



**DIRECTORY OF GRANT AWARDS
2014 GRANT CYCLE**

**NEW JERSEY COMMISSION ON
SPINAL CORD RESEARCH**

2014 GRANT CYCLE

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

JUNE 2014

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 2014 grant cycle. The research projects are not categorized, or listed in any particular order.

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

Please feel free to contact the New Jersey Commission on Spinal Cord Research at P.O. Box 360, 369 S. Warren Street, Trenton, New Jersey, 08625. The Commission's office can be reached by telephone at 609-292-4055, by fax at 609-943-4213, or by e-mail at NJCSCR@doh.state.nj.us.

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

2014 MEMBERSHIP INFORMATION

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INDIVIDUAL RESEARCH GRANT RECIPIENTS:

Mladen-Roko Rasin, M.D., Ph.D.
Rutgers, The State University of NJ
Biomedical & Health Sciences

Grant Award: \$600,000

Project Title: *Semaphorin Signaling and Regeneration of Corticospinal Circuitry*

The proposed studies will identify novel roles of sema-plexin signaling in CS axon growth both during development and after SCI.

A spinal cord injury (SCI) is a trauma to the spine that destroys some or all descending corticospinal (CS) and ascending sensory axons traveling through the site of injury. SCI irreversibly damages CS axons and alters activity in the neocortical regions that receive sensory afferents. As a result, reorganization of sensorimotor cortices occurs, which sometimes contributes to functional recovery, but other times results in erroneous or maladaptive outcomes. As a consequence of SCI, approximately 1,275,000 people in the U.S. are currently living with paralysis. Because complete regeneration after SCI is uncommon, a better understanding of SCI pathogenesis and its molecular mechanisms are needed. Recently, experimental manipulations of molecular pathways in sensorimotor neocortices were found to enhance regeneration and improve functional plasticity after SCI, indicating that a greater understanding of the molecular mechanisms underlying adaptive and/or maladaptive responses to SCI may advance efforts to promote regeneration and recovery. Identification of the molecular mechanisms that regulate CS axon growth during development and after SCI is necessary for creating new therapies for SCI.

Therefore, our objectives are to examine the specific roles of semaphorin, an inhibitory axon guidance molecule, and its associated receptor Plexin in the regulation of developing CS axons in the developing and adult spinal cord with or without SCI. We found, for the first time, that a subset of CS axons is eliminated during early postnatal development in mice, and semaphorin-Plexin signaling controls the axon elimination. Furthermore, we found that defects in the axon elimination affect neural circuit formation and motor behavior. Collectively, our data revealed that semaphorin-Plexin signaling have a role in inhibition of axon growth during early postnatal development. This findings lead into a hypothesis that the same signaling pathway has a role in inhibiting axon regeneration in the adult spinal cord after SCI. Indeed, our preliminary findings show that adult depletion of Plexin receptor in mice model promotes regeneration of injured CS axons after SCI. These results suggest that semaphorin-Plexin signaling inhibits regeneration of injured CS axons after SCI in the adult spinal cord. Thus, manipulations of the semaphorin-Plexin signaling pathway should promote post-SCI regenerative efforts, which will be tested in this proposal. We anticipate that our findings will contribute to the development of advanced treatment approaches for people with devastating SCI-induced motor deficits in New Jersey and throughout the world.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Monica Driscoll, Ph.D.
Rutgers, The State University of NJ
Molecular Biology & Biochemistry

Grant Award: \$350,000

Project Title: *Probing In vivo Mechanisms by which Exercise Enhances Regeneration of Individual Severed Neurons*

We will investigate the molecular mechanisms by which exercise promotes neuronal regeneration in vivo at the single axon level, work that should suggest novel options for reparative therapies.

In spinal cord injury axons are often sheared, causing a loss of neuronal connectivity and impaired function. The rapid regeneration of severed neurons is an obvious goal for the treatment of spinal cord injury, yet knowledge of molecular mechanisms that actively promote neuronal regrowth and reconnection in the living animal remains too limited to be applied for effective repair.

