Dear Friends and Colleagues,

This year has seen great progress in our research programs targeting paralysis. Five FDA-approved clinical trials targeting spinal cord injury (SCI) and peripheral nerve injury continue to provide exciting findings. The Phase 1 safety trial evaluating autologous human Schwann cell transplantation in subacute injury subjects is nearing completion with promising results. Millions of Schwann cells have been successfully transplanted into four subjects with no adverse effects. Based on these promising results, we have now obtained permission from the FDA to test this therapy in chronically injured individuals for the first time. This chronic SCI trial will be the first to combine cell transplantation with extensive rehabilitation. Our FDA approved trial for repairing a severe peripheral nerve injury has also shown promise in promoting return of motor and sensory function in the leg of one subject. To treat neuropathic pain after SCI, we are testing the beneficial effects of Deep Brain Stimulation. This FDA approved program has already resulted in encouraging findings that suggest a new strategy for addressing this difficult to treat condition experienced by many individuals living with SCI. Our Brain-Machine Interface FDA program is merging biological and biomedical disciplines to show proof-of-concept of operating an upper extremity neural prosthetic thereby enhancing independence. Finally, another FDA approved trial testing the safety and efficacy of adult mesenchymal stem cells has also shown encouraging results in one subject. Together these reparative trials represent the most comprehensive program in the world testing experimental therapies for spinal cord injury and related disorders.

The benefits of therapeutic hypothermia and targeted temperature management in acute brain and spinal cord injured patients continue to be recognized. Over 40 acutely injured SCI patients have undergone this experimental therapy that is showing long term benefits in neurologic function. In the area of traumatic brain injury, the most severely injured individuals are also being treated with cooling strategies in an international multicenter clinical trial. These neuroprotective programs are additional examples of how Miami Project-led basic and translational studies have been successfully moved into the clinic.

Multiple clinical programs including our Miami Project “Boot Camp” are actively investigating other aspects of SCI that may also improve function. Our ultimate goal is to combine the state-of-the-art rehabilitation and conditioning strategies with cell therapies and other regenerative approaches to target functional recovery, neuropathic pain, male fertility, spasticity, and bladder function. The Miami Project is committed to developing whole life strategies that can maximize quality of life and good health as our scientists continue to strive to develop new therapeutic interventions.

Barth Green, M.D., F.A.C.S.
W. Dalton Dietrich, Ph.D.
Discovery research, which fuels our translational and clinical programs, is clarifying molecular and cellular mechanisms underlying cell death, axonal regeneration, and circuit repair. Ultimately, this knowledge will be combined with our current therapeutic interventions to maximize functional recovery. The clarification of critical gaps in our knowledge regarding axonal regeneration and circuit plasticity will improve our chances of developing successful cures for paralysis.

The Miami Project to Cure Paralysis was established in 1985 to develop novel therapies to improve function in paralyzed individuals. Today, our discoveries are being successfully translated to people and are changing the way we provide clinical care. Our program is unique in that it touches upon multiple areas of medical research including education, discovery, translational and clinical trials. These are very exciting times within The Miami Project to Cure Paralysis and we thank our friends, colleagues, and research participants for their long-term support and commitment to our research.

Sincerely,

W. Dalton Dietrich, Ph.D.
Scientific Director, The Miami Project to Cure Paralysis
Kinetic Concepts Distinguished Chair in Neurosurgery
Senior Associate Dean for Discovery Science
Professor of Neurological Surgery,
Neurology and Cell Biology

Barth A. Green, MD
Co-Founder and Chairman, The Miami Project to Cure Paralysis
Professor and Chairman, Department of Neurological Surgery
Professor, Departments of Orthopaedics
and Rehabilitation Medicine
University of Miami Miller School of Medicine
Message from the Chairman, Dr. Barth A. Green and Scientific Director, Dr. W. Dalton Dietrich

Fundraising, Administrative, and Scientific Support Staff

RESEARCH HIGHLIGHTS

Phase I Chronic Schwann Cell Trial

Monica Perez, PT, PhD, Martin Oudega, PhD, Join The Miami Project

Hyperthermia in Neurotrauma

Faculty Highlight Mousumi Ghosh, PhD

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Active Clinical Studies and Trials

Educational Outreach

Research Funding in 2014

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Scientific Research Publications 2014

On the Cover

Schwann cell transplant: host cord interface in chronic spinal cord injury model
The Miami Project scientific team is grateful for the dedication and hard work of the fundraising, administrative, and scientific support staff. This incredible group of people spend countless hours providing direct clerical and administrative support to the research staff, and raising the precious private funds to support Miami Project research endeavors.

**Fundraising, Administrative, and Scientific Support Staff**

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*Post-doctoral Fellows*

Graduate Students  

Medical/Residents/Observorships  

Undergraduate Students  

Volunteers  

Other students  

Research Staff
At long last, we have begun our first clinical trial testing autologous human Schwann cell (ahSC) transplantation in people living with chronic spinal cord injury (SCI). This is also a Phase I trial focused on safety and feasibility outcomes. Since October 2012, we have been conducting a separate Phase I trial targeting sub-acute SCI.

