This year has already been one of the most exciting to date in the history of The Miami Project to Cure Paralysis. Following approval from the FDA to initiate a Phase I Safety Trial in people with subacute (recent) spinal cord injury (SCI), Miami Project scientists and clinicians received ethics permission from the University of Miami Miller School of Medicine to begin enrollment for this important trial. In November we recruited our first subject and in December successfully transplanted millions of his own Schwann cells into the injury. The operation went smoothly, and we are in the process of recruiting our next subjects. This critical dose escalation safety trial will provide a basis for future trials where subjects with chronic paralysis (those paralyzed for a year or more) will be treated with this novel cell therapy. These are very exciting times for The Miami Project scientific community as we continue to translate our discoveries into people to make a difference in their lives. We greatly appreciate the support of our donors and scientific colleagues who are helping to provide critical resources as we continue to move our investigations forward.

As previously mentioned, in the near future, we plan on extending these cell therapies to subjects with chronic SCI. Based on encouraging preclinical studies, it appears that Schwann cell transplantation also represents a logical cellular approach to repairing the nervous system years after the primary insult. To maximize our chances of seeing improvements in chronically injured SCI subjects, we have initiated an exciting Boot Camp in The Miami Project that will help condition and train selected individuals to maximize their chances of having a good result with the cell therapies. Thus, a series of approaches including dietary considerations, conditioning regimens, and neurorehabilitation strategies are being combined to maximize improvements in function. The Miami Project has recently obtained a state-of-the-art eLegs robotic exoskeleton for walking and we are investigating its utility for rehabilitation, conditioning, or as a mobility device in people living with paralysis. We feel that Schwann cell transplantation and subsequent combination approaches, together with these conditioning and rehabilitation strategies, may be an exciting future therapeutic to make a meaningful difference to people living with the SCI.

The Miami Project is also beginning to work more closely with various biotech companies to help translate some of their products and discoveries to the paralysis population. A recent development is our work with Medtronic to test a state-of-the-art brain-machine interface to enhance upper extremity function in people with chronic cervical SCI. Brain signal processing and electrical monitoring equipment
along with muscle stimulators will allow commands from the brain to be transmitted to upper extremity muscles to enhance motor function in selected subjects. New approaches for deep brain stimulation are also proving advantageous in promoting sensory and motor function in animal models of SCI and a clinical trial will begin this year targeting unresponsive pain in chronically injured individuals. Our ultimate goal will be to combine exciting biomedical and rehabilitation approaches with biological therapies to maximize repair and recovery processes.

The Miami Project scientists continue to receive new funding from various spinal cord foundations, as well as the National Institutes of Health and the Department of Defense (DoD). Many of the discoveries and clinical studies that we are testing in the civilian population are relevant to our military personnel who also have a high incidence of SCI and traumatic brain injury (TBI). Indeed, new DoD funding is currently supporting studies on the detrimental effects of repetitive concussion that may occur in individuals during various sporting events as well as in war situations throughout the world. A new multi-center therapeutic hypothermia trial is being initiated that will test for the first time whether mild cooling prior to decompression surgery in patients with severe TBI can have dramatic effects on improving outcome. Again, these are excellent examples of how discoveries within The Miami Project are being successfully translated to our patient populations.

Currently, there are limited pharmacological agents that can be used to protect the injured spinal cord from secondary injury mechanisms. A variety of drug therapies have failed to show significant benefits in the acute SCI populations. Our drug discovery program has identified novel molecules and cell signaling pathways that promote axonal regeneration better than currently available agents. Miami Project scientists also continue to investigate the therapeutic effects of hypothermia in patients with acute cervical SCI. A total of 35 participants have now been treated with therapeutic hypothermia and current results appear to be extremely encouraging. Indeed, at one year following injury, a significant percentage of conversion from complete paralysis to incomplete paralysis is being seen in the cooled population. Our scientists and clinicians are submitting multi-center trial grant applications to rigorously test the benefits of therapeutic hypothermia in this patient population as well.

We continue to concentrate on various quality of life issues that are important to people living with paralysis. Fertility problems in men living with SCI continue to be investigated and a new clinical trial testing a novel therapeutic target is being conducted. Another important quality of life issue involves the high incidence of neuropathic pain that is seen in our subjects living with paralysis. Clinical studies are underway to evaluate various factors that influence neuropathic pain. The Project continues to represent a unique scientific environment by which discovery, translational, and clinical research comes together with the ultimate goal of advancing new therapies to protect and promote recovery in our SCI population. This issue of our magazine covers all of our research endeavors and accomplishments during 2012 and highlights advances in many of our programs. These are indeed exciting times within The Miami Project, and we thank our friends, colleagues, and research participants for their long-term support and commitment to our research. 2013 is already turning out to be a special year, and we thank everyone for their support.

Sincerely,

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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.

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Brain Stimulation to Reduce Pain and Autonomic Problems

Can an electrical stimulation to the brain permanently reduce some debilitating symptoms of spinal cord injury (SCI), such as pain and the episodes of high blood pressure called autonomic dysreflexia? Dr. Ian Hentall and his collaborators, Drs. Jonathan Jagid, Eva Widerström-Noga, Alberto Martinez-Arizala, and Bruno Gallo, recently received funding from the Department of Defense to conduct a clinical trial to test this very question.

The basis for this clinical trial is rooted in Dr. Hentall’s pre-clinical research (funded in part by the Kleberg Foundation) as well as advances in the field of deep brain stimulation (DBS). The figure below illustrates some of the pre-clinical evidence generated by Dr. Hentall. There is a region in the midbrain called the Periaqueductal Gray, or PAG, where...
electrical stimulation triggers the release of pain relieving molecules. Dr. Hentall has demonstrated that a few weeks of stimulation in the PAG after SCI reduces pain sensitivity, improves autonomic control of the intestines and breathing, reduces the development of autonomic dysreflexia, and enhances movement. These changes are likely a result of alterations in various cellular signaling pathways that enhance growth in the damaged spinal cord. The details of these various experiments have been published in peer-reviewed scientific journals.

Deep brain stimulation (DBS) involves a surgical procedure to implant a “brain pacemaker”. The device sends different patterns of electrical stimulation to a specific region of the brain to interrupt pathways that are not functioning correctly. Currently, DBS is approved by the Food and Drug Administration (FDA) for use in individuals with advanced Parkinson’s disease or essential tremor whose symptoms are inadequately controlled by medication. The electrode is placed deep in the brain. This has been performed in over 100,000 people and the procedure and technology have been proven to be safe and effective. DBS has been used in the PAG in a few hundred people experiencing treatment-resistant chronic pain. Approximately 40 of those individuals had SCI. The results have been variable because those trials were all done differently using various stimulation patterns and targets, injury types, pain symptoms, and durations of follow-up. So the question of whether DBS can effectively reduce SCI-induced pain remains unanswered, plus nobody seems to have looked at permanent benefits of this stimulation after SCI or at symptoms other than pain.

Our multi-disciplinary team will attempt to answer these questions. Dr. Hentall has partnered with neurosurgeon Dr. Jonathan Jagid, who is very experienced with DBS surgery and technology. Dr. Jagid also partners with neurologist and clinical neurophysiologist Dr. Bruno Gallo, who will fine-tune the stimulators on a monthly basis to adapt to the needs of each individual. Dr. Eva Widerström-Noga is an expert in SCI-induced pain and Dr. Alberto Martinez-Arizala is head of the SCI Clinic at the Miami Veterans Administration Hospital, and an expert in clinically managing secondary complications associated with living with SCI. With their collective expertise, a very well controlled trial can be conducted to comprehensively evaluate the usefulness of DBS to manage pain and potentially prevent the onset of life threatening autonomic dysreflexia.

