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 2015

THE MIAMI PROJECT TO CURE PARALYSIS

UHealth UNIVERSITY OF MIAMI HEALTH SYSTEM

UNIVERSITY OF MIAMI MILLER SCHOOL of MEDICINE

Drs. Barth A. Green, W. Dalton Dietrich and Allan D. Levi

Dear Friends and Colleagues,

The Miami Project to Cure Paralysis and the Department of Neurological Surgery continue to make significant advances in the areas of discovery research, translational studies, and clinical investigations for brain and spinal cord injury (SCI). Basic neuroscience research, which is fueling our translational and clinical programs, is uncovering basic mechanisms of cell death and axonal regeneration. Innovative screening strategies are identifying novel cellular and molecular therapeutic targets to promote recovery. In addition to clarifying the mechanisms underlying cellular repair, the importance of inhibitory signals produced by the injured tissue that block successful regeneration are being identified. Together these studies are providing the necessary knowledge for understanding how best to utilize and possibly combine different treatment interventions to maximize protection and recovery mechanisms after injury.

With this new information, Miami Project scientists are testing exciting hypotheses in clinically relevant injury models. Drug discovery programs are characterizing novel compounds in translational models of trauma, stroke, and neurodegenerative diseases including muscular sclerosis. Positive findings are replicated and, based on results, considered for clinical studies. A current area of translational research is the area of therapeutic hypothermia and temperature management. This approach to protecting and improving outcome in injury models has been successfully translated to severe spinal cord and brain injured patients. More recently the importance of brain temperature in concussion has also been discovered. This and other observations are changing the way we treat patients with different injury severities to minimize long-term deficits and syndromes including age-related neurodegenerative disorders.

Over the last several years our scientists and clinicians have been successful in translating several treatment strategies into the clinic using well-designed clinical studies and Food and Drug Administration (FDA) approved trials. In terms of cellular transplantation, our Faculty are active in clinical trials utilizing Schwann cells and fetal neural stem cells in SCI subjects with complete and incomplete paralysis. The Miami Project has now completed enrollment in its first Phase I dose escalation safety trial with human Schwann cells for subacute SCI. These transplanted subjects are evaluated over several years to assess safety and efficacy. Consistent with our mission of treating subjects living with SCI, a second Schwann cell Phase I trial targeting chronic SCI has been initiated. We have already transplanted two subjects who underwent an extensive exercise and rehabilitation protocol before and following Schwann cell transplantation. We are recruiting additional subjects for this ground breaking trial that for the first time combines an extensive exercise and rehabilitation protocol with a cellular therapy. In addition to Schwann cells, we are engaged in an industry-sponsored, multi-center, Phase II trial using fetal neural stem cells to repair the injured cervical spinal cord. This FDA approved trial is supported by a company that has already completed a Phase I trial targeting subjects with thoracic SCI with outcome assessments being conducted to monitor sensory improvements.

Other clinical studies are testing the benefits of direct brain stimulation on spinal circuit reorganization and the modulation of arm and hand function. Neuropathic pain is an important consequence of SCI and our investigators are discovering the mechanisms underlying pain generation and conducting an FDA approved trial on the effects of deep brain stimulation. The combination of our proven biological approaches for treatment such as cell therapies and future approaches using neuromodulation and brain stimulation strategies appear to be an exciting direction for future research.

Investigations using therapeutic hypothermia continue to move forward for brain and spinal cord injury. Over the last several years, success has been observed with treating severe SCI with cooling protocols. Subject recruitment for a multicenter trial using therapeutic hypothermia in severe Traumatic Brain Injury (TBI) patients is also currently underway. Taken together, these clinical trials are all excellent examples on how our discovery, translational, and clinical research programs are changing the way we treat people with these devastating injuries.

Our Educational Outreach and Training Programs continue to contribute to the mission of The Miami Project. We are reaching out to individuals throughout the United States and abroad providing clinical information, resources, and news regarding progress in research and care. Over 2,500 individuals living with SCI have volunteered to be in our research registry and in 2015 alone 859 individuals participated in our active studies. With future completion of the Christine E. Lynn Rehabilitation Center for The Miami Project at the University of Miami and Jackson Memorial Hospital, these programs will only continue to grow as we help individuals with acute, subacute, and chronic injuries.

Yes, these are very exciting times for The Miami Project and we greatly appreciate the critical support from our friends and colleagues that are helping to move these investigations forward. The Miami Project to Cure Paralysis was established in 1985 to develop new therapies to improve function in paralyzed individuals. Thus, while we are enthusiastic about our current accomplishments and multi-disciplinary research programs, we are most eager about the future as we continue to move new treatments forward to treat paralysis.

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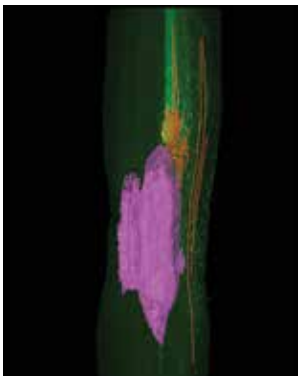

On the Cover

3D image of rat spinal cord injury showing the cavity (purple) and corticospinal tract (red).

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Sustainable Impact Project for Male Fertility After SCI

Individual living with SCI who was able to father a child with the help of The Miami Project Male Fertility research program

Dr. Nancy Brackett and colleagues, Drs. Charles Lynne, Kim Anderson-Erisman, and Emad Ibrahim, were recently awarded a special grant by the Craig H. Neilsen Foundation (CHNF). One of the grant funding programs sponsored by CHNF involves quality of life Sustainable Impact Projects (SIP). To qualify as a SIP, the project must be innovative, have a high likelihood of impacting the delivery of services and care, and address an important gap in service for individuals living with SCI and their families. The project that was funded is titled "Management of Infertility in Men with SCI: An Educational Program for Practitioners and Clients".

Drs. Nancy Brackett and Charles Lynne

This is a very important topic as the majority of men with SCI are infertile; 80% of the people living with trauma-induced SCI in the United States are male, and about half of the injuries occur in people between the ages of 16 and 30 who will go on to live many years with their SCI. Hence, many of these individuals will be at or reach a period in their lives during which they want to start a family. Dr. Brackett has spent her career investigating why men with SCI are infertile and contributing factors include ejaculatory dysfunction resulting from damage to the spinal cord and abnormal semen quality. As a result of these problems, couples with a male partner with SCI who are trying to achieve pregnancy are often told that they must undergo invasive and expensive procedures such as in vitro fertilization (IVF).

This sustainable impact project will address the gap in service due to the lack of appropriate resources for the management of infertility in men with SCI. The medical and lay communities are generally unaware that enough motile sperm can often be obtained from a man with SCI in a non-invasive manner (e.g. by vibrostimulation) and that this can allow for the possibility of less invasive and less expensive methods of achieving pregnancy, such as intrauterine insemination or even intravaginal insemination at home. This project will create an educational program to train healthcare providers and educate clients in the topic of management of infertility in men with SCI. The trainees will then become the trainers of others at their institution thereby providing sustainable education. Over time, a standard of care will evolve through repeated usage of proven methods.

During the 3 years of the grant, they will go to at least 16 centers to provide hands-on training, they will host at least 20 training workshops at The Miami Project, and conduct 12-16 seminars or webinars for SCI support groups. A website will also be created with information for healthcare providers and clients. Dr. Brackett and her team created an information guide, titled "*Male Fertility Following Spinal Cord Injury: A Guide for Patient*s", which is available in hardcopy and pdf formats on The Miami Project website. The first edition of this guide was in published in 2000 and the second edition was published in 2011. They will update this booklet as part of this project.

This SIP is expected to impact the quality of life for individuals with spinal cord injury by 1) establishing a standard of care for the management of infertility in men with SCI, 2) training healthcare providers in the optimal methods of semen retrieval in men with SCI, and 3) providing SCI clients with readily available, current information on options for fertility after SCI.

Trainee Highlights

Graduate student Amber Hackett wins award at the International Symposium on Neural Regeneration

Congratulations to graduate student Amber Hackett for winning the Best Poster Award as well as a Travel Award at the International Symposium on Neural Regeneration held at the Asilomar Conference Grounds in California in December 2015! Amber is a graduate student in the laboratory of Dr. Jae Lee and her research is targeted toward understanding how progenitor cells contribute to the scar after contusive spinal cord injury (SCI). The scar that is formed by the cells that reside in the spinal cord is called the glial scar. The role of astrocytes in glial scar formation has been heavily studied, however, recent evidence indicate that another type of cell, called oligodendrocyte progenitor cells (OPCs), also contribute to the glial scar. In the uninjured spinal cord, OPCs are uniformly distributed and slowly mature into oligodendrocytes, the cells that wrap nerve fibers and help them to efficiently transmit information. Her research found that after SCI, not only do OPCs enhance their maturation into oligodendrocytes (replacing oligodendrocytes that have died after the injury), but they also mature into astrocytes. In addition to maturing into these two cell types, they also proliferate and self-renew around the injury site. Amber wanted to know whether the scar could be changed by manipulating certain molecules in OPCs. Knowing that a molecule called STAT3 is highly activated in OPCs in the glial scar after SCI, she decided to use genetic tools to delete the STAT3 gene from OPCs to study its role in scar formation. Surprisingly, deletion of the STAT3 gene did not affect the ability of OPCs to proliferate and self-renew, but rather it decreased their ability to mature into oligodendrocytes. This suggested that STAT3 is important in the ability of OPCs to replace oligodendrocytes that die after SCI. Her next question was what would happen if OPCs had more STAT3? To do this, she genetically deleted a molecule called SOCS3, which normally serves as a brake for STAT3. Deletion of the SOCS3 gene led to increased proliferation and self-renewal of OPCs that gave rise to more oligodendrocytes and astrocytes. Can the increased production of oligodendrocytes improve the functional impairments caused by the injury by successfully replacing those that died? How does the increased density of OPCs within the scar affect nerve fiber growth? These are exciting questions that Dr. Lee's laboratory is still trying to answer.

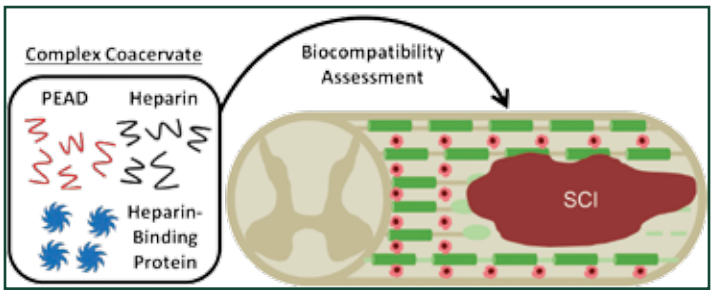
Graduate student Zachary Balmuth-Loris awarded a prestigious fellowship from the American Heart Association

Zak is a graduate student in the laboratory of Dr. Dalton Dietrich. His Ph.D. thesis and the subject of this 2 year fellowship is to investigate the beneficial effects of the proneurogenic compound P7C3-A20 (A20) in a model of focal cerebral ischemia (stroke) and to determine the cellular and molecular mechanisms underlying protection and repair. Focal cerebral ischemia is a devastating condition that leads to brain atrophy and cognitive impairments and very few therapeutic interventions are available. However, there is an increase in adult neurogenesis following ischemia, believed to provide an internal repair mechanism. The neuroprotective compound (A20) has been shown to inhibit neuronal death, prevent axonal degeneration, reduce brain atrophy, and improve cognitive function in other neurodegeneration models, but never stroke. The goal of this project is to determine if A20 is neuroprotective after focal cerebral ischemia. Zak will use two different model systems, rat and mouse, to administer a transient middle cerebral artery occlusion while examining sensorimotor (cylinder, grid walk, and adhesive tape removal test) and learning and memory cognitive (Morris water maze) behavioral tests over chronic time points (6 weeks). Neurogenesis will be examined in both neurogenic niches (the subgranular zone and subventricular zone) as well as brain atrophy. The novel tissue clearing technique CLARITY will be used to make 3D reconstructions of the ischemic brain in order to better resolve what events are occurring post injury. The endpoint of his two year study is to determine if A20 is a viable therapeutic target to combat stroke, which can be delivered immediately following symptoms while extending the therapeutic window.

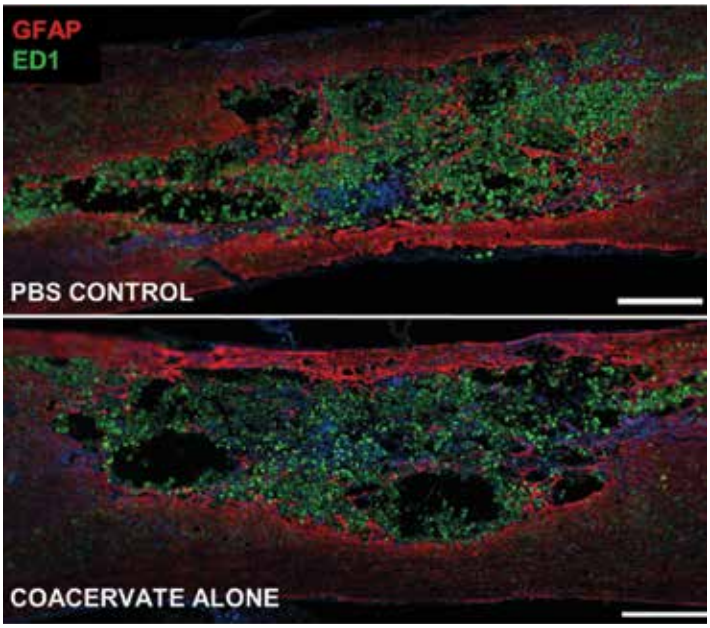
Growth Factor
Delivery Mechanisms

There has been a lot of research over the years about growth factors and their potential use in spinal cord injury repair. Growth factors are important during the development of the nervous system as well as after injury. There are many different growth factors that can influence repair in diverse ways. In the injured spinal cord, the two main events certain growth factors can do is 1) create a "good" environment to promote cell survival, and 2) stimulate sprouting or regeneration of damaged axons. Now, the body's natural production of growth factors after spinal cord injury is not enough to induce repair. A possible therapeutic strategy is to deliver extra growth factors to the injury site. However, growth factors tend to not be very stable when introduced into the spinal cord from an external source. Hence, there is much research focusing on biocompatible mechanisms for delivery of growth factors after spinal cord injury.

Dr. Martin Oudega focuses one area of his research on this topic. He and his colleagues recently tested the compatibility of a complex biomaterial that could potentially be used to deliver growth factors in a stable, sustainable manner (Rauck et al., 2015, *Acta Biomaterialia* 11:204-211). The diagram shows the different components of the biomaterial that come together to form complex droplets that can be injected into the spinal cord injury site.



An important safety step is to make sure the complex droplets are biocompatible and do not cause additional damage to the spinal cord. They found that the complex biomaterial droplets:



1. Did not worsen the inflammatory response,
2. Did not worsen glial scarring,
3. Did not cause more spinal cord tissue to die,
4. Did not reduce the number of nerve fibers above or below the injury site,
5. Did not worsen spontaneous motor recovery that naturally occurs in rats after this type of spinal cord injury.

Those are all very important findings because you would not want a delivery material to worsen the already injured tissue and possibly prevent recovery from occurring.

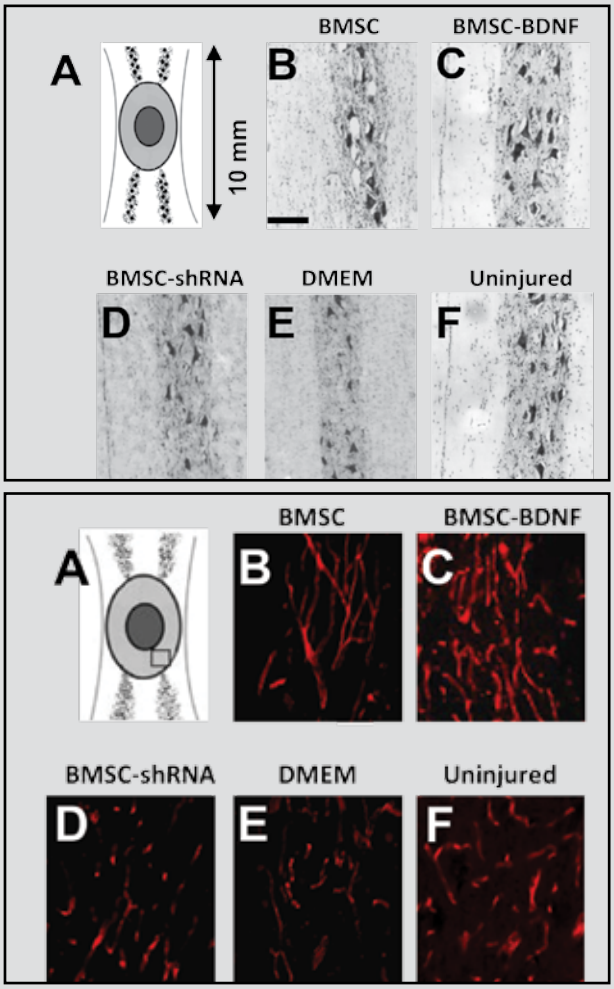
Another growth factor delivery mechanism that Dr. Oudega has investigated is cell transplantation. Bone marrow-derived mesenchymal stem cells (BMSCs) have been transplanted in the acutely and chronically injured spinal cord in adult rats. When transplanted acutely after injury the BMSCs have a neuroprotective effect, but when

transplanted chronically after injury this effect appears to be lost. See our previous articles in The Project 2012 and The Project 2013.