The central goal of our work is to identify the molecules that promote regeneration of injured neurons. To accomplish this, we exploit the powerful *C. elegans* model, which offers unique advantages. *C. elegans* is a simple transparent invertebrate nematode with a nervous system of only 302 neurons. We can directly visualize fluorescently labeled neurons, induce single axon breaks using a laser, and monitor regeneration of that neuron (some *C. elegans* neurons can regenerate, some cannot). We also can systematically reduce the activity of each gene to test its importance in regeneration and reconnection. Since most basic biological processes—including molecular pathways that promote regeneration—are conserved from *C. elegans* to humans, we expect that work in *C. elegans* should provide novel insight into the mechanisms regulating neuronal regeneration and repair in humans.

**Exercise stimulates functional recovery in SCI, but the mechanisms mediating this response in neurons native context are essentially unknown. We recently developed a swimming exercise regimen that improves *C. elegans* physical performance—these tiny animals can train. Moreover, we have made the exciting observation that exercise training can enhance the regeneration capacity of injured neurons. We are thus uniquely poised to unleash the molecular genetic and cell biological approaches available in this system to identify the mechanisms via which molecules and cells signal to enhance regeneration consequent to exercise.

We propose four experimental objectives:

1) DEFINE THE RELATIONSHIP BETWEEN EXERCISE AND REGENERATION CAPACITY FOR INDIVIDUAL INJURED NEURONS IN THEIR NATURAL CONTEXT. We will establish the effect of exercise on the regeneration proficiency of specific sensory and motor neurons, and determine the timeframe in which exercise must occur. We will ask whether neurons that are unable to regenerate might be activated for repair by exercise, and whether exercise might delay the onset of age-dependent shutdown in regeneration capacity.

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2) IDENTIFY EXERCISE PATHWAY GENES THAT MODULATE ENHANCED REGENERATION. How conserved molecules of exercise biology influence recovery from axotomy is unknown. We will ask whether nematode orthologs of mammalian exercise genes are needed for exercise-potentiated regeneration. We hypothesize that we might identify specific sub-pathways that are particularly important for regeneration.

3) TEST DRUGS THAT INCREASE EXERCISE PERFORMANCE ACROSS PHYLA FOR PROMOTION OF NEURON REGENERATION AT THE SINGLE AXON LEVEL. We will address whether two drugs that impact exercise performance can improve in vivo regeneration consequent to axotomy. Because both drugs are efficacious in mammalian models, our studies may suggest novel and specific interventions to stimulate regeneration.

4) DETERMINE WHETHER EXERCISE SIGNALING IS NEEDED DIRECTLY IN NEURONS FOR ENHANCED REGENERATION. We will manipulate exercise signaling only in specific tissues and determine impact on exercise-associated potentiation of regeneration. Distinguishing the cellular/tissue circuits by which exercise enhances regeneration is critical for full mechanistic understanding and for consideration of where to activate pathways to enhance neuronal repair.

In sum, our study will provide some of the first molecular insight into the impact of exercise on isolated injured neurons in vivo and as such might ultimately suggest novel therapeutic strategies.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Jeanne Zanca, Ph.D.
Kessler Foundation

Grant Award: \$450,635

Project Title: *Improving Functioning in Persons with Chronic Pain Post-SCI through Virtual Classroom Delivery of a Mindfulness-Based Chronic Pain Management Program*

This project will examine the feasibility and potential benefits of a web-based Mindfulness-Based Chronic Pain Management intervention for persons with chronic pain post-SCI.

WHY IS THIS STUDY BEING DONE? Chronic pain is common among people with SCI, is often severe, and can interfere significantly with daily life. Medications are the most common method for treating chronic pain in people with SCI, but these provide only partial relief from pain and can produce side effects like constipation or sleepiness that reduce quality of life. Other pain treatments include surgery, physical therapy, massage, and others, but none of these has been found to be consistently effective in reducing pain. Because current treatments (used alone or in combination) do not eliminate pain for most individuals, it is important for us to identify ways to reduce the negative effects of pain on daily life and well-being, so that people with pain can live happy, healthy, and productive lives, even if some pain still remains after other treatments are used.