The team has already obtained FDA approval to use the Medtronic Activa PC DBS device in up to 12 participants in a Feasibility Clinical Investigation. The study is collaborative between the University of Miami and the Miami Veterans Administration Hospital. The group is in the process of obtaining ethical approval from both institutions, after which enrollment will begin. The end goals of the trial are to use DBS to (1) immediately block ongoing or intermittent SCI pain without acute or long-term adverse reactions, (2) simultaneously reduce spontaneous or evoked autonomic dysreflexia, and (3) gradually lead to permanent improvements in pain and autonomic symptoms of SCI. If the method works, it will be a fairly simple matter to go forward with further study and eventual clinical application, since no further device development or preclinical research would be required.
RegenBase

a searchable, comprehensive information framework and knowledge base that will advance the field of axon regeneration

The spinal cord injury (SCI) research community, like other research communities, has been discussing the difficulties of replicating important studies as well as challenges with identifying information in the research literature that can lead to novel therapeutic strategies. One way of attacking this problem is “RegenBase”, a knowledge base being developed at The Miami Project by Drs. Vance Lemmon and John Bixby and their University of Miami collaborators Drs. Stephan Schürer and Ubbo Visser. The overall goal of the program is to develop a searchable, comprehensive information framework and knowledge base that will advance the field of axon regeneration, thereby aiding the discovery of therapeutically relevant genes or drugs for future clinical trials. This project is being funded by a grant awarded in 2012 from the National Institute of Neurological Disease and Stroke at the National Institutes of Health (NIH). The specific goals of RegenBase are to:

1. Develop minimal information standards for *in vitro* studies of neurite growth and guidance
2. Develop minimal information standards for *in vivo* studies of nervous system regeneration and repair
3. Develop an ontology that defines key concepts and their relationships to describe knowledge about neuronal regeneration
4. Curate (find, group, organize, share) information in the neuronal regeneration domain
5. Develop a searchable knowledge base in the neuronal regeneration domain
A special meeting held October 10-12, 2012 was focused on the first 2 goals described above. The meeting was called “Growth Cones and Axon Regeneration: Entering the Age of Informatics” and was funded by the National Institute of Child Health and Human Development at the NIH, the Japan Society for the Promotion of Sciences, and The Miami Project. Invited participants were leading scientists from the United States and Japan whose research is focused on nervous system regeneration and repair. The meeting comprised formal presentations and breakout discussion sessions. With only 25 senior scientists and 11 post-doctoral fellows and PhD students, the environment was ripe for collaboration.

The first day began with the concepts of minimal information reporting and biomedical ontologies. These are important because the biology of axon regeneration is complex, and sharing information across laboratories requires that there be some degree of uniformity in reporting core data. The day progressed to identification of the minimum information needed to describe “petri dish” experiments evaluating the migration and guidance of growth cones (Minimal Information about an Axon Growth Experiment; MIAGE). Growth cones are at the leading edge of growing neurites and are the “business end”; they sense, move, integrate, and adapt to their local environment. Thus, understanding and controlling them are key to successful regeneration. There were also presentations by the participants about their research. The next day involved discussing the minimal information needed to describe animal experiments targeting regeneration after SCI (Minimal Information about a Spinal Cord Injury experiment; MIASCI), as well as additional research talks. The last day featured research talks and a mentoring session for PhD students and Post-docs in attendance.

The information collected from the breakout sessions is currently being used to develop proposals for minimal information standards by faculty at The Miami Project. These will be circulated to the meeting participants and will next be distributed to the research community for feedback. After a period of comment, the revised MIAGE and MIASCI standards will be recommended to scientists and journal editors and also used to incorporate information into the evolving RegenBase knowledge base.
Dr. James Guest is an Associate Professor in the University of Miami department of Neurological Surgery and a faculty member of The Miami Project to Cure Paralysis. Dr. Guest hails from Canada; he earned his Bachelor’s and Medical degrees at the University of Alberta. He earned his PhD, however, here at the University of Miami with the late Dr. Richard Bunge in 1996. That’s when he started working with Schwann cells and pursuing pre-clinical studies to support their potential for clinical application.

Dr. Guest didn’t start out knowing this would be his calling, however. As a boy he was interested in science and participated in school science fairs, but as he went through high school his interests shifted towards political science, history, sports, and hands-on craftsman work. He actually started college thinking of becoming a lawyer, but after 2 years he decided it wasn’t for him and took some time off. He worked for a year at a chemical plant as a power engineer to make some travel money and then headed across to Southeast Asia for 3 years as a volunteer with UNICEF, the Red Cross, and other organizations. Those travels moved him and had a significant impact on his future. For example, he spent a year working on the border of Thailand and Cambodia where he was trained to perform veterinary procedures on water buffalo – undoubtedly a contributor to his success with large animal studies now. Later he started doing wound care for children who had lost limbs from mines or had limb abscesses. That was his initial exposure to using his hands for medical purposes and he found it gratifying. After those experiences he made the decision to go into medical school as a surgeon or infectious disease specialist. He has continued to volunteer his time in developing countries, most recently in Haiti since the devastating earthquake in 2010 through Project Medishare. During neurosurgical training in Vancouver, he spent several months as the resident on the acute spinal cord injury (SCI) unit and realized that the available treatments did not repair the spinal cord, and determined to use his career to develop restorative treatments for SCI.

To achieve neurological recovery after acute and chronic SCI. To do so he uses large animal models to increase the relevance of the pre-clinical testing to address key questions of efficacy and safety. His pre-clinical research in large animal models was critical in our Investigational New Drug application to the Food and Drug Administration regarding transplantation of Schwann cells after sub-acute SCI. His group uses advanced histological, behavioral, electrophysiologic, MRI, and ultrasound techniques. They have worked on designing devices to deliver cells and therapeutics in a minimally injurious manner. Currently, they are testing the transplantation of autologous Schwann cells and skin-derived precursor cells to repair tracts of the injured spinal cord. In addition, they are testing the combination of cell transplantation, intensive rehabilitation, and epidural electrical stimulation for safety and efficacy in chronic SCI models.

Other areas of research Dr. Guest specializes in include studies of human post-mortem spinal cord tissue, intra-operative human spinal cord conduction studies, research design for clinical trials, supervision of clinical trials, and assessment of stem cell studies. He is Co-PI of our Phase I Schwann cell trial with Dr. Allan Levi and is the Site-PI for the North American Clinical Trials Network sponsored by the Christopher and Dana Reeve Foundation. All-in-all, Dr. Guest is a well-rounded clinician scientist and a valued member of The Miami Project faculty.
Hypothermia has been recommended since 2005 by the American Heart Association Guidelines for CPR and Emergency Cardiovascular Care to use immediately after cardiac arrest. It also has a long history of research regarding traumatic brain injury (TBI). The pre-clinical research has demonstrated robust neuroprotection induced by therapeutic hypothermia. The clinical trials, however, evaluating therapeutic hypothermia after TBI have had mixed results. One of the problems appears to be that the variability across sustained TBIs may be even greater than the variability across SCI. Miami Project faculty members, Drs. Shoji Yokobori, Ross Bullock, Dalton Dietrich, and Helen Bramlett, and colleagues have been pursuing the question of whether there are subsets of TBI in which therapeutic hypothermia may be most effective. It appears that the presence of a subdural hematoma shortly after TBI may be a key factor.

