DIRECTORY OF GRANT AWARDS
2019 GRANT CYCLE

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

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DIRECTORY OF GRANT AWARDS FOR SPINAL CORD INJURY AND DISEASE RESEARCH

MAY 2019

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 2019 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, 369 S. Warren Street, 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.nj.gov.

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.

2019 MEMBERSHIP INFORMATION

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CSCR19IRG012
Michael Matise, Ph.D.
Rutgers University Biomedical & Health Sciences
Robert Wood Johnson Medical School - $600,000

Restoration of Tissue Homeostasis by Hh-Responsive Astrocytes Following Spinal Cord Injury

We will test whether Hh signing is required in a newly identified subset of functionally and molecularly distinct astrocytes for their role in repairing the blood-brain barrier following SCI.

The goal of the proposed project is to gain a better understanding of the cellular and molecular mechanisms that regulate the response to, and repair of, traumatic spinal cord injuries (SCI) in a rodent model system. We have discovered that a subset of glial cell (astrocytes) exhibit unique properties that distinguish them from other similar cells in the spinal cord. In particular, these cells are under the control of an important signaling pathway mediated by a secreted factor known as Sonic Hedgehog (Shh). These cells exhibit a unique function in that they appear to comprise a subset of astrocytes that respond to SCI by migrating to the injury site. There, our data suggests that they play a key role in repairing damage to the blood-brain/spinal cord barrier (BBB), a critical diffusion barrier that normally inhibits the infiltration of circulating plasma proteins and compounds into the CNS from the blood stream and in doing so maintains its unique "privileged" immune status. Disruption of the BBB commonly occurs following SCI and can lead to numerous secondary consequences. BBB disruption is also recognized as a critical early event in the etiology of many diseases affecting the CNS and spinal cord, including Multiple Sclerosis (MS) and Amyotrophic Lateral Sclerosis (ALS). Functional recovery from SCI requires the restoration of normal BBB function. However, our current knowledge of the specific roles that different spinal cord cell types and signaling pathways play in maintaining or repairing the BBB is lacking.

Our study will comprise two specific aims. In Aim 1 we will test the hypothesis that these specific, genetically and functionally unique GM astrocytes are required to establish and/or maintain the BBB after penetrating spinal cord lesions that model traumatic SCI. These studies will combine conditional mutagenesis, genetic lineage tracing, and surgically induced SCI.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CSCR19IRG018
Trevor Dyson-Hudson, Ph.D.
Kessler Foundation - $548,468

Autologous Micro-Fragmented Adipose Tissue Injection for Shoulder Overuse Injuries in Wheelchair Users with Spinal Cord Injury: A Randomized Controlled Trial

This is a randomized controlled trial to determine the efficacy of autologous micro-fragmented adipose tissue injection for recalcitrant rotator cuff disease in persons with spinal cord injury.

The overall purpose of this study is to determine the effectiveness of autologous, micro-fragmented adipose tissue injection in the treatment of a chronic shoulder pain in individuals with spinal cord injury (SCI). Shoulder pain is a common medical complication occurring in those with SCI and is caused by overuse due to an increased reliance on the upper limbs for wheelchair mobility and other activities of daily living. Often referred to as "wheelchair user's shoulder", shoulder pain can lead to substantial disability in individuals with SCI, resulting in decreased functional independence and increasing the risk for other medical complications.

Although shoulder pain has long been recognized as a significant problem in individuals with SCI, very little research has been conducted to identify suitable treatments. Current guidelines recommend conservative treatments such as rest, medications such as nonsteroidal anti-inflammatory drugs and corticosteroid injections, modalities such as heat, ice, and ultrasound, and exercises. Unfortunately, the effectiveness of these treatments in individuals with spinal cord injury is unknown and some are known to have negative side-effects or may be inappropriate for individuals with SCI. If these treatment options fail, then rotator cuff surgery may be the only option. There is clearly a need for further research into appropriate treatments for chronic shoulder pain in individuals with SCI that are effective, have minimal side effects, and maintain functional independence.

