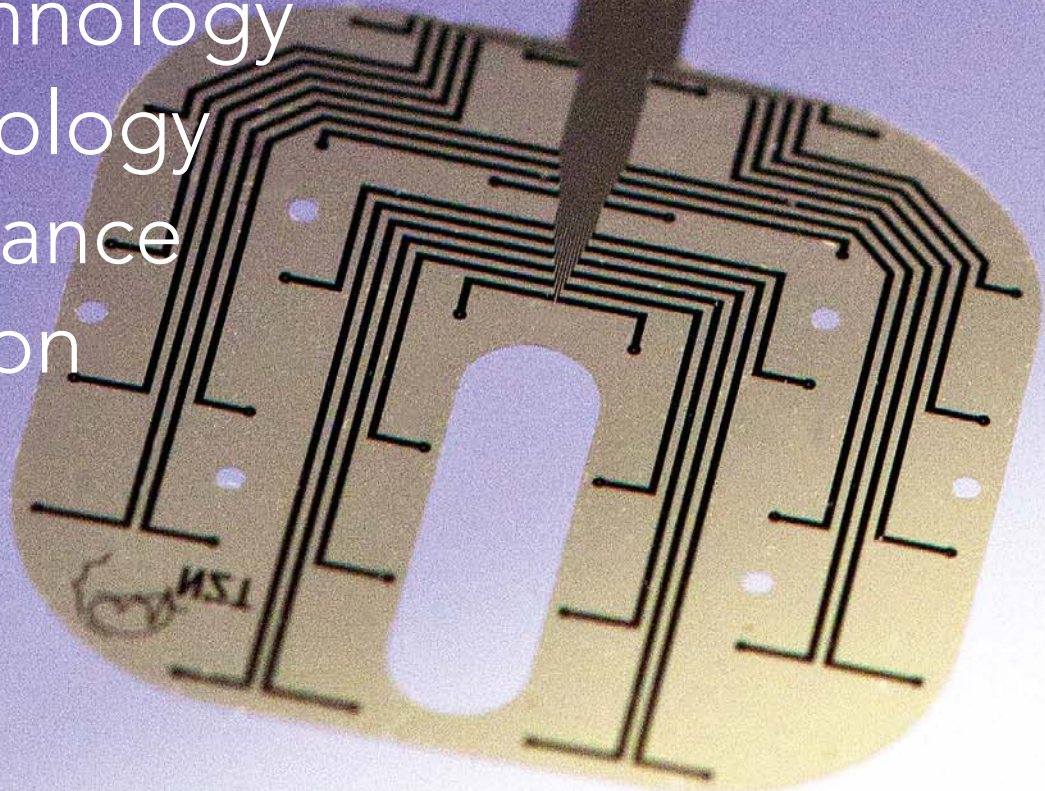


Winter 2012

THE PROJECT

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

The Merging
of Technology
and Biology
to Enhance
Function



The Miami Project To Cure Paralysis
Research Review

2011



UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE



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

This year promises to be one of the most exciting periods of discovery and translational progress for The Miami Project to Cure Paralysis. We are in the final stages of seeking permission from the FDA to initiate a Phase I **safety trial** in people with subacute spinal cord injury (SCI) using our human Schwann cell transplantation procedures. Therapeutic hypothermia studies continue to move forward and federal funding for a 17-center multi-center trial to test the efficacy of early cooling in a large number of individuals with acute spinal cord injury is being requested this year. Basic science discoveries continue to provide exciting information regarding mechanisms of axonal regeneration and combination approaches to promote more complete functional recovery in preclinical models of SCI. The potential use of cutting-edge bioengineering approaches to promote walking and hand function are becoming a reality within The Project as our scientists reach out to various biotechnological companies to build alliances to target paralysis. We greatly appreciate the support of our donors and scientific colleagues who are helping to provide critical resources as we move our investigations forward.

In this edition of our Research Review, several exciting areas of discovery are highlighted. Novel therapeutic interventions that target the acute injury setting to prevent secondary injury mechanisms provide hope for a better understanding of the injury process and repair strategies. In the area of acute protection, it is possible that cooling plus the addition of novel pharmacological interventions could provide more complete protection and functional recovery in combination rather than separately. Thus, continued investigations toward understanding mechanisms of neuronal cell death are important to the field and The Project's ultimate goal of protecting against spinal cord injury.

