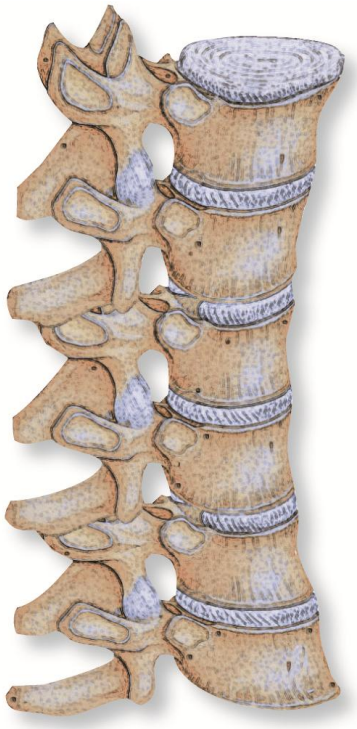
NEW YORK STATE | Department of Health
Wadsworth Center



SPINAL CORD INJURY RESEARCH BOARD

NYS SCIRB Annual Report

January 1, 2025, to December 31, 2025

I. INTRODUCTION

A spinal cord injury (SCI) was once thought of as incurable. The basic science carried out by researchers in this field, much of it accomplished in New York State, has served as an important stimulus for the clinical trials now underway in fields as diverse as neurorehabilitation, axon growth, cell biology, and robotics. Although it is not yet possible to reliably repair the human spinal cord, there are new treatments that improve the lives of SCI patients, and continued scientific explorations offer hope for doing more.

SCIs contribute to significant disability, illness, and death in the United States. Each year approximately 1,100 New York residents suffer traumatic SCIs[1] joining approximately 305,000 people living in the United States who have SCI.[2] The personal and economic costs to these individuals, their families, and society are immense.

Most frequently, these injuries are caused by motor vehicle accidents, falls, sports injuries, or acts of violence. SCI results in an abrupt change in the quality of life for those affected. Injuries to the spine near the head can result in quadriplegia, with the loss of motor control, sensation, and function of the arms, legs, bowel, bladder, chest, abdomen, and diaphragm. Injuries to the lower spine can result in loss of sensation and movement in the lower body, and loss of bowel and bladder control. Both types of injuries can result in significant chronic pain.

In addition to societal and individual costs incurred for medical care and through loss of productivity, there are significant costs for home and vehicle modifications, equipment purchase, medications, and personal assistance services. The National SCI Statistical Center reported that first-year costs for an individual with SCI range from approximately $447,037 to more than $1,369,755, with annual costs thereafter ranging from approximately $54,298 to $237,862.[2] These expenses are borne by individuals, their families, and society at large.

The New York State Spinal Cord Injury Research Board (SCIRB) was created in 1998 to solicit, review, and support proposals from leading New York State researchers in their efforts to find a cure for SCI. The Spinal Cord Injury Research Trust Fund (Trust Fund) was established to fund this research. It is financed primarily by a portion of surcharges on moving traffic violations, because motor vehicle accidents are the leading cause of SCI, followed by falls.[2] The SCIRB and Trust Fund are authorized by Title IV (Sections 250 through 251) of Article 2 of the Public Health Law (PBH) and Section 99-f of Article 6 of the State Finance Law (STF).

The SCIRB first convened in August 1999. The SCIRB is required to report annually to the Governor and Legislature on funds appropriated for SCI research and the progress of the SCIRB in terms of the results of its SCI research efforts.

1 New York State Department of Health, Bureau of Occupational Health and Injury Prevention, 2019 data

2 "Spinal Cord Injury Facts and Figures at a Glance." *National Spinal Cord Injury Statistical Center.* University of Alabama at Birmingham, 2024. Web. 29 August 2024. https://www.nscisc.uab.edu/

The SCIRB's mission and goal is to:

1. Seek major advances toward a cure and not simply incremental gains or incremental improvements for SCI patients.

2. Support research that tests novel hypotheses and/or advances innovative research approaches that could move the field of SCI research significantly forward toward discovering a cure for SCI.

The SCIRB's mission is to stimulate high-quality, innovative SCI research that will help promote treatment and cure for SCI, including methods reversing paralysis or restoring function caused by injury, or for minimizing or preventing damage occurring during acute phases of injury. To achieve this mission, the SCIRB advises the New York State Department of Health, Wadsworth Center, and Extramural Grants Administration regarding funding opportunities for competitive research awards to support New York State scientists and their collaborators from a variety of biomedical disciplines.

The SCIRB is responsible for advising the Commissioner of Health on research proposals from leading New York State researchers in their efforts to find a cure for SCI. Information about the SCIRB can be found at the Wadsworth Center's website: https://www.wadsworth.org/extramural/spinalcord.

The SCIRB appreciates the opportunity to serve the citizens of New York State by focusing on the important public health problem while stimulating economic growth through scientific research, investigation, and discovery. The SCIRB looks forward to providing additional financial support for such highly meritorious SCI research in the coming years.

II. SCIRB ORGANIZATION AND MEMBERSHIP

The SCIRB is comprised of 13 members appointed by the Governor and legislative leaders (see Appendix 3). By the end of 2025 the current composition of the SCIRB included three (2) researchers, seven (8) clinicians, and two (2) spinal cord-injured persons. Members serve four-year terms. Two (2) new appointments were made in 2025 and one (1) to be filled by the by the Speaker of the Assembly.

III. SCIRB OPERATIONS

In State Fiscal Year 2025-26, $8.5 million was programmed to support SCI research.
two (2) procurements had been released by the New York State Department of Health, Wadsworth Center, Extramural Grants Administration on behalf of the SCIRB.

Meetings are announced at least one week in advance whenever possible and are open to the public (in-person and virtually) in accordance with Open meetings law (Article 7 of the Public Officers Law). Meeting agendas are posted on the Wadsworth Center's Website at: https://www.wadsworth.org/extramural/spinalcord/meetings.

A recording of each meeting is available via the Department of Health's public Website https://www.health.ny.gov/events/webcasts/archivew/ for at least 30 days after the meeting, opening the proceedings to a wide audience.

The SCIRB Bylaws were amended in 2024 to updated language to be homogenous with Open Meetings Law and to include the newly adopted provisions found within Section 103-a(c). The bylaws can be found at https://www.wadsworth.org/extramural/spinalcord/advisory-board/statutes-bylaws.

IV. MAJOR ACTIVITIES OF THE SCIRB

Business Meetings

At its **April 11, 2025**, meeting, the Board welcomed Dr. Shelly Hsieh to the Board. The SCIRB voted and recommended funding for three (3) awards from the "Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 6)" RFA for a total of $491,790. They also voted to increase the possible number of penalties per application from 0.1 to 1.0, allowing for multiple penalties in each application at 0.1 each.

At its **October 10, 2025**, meeting the Board welcomed Dr. Ann Spungen. The SCIRB recommended funding for two (2) awards from the "Translational Research Projects in Spinal Cord Injury (Round 7)" Request for Applications (RFA) for a total of $10,893,507. These awards will begin in March 2026.

A tabular summary of these procurements can be found in Appendix 1.

Previously Recommended SCI Research Contracts

In July 2025, thirteen (13) Institutional Support for SCI Research in New York State (Round 7) contracts began their second year. The scientific progress resulting from these five (5) year awards can be found in Appendix 2.

In August 2025, eight (8) Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 5) completed their final year. The scientific progress resulting from these two (2) year awards can be found in Appendix 2.

By November 2025, one (1) PART award from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 4) completed their final year. The scientific progress resulting from this three (3) year award can be found in Appendix 2.

By September 2025, One (1) IDEA award from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 5) requested a 12-month contract extension. In September 2025, three (3) PART awards from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 5) completed their final year. Two, (2) PART awards from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 5) requested 12-month contract extensions. The scientific progress resulting from these two (2) and three (3) year awards, respectively, can be found in Appendix 2.

In September 2025, four (4) IDEA awards from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 6) completed their final year. In October 2025, four (4) PART awards from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activities (IDEA) in Spinal Cord Injury (Round 6) began their final year. The scientific progress

resulting from these two (2) and three (3) year awards, respectively, can be found in Appendix 2.

In October 2025, two (2) awards from Translational Research Projects in Spinal Cord Injury (Round 4) contracts began their third year. The scientific progress resulting from these four (4) year awards can be found in Appendix 2.

In July 2025, nine (9) awards from Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury (Round 7) began their first year. The scientific progress resulting from these two (2) and three (3) year awards, respectively, can be found in Appendix 2.

