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THE MIAMI PROJECT TO CURE PARALYSIS

Winter 2011

THE PROJECT

A Publication of The Miami Project To Cure Paralysis & The Buoniconti Fund To Cure Paralysis



The Miami Project To Cure Paralysis
Research Review

2010



UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE



A message from the
Chairman and the
Scientific Director
Barth Green, M.D., F.A.C.S.
W. Dalton Dietrich, Ph.D.

Over the past 25 years, Miami Project scientists have made discoveries that have changed the way we think about how we treat people with paralysis due to spinal cord injury. Basic and clinical research efforts have thus laid the framework for clinical trials targeting this devastating injury. Significant progress in prevention, protection, repair, and rehabilitation have all contributed to our current notion that new treatments will make differences in people's lives that may not yet have spinal cord injury or individuals living with paralysis today. This optimism is based on solid, replicated findings that show that specific therapeutic strategies promoted by Miami Project scientists can be protective and promote functional recovery when initiated after the injury. New findings also show single or combination treatments including Schwann cell therapy promotes axonal growth and improved functional recovery even when these treatments are initiated after chronic injury. This New Year will certainly be a most exciting one for the Project with new discoveries and treatments being tested in the clinical setting.

In the areas of cellular **protection**, our scientists have identified new injury mechanisms that merit evaluation as targets for preventing neuronal cell death after injury. Inflammatory cascades, as well as intracellular signaling mechanisms, appear to determine whether cells die or live after injury. In the area of therapeutic hypothermia, a multicenter trial involving hundreds of subjects with acute spinal cord injury will be advanced this year. Hopefully, through such a randomized, multi-center trial, therapeutic hypothermia will be shown to have benefits in the largest groups of participants to date with severe spinal cord injury. The results of such a trial involving this novel treatment would not need to go through all of the clinical trial stages associated with FDA approval and could immediately change the way we treat individuals with acute injuries. **Reparative** medicine is an exciting focus of The Miami Project mission. High content screening approaches are identifying novel genes and other factors that play a critical role in successful axon growth. Our scientists are studying various cell therapy approaches including Schwann cells and multiple types of stem cells. Regeneration approaches are evolving into strategies evaluating the addition of growth-promoting factors or the neutralization of powerful factors that inhibit axonal growth. The results will provide a rationale for developing single or combinatorial treatments

that better enhance regeneration and promote recovery. Our researchers are now moving forward with a Phase I Safety Trial to use a subject's own Schwann cells to repair their nervous system. Working with the FDA, this process is being finalized and this year an IND application will be submitted to the FDA for permission to start these treatments in a select number of people with acute injuries. This is another outstanding example of how Miami Project science is being translated to the clinic to treat people with these devastating injuries.

Rehabilitation strategies are an essential component of developing cures for spinal cord injury. Miami Project research continues to show promise in enhancing circuit plasticity through robotic training and electrical stimulation. The spinal cord field has embraced the use of various rehabilitation approaches that may one day be combined with neuroprotective and reparative strategies to enhance maximum recovery in people with spinal cord injury. Robotic walking machines and upper extremity rehabilitation approaches, as well as whole body vibration, are just a few strategies that are currently being studied in our subject population to enhance recovery. The elimination of pain and disruptive muscle spasms are critical for successful rehabilitation and Miami Project researchers are making key discoveries toward these goals. Our spinal cord community is aging and with that many age-related disorders are emerging in this population. It is critical that we understand these aging processes so that exercise conditioning strategies and treatments can be initiated to prevent age-related problems including cardiovascular disease and diabetes, to name a few. Investigators in The Miami Project are concentrating on this important research topic and conducting clinical studies that will provide new information on how best to inhibit these processes. Only through such a program will our spinal cord injured population continue to be healthy and have the best chance to regain function when new reparative discoveries are moved to the clinic.

Curing spinal cord injury is a complicated problem, but Miami Project scientists are attacking this problem from multiple disciplines using state-of-the-art approaches to develop treatments that incrementally restore function. We envision a cure to be composed of multiple types of treatments. For example, a neuroprotective intervention administered early after injury, followed by cell replacement, scar removal, and regeneration treatments administered at various later times post-injury. Throughout that whole process, targeted rehabilitation treatments would be essential.

Finally, our educational and outreach programs provide information and valuable resources for our spinal cord injury community. These programs are critical to individuals living with paralysis to help them understand the research that is progressing and appropriate clinical programs that they can reach out to obtain care and support. Only through such a holistic approach of treating spinal cord injury as a complex problem will Miami Project scientists and our colleagues be able to successfully treat this condition and continue to provide hope for curing this devastating disorder that affects so many individuals.

This coming year will be a most exciting one for The Miami Project to Cure Paralysis and University of Miami Miller School of Medicine as we make new discoveries and continue to use this information to develop new treatments for spinal cord injury. We thank our many friends, individuals and foundations for continuing to help us achieve our goals. Thank you for your continued support, and we look forward to a most exciting and productive 2011.

W. Dalton Dietrich, III, Ph.D.
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The Miami Project to Cure Paralysis
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RESEARCH REVIEW 2010

- 2 Message from the Chairman, Dr. Barth A. Green and
Scientific Director, Dr. W. Dalton Dietrich
- 5 Fundraising, Administrative and Scientific Support Staff

THE MIAMI PROJECT 25 YEARS OF SCIENCE

- 10 Research Achievements

FEATURE ARTICLE

- 14 An International Presence

RESEARCH HIGHLIGHTS

- 6 Human SCI Tissue Bank
- 8 Inhibition and Acceleration
- 19 New Faculty
- 20 Can Our Neurotrauma Discoveries Be Replicated?
- 22 Faculty Spotlight: Helen Bramlett, Ph.D.
- 24 Research Funding
- 28 **Faculty Profiles**
- 37 Gail F. Beach Lecture Series/Student Research
- 38 Education Outreach
- 39 Research Publications 2010



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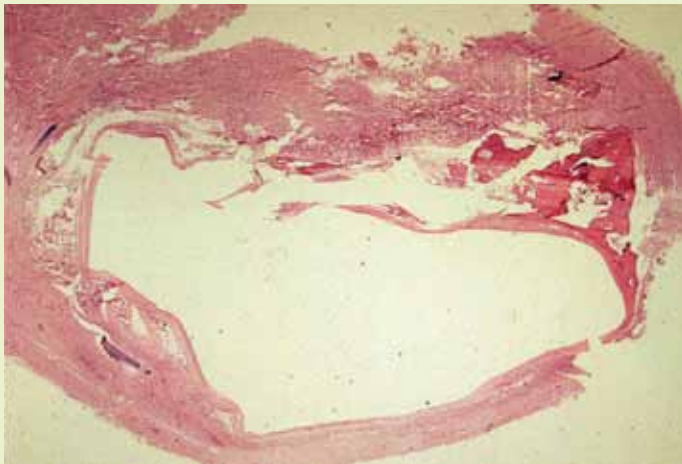
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Human SCI Tissue Bank: A Critical Resource for Understanding Human SCI



A large, fluid-filled cavity, called a cyst, often forms at the injury site in the human spinal cord (left). In some people, these cavities can further develop into syrinxes, which enlarge with increasing pressure and can eventually cause loss of sensation and additional muscle weakness.

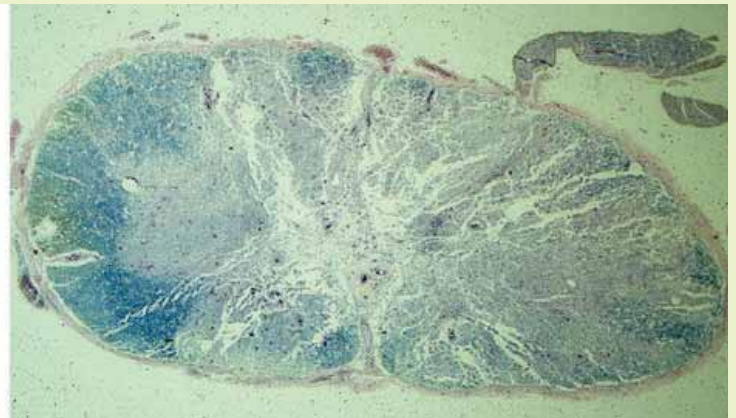
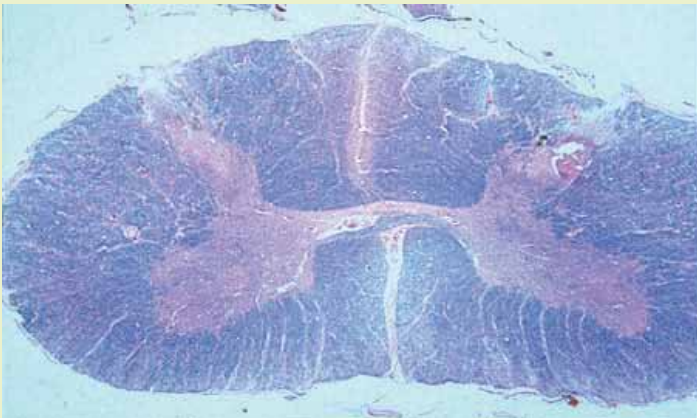
On the opposite page are images of human spinal cord samples illustrating the widespread damage resulting from trauma (far right) compared to non-injured, healthy tissue.

In our efforts to develop treatments for spinal cord injury (SCI), it is important that we use animal research models that appropriately represent what happens in humans. In order to design those models, we need to more thoroughly document and update our understanding of what happens in the human spinal cord after injury. When Dr. Richard Bunge joined The Miami Project as the Scientific Director in 1989, he decided to create a human SCI tissue bank to address that need. At the time, only one other such tissue bank existed, which was maintained by Dr. Byron Kakulas in Australia.

By 1990, The Miami Project to Cure Paralysis **Human SCI Tissue Bank** had been established. This was a collaborative effort involving University of Miami faculty (Drs. Richard Bunge, Robert Quencer, Michael Norenberg, and several of their trainees), Jackson Memorial Hospital, and the Miami-Dade Medical Examiner Department. The first publication from this initiative came in 1992 describing acute traumatic central cord syndrome. This is one of the most common types of incomplete cervical injury with a characteristic pattern of paralysis hallmarked by greater weakness in the arms and hands than in the legs. It had been thought for many years that the symptoms resulting from this type of injury were always a result of damage that was restricted to the center area of the spinal cord with significant bleeding at the site of damage. Dr. Bunge and colleagues discovered in the 1992 study that **in some cases** of central cord syndrome there was actually little to no evidence of bleeding in the injury core. Rather, there was significant axonal (nerve fibers) damage spread diffusely throughout the outer areas of the cervical cord. This discovery is very important with respect to the development of treatments to repair the appropriate areas of the spinal cord.

Another important finding had to do with Schwann cells, which was published in 2000. Schwann cells are normally not present in the spinal cord. However, after injury to the spinal cord, Schwann cells can enter the spinal cord and rapidly increase in number. When this occurs it is called schwannosis. It is thought that this occurs in roughly half of the people with SCI, however, the occurrence of schwannosis does not appear to be related to the severity or type of injury to the spinal cord. It appears to occur in areas where there is a reduced glial scar. They also found


around the damaged area. New blood vessels will also begin to enter the injury site. The **late phase** is the final phase and continues for months or years. Many different things can happen during this chronic period, such as dieback of axons, solidification of the scar, schwannosis, and the formation of fluid-filled cavities within the injury site. In some people, these cavities can further develop into syrinxes, which enlarge with increasing pressure and can eventually cause loss of sensation and additional muscle weakness.

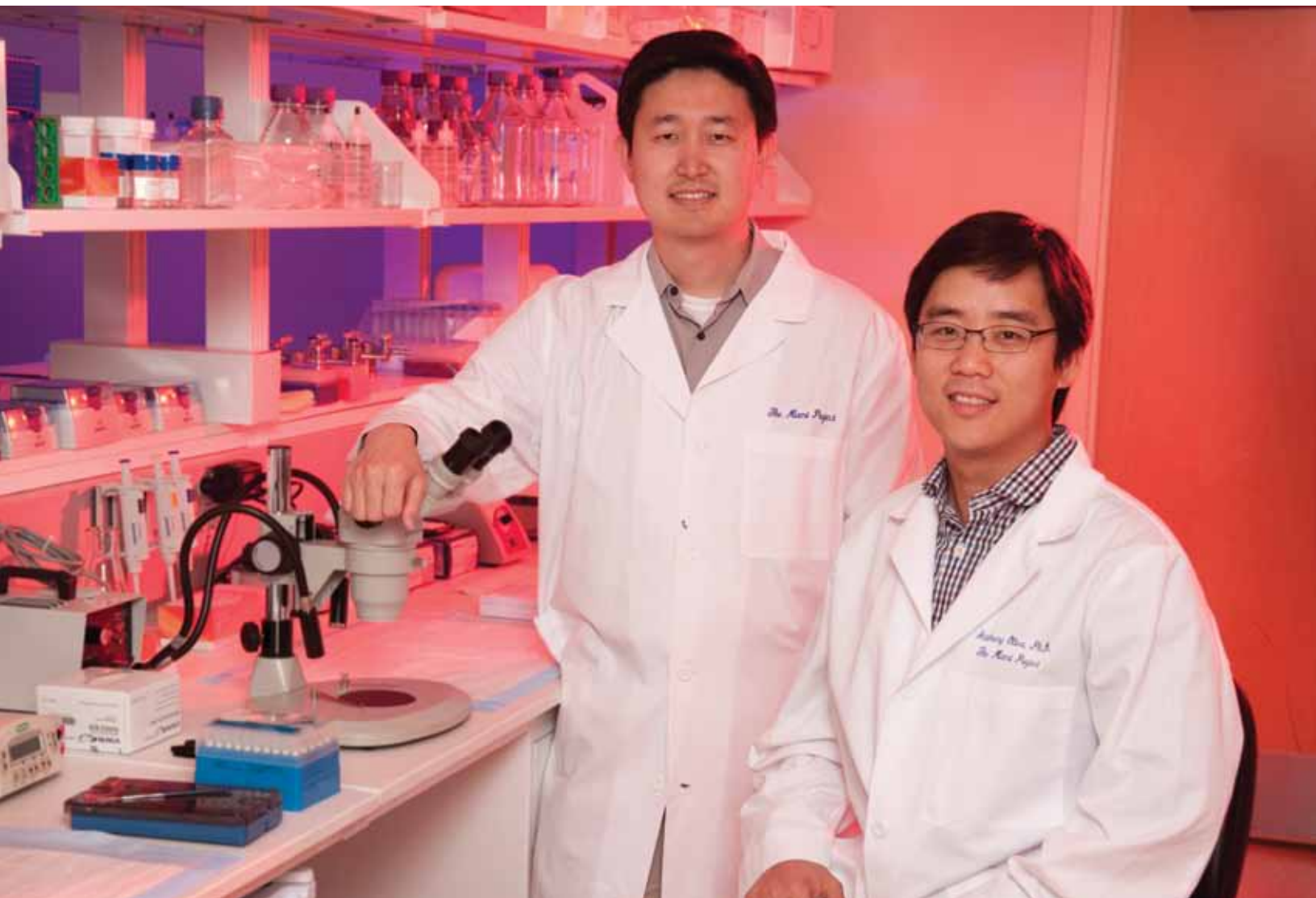


many axons “wandering” within the schwannosis. Such schwannosis, our scientists believe, may provide a barrier to the spontaneous regenerative processes that the spinal cord naturally attempts after injury.