One of the growth factors secreted by BMSCs is the neurotrophin, brain-derived neurotrophic factor (BDNF). BDNF can protect neurons as well as blood vessels. Dr. Oudega investigated the role of BMSC-secreted BDNF in spinal cord repair (Ritfield et al., 2015, *Cell Transplantation* 24:2209-2220). The cells were transplanted into the contused spinal cord three days after injury (this would be considered in the acute time frame). They used gene therapy techniques to create BMSCs that were hyper-secreting BDNF (BMSC-BDNF) or, as a control, not secreting any BDNF at all (BMSC-shRNA).

They compared the effects of transplanting normal BMSCs into the injury with those of transplanting hyper-secreting BMSC-BDNF or silenced BMSC-shRNA. BMSCs hypersecreting BDNF had a neuroprotective effect on motoneurons around the contusion – a greater number survived compared to transplanting normal BMSCs. They also examined the effect on blood vessels in the injury site. It is important to have blood vessels present in the damaged tissue because they provide oxygen as well as other molecules to promote tissue survival. They found that the hyper-secreting BMSC-BDNF very significantly increased the number of blood vessels in the injury site. Interestingly, silencing the release of BDNF had a negative impact on blood vessels. There was a 76% decrease in the blood vessel density in the injury site in animals transplanted with BMSC-shRNA compared to those transplanted with regular BMSC.

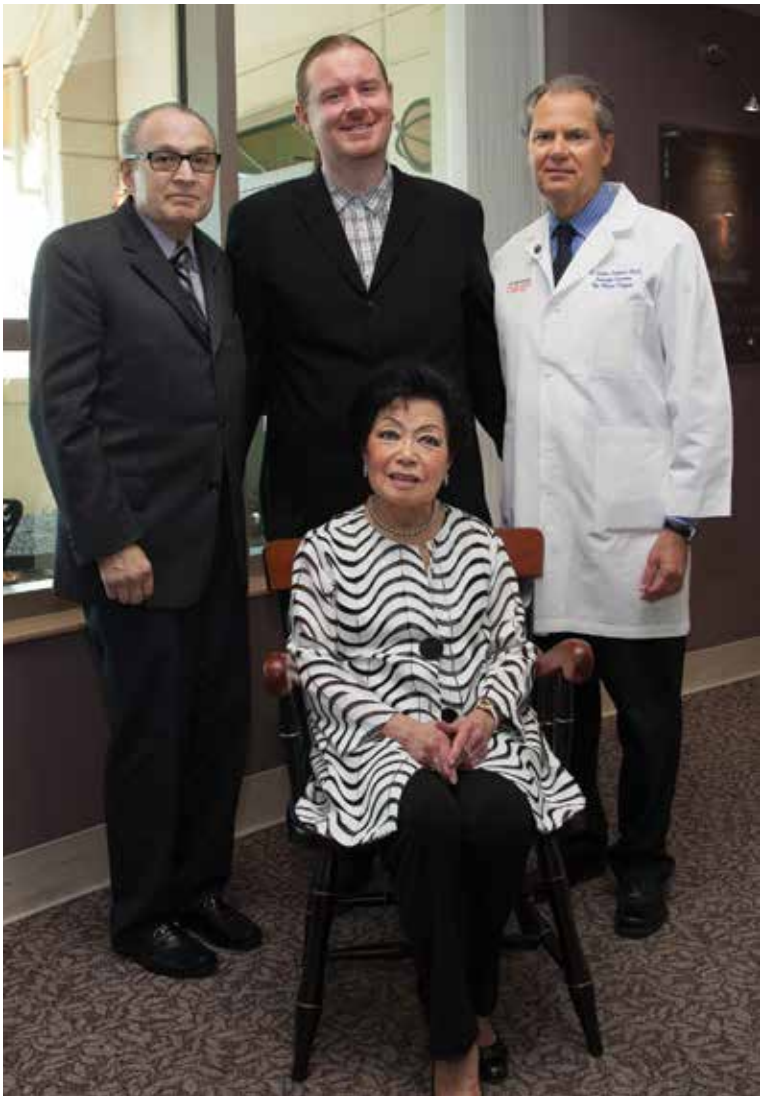
Overall, Dr. Oudega and his colleagues have demonstrated the feasibility of two different mechanisms for delivery growth factors in a sustainable way to the injury site. Research still needs to be done regarding dose optimization, delivering multiple growth factors, and cell transplant survival.



Martin Oudega, Ph.D.

The John M. and Jocelyn H.K. Watkins Distinguished Chair in Cell Therapies

"We are so happy to celebrate the contributions of Jo and her extraordinary husband John in helping us move forward in a continued leadership role in cellular therapies. Their friendship over the past few decades has been instrumental in our success as an organization"



Jocelyn H. K. Watkins (seated) with Drs. Barth Green, Damien Pearse, and Dalton Dietrich

In January 2013 The Miami Project to Cure Paralysis at the University of Miami Miller School of Medicine announced the establishment of The John M. and Jocelyn H.K. Watkins Distinguished Chair in Cell Therapies at a celebratory dinner at The Miami Project. The Chair was established from a gift from John and Jocelyn Watkins to support a leading researcher in cellular therapies as part of The Miami Project's mission of finding solutions to the problems of spinal cord and brain injuries.

The evening in 2013 included touching tributes from Miami Project founders Dr. Barth Green and Nick and Marc Buoniconti. University of Miami President Donna Shalala, Dean of the Miller School of Medicine Dr. Pascal Goldschmidt, and Miami Project Scientific Director Dr. Dalton Dietrich also shared some moving words about John and Jocelyn Watkins during the inspirational evening. "By coincidence or by destiny, this year marked the 25 years of our association with The Miami Project and it is an honor to bring to fruition something that John and I talked about for quite a long time. My wish and my hope is with the establishment of this endowed chair, it offers another step forward to the day our scientists will succeed in finding that which we have all been looking and praying for, and to be able to announce to the world in the not too distant future that they have found a cure for spinal cord injuries," said Jocelyn Watkins.

"We are so happy to celebrate the contributions of Jo and her extraordinary husband John in helping us move forward in a continued leadership role in cellular therapies. Their friendship over the past few decades has been instrumental in our success as an organization," said Dr. Green.

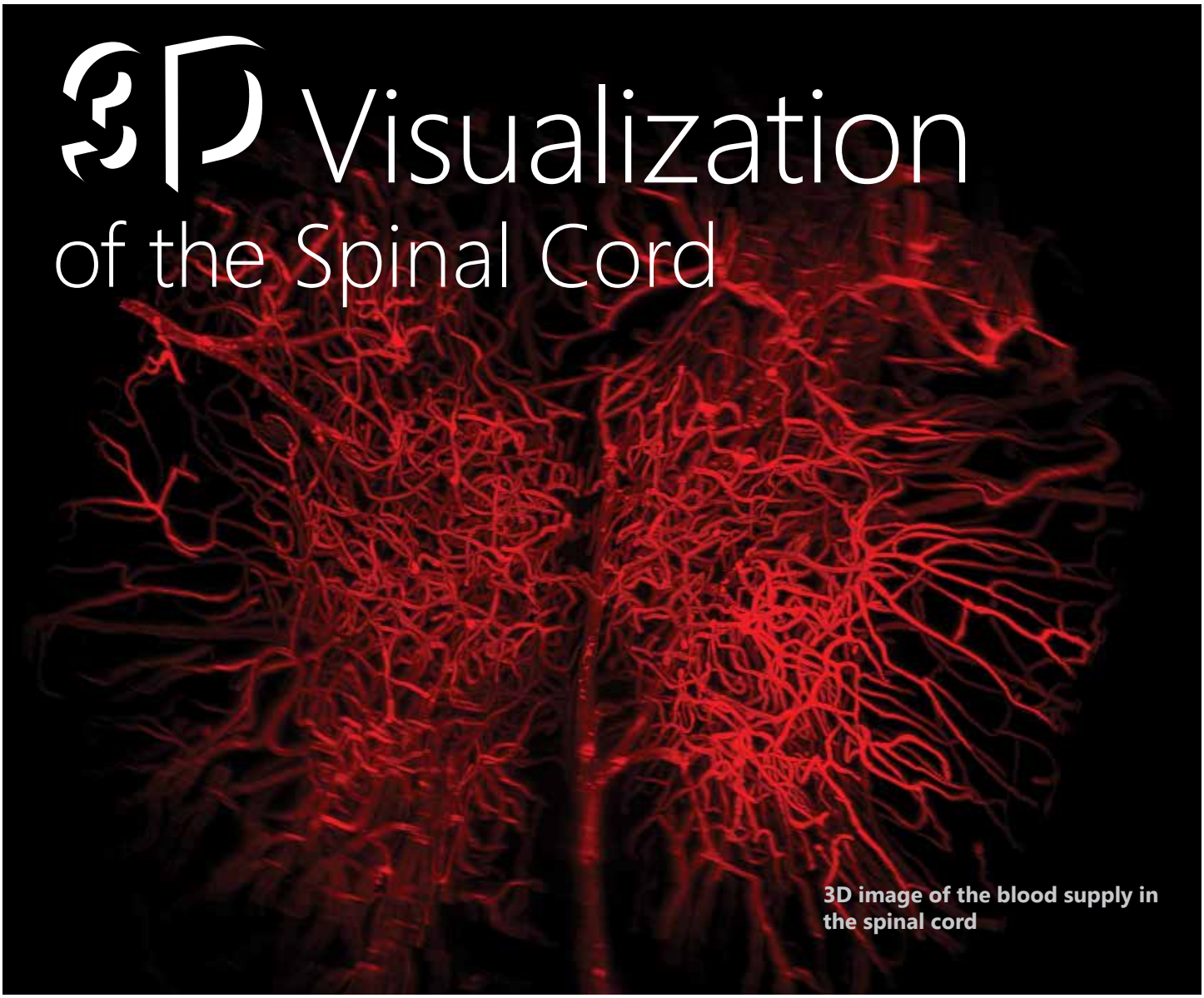
Jocelyn Watkins and her late husband John are generous but unlikely philanthropists. John was severely spinal cord injured, becoming a quadriplegic by a rogue wave while on vacation in St. Lucia in August of 1987. His body was broken but not his brilliant mind or his loving heart, leading he and Jo to many generous acts. They established the Fa Bené Foundation, originally established in 1989 to support The Miami Project to Cure Paralysis, and other charities that touched their hearts. John was an executive at Colgate Palmolive Company where he enjoyed a rapid ascent as a corporate officer and Senior Executive Vice President. In his career he developed marketing strategy, which according to Ian Cook, the present Colgate Chairman, President and CEO, that even today, "casts an enormous shadow at Colgate." Showing great strength after his accident, John used his business know-how to lecture at the University of Miami's School of Business and he enjoyed every moment.

"John and Jocelyn Watkins have been good friends to The University of Miami and The Miami Project. They have given generously over the years and have made a difference in countless lives in this community and beyond. Before his passing, John couldn't move much of his body, but each day helped to move others to help those less fortunate," noted Shalala.

In addition to a sharp mind and warm heart, those close to John will also recall his keen sense of humor, often quoting, "As a quadriplegic, I don't wear out shoes." He was also very spiritual and dedicated to his Church and family. He was passionate about children, particularly those in harm's way around the world. On January 3, 2010, The Miami Herald included John in an article about people who made a difference in the community. John was selected from scores of Miami's movers and shakers. At John's memorial service in Key Biscayne, Florida at St. Christopher's on February 6, 2009, Dr. Barth Green, who treated John after he was life-flighted in from St. Lucia, recalled that "his chances of survival were poor at best." John lived on for over 20 years helping those in need in our community and beyond.

In February 2010 the official announcement was made at a luncheon attended by Jocelyn and friends that the Watkins Endowed Chair has been given to Dr. Damien D. Pearse, Professor in the Department of Neurological Surgery at the Miami Project to Cure Paralysis. This decision was made following a national search to identify the best candidate that would fulfill the endowed chair requirements. Dr. Pearse's research focuses on the investigation of novel strategies to protect and repair the injured spinal cord. He and his research team have been integral to our success over the past several years to obtain FDA approval for our Schwann cell therapy programs, both for the subacute and chronic Phase I clinical trials. Thus, while Dr. Pearse continues to conduct basic research on spinal cord injury and test strategies to promote functional recovery, he is deeply involved with providing the critical data necessary to obtain permission to move future treatments forward. "I sincerely thank Jocelyn and John Watkins for this very special honor. The critical support that will be generated by the endowed chair will allow my laboratory and The Miami Project to continue to develop new treatments for our spinal cord injured population," said Damien Pearse.

3D Visualization of the Spinal Cord



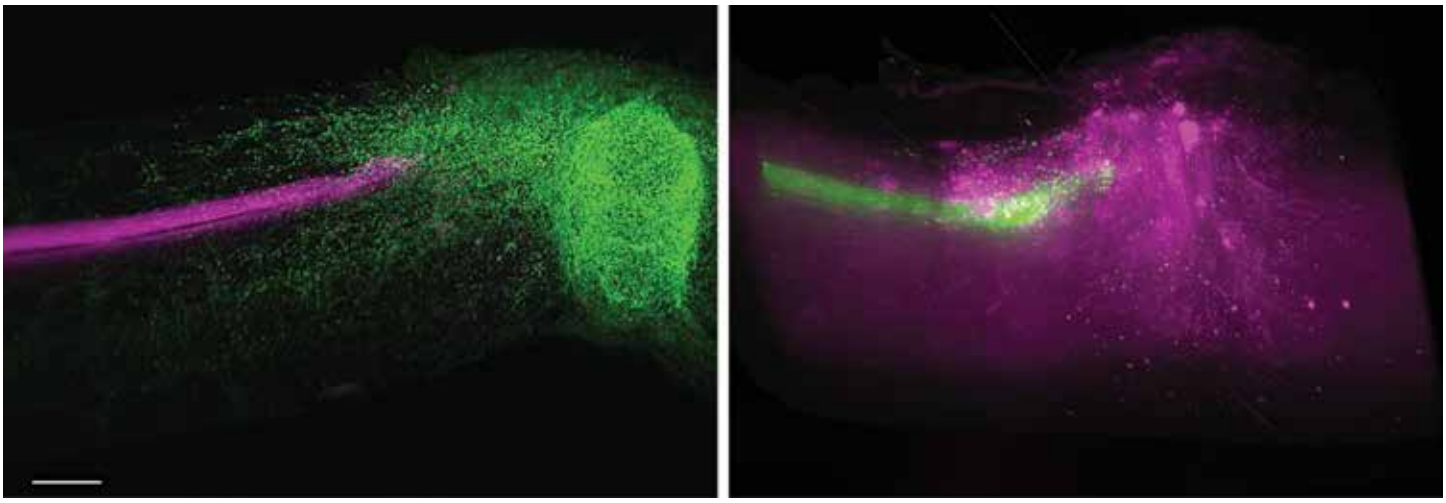
3D image of the blood supply in the spinal cord

The spinal cord is a very complex part of the body. Often times, we try to simplify the explanation of the spinal cord by saying it is like a "bundle of wires". This helps people conceptualize the idea of the spinal cord relaying information. And when one looks at a model of the spinal cord it can tend to look like a big piece of spaghetti to the lay person; however, there is much more inside.

For over a century researchers have been figuring out how to visualize the spinal cord and all of its circuitry. Advances in technology have enabled the field to understand what the spinal cord looks like before injury, after injury, and during attempts at repair. Measuring regeneration of axons is very important and using traditional imaging reconstruction methods is quite labor intensive and slow. **A team of researchers at The Miami Project recently developed a new technique for visualizing more axons with more accuracy in less time** ("3D Imaging of Axons in Transparent Spinal Cords from Rodents and Nonhuman Primates", *eNeuro*. 2(2). doi: 10.1523/ENEURO.0001-15.2015; Team: Cynthia Soderblom, Do-Hun Lee, Abdul Dawood, Melissa Carballosa, Andrea Jimena Santamaria, Francisco D. Benavides, Stanislava Jergova, Robert M. Grumbles, Christine K. Thomas, Kevin K. Park, James David Guest, Vance P. Lemmon, Jae K. Lee, Pantelis Tsoulfas).