In the area of repair for chronic injuries, the scientific field could not be more exciting. Novel molecules are being identified that can potentially target both intrinsic and extrinsic mechanisms for successful axonal regeneration and provide novel therapies for the chronically injured who are living with paralysis. For example, federal support is helping us to move

a newly identified molecule that enhances regeneration forward in preparation for future clinical trials targeting axonal regeneration. Other novel therapies utilizing new gene therapies are targeting molecules that one day could be used in combination with other therapeutic strategies, including human Schwann cell transplantation. To further enhance long track regeneration, research collaborations using novel scaffolding materials to enhance axonal growth across gaps in the spinal cord are being evaluated. Because SCI is a heterogeneous condition, it is envisioned that different therapeutic interventions may be most appropriate depending on the severity of injury and degrees of structural damage. Thus, investigating multiple ways to protect and repair the nervous system is extremely important.

Neurorehabilitation work is also being initiated to be used in future trials as a means to enhance reparative strategies in individuals living with chronic spinal cord injury. A new study is being developed to establish baseline responses to protocols involving exercise conditioning and neurorehabilitation strategies in the different groups of chronic SCI (complete, incomplete, thoracic, cervical). That data will be used in the future when we are ready to amend our Investigational New Drug (IND application) targeting human Schwann cell transplantation in chronically injured individuals. For that clinical trial, which would be initiated after we establish safety in the subacute Schwann cell transplantation trial, we will combine Schwann cell transplantation with exercise conditioning and rehabilitation to maximize the potential amount of recovery. The potential use of recently developed robotic exoskeleton systems to enhance walking as well as novel brain-machine interface technology could be coupled with our established rehabilitation studies to further enhance function. Thus, the potential merging of biological and engineering approaches to target SCI is a very exciting area of investigation for Miami Project researchers.

We continue to concentrate on quality of life issues which affect people living with paralysis. Our pain group is testing novel therapies and continuing to understand the underlying mechanisms for abnormal sensation in our subjects. Fertility problems in men living with paralysis continue to be investigated with our goal of providing a clearer understanding of how to treat this condition. New concerns regarding the effects of aging with SCI are prompting our researchers to further target their clinical investigations in this area. Currently, approximately 17 active clinical trials are ongoing in the Lois Pope LIFE Center that are hypothesis-driven programs resulting in new information that is changing the way we think about consequences of spinal cord injury. In 2011, active trials enrolled over 500 individuals with chronic SCI, and we are grateful to all of our research participants for contributing to our knowledge regarding SCI and providing new information for future clinical studies. The Project therefore represents 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. These indeed are exciting times, and we again thank our friends and colleagues for their long-term support and commitment to our program. 2012 is going to be an outstanding year, and we thank everyone for their support of our research programs.

W. Dalton Dietrich, III, Ph.D.
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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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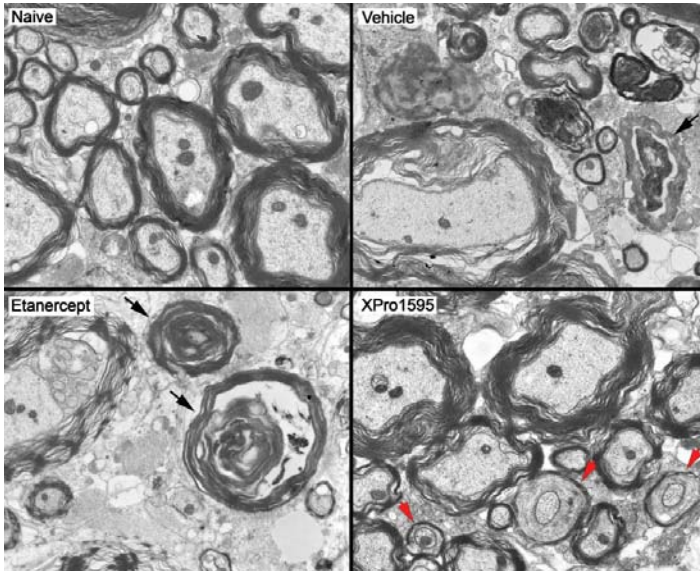


The *Yin* and *Yang* of Targeting TNF in Neurologic Disease

Dr. Roberta Brambilla, a junior faculty member at The Miami Project, published results in 2011 that are key to unraveling the confusion surrounding an important immune signaling molecule involved in the disease progression of multiple sclerosis (MS). This is important for spinal cord injury (SCI) as well because many of the tissue damaging processes associated with MS are also associated with SCI, particularly the loss of insulation (demyelination) around individual nerve fibers (axons) and damage to axons themselves.