As we announced in October 2014, we obtained FDA approval after having submitted for review additional data regarding transplantation of Schwann cells into rodents and some pigs with chronic SCI. We now have ethics approval from the University of Miami Institutional Review Board and are open for enrollment.

This new trial will be primarily focused on safety, but in addition it will involve a preliminary evaluation of the efficacy of combining Schwann cells with exercise and rehabilitation. For humans with chronic SCI, we hypothesize that axons might show improved function if myelin repair is induced with the implantation of ahSC. In addition, spinal cord cavitation may be reduced and neural sprouting and plasticity may be enhanced via neurotrophic effects. In this trial, participants will receive fitness conditioning and locomotor rehabilitation prior to transplantation in order to validate the stability of their neurological baseline and enhance their ability to undergo surgery with few complications. They will also receive fitness conditioning and rehabilitation post-transplantation to maintain health and promote neuronal activity and potential neuroplasticity.

We only have FDA approval to transplant a maximum of 10 people – remember that it is a Phase I safety trial. In order to reduce risk, there are a number of inclusion and exclusion criteria. Some of which are listed here.
Participant inclusion criteria:
- Persons with traumatic SCI that occurred a minimum of 12 months prior to enrollment;
- Between the ages of 18 and 65 years at last birthday;
- SCI between cervical level C5 and thoracic level T12 as defined by the most caudal level of intact motor and sensory function on the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI);
- ASIA Impairment Scale (AIS) grade A, B, or C at time of enrollment;
- Spinal cord lesion size that is less than or equal to 3 cm in length and less than or equal to 2 cc in volume when viewed on magnetic resonance imaging (MRI)

Participant exclusion criteria (not all are listed here):
- Persons with penetrating injury of the spinal cord or complete transection of the cord, as identified by MRI;
- Persons with a cavity structure that would preclude successful transplantation, as identified by MRI;
- Intolerance to functional electrical stimulation of muscles;
- Presence of disease that might interfere with participant safety, compliance, or evaluation of the condition under study;
- Body Mass Index (BMI) > 35;
- Persons with pre-existing conditions that would preclude satisfactory sural nerve harvest;

We will be staggering enrollment in 2 cohorts. Progression through the cohorts is based on safety, going from low risk to higher risk, and there are certain lock-out periods between participants.

Cohort 1: Thoracic Injuries with Grades A, B, C
We will enroll up to 4 participants who have thoracic spinal cord injuries between the levels of T2 to T12 with Grades A, B, or C in cohort 1.
We will enroll 2 participants with Grade A injuries before we enroll any participants with Grades B or C injuries.

Cohort 2: Cervical Injuries with Grades A, B, C
We will enroll up to 6 participants with cervical spinal cord injuries between the levels of C5 to T1 with Grades A, B, or C in cohort 2.
We will enroll 2 participants with Grade A injuries before we enroll any participants with Grades B or C injuries.

There are 5 stages of Screening to progress through before the actual Schwann cell transplantation occurs and each participant’s time commitment to the trial will be approximately 10 months. They will be followed in a separate long-term monitoring protocol annually for a total of 5 years post-transplantation.

One of the stages involves harvesting a segment of each participant’s own Schwann cells from one of their sural nerves, a sensory nerve above the ankle. The Schwann cells will then be derived from the nerve and processed.
in a culturing facility to generate the number of cells necessary for transplantation, and to undergo a purification process. All procedures will be conducted in Miami at the University of Miami Miller School of Medicine. Because the Schwann cells are obtained from each individual participant, there is reduced concern of immune rejection and immunosuppressant medication is not required. Once the cells are removed from the participant, they have to be handled in accordance to current Good Manufacturing Practices (GMP). Because the cells will eventually be injected into the spinal cord, this process is required to ensure that the cells are prepared consistently and without contaminants.

Another stage before the transplantation, which will resume after the transplantation, involves the fitness and locomotor rehabilitation training. This involves at-home and on-site components that must be completed every week. So, the individuals that end up qualifying and agreeing to participate have a very large commitment to think about.

All procedures for this research study are for research purposes only, and, therefore, are free of charge. However, participants not local to Miami will need to relocate here for at least 10 months. For those non-local participants, we have a housing program available free of charge once they start the pre-transplantation fitness and locomotor rehabilitation training program. No travel or food expenses will be covered. There are strict regulations on the amount of money people can receive to participate in clinical trials; this is to prevent individuals from participating in risky interventions just for the money.

To find out more information about the trial and prescreening, contact The Miami Project Education Department at 305-243-7108 or MPinfo@med.miami.edu.