What is a subdural hematoma? In simple terms, it is basically when a blood clot forms between the surface of the brain and the thin membrane surrounding the brain (the dura). These occur in about 20% of all severe TBI's and are very life-threatening. When the subdural hematoma is large or associated with coma, neurosurgeons need to surgically open the skull (perform a craniotomy) and remove the hematoma/blood clot. The blood clot can reduce or stop blood flow to areas of the brain and when it is removed there is a high chance of a reperfusion injury occurring as the blood re-enters those regions of the brain. Drs. Yokobori, Bullock, Dietrich, and Bramlett have demonstrated in an animal model that inducing hypothermia prior to removing the blood clot can reduce the damage caused by reperfusion. The Miami Project is also now involved with H.O.P.E.S.

H.O.P.E.S. is a clinical trial testing HypOthermia for Patients requiring Evacuation of Subdural Hematoma. This is a multi-center collaboration between scientists in the United States and Japan. The sites are the University of Texas Houston, University of Miami, University of Pittsburg, and Nippon Medical Center in Japan. It will be a randomized controlled trial for individuals that have sustained a TBI plus developed an acute subdural hematoma that needs to surgically be removed. Cooling will be induced using a device similar to that we use when cooling people acutely after SCI. In addition to measuring functional and cognitive outcomes, they will also be measuring biomarkers. Look in our Fall 2012 PROJECT magazine for a great article on biomarkers! The end goal is to determine whether this subset of individuals with a severe TBI can benefit from therapeutic management of their temperature during a necessary surgical procedure. This is another example of how the translational, multi-disciplinary research efforts of The Miami Project can truly help change medicine.
We want to take this opportunity to highlight a couple of research studies that have been accepted for publication recently in high profile journals.

Dr. Eva Widerström-Noga and colleagues recently published a study in the prominent journal *PAIN* identifying a significant biomarker for severe neuropathic pain associated with spinal cord injury (SCI). The study used imaging of the brain on individuals living with SCI without neuropathic pain, with low-impact neuropathic pain, or high-impact neuropathic pain compared to pain-free able-bodied controls. The anterior cingulate cortex (ACC) is an area of the brain that has been found to be involved with integrating and modulating pain and affective distress. Dr. Widerström-Noga found that in individuals with SCI living with severe neuropathic pain that was impacting their psychological and social realm, there were metabolite concentrations suggesting reduced neuronal activity and increased glial activity in the ACC. These findings are supported by previous animal research of similar mechanisms contributing to neuropathic pain after SCI. Brain imaging can give us quantitative, objective measures of a qualitative, subjective experience such as pain. This is important because having such a biomarker can allow us to quantitatively evaluate pain severity and treatment efficacy. The utility of this biomarker will need to be validated across different types of neuropathic pain phenotypes and tested in clinical trials targeting pain outcomes.


Drs. John Bethea and Mark Nash and colleagues recently published a study in the *PLoS ONE* journal evaluating cardiovascular disease risk factor gene expression in a mouse model of chronic SCI and advanced age. As humans with SCI live longer, the prevalence of neuroendocrine/metabolic disorders and increased risk factors for cardiovascular disease is becoming well known. However, the biologic mechanisms leading to these disorders have not been well explored. The team demonstrated in this pre-clinical study that several genes involved in leptin resistance are activated in chronic SCI. Additionally, adipokine gene products are altered after SCI as well as with advanced age. Adipokine-mediated inflammatory responses and leptin resistance can both contribute to altered energy metabolism, which can contribute to obesity, diabetes, and cardiovascular disease. These pre-clinical findings are important in enabling us to begin understanding the mechanisms leading to risk factors that we know are present in the clinical population. The end goal would be to develop therapeutic measures to counteract the dysregulated mechanisms.

*PLoS ONE* (7(7): e41073. doi:10.1371/journal.pone.0041073) *Alterations in Mouse Hypothalamic Adipokine Gene Expression and Leptin Signaling following Chronic Spinal Cord Injury and with Advanced Age*. Bigford GE, Bracchi-Ricard VC, Nash MS, Bethea JR.
The “go to” source for information about spinal cord injury

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. The department answers phone calls and emails to provide people with information about all of our research programs as well as provide information about injury prevention, clinical care referral, resources for living with paralysis, and advice about unproven therapies around the world. We also conduct numerous tours and lecturers about our research. The top graph to the left shows the total number of people reached each month during 2012 outreach activities. The Education department also assists all of The Miami Project clinical research faculty with recruitment for their clinical studies. The top graph to the right shows that during 2012, about 500 people were able to participate in our studies targeting chronic spinal cord injury (SCI). In addition, Dr. Anderson-Erisman created a comprehensive resource page on The Miami Project webpage to provide individuals with tools for staying healthy while living with paralysis, www.themiamiproject.org/stayinghealthy. This includes information about stretching, exercising, diet, nutrition, sports and leisure activities.
On February 18, 2012 the Education department hosted the 2nd Annual Miami Project Community Open House. We opened up our doors to the public for an afternoon packed full of information. The first session was focused on basic science repair strategies for chronic SCI. Dr. Jae Lee spoke about scar tissue, Dr. Damien Pearse spoke about replacing dead cells, and Dr. Vance Lemmon spoke about long distance regeneration. This was followed by a session on clinical science relevant to chronic injury. Dr. Christine Thomas spoke about muscle spasticity, Dr. Eva Widerström-Noga spoke about neuropathic pain, and Dr. Justin Sanchez spoke about new strategies in brain machine interface technology. The final component of the day was behind-the-scenes tours of three laboratories, including a cell culture lab, regeneration lab, and human exercise lab. There were over 125 community members in attendance and the event was a great success! The 3rd Annual Community Open House is scheduled for April 20, 2013.

The Education Department also participated in the 3rd Annual Brain Fair as well as Take Your Child to Work Day, hosted Disability Mentoring Day, had an educational booth at the National Neurotrauma Society annual meeting, 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.
A major role of The Miami Project is to provide education and training for the next generation of neuroscientists. This aspect of The Miami Project’s mission is equally as important as conducting the research that will lead to treatments. Our long-term educational goal is to increase the number of scientists and laboratories working on paralysis research and central nervous system disorders around the world. Students and young scientists beginning their careers gain skills from The Miami Project’s state-of-the-art comprehensive research and academic environment.

The Miami Project Summer Student Research Fellowship is offered to a handful of stellar students each summer eager to work in the laboratory of a Miami Project faculty member. In 2012, the following students were awarded this fellowship: Benjamin Bowe – Pearse lab; Chelsea Cosner – Sagen lab; Giselle Fontela – Thomas lab; Sopiko Jimsheleishvili – Liebl lab; Caleb Pitcairn – Lemmon lab; Nrithya Sundararaman – Bethea lab; Julia White – Monje lab.

These 7 students plus 8 other exceptional summer students wrote an abstract about their specific research project and presented a poster at the 2nd Miami Project Summer Student Research Session on August 1, 2012. Caleb Pitcairn won the David Hovda Outstanding Student Research Poster Award!