So what is this molecule? Well, its' official name is Tumor Necrosis Factor, but let's just call it TNF for short. TNF comes in two forms and they have opposing activities. The first form is attached to cells and it is called transmembrane TNF or tmTNF. This is the good form because it promotes cell survival, a reduction of inflammation, and the formation of myelin. The second form is not attached to cells; it moves around the body and it is called soluble TNF or sTNF. sTNF

They found that **inhibiting** just the soluble form of TNF with XPro led to a **significant improvement** in motor function, promoted axon survival, and **stimulated the reformation** of healthy myelin around demyelinated axons.




Axons wrapped with myelin, under various experimental conditions, in the thoracic region of the spinal cord: Naive = from a healthy mouse; Vehicle = from a mouse model of Multiple Sclerosis (MS); Etanercept = MS mouse treated with the drug etanercept; XPro1595 = MS mouse treated with the drug XPro1595. The black arrows point to completely collapsed, damaged axons in vehicle and etanercept, which are not seen as often with XPro. In the XPro picture, the red arrows point to remyelinating axons.

is bad since it causes cell death and chronic inflammation. Normally, these two forms of TNF work together to keep the system balanced. During diseases such as progressive MS, however, the balances appear to get shifted more towards the negative activities triggered by sTNF.

Dr. Brambilla, in collaboration with senior faculty member, Dr. John Bethea, demonstrated the effects of selectively inhibiting sTNF in an animal model of MS. They were clever in that they compared the effects of 2 drugs that inhibit TNF; XPro1595, which selectively inhibits only the sTNF form, and etanercept, more commonly known as Enbrel, which non-selectively inhibits both forms of TNF. This enabled them to tease out the different mechanisms by which each form contributes to the disease progression. They found that inhibiting just the soluble form of TNF with XPro led to a significant improvement in motor function, promoted axon survival, and stimulated the reformation of healthy myelin around demyelinated axons. Wow! So, instead of trying to knock out all TNF activity with a broad

acting drug like Enbrel, its better to block the bad guy, sTNF, and leave the good guy, tmTNF, free to promote tissue repair. The research team took this a step further and evaluated post-mortem spinal cord tissue samples from three individuals that had chronic, progressive MS. They found the same characteristics indicative of sTNF and tmTNF activity in the human diseased tissue as they found in their animal model tissue. This is important because it demonstrates that the animal model is mimicking the human disease in a similar fashion and the results they observed with XPro in the animal model will likely translate to the human.

Her data was so compelling that the reviewers accepted her manuscript without requiring any modifications or additional data. That's rare for any scientist! In fact, one reviewer went so far as to state that "the authors have addressed a very important area of research and have 'demystified' the issues around TNF that plagued the field for over a decade; congratulations to the authors for this work that truly advances our knowledge." The manuscript was published in the highly regarded journal called *Brain* (2011, volume 134, pages 2736-2754). The results were also noticed by the Society for Neuroscience and were featured in their Hot Topics for the press at the annual meeting in November 2011 in Washington, DC.

The company that manufactures XPro1595, Xencor, recently obtained FDA approval to begin a clinical trial testing the drug in rheumatoid arthritis, another progressive inflammatory disease involving TNF (for more details see www.xencor.com). While the rheumatoid arthritis clinical trials are being planned, based on the promising data obtained with XPro1595 by various researchers in models of neurodegenerative diseases, including the studies by Drs. Brambilla and Bethea, Xencor is now seeking partnership with other pharmaceutical companies to license XPro1595 for use in neurological disease, MS in particular. Those other companies would then pursue clinical trials with XPro1595 unique to their interests. Thanks to the hard work of Dr. Brambilla, Dr. Bethea, and their research teams another mystery is unraveled in the disease arena involving inflammation! 