WHAT WILL THE STUDY TEACH US? The proposed study will examine how well we can implement a web-based treatment program known as Mindfulness-Based Chronic Pain Management in persons with chronic pain after SCI. It will also assess what benefits this treatment has for them. Mindfulness-Based Chronic Pain Management aims to use the connections between the mind and body to affect how pain is experienced and reduce the suffering associated with pain. It is a 10 week program that includes weekly classes of approximately 1.5 hours each as well as daily homework assignments. Participants in the class are taught to think about their pain in a way that separates the sensation of pain (awareness of something that hurts) from the thoughts and feelings that pain creates (such as thoughts that it will never end, or feelings of sadness or anxiety). Interventions that are based on the concept of mindfulness have been found to improve pain coping, increase ability to do daily activities, and promote greater mental health in people who are dealing with chronic pain, but do not have SCI. Prior studies have also shown that the Mindfulness-Based Chronic Pain Management program has benefits for persons with chronic pain whether delivered face-to-face or delivered through live web-based video and sound. We want to see if a web-based Mindfulness-Based Chronic Pain Management program is feasible to deliver, and acceptable to persons with SCI, and assess the amount of improvement that program participants experience relative to those who participate in a web-based education program about health and functioning that does not include content related to mindfulness or pain.

WHAT WILL HAPPEN IN THE STUDY? In this study, we will enroll 80 participants who have had spinal cord injury for at least 1 year and pain of moderate or greater intensity for three months or more. After collecting information about their spinal cord injury, pain, and functioning, we will randomly select (like the flip of a coin) one half of these participants to participate in the web-based Mindfulness-Based Chronic Pain Management program. The other half of the participants will participate in the health and functioning web-based education series. Participants will complete questionnaires about pain, functioning, well-being and other topics before and after they complete the courses so we can examine changes over time.

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HOW WILL THIS STUDY BENEFIT PERSONS WITH SCI? The proposed study will help identify a low-cost, low-risk treatment option that can be combined with other treatments (such as medications) to maximize functioning and quality of life in people with chronic pain after SCI. It will do this by providing the information that researchers need to design the larger-scale, multi-site studies that will provide evidence to clinicians, consumers, and insurers to support the use of Mindfulness-Based Chronic Pain Management to improve functioning and well-being in people with chronic pain after SCI.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Bonnie Firestein, Ph.D.
Rutgers-Cell Biology & Neuroscience

Grant Award: \$600,000

Project Title: *Spinal Cord Motor Neuron-Based Biodegradable Neural Interface Design*

Our goal is to devise a prosthetic that uses biocompatible, biodegradable nanofibers that release protective compounds to align muscle cells and spare neurons from secondary injury due to SCI.

A major issue for patients who have suffered a SCI is loss of motor control and function. Manufacturing a device that would improve communication between neurons and muscle cells or artificial limbs would significantly improve quality of life.

Using previous funding from the NJCSCR, we have devised a prosthesis that uses cultured neurons and muscle cells to study how we can improve connections between the two. In this new proposal, we improve upon and extend this prosthetic to use a biocompatible, biodegradable material platform to not only increase connectivity between neurons and muscle cells, but also to release protective compounds so that the neurons will survive injury due to SCI.

At this stage, our work is performed on cells, but as we improve upon our design, we anticipate a prosthetic that can be implanted into the injured patient. The optimization of our device will improve motor function, allowing injured patients to perform activities that they were previously incapable of performing.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

FELLOWSHIP GRANT RECIPIENTS:

Siliang Wu
New Jersey Institute of Technology

Grant Award: \$60,000

Project Title: *An Electroactive Scaffold for Schwann Cell-Induced Spinal Cord Repair*

Develop a novel Schwann cell supported piezoelectric conduit for spinal cord repair.

In the United States alone, there are close to 1 million persons with damaged spinal cords. Spinal cord injury (SCI) is a devastating condition for which there is no cure. Bioengineering efforts have been focused on developing biomaterials that promote the regeneration of axons across lesions. Although these materials show promise, directing axons from the biomaterial conduit back into the spinal cord to connect with host synaptic pathways remains to be achieved.