More information about all of our clinical trials and studies is available at http://www.themiamiproject.org/trials.
Two New Faculty Join The Miami Project Team

Monica Perez, PT, Ph.D.
The Miami Project is very happy to announce that Dr. Monica Perez will be joining us as a new clinical research faculty! Dr. Perez is joining us from the University of Pittsburgh. She actually earned her PhD degree in the Department of Physical Therapy at the University of Miami in 2003. From there she did a post-doctoral fellowship at the University of Copenhagen followed by a fellowship at the National Institute of Neurological Disorders and Stroke (NINDS). Her research focuses on neural control of movement, particularly the corticospinal tract. She is currently funded to investigate Neural control of bilateral hand and arm movements after SCI (NINDS), Corticospinal function after human SCI (NINDS), Enhancement of hand motor function after cervical SCI (Veterans Affairs), and Role of the motor cortex in recovery of hand function after SCI (Craig H. Nielsen Foundation, CHNF). “I am extremely happy to have the opportunity to join The Miami Project to Cure Paralysis. The goal of my research is to understand how the brain and spinal cord contribute to control residual voluntary movement after SCI. Our mechanistic approach is used to develop strategies to facilitate voluntary motor output. For the next years our research will focus on two main areas. First, we will work on protocols to maximize plasticity at different sites within the central nervous system to enhance voluntary motor output using noninvasive stimulation techniques and motor training. Second, we will combine methodologies to better characterize SCI and their impact on the neural control of movement. These methodologies include mapping of multiple motor cortical regions, estimations of activity in the corticospinal pathway and their input to spinal motoneurones, and coupling between motor cortical areas and different muscle groups.”

Martin Oudega, Ph.D.
Dr. Martin Oudega will be joining us as a new basic science research faculty! Dr. Oudega earned his PhD at the University of Leiden in the Netherlands. He did a post-doctoral fellowship at the University of California, San Diego and then at the University of Miami as well. He became faculty at Johns Hopkins University and then the University of Pittsburgh. “I am thrilled to join The Miami Project and to start working with its great scientists and wonderful administrative and technical supporting staff. My main research focus is on developing cell-based strategies for repair of anatomical damage and improving functional impairments after SCI. I am particularly interested in the molecular mechanisms underlying cell transplant-mediated repair and in how natural and synthetic biomaterials can augment the repair potential of intraspinal cell transplants.” He is currently funded to investigate ESHU for optimizing BMSC transplant survival and their spinal cord repair efficacy (Wings for Life), Role of Ang-1 in vascular stabilization in BMSC-mediated tissue spinal cord repair (CHNF), and Fibronectin for enhancing BMSC-mediated spinal cord repair (Morton Foundation).

Congratulations to Drs. Perez and Oudega and welcome to the family!
Our researchers have demonstrated over several years the importance of temperature in neurotrauma; particularly, how lowering the temperature (hypothermia) can be therapeutic. This research directly led to the ongoing trial at the University of Miami and Jackson Memorial Hospital evaluating the safety and efficacy of mild therapeutic hypothermia in acute cervical spinal cord injury (SCI). It also led to the current HOPES trial, HypOthermia for Patients requiring Evacuation of Sudural Hematoma, a randomized-controlled trial for individuals that sustained a severe traumatic brain injury (TBI) plus developed an acute subdural hematoma that requires surgical removal. Hypothermia is used during the surgical removal of the hematoma. What about elevated temperature, hyperthermia? Dr. Dietrich and others have shown that hyperthermia after moderate to severe TBI plus developed an acute subdural hematoma that requires surgical removal. Hypothermia is used during the surgical removal of the hematoma. What about elevated temperature, hyperthermia? Dr. Dietrich and others have shown that hyperthermia after moderate to severe TBI can worsen tissue damage and outcome in experimental models. In the clinical setting, fever can significantly worsen morbidity and mortality after severe TBI. But what about all the mild TBIs and concussions that occur? Is temperature management important there?

Drs. Coleen Atkins and Dalton Dietrich recently investigated whether hyperthermia at the time of a mild TBI worsened/aggravated associated cognitive deficits. In addition to a couple control groups, they tested the following injury/temperature conditions:

1. Normothermic mTBI – a mild TBI was administered while the brain and body were at 98.6°F, then that temperature was maintained for 4 hours;

2. Hyperthermic mTBI – a mild TBI was administered while the brain and body were at 102.2°F, then that temperature was maintained for 4 hours;

3. Hyperthermic/normothermic mTBI (cooled hyperthermic) – a mild TBI was administered while the body and brain were at 102.2°F; that temperature was maintained for 15 minutes, then cooled to 98.6°F and maintained for 4 hours.

