DIRECTORY OF GRANT AWARDS
2022 GRANT CYCLE

NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

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DIRECTORY OF GRANT AWARDS FOR SPINAL CORD INJURY AND DISEASE RESEARCH

JANUARY 2022

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 2022 grant cycle. The research projects are not categorized or listed in any order.

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

Please feel free to contact the New Jersey Commission on Spinal Cord Research at P.O. Box 360, 25 S. Stockton Street, 2nd Floor, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-913-5005, 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.

2022 MEMBERSHIP INFORMATION

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COMMISSION PERSONNEL

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR22ERG009
Kessler Foundation
Silvana Lopes Costa, Ph.D. - $199,800

Project Title:
Using Eye Movements as a Biomarker of Dual-Diagnosis in Acute Spinal Cord Injury: A Proof-of-Concept Study

Examine the feasibility of using eye movements as a biomarker of cognitive dysfunction in persons with acute traumatic spinal cord injury with concomitant brain injury, termed dual diagnosis.

There are approximately 17,500 new traumatic spinal cord injuries (tSCI) each year, with roughly 285,000 persons living with tSCI in the US alone. While tSCI is defined primarily by motor and sensory impairments, an increased number of research studies have shown that cognitive impairments (impairments in the ability to perform complex operations such as reading and understanding a book) are frequent in both acute (less than 1 year after injury) and chronic (>1 year after the injury) tSCI. Specifically, it is estimated that as many as 60% of individuals with tSCI display some degree of cognitive impairment.

A dual-diagnosis of tSCI and traumatic brain injury (TBI; tSCI-TBI) occurs when patients have specific clinical and diagnostic features of both disorders resulting from trauma. Dual diagnosis is estimated to affect between 25-60% of the tSCI population. Studies have shown that individuals with tSCI-TBI show poorer outcome following rehabilitation with decreased quality of life. Diagnosis of tSCI-TBI is frequently performed retrospectively by examining acute care medical records. However, emergency medical services and/ or acute care medical records often do not contain basic information necessary to diagnose the presence and severity of TBI, especially in the presence of life-threatening issues such as those often caused by spinal trauma. Accurately identifying tSCI-TBI is therefore one of the biggest challenges clinicians and researchers face when examining cognitive functions and treating individuals with tSCI. Thus, there exists a need to develop more sensitive measures to identify the presence of TBI in tSCI during acute and chronic phases.

The present study aims to examine the feasibility of using eye movements as a biomarker of cognitive dysfunction in tSCI in two subgroups of individuals with acute tSCI: (1) tSCI (i.e., no history of TBI at the time of the traumatic event) (2) tSCI-TBI (moderate to severe TBI); in both cases the a group of able-bodied individuals will serve as a comparator sample (participants without tSCI).

The present proposal is highly relevant to the mission of the NJCSCR and its research program in several ways. First, the current study proposes innovative approach to the identification of cognitive deficits in tSCI, using eye movements as a biomarker of brain dysfunction. Eye movements have been successfully used in other neurological pathologies such as Parkinson's disease, dementia and TBI, to study brain pathology and disease progression, but they have not yet been examined in tSCI. Second, the current study will increase our understanding of

cognitive dysfunction in acute tSCI by examining the difference between individuals with tSCI with and without concomitant TBI. This is a fundamental step to diagnose and treat cognitive impairments in tSCI, a frequent and debilitating secondary biological condition resulting from tSCI. Third, the current study will provide information on the impact of cognitive deficits on QOL in acute tSCI, which has been shown to be substantially reduced in other cognitively impaired neurological populations. Fourth, this proposal will provide preliminary data which can be used to inform best practices, namely identifying the factors that dictate the need to examine different aspects of cognition in different tSCI groups (tSCI-TBI and tSCI). Finally, the current proposal will allow the research team (with a junior PI) to collect preliminary data and test the feasibility of this line of research. Results will be used as leverage to develop and apply for NIH funding to conduct a larger-scale research study. Thus, the current proposal is a fundamental step in the development of efficient assessments and rehabilitation programs, which will increase QOL and community integration in persons with tSCI, the primary goal of the NJCSCR.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR22ERG018
Rutgers, The State University of New Jersey
Biomedical & Health Sciences
New Jersey Medical School
Sridhar Kannurpatti, Ph.D. - $193,911

Project Title:
Imaging pain after Cervical Spinal Cord Injury and Assessment of a Novel Flavinoid Treatment

The ability of kaempferol (a natural flavinoid) to modify sensorimotor reorganization after a cervical SCI in rats and consequently diminish pain behavioral outcomes will be investigated.