One of the most important publications was in 2004, which was a review of the sequence of events contributing to the pathology of human SCI. There are many phases of events that occur after the initial (primary) injury. The **immediate phase** is within the first 1-2 hours and, surprisingly, not many biologic processes are occurring aside from the mechanical disruption caused by the primary injury. This may be the ideal time window for therapies targeting prevention of secondary injury events. The **acute phase** is between 2 to 48 hours. During this period, a significant amount of swelling, bleeding, and inflammation occurs at the injury site. These contribute to negative changes in nerve cells, axons, and glial cells that were not initially damaged. The **intermediate phase** begins after the first couple of days and persists for weeks. During this time, many different types of cells will enter the injury site to clear away the dead tissue and begin forming a scar

Other key discoveries have been made by external scientists using the tissue bank. These include a detailed description of the response of the immune system triggered by SCI by Dr. Lynne Weaver as well as abnormal sprouting of sensory fibers that can contribute to the development of pain and altered cardiovascular control by Dr. Andrei Krassioukov.

After Dr. Richard Bunge passed away, Dr. Michael Norenberg took over the human SCI tissue bank. The tissue bank is still active today and, thanks to Dr. Norenberg, The Miami Project is able to continue to provide this important resource to the SCI research field. The tissue bank is available to scientists wishing to address specific research questions and/or to correlate human pathology to animal findings. All of the past, present, and future results from the human SCI tissue bank will significantly contribute to the development and proper targeting of interventions to repair the damaged spinal cord. Individuals with SCI wishing to donate their spinal cord to our research program should contact our Education office for more information (305-243-7108). 



Dr. Jae Lee and Dr. Kevin Park

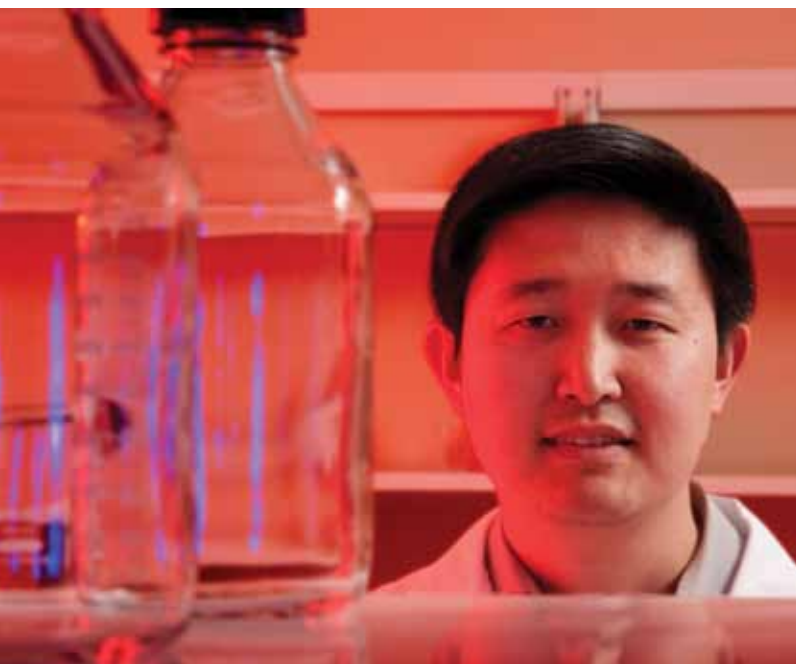
Rising Stars Recruited to Tackle Regeneration from Opposing Angles: **Inhibition and Acceleration**

The Miami Project is proud to have recruited two new faculty members who are rising stars in the field of regeneration. Dr. Jae Lee joins us from the University of California, San Diego and Dr. Kevin Park hails from Harvard University. Both faculty members are studying regeneration, but from opposite angles. Lee is focused on factors that are present after spinal cord injury (SCI) that prevent, i.e. inhibit, damaged axons (nerve fibers) from regenerating. These are referred to as external, or extrinsic, factors because they come from the environment surrounding the damaged axons. Park, on the other hand, is focused on factors that stimulate damaged axons to regenerate. These are referred to as internal, or intrinsic, factors because they come from the nerve cells that actually have axon damage. Both aspects are critical in the development of treatments that significantly repair the injured spinal cord.

Jae Lee: The Inhibitor

Dr. Lee has two immediate research goals upon joining The Miami Project. First, he would like to investigate how axon sprouting induced by blocking inhibitors can be used to promote functional recovery after SCI. His research as a post-doctoral fellow demonstrated that even though blocking specific inhibitory chemicals did not promote regeneration of injured axons, it did allow sprouting of uninjured axons in regions away from the injury site. His next goal is to harness that sprouting ability to promote meaningful behavioral recovery. His second research goal is to understand the role of specific cells that invade the injury site after SCI. These cells, which are normally not present in the spinal cord, are thought to play a role in developing the scar that forms after injury. The scar is very inhibitory to regenerating axons. These invading cells are not always restricted to the injury site and can actually spread to more distant regions. Dr. Lee would like to investigate how resident cells in the spinal cord respond to these invading cells and whether this interaction can be targeted for therapeutic purposes.

His long term research goal is to clarify the mechanisms that create an inhibitory environment after injury. Currently, we know which cells can produce what types of inhibitory molecules, but we need a better understanding of how these cells act in concert and the relative significance of the different inhibitory molecules they produce in order to identify an effective therapeutic target to treat SCI.



Kevin Park: The Accelerator

After SCI, damaged axons spontaneously attempt to regenerate themselves, but the attempt is unsuccessful. Dr. Park is interested in understanding the intrinsic mechanisms that account for failure of axon regeneration after SCI. In his post-doctoral research he identified several key proteins present within nerve cells that block regeneration. In particular, two genes called PTEN and TSC1, which are known to restrict cell growth during development, were identified as major suppressors of axon regeneration after injury. Silencing these genes was sufficient to stimulate robust re-growth of axons. His research goal in his lab at The Miami Project is to further extend his previous findings in order to better understand the intrinsic mechanisms controlling the robust axon regeneration. Some of the important questions that he will be addressing are:

1. *What is the precise intracellular mechanism underlying the axon regeneration seen after silencing PTEN or TSC1?*
2. *Are those regenerating axons able to reform and sustain functional connections?*
3. *Can we use combinatorial strategies together with PTEN deletion to further improve axon regeneration and functional recovery?*

Successful functional recovery after SCI requires multiple steps. Firstly, nerve cells with damaged axons must remain healthy and viable in order to re-grow those axons. Secondly, correct pathfinding of regenerating axons into their target regions is important for proper functional outcomes. Thirdly, regenerating axons require remyelination, i.e. insulation, in order to communicate efficiently. Dr. Park's long term research goals are to study these important processes which are so vital for meaningful gain of sensory and motor functions.

The recruitment of these two fine young investigators is a coup for The Miami Project! Successfully recruiting these two outstanding young scientists to the University of Miami Miller School of Medicine is an exciting step in the continued advancement of the mission of The Miami Project. Drs. Lee and Park bring new cutting edge experimental tools to our multidisciplinary regenerative programs and new fundamental questions to be answered. Their specific programs will be integrated into many of the existing scientific programs of the Project and will help us reach our goal of discovering and testing new treatments for people living with paralysis. 🧠

The Miami Project to Cure Paralysis RESEARCH ACHIEVEMENTS



The broad scope of research carried out at The Miami Project has focused on answering questions that help define human spinal cord injury and reveal strategies for the repair of damaged spinal tissue. The team has also made advances in knowledge that have improved the current care of people with SCI. Over the last 25 years, The Miami Project has made claim to several scientific achievements.

Pioneered the concept of a multidisciplinary approach to SCI research; assembled the most comprehensive team of researchers to address the multifaceted problems of spinal cord injury.

First to build a state-of-the art SCI research facility that under one roof houses the tools and technology that in the hands of researchers will provide advances to find a cure.

HUMAN DISCOVERIES

Established the largest collection of postmortem human spinal cord tissue in the Western Hemisphere. Pioneering anatomical observations and physiological recordings have revolutionized the understanding of human injury.

First to show conclusive evidence of chronic demyelination after SCI in humans.

First to conceive and develop a novel intraoperative monitoring technique that makes spine surgery safer. The technique is now used nation-wide and reduces the risk of paralysis during pedicle screw placement surgery.

First to provide evidence that humans possess specialized nerve circuitry that influences walking and could possibly be enhanced by rehabilitation training. These observations contributed to the development of body weight support gait training. Miami Project investigators are currently adding to the body of knowledge regarding the effectiveness of this rehabilitative training.

First to show that grip strength and sensory/motor function can be improved in people with chronic SCI by using a task practice based therapy that influences the neural circuitry for controlling arms and hands.

Completed extensive testing of a computer-driven Parastep® 1 assisted-walking system. Showed its ability to enhance cardiovascular and conditioning effects and provided supporting evidence for approval by Medicare to reimburse for the device.

First to offer proof that poor sperm motility in men with SCI is a result of chronic inflammation. New knowledge and assistive reproductive procedures have afforded the opportunity for men with SCI to father biological children. Recent Miami Project findings reveal the possibility of a rational treatment for the infertility.

Discovered that semen retrieval by penile vibratory stimulation should be the treatment of first choice for anejaculatory men with SCI because semen quality is better than when obtained by electroejaculation.

Developed new strategies for the multidisciplinary evaluation of SCI pain. The comprehensive state-of-the-art approach targets pathological, physiological, psychological, and social aspects of pain in order to tailor individual treatment strategies. This combination of methods will be useful in evaluating the outcomes of spinal cord injury clinical trials.

Partnered in the first multi-center trial establishing safety and effectiveness of electronically-stimulated cycling in persons with SCI.

Provided first evidence that cardiac structural decay was reversible after electrically-stimulated cycling in persons with SCI.

Undertook first studies establishing benefits of circuit resistance exercise training on attributes of fitness and lipid disorders in persons with both paraplegia and tetraplegia.

Provided first evidence of immune system suppression as an infection risk accompanying tetraplegia.

Led only randomized multi-center trial and published the first manuscript providing evidence for beneficial effects of drug therapy on cardiovascular disease risks in persons with tetraplegia.

Provided first evidence of exaggerated post-prandial lipemia as a silent cardiac risk in persons with SCI.

Provided first evidence for linkage of post-prandial lipemia and pro-atherogenic inflammatory vascular activity.

Currently leading the first large-scale multi-center trial examining lifestyle intervention on diabetes prevention after SCI.

Generated preliminary results that indicate that perceived life interference is related to both neuropathic pain symptom severity and objective signs such as brain metabolites, using Magnetic Resonance Spectroscopy. Specifically, the metabolites associated with neuronal dysfunction or increased numbers of glial cells appear to be important.

The Mami Project to Cure Paralysis RESEARCH ACHIEVEMENTS Continued



First to attempt to directly activate the brain to improve hand function in individuals with cervical SCI. Using transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) hope to improve the ability of the brain to drive information through the remaining spinal pathways and thereby improve hand function.

First to show that muscle weakness is greater with long-term baclofen use and paralysis than with paralysis alone. This weakness makes the whole muscle more fatigable. Restoring the strength and speed of paralyzed muscles to pre-injury levels may require more extensive therapy when baclofen is used chronically. The short-term benefits of baclofen on spasticity (e.g. management of muscle spasms that may otherwise hinder movement or social interactions) therefore have to be considered in relation to its possible long-term effects on muscle rehabilitation.

Demonstrated that the fatigability of the muscle fibers themselves increases after SCI, largely due to lack of muscle use. Transmission of the signals across the neuromuscular junction remains effective, however.



BASIC SCIENCE DISCOVERIES

Designed novel experimental strategies including mild lowering of body temperature (hypothermia) to limit secondary damage following SCI. Promising effects with Interleukin-10 and the inactivation of NFkappaB are also under investigation.

Discovered that the adult nervous system has a remarkable capacity to accept and integrate transplants of neuronal cell lines. Demonstrated that embryonic neurons can reconnect to muscle and restore its function in animals.

Initiated studies to explore whether neural precursor cells or stem cells can be developed and stimulated to mature into different types of nervous system cells.

First to establish optimal laboratory methods to isolate and expand human Schwann cells in culture from adult peripheral nerves – which represent critical steps for the use of autologous Schwann cells grafts for neural repair.