Regenerative medicine focuses on the repair or replacement of tissue lost to injury, disease, or age through self-healing and cell-based-therapies. Micro-fragmented adipose tissue injection is a type of regenerative medicine and rehabilitative medicine treatment that uses a person's fat or adipose tissue to fill joint and muscle defects, like shoulder injuries. Adipose tissue is also thought to contain growth factors and cells that may stimulate tissue healing. There is some evidence that an adipose tissue injection alleviates shoulder pain in able-bodied individuals who have shoulder pain. Results from a recent study in a small group of individuals with SCI who had shoulder pain were also promising. However, in order to better understand how this treatment works and whether it is effective, we need to continue studying it in a larger group of individuals with SCI and compare it to a conventional treatment, such as a corticosteroid injection.

The purpose of this study is to determine the effectiveness of micro-fragmented adipose tissue injection in the treatment of a chronic shoulder pain in persons with SCI. During the course of this study, 28 individuals with chronic SCI who have shoulder pain that has not responded to regular, conservative treatment will be randomly assigned (by a coin toss) to one of two treatment groups: 1) a micro-fragmented adipose tissue injection treatment group; or 2) an alternate ("control") group treated with a traditional corticosteroid injection. We will then follow

people for six months to see how both treatments work and to compare changes in shoulder pain and function. Our goal is to show that micro-fragmented adipose tissue injection works better than conventional treatments to alleviate chronic shoulder pain in individuals with SCI and potentially improve their quality of life. Achievement of the proposed goals will have a significant impact on the treatment of shoulder pain in persons with SCI. This study will identify an effective and promising rehabilitative treatment that will be an alternative to rotator cuff surgery in people with SCI who have overuse-related shoulder pain that does not respond to conventional treatments.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CSCR19IRG021
Erica Weber, Ph.D.
Kessler Foundation - $592,177

Development and Validation of an Abbreviated Cognitive Screening Battery for Individuals with Spinal Cord Injury

This project will validate the use of a brief, abbreviated cognitive screening battery, developed from established, motor-free neuropsychological tests that are sensitive to SCI-related impairment.

Traumatic spinal cord injury (SCI) is a significant public health concern as it affects approximately 17,500 persons in the US per year, who incur lifetime costs ranging from $1.6 to $4.8 million each. Researchers and clinicians alike have begun to pay greater attention to cognitive difficulties in persons with SCI, as many individuals experience problems with their thinking abilities (like memory and attention) after sustaining their injury. These cognitive problems often cause problems in the daily lives of persons with SCI, as it can affect their ability to benefit from other types of rehabilitation (PT, OT), how independently they are able to care for themselves, and how well they can re-integrate into their communities. As such, assessment of cognition is important to promoting positive health and everyday outcomes in those with SCI. Despite this need to evaluate thinking abilities after SCI, cognitive functioning is not usually assessed in individuals with SCI in the clinic, most likely because it is time- and labor-intensive, expensive, and often requires hand and arm functioning for completion of many cognitive tests.

This project proposal seeks to develop and test a brief cognitive screening tool, created from abbreviated portions of common, well-regarded, motor-free neuropsychological tests. A total of 240 participants with SCI (recruited by three current or recent SCI Model System sites: Kessler Foundation, Craig Hospital, and the University of Washington) will undergo an assessment of cognitive functioning, in the context of a broader evaluation that will help us better understand their medical history, mental health symptoms, quality of life, and daily living. Supported by our strong preliminary data, previous experience in carrying out similar projects in other neurological disorders, and the expertise of our multi-site SCIMS-based team, the rigorous testing of this collection of abbreviated tests as proposed by this study protocol will allow cognitive screening to become more routine and valuable in SCI clinics. In turn, this project will yield critical advancements in the field that improve resource-effectiveness of neuropsychological referrals, lead to greater identification of cognitive impairment, and ultimately enhance important health and daily living outcomes for individuals with SCI.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CSCR19IRG019
Nancy Chiaravalloti, Ph.D.
Kessler Foundation - $597,773

Longitudinal Changes in Cognition and Hemodynamics in Individuals with Spinal Cord Injury

We will document longitudinal changes in SCI compared to healthies in cognitive, cardio and cerebrovascular function, as well as their relationship to each other and patterns of cerebral activation.