Nationally over 200,000 people live with chronic physical disabilities and chronic pain after sustaining spinal cord injuries (SCI) in the United States and New Jersey accounts for at least a few thousand of these patients. Cervical spinal injuries are the most frequent (62% of all SCIs) leading to sensorimotor disabilities accompanied by chronic neuropathic pain. While most patients with SCI develop neuropathic pain at some point during their rehabilitation, current clinical data suggests the prescription of opioid-based medicines for longer durations and at higher morphine-equivalent doses as the only effective option for SCI pain management. Pain also hinders motor recovery during SCI rehabilitation in humans due to overlap of motor and sensory pain pathways and competition between them. This gap in understanding the exact nature of spine and brain reorganization after an SCI in preclinical animal models, using imaging measures similar to that available in the clinic on SCI patients, is an impediment to the development of novel paint treatments.

The proposed study aims to characterize imaging biomarkers related to pain across both the spinal cord and the brain and test a novel (non-opioid) compound on its ability to prevent the development of pain after a cervical SCI. Our prior studies on this naturally occurring compound, kaempferol (generally present in vegetables and fruits in trace quantities) established it as a successful treatment against traumatic brain injury (TBI) in rats. Our recent investigations testing the effect of kaempferol treatment in the rat model of cervical SCI showed promising results, where it prevented the development of pain after SCI. The proposed study will explore further on kaempferol's ability to modify sensorimotor reorganization after an SCI using imaging and the specific kaempferol-induced changes in the spinal cord and brain that associate with the diminished pain behavior. The successful outcomes of this project will lead to a potential non-opioid based treatment to prevent pain after SCI that can be clinically translated SCI patients.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR22ERG014
Rutgers, The State University of New Jersey
Biomedical & Health Sciences
Stella Elkabes, Ph.D. - $200,000

Project Title:
Neuropathic Pain in Spinal Cord Injury: A New Target and Underlying Mechanisms

The role of the neuronal calcium extrusion pump, plasma membrane calcium ATPase 2, in neuropathic pain mechanisms in the dorsal horn will be investigated following a spinal cord contusion injury.

One of the major complications associated with spinal cord injury (SCI) is the development of chronic neuropathic pain, which affects over 50% of individuals with SCI. This debilitating condition severely reduces the quality of life, has a high priority for the affected population, and is challenging to treat because available therapies, which include opioids, are not effective and have serious adverse effects. Despite advances, our knowledge of the mechanisms underlying neuropathic pain in SCI is limited and there is an urgent need for the discovery of novel mechanisms that can help the identification of new targets for therapeutic interventions. This could facilitate the development of more effective and better-targeted treatment strategies.

Studies performed in the laboratory found a coincidence between a reduction in the level of a calcium pump, namely plasma membrane calcium ATPase 2 (PMCA2) in the spinal cord (SC), and increased sensitivity to pain in mice affected by SCI as well as mice with a paralytic, inflammatory disease that mimics multiple sclerosis (MS). The reduction in PMCA2 occurred in SC regions involved in pain mechanisms. In the case of the MS model, the decrease in PMCA2 was observed only in the diseased mice that manifested neuropathic in addition to motor deficits. In contrast, PMCA2 levels were not altered in mice that displayed motor disability without neuropathic pain. This further supported the potential involvement of PMCA2 in neuropathic pain mechanisms. However, the causal link between a reduction in PMCA2 and neuropathic pain has not been established.

In the SC, PMCA2 is found exclusively in nerve cells, including those that mediate pain mechanisms and convey pain information from the SC to the brain. PMCA2 expels extra calcium ions from inside the nerve cell to the environment outside of the cell in order to maintain a proper calcium balance. This is an important function because an accumulation of calcium inside nerve cells activates mechanisms that cause overexcitability of the cells, which is believed to be a cause of neuropathic pain. Moreover, increased calcium inside nerve cells promotes the production of molecules that foster pain. After injury, a decrease in PMCA2 in nerve cells that mediate pain could elevate calcium levels within the cell, activating thus mechanisms of neuropathic pain.

The studies proposed in the present application will establish the causal link between a decrease in PMCA2 in the SC and increased sensitivity to pain and will determine whether restoration of PMCA2 in the SC, by use of gene delivery, alleviates neuropathic pain in subacute and chronic SCI. In addition, the mechanisms leading to neuropathic pain following a reduction in PMCA2

will be explored. The investigations will be performed in both male and female mice to determine whether the involvement of PMCA2 in pain mechanisms shows sex bias.

It is anticipated that the studies will identify PMCA2 as a new target for therapeutic interventions and will advance the understanding of mechanisms underlying neuropathic pain in SCI.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR22ERG026
New Jersey Institute of Technology
Bharat Biswal, Ph.D. - $199,887

Project Title:
Investigating Altered Brain Connectivity after SCI using fNIRS

We propose to use fNIRS, a relatively new neuroimaging method, to determine the neurovascular correlates of cognitive function and cerebrovascular reactivity in patients with spinal cord injury.