First to demonstrate remarkable improvement in walking function in animals using an innovative treatment that combined Schwann cell grafts with the administration of a cell messenger molecule (cyclic AMP) and the drug rolipram.

Created bioengineered cell line transplants that show promise in the treatment of chronic SCI pain.

Identified a signaling pathway that is activated during traumatic brain injury (TBI) within astrocytes and increases inflammatory gene expression in astrocytes, which exacerbates injury.

Used a novel aquaporin inhibitor to regulate tissue swelling after injury.

Established that systemic administration of just one dose of the immune-modulating drug rapamycin, a dose already well-tolerated in human cancer patients and given at a feasible therapeutic time window after brain injury, reduced the severity of seizures observed at 12 weeks after experimental TBI in rats.

First to demonstrate that there are TBI-induced deficits in the activation of molecules known to be critical for hippocampal learning.

First demonstration in animals that deep brain stimulation of serotonin-containing neurons promotes recovery from SCI or TBI.

Proposed and confirmed new theory that specific brainstem nuclei both detect traumatic brain and spinal cord injury and control their endogenous repair.

Discovered novel compound to promote regeneration *in vivo*.

Identified new family of genes that regulate the intrinsic ability of axons to regenerate.

First large screen of kinases in regeneration in mammalian neurons.

First to discover a role for cancer genes in regeneration.

Identified new descending pathways, originating in the brainstem, that regulate the spinal neurons controlling walking. This analysis has resulted in the identification of a new therapeutic target for the control of walking and research toward development of pharmacological interventions.


First to show that an endothelial bridge across the injury site forms within 7 days of contusion, this could be a bridge for early axonal growth, but disappears for a week or two before reappearing.

Demonstrated that the addition of olfactory ensheathing cells injected into the stumps beside a Schwann cell bridge leads to long distance axonal regeneration after complete transection.

Provided striking evidence that methylprednisolone improves axonal regeneration into Schwann cell bridges in transected adult rat thoracic spinal cord.

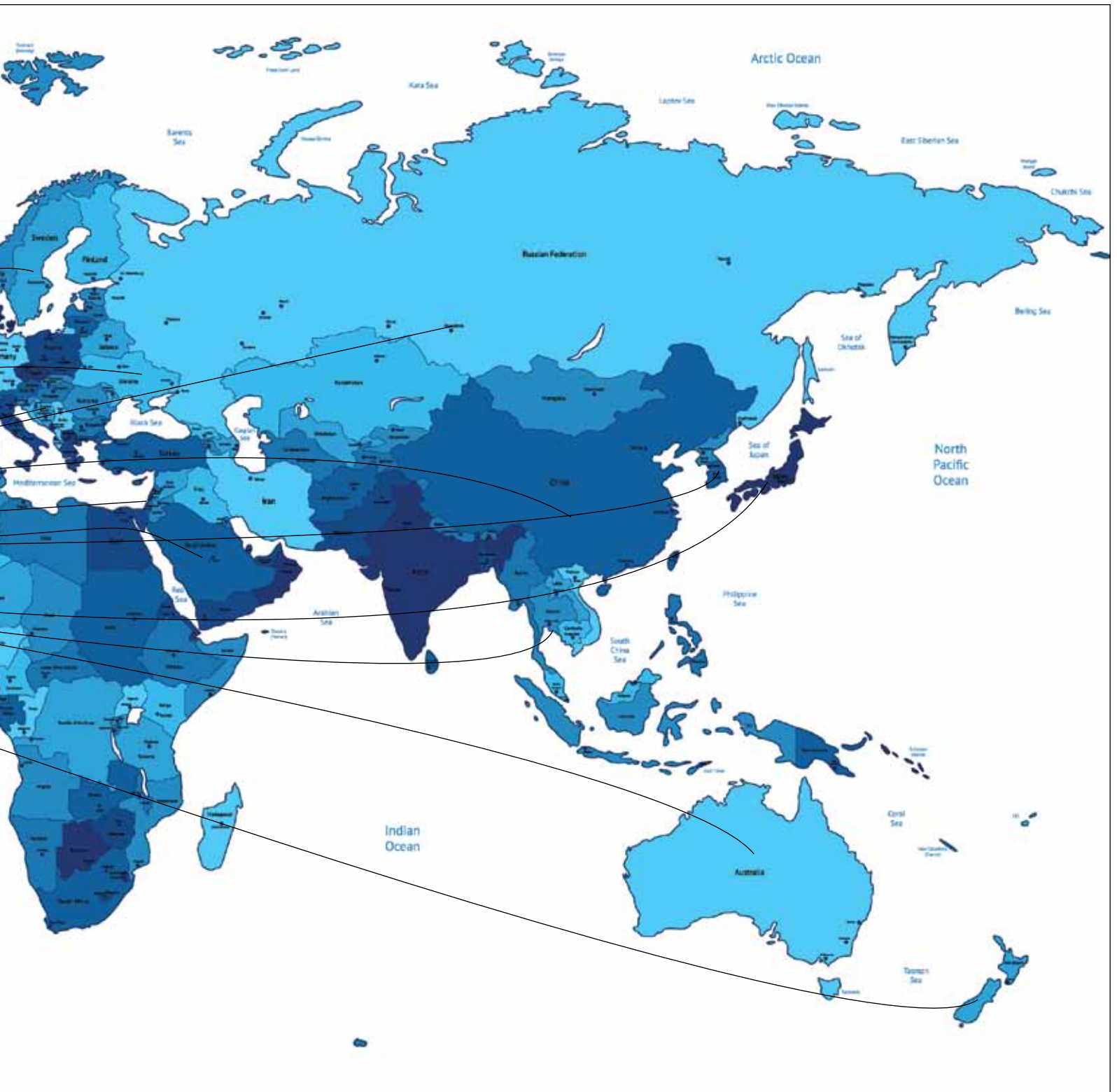
Established that the combination of neurotrophins BDNF and NT3 promotes supraspinal axonal regeneration into Schwann cell bridges following complete transection in adult rat thoracic spinal cord.

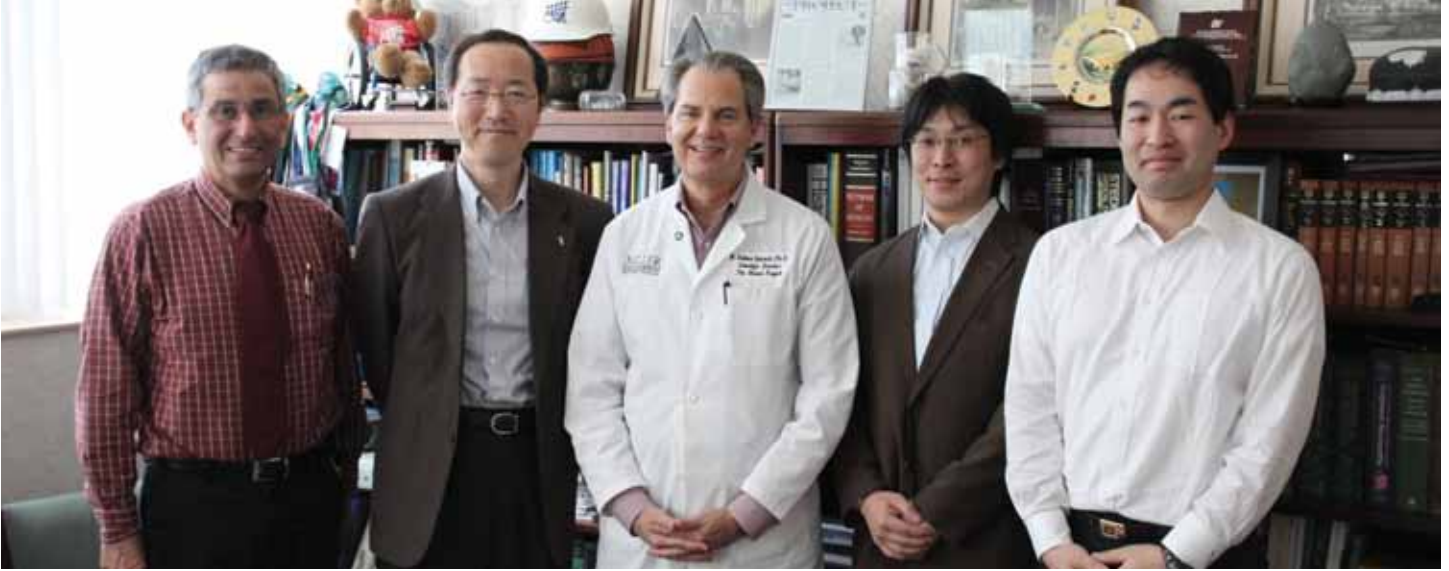
Revealed that NT3 delivered into a muscle is transported to the motor neurons which secreted it. This correlated with increased sprouting of corticospinal tract axons and improvements in walking across a horizontal ladder.

Discovered that by changing the application of a cell delivery matrix, the host/Schwann cell bridge interface is changed and becomes highly irregular with many astrocyte processes extending into the bridge. This is associated with a significant increase in the number of brainstem axons regenerating into the Schwann cell bridge. 

THE MIAMI PROJECT - AN INTERNATIONAL PRESENCE








Dr. Ozawa (second from left) worked in The Miami Project 10 years ago and is now the Chair of a clinical department in Japan. He recently visited us and is pictured here with Dr. Dalton Dietrich (center), Dr. Alex Marcillo (left), and two of his junior colleagues (right) from Japan that he has trained as a result of The Miami Project.

The Miami Project Reaches Across the World

Over the last
25 years, The
Miami Project has
touched multiple
countries across
the world with this
education and
training.

In 1985, when The Miami Project was founded, there were relatively few researchers who specialized in studying spinal cord injury. Hence, a major role of The Miami Project has been to provide education and training for the next generation of neuroscientists. This aspect of The Miami Project's mission is equally as important as conducting the research that will lead to a cure. Our long-term educational goal is to increase the number of scientists and laboratories working on paralysis research and central nervous system disorders around the world. Students and young scientists beginning their careers gain skills from The Miami Project's state-of-the-art comprehensive research and academic environment. The Miami Project has also provided specialized training to visiting scientists who go back to their respective countries to continue their research and to train their colleagues and students.

Over the last 25 years, The Miami Project has touched multiple countries across the world with this education and training. Now there are a plethora of researchers who specialize in spinal cord injury. The field understands so much more about what happens in the spinal cord after injury and has discovered key mechanisms in which we can intervene with therapeutic strategies. There are now multiple Phase I clinical trials being conducted to evaluate different interventions. The Miami Project is proud to have trained over 175 post-doctoral fellows, graduate students, and visiting scholars. There have been an uncountable number of undergraduate students and high schools students who have rotated through our laboratories and there have been 69 faculty members. 

Past and Present Faculty

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Bunge, Richard P.	Miami, FL
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Fitzpatrick, Susan M.	St. Louis, MO
Green, Barth A.	Miami, FL
Greenberg, Jonathan	Orlando, FL
Grimpe, Barbara	Germany
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Holets, Vicky R.	Silver Spring, MD
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Sagen, Jacqueline	Miami, FL
Sanchez, Justin C.	Miami, FL
Sipski, Marca Lee	Reno, NV
Seiger, Åke	Sweden
Suarez, George M.	Miami, FL
Sweetnam, Paul	Brighton, MA
Tepavac, Dejan M.	Miami, FL
Thomas, Christine K.	Miami, FL
Tsoufias, Pantelis	Miami, FL
Watson, Brant D.	Miami, FL
Whittemore, Scott R.	Louisville, KY
Widerström-Noga, Eva	Miami, FL
Wood, Patrick M.	Seattle, WA
Yezierski, Robert P.	Gainesville, FL

Post-doctoral Fellows

Alexeeva, Natalia	Syracuse, NY
Baena, Renato C.	São Paulo, Brazil
Bao, Ying-Hui	China
Basu, Sarmistha	Petaluma, CA
Berrocal, Yerko	Ft. Lauderdale, FL
Bingham, Stephanie	Miami, FL
Blaschuk, Katharine L.	Cambridge, UK
Blits, Bas	The Netherlands
Blithe, Anthony	Calgary, Canada
Brewer, Kori L.	Greenville, NC
Brindle, Ted	Miami, FL
Broton, James	Miami, FL
Brulmley, Dawn	Pocatello, ID
Bulter, Jane E.	Sydney, Australia
Casas, Carlos E.	Miami, FL
Casella, Gizelda T.	Miami, FL
Castellanos, Dan	Miami, FL
Chen, Aqing	Boston, MA
Chen, Shibing	China
Cheng, Ling	San Francisco, CA
Cheon, Jin-Souk	South Korea
Cohen, Daniel	Baltimore, MD
Currier, Paul F.	Boston, MA
Enomoto, Mitsuhiro	Japan
Esipenko, Vladimir	Kiev, Ukraine
Farahvar, Arash	Rochester, NY
Flora, Govinder	Washington, DC
Fortun, Jenny	Miami, FL