The general population is aging; today 12% of the US population is older than 65 and it is estimated that by 2020 the number of people in the US older than 65 will outnumber children younger than 5. Similar to the general population, the spinal cord injury (SCI) population is also aging and it is estimated that 14% of persons with SCI are older than 60. However, despite the fact that persons with SCI are living longer, life expectancy remains below that of the general population, with cardiovascular and cerebrovascular diseases accounting for more than 25% of all deaths since 1995. It has been proposed that the SCI population represents a model of accelerated cardiovascular aging and that decentralized cardiovascular autonomic control may play a role.

Similar to the non-injured population, as people with SCI get older, they are faced with the increased likelihood of developing age-associated diseases like cardiovascular disease and stroke (cerebrovascular disease). In fact, people with SCI are 5-times more likely to have had a stroke than people without SCI, which may be due to the secondary complications of the SCI, such as the inability to control heart rate and blood pressure. Furthermore, because of damage to the nervous system it is often more difficult to prevent and treat diseases and illness in the SCI population, which may worsen disease progression and reduce life expectancy. In addition to cardiovascular and cerebrovascular disease, people with SCI are reported to have impaired thinking (cognitive) abilities at a relatively young age, and as many as 60% of individuals with SCI have functional deficits in memory, information processing and executive function. In the general population, there is an association between aging and the development of cognitive deficits that may be related to cardiovascular and cerebrovascular dysfunction.

Recent evidence from our group has documented a significant relationship between cardiovascular and cerebrovascular dysfunction and poorer cognitive performance in person with SCI. We have additionally shown changes in the way the brain processes and remembers information in persons with SCI. However, understanding how cardiovascular, cerebrovascular and cognitive function change over time in persons with SCI compared to age-matched controls, will aid in the development of timely intervention strategies to prevent or ameliorate the pronounced functional deficits reported in the SCI population. The currently proposed project represents an important step forward in a continuing line of work that aims to understand the etiology of the prevalent cognitive disorders in the SCI population to develop and guide clinical treatment strategies in promoting independence, social integration and overall quality of life of persons living with SCI. We will document 3-5 years and 6-8 year longitudinal changes in individuals with SCI compared to age-matched healthy controls. We will compare cognitive, cardiovascular and cerebrovascular function between the groups, explore the relationship between cognitive dysfunction and cardiovascular and cerebrovascular dysfunction among

persons with SCI as compared to AM healthy controls and determine regional patterns of cerebral activation on fMRI in individuals with SCI as compared to healthy controls. We will additionally examine the incidence of dementia in persons with SCI based on individuals in our longitudinal cohort. There are few studies examining the frequency of dementia in this population. It is particularly important to understand the relative dementia risk in this population given the increased prevalence of cognitive deficits consistently reported in persons with SCI and the fact that the SCI population is aging.

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INDIVIDUAL RESEARCH GRANT RECIPIENT:

CSCR19IRG007
Steven Zheng, Ph.D.
Rutgers University Biomedical and Health Sciences
Cancer Institute of New Jersey - $600,000

Role of MAF1 in the Neuroprotection and Axonal Regeneration after Spinal Cord Injury

This project will investigate the negative role of MAF1 in the growth and survival of spinal neurons, and explore MAF1 as a potential therapeutic target for treatment of spinal cord injury.