Sustaining a mild TBI while hyperthermic caused greater brain tissue damage compared to a mild TBI while normothermic. Interestingly, bringing the hyperthermic brain temperature down to normal within 15 minutes post-injury significantly reduced the amount of tissue damage. This also had an effect on memory. Sustaining a mild TBI while normothermic had no effect on long-term memory, but sustaining a mild TBI while hyperthermic caused persistent deficits in long-term memory. These long-term memory deficits were prevented by cooling hyperthermic mild TBI animals to normothermia within 15 min after the mild TBI. Sustaining a mild TBI while normothermic or hyperthermic caused persistent deficits in working memory, which were not improved by cooling, however. Overall, these results suggest that temperature management strategies immediately after mild TBI may be promising to pursue clinically.
Dr. Mousumi Ghosh is a new Research Assistant Professor in the Department of Neurological Surgery and The Miami Project. Dr. Ghosh, a native of India, holds her Bachelors and Masters degrees in Chemistry and Microbiology from the University of Poona, India. While an undergraduate, she became interested in academic research and earned her PhD in Biochemistry in 1997 from the University of Calcutta, India. Her postdoctoral training focused on studying cell-signaling mechanisms and protein-protein interactions between the heterotrimeric G proteins and their downstream signaling targets at the University of Rochester, NY, under Dr. Alan Smrcka. She then joined The Miami Project in 2007 as a postdoctoral associate with Dr. Damien Pearse, where she began developing methods for altering glial cell reactivity and cell-to-cell interactions in response to central nervous system (CNS) injury or disease to promote neuroprotection and repair. During this time Dr. Ghosh investigated 1) the surface modification of Schwann cells to enhance their capacity for migration and axon regeneration following transplantation within the injured spinal cord, 2) microglia phenotypic conversion to alter their properties from inflammatory to reparative, and 3) the manipulation of intracellular signaling pathways in astrocytes to abolish their reactivity and production of axon growth inhibitory matrix molecules. Dr. Ghosh’s research in spinal cord injury repair was recognized by The Sam Schmidt Paralysis Foundation and The American Spinal Injury Association through The Outstanding Young Investigator Award given to her in 2009.

The present focus of Dr. Ghosh’s laboratory is on altering the hostile environment of the injured or diseased CNS to one that is conducive to repair through conversion of microglia and macrophages from a cytotoxic M1 (“bad”) to a reparative M2 (“good”) state. By understanding the signals that govern macrophage-microglia phenotype, she aims to develop novel, molecular, and immuno-pharmacological therapeutic strategies to promote M1 to M2 conversion of these cells to induce neuroprotection, neuroplasticity, and/or disease remission. Her laboratory is also interested in understanding how altering the immunophenotypical profile of macrophages and microglia can affect host glial responses, including the formation of the glial scar and oligodendrocyte migration and myelination as well as influence the ability of transplanted cells, such as Schwann cells and stem cells, to mediate neurorepair.
Can Whole Body Vibration Influence Bone Health After (Spinal Cord Injury) SCI?

As many of our readers know, SCI causes many more problems aside from not being able to move. One big problem is bone density loss, which can lead to osteoporosis. Putting weight on bones (weight bearing) and having muscle contractions are two important components of maintaining healthy bones. Healthy bone metabolism is a balance between old bone degradation (resorption) and new bone formation. SCI alters bone metabolism; there is an increase in bone resorption, but a decrease in new bone formation. This leads to an overall loss of bone density.

Vibration is a component of weight bearing and whole body vibration has been investigated by many research groups as a therapeutic intervention for osteoporosis, especially in post-menopausal women. The potential benefits of whole body vibration have been investigated for other body systems as well. In fact, in our 2010 winter edition of the Research Review we wrote an article about the effect of whole body vibration on muscle spasticity in people with motor incomplete SCI. Seeing those beneficial results promoted an interest in going “back to the bench” to evaluate how/if vibration alters bone metabolism after SCI.

Drs. Helen Bramlett and Dalton Dietrich, along with colleagues in New York, tested the effect of low-intensity, high-frequency mechanical vibration (LIV) in rodents that had a moderate mid-thoracic spinal contusion (Bramlett et al., 2014, Osteoporos. Int.). They waited for 28 days before starting LIV for a couple reasons: 1) to mimic the clinical situation of several weeks passing after SCI before rehabilitation begins and 2) animals with this type of injury begin to regain weight-bearing ability by that time and it was hypothesized that weight bearing might enhance any benefits due to LIV. LIV was given 2x/day (15 minutes/session), 5 days/week for 35 days. The vibration frequency delivered was in the 40 Hz range, which was similar to what Ness and Field-Fote (2009, Gait & Posture) did in humans with SCI.

They found that LIV administered at that time point, dose, and duration did not alter gross bone mineral density or trabecular bone architecture in that experimental model of SCI. However, they did identify some significant changes in bone metabolism. Osteoblasts are the cells associated with bone formation and the chemical osteocalcin is secreted only by osteoblasts, so osteocalcin is a biomarker of bone formation. The SCI itself resulted in decreased osteocalcin biomarker levels in the blood, which was increased back to normal levels by LIV. This suggests that LIV has a positive effect on new bone formation.

Additionally, there appeared to be an effect on certain aspects of bone resorption. Osteoclastogenesis is the development of osteoclasts and osteoclasts are the cells associated with bone resorption. In this experiment, the SCI resulted in increased osteoclastogenic potential of bone marrow precursor cells and LIV reduced this potential by 70%. This suggests that LIV may be reducing some components of the increased bone resorption induced by SCI.

Though bone metabolism is a complicated process, just like everything else with SCI, it appears that LIV is worth pursuing more as a therapeutic intervention for bone health after SCI!
...we support the idea that a combination of interventions is required to promote the most repair and functional improvement in people.