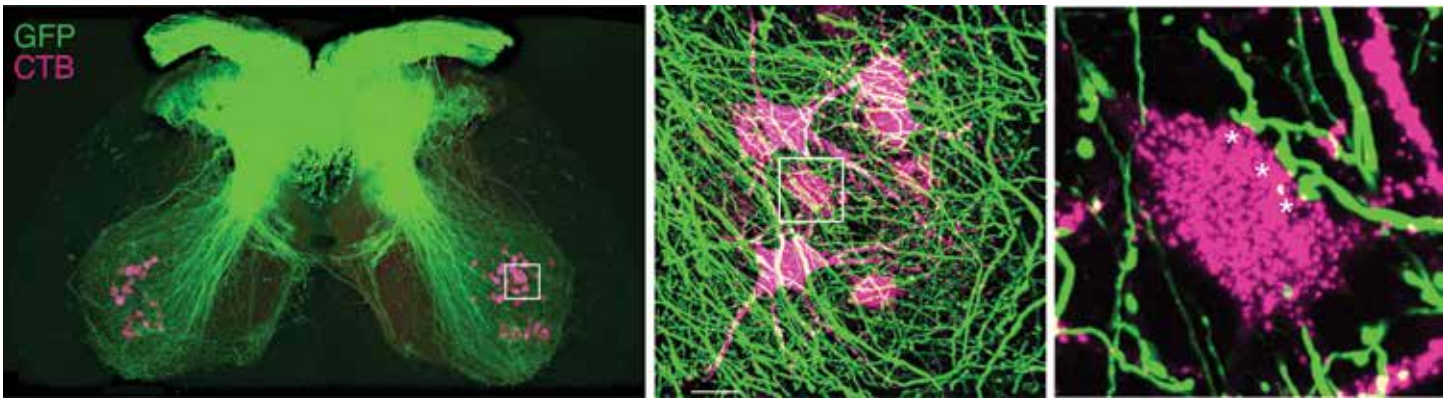
Using high tech light sheet fluorescence microscopy and a special technique for clearing tissue (tetrahydrofuran-based tissue clearing), researchers are able use the whole spinal cord without having to physically cut it into thin sections. In addition to that, the team at The Miami Project used adeno-associated viruses and chemical tracers to label axons in mice, rats, and nonhuman primates. What does all of that mean? Well, a picture is worth a thousand words…

FIGURE 1



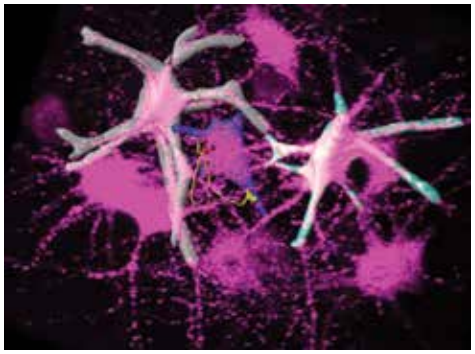
Four weeks after a spinal cord injury in mice, the corticospinal tract axons (magenta in the left photo, green in the right photo) are damaged and cannot regenerate past the fibrotic scar (green in left photo) and astroglial scar (magenta in right photo).

FIGURE 2



Left photo: Cross-section of the rat lumbar spinal cord (green) with the gastrocnemius motor neuron pool (magenta).
Middle photo: High magnification of Motorneurons (magenta) in left photo surrounded by sensory fibers (green).
Right photo: A single motorneuron (magenta) with 3 synaptic boutons (green with asterisks).

FIGURE 3



Individual motorneuron (blue) with synaptic connections (red dots) from afferent axons (yellow).

FIGURE 4A

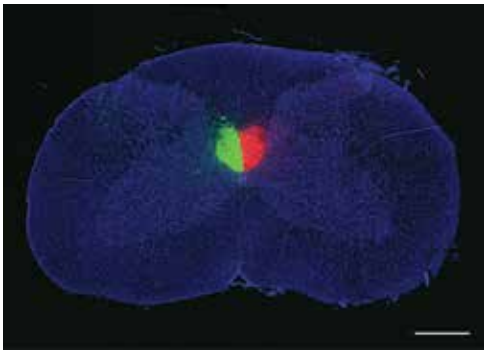
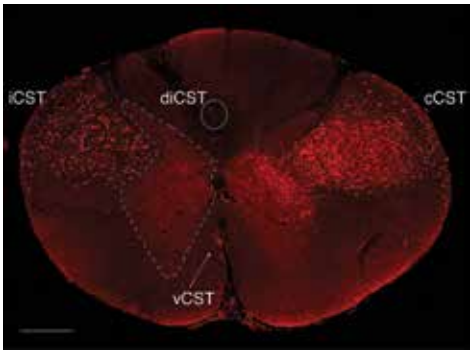


FIGURE 4B



The corticospinal tract is located in different locations within the spinal cord of the rat (Figure 4A, corticospinal tract is in the center labeled green and red) versus non-human primate (Figure 4B, corticospinal tract is on the outer edges).

The Miami Project clinical researchers currently have several clinical trials and clinical studies available for people who have had a spinal cord injury or traumatic brain injury; some are for acute injuries and some are for chronic injuries. The clinical trials are testing the safety and efficacy of different neuroprotective, reparative, or modulatory interventions. The clinical studies are investigating questions regarding activity, rehabilitation training, sleep, male fertility, pain, aging, and motor control and neuroplasticity.

If you would like to be considered for these or future Miami Project trials or studies, please see call The Miami Project Education Office at 305-243-7108.

Survey

•International Spinal Cord Injury (SCI) Basic Pain Data Set Survey for Self-Report Measure

Activity Modifying

•Clinically Meaningful Changes in Wheelchair Propulsion Stress
•Training Programs to Improve Outcomes for Individuals with SCI
•Fitness and Independence after SCI: Defining Meaningful Change and Thresholds
•Cardiorespiratory Responses to Intermittent Hypoxia Exposure in Individuals with SCI
•Effects of Acute Bionic Ambulation on Metabolism, Dysglycemia, and Cardiovascular-Autonomic Functions in Persons with SCI

Male Fertility

•Fertility Evaluation
•Treatment for Infertility

Rehabilitation

•Quantifying Spasticity in Activities of Daily Living

Aging

•Telomeres as an Aging and Health Biomarker in Persons with SCI

Sleep

•Sleep Disordered Breathing in Chronic SCI: A Randomized Controlled Trial of Treatment Impact on Cognition, Quality of Life, and Cardiovascular Disease

Motor Control and Spasticity

•Bilateral Control of Arm Movement After SCI
•Synchronization of Corticospinal Volleys After SCI
•Bilateral Force Coupling After SCI
•Reorganization of Motor Cortical Representations After SCI
•Spike-Timing Dependent Plasticity After SCI

Pain

•Perspectives on Management of Severe Neuropathic Pain After SCI

SCI TRIALS

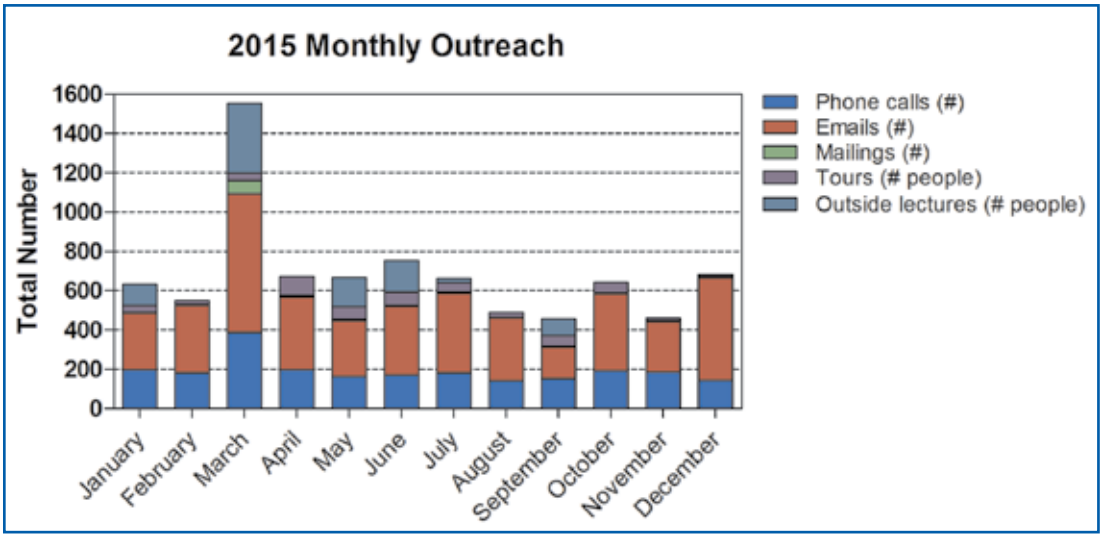
TREATMENT	POPULATION	PHASES 1	PHASES 2
Autologous Schwann Cells	Acute SCI	Closed to enrollment	
Autologous Schwann Cells	Chronic SCI	Enrolling	
Biomarkers of SCI	Acute SCI	Enrolling	
Nactn	Acute SCI	Enrolling	
Riluzole	Acute SCI	Completed	Enrolling
Therapeutic Hypothermia	Acute SCI	Enrolling	
HuCNS-SC® Stem Cells	Chronic SCI	Completed	Enrolling
DBS	Chronic SCI	Enrolling	
BMI	Chronic SCI	Pending	

TBI TRIALS

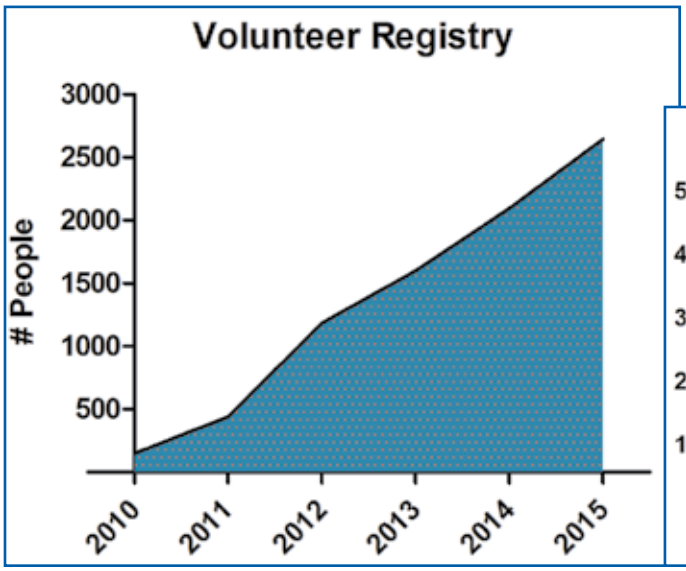
TREATMENT	POPULATION	PHASES 1	PHASES 2
Biomarkers of TBI	Acute TBI CSF & Serum	Enrolling	
Biomarkers of TBI	Acute TBI Cytokine Microdialysis	Enrolling	
Track TBI	Acute TBI Mild - Severe	Completed	Enrolling
TBI Registry	Acute TBI Mild - Severe	Enrolling	
Therapeutic Hypothermia (H.O.P.E.S.)	Acute, Severe TBI	Enrolling	

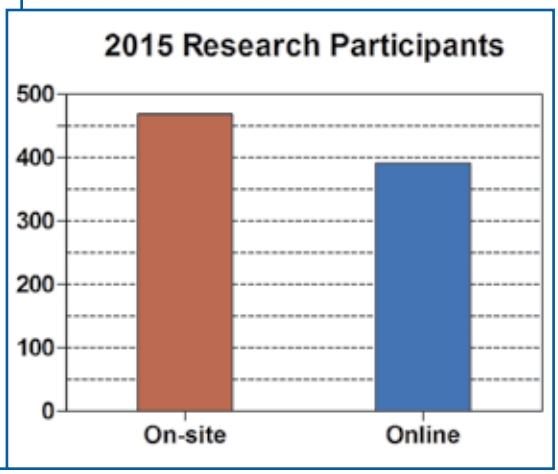
The Miami Project Believes That An Important Component Of Developing Treatments For Paralysis Involves Communication With The Community

The Education department, directed by Kim Anderson-Erisman, Ph.D., is responsible for helping thousands of our community members each year. The other valuable members of the department are Maria Chagoyen, Danielle Cilien, and Letitia Fisher. Each year the department answers thousands of phone calls and emails to provide people with information about all of our research programs and clinical studies as well as provide information about rehabilitation resources, clinical care referral, resources for living with paralysis, and advice about research from around the world. We also conduct numerous tours and lecturers about our research. The graph shows the total number of people interacted with each month during 2015 outreach activities.



The Education department also assists all of The Miami Project clinical research faculty with recruitment for their clinical studies and trials. To participate in research studies individuals must first complete an Intake form, which provides us with preliminary injury characteristics. Then you receive a phone call from us to discuss the studies that you pre-qualify for and determine whether you are interested in proceeding with any studies. If so, we set up an appointment for you to come to our research center for a neurologic exam ("ASIA") and introduction to the laboratories. The graph to the left shows the cumulative number of individuals since 2010 that have volunteered to be contacted regarding research studies for which they may qualify. The graph below shows the number of people that participated in our studies during 2015. Between on-site participants at our research center and online participants in surveys, 859 people contributed to our studies. Thank you!



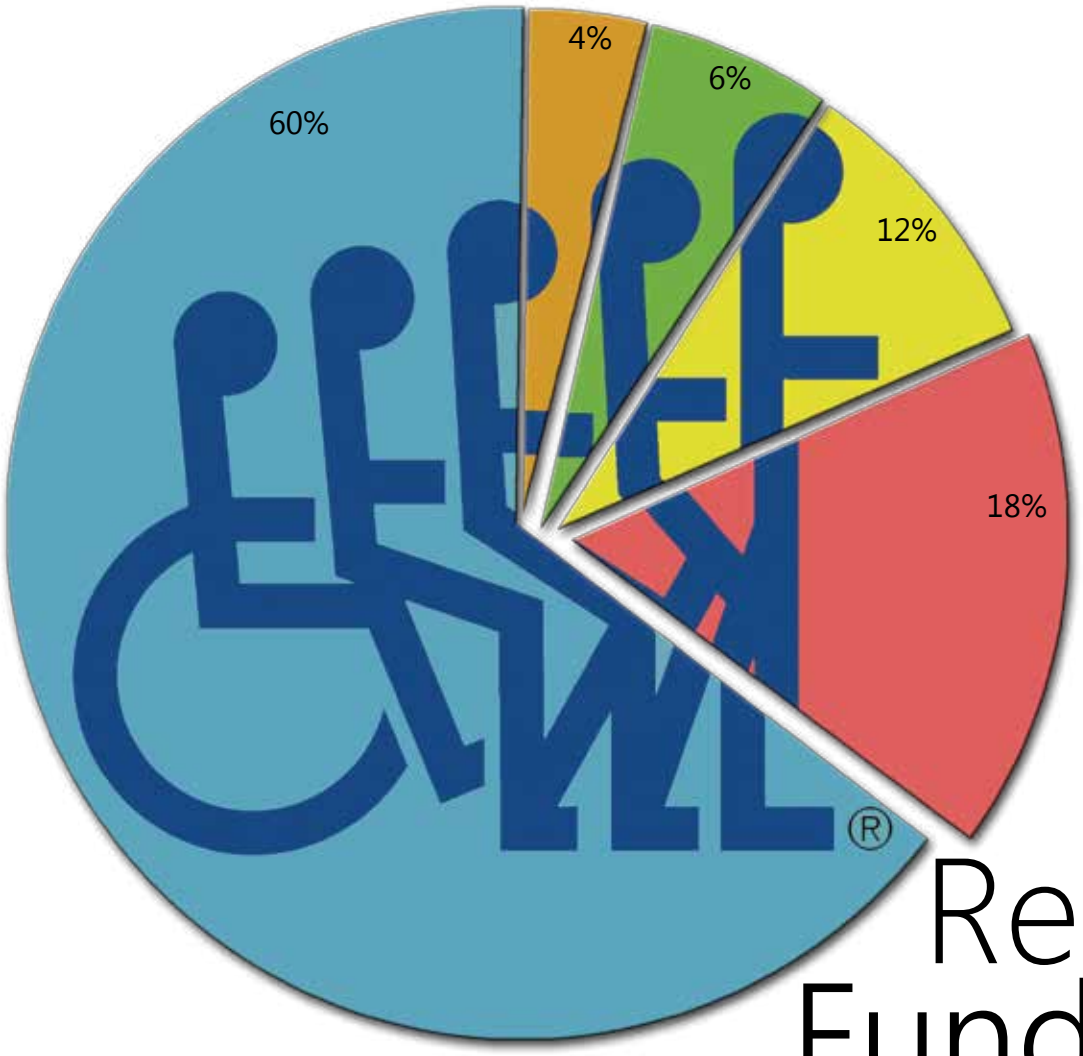


We enjoy this opportunity to open up our doors to the public to answer questions and share information...