A Blueprint for Neurotherapeutic Drug Development

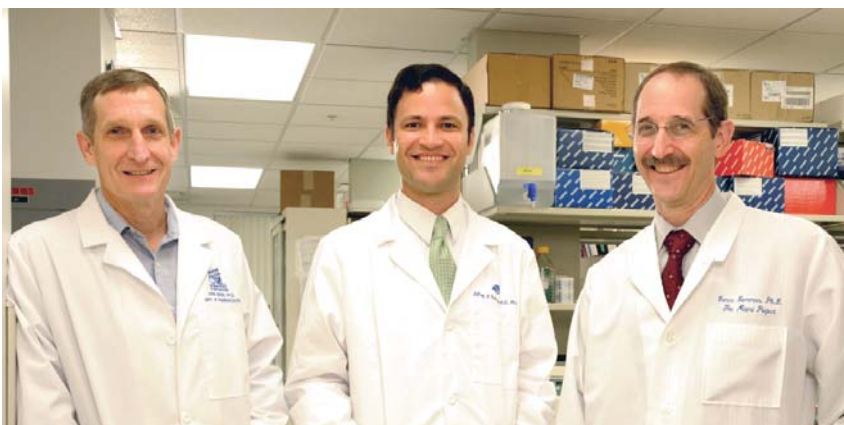


The Lemmon-Bixby lab

The ability to induce regeneration of damaged nerve fibers (axons) in the central nervous system (CNS) has been a significant challenge to the neural regeneration field for decades. This neurotherapeutic target is important not only to spinal cord injury, but also to traumatic brain injury, optic nerve injury, and many other neurological diseases. For so long this has appeared as an insurmountable obstacle, but during the past few years Miami Project faculty members John Bixby, Ph.D. and Vance Lemmon, Ph.D. have been making significant headway.

...this project was selected to be part of the National Institutes of Health (NIH) **Blueprint Neurotherapeutics Network** to develop drugs that can be used in clinical trials.

You may recall from previous magazine and newsletter articles that Drs. Lemmon and Bixby have developed a special laboratory that utilizes “high throughput” screening technology to discover novel genes and drugs that stimulate or inhibit regeneration in cell culture. Their laboratory can



Drs. John Bixby, Jeffrey Goldberg, and Vance Lemmon

Jeffrey Goldberg, also at the University of Miami, and Prof. Young-Tae Chang at the National University of Singapore. They have identified four compounds that enhance axon growth of a variety of neurons in inhibitory environments. One of these has been found to enhance regeneration in an acute spinal cord injury model as well as an optic nerve injury model (see Figure 1). That compound is called **F05**.

So, how do we move this exciting compound forward to determine if it has potential as a neurotherapeutic drug to test in clinical trials? Can we just take this compound, F05, as is, design a clinical trial, and start giving it to humans?

Unfortunately, it's not that simple. However, this project was selected to be part of the National Institutes of Health (NIH) **Blueprint Neurotherapeutics Network** to develop drugs that can be used in clinical trials. When a compound, like F05, is shown to be promising in an academic setting, such as ours, it must go through a rigorous drug development pipeline (see Figure 2) before it can be tested in humans. This pipeline is often called the valley of death because most basic science researchers cannot obtain the resources to perform all the “boring, but critical” tests necessary to develop the compound to a point where it becomes attractive to the pharmaceutical industry, and most pharmaceutical companies hesitate to invest in the neurotherapeutics drug development pipeline too early because of a long track record of failure, lack of clinically validated targets, and the fact that many CNS disorders affect relatively small populations in comparison to more widespread diseases such as cancer or heart disease. As a consequence, many potentially promising discoveries never make it through the pipeline.

literally test hundreds of genes or drugs in hundreds of thousands of neurons each week and obtain quantitative information about cell morphology and gene expression. Exciting “hits” (i.e. those genes/drugs that strongly stimulate or inhibit nerve growth) can then be investigated more thoroughly in animal models of CNS regeneration.

One of their recent projects has been to screen a novel chemical compound library to identify compounds that can overcome the regeneration-inhibitory effects of the injured CNS. They have been working on this in collaboration with Dr.