**Engineered Schwann Cell Grafts**

Many years of animal research and many scientists have demonstrated that Schwann cells transplanted into the spinal cord injury (SCI) site can create an environment that promotes various activities important for repair. Indeed we now have two Phase I clinical trials testing the safety of transplanting Schwann cells by themselves. However, we also know that Schwann cells in combination with other treatments can promote more repair — remember, the spinal cord is very complex and we support the idea that a combination of interventions is required to promote the most repair and functional improvement in people.

Drs. Mary Bunge, Damien Pearse, and colleagues recently published new results from a very exciting combination strategy (Journal of Neuroscience, 2014, 34(5):1838–1855). The “players” in the combination strategy were:

1. rat Schwann cells,
2. D15A – this is a growth factor that has been modified to act as two growth factors (Neurotrophin-3 and Brain-derived neurotrophic factor), and
3. Chondroitinase ABC (ChABC) – an enzyme that can break apart many of the proteins that are found in scar tissue surrounding the SCI site.

In addition to multiple experimental controls, they transplanted the following combinations one week after a mid-thoracic contusion injury in rodents:

1. Schwann cells that secrete D15A only
2. Schwann cells that secrete ChABC only
3. Schwann cells that secrete BOTH D15A and ChABC

They followed the animals for 3 months and then analyzed many different aspects of repair and function. They found that the transplanted Schwann cells that had been engineered to secrete D15A and ChABC at the same time had the best effect. The main results from that combination showed:

1. the greatest number of Schwann cells surviving in the graft site as well as the greatest number of axons that were myelinated (insulated) by Schwann cells,
2. more nerve fibers from the brainstem grew into the graft as well as the host tissue around and below the graft,
3. more nerve fibers from the cortex of the brain remained closer to the graft (did not die back) and grew/sprouted around and below the graft,
4. a significant improvement in aspects of locomotion, and
5. a reduction in pain-like sensations.

These results are very exciting because they show that Schwann cell grafts engineered to secrete a multifunctioning growth factor in addition to altering the scar composition lead to more axonal regeneration and functional improvement than either strategy administered alone. These are the kind of animal experiments that will help guide us as we move forward into testing combination treatments in future clinical trials.
The Miami Project clinical researchers currently have several clinical trials and clinical studies available for people who have had a spinal cord injury; some are for acute injuries and some are for chronic injuries. The clinical trials are testing the safety and efficacy of different neuroprotective, repairative, or modulatory interventions. The clinical studies are investigating questions regarding exercise science, nutrition, rehabilitation training, pain, male fertility, aging, and brain-machine interface technology.
If you would like to be considered for these or future Miami Project trials or studies, please call The Miami Project Education Office at 305-243-7108.

### Biological Trials

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<td>C4-C8 AIS A, B, C</td>
<td>C5-C7 AIS A, B, C</td>
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### Online Surveys

- Pain After SCI  
  [www.surveymonkey.com/s/SCIpain](http://www.surveymonkey.com/s/SCIpain)
- Basic Pain Dataset Self-Report  
  [www.surveymonkey.com/s/paindataset](http://www.surveymonkey.com/s/paindataset)

### Activity and Nutrient Modifying

- Cardiometabolic Risk, Obesity, and Cardiovascular Disease in SCI
- Effect of an Omega-3 Supplement Intervention on Cardiometabolic Health
- Obesity/Overweight in Early and Chronic SCI: Lifestyle Intervention Program
- Clinically Meaningful Changes in Wheelchair Propulsion Stress
- Training Programs to Improve Outcomes for Individuals with SCI

### Male Fertility

- Fertility Evaluation
- Treatment for Infertility

### Spasticity

- Quantifying Spasticity in Activities of Daily Living

### Aging

- Telomeres as an Aging and Health Biomarker in Persons with SCI
- Muscle Weakness and Fatigue with Age After SCI
- Impact of Time Post-Injury on the Bladder Inflammatory Profile

### Brain Machine Interface

- Treatment for Pain and Autonomic Dysreflexia in SCI with Deep Brain Stimulation
- Assessment of Candidates and Design Considerations for Neuroprosthetic Devices for Chronic SCI
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, Letitia Fisher, and Kathleen Gilsenan. 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, 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 reached each month during 2014 outreach activities. The Education department also assists all of The Miami Project clinical research faculty with recruitment for their clinical studies. 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.

On April 5, 2014 the Education department hosted the 4th 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 Health & Wellness related to spinal cord injury (featuring Drs. Mark Nash, Rachel Cowan, Christine Thomas, Eva Widerström-Noga, and Diana Cardenas). This included cardiovascular issues in relation to diet and exercise, in addition to chronic inflammation and sleep disruptions. Mobility was also discussed, particularly how it is impacted by strength, the environment, and wheelchair

The Miami Project believes that an important component of developing treatments for paralysis involves communication with the community.
configuration, with suggestions on how each of these factors might be manipulated to enhance mobility. Chronic pain is a significant problem to many people living with SCI and input was provided about the bio-psycho-social aspects of pain and their interactions.

This was followed by a Meet the Scientists session in which the audience met 5 of our faculty (Drs. Damien Pearse, Paula Monje, Pantelis Tsoufas, Vance Lemmon, and Brian Noga), heard brief explanations of their current research, and had the opportunity to ask questions. The final component of the day was Behind-the-Scenes tours of four laboratories, including a cell culture lab, regeneration and imaging lab, human locomotor and functional electrical stimulation lab, and human sensory lab. The 5th Annual Community Open House is scheduled for April of 2015.