Gajavelli, Shyam	Miami, FL
Gamez, Eduardo	Rochester, NY
Gonzalez-Brito, Manny	Miami, FL
Gorman, Adrienne L	Ft. Lauderdale, FL
Griffin, Lisa	Austin, TX
Guénard, Veronique	Switzerland
Guenot, Marc	France
Harumitsu, Hirata	Japan
Hemstapat, Annie	Bangkok, Thailand
Hill, Caitlin E.	White Plains, NY
Hill Esther H.	Moffett Field, CA
Horky, Laura L.	Boston, MA
Hu, Wenhui	Chicago, IL
Huizinga, Carla	The Netherlands
Humphrey, Martin F.	Perth, Australia
Ittah, Avner	Ft. Lauderdale, FL
Jain, Anjana	Atlanta, GA
Johnson, Dawn M.	Miami, FL
Joseph, Gravid	Miami, FL
Klein, Cliff S.	Toronto, Canada
Koshinaga, Morimichi	Tokyo, Japan
Kozhina, Galina	Moscow, Russia
Lee, Jeung W.	Wayne, NJ
Lee, Suni	Japan
Leme, Ricardo L.	São Paulo, Brazil
Li, Feiya	New Haven, CT
Li, Xiuming	Miami, FL
Liu, Shanliang	Richmond, VA
Meijs, Matthijs F.	The Netherlands
Melinek, Rosemary	Miami, FL
Miranda, Jorge D.	Puerto Rico
Moon, Lawrence D.	London, UK
Mulder, Mashca	The Netherlands
Nakamura, Yukiko	Osaka, Japan
Nandoe, Rishi D.	The Netherlands
Paino, Carlos L.	Madrid, Spain
Pardinas, Jose	La Jolla, CA
Patist, Carla M.	The Netherlands
Pereira, Francisco C.	São Paulo, Brazil
Plant, Giles W.	Stanford, CA
Plunkett, Jeffrey A.	Miami, FL
Raval, Ami P.	Miami, FL
Rosano, Caterina	Pittsburgh, PA
Runko, Erik A.	Bethesda, MD
Sanders, Matthew J.	Milwaukee, WI
Schmidt-Kastner, Prabha	Canada
Singh, Amanpreet	Tarrytown, NY
Stubley, Leigh Ann	Miami, FL
Suys, Sonia	Virginia Beach, VA
Suzuki, Takamoto	Tokyo, Japan

Taberner, Annette	Ft. Lauderdale, FL
Takami, Toshihiro	Osaka, Japan
Tando, So	Kyoto, Japan
Tapenas-Castillo, Alexis	Miami, FL
Tay, Bobby K.-B.	San Francisco, CA
Timmer, Leo	The Netherlands
Urrea, Carlos	Philadelphia, PA
Usher, Lynn	Cali, Columbia
Vitarbo, Elizabeth	Jacksonville, FL
Voda, Jan	Miami, FL
Wanner, Ina B.	Los Angeles, CA
Willson, Christopher	Louisville, KY
Wu, Wendong	Japan
Xu, Xiao Ming	Indianapolis, IN
Yan, Heng-Lin	West Haven, CT
Yu, Chen-Guang	Lexington, KY



Past Miami Project trainees Valerie Obremski, Xiao Ming Xu, Thomas Morrissey, Veronique Guenard, and Allan Levi working together in the laboratory.

Visiting Scholars

Bakels, Robert	The Netherlands
Bes, Jean-Claude	France
Bigland-Ritchie, Brenda	New Haven, CT
Cho, Kyoung-Suoh	Korea
Ciscar, Edith L.	France
Dagberg, Bjorn	Sweden
Dalton, Paul	England
Devon, Richard	Canada
Emery, Evelyne	France
Frisch, Gilles	France
Gordon, Tessa	anada
Gurwitz, David	Israel
Hager-Ross, Charlotte	Sweden
Hausmann, Oliver	Switzerland
Hayashi, Nariyaki	Japan
Khalfallah, Mansour	France
Kitao, Kinjai	Japan
Kinoshita, Kosaku	Japan
Lee, Won-Hyung	China
Matsushita, Yoshitaro	Japan
Menei, Philippe	France
Montero-Menei, Claudia	France
Nagashima, Hideki	Japan
Ozawa, Hiroshi	Japan
Park, Byund-Kim	Korea
Park, Sah-Hoon	Korea
Potter, Elizabeth	Chicago, IL
Ramon-Cueto, Almundena	Spain
Ross, Bruce	New Zealand
Rotshenker, Shlomo	Israel
Salvador, Sebastian	Spain
Schwirtlich, Laszlo	Serbia
Sesodia, Sanjay	Miami Shores, FL

Silverman, William	Miami, FL
Sohn, Jin-Hun	Korea
van der Woude, Luca	The Netherlands
Weaver, Lynne	Canada
Westling, Göran	Sweden
Yanagawa, Youichi	Japan
Yu, Zhao Ying	China
Zijdewind, Clasina	The Netherlands
Zijdewind, Inge	The Netherlands

Graduate students

Abulafia, Denise	Mexico City
Akcin, Mehmet	Miami, FL
Beekhuizen, Kristina	Miami, FL
Buscher, William	Pittsburg, PA
Cameron, Tracy	Toronto, Canada
Cannon, Allison	Miami, FL
Chen, Bo	Cambridge, MA
Cruz, Yenisel	Miami, FL
Danton, Gary	Miami, FL
Darr, Andrew	Miami, FL
Dimitropoulou, Anastasia,	Belgium
Dyrehag, Larserik	Sweden
Golden, Kevin	Boston, MA
Farrell, Lisa R.	Davie, FL
Furmanski, Orion	Baltimore, MD
Hoffman, Larisa Reed	Denver, CO
Jovovic, Milan	Belgrade, Serbia
Medri, Edward	Washington, DC
Mendes, Shannon W.	Boston, MA
Morrissey, Thomas K.	Jacksonville, FL
Nelson, Gary	Miami, FL
Obremski, Valerie	Orlando, FL

Passineau, Michael J.	Pittsburg, PA
Pendergast, Julie S.	Nashville, TN
Perez, Monica	Pittsburg, PA
Pinzon, Alberto	New York, NY
Rind, Howard	San Diego, CA
Rodenas-Ruano, Alma	New York, NY
Rosendahl, Andrew	New York, NY
Schaal, Sandra M.	Washington, DC
Schumm, Michael	Germany
Shihabuddin, Lamya	Framingham, MA
Smith, Robin	San Francisco, CA
Stagliano, Nancy	San Francisco, CA
Stepanek, Laurie	San Francisco, CA
Va, Natalie	Miami, FL
Van de Ven, Ingrid	The Netherlands
Van Elk, Niek	The Netherlands
Wahman, Kerstin	Sweden
Winslow, Jeffrey	Miami, FL

This partial list of 245 people, and where they are currently located, demonstrates the success of one of The Miami Project's education goals of increasing the number of neuroscientists in our field. As demonstrated with the map on the previous page, The Miami Project reaches across the world and is changing the future of spinal cord injury.

New Faculty Highlights

The Miami Project welcomes four additional faculty members to our team. Drs. Brambilla and Vaccari were both post-doctoral fellows here that have been promoted to the Research Assistant Professor level to pursue their research more independently. Dr. Keane has been a long-standing member of the neuroscience community at the University of Miami and is collaborating with several of our faculty members. Dr. Sanchez was recently recruited to the Biomedical Engineering department at the university and has joined us to expand our research into neuroengineering prosthetics to restore function in people living with spinal cord injury (SCI). Read on to learn more about each of these fine researchers.



Roberta Brambilla, Ph.D.

The main focus of Dr. Brambilla's research has been to understand the role of neuroinflammation in the pathophysiology of neurodegenerative disorders (e.g., SCI and multiple sclerosis), with a specific interest in the contribution of astrocytes,

a type of glial cell that represents the most abundant cell population in the nervous system. In parallel to continuing to explore the role of astrocytes in the diseased nervous system in collaboration with Dr. Bethea, Dr. Brambilla is developing two specific lines of research in the area of neuroimmunology which focus on: 1) investigating the role of tumor necrosis factor, TNF, in the processes of demyelination and remyelination and 2) investigating the occurrence of neuropathic pain associated with multiple sclerosis.



Juan Pablo de Rivero Vaccari, Ph.D.

Dr. Vaccari's research focuses on understanding early inflammatory events in central nervous system (CNS) trauma and neurodegenerative diseases. Currently, his laboratory is focusing on the effects of pattern recognition receptor (PRR)-activation after

SCI and neurodegenerative diseases. Rig-like Receptors (RLRs) are a novel type of PRRs that are activated following viral infections. Many of the proteins that have deleterious effects on the outcome of CNS injury and disease are activated following RLR stimulation after SCI. Therefore, his current research focuses on RLRs as a therapeutic target and a novel approach to decrease the effects of the secondary injury cascade after SCI.


Robert Keane, Ph.D.

Innate immunity is the first line of defense against pathogens and host-derived signals of cellular stress. The innate immune response engages an array of receptors to detect stress signals and pathogens and activates cells of the adaptive immune response. Dr. Keane's research focuses on investigating mechanisms that direct normal innate immunity and its dysregulation in CNS injury and disease. Agonists and activation mechanisms of inflammasomes are investigated. Regulatory mechanisms that potentiate or limit inflammasome activation after injury have been identified, as well as emerging links between innate immunity and Alzheimer's disease.



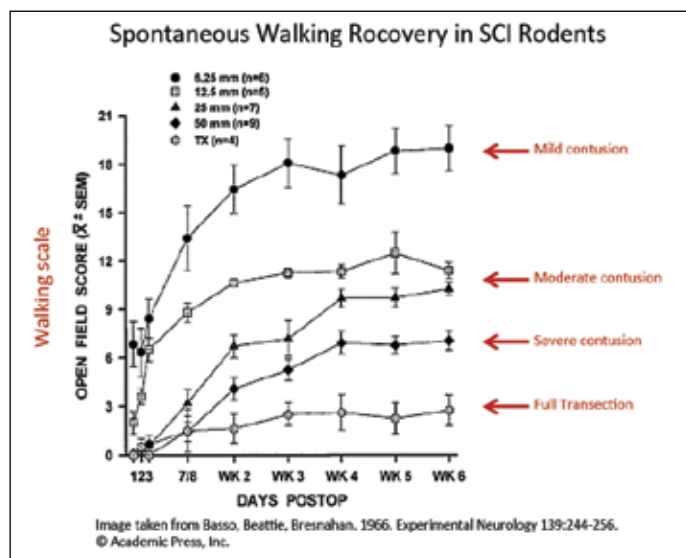
Justin Sanchez, Ph.D.

The goals of Dr. Sanchez' research and the establishment of the Neuroprosthetic Research Group are to develop brain-machine interfaces (BMI) to restore communication and control to people with neurological impairments. The approach is to directly interface with the central and peripheral

nervous system, derive the coding of sensorimotor control, and send commands to bionic devices. The laboratory uses electrophysiological and neural computational tools to seamlessly interface these devices with the nervous system. This translational research initiative operates at the crossroads between basic neural engineering research, neuroscience, and clinical care. 

Can Our Neurotrauma Discoveries Be Replicated?

Over the last several decades, thousands of scientific papers have been written summarizing new discoveries that are relevant to the area of brain and spinal cord injury (SCI). Injury mechanisms responsible for irreversible cell death as well as exciting new treatment strategies to protect and promote recovery of function in clinically



Examples of spontaneous recovery of walking after different injury severities.

relevant animal models have been frequently publicized. Nevertheless, today there are actually few proven treatments that can be given to a person with acute or chronic neurotrauma to improve function and quality of life. This **lack of a successful translation of findings from the bench to the bedside is extremely puzzling** to both scientists and the lay public who frequently read in the popular press that a new treatment has been discovered to treat a human disorder.

One potential reason for this lack of successful translation to the clinic is that our animal models or outcome measures may not be clinically relevant and therefore do not completely reproduce the clinical conditions that occur in our neurotrauma populations. For SCI, laboratory-bred rodents are the most common animal model used. We can create a mild, moderate, or severe contusion injury to the spinal cord, which is the most common type of human injury, or we can create transection (cut/stab) injuries, which are quite uncommon in humans. The spinal cord tissue damage produced by contusions versus transections

is very different, which influences the effectiveness of therapeutic treatments. Using a scale that measures walking ability in rodents, we can evaluate the natural recovery or treatment-induced recovery that occurs after the different types of injury. Even though we can create contusion injuries in rodents that look very much like human injuries, rodents experience a significant amount of natural recovery of walking function compared to humans (see graph). A severe contusion, which would eliminate all movement and feeling below the injury level in humans, still yields a significant degree of movement below the injury level in rodents. Hence, even though contusion injuries produce the same kind of tissue damage in rodents and humans, they do not produce the same kind of behavioral deficits. This complicates our research.

Another potential concern is that the published data may not be robust enough to produce clinically relevant and discernable changes in a heterogeneous population. As we know, no two spinal cord injuries are identical. This creates a high degree of variability in the human SCI population and a very strong functional improvement would be necessary in order to be measurable above the variability.

In an attempt to potentially replicate published findings and evaluate the consistency and robustness of a finding, recent **replication studies** have been **funded** by the **National Institutes of Health (NIH)** to help **promote the translation** of exciting SCI findings to the clinic. In 2000, two institutions, the Reeve-Irvine Research Center, University of California, Irvine and The Miami Project to Cure Paralysis, University of Miami successfully competed for five-year funding to contract work targeting these replication studies. During the replication process, investigators were consulted by leading SCI research authorities regarding what specific papers should be considered for replication. Once this process was completed, the scientists involved with the replication contacted the authors of the originally published data to clarify any details that were not clearly described in the publications. Then, the replication experiment was duplicated in the exact manner as the original experiment. To date, **eight published papers have been attempted to be replicated** by these SCI centers of excellence. Interestingly, **the majority of these studies have been unable to replicate the originally published results**. This indicates that more investigations are required before these treatments are tested in people with SCI. It is felt that this need to replicate findings will ultimately identify pre-clinical experimental therapies that will promote the chances of successful translation to the clinic.

Recently, a third institution, Ohio State University, was awarded a replication contract by NIH as well. After a first attempt at replicating a study failed, they discovered that the original authors had injured the spinal cords at a very slightly different angle than the investigators replicating the study. **That slight difference actually mattered.** They were able to successfully replicate the published results on the third attempt.