Summer Student Research Projects:

1. Immunocytochemistry and Confocal Imaging of Whole Mount Nervous System Tissue, Benjamin Bowe

2. Novel Therapeutic Applications of CGRP8-37 for SCI Neuropathic Pain and Migraines, Chelsea Cosner

3. Attenuation of Spinal Cord Injury-induced Pain by Intraspinal Transplantation of Recombinant Neuroprogenitor Cells in Rats, Catherine Gordon

4. Investigation of mRNA-binding Protein Overexpression on Neurite Growth, Caleb Pitcairn

5. Walking-like Movements Produced by Reinnervated Hindlimb Muscles in Response to Stimulation of Transplanted Embryonic Cells, Giselle Fontela

6. Developing an Astrocyte-Specific Viral Expression System to Characterize Reactive Astrogliosis, Joaquin Jimenez

7. Plasticity of Schwann Cell Morphology in Vitro, Julia White

8. Design of SHG/EM2 Construct to Alleviate Spinal Cord Injury Induced Pain, Karen Velarde, Leslie Seijo


10. Myelin Expression in the Brain of TNF Receptor Knockout Mice, Nrithya Sundararaman

11. MicroRNA Overexpression in Neurons in Culture, Ryan Kowalsky

12. Rolipram Rescues Cognitive Impairments Resulting From Traumatic Brain Injury, Rosmery Santos

13. Examining the Association of Eph Receptors using Bimolecular Fluorescence Complementation (BiFC), Sopiko Jimsheleishvili

The Miami Project has a multi-disciplinary group of scientists that are all doing research to understand and better treat neuropathic pain. This kind of pain differs a lot from physiological pain we all know. For example, when we cut our finger it feels painful for a couple of days, but as the wound heals the pain goes away. Neuropathic pain stays much longer, often for years, and it responds poorly to pain-killer drugs. Spinal cord injury (SCI) induced neuropathic pain is an extremely complex problem. Pain is not just “all in the head”. There are biologic changes that occur in the spinal cord as a direct result of injury. So, aside from losing sensation after SCI, spontaneous and/or evoked pain can develop. Some of the changes we know occur after SCI to contribute to the development of pain are:

1. Neuronal hyperexcitability
   a. Receptor changes, eg. NMDA & other glutamate receptors, and ion channel changes, eg. Sodium channels
   b. Increased release of excitatory substances
   c. Loss of endogenous inhibitory tone (disinhibition; loss of GABA interneurons in spinal cord; altered descending inhibition)

2. Neuroplasticity
   a. Structural changes, e.g. sprouting and rearrangement of pain fibers entering the spinal cord from the periphery

3. Pain “generator” in the brain and spinal cord

4. Glia activation (astrocytes and microglia)
Combination Treatments

As you can see, there are many mechanisms contributing to neuropathic pain. As a result, it may be more effective to try to target multiple mechanisms at the same time with a combination approach. Dr. Jacqueline Sagen has been doing just that; she performs basic science research to determine and target multiple biologic mechanisms contributing to chronic neuropathic pain. She uses cell transplantation as well as drugs to target pain mechanisms in animal models. The goal of combination treatments is to induce an effect that is better than when each treatment is given separately. This is called additive. If the additive effect is better than expected, then it is called supra-additive or synergistic. In that situation the total dose of the combination might be lower than if given separately, which would be a good thing because lower doses usually cause fewer side effects.

In 2009, Dr. Sagen’s laboratory demonstrated that acetaminophen, which acts in part by inhibiting the degradation of naturally occurring cannabinoids in the body, in combination with morphine or gabapentin has a greater effectiveness (synergistic) on reducing pain than either drug alone. Her lab also discovered that 2 types of small proteins (peptides) derived from the marine cone snail were very effective when given in combination at reducing pain responses in spinal injured animals. These identified promising targets are being utilized in the generation of engineered cells and gene therapy vectors to produce sustained delivery of analgesic peptides for long-term pain alleviation.

In 2012, her group focused on blocking hyperactive excitatory receptors (using ketamine or histogranin) and activating hypoactive inhibitory neurons (using baclofen or muscimol) in the dorsal horn of the spinal cord. These drugs were delivered separately or in combinations to the intrathecal space, similar to how a “Baclofen pump” works in humans. They administered the drugs to the intrathecal space on purpose, rather than oral or systemically, because fewer side effects occur when drugs are given intrathecally. Dr. Sagen’s lab found that the only combination that resulted in a synergistic reduction of pain was the combination of Baclofen and ketamine. This, in effect, “quieted” the overactive excitatory neurons and “woke up” the underactive inhibitory neurons to somewhat reset the system. This suggests that these are good targets to pursue therapeutically.

Another way to deliver combination analgesic drugs locally to avoid systemic side effects is to use cells as minipumps - either engineered cells capable of releasing analgesic substances or endogenous cells converted to release recombinant virus-encoding analgesics. As chronic neuropathic pain involves reduced inhibition and enhanced excitation of neurons in the spinal cord, targeting both of these mechanisms at the same time using cell or gene therapy may be a promising approach for long-term pain reduction. Recently, Dr. Sagen’s lab has developed recombinant neural stem cells that are able to release an inhibitory neurotransmitter (GABA) and a peptide antagonist of excitatory receptors (serine-histogranin). The cells are therefore able to target both the inhibitory and excitatory processes and restore the balance between them. Injection of such cells into the spinal cord helped to reduce neuropathic pain symptoms in animals with SCI. Dr. Sagen’s lab is currently working on several recombinant plasmids encoding genes from the marine cone snail that were found to be effective in the combination studies above. These will be ready to test in SCI pain models to find out the best combination approaches to beat the pain. One thing is clear, however, and that is that targeting just one mechanism contributing to neuropathic pain is likely not going to be good enough. So, Dr. Sagen is forging down the right track with combination treatments.
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 2012.

**Craig H. Neilson Foundation**
Dr. Nancy Brackett (P.I.)
- Inflammasome Signaling and Sperm Cell Function
- Improving Reproductive Function in Men with Spinal Cord Injury

Dr. Stanislava Jergova (P.I. – Post-doctoral Fellowship), Dr. Jacqueline Sagen (Sponsor)
- Recombinant Stem Cell Therapy for Spinal Cord Injury Pain

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

Dr. Daniel Liebl (P.I.)
- A Novel Mechanism to Block Oligodendrocyte Cell Death Following SCI

Dr. Mark Nash (P.I.)
- Effects of Salsalate Monotherapy on Prandial-Induced Vascular Inflammation in Overweight Persons with SCI
- Effects of Exercise on Prandial Lipemia and Fat Oxidation After Tetraplegia
- A Model Community/Home-based Exercise Program for SCI

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

Dr. Eva Widerström-Noga (P.I.), Dr. Alberto Martinez-Arizala (Co-I.)
- Utility of Quantitative Sensory Testing in SCI-related Pain

**Department of Defense (DOD) Defense Advanced Research Projects Agency (DARPA)**
Dr. Justin Sanchez (P.I.)
- Tissue, Electrical, and Material Responses in Electrode Failure

**Abramson Foundation**
Dr. Pantelis Tsouffas (P.I.)
- Neural Stem Cells for Spinal Cord Injury

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

**Christopher & Dana Reeve Foundation**
Dr. Mary Bartlett Bunge (P.I.)
- Studies of Schwann Cell Transplantation
- Research Consortium on Spinal Cord Injury: Studies of Schwann Cell Transplantation

Dr. James Guest (Center P.I.)
- North American Clinical Trials Network

Dr. Brian Noga (P.I.), Dr. Ian Hentall (Co-I.)
- Therapeutic Potential of DBS for Improving Walking Following Incomplete Spinal Cord Injury
-Creating the Synthetic Brain Through Hybrid Computational and Biological Systems: Repairing and Replacing Neural Networks
-Responsive Neurorehabilitation Using an Advanced Brain Monitoring BCI