There are as many as 17,500 new spinal cord injury (SCI) cases nationwide and over 300 in New Jersey each year. SCI has long-term deliberating effects on the injured individuals, and heavy burden on their families and the health care system. Currently, no effective treatment is available. There is an urgent need for new therapies.

A major challenge for recovery from SCI is to regain the growth ability of adult spinal nerves, which is lost due to restrained activity of mTOR, a master regulator of axonal growth. Recent studies have shown that stimulating mTOR by deletion of PTEN leads to regeneration of brain and spinal nerves. Unfortunately, removing PTEN is known to cause cancers in mice and men. Therefore, it is important to find new targets to activate mTOR without severe adverse effects.

In our preliminary study, we discovered that knockdown of MAF1 promotes the growth and survival of brain neurons. Maf1 inhibition does not appear to have the negative consequences suffered from PTEN blockage. In this application, we will study MAF1 in spinal neurons and test whether Maf1 inhibition has also stimulate the regeneration and survival of spinal neurons. If successful, the proposed studies will help lay groundwork for developing novel therapeutic drugs for treating SCI.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR19ERG004
Martin L. Yarmush, M.D., Ph.D.
Rutgers University Biomedical and Health Sciences
Cancer Institute of New Jersey - $200,000

Autonomous Early Detection and Treatment of Pressure Wound after Spinal Cord Injury

We will monitor galvanic skin responses, recorded differentially from normal and pressure wounded skin to detect invisible onset of pressure ulcers and guide healing using electrical stimulation.

Pressure ulcers, with an incidence of over 50%, are serious secondary complications in spinal cord injury patients. The loss of sensation and mobility makes SCI patients very prone to develop pressure ulcers that rapidly progress to chronic stages where current treatment modalities fail. The chronic pressure ulcers are prone to bacterial infections and sepsis leading to patient death. SCI patients depend on skilled nursing care which currently is expensive and results in delayed treatment due to inadequate pressure ulcer diagnostic tools. The delayed treatment and the absence of options for successful chronic wound treatment makes pressure ulcer treatment a nationwide healthcare priority.

SCI results in a loss of endogenous autoregulatory function of skin necessary to withstand normal pressure. The exposure of skin to the pressure of critical intensity and duration in SCI patients occludes the normal blood circulation depriving cells of oxygen and other nutrients. The changes in subepithelial and interstitial fluid introduced by such deprivation of nutrients along with the local increase in pressure triggers ischemia and necrosis of regional cells and thereby the onset of a pressure ulcer. A mechanism to track and restore such changes can be developed for therapeutic pressure ulcer intervention in SCI patients.

The goal of these studies is to track pressure induced changes on circulation and in interstitial fluid using GSR and restore them using electrical stimulation to develop a clinically relevant multimodal pressure ulcer treatment for SCI patients.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR19ERG008
Treena Arinzeh, Ph.D.
New Jersey Institute of Technology - $200,000

A Novel Combination Strategy Using Schwann Cells and a Bifunctional Conduit for Spinal Cord Repair

This study will evaluate the use of a bifunctional conduit that provides both physical and biochemical cues in combination with Schwann cells for spinal cord repair.

In the United States alone, there are approximately 300,000 individuals living with a spinal cord injury (SCI). SCI is a devastating condition for which there is no cure. Bioengineering efforts have been focused on developing biomaterials that promote the regeneration of axons across lesions. Although these materials show promise, the overall effect is limited, and many axons fail to traverse the lesion. In addition, directing the axons across the lesion back into the spinal cord to integrate with host pathways remains to be achieved. Recent efforts, therefore, have been exploring combination strategies using conduits with cells and/or neurotrophic or neuroprotective factors.