Why is it important to independently replicate someone else's research? A critical component of research is to eliminate bias. Most scientists spend their careers doing research because they love it and truly want to help people with discoveries borne from their hard work. There is the possibility that a scientist may believe in their therapy so strongly that they unintentionally introduce bias into their experiments that lead to positive results. When those results lead to the consideration of testing that therapy in humans, the stakes are raised significantly. Firstly, conducting clinical trials costs billions of dollars. Wasting that amount of money on a therapy that may be based on biased results is a travesty and has many negative ramifications. Secondly, **human life is now at stake.** There is risk associated with everything when it is first tested in humans because it's never been done before. Negative outcomes can occur and have occurred in the past. As a result, the majority of scientists believe that therapies that are being considered for human testing should be replicated at least once in a laboratory independent of the developers. The idea being that the independent lab is not invested in the therapy and, therefore, will be less likely to introduce bias into the experiments.

As described previously, however, one lab trying to exactly replicate another lab's results is not easy and has thus far been unsuccessful for SCI. So how do we tackle this problem in a better way?

A new approach to the same problem

Along the same lines of emphasizing independent replication of findings, a new program has been recently funded by the Department of Defense (DOD) to support similar multi-institutional investigations in the area of experimental traumatic brain injury (TBI). TBI is a major problem in the U.S. for civilians as well as for our warriors who have been injured in the wars of Afghanistan and Iraq. It is felt that independent verification of exciting new therapies will help promote the successful translation of these TBI treatments to emergency rooms around the country as well as to the battlefield situation. Several institutions working together

have therefore successfully received funding from the DOD to collaborate in these novel treatment studies targeting experimental TBI. **Operation Brain Trauma Therapy** will include neurotrauma centers at The Miami Project to Cure Paralysis, the University of Pittsburgh, Walter Reed Army Institute of Research, Virginia Commonwealth University, and Banyan Biomarker, Inc. Instead of one lab attempting to exactly replicate another lab's results, this consortium will **screen drugs in a variety of well-established preclinical models** to find those that hold the greatest promise. Those **drugs that are most successful in multiple models at multiple institutions will advance** to higher tiers of experiments involving greater complexity that better mimic the true clinical situation. The most promising drugs will then be considered for clinical trials. The rationale for using different models across different institutions is that, like SCI, TBI is a very heterogeneous injury, and if a drug is found to be efficacious in multiple laboratories then it may have the best chance of working in this heterogeneous human population which demonstrates complex pathologies.

In this regard, it should be emphasized that Miami Project researchers were the first to discover the importance of mild cooling as a protective treatment for acute cerebral ischemia and neurotrauma. This is one of the few examples of the successful translation of a new treatment to the clinic where mild cooling is now being used to treat a variety of patient populations including cardiac arrest, term babies with neurological insults, acute stroke as well as brain and spinal cord trauma. It is anticipated that these types of studies supported by the NIH or the DOD will go a long way toward identifying new treatments that will produce more significant functional improvements, both in the acute as well as more chronic injury settings. 

Replication Studies of Acute Neuroprotective Agents

A re-assessment of erythropoietin as a neuroprotective agent following rat spinal cord compression or contusion injury. *Experimental Neurology* 213 (2008) 129–136

A re-assessment of minocycline as a neuroprotective agent in a rat spinal cord contusion model. *Brain Research* 1243 (2008) 146–151

Anti-CD11d monoclonal antibody treatment for rat spinal cord compression injury. *Experimental Neurology* (2010), doi:10.1016/j.expneurol.2010.11.015

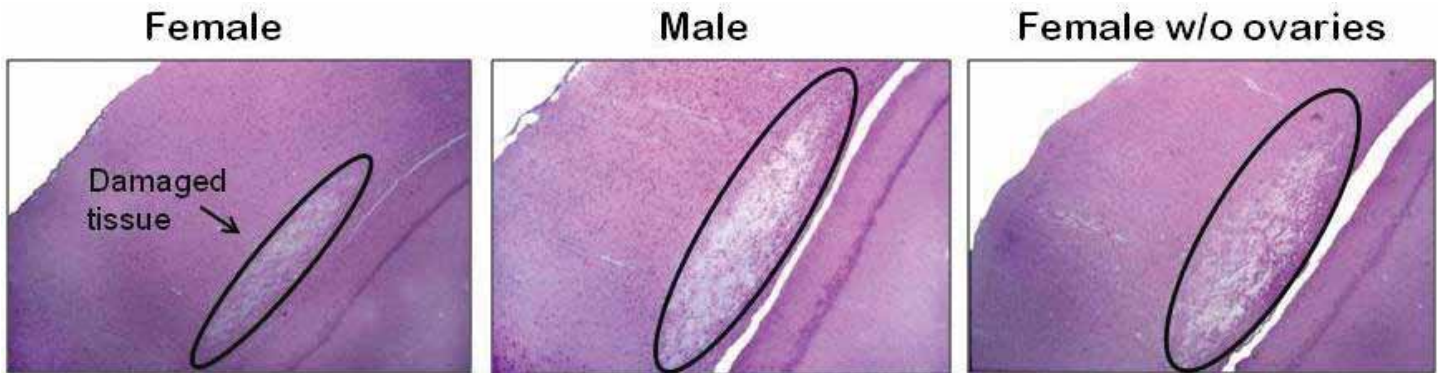
A re-assessment of P2X7 receptor inhibition as a neuroprotective strategy in rat models of contusion injury. Involved 2 different P2X7 receptor inhibitors, PPADS and Brilliant Blue G. *Experimental Neurology*, submitted for review



Faculty Spotlight on Helen M. Bramlett, Ph.D.

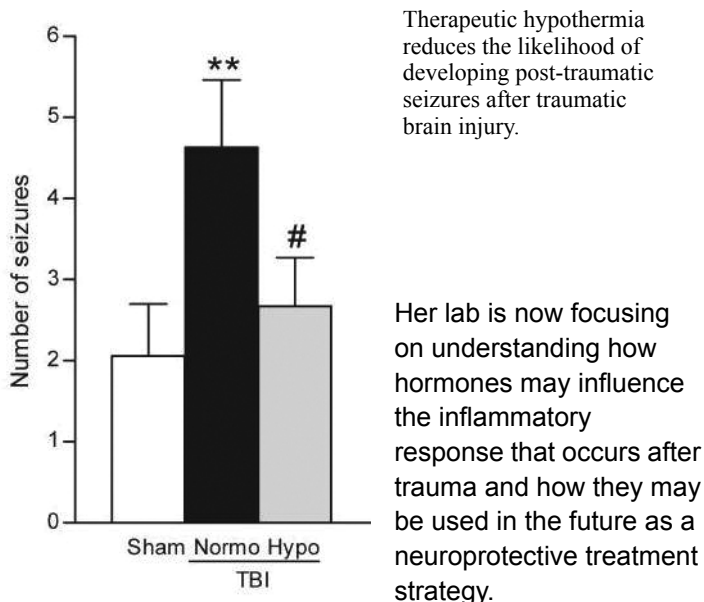
In 2001, her lab was the first to demonstrate that the amount of estrogen-based hormones naturally present in female rodents during a traumatic brain injury (TBI) is protective for the brain tissue.

Dr. Helen Bramlett is an Associate Professor of Neurological Surgery and has been a faculty member with The Miami Project since 2001. Her research focuses on trauma to the brain and spinal cord. Previous studies have investigated how hormones influence injury. Most recently, mechanisms underlying progressive damage and relationships to late occurring neurodegenerative diseases are a focus of her laboratory.




Females that are producing estrogen sustain less tissue damage after traumatic brain injury compared to males or females that are not producing estrogen.

In 2001, her lab was the first to demonstrate that the amount of estrogen-based hormones naturally present in female rodents during a traumatic brain injury (TBI) is protective for the brain tissue. She demonstrated this by comparing female rats to male rats as well as to other female rats that were no longer producing estrogen (did not have their ovaries). The figure above shows that females producing estrogen have a smaller amount of tissue damage after TBI.



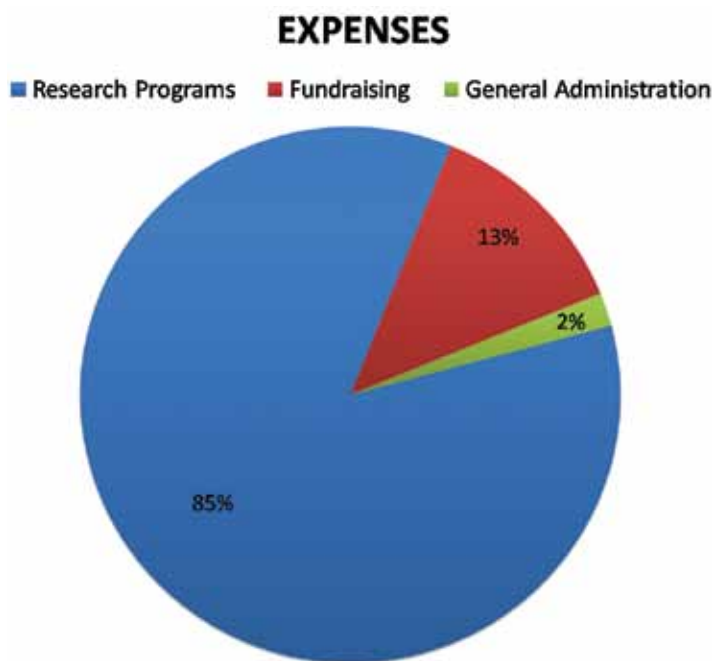
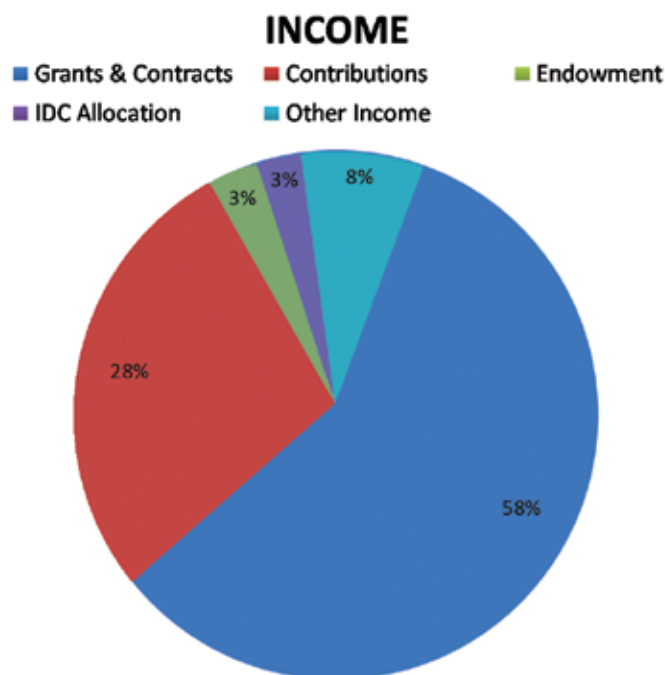
Other studies in her lab are evaluating the long-term changes that occur in the brain after injury. In 2002, her lab produced a quantitative analysis verifying that a progressive loss of brain tissue continues to occur for several months after a TBI. This includes chronic changes in axons that actually survived the initial injury. Another progressive change that occurs after TBI is

the development of seizure activity, a phenomenon known as post-traumatic epilepsy. Recently her lab published data demonstrating that this seizure activity actually worsens tissue damage. In 2010, Dr. Bramlett successfully competed for a Merit Review Grant from the Veterans Administration Biological Laboratory Research and Development program to develop novel treatment strategies for post-traumatic epilepsy. She has a joint faculty appointment at the Bruce W. Carter Department of Veterans Affairs Medical Center here in Miami. Initial experiments indicate that using hypothermia as a treatment strategy for TBI can also reduce the susceptibility to post-traumatic seizures. The graph demonstrates that hypothermia significantly reduces the number of seizures that occur when challenged.

Dr. Bramlett also wears many other hats. She has been instrumental in the NIH-funded spinal cord injury replication studies that The Miami Project has been conducting. So far, five acute treatment strategies have been attempted to be replicated. She is also a Co-Investigator on a newly funded multi-center Department of Defense program to test new drugs that may be used to treat our wounded warriors. These projects are discussed in more detail in another article in this issue discussing the need for replication. At the University she teaches neuroanatomy to undergraduate and graduate students, and serves on the Program in Biomedical Science admissions committee as well as the Institutional Animal Care and Use Committee. She has also served as the President of the Miami Chapter of the Society for Neuroscience, sat on many grant review committees, and next year she will be the new Vice-President for the National Neurotrauma Society. Dr. Bramlett contributes significantly to the mission of The Miami Project and is a highly valued faculty member. 

Each year, Miami Project scientists seek funding for their research by submitting proposals to the National Institutes of Health, the premier scientific body in the United States, as well as other funding agencies and foundations.

Their scientific peers rate the merits of these proposed experiments in a highly competitive process and only the best are funded. The agencies and organizations listed below supported the Principal Investigator(s) and the scientific project(s) indicated during 2010.



Abramson Foundation

Dr. Pantelis Tsoulfas (P.I.)

-Neural stem cells for spinal cord injury

Christopher & Dana Reeve Foundation

Dr. Mary Bartlett Bunge (P.I.)

-Studies of Schwann Cell Transplantation

Dr. James Guest (Center P.I.)

-North American Clinical Trials Network

Craig H. Neilsen Foundation

Dr. John Bethea (P.I.)

Dr. Roberta Brambilla (Co-I.)

-The Role of Astroglial-NF- κ B in Regenerative Sprouting and Neuroprotection

Dr. Murray Blackmore (P.I.)

Dr. Vance Lemmon (Co-I.)

-Functional Testing of Regeneration-Associated Genes in Spinal Cord Injury

Dr. Nancy Brackett (P.I.)

-Inflammasome signaling and sperm cell function

Damien Pearse (Mentor)

(Postdoctoral Fellow Award, Dr. Mousumi Ghosh)

-Promoting the migratory capacity of implanted Schwann cells after SCI to enhance regeneration, remyelination and recovery

Dr. Ian Hentall (P.I.)

-Chronic Brainstem Stimulation to Improve Recovery After Spinal Cord Injury

Dr. Robert Keane (P.I.)