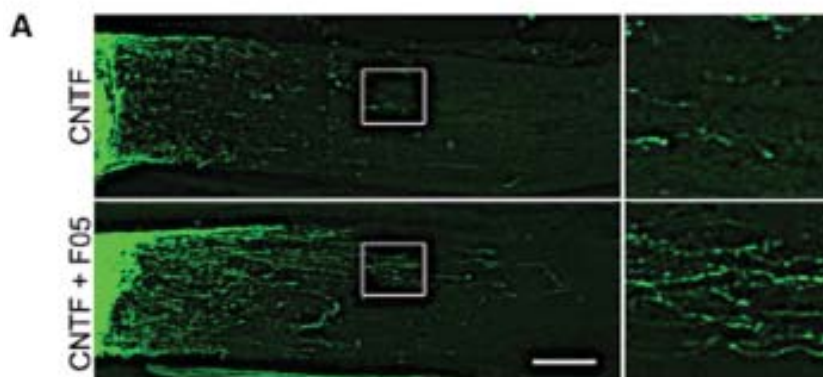


Figure 1. F05 stimulates significant regeneration of damaged axons (green) in an optic nerve injury model when the cell bodies are kept alive with a growth factor (CNTF).

Blueprint Neurotherapeutics Scope

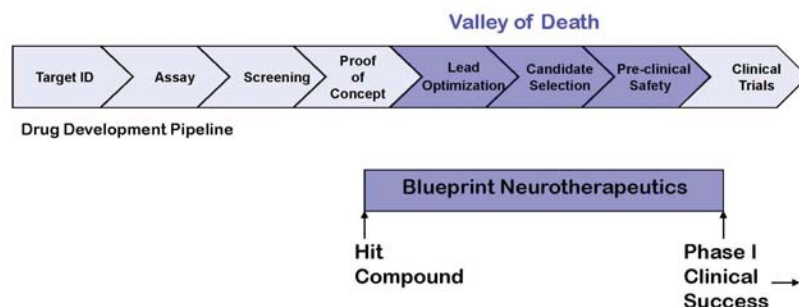


Figure 2. This diagram depicts the multiple processes that must occur from the time a target drug is discovered through completion of clinical trials. The “valley of death” constitutes all of the processes required to take a compound from proof of concept experiments to full-fledged clinical trials, and this is where the NIH Blueprint Neurotherapeutic Network has stepped in to assist academic centers with promising therapeutic compounds.

Fortunately, NIH recognized this problem and developed the Blueprint Neurotherapeutics Network to try to facilitate translation of basic discoveries to the clinic. After a highly competitive process, Drs. Lemmon, Bixby, and Goldberg were 1 of only 7 projects to be funded in the initial round. Their team will perform all of the biological activity and efficacy testing of F05 and new derivatives that are developed and they will also have access to millions of dollars worth of services that are normally available only to pharmaceutical and biotechnology companies.

Hopefully, this will **stimulate** pharmaceutical companies to **license** the most **promising** neurotherapeutic drugs and **invest** in the **clinical trials** needed to bring them to market.

Before F05 can move into clinical trials, its chemical structure must be redesigned to convert it into a safe and effective drug. This process is called chemical optimization and it involves the creation of hundreds of different chemical variations of F05, which must be tested and retested in cell-based systems and animal models to find one with the desired effects. This is what pharmaceutical companies, not academic centers, are designed to do on a large scale. Promising variants that are developed will undergo medicinal chemistry testing, pharmacology and toxicology testing, and Good Manufacturing Practices formulation. This will all be performed by contract research organizations that usually provide these services to the biotechnology and pharmaceutical industries.

Each project in the Neurotherapeutics Network, including the F05 project, is directed by a Lead Development Team (LDT) consisting of academicians, consultants from the pharmaceutical industry, and NIH staff (see Figure 3). Under the direction of the LDT, the F05 project is currently perfecting the biological assay, testing the drug-like properties of F05 and the other three “hits”, and designing and producing F05 derivatives for biological testing. The LDT has set milestones and deliverables, and confers biweekly to ensure that the project keeps on task.