The goal here is to improve axon regeneration across a Schwann cell (SC)-containing conduit and into the host cord to improve functional recovery by using a novel tissue engineering strategy. These studies bring together the PI, Dr. Treena Livingston Arinzeh, who has expertise in tissue engineering and biomaterials, with an established investigator in SCI research, Dr. Martin Oudega, to develop a novel, combination strategy and more translatable approach in spinal cord repair. SCs in combination with a bifunctional conduit that has both physical and biochemical properties will be used in the proposed studies to promote axonal growth. The bifunctional conduit consists of aligned fibers that have piezoelectric activity, which provides electrical activity without having to apply external electrodes, provide contact guidance for directional growth of the axons, and release zinc (Zn) to promote SC survival and axonal regeneration. The conduit is also biodegradable, which allows for full integration over time. The unique combination of SC transplantation with a degradable piezoelectric conduit may be an effective and translatable strategy leading to clinical trials. The Miami Project, where Dr. Martin Oudega is a Research Associate Professor, is currently conducting autologous human SC transplantation for human SCI. Studies proposed here will complement the ongoing clinical trial by developing novel SC combination strategies to improve functional recovery. If findings in the proposed animal studies show promise, the path to a clinical trial will be faster since SCs are currently in a clinical trial and the proposed biomaterials also are approved by the FDA.

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FELLOWSHIP RESEARCH GRANT RECIPIENT:

CSCR19FEL002
Nofar Engelhard
Rutgers University - $60,000

Characterizing a Novel Spinal Cord Population: Role In Both Locomotive Control and Recovery from Spinal Cord Injury

We target a new spinal cord neuronal population to characterize its connectivity, reveal its role in locomotion, and establish its importance for recovery after spinal cord injury.

Walking requires the synchronization of various muscles, which depends on the orchestrated activity of numerous elements in our spinal cord. Damage to these intricate circuits (spinal cord injury) can result in loss of control over motor functions such as walking (locomotion). The main cause for spinal cord injury is car accidents: in New Jersey alone, there are over 250,000 annual accidents - of which 20% result in injuries. Although no treatment can restore one's ability to walk, rehabilitation strategies show some success in improving motor function, suggesting that providing stimulation to the spinal cord cause the induction of neural circuits change, serving as the mechanism of the improved motor control. This capability of neural circuits to change their connection pattern and to reorganize to form new circuits, is broadly termed- plasticity. Indeed, animal research supports the notion that spinal cord is capable of spontaneous plastic reorganizations after spinal cord injury; processes that can be further engaged by rehabilitation.

Thus, to develop better therapies for restoration of motor control after spinal cord injury, we must identify and characterize the spinal cord elements participating in plasticity- induced recovery of motor function. Circuits involved, are suggested to possess some or all of the following properties: they 1) are modulated by external information about touch, body posture, and position, 2) have the ability to directly contribute to movement, and 3) have a role in synchronizing activity across the body. Identifying these circuits will allow for a better understanding of the plasticity processes that underlie functional recovery following spinal cord injury; knowledge that can used for optimization of therapeutic approaches.

We use advanced mouse genetic tools, allowing us to both visualize, and manipulate specific spinal cord neuronal populations. Combined with our sensitive behavioral paradigms, we can characterize their connections within the spinal cord, and identify their role in locomotion, in both the healthy and injured animal. Our preliminary work identifies a new spinal cord neuronal population, termed IZ-PV+. Our results suggest that a spinal cord IZ-PV+ microcircuit exhibits all the major characteristics of circuits participating in plasticity- induced functional recovery and is thus, likely to be important in both locomotive control and recovery from spinal cord injury. We propose to thoroughly characterize the circuit in which IZ-PV+ neurons reside, their projection patterns across the spinal cord and their role in locomotion of the healthy animal. This proposal will set the groundwork for our future work, in which we will examine IZ-PV+ contribution to locomotion and recovery from spinal cord injury. We argue: to better understand how specific spinal cord neuronal populations reorganize after injury to improve recovery, we

must first characterize them in the healthy animal. We hope that research such as ours will open the door for similar work, designed to characterize additional spinal cord circuits in health and disease. Expanding our knowledge about specific spinal cord subpopulations will supply an arsenal of potential therapeutic targets, with different potential clinical advantages that could be used for personalized treatment of spinal cord injury.