In September 2025, three (3) awards from Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 6) began their first year. The scientific progress resulting from these two (2) year awards can be found in Appendix 2.

Funding Opportunities

- Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 7)
- Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activities (IDEA)in Spinal Cord Injury (Round 8)

NYS SCI Research Symposium

The SCIRB discussed scheduling a future NYS SCI Research Symposium at their business meetings in 2025. A future symposium would highlight recent advances and developments in basic and translational SCI research, feature presentations of the research supported by the Program, and invite international/national speakers to present new discoveries.

A subcommittee was created to investigate the feasibility of holding a Symposium includes four SCIRB members and a representative from NYS Department of Health, Wadsworth Center, Extramural Grants Administration to act as a liaison for the Department of Health. This subcommittee met twice during 2025 in a preliminary capacity.

Appendix 1

Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 6)

Organization	Fellow and PI	Project Title	Recommended Funding
Winifred Masterson Burke Medical Research Institute	Edmund Hollis, Ph.D. & Caroline Machado, Post-Doctoral Fellow	Corticospinal dendritic dynamics during SCI rehabilitation	$192,000
Icahn School of Medicine at Mount Sinai	Jongyan Zou, MD, Ph.D. & Swagata Dey, Post-Doctoral Fellow	The role of guidance molecule PlexinB1 in astrocytosis and wound compaction in SCI	$192,000
Syracuse University	Victor Duenas, Ph.D. & Evan Tulsky, Pre-Doctoral Fellow	Development of a robotic leg stretching protocol to mitigate spasticity in people with SCI	$107,790
		Total (3 Awards)	**$491,790**

Translation Research Projects in Spinal Cord Injury (Round 7)

Organization	PI	Project Title	Recommended Funding
Columbia University	Jason B. Carmel	Epidural versus transcutaneous cervical spinal cord stimulation to improve arm and hand function in chronic spinal cord injury	$5,777,635
Columbia University	Sunil K. Agrawal	Improving Seated Postural Control in People with Spinal Cord Injury with a Robotic Trunk Support Trainer (TruST)	$5,115,872
		Total (2 Awards)	$10,893,507

Appendix 2

Scientific Progress Resulting from SCI Research Board Funded Projects

Institutional Support for SCI in New York State (Round 7)
Contract Term 07/01/2023-06/30/2028

Progress Reporting Period
01/01/2025-6/30/2025

13 Awards, Procurement Total: $3,900,000

1. **Winifred Burke Medical Research Institute**
   Funding was used to support the Core Manager at the Structural and Functional Imaging Core at Burke Neurological Institute (BNI). The Structural and Functional Imaging Core is used by all SCI researchers at BNI to produce scientific results and discoveries, support future funding applications, and generate high quality images for scientific talks and publications. Funds were also used to provide salary support to the Director of BNI.

2. **The Research Foundation for SUNY – Stony Brook**
   Several pieces of equipment were purchased using the SCIRB funds: *HTEC-600 All-in-One Stand-Alone HPLC-ECD system with Clarity Data System Analysis Software, basic reagents and supplies for producing tissue samples, and miscellaneous glass electrode fabricating supplies.*

   Equipment is being used in a collaborative pilot project to continue to obtain preliminary data investigating serotonin-dependent BDNF pathway-mediated neuroplasticity in histological sections of lumbosacral spinal cord regions controlling bladder function in response to novel task-specific training in bladder function. The new Biochemical Assay/Analysis Core equipment (ultrasonic homogenizer) are currently being used to process lumbosacral spinal cord tissue samples to obtain total protein homogenates that will be used to obtain preliminary biochemical assay data for this pilot project. Once additional histological data and preliminary biochemical assay data are obtained in this pilot project, the preliminary findings will be presented at a scientific conference (*e.g.*, American Physiology Summit 2026, or Society for Neuroscience 2026).

3. **The Research Foundation for SUNY – Downstate Health Sciences University**
   Funding was used to support a Postdoctoral Researcher's effort on a project aims to leverage the most detailed biophysical model of motor cortex (M1) neural circuits to characterize how low-dimensional latent dynamics, associated with behavior, are represented in EEG signals. This research has contributed to an R01 grant proposal submitted to NIH "AI-based automated development of multiscale brain circuit models" and the creation of a Center for AI in Mental Health, funded by the SUNY STRIVE program.

4. **Bronx Veterans Medical Research Foundation**
   Funding was used to support equipment that is used by multiple investigators within the Spinal Cord Damage Research Center. These include: Lokomat, DXA and Leica Cryostat. Studies supported by the equipment include understanding the effects of a multi-drug treatment regimen on tracts that survived SCI.

5. **Icahn School of Medicine at Mount Sinai**
   Funding was used to support staff in their project design, data interpretation, and manuscript preparation.

6. **Regenerative Research Foundation**
   Funds were used to partially support Dr. Hill's (Principal Investigator) salary. These funds have enabled her to work on grant writing and generating preliminary data (staining and examination of tissue sections) for a follow up study to prior work (PMCID: PMC9635187), complete work associated with obtaining the necessary regulatory approvals for SCI studies (IACUC and IBC) and manage the SCI studies at the RRF.

   Dr. Hill's lab is dedicated to spinal cord injury repair and the development and preclinical testing of interventions to promote recovery from SCI. Partial funding of Dr. Hill's salary allows her dedicated time to write, generate new ideas, maintain regulatory compliance and perform experiments necessary to generate preliminary data that will be used to submit an upcoming grant application.

7. **University of Rochester**
   Funding was used to partially support the Principal Investigator's effort, as well as the effort of new staff who have joined the research team. The funds have aided in the recruitment, training and retention of staff.

8. **Research Foundation of CUNY – Staten Island**
   In Year 1, Equipment purchased was purchased and installed to support SCI research and especially to develop a lab station for bladder studies after transspinal stimulation and locomotor training in people with SCI. Researchers used the equipment to record transspinal evoked potentials in people with SCI during assisted stepping with the Lokomat. Further, the sterilization equipment was used for urodynamics tests performed in people with SCI after transspinal stimulation for recovery of somatic and non-somatic functions. These funds supported partial salary support for Dr. Abdullah Sayed Ahmad.

9. **The Feinstein Institute for Medical Research**
   Funding supported salaries and the purchase of equipment and supplies, 3 separate projects that aim to improve the understanding of factors that influence health and physical function in persons with traumatic spinal cord injury (SCI). Funding for Project 1, "Immunological Profiles in Veterans with Chronic SCI" will assist in performing systemic immunological profiling of Veterans with chronic SCI (PI: Bloom) and to explore potential correlations with anti-COVID antibodies measured in samples from the same individuals.

Funding for Project 2, “Vaccine Responsiveness in People with SCI” will be used to assist in expanding inclusion criteria beyond that of a funded DOD study, (W81XWH2211032, Biomarkers of Immune Dysfunction and Vaccine Responsiveness in People with Chronic Traumatic SCI, (SCIVAX)" (PI: Bloom). Funding will partially support inclusion of persons with SCI who satisfy all other inclusion/exclusion criteria, and present at the Dept. of Physical Medicine and Rehabilitation outpatient SCI clinic for a flu or COVID-19 vaccine/booster to promote their health, but are less than one year from initial injury Funding for Project 3 (PI: Song), “Low intensity trans-spinal focused ultrasound stimulation (tsFUS) for the treatment of neuropathic pain” will be used to assist with the study the mechanism of tsFUS in the spinal circuit, and to develop a novel neuromodulation strategy for pain control after spinal cord injury.

10. Rensselaer Polytechnic Institute

The NYSCRIB funding is used to support our staff member Dr. John Leman, who manages the lab day-today activities. Dr. Leman benefited from a rich set of training and professional development opportunities while working on the NYS DOH SCIRB Institutional Support–funded project focused on developing biomaterials from estrogen pro-drugs for spinal cord injury applications. Through this support, he regularly attended scientific seminars, workshops, and invited talks that strengthened his expertise in biomaterials design, neurotrauma, and drug-delivery strategies. He also participated in regional and national conferences, where he presented research findings, broadened his professional network, and gained exposure to advancements across the field. In addition, Dr. Leman refined his leadership and mentoring skills by supervising undergraduate researchers in the lab at RPI, guiding their experimental training, fostering their scientific development, and managing day-to-day research activities. Taken together, these experiences provided him with strong technical, professional, and mentoring foundations that will continue to support his career trajectory

11. The Trustees of Columbia University in the City of New York

Funding will be used by the Robotics and Rehabilitation Lab at Columbia University to develop robotics for trunk and neck control for measurement and active control, with the goal of investigating the coordination and control of head and trunk motion while sitting and standing during tasks performed in augmented reality. Funding will assist with the characterization of spinal cord injury patients and compare with age-matched healthy adults. Funding will be used by the Movement Recovery Lab at Columbia to test multi-segment spinal cord stimulation to uncover its principles and maximize selectivity of individual muscles in rats.