-Inflammasome Regulation Following Spinal Cord Injury

Dr. Mark Nash (P.I.)

-Effects of Exercise on Prandial Lipemia and Fat Oxidation After Tetraplegia

-Effects of Salsalate on Prandial-Induced Vascular Inflammation after SCI

-A Model Community/Home-Based Exercise Program for SCI

Dr. Jacqueline Sagen (P.I.)

-Identification and Rapid Screening of Novel Treatments for SCI Pain

Dr. Christine Thomas (P.I.)
-Automatic analysis of spasms in human muscles paralyzed by spinal injury

Dr. Eva Widerström-Noga (P.I.)
Alberto Martinez-Arizala (Co-I.)
-Utility of quantitative sensory testing in SCI-related neuropathic pain

Department of Defense (DOD) Spinal Cord Injury Research Program (SCIRP) of the Office of the Congressionally Directed Medical Research Programs

Dr. M. Ross Bullock (P.I.)
-Clinical Phase IIB Trial of Oxyocyte perfluorocarbon in Severe Human Traumatic Brain injury

Dr. Jed Hartings (P.I.)
Dr. M. Ross Bullock (Co-I.)
-Spreading Depressions as Secondary Insults after Traumatic Injury to the Human Brain

Dr. Ian Hentall (P.I.)
-Electrical Stimulation of the Midbrain to Promote Recovery from Traumatic Forebrain Injury

Dr. Mark Nash (P.I.)
-Obesity/Overweight in Persons with Early and Chronic SCI: A Randomized, Multicenter, Controlled Lifestyle Intervention

Dr. Damien Pearse (P.I.)
Dr. Mary Bartlett Bunge (Co-I.)
Dr. James Guest (Co-I.)
-Schwann Cell Implantation for SCI Repair: Optimization of Dosing, Long-Term Cell Persistence, and the Evaluation of Toxicity and Tumorigenicity

Dr. Damien Pearse (Partner P.I.)
-Site-directed Nanotherapeutics to Abrogate Relapsing/Remitting Multiple Sclerosis and Promote Remyelination Repair

Dr. Frank Tortella (P.I.)
Dr. M. Ross Bullock (Co-I.)
-Treatment of Traumatic Brain Injury using the neuroprotectant NNZ2566

Fa Bene Foundation

Dr. Damien Pearse (P.I.)
-Cellular therapies for chronic spinal cord injury repair

Florida Department of Health Bureau of Emergency Medical Services

Dr. Gillian Hotz (P.I.)
-WalkSafe Florida State Implementation

Florida Department of Transportation

Dr. Gillian Hotz (P.I.)
-Safe Route to School-WalkSafe County Program
-WalkSafe Miami-Dade

-WalkSafe Tool Kit
-BikeSafe Program

International Spinal Research Trust

Dr. James Guest (Center P.I.)
-Comparison of Schwann cells and Skin-derived precursor cells for repair of demyelination in the primate corticospinal tract

McKnight Brain Research Foundation – University of Florida

Dr. Mary Bartlett Bunge (P.I.)
-Transplantation of Adult Neural Progenitors (AHNPS) into the Contused Adult Rat Spinal Cord

Medtronic Spinal and Biologics

Dr. Barth Green (Co-I.)
-Pivotal IDE Study of the Bryan Cervical Disc Prosthesis in the Treatment of Degenerative Disc Disease

Miami-Dade County Health Department via Center of Disease Control

Dr. Gillian Hotz (P.I.)
-Community Putting Prevention to Work – Safe Routes to School

Miami Dade Metropolitan Planning Organization

Dr. Gillian Hotz (P.I.)
-BikeSafe Project

National Human Genome Research Institute

Dr. Vance Lemmon (P.I.)
-Bioassay Ontology and Software Tools to Integrate and Analyze Diverse Data Sets

National Institute on Aging

Dr. Coleen Atkins (P.I.)
-Modulation of the Cyclic AMP Pathway after Traumatic Brain Injury in Aged Animals

National Institute of Child Health & Human Development

Dr. John Bixby (P.I.)
Dr. Murray Blackmore (Co-I.)
Dr. Vance Lemmon (Co-I.)
-Combination therapy in SCI: proof of concept for new compounds and candidate genes

Dr. Edelle Field-Fote (P.I.)
-Adaptive control of flexion withdrawal reflex stimulator for locomotor rehabilitation

Dr. Edelle Field-Fote (P.I.)
Dr. Diana Cardenas (Co-I.)
Dr. Mark S. Nash (Co-I.)
-Improving Hand and Arm Function in Individuals with SCI; Plus American Recovery and Reinvestment Act Supplement grant

Dr. Vance Lemmon (P.I.)
 Dr. John Bixby (Co-I.)
 -Novel Gene Targets for CNS Axonal Regeneration

National Institute for Disability and Rehabilitation Research

Dr. Mark Nash (P.I.)
 -Exercise Interventions for Spinal Cord Injured Adults with Obesity-related Secondary Disorders
 -Sleep Disordered Breathing in Persons with Chronic Tetraplegia: Characterization and Intervention

Dr. Suzanne Groah (P.I.)
 Dr. Mark Nash (Co-I.)
 -Rehabilitation Research and Training Center on Secondary Conditions in SCI

Dr. Gillian Hotz (P.I.)
 -Investigating the Effects of Snoezelen in Children Recovering from Severe Brain Injury

National Institute of Neurological Disorders & Stroke

Dr. Coleen Atkins (P.I.)
 -Rehabilitation Strategies for Memory Dysfunction after Traumatic Brain Injury

Dr. Mary Bartlett Bunge (P.I.)
 Dr. Paula Monje (Co-I.)
 Dr. Patrick Wood (Co-I.)
 -Cytological Studies of Developing and Mature Neurons

Dr. John Bixby (P.I.)
 Dr. Vance Lemmon (Co-I.)
 -Novel compounds that overcome glial inhibition of axonal regeneration; Plus American Recovery and Reinvestment Act Supplement grant

Dr. John Bixby (P.I.)
 -RPTPs in the growth of vertebrate axons
 -Predoctoral training in the neurosciences
 -Mechanisms underlying inhibition of regeneration in CNS axons

Dr. John Bethea (P.I.)
 Dr. Roberta Brambilla (Co-I.)
 -The Role of Astroglial-NF- κ B in SCI
 -Astrocytes Play a Critical Role in the Pathology of EAE

Dr. Akira Chiba (P.I.)
 Dr. Vance Lemmon (Co-I.)
 -In situ Protein-Protein Interaction Networks (PIN) of Neurons

Dr. Ramon Diaz-Arastia (P.I.)
 Dr. M. Ross Bullock (Co-I.)
 -Phase II, randomized controlled trial of brain tissue oxygen monitoring

Dr. W. Dalton Dietrich (P.I.)
 Dr. Helen Bramlett (Co-I.)
 -Efficacy of Necrostatins on Post-traumatic Epilepsy

Dr. W. Dalton Dietrich (P.I.)
 Dr. Coleen Atkins (Co-I.)
 -Cyclic Nucleotide Regulation in Traumatic Brain Injury

Dr. W. Dalton Dietrich (P.I.)
 Dr. John Bixby (Co-I.)
 Dr. Damien Pearse (Co-I.)
 -Training Program in CNS Injury and Repair

Dr. W. Dalton Dietrich (P.I.)
 Dr. Helen Bramlett (Co-I.)
 -The Importance of Temperature on Inflammation after TBI

Dr. W. Dalton Dietrich (P.I.)
 Dr. Helen Bramlett (Co-I.)
 Dr. Daniel Liebl (Co-I.)
 Dr. Pantelis Tsoulfas (Co-I.)
 -Mechanisms of Recovery Following Traumatic Brain Injury

Dr. Robert Keane (P.I.)
 -Inflammasome Regulation After Spinal Cord Injury

Dr. Daniel Liebl (P.I.)
 -Ephrins Regulate Stem Cell Proliferation following Traumatic Brain Injury
 -Regulation of Synaptic Formation & Efficacy Following Traumatic Brain Injury

Dr. Allan Levi (P.I.)
 -Transplantation of autologous Schwann cells for the repair of segmental peripheral nerve defects.

Dr. Andrew Maudsley (P.I.)
 Dr. Eva Widerström-Noga (Co-I.)
 -Volumetric MRSI Evaluation of Traumatic Brain Injury

Dr. Brian Noga (P.I.)
 -Control of Spinal Locomotor Activity by Monoamines

Dr. Damien Pearse (P.I.)
 Dr. Mary Bartlett Bunge (Co-I.)
 Dr. Brian Noga (Co-I.)
 Dr. Patrick Wood (Co-I.)
 -Axon Regeneration: Synergistic Actions of the MAPK and Cyclic AMP Pathways

Dr. Jacqueline Sagen (P.I.)
 -Translational Model for Novel Therapeutics in Spinal Cord Injury Pain

Dr. Jacqueline Sagen (P.I.)
 Dr. Ian Hentall (Co-I.)
 -Neural Transplants and Spinal Neuropathic Pain Processes

Dr. Christine Thomas (P.I.)
 -Muscle function in human cervical spinal cord injury
 -Rescue of Denervated Muscle

Dr. Grace Zhai (P.I.)
 Dr. Pantelis Tsoulfas (Co-I.)
 -Mechanisms of Neuronal Maintenance and Protection

New York State Department of Health

Dr. Damien Pearse (Co-I.)
 -Manipulation of Glycans in Repair of Spinal Cord Injury

Pfizer, Inc./ United Biosource Corp.

Dr. Diana Cardenas (Site P.I.)
 -A 17-week Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Centered Study of Pregabalin for Treatment of Chronic Central Neuropathic Pain After Spinal Cord Injury

Paralyzed Veterans of America Education Foundation

Dr. Mark S. Nash (Mentor)
 (Post-doctoral Fellow Award, Dr. Rachel Cowan)
 -From Research into the Clinic: The Manual Wheelchair Propulsion Database

Ralph C. Wilson Medical Research Foundation

Dr. Mary Bartlett Bunge (P.I.)
 -Development of Improved Conduits to Introduce Cells, Growth Factors and Extracellular Matrices into the Injured Rat Spinal Cord for Effective Repair

Dr. Jacqueline Sagen (P.I.)
 -Cell and gene therapy strategies for delivery of novel marine snail peptides in chronic spinal cord injury pain

State of Florida James and Esther King Biomedical Research Program

Dr. John Bixby (P.I.)
 Dr. Murray Blackmore (Co-I.)
 Dr. Vance Lemmon (Co-I.)
 -Combination therapy in SCI: proof of concept for new compounds and candidate genes

The Children's Trust

Dr. Gillian Hotz (P.I.)
 -WalkSafe Children's Trust

University of Miami Interdisciplinary Research Program

Dr. Ian Hentall (P.I.)
 -Whole Body Pharmacological Profiling and Imaging of FAST Probes

University of Miami Stanley J. Glaser Foundation

Dr. Coleen Atkins (P.I.)
 -Rehabilitation Strategies for Cognitive Disabilities after Traumatic Brain Injury

U S Army Medical Research & Material Command

Dr. Helen Bramlett (P.I.)
 -Pathophysiology of Polytrauma and Novel Treatment Strategies

Dr. W. Dalton Dietrich (P.I.)
 Dr. John Bixby (Co-I.)
 Dr. Murray Blackmore (Co-I.)
 Dr. Vance Lemmon (Co-I.)
 Dr. Daniel Liebl (Co-I.)
 Dr. Damien Pearse (Co-I.)
 Dr. Pantelis Tsoulfas (Co-I.)
 -Battlefield Exercise and Combat Related Spinal Cord Injury: Neuroprotection and Repair after SCI

Dr. W. Dalton Dietrich (P.I.)
 Dr. Helen Bramlett (Co-I.)
 -The Use of Lentiviral-Vector-Mediated Transduction of Neural Progenitor Cells to Repair the Brain after Traumatic Brain Injury

Veterans Administration Biological Laboratory Research and Development

Dr. Helen Bramlett (P.I.)
 -Novel Treatment Strategies for Treating Posttraumatic Epilepsy

Veterans Administration Rehabilitation Research and Development

Dr. Robert Jackson (P.I.)
 Dr. Diana Cardenas (Co-I.)
 -Rehabilitation of IPF patients: Effects of exercise and oxidant stress

Dr. Eva Widerström-Noga (P.I.)
 Dr. Diana Cardenas (Co-I.)
 Dr. Alberto Martinez-Arizala (Co-I.)
 -Magnetic resonance spectroscopy as a diagnostic and outcome measure in clinical pain trials involving people with spinal cord injury

Wings for Life Foundation

Dr. Damien Pearse (P.I.)
 -Transcriptional Activation of Endogenous and Exogenous Neural Precursor cells for SCI Repair

The faculty of The Miami Project are a talented multidisciplinary team. In the following Profiles, each faculty member describes their specific research focus and highlights of recent progress.



My research interest is the pathobiology and treatment of CNS injury in both the acute and chronic setting. Animal models of cerebral ischemia, and brain and spinal cord trauma are utilized to investigate the mechanisms of tissue injury. The ultimate goal is to target specific injury processes for pharmacological intervention, including the addition of growth factors, to promote circuit plasticity, regeneration, and recovery of function.

W. DALTON DIETRICH, PH.D.

Scientific Director

Kinetic Concepts Distinguished Chair in Neurosurgery

Professor, Departments of Neurological Surgery, Neurology, and Cell Biology & Anatomy

Senior Associate Dean for Discovery Science

Neuroprotection and Improved Recovery of Function following CNS Trauma



A major focus of my research lies in the development of methods to surgically prevent further neurological deterioration and to promote neurological recovery in the chronic spinal cord injury (SCI) patient. The two procedures that we are researching include the delayed decompression of spinal cord and nerve roots and the surgical treatment of spinal cord cysts and tethering from scar tissue. I am also collaborating with Drs. Robert Quencer, Blair Calancie, and Michael Norenberg on the Human Spinal Cord Injury Model project. This very important research program correlates a patient's neurological function with their neurophysiological (electrical) status and imaging studies.