Images from our 2015 Open House, including (counterclockwise beginning above) the imaging laboratory, clinical trials discussion, cell culture lab display, and one of our faculty members (Dr. Rachel Cowan) speaking with a young guest.

On April 11, 2015 the Education department hosted the 5th Annual Miami Project Community Open House. **We enjoy this opportunity to open up our doors to the public to answer questions and share information, as well as to hear direct input from our community.** The afternoon began with an interactive session about our *Current Clinical Trials* for spinal cord injury (featuring Drs. Allan Levi, Jonathan Jagid, Rachel Cowan, Christine Thomas, Monica Perez, Dalton Dietrich, and Kim Anderson-Erisman). This included discussions around Schwann cells, stem cells, deep brain stimulation for pain, fitness, and rehabilitation. This was followed by a session about the *Hurdles in Translation from Lab to Clinic*. Dr. Dalton Dietrich spoke about replication of results in animal experiments, Dr. Vance Lemmon discussed the need for minimum information standards for SCI experiments, and Dr. Damien Pearse presented information about preclinical data required by the FDA. The final component of the day was *Behind-the-Scenes* tours of four laboratories, including a cell culture lab, high-content screening and imaging lab, brain surgery and measuring activity lab, and human brain-spinal cord connections lab. The 6th Annual Community Open House is scheduled for April 9, 2016.

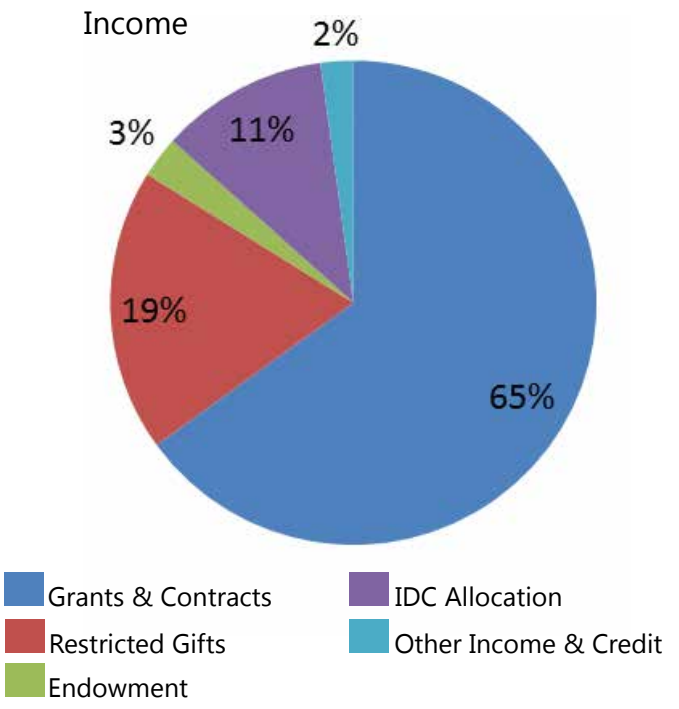
If you have questions, don't hesitate to email us at mpinfo@med.miami.edu or call us at 305-243-7108.

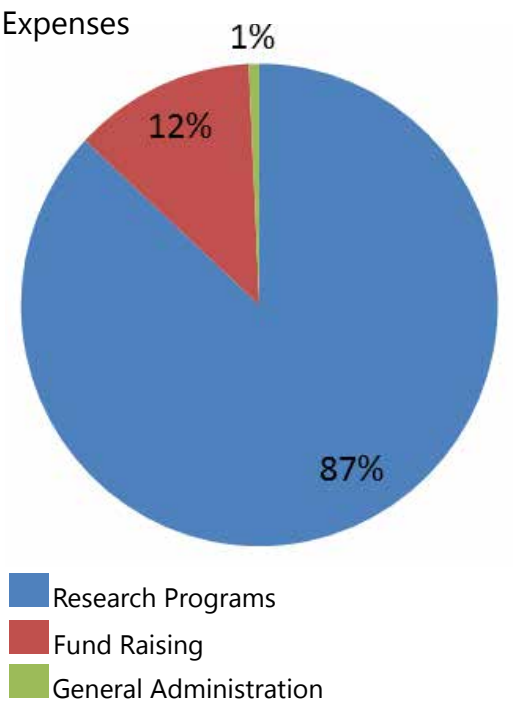


Research Funding

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 2015.





American Heart Association Scientific Development Grant
Dr. Juan Pablo De Rivero Vaccari (P.I.)
-Activation of Rig-like Receptor Signaling after Focal Cerebral Ischemia

Bryon Reisch Paralysis Foundation
Dr. Kim Anderson-Erisman (P.I.)
-The Safety of Autologous Human Schwann Cells in Subjects with Chronic SCI Receiving Rehabilitation

Christopher & Dana Reeve Foundation
Dr. James Guest (Center P.I.)
-North American Clinical Trials Network

Craig H. Neilsen Foundation
Dr. Kim Anderson-Erisman (P.I.)
-Miami Project Education Program

Dr. Nancy Brackett (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)
-Improving Reproductive Function in Men with Spinal Cord Injury

Dr. Nancy Brackett (P.I.), Dr. Kim Anderson-Erisman (Co-I.)
-Management of Infertility in Men with SCI: An Educational Program for Practitioners and Clients

Dr. James Guest (P.I.)
-Neuroprotective Effects of Internal Decompression of the Spinal Cord

Dr. Paula Monje (P.I.)
-Identity-function Definitions for Transplantable Human Schwann Cells

Dr. Mark Nash (P.I.)
-A Time-Course Study of Experimental Cardiometabolic Risk/Disease after SCI

Dr. Martin Oudega (P.I.)
-Role of Ang-1 in Vascular Stabilization in BMSC-mediated Spinal Cord Repair

Dr. Monica Perez (P.I.)
-Corticospinal Excitability of Leg Muscles After Spinal Cord Injury

Dr. Urs Rutishauser (P.I.), Dr. Damien Pearse (Co-I.)
-Optimization of PST-Engineered Schwann Cells for SCI Repair

Dr. Christine Thomas (P.I.)
-Weakness and Fatigue with Age after Spinal Cord Injury

Danish Medical Research Council
Dr. Roberta Brambilla (P.I.), Dr. Kate Lambertsen (P.I.)

Clockwise from top left: Stephanie Lee, Nicole Wilson, Dr. Hassan Al-Ali, Camilla Hansen, Poincyane Assis-Nascimento, Dr. Mehran Tehran

-Microglial-derived Transmembrane TNF Versus Soluble TNF: The Good and the Bad?

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

Dr. Rachel Cowan (P.I.)
-Fitness and Independence After SCI: Defining meaningful Change and Thresholds

Dr. W. Dalton Dietrich (P.I.), Dr. Michael Wang (Partner P.I.)
-Biomarkers for Spinal Cord Injury-Related Medical Complications

Dr. W. Dalton Dietrich (P.I.), Dr. John Bixby (Co-I.), Dr. Helen Bramlett (Co-I.), Dr. Jae Lee (Co-I.), Dr. Vance Lemmon (Co-I.), Dr. Daniel Liebl (Co-I.), Dr. Kevin Park (Co-I.), Dr. Pantelis Tsoulfas (Co-I.)
-Battlefield Exercise and Combat Related Spinal Cord Injury

Dr. Jonathan Jagid, (P.I.), Dr. Ian Hentall (Co-I.), Dr. Alberto Martinez-Arizala (Co-I.), Dr. Eva Widerström-Noga (Co-I.)
-Treatment of Pain and Autonomic Dysreflexia in Spinal Cord Injury with Deep Brain Stimulation

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

Dr. Brian Noga (P.I.), Dr. James Guest (Co-I.)
-Gait Ignition Using DBS Following SCI

Dr. Kevin K. Park (P.I.)
-Novel Combinatory Approaches to Repair Visual System After Optic Nerve Damage

Dr. Damien Pearse (P.I.), Dr. Howard Levene (Partner P.I.)
-Translation of Novel PDE4 Inhibitors for the Treatment of Acute Spinal Cord Injury

Dr. Shirin Shafazand (P.I.), Dr. Mark S. Nash (Co-P.I.)
-Neuro-cognitive Decline and Sleep-Disordered Breathing After SCI

Dr. Eva Widerström-Noga (P.I.), Dr. Kim Anderson-Erisman (Co-I.), Dr. Alberto Martinez-Arizala (Co-I.)
-Experiences of Living with Persistent Pain After a Spinal Cord Injury

Dr. Eva Widerström-Noga (P.I.), Dr. Kim Anderson-Erisman (Co-I.), Dr. Alberto Martinez-Arizala (Co-I.)
-Perspectives in Management of Severe Neuropathic Pain After a Spinal Cord Injury

Department of Defense (DoD) Psychological Health and Traumatic Brain Injury Program of the Office of Congressionally Directed Medical Research Programs
Dr. W. Dalton Dietrich (P.I.), Dr. Helen Bramlett (Co-I.)
-Operation Brain Trauma Therapy
-The Importance of Temperature in the Pathophysiology of Mild Repetitive Brain Injury
-The Use of Pro-Neurogenic Molecules to Promote Recovery of Function Following Acute and Chronic Traumatic Brain Injury

Dr. M. Ross Bullock (P.I.)
-Preclinical Evaluation of FDA Approved Human Neural Stem Cells in a Rat Model of Severe Traumatic Brain Injury

Dr. Eva Widerström-Noga (P.I.)
-Utility of MRS Brain Biomarkers of Pain Phenotypes after TBI

E. Matilda Ziegler Foundation for the Blind
Dr. Kevin Park (P.I.)
-Novel Combinatorial Approaches to Enhance Retinal Ganglion Cell Survival and Axon Regeneration after Optic Nerve Injury

FISM Fondazione Italiana Sclerosi Multipla (Italian Multiple Sclerosis Foundation)
Dr. Roberta Brambilla (P.I.)
-The Pro-Remyelination Effect of Transmembrane Tumor Necrosis Factor: Investigation Into the Role of Tumor Necrosis Factor Receptor 2

Florida Department of Transportation
Dr. Gillian Hotz (P.I.)
-WalkSafe/Bikesafe Project, Public Service Announcement Marketing Campaign, Safe Routes to School

GE/NFL Head Health Challenge
Dr. Gillian Hotz (P.I.)
-Advanced MRI Applications for Mild Traumatic Brain Injury

International Spinal Research Trust
Dr. James Guest (Center P.I.)
-Cellular Trials to Support Corticospinal Axon Regeneration in Non-Human Primates

Medtronic Spinal and Biologics
Dr. Allan Levi (Site-P.I.), Dr. Barth Green (Co-I.)
-Study of the Bryan Cervical Disc Prosthesis in the Treatment of Degenerative Disc Disease – Pivotal IDE Study

National Eye Institute
Dr. Kevin K. Park (P.I.)
-Regeneration and Reconnection of Damaged Optic Nerve

National Institute of Child Health and Human Development
Dr. Vance Lemmon (P.I.), Dr. John Bixby (P.I.)
-Novel Gene Targets for CNS Axonal Regeneration

National Institute on Disability, Independent Living, and Rehabilitation Research
Dr. Diana Cardenas (P.I.), Dr. Rachel Cowan (Co-I.), Dr. Mark Nash (Co-I.)
-South Florida Spinal Cord Injury Model Systems

Dr. Michael Boninger (P.I.), Dr. Kevin Dalal (Site P.I., Miami), Dr. Rachel Cowan (Site Co-P.I., Miami)
-Collaboration on Mobility Training

Dr. Mark Nash (P.I.), Dr. Kim Anderson-Erisman (Co-I.), Dr. Rachel Cowan (Co-I.), Dr. Eva Widerström-Noga (Co-I.)
-A Lifestyle Intervention Targeting Enhanced Health and Function for Persons with Chronic SCI in Caregiver/Care-Receiver Relationships: Effects of Caregiver Co-Treatment

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

Dr. Heather Taylor (P.I.), Dr. Eva Widerström-Noga (Co-I.)
-The Relations among Pain, Depression, and Resilience and their Prediction of Life Satisfaction in Men and Women with Spinal Cord Injury

National Institute of Neurological Disorders & Stroke
Dr. Kim Anderson-Erisman (P.I.), Dr. W. Dalton Dietrich (P.I.)
-NIH Neurotrauma Summer Research Experience Program

Dr. Coleen Atkins (P.I.)
-Rehabilitation Strategies for Memory Dysfunction after Traumatic Brain Injury
-The Role of Phosphodiesterase 4B in Inflammation after Trauma (Fellowship)

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

Dr. Mark Gurney (P.I.), Dr. Coleen Atkins (Subcontract-P.I.)
-PDE4B Inhibitors for Treating Brain Injury

Dr. Mary Bartlett Bunge (P.I.), Dr. John Bethea (Co-P.I.), Dr. Ian Hentall (Co-I.), Dr. Paula Monje (Co-I.), Dr. Kevin Park (Co-I.), Dr. Patrick Wood (Co-I.)
-Cytological Studies of Developing and Mature Neurons

Dr. Roberta Brambilla (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)
-Molecular Mechanisms of the Protective Function of Oligodendroglial TNFR2: A New Therapeutic Target in Neuro-immune Disease

Dr. Roberta Brambilla (P.I.)
-Does Microglial TNFR2 Contribute to the Protective Role of Membrane TNF in EAE?

Dr. Helen Bramlett (P.I.), Dr. W. Dalton Dietrich (P.I.), Dr. Daniel Liebl (P.I.)
-A Novel Combination Strategy for Protection and Repair After TBI

Dr. Helen Bramlett (P.I.)
-33rd Annual National Neurotrauma Society Symposium

Dr. W. Dalton Dietrich (P.I.), Dr. Robert Keane (Co-P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)
-Therapeutic Neutralization of the Inflammasome after Spinal Cord Injury

Dr. Edelle Field-Fote (P.I.), Dr. Eva Widerström-Noga (Co-I.)
-Dose-response Effects of Whole Body Vibration on Spasticity and Walking in SCI

Dr. Gillian Hotz (Site-P.I.), Dr. Ross Bullock (Site Co-P.I)
-Transforming Research and Clinical Knowledge in Traumatic Brain Injury

Dr. Jae Lee (P.I.)
-Role of Fibroblasts in Axon Regeneration After SCI
-Translational Profile of Perivascular Fibroblasts After Spinal Cord Injury
-RAP as a Therapeutic Compound for Neuronal Regeneration After Spinal Cord Injury (Sub-contract)

Dr. Vance Lemmon (P.I.), Dr. John Bixby (P.I.), Dr. Stephan Schürer (P.I.)
-Regenbase: A Searchable Database to Organize Regeneration Knowledge via Ontologies

Dr. Daniel Liebl (P.I.)
-Ephrins Regulate Stem Cell Proliferation following Traumatic Brain Injury

Dr. Avi Ma'ayan (P.I.), Dr. Stephan Schürer (P.I.), Dr. Vance Lemmon (Co-I.)
-Data Coordination and Integration Center for LINCS-BD2K

Dr. Paula Monje (P.I.)
-Phenotypic and Functional Analysis of Human Schwann Cells for Potency Assay Development

Dr. Brian Noga (P.I.), Dr. James Guest (Co-I.)
-Gait Induction After SCI

Dr. Damien Pearse (P.I.)
-Therapeutic Targeting of Intracellular Mechanisms Involved in Glial Scar Formation

Dr. Monica Perez (P.I.)
-Neural Control of Bilateral Hand and Arm Movements After Spinal Cord Injury
-Corticospinal Function After Human Spinal Cord Injury

Dr. Gaofeng Wang (PI.), Dr. Mary Bartlett Bunge (Co-I.)
-Epigenetic Prevention of Diabetic Neuropathy by Vitamin C

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

National Scientific and Technical Research Council (CONICET, Argentina)
Dr. Paula Monje (P.I.), Dr. Patricia Setton-Avruj (P.I.)
-Signal Transduction Pathways Underlying the Pro-differentiating Effect of Iron in Schwann cells: A Comparison Between Rodent and Human Schwann Cells

-Transplantation of Bone Marrow Stromal Cells and Schwann Cells for Peripheral Nerve Repair