The education department also participated in the 5th Annual Brain Fair with a Build-a-Spinal Cord exhibit/activity and gave invited lectures to multiple SCI consumer groups. If you have questions, don’t hesitate to email us at mpinfo@med.miami.edu or call us at 305-243-7108.

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.

November 5, 2014
Vittorio Gallo, PhD
Children’s National Medical Center
Washington, DC

December 3, 2014
Pramod Dash, PhD
University of Texas Medical School at Houston
Houston, TX

January 7, 2015
Susan Harkema, PhD
University of Louisville – Louisville, KY

February 4, 2015
Armin Curt, MD, FRCPC
University of Zurich – Zurich, Switzerland

March 4, 2015
V. Reggie Edgerton, PhD
University of California, Los Angeles
Los Angeles, CA

April 1, 2015
Larry M. Jordan, PhD
University of Manitoba – Winnipeg, Canada

May 6, 2015
T. George Hornby, PhD, PT
University of Illinois at Chicago – Chicago, IL
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 2014.

**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 – Screening

**Children’s Tumor Foundation**
Dr. Cristina Fernandez-Valle (P.I.), Dr. Paula Monje (Co-I.)
-Creation of Human Merlin-Null Schwann cells for NF2 Studies

**Christopher & Dana Reeve Foundation**
Dr. James Guest (Center P.I.)
-North American Clinical Trials Network
-CTN7-2014: Safety and Pharmacokinetics of Riluzole in Patients

**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. Robert Keane (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)
-Inflammasome Regulation Following Spinal Cord Injury

Dr. Daniel Liebl (P.I.)
-A Novel Eph Receptor-Mediated Mechanism of Cell Death Following Spinal Cord Injury

Dr. Brian Noga (P.I.), Dr. Ian Hentall (Co-I.)
-Acute Facilitation of Walking After SCI Using Deep Brain Stimulation
Dr. Kevin Park (P.I.), Dr. Jae Lee (Co-I.)  
-Novel Combinatorial Approaches to Promote Axon Regrowth After Chronic SCI

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

Dr. Jacqueline Sagen (P.I.)  
-Utilizing Designer Genes to Alleviate Chronic SCI Pain

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

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

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

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

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

**Department of Defense US Army Medical Research and Materiel Command (DAMD)**

Dr. M. Ross Bullock (P.I.)  
-Clinical Phase IIB Trial of Oxycyte Perfluorocarbon in Severe Human Traumatic Brain Injury  
-Laboratory studies evaluating PFC in models of Penetrating and Closed 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, Social Marketing Campaign, and School-Specific Action Plan

**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 Football League Charities Medical Research**  
Dr. Coleen Atkins (P.I.)  
-The Effects of Mild Hyperthermia on Outcome after Mild Traumatic Brain Injury

**National Heart, Lung, and Blood Institute**  
Dr. Stephan Schürer (P.I.), Dr. Vance Lemmon (Co-I.)  
-LINCS Information FramEwork (LIFE) to integrate and Analyze Diverse Data Sets

**National Human Genome Research Institute**  
Dr. Vance Lemmon (P.I.)  
-Bioassay Ontology and Software Tools to Integrate and Analyze Diverse Data Sets

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

**National Institute of Disability & 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.)  
-Sleep Disordered Breathing in Persons with Chronic Tetraplegia: Characterization and Intervention  
-Dr. Suzanne Groah (P.I), Dr. Mark Nash (Co-I.)  
-Rehabilitation Research and Training Center on Secondary Conditions in SCI

**National Institute of Neurological Disorders & Stroke**  
Dr. Kim Anderson-Erisman (Co-P.I.), Dr. W. Dalton Dietrich (Co-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. Mary Bartlett Bunge (Co-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. John Bixby (P.I.), Dr. Vance Lemmon (Co-I.)  
-Novel Compounds that Overcome Glial Inhibition of Axonal Regeneration  
-Dr. W. Dalton Dietrich (P.I.), Dr. Helen Bramlett (Co-I.), Dr. Coleen Atkins (Co-I.)  
-The Importance of Temperature on Inflammation after TBI  
-Cyclic Nucleotide Regulation in Traumatic Brain Injury  
-Dr. W. Dalton Dietrich (P.I.), Dr. Robert Keane (Co-P.I.)  
-Therapeutic Neutralization of the Inflammasome after Spinal Cord Injury  
-Dr. Gillian Hotz (Site-P.I.), Dr. M. 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  
-Eph Receptors Regulate Vascular Growth Following Traumatic Brain Injury (Fellowship)  
-Modulating Post-injury Gliotransmitter Levels leads to improved Synaptic Function (Fellowship)  
-Dr. Paula Monje (P.I.)  
-Phenotypic and Functional Analysis of Human Schwann Cells for Potency Assay Development
Dr. Damien Pearse (P.I.)
- Therapeutic Targeting of Intracellular Mechanisms Involved in Glial Scar Formation