**Department of Defense (DOD) Spinal Cord Injury Research Program of the Office of the Congressionally Directed Medical Research Programs**
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. Jae Lee (Co-I.), Dr. Vance Lemmon (Co-I.), Dr. Daniel Liebl (Co-I.), Dr. Kevin Park (Co-I.), Dr. Pantelis Tsoufas (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.)
-Site-directed Nanotherapeutics to Abrogate Relapsing/Remitting Multiple Sclerosis and Promote Remyelination Repair

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

Dr. M. Ross Bullock (P.I.)
-Laboratory Studies to Evaluate Perfluorocarbon in Models of Traumatic Brain Injury

Dr. W. Dalton Dietrich (P.I.), Dr. Helen Bramlett (Co-I.)
-Operation Brain Trauma Therapy
-Operation Brain Trauma Therapy
-The Importance of Temperature in the Pathophysiology of Mild Repetitive Brain Injury

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

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

**Department of Defense (DoD) United States Army Medical Research Acquisition Activity**

Dr. W. Dalton Dietrich (P.I.), Dr. Helen Bramlett (Co-I.)
-Operation Brain Trauma Therapy

**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

**Florida Department of Transportation**

Dr. Gillian Hotz (P.I.)
-Safe Route to School-WalkSafe County Program
-Statewide WalkSafe Program and Tech Center
-WalkSafe Miami-Dade
-WalkSafe Tool Kit
-BikeSafe Program
-Transportation Enhancement

**International Collaboration on Repair Discoveries**

Dr. Rachel Cowan (Distinguished Visiting Scholar)
-Measurement Properties of Wheelchair Propulsion Tests: Minimal Clinical Important Difference and Smallest Detectable Difference

**International Spinal Research Trust**

Dr. James Guest (Center P.I.)
-Comparison of Schwann Cells and Skin-derived Precursor Cells for Repair of Demyelination in the Primate Corticospinal Tract

**KiDZ Neuroscience Center**

Dr. Gillian Hotz (P.I.)
-Accelerometer Study
-Countywide Concussion Surveillance System
Medtronic Spinal and Biologics
Dr. Barth Green (Co-I.)
-Pivotal IDE Study of the Bryan Cervical Disc Prosthesis in the Treatment of Degenerative Disc Disease

National Center for Medical Rehabilitation Research in the National Institute of Child Health and Human Development and the National Institute of Neurological Disorders and Stroke
Dr. Christine Thomas (P.I.)
-Verifying Automatic Analysis of Muscle Spasms in Large Datasets

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. David Fuller (P.I.), Dr. Justin Sanchez (Co-I.)
-Training Novel Host-Graft Circuits to Enhance Spinal Cord Repair

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 & Human Development
Dr. Edelle Field-Fote (P.I.), Dr. Diana Cardenas (Co-I.), Dr. Mark Nash (Co-I.)
-Improving Hand and Arm Function in Individuals with SCI

National Institute of Disability & Rehabilitation Research
Dr. Diana Cardenas (P.I.), Dr. Rachel Cowan (Co-I.), Dr. Mark Nash (Co-I.)
-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.)
-Exercise Interventions for Spinal Cord Injured Adults with Obesity-related Secondary Disorders

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

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

Dr. John Bixby (P.I.), Dr. Vance Lemmon (Co-I.)
-Novel Compounds that Overcome Glial Inhibition of Axonal Regeneration

Dr. John Bixby (P.I.), Dr. Vance Lemmon (Co-P.I.), Dr. Jeff Goldberg (Co-P.I.)
-Triazine-based Compounds to Promote Regeneration in Optic Neuropathies

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

National Institute of Neurological Disorders & Stroke
Dr. Jesse Brodkin (P.I.), Dr. Jacqueline Sagen (Subcontractor for Small Business Innovation Research award)
-Using a Multi-touch Screen to Automate Pain Assessment

Dr. Ramon Diaz-Arastia (P.I.), Dr. M. Ross Bullock (Co-I.)
-Phase II, Randomized Controlled Trial of Brain Tissue Oxygen Monitoring

Dr. W. Dalton Dietrich (P.I.), Dr. Helen Bramlett (Co-I.)
-Mechanisms of Recovery Following Traumatic Brain Injury
-Efficacy of Necrostatins on Post-traumatic Epilepsy (via American Recovery and Reinvestment Act)

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

Dr. Jae Lee (P.I.)
-Role of Fibroblasts in Axon Regeneration After SCI
Dr. Allan Levi (P.I.)
- Transplantation of Autologous Schwann Cells for the Repair of Segmental Peripheral Nerve Defects

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

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

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

Dr. Michael Norenberg (P.I.), Dr. John Bethea (Co-I.)
- NF-kappaB in Astrocyte Swelling/Brain Edema Associated with Acute Liver Failure

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

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

Dr. Jacqueline Sagen (P.I.)
- Potent Analgesic Conopeptides for Treatment of Chronic Spinal Cord Injury Pain

Dr. Justin Sanchez (P.I.)
- Neural Correlates of Tourette Syndrome

Dr. Christine Thomas (P.I.)
- Muscle Function in Human Cervical Spinal Cord Injury
- Rescue of Denervated Muscle

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

Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation
Dr. Ian Hentall (P.I.)
- Trophic Brainstem Stimulation for Autonomic Dysfunction after Spinal Cord Injury

The Hearsts Foundation
Dr. James Guest (P.I.)
- Pivotal Pre-Clinical Studies for Transplantation of Schwann Cells in Chronic Spinal Cord Injury

The Karl Kirchgessner Foundation
Dr. Kevin Park (P.I.)
- Developing PTEN shRNA-mediated Combinatorial Approaches to Improve Optic Nerve Regeneration

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

University of Miami Stanley J. Glaser Foundation
Dr. Coleen Atkins (P.I.)
- Rehabilitation Strategies for Cognitive Disabilities after Traumatic Brain Injury

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

Veterans Administration Rehabilitation Research and Development
Dr. Robert Jackson (P.I.), Dr. Diana Cardenas (Co-I.)
- Rehabilitation of IPF Patients: Effects of Exercise and Oxidant Stress

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

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

State of Florida James and Esther King Biomedical Research Program
Dr. John Bixby (P.I.), Dr. Murray Blackmore (Co-I.), Dr. Vance Lemmon (Co-I.)
- Combination Therapy in SCI: Proof of Concept for New Compounds and Candidate Genes
The “Scar”... what is it, really?

We all hear about scar tissue and how much of a barrier it is to repairing the chronically injured spinal cord, but what is it really and how do we overcome it? Dr. Jae Lee joined The Miami Project faculty in 2010 focused on answering this very question. Scar tissue begins to develop around the injury site several weeks after the injury occurs and continues to change for several months, possibly years. It is initially the body’s natural effort to enclose the injury site to prevent it from getting bigger. This is actually important because scientists have shown that if you disrupt the formation of the scar, the injury site “spreads out” and interferes with some of the spontaneous recovery that occurs over time.

However, once the scar is formed it becomes an inhibitory barrier to axon regeneration. The figure above illustrates this very well. Corticospinal axons are colored red; these are axons whose cell bodies are located in the cortex of the brain and they are very important for directing voluntary control of skilled movements. Serotonergic axons are colored green; these are axons from cell bodies largely located in the midbrain and brainstem and they are important for many types of movements, including locomotion. The figure clearly demonstrates that these axons are still present long after the spinal cord injury (SCI) has occurred, but they cannot move past the scarred injury site.