Spinal cord injury (SCI) is characterized by damage to the spinal cord which can either temporarily or permanently alter its function. This leads to neurological changes in both the spinal and supraspinal levels of the central nervous system. Rehabilitation often focuses on the spinal cord itself and neglects direct observation of neural activity, partly due to the high costs of routine functional magnetic resonance imaging (fMRI) procedures. Due to the lack of neuroimaging studies investigating the neurovascular dynamics after SCI, it is not clear how functional brain reorganization is altered in cognitive processing areas after SCI. This is important to understand since individuals with SCI have a 13 times greater risk of cognitive impairment than able-bodied individuals and commonly report symptoms of depression and anxiety, which may interfere with rehabilitation.

Therefore, we plan to use functional near-infrared spectroscopy (fNIRS) to investigate cognitive function in individuals with SCI. This technology uses light to quantify the brain's hemodynamic changes and is more portable and suitable for studying SCI than fMRI. By using fNIRS, we can detect functional brain differences between individuals with SCI and able-bodied individuals, in both cognitive task and resting conditions. We will evaluate cognitive performance on working memory and attention tasks. Additionally, we will evaluate neurovascular function using a breath-hold task. This study will provide insight on brain reorganization in cognitive processing areas after SCI, which will aid in our understanding of the neuropsychological consequences after SCI. Our goal is to progress the development of effective rehabilitation treatments and biomarkers for successful recovery using fNIRS.

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EXPLORATORY RESEARCH GRANT RECIPIENT:

CSCR22ERG023
Rutgers, The State University of New Jersey
Department Chemistry & Chemical Biology
KiBum Lee, Ph.D. - $200,000

Project Title:
Direct Conversion of Reactive Astrocytes into Neurons for Combined Immunomodulatory and Cell Replacement Therapy after Spinal Cord Injury

This exploratory proposal aims to develop a nanoparticle-based transcription factor for both immunomodulatory and cell replacement therapy for the treatment of spinal cord injury.

Trauma to the spinal cord can result in devastating deficits. However, unlike many other areas of the body, the spinal cord cannot regenerate after injury leading to long term, incurable deficits. One of the reasons for this is the complex and inhibitory environment of the spinal cord that is highly inflammatory and made up of the glial and fibrotic scar. One of the significant components of this scar is reactive A1 astrocytes that promote inflammation and inhibit axon regeneration.

To this end, we aim to mitigate the inflammatory environment while simultaneously providing a cell source for cell replacement therapy by converting A1 reactive astrocytes into functional neurons. This process is termed trans differentiation and has been demonstrated using viral vectors that express the transcription factors ASCL1 or NeuroD1. However, the use of viral vectors for therapies is limited by the many side effects caused by viral vectors including immunogenicity, genomic integration, and cytotoxicity.

In order to overcome these limitations, our lab has developed a platform termed NanoScript that can replicate the structure and function of natural transcription factors using a synthetic nanoparticle-based system. This proposal aims to develop a novel biodegradable peptide NanoScript that targets ASCL1 and NeuroD1 to study the direct conversion of reactive astrocytes into functional neurons both in vitro and in vivo. These studies will give us a further understanding of the role of A1 astrocytes in neuroinflammation as well as provide a therapeutic strategy for bridging the lesion left after spinal cord injury.

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FELLOWSHIP RESEARCH GRANT RECIPIENT:

CSCR22FEL011
Rutgers, The State University of New Jersey
W. M. Keck Center for Collaborative Neuroscience
Mark Gradwell, Ph.D. - $150,000

Project Title:
Identifying spinal circuits contributing to maladaptive plasticity following SCI

We genetically target a new subpopulation of excitatory interneuron, 5-HT6R-expressing neurons, to determine their intrinsic excitability, connectivity, and functional role before and after SCI.

Over 1.2 million people in the United States, and 6000 New Jersey residents live with spinal cord injury (SCI). Annually, roughly 500 New Jersey residents are hospitalized with SCI. In these patients, the prevalence of SCI associated pain and muscle spasticity is alarmingly high, with > 70% of the injury population suffering from chronic neuropathic pain and > 80% exhibiting muscle spasticity. These conditions have proven difficult to treat, largely due to a limited understanding of the cells within the spinal cord that are responsible for their development. Without first identifying the cells responsible for the development of pain and spasticity it is challenging to develop targeted therapeutic interventions. The reason it has been challenging to identify these cells to date is because there are many different cell types, all with different roles within the spinal cord. Until recently we have not had the appropriate tools to study specific neuron types to better understand these roles.