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

Robert J. Kleberg, Jr., and Helen C. Kleberg Foundation
Dr. Kim Anderson-Erisman (P.I.), Dr. Rachel Cowan (Co-I.), Dr. Edelle Field-Fote (Co-I.), Dr. Mark Nash (Co-I.), Dr. Christine Thomas (Co-I.), Dr. Eva Widerström-Noga (Co-I.)
- Exercise and Locomotor Training Required for Clinical Trials Targeting Chronic Spinal Cord Injury

Paralyzed Veterans of America Foundation
Dr. Mousumi Ghosh (P.I.), Dr. Damien Pearse (Co-I.)
- Down-Regulating PDE4A in Astrocytes to Promote Axon Regeneration After SCI

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.)

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

University of Miami SAC Awards
Dr. Robert Keane (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)
- Therapeutic Neutralization of the Inflammasome after Spinal Cord Injury

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

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

- Rehabilitation of IPF Patients: Effects of Exercise and Oxidant Stress

Dr. Robert Jackson (P.I.), Dr. Diana Cardenas (Co-I.)
- Enhancing the Reparative Efficacy of Schwann Cells Following Chronic SCI
The Miami Project To Cure Paralysis

Faculty Profiles

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, III, PH.D.
Scientific Director, The Miami Project
Kinetic Concepts Distinguished Chair in Neurosurgery
Senior Associate Dean for Discovery Science
Professor, Departments of Neurological Surgery, Neurology, and Cell Biology & Anatomy

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

BARTH A. GREEN, M.D., F.A.C.S.
Co-Founder, The Miami Project
Professor and Chairman, Department of Neurological Surgery

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.
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), and genetically engineering SCs before transplantation to improve their growth factor-secretion capability or neurons to enhance their ability to regrow axons, and testing matrices for efficacy after injury. We pay particular attention to the interface 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, Sylvester Cancer Center, Vice Provost for Research
VANCE LEMMON, PH.D.
Walter G. Ross Distinguished Chair in Developmental Neuroscience
Professor, Department of Neurological Surgery
High Content Screening and Functional Genomics of the Nervous System
Our laboratory has developed methods to test thousands of genes or chemicals in hundreds of thousands of neurons each week and obtain quantitative information about cell morphology and gene expression. This “high throughput” capability allows us to tackle questions about development and regeneration using systems biology approaches. The Lemmon-Bixby lab has 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 hundreds of kinases by overexpression and have also tested >1500 kinase inhibitors, many of which strongly promote neurite growth in vitro. Using machine learning and cheminformatics (collaboration with Dr. Stephan Schürer) we can identify critical kinases and their signaling networks as well as potential lead therapeutic compounds. A second project is based on the observation that peripheral sensory neurons initiate a genetic program appropriate for axonal regeneration after injury. Our laboratory is combining next-generation sequencing with cell-based phenotypic screening to identify genes and microRNAs that are part of this genetic program. Finally, in collaboration with Dr. S. Schürer and Dr. Ubbo Visser, we are developing RegenBase, an information system that integrates diverse data on nerve regeneration after spinal cord injury with data from other information resources.
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 are near completion of a two year grant from the Department of Defense to evaluate the neuroprotective effect of Perfluorocarbons 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. We are also evaluating hypothermia neuroprotection, in humans and animals, using novel biomarkers. We are also obtaining pilot data with FDA approved Human stem cells, transplanted into the rat brain, as therapy for Penetrating TBI.

DIANA CARDENAS, M.D., M.H.A.
Professor and Chair, Department of Rehabilitation Medicine
Chief of Service & Medical Director, Department of Rehabilitation Medicine
Pain Interventions and Prevention of Urinary Tract Infections
The goals of my research are to help find therapeutic interventions that improve recovery, reduce secondary conditions, and create a better life for persons with SCI and other conditions that impair physical or cognitive function. Currently, my research focus is in the areas of neuropathic pain and neurogenic bladder management.

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.

ALLAN D. LEVI, M.D., PH.D., F.A.C.S.
Professor, Departments of Neurological Surgery, Orthopedics, and Rehabilitation Medicine
Chief of Neurospine Service, Jackson Memorial Hospital/Chief of Neurosurgery, University of Miami 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.

**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, Rehabilitation Medicine, and Kinesiology & Sports Sciences  
Physiological Assessment of Secondary Complications following SCI: Electrical Stimulation, Cardiometabolic and Vascular Pathophysiology, Cardioendocrine Pathology, and Exercise and Dietary Biochemistry  
One of the enduring goals of The Miami Project has been to test and then translate strategies that optimize health of persons with SCI. A significant target for this strategy has focused on physical activity to lessen secondary risks of SCI associated with physical deconditioning 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 of prescription and non-prescription agents that reduce hazards of fasting and postprandial lipid disorders, dysglycemia, and vascular inflammatory stress.