BARTH A. GREEN, M.D.

Co-Founder

**Professor and Chairman, Department of Neurological Surgery
Surgical Interventions**

**JOHN R. BETHEA, PH.D.**

Professor, Departments of Microbiology & Immunology and Neurological Surgery
Immunological Consequences of SCI and The Development of Neuroprotective Strategies

In my laboratory we are studying spinal cord injury (SCI) and diseases of the nervous system such as Multiple Sclerosis (MS) to try to understand the cellular and molecular mechanisms that contribute to astrogliosis and secondary neuronal cell death. To this end, my laboratory has two main research objectives. First, we are studying the neuro-inflammatory response that occurs following SCI and second, we are developing novel therapies for SCI and diseases of the central nervous system.

JOHN BIXBY, PH.D.

Professor, Departments of Molecular & Cellular Pharmacology and Neurological Surgery

Senior Associate Dean for Graduate & Postdoctoral Studies

VANCE LEMMON, PH.D.

Walter G. Ross Distinguished Chair in Developmental Neuroscience

Professor, Department of Neurological Surgery

High Content Screening and Functional Genomics of the Nervous System

Our laboratory has developed methods to test hundreds of genes in hundreds of thousands of neurons each week and obtain quantitative information about cell morphology and gene expression. This “high throughput” capability allows us to tackle questions about development and regeneration using Systems Biology approaches. The Lemmon-Bixby lab has four ongoing projects related to axon regeneration. The first project springs from the fact that neurons in the peripheral nervous system are able to regenerate while neurons in the central nervous system (CNS) are not. By analyzing data from several molecular biological approaches we were able to identify 900 genes that are preferentially expressed in regenerating peripheral neurons. Our second project is based on the fact that young CNS neurons have a greater regenerative capacity than old CNS neurons (collaboration with Dr. Jeff Goldberg). We have used DNA microarray data to generate a list of 800 candidate genes. The third project is to test effects of overexpression of known signaling proteins (kinases and phosphatases). In this screen we have tested 724 genes, and have found a high percentage with significant effects on neurite growth (about 40 total). The data from this screen is allowing us to begin to build models of neuronal signaling networks underlying axon regeneration. The fourth project is to screen a chemical compound library to identify compounds that can overcome the regeneration-inhibitory effects of the injured CNS (collaboration with Prof. Young-Tae Chang, National University of Singapore).

**M. ROSS BULLOCK, M.D., PH.D.**

Professor, Department of Neurological Surgery

Director, Clinical Neurotrauma

Preclinical Mechanistic and Neuroprotection Research in Traumatic Brain Injury and Clinical trials, and Neuromonitoring Techniques in the Injured Brain

An important focus in my laboratory is the possibility of promoting repair by augmenting endogenous progenitor cells or by using cell transplantation strategies. We are currently working on modulating neurogenesis and thus improving cognitive recovery after neurotrauma.



MARY BARTLETT BUNGE, PH.D.

**Christine E. Lynn Distinguished Professor in Neuroscience
Professor, Departments of Cell Biology & Anatomy, Neurological Surgery, and
Neurology**

Development of Combination Strategies to Repair the Injured Spinal Cord

The goal in my laboratory is to foster regeneration of axons across and beyond a spinal cord injury (SCI). To improve regeneration of axons after SCI, we are investigating interference in the accumulation of proteoglycans (molecules that inhibit axonal growth), improved survival of transplanted Schwann cells, and genetic engineering of these cells before transplantation to improve their neurotrophic factor-secreting capability or of neurons to enhance their ability to regenerate axons after injury.

DIANA CARDENAS, M.D., M.H.A.

**Professor and Chair, Department of Rehabilitation Medicine
Chief of Service & Medical Director, Department of Rehabilitation Medicine
Pain Interventions and Prevention of Urinary Tract Infections**

The goals of my research are to help find therapeutic interventions that improve recovery, reduce secondary conditions, and create a better life for persons with SCI and other conditions that impair physical or cognitive function. Currently, my research focus is in the areas of neuropathic pain and neurogenic bladder management.



EDELLE C. FIELD-FOTE, PH.D., P.T.

**Professor, Departments of Physical Therapy and Neurological Surgery
Motor Restoration after Spinal Cord Injury**

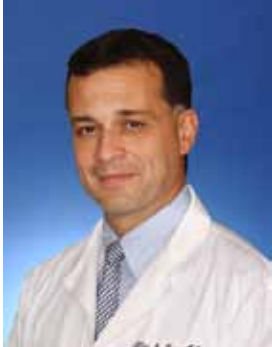
The studies in the Neuromotor Rehabilitation Research Laboratory cross the boundaries of basic neurophysiology of the brain and spinal cord and applied neurophysiology related to neuroplasticity and motor learning. We want to understand which interventions best promote recovery of function. Some of the rehabilitation studies focus on recovery of hand and arm function, while others are aimed at walking function.

ROBERT W. KEANE, PH.D.

**Professor, Department of Physiology & Biophysics
Regulation of Innate Immunity after CNS Trauma**

Innate immunity is the first line of defense against pathogens and host-derived signals of cellular stress. My research focuses on investigating mechanisms that direct normal innate immunity and its dysregulation in central nervous system injury and disease, including (1) agonists and activation mechanisms of inflammasomes, (2) regulatory mechanisms that potentiate or limit inflammasome activation after injury, and (3) emerging links between innate immunity and Alzheimer's disease.





ALLAN D. LEVI, M.D., PH.D.

Professor, Departments of Neurological Surgery, Orthopedics, and Rehabilitation Medicine

Chief of Neurospine Service, Jackson Memorial Hospital

Cellular Transplantation Strategies after Spinal Cord Injury

My research interests have focused on developing cellular transplantation strategies to repair injuries within both the human central and peripheral nervous system. My current interests involve (1) further studies on the human Schwann cells extensively expanded in cell culture to determine whether the functional capacity of these cells with respect to myelination and regeneration are retained when compared to primary Schwann cell cultures and (2) the development and characterization of a model of a peripheral nerve

injury with a lengthy gap in the rat so that we can further characterize the influence of transplanted Schwann cell grafts within a collagen based channel on peripheral nerve regeneration.

MARK S. NASH, PH.D., F.A.C.S.M.

Professor, Departments of Neurological Surgery, Rehabilitation Medicine, and Kinesiology & Sports Sciences

Physiological Assessment of Secondary Complications following SCI: Electrical Stimulation, Cardiometabolic and Vascular Physiology, Cardiovascular Pathology, and Exercise and Dietary Biochemistry

One of the enduring goals of The Miami Project has been to test and implement strategies that optimize health of persons with SCI. A significant target for this strategy has focused on physical activity to lessen secondary risks of SCI associated with physical deconditioning. We also examine complementary themes to validate exercise prescription after SCI, identify optimal dietary composition, and use of prescription and non-prescription agents that reduce hazards of fasting and postprandial lipid disorders, dysglycemia, and vascular inflammatory stress.



JACQUELINE SAGEN, PH.D., M.B.A.

Professor, Department of Neurological Surgery

Cellular Implants for the Alleviation of Chronic Pain and CNS Injury

Our laboratory continues to explore novel and more effective strategies in the therapeutic management of chronic debilitating pain. Our recent research is focused on (1) identification of more effective analgesic agents and combinations for alleviating pain using SCI models and (2) development of emerging therapeutic interventions, including cell transplantation and gene therapy, which have the potential to provide long-term alleviation in people with intractable pain, overcoming the need for repeated pharmacologic administration.

CHRISTINE K. THOMAS, PH.D.

Professor, Department of Neurological Surgery

Neuromuscular Weakness, Fatigue, Spasms, and Regeneration

Our laboratory is currently asking two main questions regarding SCI. First, in studies on people with SCI, we want to understand how well involuntary contractions of paralyzed muscles (spasms) are managed by exercise or by taking baclofen, a drug that is commonly used to control spasticity. Second, in our animal studies, we are exploring how to replace neurons that die because of SCI. Neuron death is common at the injury site and results in severe muscle weakness.





PATRICK M. WOOD, PH.D.

Research Professor, Department of Neurological Surgery

Changes in the Molecular and Biological Properties of Human Schwann Cells

Schwann cells have shown promise in animal studies in promoting recovery from SCI. We have developed protocols that allow the generation, from a small biopsy of human peripheral nerve, of large numbers of a person's own Schwann cells that can be transplanted back into their injured spinal cord. Efficient growth of human Schwann cells in culture requires the addition of recombinant neuregulin and the cAMP enhancer forskolin. To better understand the effects of these reagents on Schwann cells, we are performing basic research to determine the mechanisms by which neuregulin and cAMP enhancers promote interaction between axons and Schwann cells, including axon-

induced proliferation and the formation of myelin sheaths.

NANCY L. BRACKETT, PH.D., H.C.L.D.

Research Associate Professor, Departments of Urology and Neurological Surgery

Male Fertility following Spinal Cord Injury

Our research is focused on understanding and improving impairments to male fertility which occur following SCI. A major aim is to determine the cause of impaired semen quality in men with SCI. Our recent evidence indicates that the problem is related to the seminal plasma. Our current research is investigating inflammatory factors, including semen cytokine levels, as contributors to the problem. Our ultimate goal is to develop therapies to normalize semen quality in men with SCI, so that chances of biological fatherhood are increased.



HELEN M. BRAMLETT, PH.D.

Associate Professor, Department of Neurological Surgery

The Pathophysiology and Treatment of CNS Injury

The focus of my neurotrauma laboratory is to investigate both acute and long-term consequences of brain and spinal cord trauma. My current research interests are on the pathophysiology of traumatic brain and spinal cord injury with an emphasis on the pathogenesis of progressive white matter damage as well as the benefits of therapeutic hypothermia. My laboratory is also investigating mechanistic events leading to the development of posttraumatic epilepsy. Additionally, my current work is also focusing on complex traumatic brain injury models that mimic polytrauma as this type of injury has become more prevalent in combat areas.

JAMES D. GUEST, M.D., PH.D.

Associate Professor, Department of Neurological Surgery

Cellular and Molecular Strategies to Achieve Long Tract Regeneration in the Spinal Cord

The current focus of my laboratory is on the transplantation of autologous glial cells to repair tracts of the injured spinal cord. We utilize several types of animal models with an emphasis on solving translational questions related to human clinical application and collaborate with other researchers in the development of relevant devices. Other areas of research include studies of human post-mortem spinal cord tissue, intra-operative human spinal cord conduction studies, and research design for human clinical trials.





IAN D. HENTALL, PH.D.

**Research Associate Professor, Department of Neurological Surgery
Brainstem Influences on Neurotrauma**

Our research is centered on the general idea that serotonin-containing brainstem neurons influence natural repair processes following brain or spinal cord injury. We study in rats (1) how these brainstem (raphé) neurons respond during injury; (2) how raphé activity influences restorative molecular mechanisms in damaged regions; and (3) how recovery from traumatic spinal cord or brain injury is improved by prolonged electrical stimulation of these nuclei, a procedure with potential for treating acute injury in man.

GILLIAN A. HOTZ, PH.D.

**Associate Research Professor, Department of Neurological Surgery
Co-Director, Pediatric Brain & Spinal Cord Injury Program
Director, Neurotrauma Outcome Research, Concussion, WalkSafe™ & BikeSafe™ Programs**

As a behavioral neuroscientist my clinical interests have always been investigating the neurocognitive deficits of those individuals that have sustained a traumatic and acquired brain injury. I have co-authored two neurocognitive tests, The Brief Test of Head Injury for adults and the Pediatric Test of Brain Injury for children. My research has also focused on injury prevention and I have developed the WalkSafe program and now the BikeSafe program. As the Director of the Concussion Program we have a comprehensive program including neurologic evaluation, neuroimaging, neuropharmacological management, and neuropsychological testing using ImPACT, a computerized neurocognitive screening measure.



DANIEL J. LIEBL, PH.D.

**Associate Professor, Department of Neurological Surgery
Director, Neuroscience Graduate Program
Function of Growth and Guidance Molecules in the Developing and Regenerating Nervous Systems**

The goal of my laboratory is to identify the mechanisms that lead to CNS pathophysiology and its regenerative potential. We focus on a family of molecules, called ephrins and Eph receptors, which play important roles in the developing, regenerating, and injured nervous systems. Specifically, we are currently interested in areas of adult neurogenesis, neuroprotection, synaptic plasticity, regeneration, and therapeutic strategies. Overall, our approach is to develop novel strategies to minimize CNS damage and maximize

regeneration, which can be best achieved through a comprehensive mechanistic approach.

ALBERTO MARTINEZ-ARIZALA, M.D.

**Clinical Associate Professor, Departments of Neurology, Neurological Surgery, and Orthopaedics & Rehabilitation
Pathophysiology and Treatment of Secondary Complications in Spinal Cord Injury**

My research interests focus on common complications that are seen following spinal cord injury: pain, spasticity, syringomyelia, and tethered cord syndrome. My interests include investigating the basis for the development of the different spasticity and pain profiles in the spinal cord injured population and to study potential novel treatments for those conditions.





BRIAN R. NOGA, PH.D.

**Research Associate Professor, Department of Neurological Surgery
Brain and Spinal Mechanisms Controlling Walking**

Our long-term goal is to develop and optimize treatments for spinal cord injury based on transmitter enhancement strategies that include deep brain stimulation, delivery of neurotransmitters or similarly acting drugs, or transplantation of cells secreting these substances. Of the many possible neurotransmitter candidates that could be used for this purpose, monoamines hold particular promise. We have concentrated our recent research effort on understanding the role monoamines play in the control of walking in normal and injured spinal cord.

DAMIEN D. PEARSE, PH.D.