Paralyzed Veterans Affairs
Dr. Monica Perez (P.I.)
-Targeting the Ipsilateral M1 to Improve Hand Opening-Closing After SCI (Fellowship)
-Synchronization of Corticospinal Volleys After Tetraplegia (Fellowship)

Pfizer, Inc.
Dr. Michael Wang (Site P.I.)
-STRIVE Staphylococcus Vaccine Trial for Elective Spinal Surgery

Sheila and David Fuente Neuropathic Pain Program
Dr. Jacqueline Sagen (P.I.)
-Development of a Phantom Limb Pain Model for Novel Therapeutic Interventions

State of Florida Brain and Spinal Cord Injury Program, Department of Health, and Red Light Camera Fund
-These three state funds contribute to several research programs within The Miami Project to Cure Paralysis

StemCells, Inc.
Dr. Allan Levi (Site-P.I.), Dr. Kim Anderson-Erisman (Co-I.)
-A Single-Blind, Randomized, Parallel Arm, Phase II Proof-of-Concept Study of the Safety and Efficacy of HUCNS-SC Transplantation in Cervical Spinal Cord Injury

Morton Cure Paralysis Fund
Dr. Martin Oudega (P.I.)
-Fibronectin for Enhancing BMSC-mediated Spinal Cord Repair

The Pew Charitable Trusts
Dr. Kevin Park (P.I.)
-Visual System Repair Following Optic Nerve Damage

UM Dean's Bridge Funding Program
Dr. Daniel Liebl (P.I.)
-Molecular Mechanisms of Synaptic Dysfunction Following TBI

US Army Medical Research and Material Command
Dr. Treena Arinzeh (P.I.), Dr. Mary Bartlett Bunge (Sub-site P.I.)
-A Combination Tissue Engineering Strategy for Schwann Cell-Induced Spinal Cord Repair

Veterans Administration Biological Laboratory Research and Development
Dr. Helen Bramlett (P.I.)
-Novel Treatment Strategies for Targeting Post-Traumatic Epilepsy

Dr. Michael Norenberg (P.I.), Dr. Helen Bramlett (Co-I.)
-Chronic Traumatic Encephalopathy: Role of Astrocytes

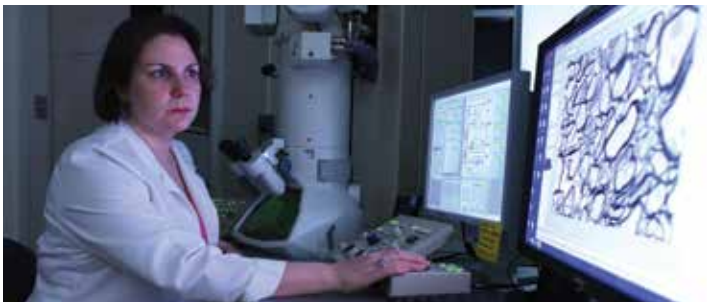
Veterans Administration Rehabilitation Research and Development
Dr. Victor Arvanian (P.I.), Dr. Damien Pearse (Co-I.)
-Enhancing Plasticity in a Damaged Spinal Cord to Repair Transmission and Function

Dr. Martin Oudega (P.I.), Dr. Monica Perez (P.I.)
-Maximizing Spike Timing-Dependent Plasticity After Spinal Cord Injury

Dr. Damien Pearse (P.I.), Dr. Moushumi Ghosh (Co-I.)
-Enhancing the Reparative Efficacy of Schwann Cells Following Chronic SCI

Dr. Monica Perez (P.I.)
-Enhancement of Hand Motor Function After Cervical Spinal Cord Injury

Wings for Life
Dr. Martin Oudega (P.I.)
-ESHU for Optimizing BMSC Transplant Survival and Spinal Cord Repair Efficacy


Scientific staff member, Vania Almeida, analyzing tissue

Meet our Faculty

The Miami Project To Cure Paralysis

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.

W. DALTON DIETRICH, PH.D.

Scientific Director
Kinetic Concepts Distinguished Chair in Neurosurgery
Senior Associate Dean for Discovery Science Professor, Departments of Neurological Surgery, Neurology, and Cell Biology

Neuroprotection and Improved Recovery of Function following CNS Trauma

My research interest is the pathobiology and treatment of Central Nervous System (CNS) injury in both the acute and chronic setting. Animal models of spinal cord injury, traumatic brain injury, and stroke are utilized to investigate the cellular and molecular mechanisms of tissue injury. The ultimate goal is to target secondary injury processes for various interventions that may protect vulnerable cell types or promote reparative processes to enhance neuroprotection, circuit plasticity, and recovery of function. The use of therapeutic hypothermia and targeted temperature management in preclinical and clinical settings is currently a focus of discovery and clinical investigations in the laboratory.

BARTH A. GREEN, M.D., F.A.C.S.

Professor of Neurological Surgery, Neurology, Orthopaedics, and Physical Medicine & Rehabilitation
Co-Founder and Chairman, The Miami Project to Cure Paralysis
Executive Dean for Global Health and Community Service

Translational Interventions

Over the recent years my research efforts have mainly involved taking the cutting edge basic neuroscience work product and data created by our Miami Project team from the bench to our UM affiliated clinics and hospitals. A good example of such translational research efforts has included the use of modest hypothermia for neuroprotection both in cases of acute spinal cord injury and for use in the operating room for patients undergoing high risk spinal cord surgery. I am also privileged to be able to collaborate with The Miami Project cellular transplantation programs and have been working on projects involving adult mesenchymal stem cells as well as being part of the major effort transforming our successful Schwann cell laboratory model into clinical trials. Another area of clinical interest and research includes the diagnosis and treatment of Chiari I malformation with and without syringomyelia.

ALLAN D. LEVI, M.D., PH.D., F.A.C.S.

Professor, Departments of Neurological Surgery, Orthopedics, and Physical Medicine & Rehabilitation
Chairman, Departments of Neurological Surgery
Chief of Neurosurgery, Jackson Memorial Hospital

Cellular Transplantation Strategies after SCI/Systemic Hypothermia after Acute SCI

My clinical research interests currently focus on developing cellular transplantation strategies to repair injuries within both the human central and peripheral nervous system. I am currently Co-PI on our clinical trial "Transplantation of Autologous Human Schwann Cells (SCs) to Repair the Injured Spinal Cord - Phase I - safety study". This represents a first-in-man dose escalation study of autologous human SCs for patients with sub-acute thoracic SCI (T3 to T11). We are also very interested in the use of SCs for peripheral nerve injuries with long segmental defects and have performed such a transplantation in a patient with a significant acute sciatic nerve injury. Hypothermia continues to show promise in a variety of acute central nervous system injuries. There are various factors that need to be considered with systemic cooling of the SCI patient, including methods of cooling, window from injury to initiation, duration and depth of hypothermia, rate of re-warming, etc. While

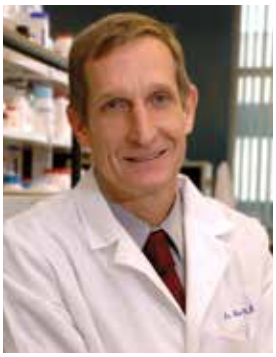
profound levels of hypothermia (T <32˚C) can be difficult to administer and are subject to increased complication rates, mild (modest) levels of hypothermia (T 32-34˚C) have been shown to provide significant protection against traumatic and ischemic neuronal cell death. I am currently the PI of our institutional protocol studying systemic hypothermia induced via an intravascular catheter and continued for 48 hours after acute cervical SCI.

MARY BARTLETT BUNGE, PH.D.

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

Development of Combination Strategies with Schwann Cells 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, we are investigating reducing the accumulation of proteoglycans (molecules that inhibit axonal growth), improving survival of transplanted Schwann cells (SCs), genetically engineering SCs before transplantation to improve their growth factor-secretion capability or neurons to enhance their ability to regrow axons, and testing matrices (in which the SCs are transplanted) for efficacy after injury. We pay particular attention to the interfaces between the SC implant and the host spinal cord.



JOHN BIXBY, PH.D.

Professor, Departments of Molecular & Cellular Pharmacology and Neurological Surgery, Center for Computational Sciences, Institute for Human Genomics
Vice Provost for Research

VANCE LEMMON, PH.D.

Walter G. Ross Distinguished Chair in Developmental Neuroscience
Professor, Department of Neurological Surgery, Center for Computational Sciences, Institute for Human Genomics, Sylvester Cancer Center

High Content Screening and Functional Genomics of the Nervous System

Our laboratory has developed methods to test thousands of genes or chemicals in hundreds of thousands of neurons each week to obtain quantitative information about cell morphology and gene expression. This "high throughput" capability allows us to tackle questions about axon growth and regeneration using systems biology approaches, and to take them into animal models of injury. **The Lemmon-Bixby lab** has several ongoing projects related to axon regeneration. One project is to test the roles of known signaling proteins called protein kinases. In this screen we have tested >1600 kinase inhibitors, many of which strongly promote neurite growth in vitro. Using bioinformatics, biochemistry, and machine learning we can identify critical kinases and their signaling networks as well as potential lead therapeutic compounds, one of which has proven active in two different models of spinal cord injury. A second project is based on the observation that injured peripheral sensory neurons initiate a genetic program appropriate for axonal regeneration. Our laboratory has combined next-generation sequencing with cell-based phenotypic screening to identify genes, especially transcription factors, and microRNAs that appear to regulate this genetic program, and is testing them in vitro and in vivo. Finally, in collaboration with Dr. S. Schürer, Dr. Ubbo Visser, and Drs. Nigam Shah and Alison Callahan (Stanford), we are developing RegenBase, an information system that includes an online tool for annotation of data and metadata, a knowledge base of diverse data on nerve regeneration, and an ontology that allows structured queries of the database.

HELEN M. BRAMLETT, PH.D.

Professor, Departments of Neurological Surgery and Psychology, Undergraduate Neuroscience Program Director, and Health Scientist Veterans Affairs

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, our 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.

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

We recently completed an extensive series of studies funded by the Department of Defense (DoD) to evaluate the neuroprotective effect of Perfluorocarbons (PFC) in four rodent models of traumatic brain injury (penetrating brain injury, closed traumatic brain injury with secondary hypoxia, tissue culture with stretch injury, and mechanistic and safety studies). These oxygen carriers have shown benefit in previous studies involving fluid percussion injury and subdural hematoma models. Unfortunately, we could not demonstrate efficacy with 3 of the PFC's tested. We are also evaluating hypothermia neuroprotection, in humans and animals, using novel biomarkers. We are currently funded by the DoD to obtain efficacy and safety data with FDA approved human stem cells, transplanted into the rat brain, as therapy for Penetrating TBI.

ROBERT W. KEANE, PH.D.

Professor, Departments of Physiology & Biophysics, and Neurological Surgery

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 data linking inflammasome proteins as biomarkers for CNS injury.

DANIEL J. LIEBL, PH.D.

Professor, Department of Neurological Surgery

Molecular Mechanisms that Regulate Cellular Dysfunction and Death Following CNS Injury, and Mechanisms to Promote Regeneration and Recovery.

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, apoptotic cell death, synaptic plasticity, regeneration, and therapeutic strategies. Overall, our approach is to

develop novel strategies to minimize CNS damage and maximize regeneration/tissue repair, which can be best achieved through a comprehensive mechanistic approach.

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

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

Physiological Assessment of Secondary Complications following SCI: Electrical Stimulation, Cardiometabolic and Vascular Pathophysiology, Autonomic Pathophysiology, Exercise and Biochemistry, Exoskeletons/Orthoses for Health and Function

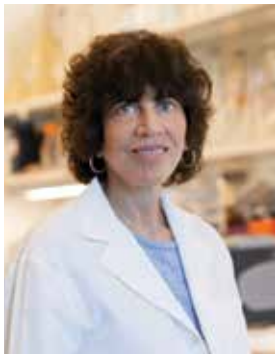
One of the enduring goals of The Miami Project has been to test and then translate strategies that optimize health and function of persons with SCI. This research has focused on physical activity to lessen secondary risks of SCI associated with physical deconditioning and an accelerated trajectory of cardioendocrine disease. We also examine complementary themes to validate exercise prescription after SCI, identify optimal dietary composition and causes for overeating, and use agents that reduce hazards of fasting and postprandial lipid disorders, dysglycemia, and vascular inflammatory stress, and autonomic/immune system dysregulation. We study the metabolism of bionic ambulation and it's effects on post-injury disease and function.

DAMIEN D. PEARSE, PH.D.

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.



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

Professor, Department of Neurological Surgery

Cellular Implants and Gene Therapy for the Alleviation of Chronic Pain

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) developing and refining more clinically relevant chronic pain models following injury to the nervous system in order to test novel treatments and (2) designing novel 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.

THOMAS J. SICK, PH.D.

Professor of Neurology and Physiology/Biophysics

Cellular and Neuronal Circuit Alterations after Traumatic Brian Injury That Contribute to Cognitive Decline and Epilepsy

My laboratory is conducting electrophysiological assessments of neuron and brain circuit alterations that occur after traumatic brain injury. Long-term clinical consequences of brain injury include declines in cognitive function and in many cases the development of epilepsy. We are trying to understand how circuits in the brain change over time after injury and how these changes might lead to alterations of brain function and behavior.

CHRISTINE K. THOMAS, PH.D.

Professor, Department of Neurological Surgery, and Physiology & Biophysics

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 age at SCI and SCI duration impact muscle strength because injured people report new declines in physical function at 45-50 years of age. Second, in our animal studies, we are exploring how to protect neurons from death because of SCI. Neuron death is common at the injury site and results in severe muscle weakness.

MICHAEL Y. WANG, M.D., F.A.C.S.

Professor, Departments of Neurological Surgery and Physical Medicine & Rehabilitation

Spinal Cord Injury Outcomes

My primary research has been in the investigation of SCI Outcomes. I work with Miami Project researchers Drs. Allan Levi and Barth Green in studying the clinical effects of Hypothermia. Currently, a multi-center randomized, prospective study on the effects of hypothermia in SCI is planned. In addition, I am studying the clinical application of SCI biomarkers to predict the effects of both injuries as well as therapeutic interventions with Drs. Dalton Dietrich and Ross Bullock.

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

Research Professor, Departments of Neurological Surgery and Urology

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.

JAMES D. GUEST, M.D., PH.D., F.A.C.S., F.R.C.S.(C)

Clinical Professor, Department of Neurological Surgery

Augmented Recovery after SCI; Application of Therapeutic Combinations in Preclinical Studies, and Early Phase Clinical Trials

Recognizing that combined therapeutic approaches are needed to enhance recovery after traumatic SCI, we currently combine cell therapy with rehabilitation, and electrical stimulation. The lab group has members ranging from senior and junior medical faculty to postdoctoral students, medical, and undergraduate students. We use large animal models to increase the relevance of the pre-clinical testing to address key questions of efficacy and safety important to the FDA. Therapeutics testing emulates human application as fully as possible; we use advanced histological, behavioral, electrophysiological, MRI, and ultrasound techniques. We design devices to deliver cells and therapeutics in a minimally injurious manner. Dr. Guest is also active in clinical trial design and execution through participation in the North American Clinical Trials Network and SCOPE (Spinal cord outcomes partnership endeavor).

GILLIAN A. HOTZ, PH.D.

Research Professor, Department of Neurological Surgery
Director, KiDZ Neuroscience Center
Director, 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, preventing brain and spinal cord injuries in children, and I have developed the WalkSafe program, which has been shown to decrease the number of elementary school age children that get hit by cars, and now the BikeSafe program to educate middle school age children on bicycle safety skills. As the Director of the Concussion Program we have a comprehensive countywide concussion care program including neurologic evaluation, neuroimaging, neuropharmacological management, and neuropsychological testing using ImPACT, a computerized neurocognitive screening measure. I am the PI on many local and federal grants funding Safe Routes to School initiatives, Transportation Alternative Programs, and Track TBI.

ALBERTO MARTINEZ-ARIZALA, M.D.

Clinical Professor, Departments of Neurology, Neurological Surgery, and Physical Medicine & Rehabilitation
Chief, SCI Service Miami VA Medical Center

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.

EVA WIDERSTRÖM-NOGA, D.D.S., PH.D.

Research Professor, Departments of Neurological Surgery, Physical Medicine & Rehabilitation, and Health Scientist Veterans Affairs

SCI-related Neuropathic Pain Phenotypes and Biomarkers

My research program is focused on the identification of clinical correlates of underlying

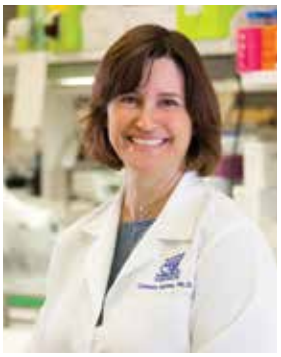
mechanisms of neuropathic pain associated with neurological trauma in order to facilitate the translation of basic research findings to treatments tailored to specific mechanisms. We are also examining the personal experiences of people living with chronic pain and SCI to increase our understanding about factors that help or hinder obtaining optimal pain relief. My research program is highly collaborative and includes extensive interdisciplinary protocols for a multimodal evaluation of self-reported pain symptoms and its psychosocial impact, quantitative assessment of neurological function, and biomarkers including non-invasive brain imaging and genetic polymorphism.