The main component of the scar that you tend to hear about has to do with cells called astrocytes (colored blue in the figure above). Sometimes the scar will be referred to as the astroglial scar, or glial scar for short, because astrocytes are a type of glial cell. Glial cells are sometimes called the “glue” of the nervous system, but they do more than just hold everything together. After an injury to the spinal cord, glial cells are involved with removing dead cells and walling off the injury. However, astrocytes are not the only component of scar tissue. Dr. Lee
has been focusing on the fibrotic scar as well, which is in the interior of the injury site (see figure to the right). The fibrotic scar is made up of chemicals released by a type of cell called a fibroblast. The chemicals released by fibroblasts give structure to tissue and are important in normal wound healing processes of the skin. Dr. Lee was one of the first to show evidence that these fibroblasts enter the spinal cord from the microscopic blood vessels within the cord that get damaged during the injury. Since a major function of fibroblasts is to release a chemical called fibronectin, Dr. Lee’s group has been investigating the role of fibronectin at the injury site. While fibronectin is not expressed in the normal central nervous system (CNS = the brain and spinal cord), it is expressed at high levels after SCI. Interestingly, even though the fibronectin is released by the fibroblast cells, Dr. Lee’s recent results indicate that another type of cell, the macrophage, may be primarily responsible for the assembly of fibronectin into a matrix at the injury site, which results in the fibrotic scar. Macrophage cells are immune cells and these results suggest that the immune response after injury may also play an important role in formation of the fibrotic scar. In non-CNS tissue, fibronectin is involved in a wide range of activities important to maintaining the body, but its role in the fibrotic scar after SCI is not clear. It is clear, however, that axons cannot grow through it. In 2012 Dr. Lee received a five-year grant from the National Institutes of Health on the role of fibroblasts in axon regeneration after SCI and he is planning on submitting a similar five-year grant application on the fibronectin story sometime in 2013. Understanding the scar is critical to overcoming it as an inhibiting barrier to axonal regeneration. The Miami Project strives to have a comprehensive approach to the complex problem of repairing SCI and is happy to have Dr. Lee contributing so significantly to ultimately overcoming the scar.

Figure 2: The fibrotic scar (green) fills the injury site while surrounded by the astroglial scar.
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 & Anatomy
Neuroprotection and Improved Recovery of Function following Central Nervous System (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
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 (SCI) 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. Each of these projects involves collaborations with Miami Project basic and clinical researchers as well as the faculty from the Department of Neurological Surgery and several other collaborating departments and Centers of Excellence at the University of Miami Miller School of Medicine.
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 to Repair the Injured Spinal Cord
The goal in my laboratory is to foster regeneration of axons across and beyond a 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 neurotrophic factor-secreting capability or neurons to enhance their ability to regenerate axons after injury. We pay particular attention to the interface between the SC implant and the host spinal cord.

JOHN R. BETHEA, PH.D.
Professor, Departments of Microbiology & Immunology and Neurological Surgery
Immunological Consequences of SCI and the Development of Neuroprotective Strategies
In my laboratory we are studying SCI and diseases of the nervous system such as Multiple Sclerosis (MS) to try to understand the cellular and molecular mechanisms that contribute to astrogliosis and secondary neuronal cell death. To this end, my laboratory has two main research objectives. Firstly, we are studying the neuro-inflammatory response that occurs following SCI and, secondly, we are developing novel therapies for SCI and diseases of the CNS.

JOHN BIXBY, PH.D.
Professor, Departments of Molecular & Cellular Pharmacology and Neurological Surgery
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 based on the observation that young CNS neurons have a greater regenerative capacity than old CNS neurons (collaboration with Dr. Jeff Goldberg). We have identified a family of developmentally regulated transcription factors (proteins that bind DNA and turn on or off scores of genes) that is very important in axon regeneration. Another project is to test the roles of known signaling proteins called kinases. In this screen we have tested hundreds of kinases by overexpression and have also tested a few hundred kinase inhibitors, many of which strongly promote neurite growth in vitro. The data from this screen are allowing us to begin to build models of neuronal signaling networks underlying axon regeneration. A third 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.
M. ROSS BULLOCK, M.D., PH.D.
Professor, Department of Neurological Surgery
Director, Clinical Neurotrauma
Preclinical Mechanistic and Neuroprotection Research in Traumatic Brain Injury (TBI) and Clinical Trials, and Neuromonitoring Techniques in the Injured Brain
We have recently obtained two year funding from the Department of Defense to evaluate the neuroprotective effect of Perfluorocarbons in four rodent models of TBI (penetrating brain injury, closed TBI 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 as surrogate indicators of possible benefit.

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

EDELLE C. FIELD-FOTE, PH.D., P.T.
Professor, Departments of Physical Therapy and Neurological Surgery
Motor Restoration after Spinal Cord Injury
The studies in the Neuromotor Rehabilitation Research Laboratory cross the boundaries of basic neurophysiology and neurorehabilitation. We apply principles of neuroplasticity and motor learning to understand how interventions can be optimized and combined to promote best recovery of function. Some of our rehabilitation studies focus on recovery of hand and arm function, while others are aimed at walking function.

ROBERT W. KEANE, PH.D.
Professor, Department of Physiology & Biophysics
Regulation of Innate Immunity after CNS Trauma
Innate immunity is the first line of defense against pathogens and host-derived signals of cellular stress. My research focuses on investigating mechanisms that direct normal innate immunity and its dysregulation in CNS injury and disease, including (1) agonists and activation mechanisms of inflammasomes, (2) regulatory mechanisms that potentiate or limit inflammasome activation after injury, and (3) emerging links between innate immunity and Alzheimer’s disease.
ALLAN D. LEVI, M.D., PH.D., 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 CNS and PNS. I am Co-PI on our autologous human Schwann cells (ahSC) trial, which represents a first-in-man dose escalation study of ahSC for individuals with sub-acute thoracic SCI. Hypothermia continues to show promise in a variety of acute CNS 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. I am the PI of our trial 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  
Director, Neuroscience Graduate Program  

**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 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 & Vascular Physiology, Cardioendocrine Pathology, and Exercise & 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. We also examine complementary themes to validate exercise prescription after SCI, identify optimal dietary composition, and use of prescription and non-prescription agents that reduce hazards of fasting and postprandial lipid disorders, dysglycemia, and vascular inflammatory stress.

JACQUELINE SAGEN, PH.D., M.B.A.  
Professor, Department of Neurological Surgery  

**Cellular Implants for the Alleviation of Chronic Pain and CNS Injury**  
Our laboratory explores novel and more effective strategies in the therapeutic management of chronic pain. Our recent research is focused on (1) identification of more effective analgesic agents and combinations for alleviating pain using SCI models and (2) development of emerging therapeutic interventions, including cell transplantation and gene therapy, which have the potential to provide long-term alleviation in people with intractable pain, overcoming the need for repeated pharmacologic administration.
CHRISTINE K. THOMAS, PH.D.
Professor, Department of Neurological Surgery
Neuromuscular Weakness, Fatigue, Spasms, and Regeneration
Our laboratory is currently asking two main questions regarding SCI. First, in studies on people with SCI, we want to understand how well involuntary contractions of paralyzed muscles (spasms) are managed by exercise or by taking baclofen, a drug that is commonly used to control spasticity. Second, in our animal studies, we are exploring how to replace neurons that die because of SCI. Neuron death is common at the injury site and results in severe muscle weakness.