12. Research Foundation of CUNY obo City College of New York

Funding was utilized to support the stipend of Graduate Research Assistant, s. Chinny Oakfor. Results from Dr. Undieh’s research suggest that multiple mechanisms may be involved in the actions of various chemical compounds to promote nucleolipid biosynthesis. Ms. Okafor is conducting research to explore and clarify the mechanisms by which nonpeptide neurotrophic compounds may modulate nucleolipid biosynthesis and neurotrophic signaling. This understanding will help in prioritizing and optimizing compounds for further study as leads for SCI treatment.

13. Albany Research Institute, Inc.

This institutional grant (PI: Jonathan Wolpaw) supports three specific aims, each focused on developing a new noninvasive therapeutic approach. Data generated through this funding have led to applications to the SCIRB for clinical trials, including a controlled trial of H-reflex operant conditioning, as well as to the Nielson Foundation, the VA Office of Research and Development, and the National Institutes of Health.

Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 5)
Contract Term 09/01/2023-08/31/2025

Progress Reporting Period
03/01/2025-08/31/2025

8 Awards, Procurement Total: $1,221,359

1. **Winifred Burke Medical Research Institute**
   Yutaka Yoshida, Ph.D.; Teruko Danjo Current Fellow
   Postdoctoral: $180,581
   Restoration of Motor Function Following SCI Via Optical Stimulation

   Introduction/Background: During this period, an original applicant, Alzahraa Amer, had to move to Chicago due to her personal reason. Therefore, the fellowship has been transferred to Teruko Danjo. She has both MD and PhD and has interest in promoting motor recovery of human SCI patients. Since SCI research is new to her, she started learning SCI from members in Yoshida lab. So far, she has successfully set up the optogenetic stimulation in the cervical spinal cord.

   Progress Towards Specific Aims: During this period, the focus was on setting up skilled reaching and grasping behaviors after the cervical spinal cord injury.

   Impact: Optogenetic spinal stimulation would provide new therapeutic strategy for SCI patients.

2. **Columbia University**
   Jason B. Carmel, M.D., Ph.D.; Windsor KC Ting, Applicant Fellow
   Postdoctoral: $190,000
   Functional Dissection of the Rat Corticoreticular Pathway in SCI

   Introduction/Background: Spinal cord injury can be debilitating, and for patients, recovery of fine motor function is a top priority. Researchers proposed to study the corticoreticular pathway using neural dissection techniques and assess the effect of activating and inhibiting this pathway on fine motor function, in healthy rodents as well as after spinal cord injury.

   Progress Towards Specific Aims: For necessity, researchers developed an accurate, scalable pipeline to assess fine motor function and have preliminary evidence demonstrating reduction of corticospinal pairing physiology and abrogation of reticulospinal pairing with reticulospinal inhibition.

   Impact: This work helps researchers to understand the neural circuits implicated in normal and injured fine motor function in rodents, which they hope to directly translate to more effective treatment in humans. Support to do this work and to train a postdoctoral fellow at Columbia is in large part due to this opportunity by NYS.

3. **The Research Foundation of CUNY obo City College of New York**
John H. Martin, Ph.D.; Jasmine Pathan, Applicant Fellow, Thelma Bethea, Current Fellow
Predoctoral: $118,000
Activity and Connectivity Maintain Premotor Interneuron Viability After SCI

Introduction/Background: During the prior funding period researchers discovered that hyperreflexia in the unilateral corticospinal tract (CST) injury model for SCI mechanisms was determined by aberrant stretch reflex sprouting that is not compensated for by an inhibitory presynaptic mechanism (GABApre). We also discovered that motor neuron excitability, due to the membrane-bound protein potassium-chloride co-transporter #2 (KCC2) was unchanged. SCI and CST injury reduces motor cortex-evoked muscle potential responses (MEPs), which is a physiological marker for weakness after injury. During this funding period researchers determined, using a bilateral CST lesion to better model a midline cervical SCI, if motor cortex neuromodulation can be used to abrogate hyperreflexia and enhance muscle potential recruitment after injury.

Progress Towards Specific Aims: Hyperreflexia after bilateral CST injury produces a loss of membrane-bound KCC2, as well as glutaminergic 1A afferent sprouting without commensurate GABApre changes. Motor cortex neuromodulation promotes recovery from hyperreflexia, likely a consequence of promoting appropriate GABApre regulation of increased excitatory afferent terminals on motor neurons, as well as reinstatement of membrane-bound KCC2. Researcher shows that bilateral CST lesion produced a loss of MEP recruitment, and that motor cortex neuromodulation was able to promote MEPs to baseline levels.

Impact: Researchers have, for the first time, used motor cortex neuromodulation to abrogate hyperflexia and strengthen motor cortex-to-muscle connectivity. This can be translated to the human using non-invasive TMS; instead of epidural electrical stimulation.

4. **Rensselaer Polytechnic Institute**
Ryan J. Gilbert, Ph.D.; Edmund F. Palermo, Ph.D.; Adelle Hamilton, Applicant Fellow
Predoctoral: $122,400
Novel Poly (Pro-Gabapentin) Films to Provide Neuroprotection and Increase Neurite Extension

Introduction/Background: Neural interfaces link the nervous system with the outside world via electrodes and offer the possibility of helping people with severe sensory and motor disabilities, like those who have suffered from spinal cord injury (SCI). Following electrode insertion into the brain, the tissue gets sheared and free radical species are released which leads to neuronal death and glia activation, preventing proper interface between the electrodes and healthy brain tissue. Curcumin, a naturally occurring molecule, has antioxidant and anti-inflammatory properties and when used in polymer form, could act as an electrode coating.

Progress Towards Specific Aims: Researchers have optimized electrospinning parameters to the following: 12wt% P75 solution in HFIP, electro-spun for 20 minutes under the following conditions: 2000rpm, 18kV, 2ml/hr flow rate, 6cm gap distance. Figure 1A and 1B below portrays the clear P75 fiber alignment under 1000X and 2500X magnification from scanning electron microscopy. What is also interesting is that researchers see interconnecting branches from fiber to fiber. Through Fast Fourier Transform they have quantitatively measured the AUC to be 22.1 (AUC = 1 is perfectly aligned, AUC =100 is randomly oriented fibers). Researchers have also shown that they obtain an average coverage of 92.18% of P75 fibers over the poly-L-lactic acid (PLLA) film. This coverage is ideal as they want cells to have complete contact with the fibers rather than the film underneath for maximum efficiency. Furthermore, they measured the diameter of the fibers to be roughly 2.023μm, which is consistent with previous studies and is ideal for cell migration along the orientation of the fibers.

After characterizing fiber morphology and topography, they explored its ability to sequester free radicals and retain its antioxidant properties. They compared that of a P75 film of the same mass of the fibers by performing a 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay. Comparing P75 fibers to films, on day 0, they see that only 37.87% of the free radicals were present, meaning that the P75 fibers sequestered 67.65% of the free radicals. Whereas, at the same time point, the P75 films only sequestered 18.15% of the free radicals (Figure 3A). This is also evident in Figure 2B that depicts the color change of native purple color of DPPH to its reduced, yellow color under the fiber group. However, after 5 days of incubation with free radicals, they see that the P75 fibers had a slight decrease from 37.87% to 30.99% of free radicals remaining. This provides further evidence of a more onset reduction of DPPH from P75 at day 0. Interestingly, after 5 days of DPPH incubation, in the presence of films, 32.35% of free radicals remained, showing no significant difference from the fiber group.

When considering a biomaterial for tissue applications, the surface must not be toxic for the cells in order to promote cell proliferation and migration. For this researchers pursued an *in vitro* metabolic assay (PrestoBlue™) with primary rat Schwann cells. PrestoBlue™ contains resazurin, a non-fluorescent blue dye. Metabolically active cells with functional mitochondria, cytosolic, and microsomal enzymes reduce resazurin to resorufin, a pink, highly fluorescent compound. Where the degree of fluorescence directly correlates with the number of viable cells and their metabolic activity. After culture, when comparing P75 fibers to PLLA fibers (a well characterized polymer in Dr. Gilbert's lab), researchers see that the fluorescence intensity of the P75 fiber group is roughly double that of the PLLA fibers. Researchers may be able to infer that the Schwann are more metabolically active on P75 fibers and as such, these fibers would be a prime candidate for tissue engineering applications.