Recent efforts, therefore, have been exploring combination strategies using conduits with cells and/or neurotrophic or neuroprotective factors. Using a tissue engineering strategy, our goal is to improve axon regeneration across a Schwann cell (SC)-laden conduit/bridge and into the spinal parenchyma caudal to the injury site to improve functional recovery. Our overall hypothesis is that axonal regeneration and functional recovery are improved by utilizing an appropriate conduit with SCs that provides both physical and neurotropic cues in combination with neurotrophin release caudal to the injury. The conduit will be piezoelectric, which means it has intrinsic electrical properties, and will release neurotrophins to support axonal regeneration. A combination of cells and effective neurotrophin delivery within a piezoelectric conduit is a novel and translatable approach. Aim 1 will fabricate and characterize the piezoelectric scaffold and evaluate neurotrophin release. Aim 2 will evaluate axonal growth using the piezoelectric scaffold with or without neurotrophin release in vitro. The goal here is to establish that biomaterials can be an effective method for the controlled release of neurotrophins and will improve axonal growth. Aim 3 will evaluate axonal growth and functional recovery using the combination approach in vitro in a complete transection model. The goal is promote axon growth throughout the conduit and extend into the caudal spinal parenchyma following the controlled release of neurotrophins. This study proposes a novel tissue engineering strategy utilizing piezoelectric conduits, neurotrophins and SCs to promote axonal regeneration into, through and out of the SC bridge to improve functional recovery.

Currently, there are approximately 6,000 New Jersey residents suffering from traumatic injuries or diseases that damage the spinal cord. Our research work provides potential therapies that could improve their quality of life.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Hui Wang, Ph.D.
Rutgers – Neuroscience & Cell Biology

Grant Award: \$150,000

Project Title: *Cooperation of Shh and Fgf signaling for generating oligodendrocytes during development and following SCI*

My experiments will define the role of FGF and Shh signaling in the specification and differentiation of embryonic and adult spinal cord OPCs under normal and post-injury conditions, respectively.

Successful functional recovery following spinal cord injury (SCI) involves the production of specialized glial cells that are involved in controlling neurotransmission. Among these cells are the myelin-producing oligodendrocytes (OLs) that are generated from progenitor cells (OPCs) that are located in the adult spinal cord. It has been shown that two important cell signaling pathways are involved in this process. These are the Sonic Hedgehog (Shh) and Fibroblast Growth Factor (FGF) pathways, which are up-regulated in the spinal cord following SCI. Because these pathways have been shown to play important roles in generating glial cells in development and in some previous experiments on SCI, we believe they are likely to contribute to functional recovery. Notably, there is evidence from studies using the forebrain that both pathways cooperate to induce OLs after injury, but so far prior investigation has failed to establish this relationship in the spinal cord. Specifically, the role of FGF signaling in the production of spinal cord OLs is not thought to be as important as it is in the brain.

I have now obtained preliminary data that reveals a similar, broad requirement for FGF signaling in generating OLs in the spinal cord. In addition, prior published work from our lab has provided evidence that FGF pathway genes in the ventral spinal cord are regulated Shh signaling, suggesting a possible mechanism for pathway interactions. Together, these data provide the first evidence that the Shh and FGF pathways cooperate to generate the majority of OLs in the spinal cord. The fact that both pathways are also involved in producing OLs in adults after SCI raises the likely possibility for a similar link in adult OL stem cells.

Two aims of this proposal will address this issue. First, I will define the requirement of embryonic FGF signaling to produce ventral spinal cord OLs by extending my preliminary analysis. These studies will provide important mechanistic insights into Shh/FGF pathway cooperation that will be directly applicable to my adult SCI studies due to the conserved reactivation of developmental signaling pathways following CNS injury. Second, I will determine whether FGF signaling is required downstream of Shh adult glial progenitor cells following SCI. The overall goal of these experiments is to test whether FGF signaling is required in reactive cells to generate glial progeny (oligodendrocytes and astrocytes) downstream of Shh after SCI. Thus, these experiments will establish a definitive role for FGF signaling in the specification and differentiation of embryonic and adult spinal cord OPCs under normal and lesioned conditions, respectively. Results from my studies will provide important information on the molecular sequence of events that occurs in OL progenitors following SCI that could be used to improve treatment and recovery from this devastating problem.