GILLIAN A. HOTZ, PH.D.
Research Professor, Department of Neurological Surgery
Director, KiDZ Neuroscience Center
Director, Concussion, WalkSafe™ & BikeSafe™ Programs
Neurocognitive Deficits and Injury Prevention
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.

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.

HELEN M. BRAMLETT, PH.D.
Associate Professor, Department of Neurological Surgery
The Pathophysiology and Treatment of CNS Injury
The focus of my neurotrauma laboratory is to investigate both acute and long-term consequences of brain and spinal cord trauma. My current research interests are on the pathophysiology of TBI and SCI with an emphasis on the pathogenesis of progressive white matter damage as well as the benefits of therapeutic hypothermia. My laboratory is also investigating mechanistic events leading to the development of posttraumatic epilepsy. Additionally, my current work is also focusing on complex traumatic brain injury models that mimic polytrauma as this type of injury has become more prevalent in combat areas.
JAMES D. GUEST, M.D., PH.D., F.A.C.S., F.R.C.S.(C)
Associate Professor, Department of Neurological Surgery
Translation Studies in Cellular, Molecular, and Electrical Stimulation Strategies to Achieve Neurological Recovery After Acute and Chronic SCI
The central aim of our group is to achieve translation of therapeutic studies from animal models to early stage human trials. To this end we use some large animal models to increase the relevance of the pre-clinical testing to address key questions of efficacy and safety. The emphasis is on conducting testing of therapeutics to emulate human application as fully as possible. We design devices to deliver cells and therapeutics in a minimally injurious manner. Currently, we are testing the transplantation of autologous Schwann cells and skin-derived precursor cells to repair tracts of the injured spinal cord. In addition we are testing the combination of cell transplantation, intensive rehabilitation, and epidural electrical stimulation for safety and efficacy.

DAMIEN D. PEARSE, PH.D.
Associate Professor, Department of Neurological Surgery
Exploration and Translation of Therapeutic Strategies to Repair the Injured Spinal Cord and Brain
My laboratory focuses on several key aspects of CNS injury repair, including (1) the utility and clinical translation of exogenous and endogenously harnessed cell therapeutics (particularly when used in combinatory approaches), (2) understanding the role of, and developing therapies for, altered cyclic AMP (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.

JUSTIN C. SANCHEZ, PH.D.
Associate Professor, Department of Biomedical Engineering
Director, Neuroprosthetics Research Group
Neuroprosthetics and Neural Engineering
The goals of my research are to develop brain-machine interfaces (BMI) to restore communication and 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.
MICHAEL Y. WANG, M.D., F.A.C.S.
Associate 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.

KIM ANDERSON-ERISMAN, PH.D.
Research Associate Professor, Department of Neurological Surgery
Director of Education

Translational Investigations for Chronic SCI
My research focuses on translational investigations and bridging the gap between basic science, clinical science, and the public community living with SCI. I recently completed a multi-center clinical study evaluating the reliability and validity of the Spinal Cord Independence Measure in the US healthcare setting. My current projects focus on 1) aging related changes in bladder health after SCI and 2) determining the minimum amount of exercise and locomotor training required for clinical trials targeting chronic SCI.

NANCY L. BRACKETT, PH.D., H.C.L.D.
Research Associate Professor, Departments of Neurological Surgery and Urology

Male Fertility following SCI
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.

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 SCI or TBI 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 or chronic injury in man.
ALBERTO MARTINEZ-ARIZALA, M.D.
Clinical Associate Professor, Departments of Neurology, Neurological Surgery, and Orthopaedics & Rehabilitation
**Pathophysiology and Treatment of Secondary Complications in SCI**
My research interests focus on common complications that are seen following SCI: pain, spasticity, syringomyelia, and tethered cord syndrome. My interests include investigating the basis for the development of the different spasticity and pain profiles in the spinal cord injured population and to study potential novel treatments for those conditions.

BRIAN R. NOGA, PH.D.
Research Associate Professor, Department of Neurological Surgery
**Brain and Spinal Mechanisms Controlling Walking**
Our long-term goal is to develop and optimize treatments for SCI 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.

EVA WIDERSTRÖM-NOGA, D.D.S., PH.D.
Research Associate Professor, Departments of Neurological Surgery, Rehabilitation Medicine, Neuroscience Program, and Health Scientist Veterans Affairs
**SCI-related Neuropathic Pain Phenotypes and Biomarkers**
My research program is focused on the identification of clinical correlates of underlying mechanisms of neuropathic pain associated with neurological trauma in order to facilitate the translation of basic research findings into treatments tailored to specific mechanisms. We are also examining the personal experiences of people living with chronic pain and SCI. My research program is highly collaborative and includes extensive interdisciplinary protocols for a multimodal evaluation of pain symptoms and its psychosocial impact, quantitative assessment of neurological function, and biomarkers including non-invasive brain imaging and genetic polymorphism.

COLEEN ATKINS, PH.D.
Assistant Professor, Department of Neurological Surgery
**Developing Novel Therapies for TBI and SCI**
The research in my laboratory focuses on developing novel therapeutic interventions for TBI and 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 SCI and related neurological disorders.

HOWARD B. LEVENE, M.D., PH.D.
Assistant Professor, Department of Neurological Surgery

Schwann Cell Transplantation after SCI

One proposed therapy for SCI is to introduce cells to the injury site to help repair, restore, or support existing neurons. My research focuses 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.

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 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 SCI and other neurodegenerative conditions.

ROBERTA BRAMBILLA, PH.D.
Research Assistant Professor, Department of Neurological Surgery

Modulation of the Immune Response in Neurologic Disease

The main focus of my research has been to understand the role of neuroinflammation in the pathophysiology of neurodegenerative disorders (e.g., SCI and MS), with a specific interest in the contribution of the astrocytes, a type of glial cell that represents the most abundant cell population in the nervous system. Currently, my laboratory is developing two specific lines of research in the area of neuroimmunology, which focus on (1) investigating the role of tumor necrosis factor in the processes of demyelination and remyelination and (2) investigating the occurrence of neuropathic pain associated with MS.
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 levels 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 CNS trauma and neurodegenerative diseases. Currently, my laboratory is focusing on the effects of pattern recognition receptor (PRR)-activation after SCI and neurodegenerative diseases such as Alzheimer’s disease.

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.
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 5, 2012
Randall T. Moon, PhD
University of Washington School of Medicine - Seattle, WA
“Wnt/beta Catenin Signaling in Acute Injury and Chronic Disease”

November 7, 2012
Leigh R. Hochberg, MD, PhD
Brown University - Providence, RI
“Intracortically-Based Brain-Computer Interfaces: Turning Thought into Action”

December 5, 2012
David S. K. Magnuson, PhD
University of Louisville – Louisville, KY
“Directing Spinal Cord Plasticity: Activity-Dependent Gain and Loss of Locomotor Function after Injury”

January 9, 2013
Dwight E. Bergles, PhD
The Johns Hopkins University - Baltimore, MD
“Regenerative Capabilities of Oligodendrocyte Progenitors in the Adult CNS”

February 13, 2012
William David Richardson, PhD, FLS, FMedSci
University of London – United Kingdom
“Myelin Dynamics in Healthy Adult Mice”

March 6, 2013
Jeffrey Milbrandt, MD, PhD
Washington University School of Medicine - St. Louis, Missouri
“Demystifying Axonal Degeneration: New Therapeutic Targets Provide Hope for Peripheral Neuropathy”