**Associate Professor, Department of Neurological Surgery
Exploration and Translation of Therapeutic Strategies to Repair the Injured Spinal Cord and Brain**

My laboratory focuses on several key aspects of CNS injury repair, including (1) the utility and clinical translation of exogenous and endogenously harnessed cell therapeutics (particularly when used in combinatory approaches), (2) understanding the role of, and developing therapies for, altered cyclic AMP (adenylyl cyclase, phosphodiesterases, and PKA) and MAPK signaling in neurons and glia after CNS injury, (3) the use of nanotherapeutics for multifunctional and site-directed gene/drug targeting to the injured CNS, and (4) the application of methodologies for improved imaging of axonal regeneration and cell integration within the injured CNS such as 3D ultramicroscopy and diffusion tensor imaging.



JUSTIN C. SANCHEZ, PH.D.

**Associate Professor, Department of Biomedical Engineering
Director, Neuroprosthetics Research Group
Neuroprosthetics and Neural Engineering**

The goals of my research are to develop brain-machine interfaces (BMI) to restore communication and control to people with neurological impairments. The approach is to directly interface with the central and peripheral nervous system, derive the coding of sensorimotor control, and send commands to bionic devices. The laboratory uses electrophysiological and neural computational tools to seamlessly interface these devices with the nervous system.

PANTELIS TSOULFAS, M.D.

Associate Professor, Departments of Neurological Surgery and Cell Biology & Anatomy

Neurotrophins: Specificity of Action

My laboratory is interested in two areas of neurobiology that are significant for developing new strategies for spinal cord injury repair. Over the past years, we have worked to modify neurotrophins that are better suited for use in SCI. We are also interested in understanding the processes involved in maintaining and differentiating neural stem cells





EVA WIDERSTRÖM-NOGA, D.D.S., PH.D.

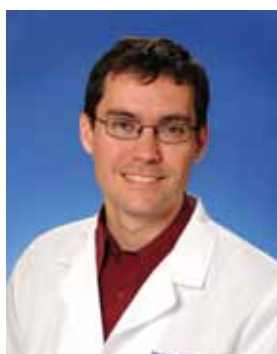
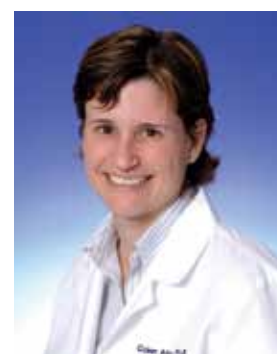
**Research Associate Professor, Departments of Neurological Surgery, Rehabilitation Medicine, Neuroscience Program, and Health Scientist Veterans Affairs
SCI-related Neuropathic Pain Phenotypes and Biomarkers**

My research program is focused on the identification of clinical correlates of the underlying mechanisms of neuropathic pain associated with neurological trauma and injury in order to facilitate translation of basic research findings and the development of tailored interventions. My research focus is highly collaborative and involves extensive interdisciplinary protocols for a multi-axial evaluation of pain symptoms and its psychosocial impact, quantitative assessment of neurological function, and biomarkers including non-invasive brain imaging and genetic polymorphism.

COLEEN ATKINS, PH.D.

**Assistant Professor, Department of Neurological Surgery
Developing Novel Therapies for Traumatic Brain Injury and Spinal Cord Injury**

The research in my laboratory focuses on developing novel therapeutic interventions for traumatic brain injury (TBI) and spinal cord injury (SCI). The research goal of my laboratory is to enhance rehabilitation and recovery by manipulating synaptic plasticity at specific levels of the neuroaxis following TBI and SCI. We have initiated preliminary studies assessing the cellular signaling pathways that are involved in synaptic plasticity at supraspinal regions after SCI, and this will be an important research direction in which we will test novel strategies to enhance recovery after SCI.



MURRAY BLACKMORE, PH.D.

**Research Assistant Professor, Department of Neurological Surgery
Gene Therapy Strategy to Boost the Intrinsic Ability of Neurons to Regenerate Axons after Spinal Cord Injury**

The goals of my laboratory are to clarify the molecular mechanisms that control the growth of axons from nerve cells, and to harness that information to create novel therapies for nervous system injury. Taking advantage of recent advances in automated microscopy, we use high content analysis to rapidly test hundreds of candidate genes in cultured neurons. Because we believe that combinations of genes will be most effective, we work to develop molecular tools that can overexpress and/or knock down multiple gene targets in a single cell. We are currently testing candidate genes in a model of spinal cord injury in rodents.

ROBERTA BRAMBILLA, PH.D.

**Research Assistant Professor, Department of Neurological Surgery
Modulation of the immune response in neurologic disease**

The main focus of my research has been to understand the role of neuroinflammation in the pathophysiology of neurodegenerative disorders (SCI and multiple sclerosis), with a specific interest in the contribution of the astrocytes, a type of glial cell that represents the most abundant cell population in the nervous system. Currently, my laboratory is developing two specific lines of research in the area of neuroimmunology, which focus on (1) investigating the role of tumor necrosis factor in the processes of demyelination and remyelination and (2) investigating the occurrence of neuropathic pain associated with multiple sclerosis.





JUAN PABLO DE RIVERO VACCARI, PH.D.

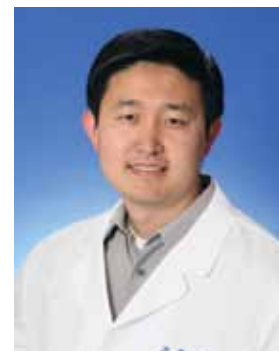
Research Assistant Professor, Department of Neurological Surgery
Underlying mechanisms of the innate immune response and contributions to various CNS diseases

My research focuses on understanding early inflammatory events in central nervous system (CNS) trauma and neurodegenerative diseases. Currently, my laboratory is focusing on the effects of pattern recognition receptor (PRR)-activation after spinal cord injury (SCI) and neurodegenerative diseases.

JAE K. LEE, PH.D.

Assistant Professor, Department of Neurological Surgery
Neutralizing inhibitors of axon regeneration; stimulating plasticity

The long term research goal in my laboratory is to elucidate the mechanisms of cellular interactions in the injured adult spinal cord that creates an environment inhibitory to axonal growth. Currently, we know which cells can produce what types of inhibitory molecules, but we need a better understanding of how these cells interact and the relative significance of the different inhibitory molecules they produce in order to identify an effective therapeutic target to treat spinal cord injury and related neurological disorders.



PAULA V. MONJE, PH.D.

Research Assistant Professor, Department of Neurological Surgery
Molecular signals controlling Schwann cell proliferation and differentiation
In vitro methods to enhance the Schwann cell's ability to promote CNS repair after transplantation

My laboratory studies basic aspects of Schwann cell biology and the use of these cells as therapeutic tools for nerve tissue regeneration. Specifically, we are investigating the role of the second messenger cAMP in the reciprocal interactions between Schwann cells and neurons underlying 1) the axonal regulation of Schwann cell proliferation and myelination during development and 2) the initiation of Schwann cell dedifferentiation, cell cycle re-entry, and re-myelination after injury. To accomplish these studies, we work intensively towards developing new cell culture methods suitable for studying cell signaling and neuron-glia interactions in both human and rodent Schwann cells.

KEVIN K. PARK, PH.D.

Assistant Professor, Department of Neurological Surgery
Intrinsic mechanisms of axon regeneration

My lab is interested in understanding the neuron's intrinsic mechanisms that account for failure of axon regeneration in the central nervous system (CNS). Previously, I and others have identified several key proteins that block axon regeneration, which are present in mature CNS neurons. In my current research, I will further extend my findings in order to better understand the mechanisms governing robust axon regeneration and also to explore the potential of developing therapeutic strategies for spinal cord injury and other neurodegenerative conditions.



Gail F. Beach Memorial Lecture Series

The Miami Project has brought many renowned neuroscientists from around the world to our campus as part of The Gail F. Beach Memorial Visiting Lectureship Series. The lectureship series is dedicated to Gail F. Beach, a schoolteacher and person with SCI, whose generosity and foresight provides outstanding educational opportunities for The Miami Project researchers and our neuroscience colleagues at the University of Miami.



Gail F. Beach visiting lecturer Dr. Kenneth S. Kosik with Dr. W. Dalton Dietrich.

September 1, 2010

Kenneth S. Kosik, M.D.

Neuroscience Research Institute,
University of California, Santa Barbara
"MicroRNAs and the Necessity for a Systems Biology"

September 15, 2010

David H. Rowitch, M.D., Ph.D.

Howard Hughes Medical Institute,
University of California, San Francisco
"Developmental Perspective on Brain Cancer"

November 3, 2010

Michael S. Beattie, Ph.D.

Brain and Spinal Injury Center,
University of California, San Francisco
"Microglial Activation, Neuronal Death and Glial Regeneration after SCI."

January 5, 2011

Charles Heckman, Ph.D.

The Feinberg School of Medicine,
Northwestern University, Chicago
"Adaptations in Electrical Properties of Motoneurons in Normal Motor Behavior, Spinal Cord Injury and ALS"

February 2, 2011

Andrew A. Pieper, M.D., Ph.D.

Southwestern Medical School,
University of Texas
"In Vivo Discovery of Molecules for Treatment of Neuropsychiatric Disease"

March 2, 2011

Phillip Popovich, Ph.D.

Center for Brain and Spinal Cord Repair, The Ohio State University
College of Medicine
"Manipulating Microglia and Macrophages to Promote Recovery after Spinal Cord Injury"

April 6, 2011

Susan Charlifue, Ph.D.

Craig Hospital
"Aging with SCI: Evidence for Premature Emergence of Secondary Complications"

Student Research



Summer Research Fellowship awardee Sarah Bobker with her mentor Dr. Nancy Brackett.

A major role of The Miami Project is to provide education and training for the next generation of neuroscientists. This is a critical component of the mission of The Miami Project. Our

long-term educational goal is to increase the number of scientists and laboratories working on paralysis research around the world so that treatments can be discovered and developed faster. Students and young scientists beginning their careers gain skills from the top-notch academic environment created by the faculty of The Miami Project. During 2010, the faculty members of The Miami Project were actively training 21 post-doctoral fellows, 19 graduate students, 60 undergraduate students, and 51 volunteer students in their laboratories. A select few received fellowship awards for their hard work, as described below.

The Summer Student Research Fellowship is offered to approximately 10 students each year eager to work in the laboratory of a Miami Project faculty member. In 2010, the following students were funded by the North Dade Medical Foundation:

- Amored Amaya – Pearse lab
- James Atkins – Thomas lab
- Sarah Bobker – Brackett lab
- Alexandra Carroll – Lemmon lab
- David Collante – Sagen lab
- Clayton Jackson – Hentall lab
- Allyson Hodgkins – Bixby lab
- Lara Kusnezov – Bunge lab
- Anne Palermo – Nash lab

The University of Miami Citizens Board also funded summer research fellowships for 2 outstanding University of Miami undergraduate students working in Miami Project laboratories. In 2010, those students were:

- Armstrong Ibe – Pearse lab
- Daryaris Morffi – Atkins lab

Dr. John Bixby received supplemental funding from the American Recovery and Reinvestment Act to fund one summer student during 2010, who was Matthew Sacino. 🇺🇸

The “go to” source for information about spinal cord injury

The education department of The Miami Project is the “go to” source for information about spinal cord injury (SCI) and traumatic brain injury (TBI) research being conducted at The Miami Project and for updates describing continuing progress toward the goal of developing treatments for SCI and TBI. Tours and lectures are given frequently. The education department also answers many broader requests for information regarding injury prevention, clinical care referral, resources for living with paralysis, and advice about unproven therapies available around the world. The graph below shows the total number of people reached each month during outreach activities.

In March 2010 the education department participated in the 1st Brain Fair in Miami where over 1,100 people were informed about the central nervous system, injury, prevention, and repair. This will be an annual community outreach event and the next Brain Fair will be held on March 19, 2011.

The education department created a “Neurotrauma Lecture Series” curriculum for high school students in Virginia. Several faculty members gave lectures as part of the curriculum that were transmitted via telecommunication to students at two campuses in Virginia.



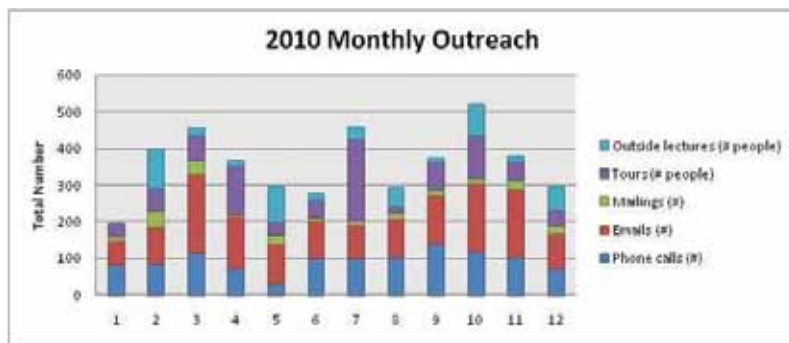
Dr. Field-Fote and Dean Pascal Goldschmidt demonstrate spinal reflexes at the Brain Fair.



Miami Project participates in Take Your Child to Work Day

We also partnered with Urgent Inc. Rites of Passage Youth Empowerment Academy for an internship program for 2 high school students interested in working during the summer. The Rites of Passage Youth Empowerment Academy empowers girls with the knowledge, skills, and opportunities to transition more successfully from adolescence to adulthood.

The education department also hosted Disability Mentoring Day, Take Your Child to Work Day, and had educational booths at the Miami Beach Abilities Explosion as well as the National Neurotrauma Society annual meeting. [CMI](#)



The number of people helped each month by the education department's various information resources.

Published studies that have passed the test of peer review are the benchmark of scientific progress. Listed here are the 2010 research publications by Miami Project scientists and colleagues.

To find links to the abstracts and complete scientific publications listed here, visit the Research Publications section of our website at www.themiamiproject.org/researchpublications



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