collaborators shows is substantially distorted in the acute aftermath of injury. Drag-reducing polymers have been used in other injury models to restore physiological perfusion including myocardial infarction and traumatic brain injury but have yet to be used to treat spinal cord injury. The proposed studies will take advantage of new developments in digital light processing by our laboratory, which can 3D-print topologies that recreate the ultrasound scans of spinal cord vasculature produced by our collaborators. Human whole blood will be perfused through in vitro models of vascular bed topologies obtained from both non-injured and injured animals to determine the effect of dragreducing polymers on hemodynamic profiles. A second microvascular model will also be used to evaluate the effects of drag-reducing polymers on arteriole-scale vasculature by incorporating smooth muscle cells. In order to validate the in vitro blood flow measurements, Doppler ultrasound as well as nonlinear ultrasound localization microscopy will measure spinal cord blood flow in a rat model of thoracic-level spinal cord injury in real-time in response to the administration of drag-reducing polymers. The microvascular model and the in vivo studies will also evaluate the effects of adding norepinephrine following injury, since this agent is often used to counteract injury-induced hypotension in a clinical setting. Moreover, combining the ultrasound measurements with mean arterial pressure monitoring will provide insight into how drag-reducing polymers affect both local and systemic blood flow in the aftermath of injury.

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Fellowship Research Grant

Wankyu Ko, Ph.D. Rutgers, The State University of New Jersey CSCR25FEL002 \$240,000

Aligned neuron-inducing hybrid graft for functional repair after spinal cord injury

Developing a biodegradable, injectable, and biocompatible hybrid graft programmed for aligned neuron differentiation, using FDA-approved materials, for direct transplantation into a lesion to repair the injured spinal cord.

Traumatic spinal cord injury (SCI) leads to severe functional impairment accompanied by neuronal loss. Researchers have identified neural stem cells (NSCs) derived from embryonic spinal cords as potential candidates to compensate for this loss. By employing advanced techniques to culture these embryonic NSCs (eNSCs), scientists can evaluate the impact of various interventions on NSCs, paving the way for further research and the potential development of new SCI therapies. Notably, human embryonic spinal cord-derived NSCs, such as NSI-566 cells, are being implanted into SCI patients to support their recovery. Studies have shown that neuronal differentiation from transplanted eNSCs promotes the healing of injured spinal cords. However, transplanted eNSCs often struggle to survive during SCI events. Moreover, the surviving cells are more prone to differentiate into astrocytes rather than neurons. Following SCI, activated astrocytes express glial fibrillary acidic protein (GFAP), leading to the formation of cystic cavities with GFAP barriers within the lesion. These GFAP barriers hinder the survival and neuronal differentiation of transplanted NSCs by releasing inflammatory cytokines into the lesion. The progressive formation of lesion cavities post-SCI also exacerbates the accumulation of inflammatory cytokines. These inflammatory processes, including proinflammatory cytokines and cystic cavities, impede the relay of neuron signals necessary for functional repair post-SCI.

We require a hybrid treatment with dual effects for functional SCI repair. Developing a hybrid treatment capable of anti-inflammation and neuron induction to treat SCI has been a major challenge due to the complicated and dynamic changes that occur in the cellular environments after SCI. The neuronal destruction (primary damage) caused by traumatic SCI, followed by the accumulation of inflammatory cytokines and the formation of an activated cystic cavity (secondary damage), hinders the recovery of damaged neurons and the survival/neuronal differentiation of transplanted cells. In particular, the neuronal signal relay between the intact and injured regions is a prerequisite for functional repair. Given the complex inhibitory environment caused by SCI, an effective approach to address these issues is strongly needed. To address this, I have developed a hybrid graft that can (1) provide a favorable environment for cellular regeneration and (2) serve as an aligned neuron differentiation scaffold to reactivate the signal relay.

A hybrid graft composed of (i) UDCA (ursodeoxycholic acid) as an anti-inflammatory drug, (ii) an injectable hydrogel conjugated with glycol chitosan (GC) and oxidized hyaluronate (oHA), (iii) embryonic spinal cord-derived neural stem cells (eNSCs), and (iv) PEDOT (Poly (3,4-ethylene dioxythiophene)) conjugated PLGA (polylactic-co-glycolic acid) fiber as an aligned neuron-inducing scaffold will be transplanted into the SCI region for the repair. UDCA, chitosan, hyaluronate, eNSCs, PEDOT, and PLGA have all been approved by the FDA as medical treatments in clinics.

While the materials mentioned for this study are already approved by the FDA as therapeutic materials, the novelty of the developing hybrid graft stems from the systematically optimized harmony among these materials to facilitate functional SCI repair. Simply adding a large number of cells into the lesion does not guarantee better recovery, as numerous processes occur simultaneously after SCI. I believe that the hybrid graft, based on its anti-inflammatory and neuron-inducing effects, will have significant implications for SCI patients.

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