My research utilizes exciting new mouse genetic tools that allow me to visualize and test the function of specific cells within the spinal cord. I will use these tools to determine how one particularly interesting cell type contributes to neuropathic pain and spasticity behaviors. Neuropathic pain and spasticity are both likely due to the over excitability of neurons that process touch information. This over excitability allows for touch signals to excite cells that communicate pain (neuropathic pain) as well as over-excite cells responsible for movement (spasticity). The cells I am interested in process touch information. Importantly, following SCI it is likely these cells become more excitable. Therefore, these cells are ideally placed to play a role in the neuropathic pain and spasticity that often develops following SCI. I will test what happens to these cells following injury – do they become more excitable? I will test who these cells talk to before and after injury – do they 'gain access' to the pain or movement cells? Finally, I will test if activating these cells causes pain behaviors or muscle spasticity or if inhibiting these cells alleviates pain and spasticity following injury.

My study provides an essential framework and key tools to improve SCI therapeutics. When sensory information arrives at the spinal cord different cells must process this information before sending it to the correct output (e.g., touch, pain, movement). Following SCI, these signals may become crossed so touch can cause pain or inappropriate movements. This work helps us to understand which cells receive the touch information, who they normally talk to, and why they might talk to someone else following injury. Once we identify the cells responsible for this crosstalk, we can begin to specifically target them with therapeutics. For example, recent

exciting evidence suggests that spatiotemporally controlled epidural electrical stimulation (EES) enables voluntary waking in SCI patients. Similarly, work using transplantation strategies to provide new neural cells to promote recovery has shown great promise. Learning more about the cells that are involved in recovery vs. pain and spasticity will help refine these approaches to selectively promote activity in cells that lead to functional recovery while avoiding activity of those that cause pain and spasticity.

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FELLOWSHIP RESEARCH GRANT RECIPIENT:

CSCR22FEL015
Rutgers, The State University of New Jersey
Biomedical & Health Sciences
Department Neuroscience & Cell Biology
Michael Rallo - $60,000

Project Title:
The Role of Hedgehog Signaling as a Mediator of Diverse Reactive Gliosis Phenotypes Following Traumatic Spinal Cord Injury

This project will evaluate the novel role of a developmental pathway, Hedgehog signaling, in regulating the cellular response to traumatic spinal cord injury.

Tissue repair and regeneration following traumatic spinal cord injury (SCI) is mediated by a coordinated multi-cellular response. Astrocytes, a predominant cell type present in the brain and spinal cord, play a critical role in maintaining the health of central nervous system (CNS) tissue (i.e., brain and spinal cord) at rest. In response to CNS injury or disease, astrocytes undergo the conserved process of reactive gliosis to repair tissue damage. While this response is observed in a variety of disease states, such as SCI and stroke, and Alzheimer's and Parkinson's diseases, there is little understanding of how this process is regulated and may contribute to disease progression or recovery.

The research proposed here will explore the novel role of Hedgehog (Hh) signaling – a pathway active during nervous system formation and implicated in recovery from CNS damage – in regulating the astrocytic response to a penetrating form of traumatic SCI. Our preliminary findings suggest that Hh signaling directs astrocytes in responding to the injury and restoring normal, healthy tissue at that site.

Targets of this pathway will be identified through state-of-the-art genetic techniques, including RNA sequencing, with the hope of uncovering novel treatment strategies. The current availability of approved pharmacologics that target Hh signaling underscores the clinical importance of studying this pathway in the setting of traumatic SCI.

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FELLOWSHIP RESEARCH GRANT RECIPIENT:

CSCR22FEL016
Rutgers, The State University of New Jersey
Department Biomedical Engineering
Zachery Finkel - $60,000

Project Title:
Safety and Efficacy Study of Gsx1 Gene Therapy for Spinal Cord Injury

We are testing the safety and effectiveness of AAV-based Gsx1 gene therapy to regenerate cells after spinal cord injury and restore locomotor function.

Spinal cord injury affects a large portion of the population and results in lower quality of life for patients. In the United States alone, 18,000 new cases of debilitating spinal cord injury (SCI) occur on average each year. Many avenues have been investigated to treat spinal cord injury, with the aim to produce more cells, the basic unit of life, into the damaged tissue. The Cai lab has recently demonstrated that lentivirus mediated Gsx1 expression promotes functional recovery after SCI in a hemi section injury mouse model. Lentivirus may cause random insertional mutation and immediate treatment is not available on site of SCI incidents. The goal of this project is to determine the safety and efficacy of Gsx1 gene therapy using adeno-associated virus (AAV) in a clinically relevant contusion SCI model and determine the time window of effective treatment. The completion of this project will advance our understanding of the molecular mechanisms of stem cell regulation in the adult injured spinal cord. Thus, this proposed project addresses the ongoing initiative of NJCSCR to develop new therapies to improve the care and quality of life of SCI patients.

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