April 3, 2013
Bruce D. Trapp, PhD
The Cleveland Clinic Foundation - Cleveland, Ohio
“Pathogenesis of Neurological Disability in Multiple Sclerosis”

May 1, 2013
Hongjun Song, PhD
Johns Hopkins University School of Medicine - Baltimore, MD
“Circuit Mechanisms Regulating Adult Neural Stem Cells and Neurogenesis”
The Miami Project is proud to have a new junior faculty member join our team in 2012, Dr. Rachel Cowan. Dr. Cowan’s current research focus is on enhancement and preservation of maximal transfer and wheelchair propulsion ability in individuals with spinal cord injury (SCI). Her training has centered on understanding and influencing human performance. At the University of North Carolina Wilmington she earned a Bachelor’s degree in physical education with an emphasis on athletic training rather than the typical emphasis on teaching. She then went on to obtain her Master’s degree at Wake Forest University focused on learning how to use exercise and fitness to delay or reverse effects of chronic disease in people over the age of fifty. From there she moved up to Pennsylvania and got her PhD in rehabilitation science and technology focusing on wheelchair biomechanics in people with SCI at the University of Pittsburgh. Dr. Cowan came to The Miami Project in 2008 to complete a post-doctoral fellowship in our applied physiology lab studying fitness levels in people with different levels of SCI.

Aside from her formal training, she also “dabbles” in computer programming. She is highly skilled in a program called MATLAB, which is a platform for writing custom solutions for data collection, data extraction, and data analysis. This is very important for large data sets with several confounding variables that could potentially influence outcome. Furthermore, Dr. Cowan is a blossoming statistics wiz! This is a great asset because she helps us consider new ways to design clinical studies, particularly because SCI has so much variability between people with the “same” injury.

What really drives Rachel Cowan though is the fact that she has a spinal cord injury herself. The reality of experiencing and living with an SCI cannot be taught in any books. The core of that drive centers around the frustrations associated with obtaining appropriate SCI healthcare, equipment, services, etc. that enable people with SCI to successfully resume life. Dr. Cowan funnels those frustrations into making a difference. To that end, her research tends to focus on providing evidence that will support changing policy. In effect, she tries to generate research that is useful immediately, for clinicians, individuals with SCI, other researchers, engineers, or companies, rather than many years down the road.

What you might not know about Dr. Cowan is that she is an avid snow skier! Her outlook on life is to explore and try new things. This ranges from sports to foods to locations. For several years after her SCI she was terrified of traveling on her own because of her SCI, but now has it down to a science after some tough love in graduate school! Welcome, Dr. Cowan, to The Miami Project faculty!
The Miami Project clinical researchers currently have 17 research studies available for people who have had a spinal cord injury for at least 1 year. They are investigating questions regarding exercise science, rehabilitation training, pain, male fertility, spasticity, sleep problems, and neuroprosthetics.

The Miami Project also has 13 clinical trials ongoing or in the planning stages to test interventional repair or neuroprotective strategies for spinal cord injury or traumatic brain injury. It has never been a more exciting time!

### Clinical Studies

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<td>Cardiometabolic Risk, Obesity and Cardiovascular Disease in People with Spinal Cord Injury</td>
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<td>Effect of an Omega-3 Supplement Intervention Program on Cardiometabolic Health in People with Spinal Cord Injury</td>
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<td>Obesity/Overweight in Persons with Early and Chronic SCI: A Randomized Multi-Center Controlled Lifestyle Intervention</td>
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<td>Male Fertility</td>
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<td>Rehabilitation</td>
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<td>Improving Hand and Arm Function in Individuals with Incomplete SCI</td>
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<td>Different Stimulation Methods Aimed at Improving Hand and Arm Function in Individuals with Incomplete SCI</td>
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<td>Prospective, Randomized Controlled Trial for Shoulder Pathology and Pain in Chronic SCI</td>
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<td>Activity in Muscles Paralyzed by SCI</td>
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<td>Spasticity</td>
<td>Direct Current Stimulation to Improve Muscle Function after Human Spinal Cord Injury</td>
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<td>Motor Unit Firing Rates After Human Spinal Cord Injury</td>
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<td>Pain</td>
<td>Experiences of living with persistent pain after a spinal cord injury</td>
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<td>International Spinal Cord Injury Basic Pain Data Set Survey for Self-Report Measure</td>
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<td>Survey to Determine the Prevalence of Sleep-Related Problems</td>
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<td>Sleep Disordered Breathing (SDB) in Persons with Chronic Tetraplegia: Characterization and Treatment</td>
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<tr>
<td>Sleep</td>
<td>Assessment of Candidates and Design Considerations for Neuroprosthetic Devices for Individuals with Chronic Spinal Cord Injury</td>
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### Clinical Trials

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<th>Treatment</th>
<th>Population</th>
<th>Pre-Clinal</th>
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<th>Phase 2</th>
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<td>AUTOLOGOUS SCHWANN CELLS</td>
<td>Acute SCI</td>
<td>Ongoing</td>
<td>Enrolling</td>
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<td>BIOMARKERS OF SCI</td>
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<td>Enrolling</td>
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<td>NACHT</td>
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<td>RILUZOLE</td>
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<td>ROLIPRAM</td>
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<td>Acute SCI</td>
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<tr>
<td>BIOMARKERS OF TBI</td>
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<td>BOOST</td>
<td>Severe TBI</td>
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<td>COSBID</td>
<td>Acute TBI</td>
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<td>Acute, Moderate or Severe TBI</td>
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<td>OXCYTE</td>
<td>Acute, Severe TBI</td>
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<td>Acute TBI</td>
<td>Pending</td>
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To find links to the abstracts and complete scientific publications listed here, visit the Research Publications section of our website at www.themiamiproject.org/researchpublications
The Miami Project and spinal cord injury (SCI) research community recently lost an excellent scientist and dear friend, Dr. Mary June Eaton.

**Significance of her work**

Dr. Eaton’s research involved the use of molecular biology techniques and investigation of various cell lines for the treatment of the consequences of SCI. Her research included work on neuronal and chromaffin rat cell lines that secrete neurotransmitters such as serotonin (5HT), GABA, galanin, and catecholamines, as well as the neurotrophin BDNF and the opioid peptide met-enkephalin. One major goal of her research was to examine the potential of these cell lines to act like biologic “minipumps” to secrete molecules to alleviate neuropathic and neurogenic pain in rodent models of tonic, peripheral, and central spinal injury by transplanting these cells into the spinal cord. Having served in the army herself as a nurse, she felt a strong commitment to use her research to find a way to help wounded soldiers with spinal cord injuries and neuropathic pain conditions.

**Working with her**

Dr. Eaton’s scientific and philosophical view was to move successful basic research to clinical applications for human medical problems “as quickly as possible”. She also applied this principle to all her work in the sense that she was always a step ahead and well organized. Working with her was therefore both inspiring and very productive. Although her work was pre-clinical, she was very aware and appreciative of all the clinical aspects of neuropathic pain that individuals with SCI face.

**Mary as a person**

Mary was a very creative and interesting individual. She approached life with the same energy as her work. She used her spare time to take flying lessons and to scuba dive among other things. She was also very interested in photography and making sculptures and jewelry. She was the type of person who never focused on the negative; rather, she always looked forward, which was one of her greatest strengths. Mary June Eaton, Ph.D., is greatly missed by her many friends and colleagues.
We've Begun

The Miami Project to Cure Paralysis Doctors Perform First FDA Approved Schwann Cell Transplantation On Spinal Cord Injured Patient