Impact: Researchers believe the impact of the project will be in the synthesis of poly(pro-drug) forms of curcumin which show quenching of ROS at the injury site. Such polymer pro-drug forms may not only negate reactive species but also act as a guidance cue to direct the migration of cells following spinal cord injury.

5. Columbia University
Sunil K. Agrawal, Ph.D.; Priya Kulkami, Applicant Fellow
Predoctoral: $116,000
Improving Trunk and Neck Coordination During Reaching Tasks with a Robotic Neck Brace in Individuals with Spinal Cord Injury

Introduction/Background: High thoracic and cervical spinal cord injury (SCI) can affect both postural control as well as head-trunk coordination. Since head and trunk coordination is known to be very important during reaching tasks, this coordination should be studied in both healthy subjects and those affected by SCI. The insights yielded by this study may be used to improve this coordination in patients with spinal cord injury. Using a robotic neck brace to provide external forces during reaching can assist this coordination and may improve reaching performance.

Progress Towards Specific Aims: A novel neck brace has been developed for the purposes of neck control relative to the trunk. This neck brace allows three degrees-of-freedom of movement, including the ability to apply a supporting vertical force to keep the head close to the neutral configuration. The neck device can control the orientation of the head relative to the shoulders and simultaneously provide a vertical supporting force on the head. A physical design of the wearable brace was constructed and was bench tested to demonstrate the feasibility of the idea. In the last six months, a human study was conducted with ten healthy subjects who wore the brace. The head-neck was controlled to be in a specific orientation while a force was applied on the head. Researchers studied several issues such as: (i) ability to keep the head-neck in a specific orientation while forces were applied, (ii) ability to apply desired forces, (iii) effect on the muscle activity of the participant, (iv) fit of the brace to the participant and its effect on performance on the brace. These aspects are currently being summarized into a scientific paper which will be submitted for a future publication to a journal.

Impact: This project may improve the way patients with SCI perform seated reaching tasks. Insights gained from characterization can answer underlying questions about head-trunk coordination and rehabilitation in people with SCI.

6. Icahn School of Medicine at Mount Sinai
Ravi Iyengar, Ph.D.; Nicholas Johnson, Applicant Fellow
Postdoctoral: $191,978
Multi-Drug Combination Effects on Physical Therapy-Enabled Recovery After SCI

Introduction/Background: Spinal Cord Injury (SCI) is a debilitating disease that affects approximates 305,000 people in the United states. SCI involves the interruption of nervous connection between the brain and the body, leading to the loss of sensation and motor function. There are no approved pharmacological interventions for SCI, but physical therapy improves function in most patients. However, functional recovery is often limited. SCI is particularly intractable because central nervous system neurons, including the spinal cord, do not intrinsically regenerate. With SCI, neurons also face extrinsic inhibitors to rengeneration. Dr. Iyengar's lab has identified drug targets to overcome both the intrinsic and extrinsic factors inhibiting functional recovery after SCI and has shown the efficacy of this drug combination in an optic nerve model of nerve

injury. The goal of this project is to show the efficacy of this drug combination for improving functional outcomes in combination with physical therapy in an animal model of SCI.

Progress Towards Specific Aims: The fellow has completed pilot experiments with mice to identify an injury severity that recapitulates severe injury in humans, in which there will be a measurable difference between the natural recovery mice experience over this time period, the recovery with physical therapy, and the recovery with the full combination of physical therapy and pharmaceutical intervention.
The proposed experiments have begun. The fellow has performed the surgeries necessary for intracranial injections and the first cohort of this experiment will be completed in the coming weeks.

Impact: By the end of this experiment, researchers expect to have shown the efficacy of a combinatorial therapy for SCI. By combining a pharmaceutical aproach and physical therapy, they anticipate that animals will show 90% or more functional recovery over just 60% without intervention. Functional recovery is the most important goal in the treatment of SCI. This project is the next step in developing a treatment for humans that provides complete or near-complete functional recovery following SCI.

7. Columbia University
Sunil K. Agrawal, Ph.D.; Chawin Ophaswongse, Applicant Fellow
Postdoctoral: $180,000
Improving Trunk Control While Seated on Wheelchairs in Individuals with Spinal Cord Injury Using Robotics

Introduction/Background: Individuals with cervical or high thoracic spinal cord injuries (SCI) often rely on wheelchairs for mobility but face significant challenges in activities of daily living (ADL) due to impaired trunk control and stability. Tasks such as eating, working at a desk, opening doors, or reaching for objects can become difficult. While passive devices may provide trunk support in wheelchairs, they often restrict mobility and limit opportunities for postural rehabilitation. To address this, researchers have developed the Wheelchair for Active Postural Support System (WRAPS), an actuated robotic torso support system. WRAPS stabilizes the trunk while allowing controlled motion during seated activities, offering SCI patients the potential to improve their postural control and better assist with ADL.

Progress Towards Specific Aims: Researchers developed a variable resistance controller in WRAPS for physical assistance around the reach workspace. They then tested the controller with able-bodies subjects to validate performance and postural stability when the robot interacting with human. A protocol was approved by Columbia Institutional Review Board (IRB), no. AAAV2487, to recruit SCI patients for experiment with goals similar to Specific Aim (I). A new EEG dataset is planned to collect to improve the quality of the signals. A new EEG acquisition pipeline is being developed for integration with the WRAPS system.

Impact: WRAPS stabilizes the trunk while allowing controlled motion during seated activities, offering SCI patients the potential to improve their postural control and better assist with ADL.

8. Cornell University

Yadong Wang, Ph.D.; Catia Dombaxe, Applicant Fellow
Predoctoral: $122,400
Examine the effects Goldfish Extracellular Matrix (ECM) Hydrogel and Chondroitinase ABC (ChABC) in Injured Mice.

Introduction/Background: Every year, half a million individuals worldwide face the devastating impact of Spinal Cord Injury (SCI), with 18,000 cases in the US alone. With no effective treatment currently available, the urgency to develop new therapies is paramount. This research unveils a groundbreaking approach inspired by the regenerative capabilities of lower vertebrates, such as goldfish. The proposed treatment involves a Hyaluronic Acid blend hydrogel delivering naturally occurring regenerative proteins found in goldfish spinal cord (gECM) and stabilized Chondroitinase ABC (ChABC) in a lipocoacervate (ChABC-LipCo). This combination therapy aims to create a growth-permissive environment for axonal regrowth and inhibit scar tissue formation in mouse models of SCI.

Progress Towards Specific Aims: Researchers successfully decellularized goldfish spinal cord tissue. The tissue harvested at 5 weeks timepoint was used to conduct proteomics and bioinformatics analysis. Through the bioinformatics analysis, we found the top 5 proteins with biological function in tissue regeneration, wound healing, and anti-inflammatory properties. Further analysis is being conducted to validate these proteins. Additionally, they finished the composition of HA-Fibrin hydrogel and tested it *in vitro* using a dorsal root ganglion (DRG) explant mouse model. Their data shows extensive neurite outgrowth and branching in DRG cultured in gECM hydrogel compared to control group.

Impact: This research promises a paradigm shift in SCI treatment, offering hope to thousands. By harnessing nature's regenerative mechanisms and combining them in an innovative therapeutic approach, this study aims to provide a novel methodology for spinal cord regeneration in mice. The potential for a minimally invasive injectable treatment could significantly enhance patient care, allowing individuals to regain lost functions and improve their overall quality of life. This journey from nature's insights to transformative therapy holds the key to revitalizing hope for those affected by SCI worldwide.

Predoctoral and Postdoctoral Fellowships in Spinal Cord Injury Research (Round 6)
Contract Term 09/01/2025-08/31/2027

Progress Reporting Period
First Progress Reports due 1/31/26

3 Awards, Procurement Total: $491,790

1. **Winifred Burke Medical Research Institute**
   Edmund Hollis, Ph.D.; Caroline Machado, Application Fellow
   Postdoctoral: $192,000
   Corticospinal dendritic dynamics during SCI rehabilitation

   Lay Abstract: The main goal of this research proposal is to determine how rehabilitation helps injured neurons reconnect and improve the recovery of movement following SCI, and to provide the resources for me to develop Fellow's mentorship and leadership skills to become an independent investigator. The central hypothesis is that rehabilitation after SCI stabilizes new synaptic connections to injured corticospinal neurons. Knowing how this works is key to developing effective therapies.