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EXPLORATORY RESEARCH GRANT RECIPIENTS:

Rakesh Pilar, Ph.D.
Kessler Foundation

Grant Award: \$194,976

Project Title: *Development of Signal Processing Toolbox for Assessing Neuromuscular Response during Electrical Stimulation*

We propose to develop a novel robust algorithm to extract artifact-free EMG signal during electrical stimulation to study the neuromuscular response of the stimulated muscle.

Traditionally, electrical stimulation (ES) has been used in SCI patients as one of the rehabilitation paradigms to assist or restore neuromuscular function in paralyzed muscles. Functional Electrical Stimulation (FES) operates on a basic principle that the application of electrical current to a muscle nerve or muscle itself can activate contraction in paralyzed muscles. When muscle contraction made either voluntarily or by ES, action potentials (APs) are generated in each muscle cell (fiber) and these APs from activated fibers can be recorded invasively using surface electrodes as electromyography (EMG). The EMG recording tells intensity or activation level of muscle contraction, patterns of AP generation which are important for understanding the neuromuscular and physiological effects created by ES. However collection of high quality EMG during ES has been difficult to achieve because of the presence of stimulus artifact. The overlap between the stimulus artifact and EMG signals obstructs the use of conventional signal filtering techniques to extract the true EMG signals from the artifact-contaminated recordings. The goal of this study is to develop a robust signal processing algorithm to extract EMG during ES and study the physiological significance of ES on neuromuscular properties of the stimulated muscle.

First aim of this study is to develop a robust signal processing algorithm for the removal of stimulus artifact from contaminated surface EMG signals during ES. Our preliminary results show that Empirical Mode Decomposition (EMD) based algorithm to extract ES artifact from stimulated EMG has a lot of potential. Although the algorithm was able to extract the major portion of the EMG, some data was lost in discarded artifact components indicating EMD alone is not sufficient to successfully isolate EMG signal. We propose to use another decomposition technique, Independent Component Analysis (ICA) to further separate the EMG. Overall, we will develop a toolbox that combines the merits of both EMD and ICA to optimize the performance and further minimize the EMG signal loss.

Second aim is to establish the validity of EMD-ICA algorithm by assessing the quality of the separated EMG before interpreting and assigning it any kind of physiological meaning. We will use a test signal consisting of sequence of only EMG (voluntary muscle activation) and electrical stimulated EMG. The algorithm will be applied 'EMG+ES' sequence and artifact-free EMG will be extracted. The various properties of this extracted EMG will be compared with voluntary 'EMG only' sequences to calculate the validation measure.

Once we establish the validity, as our third aim, we will optimize the ES parameters by analyzing changes in the filtered EMG due to varying patterns of ES for this study. Numerous tests would be required to find the optimum ES training pattern (frequency, pulse width) for each patient and for each functional task. Currently, not many mathematical models or theoretical foundations

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exist which will successfully identify the relationships between the patterns of ES and optimum neuromuscular responses. We will bridge this gap by analyzing artifact-free EMG collected during ES contractions and observing the changes in it occurring due to change in ES pattern. The properties of EMG collected during varied patterns of ES will enable us to know the effect of certain frequencies, amplitude, pulse width of ES on motor recruitment patterns and muscle fatigue. We will be the first to assess these changes by studying the pure, artifact-free EMG during stimulated contractions.

The outcomes of the study will help in understanding the direct effects of ES on muscles by getting access to high quality EMG during ES and help the clinician or researcher to modify and optimize FES training paradigms based on the target muscle response. This could have a major impact on the field of spinal cord injury research and rehabilitation.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Anita Singh, Ph.D.
Rowan University

Grant Award: \$198,437

Project Title: *Using Bioengineered Scaffold Loaded with Neurotrophins to Enhance Functional Recovery after Locomotor Training in Spinal Cord Injury Animals*

To investigate the efficacy of a combinatorial bioengineering treatment strategy using scaffold loaded with neurotrophins and treadmill training in a clinically relevant spinal cord injury animal model.