PATRICK M. WOOD, PH.D.

Research Professor (Retired), 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.



COLEEN ATKINS, PH.D.

Associate 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 found that specific synaptic plasticity signaling pathways are altered after TBI and we are currently using pharmacotherapies to target those pathways to improve behavioral recovery after TBI.

NAGI AYAD, PH.D.

Associate Professor, Department of Psychiatry and Behavioral Sciences

Cell Cycle Transitions in the Developing and Diseased Nervous Systems

The research in my laboratory focuses on cell cycle transitions in the developing nervous system. My laboratory identified essential proteins required for controlling mitotic entry and exit and also demonstrated that cell cycle proteins are present and active in the developing nervous system and fully differentiated neurons. Specifically, the research group uncovered the mechanism through which the Anaphase Promoting Complex/Cyclosome (APC/C) and other cell cycle regulators such as Wee 1 control cell proliferation, cycle exit, and differentiation. These neural progenitor cell cycle proteins are kinases, ubiquitin ligases, and epigenetic enzymes that may be targets in cancer, spinal cord injury, and traumatic brain injury. Thus, my laboratory is searching for novel molecular pathways that control neural development and are targets in multiple human maladies. This is accomplished using a multi-disciplinary approach that utilizes whole genome, siRNA, cDNA, and small molecule cell-based screens to develop therapies.

MONICA A. PEREZ, P.T., PH.D.

Associate Professor, Departments of Neurological Surgery

Motor Control in Humans with and without Spinal Cord Injury

The focus of my research is on understanding how the brain and spinal cord contribute to the control of voluntary movements in healthy humans and in individuals with spinal cord injury. This theme is mainly investigated from a neurophysiological point of view, using a combination of transcranial magnetic stimulation (TMS), magnetic resonance imaging (MRI), and peripheral nerve stimulation techniques. The population of individuals with SCI is heterogeneous. The severity of impairments depends on the site and extent of the injury. We use MRI to examine the extent to which changes in the pathophysiology of the spinal cord correlate to physiological and functional outcomes. Current research projects focus on topics such as interhemispheric interactions between primary motor cortices during unimanual and bimanual movements and corticospinal and spinal reorganization after an injury to the spinal cord.

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.

KIM ANDERSON-ERISMAN, PH.D.

Research Associate Professor, Department of Neurological Surgery

Director of Education, The Miami Project to Cure Paralysis

Translational Investigations for Chronic Spinal Cord Injury

My research focuses on translational investigations and bridging the gap between basic science, clinical science, and the public community living with SCI. My current projects focus on 1) aging related changes in bladder health after SCI, 2) determining the minimum amount of exercise and locomotor training required for clinical trials targeting chronic SCI, and 3) identifying the facilitators and barriers to clinical trial participation from the SCI consumer perspective. In addition, I direct our Schwann cell clinical trial program and collaborate with Dr. Levi regarding our participation in an industry-sponsored stem cell trial.

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 how these brainstem (raphé) neurons respond during injury, how raphé activity influences restorative molecular mechanisms in damaged regions, and how recovery from traumatic spinal cord or brain injury is improved by prolonged electrical stimulation of these nuclei or of their input areas. The procedure of deep brain stimulation has the potential for treating early chronic injury in man.

JONATHAN R. JAGID, M.D.

Clinical Associate Professor, Department of Neurological Surgery

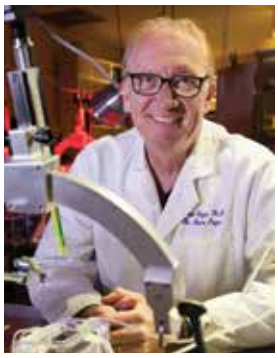
Device Interventions in SCI and TBI

My research includes projects investigating the use of Deep Brain Stimulation for spinal cord injury as well as hypothermia for traumatic brain injury. Presently, we are looking at the use of Deep Bain Stimulation of the periaqueductal gray to improve severe intractable neuropathic pain in spinal cord injured patients. In traumatic brain injury, a prospective multicenter study is underway looking at the effects of modest hypothermia on the surgical evacuation of subdural hematoma's (HOPES Trial). Shortly, we will embark on a study looking at a novel device to restore cortically controlled limb movement in spinal cord injury.

BRIAN R. NOGA, PH.D.

Research Associate Professor, Department of Neurological Surgery

Brain and Spinal Mechanisms Controlling Walking



Neuromodulation technologies are increasingly looked at as potential treatment options for paralysis associated with spinal cord injury (SCI). Deep brain stimulation is one such method that so far has had little or no application in persons with SCI even though most new and chronic injuries are incomplete. Recent work in our laboratory has pointed to a brain target for controlling walking. We are currently investigating the usefulness of stimulating this site to enhance walking in a translational large animal model of SCI.

MARTIN OUDEGA, PH.D.

Research Associate Professor, Department of Neurological Surgery

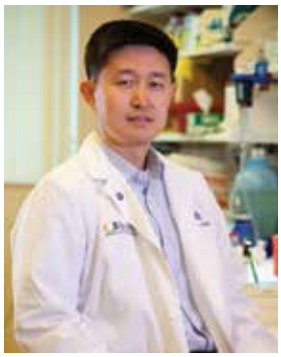
Bioengineering Cell-based Spinal Cord Repair

We employ animal models to better our understanding of the neuroanatomical and functional consequences of spinal cord injury and to use this information to generate and guide cell-based strategies to maximize functional recovery. Bioengineering principles are tightly integrated in our studies; the versatility of natural and artificial biomaterials offers important possibilities to address questions related to the failed or limited repair by cell transplants. The overall goal of our scientific efforts is to develop repair approaches that lead to significant anatomical restoration resulting in functional restoration after spinal cord injury that can be translated into the clinic.

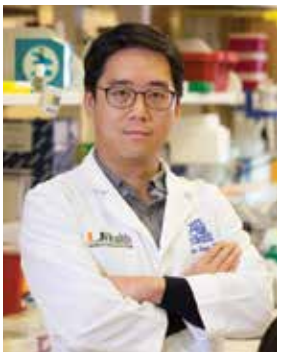
JAE K. LEE, PH.D.

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.



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.

ROBERTA BRAMBILLA, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Modulation of the Neuro-Immune Response in Neurologic Disease

The main focus of my research is to understand the role of neuroinflammation in the pathophysiology of neurodegenerative disorders (e.g., spinal cord injury and multiple sclerosis), with an interest in the contribution of glial cells, specifically the astrocytes, which represent the most abundant cell population in the nervous system, and the oligodendrocytes, which are responsible for axon myelination. Currently, my laboratory is working on two lines of research in the area of neuroimmunology, which are focused on: (1) investigating the role of tumor necrosis factor and its receptors in the processes of demyelination and remyelination, and (2) understanding how mitochondrial dysfunction in oligodendrocytes may be involved in the etiopathology of multiple sclerosis.

RACHEL E. COWAN, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Enhancement and preservation of maximal transfer and wheelchair propulsion ability

Our first focus is defining what level of fitness and 'skill' are required to independently perform transfers to and from the bed, car, shower, and ground and if these are different for various levels of SCI. Our second focus is defining how changes in fitness and wheelchair configuration can meaningfully reduce the effort required to propel a manual wheelchair and how these changes may differ by level of SCI.

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) injury. Currently, my laboratory is studying the effects of pattern recognition receptor (PRR)-activation after spinal cord injury (SCI), traumatic brain injury (TBI), and stroke. In addition, my laboratory studies how natural-aging produces inflammation in the brain, a phenomenon known as brain inflammaging, which potentially precedes the onset of age-related neurodegenerative diseases.

MOUSUMI GHOSH, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Altering Host Glial Responses following CNS Injury and Disease to Promote Repair

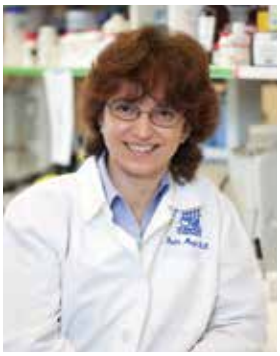
My research interests are focused on altering the hostile environment of the injured or diseased CNS to one that is conducive to repair through altering inflammation. Specifically our work focuses on delineating the intrinsic and extrinsic signals present after injury that antagonize the conversion of activated microglia and macrophages to a reparative phenotype in experimental models of CNS injury and disease, such as Multiple Sclerosis. We are also interested in understanding how altering the immunophenotypical profile of macrophages and microglia can affect host glial responses, including glial scar formation, as well as influence the ability of transplanted cells, such as Schwann cells and stem cells, to mediate neurorepair.

HOWARD B. LEVENE, M.D., PH.D., F.A.A.N.S.

Clinical Assistant Professor, Department of Neurological Surgery

Phosphodiesterase Inhibitors and Schwann Cell Transplantation after SCI

Secondary injury after spinal cord injury remains an active area for proposed therapy. With my co-PI Dr. Damien Pearse, we are investigating the effect of novel phosphodiesterase inhibitors after SCI. Phosphodiesterase inhibitors are proposed to sustain cAMP to abate cytotoxic processes during secondary injury, resulting in neuroprotection. Our work currently is transitioning from murine to porcine models. Another proposed therapy for spinal cord injury is to introduce cells to the injury site to help repair, restore, or support existing neurons. I worked with my colleagues on a large animal model to study the effect and behavior of transplanted autologous Schwann cells. I have been involved in the refinement of this animal model. This approach allows for the scientific study of the behavior of implanted cells and generates the groundwork for clinical trials. Research utilizing this model is done in collaboration with clinicians and scientists at The Miami Project such as Drs. Guest, Solano, Pearse, Wood, Bunge, and many more.



PAULA V. MONJE, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Molecular Mechanisms of Schwann cell Differentiation and Applications in Cell Therapy

Work in my laboratory combines signal transduction studies on mechanisms of Schwann cell differentiation and assay development studies on the use of Schwann cells in cell therapy. We are currently investigating the role of the second messenger cAMP in the reciprocal interactions between Schwann cells and neurons underlying the regulation of Schwann cell proliferation and myelination. We also work on the development of new in vitro systems for the growth and assessment of function of human and rodent Schwann cells. One important goal is to find reliable means to assess and improve the potency of the cells in culture prior to their use in cell transplantation strategies.

Summer Students

A major role of The Miami Project is to provide education and training for the next generation of neuroscientists. 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.

In 2015, Drs. Anderson-Erisman and Dietrich embarked on year 3 of a 5-year NIH Summer Student Research Grant, which enables a handful of stellar undergraduate students the opportunity to work in the laboratory of a Miami Project faculty member for 10 weeks during the summer. Each week, the students attended 2 lectures and participated in 1 journal club, in addition to 37 hours of hands-on laboratory work (for a total of 40 hours each week). These 13 students wrote an abstract about their specific research project and presented a poster at the 5th Miami Project Summer Student Research Session on August 7, 2015.

Summer Students and their Research Projects:

Name	Summer mentor	Summer project
Caminita, Christena	Dr. Christine Thomas	Physical Activity Duration and Intensity in Injured and Uninjured Subjects
Choi, Claire*	Dr. Roberta Brambilla	Protective Role of Microglial TNFR2 in Neuroimmune Disease
Deshane, Alok	Dr. Damien Pearse	Spatio-temporal Distribution of Nestin-Driven GFP Expression in a Transgenic Mouse Thoracic Contusion SCI Model
Desousa, Brandon	Dr. Ross Bullock	Characterization and Modulation of Stem-like Cells after a Controlled Cortical Impact Injury in Mice
Dominguez, Barbara*	Dr. Rachel Cowan	External Demands of Manual Wheelchair Propulsion
Ibrahim, Karen	Dr. Nancy Brackett	Inflammasome Activation and Semen Quality in Men With and Without SCI
Lanjewar, Alexandra	Dr. Jacqueline Sagen	NFkB as a Pathology-inducible Promoter to Modulate Gene Expression in Pain Model
Lopez, Kathryn	Dr. Brian Noga	Histological Analysis of the Spinal Cord Injury Lesion Site Reflects Benefits of Deep Brain Stimulation for Improved Walking After SCI
Macklin, Richard	Dr. Monica Perez	Sensory Examinations in the Acute and Chronic Phase of Incomplete Cervical Human Spinal Cord Injury
McGrath, Michael	Dr. Paula Monje	Transcriptome Profiling of Human and Rodent Schwann Cells: Interspecies Comparison via Next Generation RNA-Seq Technology
Sikah, Kevin	Dr. Coleen Atkins	Effects of Early Life Stress on Pathology after Mild Traumatic Brain Injury
Vallabhaneni, Ahdarsh	Dr. Mary Bunge	Can Astrocytes be Compromised without Affecting Transplanted Schwann Cells to Improve Axon Regeneration Across the Glial Scar after SCI?
Lovell, Lyndah*	Dr. Vance Lemmon	Machine Learning Demonstrates Relationship Between Kinase Activity and Regulation of Neurite Outgrowth

*award winners of the poster session

Dr. Dietrich talking with the summer students at the awards ceremony

Poster session

Students and Dr. Anderson-Erisman at the awards ceremony

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.

September 9, 2015
Valeria Cavalli, PhD
Washington University School of Medicine – St. Louis, MO

Drs. Vance Lemmon and Valeria Cavalli

October 7, 2015
Gordon Mitchell, PhD
University of Florida – Gainesville, FL

November 4, 2015
Suzanne Groah, MD, MSPH
National Rehabilitation Hospital – Washington, DC

Drs. Mark Nash with Suzanne Groah

February 3, 2016
Laura Feltri, MD
University of Buffalo (SUNY) – Buffalo, NY

March 2, 2016
John Martin, MD, PhD
The City College of New York – New York, NY

Drs. John Martin and Monica Perez

April 6, 2016
Axel Nimmerjahn, PhD
Salk Institute for Biological Studies – La Jolla, CA

Scientific Publications

JOURNAL OF NEUROTRAUMA 33:493–499 (March 1, 2016)

DOI: 10.1089/neu.2015.4064

Facilitators and Barriers to Spinal Cord Injury Clinical Trial Participation: Multi-National Perspective of People Living with Spinal Cord Injury

Kim D. Anderson,[1] Rachel E. Cowan,[1] and Jane Horsewell[2]

Abstract

These are exciting times for the translation of promising interventions for spinal cord injury (SCI) into testing wi
trials. These interventions include acute surgical decompression, neuroprotection, neural repair, cell replacement
based rehabilitation, and medical devices, including devices requiring surgical implantation. By nature, clinical
have strict inclusion and exclusion criteria, which narrow down the pool of potential participants. Meeting
numbers for properly powered trials is a daunting task. Therefore, it is important that trials are designed in a
facilitates participation. The purpose of this research study was to learn more about the factors that encourage
with the decision to participate in clinical trials from the perspective of people living with SCI. A multi-nati
was conducted, primarily online, in which 841 participants with SCI ranked 52 factors as facilitators or barr
Likert scale. There were 13 universal facilitators, five universal barriers, and three universally neutral
functionality and the number one barrier was personal
groups of people living with SCI. All of

Published studies that have passed the test of peer review are the benchmark of scientific progress. Listed here are the 2015 research publications by Miami Project scientists and colleagues.

Ahmad FU, Frenkel MB, Levi AD. (In press). Spinal stability after resection of nerve sheath tumors. *J Neurosurg Sci*.

Ahmed AI, Gajavelli S, Spurlock MS, Chieng LO, Bullock MR. (In press). Stem cells for therapy in TBI. *J R Army Med Corps.*

Al-Ali H, Lee DH, Danzi MC, Nassif H, Gautam P, Wennerberg K, Zuercher B, Drewry DH, Lee JK, Lemmon VP, Bixby JL. (2015). Rational Polypharmacology: Systematically identifying and engaging multiple drug targets to promote axon growth. *ACS Chem Biol.* 10(8):1939-1951.

Alperin N, Loftus JR, Oliu CJ, Bagci AM, Lee SH, Ertl-Wagner B, Sekula R, Lichtor T, Green BA. (2015). Imaging-based features of headaches in Chiari Malformation Type I. *Neurosurgery*. 77(1):96-103.

Anderson KD, Cowan RE, Horsewell J. (In press). Facilitators and barriers to spinal cord injury clinical trial participation: Multi-national perspective of people living with spinal cord injury. *J Neurotrauma*.