2. **Icahn School of Medicine at Mount Sinai**
   Hongyan Zou, MD., Ph.D.; Swagata Dey, Application Fellow
   Postdoctoral: $192,000
   The role of guidance molecule PlexinB1 in astrocytosis and wound compaction in SCI

   Lay Abstract: After spinal cord injury (SCI), glial cells are mobilized to form a protective barrier that separates lesion core from healthy spinal cord tissues. The glial barrier is critical to limit inflammatory spread, facilitate debris clearing, and promote wound compaction to minimize injury size and maximize repair area. Reactive astrocytes also build a glial bridge to guide regenerating axons across the injury site. However, the signaling mechanisms that orchestrate glial cell mobilization remain unclear. Recent efforts from the Zou laboratory have revealed a pivotal role of axon guidance receptor Plexin-Bs in mediating cell-cell communication and physical alignment of glial cells at lesion site after SCI. The Fellow's proposal focuses on Plexin-B1 signaling in astrocyte activation. They will test the central hypothesis that Plexin-B1 activation in reactive astrocytes facilities glial communication in building a protective glial barrier during wound healing after SCI. They will combine co-culture systems, time-lapse imaging, mouse genetics, and in vivo SCI paradigms. The new knowledge of signaling mechanisms of glial cell communication during wound healing will open doors for new strategies to enhance neural repair and functional recovery after SCI.

3. Syracuse University

Victor Duenas, Ph.D.; Evan Tulsky, Application Fellow
Predoctoral: $107,790
Development of a robotic leg stretching protocol to mitigate spasticity in people with SCI

Lay Abstract: Spasticity, which is a common condition in people with chronic spinal cord injury (SCI), negatively interferes with activities of daily living. Spasticity can lead to loss of balance, falls, injuries, and contractures. Muscles contract uncontrollably or become too stiff, thus limiting leg movement. Treatments include oral medications, surgery, and physical therapy. Stretching is a primary treatment in which physical therapists or caregivers apply manual stretches to provide relief from spasms and improve passive range of motion. However, providing repeatable and reliable stretching is caregiver intensive.

Researcher's goal is to develop an automated strategy to mitigate the debilitating effects of spasticity after a SCI through personalized muscle stretching facilitated by a powered, wearable leg device controlled by a closed-loop algorithm. The overall objectives are to 1) develop a robotic leg stretching protocol to customize the application of static and dynamic leg stretching; and 2) evaluate the stretching protocol in people with spasticity post SCI, and establish safety, satisfaction, and ease of use.

Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury Research (Round 4)
9 Total Awards; IDEA Contract Term 11/01/2021-10/31/2023; PART Contract Term 11/01/2021-10/31/2024, Procurement Total: $3,490,176

Progress Reporting Period
05/01/25-10/31/2025 (IDEA)

1 Active IDEA award during reporting period due to NCE

1. **Research foundation for SUNY Stony Brook**
   Irene C. Solomon, Ph.D.
   IDEA: $357,782
   Neuroprotective Strategies to Minimize SCI Tissue Damage and Improve Bladder and Respiratory Function

   Introduction/Background: Spinal cord injury (SCI) initiates a secondary cascade of pathological processes that leads to further cellular/tissue damage and loss. Thus, there is a need to develop, implement, and optimize therapies focused on minimizing the extent of secondary injury-related cellular/tissue damage and loss following SCI. To this end, administration of the antibiotic minocycline (MIN) and the peroxisome proliferator-activated receptor gamma agonist pioglitazone (PIO), both of which are commonly used FDA-approved clinical agents, have been shown to exert neuroprotective actions in central nervous system injury/disease. The efficacy of these agents on bladder and respiratory dysfunction following SCI are unknown. Therefore, this project is designed to investigate the neuroprotective effects of MIN, PIO, and combined MIN/PIO treatment as a pharmacology-based therapeutic strategy to minimize secondary injury-related neural tissue damage/loss and promote improvement of bladder and respiratory function in an adult rat moderate contusion SCI model.

   Progress Towards Specific Aims: Researchers have conducted additional data analysis for our experiments evaluating the effects of 7-day MIN (or baytril (BAY) control) treatment beginning at 24-hr post-SCI on reflex micturition behaviors in anesthetized rats. These analyses revealed that in ~67% of the rats treated with MIN at this time point post-SCI, in addition to the reduction in SCI-related bladder overactivity, a restoration of bladder-sphincter coordination was observed. Researchers have also continued processing of SCI tissue samples for evaluation of the lesion site, including MIN-induced changes in anti-inflammatory and neuroprotective markers. Researchers also restarted pilot experiments evaluating the effects of 7-day PIO (or PBS vehicle control) treatment following SCI on recovery of spontaneous and reflex bladder function; however, the data have not yet been analyzed.

   Future Directions: Researchers plan to continue with their assays on the SCI tissue samples from the MIN experiments as well as continue with our PIO experiments during the next reporting period.

Impact: Our study is implementing a promising non-invasive pharmacology-based neuroprotective intervention strategy using currently available FDA-approved agents to minimize SCI-induced secondary injury-related neural tissue damage/loss and promote spontaneous improvement in bladder function in an adult rat moderate contusion SCI model. This therapeutic approach could be easily integrated into clinical use to facilitate recovery of bladder function and exert a significant positive impact on quality of life in SCI patients.

Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury Research (Round 5)
9 Total Awards; IDEA Contract Term 10/01/2022-09/30/2024; PART Contract Term 10/01/2022-09/30/2025, Procurement Total: $5,750-948

Progress Reporting Period
04/01/2025-09/30/2025 (IDEA); 04/01/2025-09/30/2025 (PART)

5 Active during reporting period due to NCE

1. **Winifred Masterson Burke Medical Research Institute**
   Edmund R. Hollis, Ph.D.; Kathleen M. Friel, Ph.D.
   PART: $990,000
   Enhancing Nerve Transfer Surgery to Restore Hand and Arm Function in Chronic Tetraplegia

   Introduction/Background: Individuals who have limited use of their arms and hands because of spinal cord injury (SCI) experience a decreased quality of life and incur significant long-term care costs. Approximately one-third of people with chronic SCI could benefit considerably from nerve transfer surgery, where working nerves are transferred to paralyzed arm muscles to restore movement. Although the procedure has the potential to greatly enhance arm function, outcomes can vary. The primary objective of this research is to improve recovery for these individuals by exploring two avenues that have the potential to enhance outcomes.

   Progress Towards Specific Aims: Aim 1. Determine the effects of robot-assisted rehabilitation on dexterous hand movements and cortical motor map changes in tetraplegic individuals following nerve transfer surgery (Pilot Clinical Trial). The first aim of this study involves investigating whether robotic training of the arm that underwent nerve transfer can improve movement and strength recovery. Four participants were enrolled, three of whom have completed six weeks of robotic training at one-year post-surgery. An additional individual has had nerve transfer surgery and is currently undergoing robotic training.
   Aim 2. Determine the regeneration-promoting effects of conditioning electrical stimulation in a large animal model of radial nerve repair. All four subjects have completed behavioral and electrophysiology studies and researchers are currently performing histological studies. Evaluation of behavioral outcomes and histology is ongoing.

   Future Directions: For aim 1, Researchers will analyze data from the most recent participants to complete intensive, robotic rehabilitation during the next period.
   For aim 2, Researchers will analyze data from all animals (behavior, histology, and physiology).

   Impact: The planned research will provide crucial insights into how to optimize outcomes for individuals with SCI who undergo nerve transfer surgery.

2. **Research Foundation for SUNY Stony Brook**
Irene C. Solomon, Ph.D.; Steven J. Weissbart, M.D.
PART: $986,610
Therapeutic Intermittent Hypoxia to Reduce Detrusor Overactivity and Symptom Severity in Chronic Incomplete SCI: Translation and Mechanisms

Introduction/Background: Spinal cord injury (SCI) has a profound negative impact on lower urinary tract (LUT) function, resulting in problems with urine storage and emptying of the bladder that are associated with a high degree of morbidity and a poor quality of life. While the injured spinal cord exhibits a robust capacity for neural plasticity that promotes spontaneous functional recovery, this recovery is rarely complete, and deficits persist. Preclinical studies in our laboratory have been using neural plasticity-inducing acute intermittent hypoxia (AIH) as a strategy to reduce bladder over-activity (*i.e.*, non-voiding bladder contractions) and promote improvements in bladder function in rats with SCI. While our observations are encouraging, the impact of therapeutic AIH as a strategy to improve bladder function in humans with SCI remains to be evaluated. Moreover, the neural mechanisms that underlie AIH-induced improvements in bladder function are unknown. This project is designed to initiate translation of our work (SA1: human subjects - *proof of concept pilot study*) and evaluate possible neural mechanisms for AIH-induced improvements in LUT function (SA2: preclinical rat studies).