Spinal cord injury (SCI) is a devastating and debilitating condition that affects an estimated 227,080 to 300,938 persons in the United States with approximately 12,000 new cases occurring each year. Current treatment strategies include activity based rehabilitation therapies, such as body weight supported treadmill training (BWSTT) that utilizes the uninjured descending pathways in incomplete SCI patients and spinal circuits below the level of injury in complete SCI patients. If the descending inputs are minimal or absent, recovery in walking over-ground is never observed in SCI patients. Since the amount of spared descending input strongly regulates the extent of recovery after BWSTT, combining transplantation treatment strategies that increase the number of descending inputs by inducing neuroprotective and regenerative environment around the injured spinal cord holds most promise to further enhance the functional recovery after BWSTT. Transplantation strategies using cells genetically engineered to deliver neurotrophins, which is a neuroprotective and neuroregenerative agent, limit spinal tissue loss, promote regeneration/sprouting of injured axons, bridge the site of injury and result in some functional recovery in animal SCI models. Clinical translation of these techniques poses several problems, including rejection and issues with regulation of release, requiring more invasive approaches with additional problems associated with potential rejection and regulation of release of bioactive compounds. To overcome these limitations, we propose using bioengineered scaffold poly N-(isopropylacrylamide) – poly (ethylene glycol) (PNIPAAm-PEG), which has shown to be highly biocompatible and when functionalized to secrete a neurotropic factor can promote regeneration and functional recovery in a surgically induced SCI animal model.

In the proposed study, we aim to further investigate the efficacy of this bioengineered scaffold secreting neurotrophins as an alternative to cellular transplants in a clinically relevant contusion SCI animal model. Furthermore by incorporating BWSTT in these animals, our collaborative group will for the first time report the combinatorial effect of scaffold+neurotrophins+BWSTT in a clinically relevant contusion SCI model. Successful findings from this study will help develop a unique tissue-engineering approach with promising clinical application in incomplete SCI patients. By adding other growth promoting agents to this bioengineered scaffold, future studies can explore the beneficial effects of the proposed combinatorial treatment strategy in complete SCI animal model.

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NEW JERSEY COMMISSION ON SPINAL CORD RESEARCH

Gal Haspel, Ph.D.
NJIT

Grant Award: \$199,997

Project Title: *A Minimal Locomotion Circuit to Investigate Neuronal Regeneration*

In this exploratory grant, I propose to develop a new, compact and modular preparation in a live animal to study neuronal circuit parameters that can support recovery from spinal cord injury.

A spinal cord injury is complex. It involves processes at many levels from molecules through cells, neuronal circuits and organs to the whole animal or patient. While we have very fruitful and established experimental models at the molecular, cellular and whole animal levels, it has been difficult to isolate factors that rise from the level of the neuronal circuit and its activity: Are neuronal regeneration and plasticity affected by the circuit activity? Does it matter if the activity is similar to the naturally occurring one and if so, how similar does it need to be? How does a circuit, dedicated to locomotion deal with a lesion of a connection and with the reconnection?

My research on the neurobiology of locomotion of this animal has led me to identify a small circuit that is composed of two neurons and two opposing muscle cells that they control. In the new preparation, I combine several cutting edge technologies to enable recording and separately controlling the activity of each neuron and muscle and to perform a very precise lesion in one or the other axons of the neurons with a focused laser beam. The activity of the circuit can be recorded before, during and after the lesion as neuronal regeneration or plasticity occurs. Results, ideas and principals that will arise from these studies will be evaluated through my collaboration with a laboratory that studies a vertebrate model of spinal cord injury. The preparation will allow us to test existing hypotheses, develop new ones and contribute to our understanding of the effects of circuit activity on recovery from spinal cord injury.

When concluded, I expect this experimental preparation of a minimal locomotion circuit to be a springboard to the study of neuronal recovery from injury at the circuit and cellular levels and lead to therapeutic breakthroughs.

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