Asfour S, Elmasry S, de Rivero Vaccari JP, Travascio F. (2015). Effects of tobacco smoking on the degeneration of the intervertebral disc: A finite element study. *PLoS ONE*. 10(8):e0136137.

Asfour S, Travascio F, Elmasry S, de Rivero Vaccari JP. (2015). A computational analysis on the implications of age-related changes in the expression of cellular signals on the role of IGF-1 in intervertebral disc homeostasis. *J Biomech.* 48(2):332-339.

Bacallao K, Monje PV. (2015). Requirement of cAMP signaling for Schwann cell differentiation restricts the onset of myelination. *PLoS One*. 10 (2): e0116948.

Beckerman SR, Jimenez JE, Shi Y, Al-Ali H, Bixby JL, Lemmon VP. (2015). Phenotypic assays to identify agents that induce reactive gliosis: A counter-screen to prioritize compounds for preclinical animal studies. *Assay Drug Dev Technol*. 13(7):377-388.

Bernardes D, Brambilla R, Bracchi-Ricard V, Karmally S, Dellarole A, Carvalho-Tavares J, Bethea JR. (In press). Prior regular exercise improves clinical outcome and reduces demyelination and axonal injury in experimental autoimmune encephalomyelitis. *J Neurochem*.

Biering-Sørensen F, Alai S, Anderson K, Charlifue S, Chen Y, DeVivo M, Flanders AE, Jones L, Kleitman N, Lans A, Noonan VK, Odenkirchen J, Steeves J, Tansey K, Widerström-Noga E, Jakeman LB. (2015). Common data elements for spinal cord injury clinical research: a National Institute for Neurological Disorders and Stroke project. *Spinal Cord*. 53:265-277.

Blabe CH, Gilja V, Chestek CA, Shenoy KV, Anderson KD, Henderson JM. (2015). Assessment of brain-machine interfaces from the perspective of people with paralysis. *J Neural Eng*. 12(4):043002.

Blaya MO, Tsoulfas P, Bramlett HM, Dietrich WD. (2015). Neural progenitor cell transplantation promotes neuroprotection, enhances hippocampal neurogenesis, and improves cognitive outcomes after traumatic brain injury. *Exp Neurol*. 264:67-81.

Bloom L, Burks SS, Levi AD. (In press). Multiple recurrent postoperative spinal infections due to an unrecognized presacral abscess following placement of bicortical sacral screws: case report. *J Neurosurg Spine*.

Bramlett HM, Dietrich WD, Dixon CE, Shear DA, Schmid Maj KE, Mondello S, Wang KK, Hayes RL, Povlishock J, Tortella FC, Kochanek PM. (In press). Erythropoietin treatment in traumatic brain injury: Operation Brain Trauma Therapy. *J Neurotrauma.*

Bramlett HM, Dietrich WD. (2015). Long-term consequences of traumatic brain injury: Current status of potential mechanisms of injury and neurological outcomes. *J Neurotrauma*. 32(23):1834-48.

Brand FJ III, de Rivero Vaccari JC, Mejias, NH, Alonso OF, de Rivero Vaccari JP. (2015). RIG-I contributes to the innate immune response after cerebral ischemia. *J Inflammation.* 12:52.

Browning M, Shear DA, Bramlett HM, Dixon CE, Mondello S, Schmid Maj KE, Poloyac SM, Dietrich WD, Hayes RL, Wang KK, Povlishock J, Tortella FC, Kochanek PM. (In press). Levetiracetam treatment in traumatic brain injury: Operation Brain Trauma Therapy. *J Neurotrauma.*

Bruehl S, Ohrbach R, Sharma S, Widerstrom-Noga E, Dworkin RH, Fillingim RB, Turk DC. (In press). The ACTTION-American Pain Society Pain Taxonomy (AAPT): Approaches to demonstrating the reliability and validity of core diagnostic criteria. *J Pain.*

Bullock MR, Rehman MF, Oddo M, Miller C, Hill M. (2015). Temperature management in neurological and neurosurgical intensive care unit. *Ther Hypothermia Temp Manag*. 5(2):62-67.

Cahill KS, McCormick PC, Levi AD. (2015). A comprehensive assessment of the risk of bone morphogenetic protein use in spinal fusion surgery and postoperative cancer diagnosis. *J Neurosurg Spine*. 23(1):86-93.

Cajigas I, Burks SS, Gernsback J, Fine L, Moshiree B, Levi AD. (In press). Allergy to prolene sutures in a dural graft for chiari decompression. Case Reports in Medicine.

Calabro FJ, Perez MA. (In press). Bilateral reach-to-grasp movement asymmetries after human spinal cord injury. *J Neurophysiology*.

Chieng LO, Hubbard Z, Salgado CJ, Levi AD, Chim H. (2015). Reconstruction of open wounds as a complication of spinal surgery with flaps: A systematic review. *Neurosurg Focus*. 39(4):E17.

Cirillo J, Calabro F, Perez MA. (In press). Impaired organization of TMS-induced I-waves after human spinal cord injury. *Cerebral Cortex*.

Cirillo J, Perez MA. (2015). Subcortical contribution to late TMS-induced I-waves in intact humans. *Front Integr Neurosci*. 9:38.

Datto JP, Bastidas JC, Miller NL, Shah AK, Arheart KL, Marcillo AE, Dietrich WD, Pearse DD. (2015). Female rats demonstrate improved locomotor recovery and greater preservation of white and gray matter after traumatic spinal cord injury compared to males. *J Neurotrauma*. 32(15):1146-1157.

Datto JP, Yang J, Dietrich WD, Pearse DD. (2015). Does being female provide a neuroprotective advantage following spinal cord injury? *Neural Regen Res*. 10(10):1533-1536.

de Rivero Vaccari JC, Brand F III, Berti AF, Alonso OF, Bullock MR, de Rivero Vaccari JP. (2015). Mincle signaling in the innate immune response after traumatic brain injury. *J Neurotrauma*. 32(4):228-236.
de Rivero Vaccari JP, Brand F 3rd, Adamczak S, Lee SW, Perez-Barcena JP, Wang MY, Bullock MR, Dietrich WD, Keane RW. (In press). Exosome-mediated inflammasome signaling after central nervous system injury. *J Neurochem*.

de Rivero Vaccari JP, de Rivero Vaccari JC. (2015). Biomarkers in disease: Methods, discoveries and applications. General methods and their applications, edited by Victor Preedy and Vinood B. Patel. Inflammasome proteins as biomarkers of injury and disease. Springer. 1207-1228.

de Rivero Vaccari JP, Dietrich DW, Keane RW. (2015). Therapeutics targeting the inflammasome after central nervous system injury. *Translational Research*. pii: S1931-5244(15)00145-0.

de Rivero Vaccari JP, Patel HH, Brand FJ III, Perez-Pinzon MA, Bramlett HM, Raval AP. (In press). Estrogen receptor beta signaling alters cellular inflammasomes activity after global cerebral ischemia in reproductively senescence female rats. *J Neurochem*.

Dietrich WD. (2015). Editorial comment: New guidelines for post-cardiac arrest targeted temperature management. *Ther Hypothermia Temp Manag*. 5(4):183.

Dietrich WD. (2015). Exciting times for the journal. *Ther Hypothermia Temp Manag*. 5(2):61.

Dietrich WD. (2015). New targets for temperature management. *Ther Hypothermia Temp Manag*. 5(3):115.

Dietrich WD. (2015). Protection and repair after spinal cord injury: Accomplishments and future directions. *Top Spinal Cord Inj Rehabil*. 21(2):174-187.

Dietrich WD. (2015). Temperature management in the new year. *Ther Hypothermia Temp Manag*. 5(1):1.

Dietrich WD, Bramlett H. (2015). Therapeutic hypothermia and targeted temperature management in traumatic brain injury: Clinical challenges for successful translation. *Brain Res*. pii: S0006-8993(15)00973-00977.

Dixon CE, Bramlett HM, Dietrich WD, Shear DA, Yan HQ, Deng-Bryant Y, Mondello S, Wang KK, Hayes RL9, Empey P, Povlishock J, Tortella FC, Kochanek PM. (In press). Cyclosporine treatment in traumatic brain injury: Operation Brain Trauma Therapy. *J Neurotrauma*.

Dixon KJ, Theus MH, Nelersa CM, Mier J, Travieso LG, Yu TS, Kernie SG, Liebl DJ. (2015). Endogenous neural stem/progenitor cells stabilize the cortical microenvironment after traumatic brain injury. *J Neurotrauma*. 32(11):753-764.

Dugan EA, Sagen J. (2015). An intensive locomotor training paradigm improves neuropathic pain following spinal cord compression injury in rats. *J Neurotrauma*. 32(9):622-632.

Ellenbroek D, Kressler J, Cowan RE, Burns PA, Mendez AJ, Nash MS.

(2015). Effects of prandial challenge on triglyceridemia, glycemia, and pro-inflammatory activity in persons with chronic paraplegia. *J Spinal Cord Med*. 38(4):468-475.

Elmasry S, Asfour S, de Rivero Vaccari JP, Travascio F. (2015). Effects of tobacco smoking on the degeneration of the intervertebral disc: A finite element study. *PloS ONE*. 10(8):e0136137.

Führmann T, Ghosh M, Otero A, Goss B, Dargaville TR, Pearse DD, Dalton PD. (2015). Peptide-functionalized polymeric nanoparticles for active targeting of damaged tissue in animals with experimental autoimmune encephalomyelitis. *Neurosci Lett.* 602:126-132.

Gajavelli S, Kentaro S, Diaz J, Yokobori S, Spurlock M, Diaz D, Jackson C, Wick A, Zhao W, Leung LY, Shear D, Tortella F, Bullock MR. (2015). Glucose and oxygen metabolism after penetrating ballistic-like brain injury. *J Cereb Blood Flow Metab*. 35(5):773-780.

Ghosh M, Aguirre V, Wai K, Felfly H, Dietrich WD, Pearse DD. (2015). The interplay between cyclic AMP, MAPK, and NF-kB pathways in response to proinflammatory signals in microglia. *Biomed Res Int*. 308461.

Ghosh M, Pearse DD. (2015). The role of the serotonergic system in locomotor recovery after spinal cord injury. *Front Neural Circuits*. 8:151.

Greig E, Cornely CC, Green BA. (2015). The challenges of establishing and sustaining an overseas enterprise: One Haitian NGO's perspective. *J Craniofac Surg*. 26(4):1058-1060.

Greig E, Cornely CC, Green BA. (2015). Project Medishare's historic Haitian earthquake response. *J Craniofac Surg*. 26(4):1034-1035.

Guest J, Dietrich WD. (2015). Commentary regarding the recent publication by Tabakow et al., "Functional regeneration of supraspinal connections in a patient with transected spinal cord following transplantation of bulbar olfactory ensheathing cells with peripheral nerve bridging". *J Neurotrauma*. 32(15):1176-1178.

Harrison BJ, Venkat G, Hutson T, Rau KK, Bunge MB, Mendell LM, Gage FH, Johnson RD, Hill C, Rouchka EC, Moon L, Petruska JC. (2015). Transcriptional changes in sensory ganglia associated with primary afferent axon collateral sprouting in spared dermatome model. *Genom Data*. 6:249-252.

Hawryluk GW, Bullock MR. (2015). Design of acute neuroprotection studies. *Handb Clin Neurol*. 128:761-778.

Hentall ID, Luca CC, Widerstrom-Noga E, Vitores A, Fisher LD, Martinez-Arizala A, Jagid, JR. (In press). The midbrain central gray best suppresses chronic pain with electrical stimulation at very low pulse rates in two human cases. *Brain Research*.

Hittinger EA, Maher JL, Nash MS, Perry AC, Signorile JF, Kressler J, Jacobs KA. (2015). Ischemic preconditioning does not improve peak exercise capacity at sea level or simulated high altitude in trained male cyclists. *Appl Physiol Nutr Metab*. 40(1):65-71.

Hofstetter CP, Hofer AS, Levi AD. (In press). Exploratory meta-analysis on dose-related efficacy and morbidity of bone morphogenetic protein in spinal arthrodesis surgery. *J Neurosurg Spine*.

Hofstetter CP, Hofer AS, Wang MY. (2015). Economic impact of minimally invasive lumbar surgery. *World J Orthop*. 6(2):190-201.

Ibrahim E, Aballa TC, Roudebush WE, Lynne CM, Brackett NL. (2015). Inhibin B is lower and anti-Müllerian hormone is similar in serum of men with spinal cord injuries compared to controls. *Syst Biol Reprod Med*. 61(2):72-77.

Ibrahim E, Lynne CM, Brackett NL. (In press). Male fertility following spinal cord injury: An update. *Andrology*.

Iorgulescu JB, Patel SP, Louro J, Andrade CM, Sanchez AR, Pearse DD. (2015). Acute Putrescine supplementation with Schwann cell implantation improves sensory and serotonergic axon growth and functional recovery in spinal cord injured rats. *Neural Plast*. 186385.

Jagid J, Madhavan K, Bregy A, Desai M, Ruiz A, Quencer R, Landy HJ. (2015). Deep brain stimulation complicated by bilateral large cystic cavitation around the leads in a patient with Parkinson's disease. *BMJ Case Rep*. doi: 10.1136/bcr-2015-211470.

Kanno H, Pearse DD, Ozawa H, Itoi E, Bunge MB. (2015). Schwann cell transplantation for spinal cord injury repair: its significant therapeutic potential and prospectus. *Rev Neurosci.* 26(2):121-128.

Kochanek PM, Bramlett HM, Dixon CE, Shear DA, Dietrich WD, Schmid KE, Mondello S, Wang KK, Hayes RL, Povlishock JT, Tortella FC. (In press). Operation Brain Trauma Therapy: Approach to modeling, therapy evaluation, drug selection, and biomarker assessments for a multicenter pre-clinical drug screening consortium for acute therapies in severe traumatic brain injury. *J Neurotrauma*.

Kochanek PM, Bramlett HM, Shear DA, Dixon CE, Mondello S, Dietrich WD, Hayes RL, Wang KK, Poloyac SM, Empey P, Povlishock J, Mountney A, Browning M, Deng-Bryant Y, Yan HQ, Jackson TC, Catania M, Glushakova O, Richieri S, Tortella FC. (In press). Synthesis of findings, current investigations, and future directions: Operation Brain Trauma Therapy. *J Neurotrauma*.

Kwon BK, Streijger F, Hill CE, Anderson AJ, Bacon M, Beattie MS, Blesch A, Bradbury EJ, Brown A, Bresnahan JC, Case CC, Colburn RW, David S, Fawcett JW, Ferguson AR, Fischer I, Floyd CL, Gensel JC, Houle JD, Jakeman LB, Jeffery ND, Jones LA, Kleitman N, Kocsis J, Lu P, Magnuson DS, Marsala M, Moore SW, Mothe AJ, Oudega M, Plant GW, Rabchevsky AS, Schwab JM, Silver J, Steward O, Xu XM, Guest JD, Tetzlaff W. (2015). Large animal and primate models of spinal cord injury for the testing of novel therapies. *Exp Neurol*. 269:154-168.

Levi AD, Burks SS, Anderson KD, Dididze M, Khan A, Dietrich WD. (In press). The use of autologous Schwann cells to supplement sciatic nerve repair with a large gap - First in human experience. *Cell Transplant*.

Long J, Tazoe T, Soteropoulos DS, Perez MA. (In press). Interhemispheric connectivity during bimanual isometric force generation. *J Neurophysiology*.

Lorenzana AO, Lee JK, Mui M, Chang A, Zheng B. (2015). A surviving intact branch stabilizes remaining axon architecture after injury as revealed by in vivo imaging in the mouse spinal cord. *Neuron*. 86(4):947-954.

Lynne CM, Ibrahim E, Brackett NL. (In press). Electroejaculation and penile vibratory stimulation. In: Case studies in male fertility: Expert analysis and current controversies. E. Kim and R. Brannigan (Eds.), JP Medical Publishers, London.

Macklin RA, Brooke VJ, Calabro FJ, Ellaway PH, Perez MA. (In press). Sensory examinations after incomplete chronic cervical spinal cord injury. *Spinal Cord*.

Madsen PM, Clausen BH, Degn M, Thyssen S, Kellemann Kristensen L, Svensson M, Ditzel N, Finsen B, Deierborg T, Brambilla R, Lambertsen KL. (In press). Genetic ablation of soluble TNF with preservation of membrane TNF is associated with neuroprotection after focal cerebral ischemia. *J. Cereb. Blood Flow and Metab*.

Manzano GR, Levi AD. (2015). Cervical laminoplasty. In Handbook of Spine Surgery. Eds: A. Baaj, P. Mummaneni et al. Thieme, New York, Chapter 41.