Progress Towards Specific Aims: Researchers have continued with recruitment for the SA1 experiments evaluating the effects AIH treatment on clinical indices of LUT function in human subjects with neurogenic bladder (SCI and MS). Researchers have also continued with SA2A experiments evaluating potential contributions of serotonergic (5-HT) mechanisms in AIH-induced improvements in LUT function.

Future Directions: Researchers plan to continue with the SA1 recruitment efforts and experiments in human subjects with SCI (and MS and idiopathic OAB controls) and our SA2 preclinical mechanistic studies in rats with SCI during the next reporting period.

Impact: This project will provide novel information about the benefits of AIH therapies to improve clinical indices of bladder function and symptom severity/bother in SCI, identify potential neuromodulatory mechanisms (which have yet to be determined in SCI) that contribute to AIH therapy-induced improvements in bladder function in SCI, and lay the groundwork to enable future clinical trials and the transition of AIH therapies to clinical management of bladder dysfunction following SCI.

3. **Icahn School of Medicine at Mount Sinai**
Leif A. Havton, M.D., Ph.D. (through 12/15/2024), Noam Harel, M.D., Ph.D. (starting 12/16/2024)
PART: $926,620
Augmentation of Bladder Function by Transcutaneous Spinal Cord Stimulation After Conus Medullaris Injury in Primates

Introduction/Background: Injuries to the most caudal portion of the spinal cord, including the sacral segments of the spinal cord are referred to as conus medullaris (CM) forms of spinal cord injury (SCI). Associated lumbosacral nerve roots, referred to as the cauda equina (CE), are typically also injured in the setting of trauma to the

lower thoracic and upper lumbar spine. The overall goal for this is to explore the potential utility of non-invasive transcutaneous spinal cord stimulation (TSCS) for improving bladder emptying after a CM/CE form of spinal cord injury. The studies are performed in a non-human primate (NHP) model of an incomplete CM/CE form of SCI. An incomplete avulsion injury to ventral roots that innervate the lower urinary tract is performed in male and female rhesus macaques with the goal of achieving an LUT denervation of approximately 50%. At multiple time points after the injury for a post-operative study period of 6 months, physiologic studies of the lower urinary tract, including urodynamic bladder pressure recordings during bladder filling and emptying, are combined with transcutaneous spinal cord stimulation in NHPs under light sedation. The partial filling of the bladder is performed to activate voiding reflexes in sedated Voiding and efficiency of bladder emptying information are collected both with and without TSCS.

Progress Towards Specific Aims: During the first reporting period work was performed to meet the institutional requirement for the proposed animal studies at the California National Primate Research Center (CNPRC)/UC Davis. This included the preparation of the UC Davis Institutional Animal Care and Use Committee (IACUC) protocol for NHP research studies and assignment of training to research team members based on UC Davis training requirements for work with NHPs.

Impact: Studies of conus medullaris (CM)/cauda equina (CE) forms of spinal cord injury represent an underserved area of basic and translational research. Presently, there are no available treatments to reverse or augment neurological functions after CM/CE injuries in patient populations. If successful, our planned studies may contribute to the development of a new neuromodulation treatment strategy, using non-invasive electrical stimulation of the spinal cord, to augment voiding and bladder emptying after CM/CE injuries. Improved bladder function after spinal cord injury has been recognized by several patient groups as a high priority for improved quality of life and independence in the community.

4. Albany Research Institute, Inc.
Disha Gupta, Ph.D.
IDEA: $356,538
Operant Conditioning of Somatosensory Evoked Potentials to Improve Motor Function after SCI

Introduction/Background: This study aims to improve functional recovery in individuals with incomplete spinal cord injury (iSCI) by enhancing weakened central nervous system responses to sensory input. While most rehabilitation research focuses on restoring motor control through descending pathways, sensory impairments—often overlooked—play a crucial role in motor function. Sensory input is essential for effective movement, and its loss can limit motor rehabilitation. This study utilizes Targeted Neuroplasticity via a novel non-invasive Brain-Computer Interface (BCI) to strengthen sensory pathways and support overall recovery.

Progress Towards Specific Aims: This study has two aims: i) To develop and validate a novel somatosensory BCI that uses operant conditioning to augment

the sensory brain response; ii) Assess its impact on behavioral function and physiology. The sensory BCI system called Cortical-Evoked Potential Operant Conditioning System (C-EPOCS) has been developed and tested to support conditioning of both upper and lower limbs. Vibrotactile (sensory) and robotic (motor) assessment protocols for longitudinal testing have been optimized, including testing their inter-session reliability.

Impact: This study has resulted in the development of a) C-EPOCS–a BCI that enables realtime operant conditioning of a targeted brain response. Built upon the foundation of EPOCS—a system currently structured for processing muscle responses—C-EPOCS enables real-time processing and feedback of sensory brain responses. It supports pseudo-real-time data analysis and rapid target threshold selection; b) optimized stimulation protocol and analysis pipeline designed to reliably elicit target somatosensory cortical components, with inter-session stability; c) programmable trigger hardware, (useful for various neuroscience studies); d) vibrotactile sensory assessment system including open-source vibrotactile hardware assessment software; d) integration of neurophysiological assessment system with a robot-based kinematic evaluation system.

5. The Research Foundation of CUNY obo City College of New York
John Martin, Ph.D.
PART: $982,800
Leveraging LTP to Promote CST Axon Sprouting in the Spinal Cord

Introduction/Background: Restoring function after SCI will depend on durable plasticity to reconnect the brain, where movements are initiated, with the spinal cord below the cervical injury, where most distal arm movements are produced. Promoting reconnection through and beyond the injury currently is not yet possible. However, since most SCIs are incomplete, spared connections below the injury are an important therapy target to make spared connections more abundant and stronger. This project focuses on the corticospinal tract (CST), which is the brain circuit essential for skilled movements. Our published studies show that a neuromodulatory approach called theta burst stimulation (TBS) enhances activity-dependent CST axon sprouting and synaptogenesis. TBS also induces long-term potentiation (LTP) in the corticospinal motor system. In this project, researchers continue to study a potential link between muscle response LTP and CST axon growth with the aim of enhancing CST axon outgrowth after SCI to promote function. In Aim 1, researchers enhance motor cortex LTP to grow new CST connections in healthy rats, and in Aim 2, after cervical contusion injury. Aim 3 investigates translation from electrical neuromodulation to promote CST connections to using transcranial magnetic stimulation (TMS).

Progress Towards Specific Aims: For Aim 1, researchers observe that the combinatorial approach not only boosts axon growth, resulting in a 6-fold increase in CST density within the cervical spinal gray matter intermediate zone compared with sham controls, but leads to extensive growth in the gray matter region where motor neurons are located. There, researchers see formation of putative synaptic connections with motor neurons, suggesting a functional connection. Researchers do not yet observe that the combined approach boosts muscle response plasticity beyond that observed with TBS alone. For Aim 3 experiments, researchers have completed

the mathematical modeling estimating the electrical field induced by magnetic stimulation. Researchers also created a model for epidural electrical stimulation. Compared with the field produced by epidural electrical stimulation at a current when a motor response is produced, the field induced by TMS is both broader and less intense at levels producing similar motor effects. The modeling results show promise for translation of the electrical TBS to the human using magnetic stimulation.

Future Directions: For Aim 1 of the 4th reporting period, researchers will continue to increase the number of animals for documenting the actions of the novel combinatorial DREADD + neuromodulation protocol to identify additive versus multiplicative effects. These additional animals will also be tested for muscle response plasticity. For Aim 2, researchers are ready to begin the SCI experiments with the present anatomical results. For Aim 3, researchers will move forward with the awake-animal studies, beginning with identifying the strength of muscle response LTP evoked by TBS.