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SPINAL CORD TECHNIQUES TRAINING TRAVEL GRANT RECIPIENT:

CSCR19TTT002
Nofar Engelhard
Rutgers University - $4,000

After finishing high school, I chose to devote two years for national service in my home country, Israel. During that time, I volunteered in an organization for adults and youths with various types of disabilities, including paraplegia and quadriplegia. We, as a group of volunteers, came there to spend time with them, take part in their activities, and help them with whatever was necessary. While I already knew that I wanted to study biology, this experience made me develop a specific interest in understanding the biology of disabilities and in studying ways to improve them.

Since then, my research training has focused on dissection of specific neuronal circuits important for sensorimotor integration. Additionally, I gathered various expertise including: patch clamp electrophysiology, immunohistochemistry and behavior. I am currently during my second year of a PhD program in the lab of Dr. Victoria Abraira at Rutgers University where we are interested in studying the role of specific spinal cord circuits in sensorimotor function. To that end, our lab developed and validated the use of advanced mouse molecular genetic tool box to label, visualize and manipulate specific spinal cord circuits. It is my personal interest, which I share with my PI, Dr. Victoria Abraira, to extend our expertise to the field of spinal cord injury.

Our tools, used for genetic targeting of specific spinal cord circuits, present a great opportunity to dissect the role of specific spinal cord populations in recovery from spinal cord injury. This research is both conceptually and technically innovative and can have a profound impact of clinical approaches targeting specific spinal cord circuits to induce recovery from spinal cord injury. To achieve my goal, I would like to participate in a spinal cord technique course. Support from the New Jersey Commission on Spinal Cord Research will guarantee the necessary training to allow me to apply my unique skills (including mouse molecular genetics, spinal cord electrophysiology, anatomy, and behavior) to shed light on the circuits involved in recovery from spinal cord injury.

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SPINAL CORD TECHNIQUES TRAINING TRAVEL GRANT RECIPIENT:

CSCR19TTT003
Diego Prado De Maio
Rutgers University - $4,000

I am very interested in training in the area of neuroimmunology, a rapidly expanding field that shows significant promise. I believe spinal cord injury research is one area in particular that could greatly benefit from the application of immunology science, and I would like to gain the knowledge and skills necessary to carry this out. This course will provide me with in depth knowledge of techniques so that I will improve my surgical skills and create more repeatable data efficiently.

In this regard, I am currently working with a mouse model of decreased helper T cell immunity to determine the role of these cells in systemic lupus erythematosus and neurotrauma following a spinal cord injury. With this fellowship, I would be able to expand my current research and focus on the relationship between spinal cord injury and autoimmunity. My sponsor and I have established a plan based on current literature to investigate this actively developing area, including attending the Spinal Cord Injury Techniques Training Program at Ohio State University.

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SPINAL CORD TECHNIQUES TRAINING TRAVEL GRANT RECIPIENT:

CSCR19TTT004
Nisha Singh
Rutgers University - $4,000

As an aspiring biomedical researcher, I am interested in elucidating the molecular mechanisms underlying the secondary phase of spinal cord injury (SCI) to aid in the development of drugs and other pharmaceutical agents that can be used for treatment. In particular, identifying therapeutic targets in relevant molecular pathways, developing and optimizing modes of treatment delivery, and studying axon kinematics and pharmacokinetics, are areas that I would like to pursue. The SCI techniques training course will equip me with additional knowledge and experience that can be applied to more effectively explore these avenues of research.

Through the course, I hope to learn more about current in vivo approaches that are being used to study SCI. The course will give me a better understanding of these methodologies, their implementation, and the experimental designs associated with them. Applying these approaches to my research in conjunction with in vitro experiments will facilitate more comprehensive testing of pharmacologic agents that I identify as viable treatment options and characterizations of SCI pathology.

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