**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 combinatorial approaches), (2) understanding the role of, and developing therapies for, altered cyclic AMP (adenyl 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 for the Alleviation of Chronic Pain and CNS Injury
Our laboratory continues to explore novel and more effective strategies in the therapeutic management of chronic debilitating pain. Our recent research is focused on (1) identification of more effective analgesic agents and combinations for alleviating pain using SCI models and (2) development of emerging therapeutic interventions, including cell transplantation and gene therapy, which have the potential to provide long-term alleviation in people with intractable pain, overcoming the need for repeated pharmacologic administration.

THOMAS J. SICK, PH.D.
Professor of Neurology and Physiology/Biophysics
Cellular and Neuronal Circuit Alterations after Traumatic Brain 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
Neuromuscular Weakness, Fatigue, Spasms, and Regeneration
Our laboratory is currently asking two main questions regarding SCI. First, in studies on people with SCI, we want to understand how well involuntary contractions of paralyzed muscles (spasms) are managed by exercise or by taking baclofen, a drug that is commonly used to control spasticity. Second, in our animal studies, we are exploring how to replace neurons that die because of SCI. Neuron death is common at the injury site and results in severe muscle weakness.

MICHAEL Y. WANG, M.D., F.A.C.S.
Professor, Departments of Neurological Surgery and Rehabilitation Medicine
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 preclinical testing to address key questions of efficacy and safety important to 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 as 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, WalkSafeTM & BikeSafeTM 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.
ALBERTO MARTINEZ-ARIZALA, M.D.
Clinical Professor, Departments of Neurology, Neurological Surgery, and Rehabilitation Medicine
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, Rehabilitation Medicine, 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, 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.

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. Thus, my laboratory is searching for novel molecular pathways that control neural development and are targets in multiple human maladies.
HELEN M. BRAMLETT, PH.D.
Associate 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.

JUSTIN C. SANCHEZ, PH.D.
Associate Professor, Department of Biomedical Engineering, Director, Neuroprosthetics Research Group; Program Manager, Defense Advanced Research Projects Agency Neuroprosthetics and Neural Engineering
The goals of my research are to develop brain-machine interfaces (BMI) to restore communication and movement control to people with neurological impairments. The approach is to use technology to directly interact with the central and peripheral nervous system, interpret the internal coding of brain activity for intent, and send commands to bionic devices to trigger movements. The laboratory uses electrophysiological and neural computational tools to seamlessly interface these devices with the nervous system. I am interested in developing combined therapies (technology with rehabilitation and repair) to personalize therapeutic approaches for people living with disabilities.

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 manage 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 potential for treating early of chronic injury in man.

BRIAN R. NOGA, PH.D.
Research Associate Professor, Department of Neurological Surgery

**Brain and Spinal Mechanisms Controlling Walking**

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

COLEEN ATKINS, PH.D.
Assistant Professor, Department of Neurological Surgery

**Developing Novel Therapies for Traumatic Brain Injury and Spinal Cord Injury**

The research in my laboratory focuses on developing novel therapeutic interventions for traumatic brain injury (TBI) and spinal cord injury (SCI). The research goal of my laboratory is to enhance rehabilitation and recovery by manipulating synaptic plasticity at specific levels of the neuroaxis following TBI and SCI. We have 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.

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 has been 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 developing two specific lines of research in the area of neuroimmunology, which are focused on: (1) investigating the role of tumor necrosis factor 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 V ACCARI, 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.
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.  
Assistant Professor, Department of Neurological Surgery  
Schwann Cell Transplantation after SCI  
One proposed therapy for spinal cord injury is to introduce cells to the injury site to help repair, restore, or support existing neurons. I work 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 signals controlling Schwann cell proliferation and differentiation  
In vitro methods to enhance the Schwann cell’s potency for CNS repair  
My laboratory studies basic aspects of Schwann cell biology and their use in transplantation for CNS regeneration. Specifically, we are investigating the role of cAMP and growth factors in the reciprocal interactions between Schwann cells and neurons underlying the regulation of Schwann cell proliferation and myelination, as well as the initiation of Schwann cell dedifferentiation after injury. Our lab works intensively towards refining the use and developing new cell culture methods for the growth and assessment of function of both human and rodent Schwann cells. One important goal is to improve the quality of cultured adult Schwann cells for an intended use in clinical trials.
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 2014, Drs. Anderson-Erisman and Dietrich embarked on year 2 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 11 students wrote an abstract about their specific research project and presented a poster at the 4th Miami Project Summer Student Research Session on August 8, 2014.

**Summer Students and their Research Projects:**

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*award winners of the poster session*
Published studies that have passed the test of peer review are the benchmark of scientific progress. Listed here are the 2014 research publications by Miami Project scientists and colleagues.


Luo X, Yungher B, Park KK (2014) Application of tissue clearing and light sheet fluorescence microscopy to assess...


The Miami Project has received FDA approval to begin human clinical trials and to transplant Schwann cells in chronically spinal cord injured persons.

The Miami Project continues its quest to find more effective treatments and ultimately a cure for paralysis.

If you are interested in participating in this trial, or one of our other FDA approved human clinical trials or research studies please visit: www.themiamiproject.org/trials or call 1-800-STAND UP

Apply now to see if you qualify for one of our clinical trials or research studies.