McGuire LS, Bregy A, Sick J, Dietrich WD, Bramlett HM, Sick T. (2015). Nonconvulsive seizures as secondary insults in experimental traumatic brain injury. In: Kobeissy FH, editor. SourceBrain Neurotrauma: Molecular, neuropsychological, and rehabilitation aspects. Boca Raton (FL): CRC Press/Taylor & Francis; Chapter 12. Frontiers in Neuroengineering.

Medvid R, Ruiz A, Komotar RJ, Jagid JR, Ivan ME, Quencer RM, Desair MB. (2015). Current applications of MRI-guided laser interstitial thermal therapy in the treatment of brain neoplasms and epilepsy: A radiologic and neurosurgical overview. *AJNR Am J Neuroradiol*. 36(11):1998-2006.

Mondello S, Shear DA, Bramlett HM, Dixon CE, Schmid Maj KE, Dietrich WD, Wang KK, Hayes RL, Glushakova O, Catania M, Richieri S, Povlishock J, Tortella FC, Kochanek PM. (In press). Insight into preclinical models of traumatic brain injury using circulating brain damage biomarkers: Operation Brain Trauma Therapy. *J Neurotrauma*.

Monje PV. (2015). To myelinate or not to myelinate: Fine tuning cAMP signaling in Schwann cells to balance cell proliferation and differentiation. *Neural Regeneration Research*. 10(12):1936-1937.

Mountney A, Bramlett HM, Dixon CE, Mondello S, Dietrich WD, Wang KK, Caudle KL, Empey P, Poloyac SM, Hayes RL, Povlishock J, Tortella FC, Kochanek PM, Shear DA. (In press). Simvastatin treatment in traumatic brain injury: Operation Brain Trauma Therapy. *J Neurotrauma*.

Nash MS. (2015). Editorial note on: Optimal scaling of weight and waist circumference to height for adiposity and cardiovascular disease risk in individuals with spinal cord injury. *Spinal Cord*. 53(1):69.

Nasirinezhad F, Gajavelli S, Priddy B, Jergova S, Zadina J, Sagen J. (2015). Viral vectors encoding endomorphins and serine histogranin attenuate neuropathic pain symptoms after spinal cord injury in rats. *Mol Pain*. 11:2.

Nasirinezhad F, Jergova S, Pearson JP, Sagen J. (2015). Attenuation of persistent pain-related behavior by fatty acid amide hydrolase (FAAH) inhibitors in a rat model of HIV sensory neuropathy. *Neuropharmacology*. 95:100-109.

Ocal O, Pashkov V, Kollipara RK, Zolghadri Y, Cruz VH, Hale MA, Heath BR, Artyukhin AB, Christie AL, Tsoulfas P, Lorens JB, Swift GH, Brekken RA, Wilkie TM. (2015). A rapid in vivo screen for pancreatic ductal adenocarcinoma therapeutics. *Dis Model Mech*. 8(10):1201-1211.

Oudega M, Perez MA. (2015). Editors of Mechanisms of motor function recovery after spinal cord injury. *Research Topic in Frontiers in Integrative Neuroscience*.

Park P, Okonkwo DO, Nguyen S, Mundis GM Jr, Than KD, Deviren V, La Marca F, Fu KM, Wang MY, Uribe JS, Anand N, Fessler R, Nunley PD, Chou 4, Kanter AS, Shaffrey CI, Akbarnia BA, Passias PG, Eastlack RK, Mummaneni PV. (In press). International Spine Study Group. Can a minimal clinically important difference be achieved in elderly patients with adult spinal deformity who undergo minimally invasive spinal surgery? *World Neurosurg*.

Park P, Wang MY, Lafage V, Nguyen S, Ziewacz J, Okonkwo DO, Uribe JS, Eastlack RK, Anand N, Haque R, Fessler RG, Kanter AS, Deviren V, La Marca F, Smith JS, Shaffrey CI, Mundis GM, Mummaneni PV. (2015). Comparison of two minimally invasive surgery strategies to treat adult spinal deformity. *J Neurosurgery: Spine*. 22(4):374-380.

Park P, Wang MY, Nguyen S, Mundis GM Jr, La Marca F, Uribe JS, Anand N, Okonkwo DO, Kanter AS, Fessler R, Eastlack RK, Chou D, Deviren V, Nunley PD, Shaffrey CI, Mummaneni PV. (In press). International Spine Study Group. Comparison of complications and clinical and radiographic outcomes between non-obese and obese patients with adult spinal deformity undergoing minimally invasive surgery. *World Neurosurg*.

Park Y, Liu C, Luo T, Dietrich WD, Bramlett H, Hu B. (2015). Chaperone-mediated autophagy after traumatic brain injury. *J Neurotrauma*. 32(19):1449-1457.

Pastori C, Kapranov P, Penas C, Peschansky V, Volmar CH, Sarkaria JN, Bregy A, Komotar R, St Laurent G, Ayad NG, Wahlestedt C. (2015). The bromodomain protein BRD4 controls HOTAIR, a long noncoding RNA essential for glioblastoma proliferation. *Proc Natl Acad Sci U S A*. 112(27):8326-8331.

Patel AA, Zfass-Mendez M, Lebwohl NH, Wang MY, Green BA, Levi AD, Vanni S, Williams SK. (2015). Minimally invasive versus open lumbar fusion: A comparison of blood loss, surgical complications, and hospital course. *Iowa Orthop J*. 35:130-134.

Penas C, Govek EE, Fang Y, Ramachandran V, Daniel M, Wang W, Maloof ME, Rahaim RJ, Bibian M, Kawauchi D, Finkelstein D, Han JL, Long J, Li B, Robbins DJ, Malumbres M, Roussel MF, Roush WR, Hatten ME, Ayad NG. (2015). Casein kinase 1 is an APC/C(Cdh1) substrate that regulates cerebellar granule cell neurogenesis. *Cell Rep.* 11(2):249-260.

Penas C, Hatten ME, Ayad NG. (2015). The APC/C and CK1 in the developing brain. *Oncotarget*. 6(19):16792-16793.

Penas C, Mishra JK, Wood SD, Schürer SC, Roush WR, Ayad NG. (2015). GSK3 inhibitors stabilize Wee1 and reduce cerebellar granule cell progenitor proliferation. *Cell Cycle*. 14(3):417-424.

Perez MA, Rothwell JC. (2015). Distinct influence of hand posture on cortical activity during human grasping. *J Neurosci*. 35:4882-4889.

Perez MA. (2015). Neural control of hand movements. *Motor Control*. 19:135-141.

Perez-Cruet MJ, Fessler R, Khoo LT, Wang MY. (2015). An anatomic approach to minimally invasive spine surgery, 2nd Edition. CRC Press.

Peschansky VJ, Pastori C, Zeier Z, Motti D, Wentzel K, Velmeshev D, Magistri M, Bixby JL, Lemmon VP, Silva JP, Wahlestedt C. (2015). Changes in expression of the long non-coding RNA FMR4 associate with altered gene expression during differentiation of human neural precursor cells. *Front Genet*. 6:263.

Prak RF, Doestzada M, Thomas CK, Tepper M, Zijdewind I. (2015). Reduced voluntary drive during sustained but not during brief maximal voluntary contractions in the first dorsal interosseous weakened by spinal cord injury. *J Appl Physiol (1985)*. 119(11):1320-1329.

Rao S, Morales AA, Pearse DD. (In press). The comparative utility of Viromer RED and Lipofectamine for transient gene introduction into glial cells. *Biomed Res Int*.

Rauck BM, Novosat TL, Oudega M, Wang Y. (2015). Biocompatibility of a coacervate-based controlled release system for protein delivery to the injured spinal cord. *Acta Biomater*. 11:204-211.

Ritfeld GJ, Patel A, Chou A, Novosat TL, Castillo DG, Roos RA, Oudega M. (2015). The role of Brain-Derived Neurotrophic Factor in bone marrow stromal cell-mediated spinal cord repair. *Cell Transplant*. 24(11):2209-2220.

Ruschel J, Hellal F, Flynn KC, Dupraz S, Elliott DA, Tedeschi A, Bates M, Sliwinski C, Brook G, Dobrindt K, Peitz M, Brüstle O, Norenberg MD, Blesch A, Weidner N, Bunge MB, Bixby JL, Bradke F. (2015). Axonal regeneration. Systemic administration of epothilone B promotes axon regeneration after spinal cord injury. *Science*. 348(6232):347-352.

Scivoletto G, Glass C, Anderson KD, Galili T, Benjamini Y, Front L, Aidinoff E, Bluvshtein V, Itzkovich M, Catz A. (2015). An international age and gender controlled model for the spinal cord injury ability realization measurement index (SCI-ARMI). *Neuralrehabilitation and Neural Repair.* 29:25-32.

Serak J, Vanni S, Levi AD. (In press). The extreme lateral approach for treatment of thoracic and lumbar vertebral body metastases. *J Neurosurg Sci*.

Shear DA, Bramlett HM, Dixon CE, Dietrich WD, Deng-Bryant Y, Schmid Maj KE, Mondello S, Wang KK, Hayes RL, Povlishock J, Kochanek PM, Tortella FC. (In press). Nicotinamide treatment in traumatic brain injury: Operation Brain Trauma Therapy. *J Neurotrauma*.

Sidani C, Saraf-Lavi E, Lyapichev KA, Nadji M, Levi AD. (2015). Acute presentation of brachial plexus schwannoma secondary to infarction. *Neuroradiol J*. 28(3):333-336.

Soderblom C, Lee DH, Dawood A, Carballosa M, Jimena Santamaria A, Benavides FD, Jergova S, Grumbles RM, Thomas CK, Park KK, Guest JD, Lemmon VP, Lee JK, Tsoulfas P. (2015). 3D imaging of axons in transparent spinal cords from rodents and nonhuman primates. *eNeuro*. 2(2). doi: 10.1523/ENEURO.0001-15.2015.

Stone McGuire L, Bregy A, Sick J, Dietrich WD, Bramlett HM, Sick T. (2015). Nonconvulsive seizures as secondary insults in experimental traumatic brain injury. In: *Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects*, Kobeissy FH (ed), CRC Press, pp. 131-144.

Tazoe T, Perez MA. (2015). Effects of repetitive transcranial magnetic stimulation after spinal cord injury. *Arch Phys Med Rehabil*. 96:S145-S155.

Thirumala P, Zhou J, Krishnan R, Manem N, Umredkar S, Hamilton DK, Balzer JR, Oudega M. (In press). Diagnostic accuracy of evoked potentials for functional impairment after contusive spinal cord injury in adult rats. *J Clin Neurosci.*

Tisherman S, Bullock MR, Provencio J, Rincon F. (2015). Intraoperative temperature management. *Ther Hypothermia Temp Manag.* 5(2):68-72.

Titus DJ, Furones C, Atkins CM, Dietrich WD. (2015). Emergence of cognitive deficits after mild traumatic brain injury due to hyperthermia. *Exp Neurol*. 263:254-262.

Titus DJ, Oliva AA, Wilson NM, Atkins CM. (2015). Phosphodiesterase inhibitors as therapeutics for traumatic brain injury. *Curr Pharm Des*. 21(3):332-342.

Trojanowsky M, Vidovic D, Simanski S, Penas C, Schurer S, Ayad NG. (2015). Screening of cell cycle fusion proteins to identify kinase signaling networks. *Cell Cycle*. 14(8):1274-1281.

Tsenkina Y, Ricard J, Runko E, Quiala-Acosta MM, Mier J, Liebl DJ. (2015). EphB3 receptors function as dependence receptors to mediate oligodendrocyte cell death following contusive spinal cord injury. *Cell Death Dis.* 6:e1922.

Vayssier N, Solomon R, Severyn J, Hurley E, Greenberg J, Hotz G. (In press). Sustaining a pediatric injury prevention program through educational curriculum dissemination. *Health Promot Pract*.

Wang MY. (2015). The enemy of good is perfect. *World Neurosurg*. 83(3):299-300.

Wang J, Pearse DD. (2015). Therapeutic hypothermia in spinal cord injury: The status of its use and open questions. *Int J Mol Sci.* 16(8):16848-16879.

Wang MY, Widi G, Levi AD. (2015). The safety profile of lumbar spinal surgery in elderly patients 85 years and older. *Neurosurg Focus*. 39(4):E3.

Wang MY. (2015). Are surgeons able to foresee preoperative predictors

of a complication? *World Neurosurg*. 84(2):233-234.

Wang MY. (2015). Higher risks of complications in patients with rheumatoid arthritis. *World Neurosurg*. 84(2):226-227.

Wang MY. (2015). Physician protect thyself. *World Neurosurg*. 83(2):154.

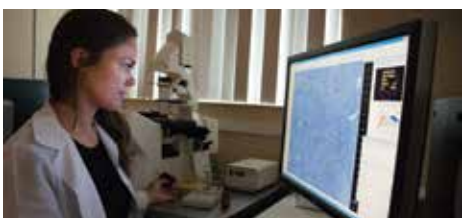
Wang MY, Sama A, Uribe JS (Eds). (2015). Lateral access minimally invasive spine surgery. Springer-Verlag Publishing, Vienna, Austria.

Wang MY, Strayer A, Harris O, Rosenberg C, Mummaneni P. (Eds.) (2015). Handbook of Neurology, Neurosurgery, and Intensive Care for Nurses & Advanced Practice Health Professionals. CRC Press, London, England.

Widerström-Noga E, Govind V, Adcock J, Levine B, Maudsley AA. (In press). Subacute pain after TBI is associated with lower insular N-Acetylaspartate concentrations. *J Neurotrauma*.

Widerström-Noga EG, Cruz-Almeida Y, Felix ER, Pattany PM. (2015). Somatosensory phenotype is associated with thalamic metabolites and pain intensity after spinal cord injury. *Pain*. 156:166-174.

Widerström-Noga EG, Felix ER, Adcock JP, Escalona M, Tibbett J. (In press). Multidimensional neuropathic pain phenotypes after spinal cord injury. *J Neurotrauma*.



Pernille Madsen

Williams RR, Venkatesh I, Pearse DD, Udvadia AJ, Bunge MB. (2015) MASH1/Ascl1a leads to GAP43 expression and axon regeneration in the adult CNS. *PLoS One*. 10(3):e0118918.

Winslow J, Martinez A, Thomas CK. (2015). Automatic identification and classification of muscle spasms in long-term EMG recordings. *IEEE J Biomed Health Inform*. 19(2):464-470.

Yokobori S, Hosein K, Wang M, Gajavelli S, Moghieb A, Zhang Z, Wang K, Bullock MR, Dietrich WD. (2015). Biomarkers in spinal cord injury. In: Biomarkers of brain injury and neurological disorders. Wang K, Zhang Z, Kobeissy F, (eds). CRC Press, pp. 341-354.

Yokobori S, Zhang Z, Moghieb A, Mondello S, Gajavelli S, Dietrich WD, Bramlett H, Hayes RL, Wang M, Wang KK, Bullock MR. (2015). Acute diagnostic biomarkers for spinal cord injury: review of the literature and preliminary research report. World Neurosurg. 83(5):867-878.

Yu H, Koilkonda RD, Chou TH, Porciatti V, Mehta A, Hentall ID, Chiodo VA, Boye SL, Hauswirth WW, Lewin AS, Guy J. (2015). Consequences of zygote injection and germline transfer of mutant human mitochondrial DNA in mice. *Proc Natl Acad Sci U S A*. 112(42):E5689-5698.

Eric Bray

Yungher BJ, Luo X, Salgueiro Y, Blackmore MG, Park KK. (2015). Viral vector-based improvement of optic nerve regeneration: characterization of individual axons' growth patterns and synaptogenesis in a visual target. *Gene Ther*. 22(10):811-821.

Zeidenberg J, Burks SS, Jose J, Subhawong TK, Levi AD. (2015). The utility of ultrasound in the assessment of traumatic peripheral nerve lesions: report of 4 cases. *Neurosurg Focus*. 39(3):E3.

Zhu Q, Gao X, Levene HB, Brown MD, Gu W. (In press). Influences of nutrition supply and pathways on the degenerative patterns in human intervertebral disc. Spine (Phila Pa 1976).

Zhu Y, Soderblom C, Krishnan V, Ashbaugh J, Bethea JR, Lee JK. (2015). Hematogenous macrophage depletion reduces the fibrotic scar and increases axonal growth after spinal cord injury. *Neurobio Dis*. 74:114-125.

Zhu Y, Soderblom C, Trojanowsky M, Lee DH, Lee JK. (2015). Fibronectin matrix assembly after spinal cord injury. *J Neurotrauma*. 32(15):1158-1167.

Alberto Vitores

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