Impact: Development of combinatorial neuromodulation strategies to boost brain to muscle response plasticity for corticospinal tract connectivity will open new directions for biological therapies for SCI. With these studies, researchers expanded their "neuromodulation toolbox" of preclinical therapies. If effective, the invasive chemogenetic neural activation approach may may be implemented non-invasively in humans using non-invasive transcranial direct current stimulation (tDCS) and pharmacological approaches. Epidural TBS stimulation, which is minimally invasive, could be replaced with non-invasive TMS.

Projects to Accelerate Research Translation (PART) and Innovative, Developmental or Exploratory Activates (IDEA) in Spinal Cord Injury Research (Round 6)
IDEA Contract Term 10/01/2023-09/30/2025; PART Contract Term 10/01/2023-09/30/2026

Progress Reporting Period
04/01/2025-09/30/2025

8 Awards, Procurement Total: $5,275,108

1. **Icahn School of Medicine at Mount Sinai**
   Thomas Bryce, M.D.
   PART: $910,611
   Biomarkers of SCI Pain Evolution During Acute Rehabilitation (BioSPEAR)

   Introduction/Background: Pain is common following spinal cord injury (SCI) and is an important factor affecting quality of life. Nearly all pain after SCI can be classified into either neuropathic (nerve) pain or nociceptive pain. There is a lot researchers do not know about how this pain develops, what predicts its onset, and the biology underlying the pain. The purpose of this research study is to document the experience of pain after SCI, its development and persistence early after injury during acute inpatient rehabilitation (AIR), a period when pain after SCI often develops; to identify a molecular biomarkers of neuropathic pain using hypothesis-driven and unbiased approaches; and to explore the relationships of biomarkers, clinical characteristics, and psychosocial factors present during AIR to the persistence of pain six months post-injury.

   Impact: The data gathered in this study are essential for designing studies to test future interventions aimed to prevent development of neuropathic pain, and to determine how current standard-of care interventions (pharmacological or non-pharmacological) may affect the establishment and trajectory of the pain. If successful, the findings from this study could lead to better, more personalized pain management strategies and could be tested further in larger clinical trials. This could ultimately change how we treat neuropathic pain following SCI, making the treatments more effective and less harmful. This could also help us better predict and manage pain in people recovering from SCI, potentially leading to more effective treatments and improved outcomes.

2. **Winifred Masterson Burke Medical Research Institute**
   Edmund Hollis, Ph.D.
   PART: $988,622
   Ephrin-Mediated Cortical Motor Circuit Rewiring

   Introduction/Background: This project investigates how rewiring spared motor circuits can restore movement after central nervous system injury. It examines how reducing axon-repelling signals reshapes these circuits and supports recovery. Using genetic and optical imaging tools, researchers will track changes in brain motor networks and test how disrupting specific brain-spinal connections or removing key brainstem neurons affects function. The findings could reveal how neural plasticity promotes recovery and guide new treatments for spinal cord injury and stroke.

Progress Towards Specific Aims: Aim 1: Researchers competed isometric pull task behavioral analysis in all three groups (an average of n=16/genotype), except the principal component analysis, we are currently processing the data from these animals (figure.1). Researchers' processed four (04) animals and added in their anatomical analysis data; we are still processing ten (10) more animals. Aim 2: Experiments are ongoing. In this period, researchers have added more mice to the calcium imaging experiments.
Aim 3: Researchers completed behavior analysis in all animals showing rehabilitation-mediated recovery. Virally delivered diptheria toxin (DT) receptor was used to ablate brainstem neurons supporting recovery. Researchers are currently processing animal tissues for anatomical assessment of injury.

Impact: The research project will provide new insight into how circuit plasticity throughout the descending motor axis can support the recovery of precision forelimb control and will provide a target for therapeutical intervention after neura injury such stroke, traumatic brain injury and spinal cord injury.

3. **Icahn School of Medicine at Mount Sinai**
Hongyan (Jenny) Zou, M.D., Ph.D.
IDEA: $360,000
Investigate Glial Communication in Neural Repair After SCI

Introduction/Background: Glial communication plays an important role for neural repair and injury resolution after spinal cord injury (SCI). In response to injury, reactive astrocytes extend long processes to corral the wound; they also longitudinally align at the injury periphery, serving as a glial bridge to guide regenerating axons across the injury site. This proposal studies how reactive astrocytes utilize axon guidance receptor Plexin-B1 to gain mechanoplasticity to control dynamics of astrocyte processes and to resolve collision.

Impact: This study discovered for the first time safeguard mechanisms used by reactive astrocytes via guidance receptor Plexin-B1 to ensure mechanocompliance of astrocytic processes against physical damage, which may trigger spatial disarray and unwanted immune responses. Reactive astrocytes also tap into the neurodevelopmental pathway of Plexin-B1 to organize the astroglial bridge to guide axon regrowth and astroglial barrier to ensure corralling and wound compaction in order to minimize lesion core and maximize repair area to expedite functional recovery after SCI.

4. **Winifred Masterson Burke Medical Research Institute**
Vibhu Sahni, Ph.D.
IDEA: $360,000
Structural Plasticity of Cortico-Brainstem Projections After SCI and Their Contributions to Functional Recovery

Introduction/Background: Spinal cord injury (SCI) damages direct connections between the cortex and the spinal cord causing paralysis. Some plasticity of these connections can mediate limited recovery after SCI. However, undamaged circuits can also exhibit plasticity, and this represents another resource for enhancing recovery

after SCI. The cortex also directly communicates with the brainstem, a critical movement control center that also communicates directly with the spinal cord. Therefore, this cortex-brainstem-spinal pathway represents another way for the cortex to communicate with the spinal cord after SCI. However, due to technical limitations in the field, whether there is plasticity in the connections between the cortex and the brainstem after SCI remains an unanswered question. Further, the contribution of these connections to functional recovery after SCI remains completely unknown.

Progress Towards Specific Aims: Researchers have made significant progress towards both Aims 1 and 2. In their previous progress report, they established and confirmed that Npy+ neurons in layer V are CBN while Cartpt+ neurons in layer V are CSN. They used StARQ, an automated machine learning pipeline, to further identify that these populations exhibit strikingly different innervation in distinct brainstem nuclei. In this report, researchers have investigated Npy+ CBN structural axonal plasticity in response to a cervical SCI. Our findings suggest that Npy^{+} CBN axons sprout into medullary regions that they do not normally innervate in uninjured controls. This could be a very interesting finding because it highlights a potentially novel circuitry that emerges in response to SCI, even though these neurons are not directly damaged by the injury itself. In Aim 2, researchers had previously reported that they have validated expression of DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) from our newly packaged AAV particles using anatomical analyses. They used the single pellet reaching task to establish that Npy+ CBN control skilled forelimb movement in uninjured mice. In the present work, researchers have performed detailed kinematic analyses using DeepLabCut, a pose estimation pipeline, to establish the precise point at which silencing these neurons results in a failure in skilled reaching. Interestingly, their results show that there is a new kind of error that emerges when Npy+ CBN are silenced. Together, these results now provide the foundation to rigorously investigate the functional contributions of this population of neurons after SCI.

Impact: There is a critical need for this work since the cortico-brainstem connections represent a significant, yet untapped resource for enhancing recovery after SCI. Their experiments will unequivocally identify the role of these connections in SCI recovery, which will have direct impact on future neurorehabilitation approaches for SCI. The hope is that these could eventually be utilized in combination with established approaches to promote motor recovery after SCI. The brainstem also plays an important function in bowel and bladder function. Therefore, these investigations and tools could also be manipulated to improve bowel and bladder function, an important goal for individuals living with SCI.

5. Bronx Veterans Medical Research Foundation
Noam Harel, M.D., Ph.D.
PART: $946,581
Optimizing Spinal Cord Associative Plasticity to Enhance Response to Hand Training in Cervical SCI

Introduction/Background: This project builds upon our prior work to pair brain and spinal cord stimulation to strengthen nerve circuits controlling weakened hand muscles after spinal cord injury (SCI). Researchers hope to expand on this “Spinal Cord Associative Plasticity” (SCAP) approach by spending more time with each participant to individually optimize every aspect of the SCAP protocol, including combining SCAP

with hand rehabilitation exercises. Researchers expect that SCAP will induce plasticity, whereas hand exercises will shape that plasticity into improved function.

Progress Towards Specific Aims: Through the date of this submission, nine participants have enrolled in the study (of a planned 12). One participant completed the study. One enrolled participant required an unexpected surgery and did not start procedures. Three participants withdrew from the study (one withdrew after 2 visits, two withdrew after 3 visits). Reasons for withdrawal have been duration of study sessions; goal for more advanced clinical trial stage; and unrelated psychiatric event. Four participants are active in the study.

Impact:
Regaining control over hand function represents the top priority for individuals with cervical SCI. Furthermore, this approach could be compatible with other future interventions, including medications and cell-based treatments.

6. University of Rochester
Bradford C. Berk, M.D., Ph.D.
IDEA: $359,294
PDE10A Treatment for Neuropathic Pain After SCI

Introduction/Background: Motor and sensory functional loss is a major consequence of spinal cord injury (SCI), severely limiting independence and quality of life. Despite this, clinically approved therapies to restore motor and sensory function remain lacking. Phosphodiesterase 10A (PDE10A), which regulates intraceullular communication has been identified as a candidate gene regulating inflammation after SCI. Researchers showed that MP-10, a PDE10A inhibitor, limited cell death by reducing inflammation and could improve motor and sensory function

Progress Towards Specific Aims: Aim 2: Determine the effect of MP-10 on chronic neuropathic pain after SCI. For this study, researchers continued treating a group of mice for 28 days to observe the chronic, long-term effects of MP-10. They found that benefits of MP-10 at day 14 were like those at day 28. The greatest benefit was in walking that significantly improved at day 28 compared to the Control SCI group.

Impact: MP-10 is a promising early neuroprotective therapy that accelerates functional recovery and establishes conditions favorable for long-term motor restoration.

7. Winifred Masterson Burke Medical Research Institute
Edmund Hollis, Ph.D.
IDEA: $360,000
The Contribution of Wallerian Degeneration to Neural Tissue Inflammation and Axon Regeneration

Introduction/Background: Following traumatic injury to the central nervous system (brain, spinal cord, or optic nerve), the regeneration of damaged neural tissue is severely limited, resulting in permanent functional deficits. Mature nerve cells in mammals are equipped with long, cable-like structures (called axons) that facilitate rapid transmission of electrical impulses among distant groups of cells. Injury to these

cables disrupts communication lines, leads to their disintegration through a process called Wallerian degeneration, and triggers an inflammatory response. The ***central hypothesis*** of this study is that WD triggers neural tissue inflammation and is necessary for axon regeneration.

Impact: For many years, it was assumed that preventing axon degeneration would universally benefit nerve repair. The studies using *Sarm1* knockout mice demonstrate that this early axon breakdown is not merely destructive but also initiates key signals that activate Schwann cells and recruit immune cells required for efficient peripheral nerve regeneration. These findings reveal that therapeutic strategies targeting SARM1 must balance axon protection with preservation of the pro-regenerative signaling that accompanies Wallerian degeneration.

This research directly addresses a major translational question: whether therapies designed to protect axons might inadvertently impair axon regrowth after traumatic injury. By defining how loss of SARM1-dependent axon degeneration alters immune responses and repair processes following spinal cord and peripheral nerve injury, the research results provide new mechanistic insight into the interplay between axon integrity, neuroinflammation, and regeneration. These discoveries establish the foundation for developing next-generation neuroprotective therapies that safeguard axons while maintaining the biological cues necessary for successful neural repair.

8. Bronx Veterans Medical Research Foundation
Welping Qin, M.D., Ph.D.
PART: $990,000
Novel Targeting Nanotherapeutics for Functional Recovery After Acute SCI

Introduction/Background: The goals of this reporting period are to: 1) continue to validate if the optimized Nano-MP can more efficiently reduce lipid peroxidation and promote neuroprotection in a rat model of contusion SCI.; and 2) to determine whether Nano-MP improves functional recovery after a contusion SCI in male rats.

Progress Towards Specific Aims: Aim 1.2: Researchers recent work suggested that the modified Nano-MP can more efficiently reduce lipid peroxidation and promote neuroprotection in a rat model of contusion SCI. Aim 2. Researchers started a new animal experiment to examine whether the modified Nano-MP improves functional recovery after a contusion SCI in male rats.

Impact:
These progresses that were made over the reporting period will allow us to move the study toward the next phase as planned.

Translational Research Projects in Spinal Cord Injury (Round 4)

Contract Term 10/01/2022-09/30/2027

Progress Reporting Period
04/01/2025-09/30/2025

2 Awards, Procurement Total: $7,566,394

1. **The Feinstein Institute for Medical Research**
   Chad Bouton, M.S.
   $3,570,469
   Constant and Cortically Modulated Transcutaneous Spinal Cord Stimulation for the Treatment of Upper Extremity Impairment

   Introduction/Background: Spinal cord injuries can cause complete or partial paralysis by disrupting the flow of information between various parts of the nervous system, making it challenging for individuals to perform daily activities and achieve independence. Our team has been researching transcutaneous spinal cord stimulation (tSCS) combined with activity-based training as an effective treatment for individuals with tetraplegia. In severe cases, additional methods are needed; our team developed a brain-computer interface (BCI) by utilizing multiple chips implanted in the brain's movement area to record and decode detailed information about movement-related activity.

   To that, researchers aim to restore arm/hand function in individuals with tetraplegia by using tSCS and a BCI. The combination of these two methods can promote changes in affected pathways and restore short-term and potentially long-term muscle control. Our study will involve participants who will receive tSCS only and participants who will receive tSCS followed by 6 months of BCI-driven tSCS.

   Progress Towards Specific Aims: Two participants have been enrolled into the study, one for each Aim. The participant for Aim 1 has begun their baseline period data collection. Researchers have been conducting calls with potential candidates for the additional slots related to Aim 1, and several candidates have visited the lab for further assessments of eligibility for the study as well. For Aim 2, one participant was successfully implanted with 5 microelectrode arrays in the motor and sensory cortices (per protocol) in March 2023 and has fully recovered from the procedure. This participant has been undergoing BCI testing, tSCS mapping, baseline sessions, and other tasks in preparation of BCI-mediated tSCS to promote recovery of upper extremity movement.

   Impact: Successful implementation of this treatment could significantly improve the quality of life by restoring arm/hand function to allow performance of activities of daily living, thereby increasing their independence.

2. The Trustees of Columbia University in the city of New York
Sunil K. Agrawal, Ph. D.
$3,995,925
Improving Balance After Spinal Cord Injury Using a Robotic Upright Stand Trainer

Introduction/Background: People with SCI show balance deficits during upright standing and walking. It has been shown that neurorehabilitation is effective in incomplete SCI. However, the rehabilitation is challenging as the subjects have difficulty maintaining a standing posture without external support. Hence, the SCI rehab is personnel intensive and physically demanding. There is also a lack of standardized training protocols, and the training is performed over many sessions. It begs the question if one can make individual training sessions more efficient and effective. The applicant's translational proposal is significant because researchers address all the above challenges using a novel robotic upright stand trainer (RobUST) that researchers have designed and tested at Columbia University. Our preliminary studies with mild and severe spinal cord injury patients show long-term changes in posture and balance in SCI due to training with RobUST.

Progress Towards Specific Aims: Years 1-3 have focused on the following Aim 1 goals: (i) Improving features of RobUST training system and the human interface, e.g. improving transparency of the system during human usage, adding virtual reality interfaces, development of 3-dimensional force fields, and testing these features in different human functions such as standing, squatting, stepping, upper body maneuvers, etc. (See Pubs 1, 2, 7 and NewPubs 1, 2, 4, 5 below) that describe how these features were tested and used within behavioral studies. The goals of Aim 2 were explored within the training data obtained with RobUST in multi-session training studies. Pubs 3, 4, 5, 6 and New Pub 3 describe how patients with RobUST responded to training in different hand holding conditions with and without RobUST. The goals of Aim 3 are being pursued in new training studies that are being performed at Kessler Rehabilitation Institute where we are exploring different templates for reaching and balance. Researchers have installed a fully functional RobUST at Kessler Rehabilitation Institute. The subcontract between Columbia University and Kessler is now in place and preliminary experiments with RobUST were performed at Kessler

Impact: SCI rehab is personnel intensive and physically demanding. Due to heterogeneity of the injury and subject-specific rehabilitation needs, there is poor scientific understanding and lack of standardized training protocols to affect outcomes. Additionally, the SCI posture training typically are long, up to 80 sessions, and expensive. This raises the question if there are ways to systematically decrease the number of training sessions by making individual sessions more efficient and effective. Researchers believe that our translational proposal is significant because this is the first research that is targeted to address all of the above challenges.

Appendix III

NEW YORK STATE SPINAL CORD INJURY RESEARCH BOARD

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2 Service Concluded During 2025