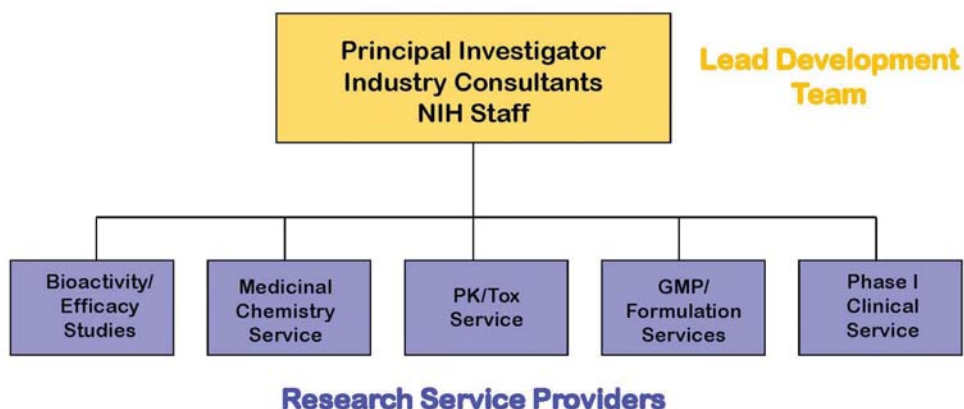


Figure 3. The operational model for each project within the Neurotherapeutic Network involves a Lead Development Team overseeing multiple drug development components carried out by research service providers.

A really important component of this relationship between our academic researchers and the industry service organizations is that NIH has ensured that our investigators will retain all intellectual property rights for any drugs they develop through the Neurotherapeutic Network. This is critical because it provides value to the end product. Drugs that successfully traverse the “valley of death” suddenly become very interesting to big pharmaceutical companies because they have potential to make it through the rigorous FDA approval process. Hopefully, this will stimulate pharmaceutical companies to license the most promising neurotherapeutic drugs and invest in the clinical trials needed to bring them to market.

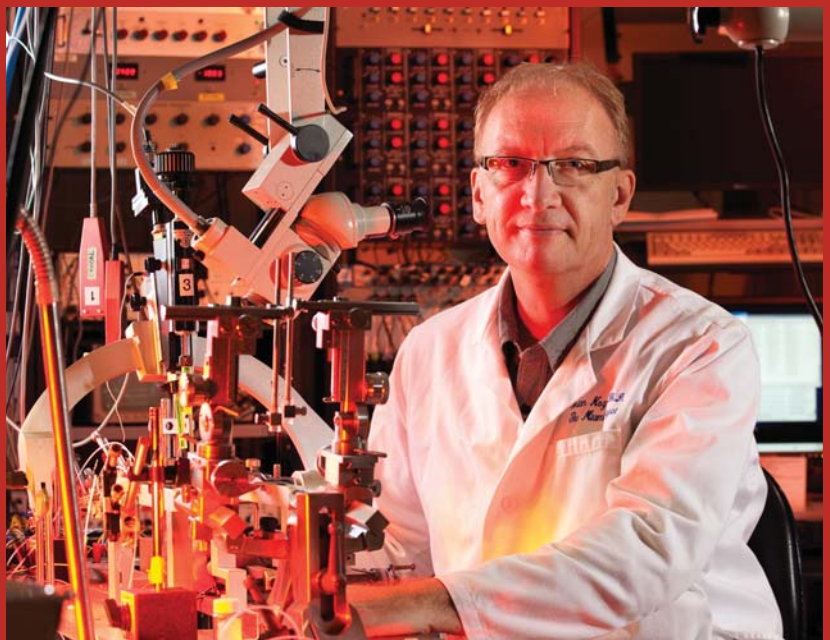
Deep Brain Stimulation and Locomotion


Did you know that electrical stimulation of a particular area in the brain can trigger the release of chemicals way down in the spinal cord that facilitate walking? Well, Miami Project faculty member Dr. Brian Noga knows this and he has been focusing his research on how to apply this after spinal cord injury.

In the healthy central nervous system (brain and spinal cord) there is a group of nerve cells (neurons) within the middle of the brain that play an important role in signaling the body to start walking or locomotion. These neurons are known as the “midbrain” locomotor region, or MLR. Each of these neurons connect (via a nerve fiber or axon) to other neurons within the brainstem transmitting the “command” for initiating locomotion as well as other neurons which provide powerful neuromodulatory influences on the walking pattern. Together, these neurons form the “descending locomotor pathways”, sending axons down to the thoracolumbar region of the spinal cord that contains the neurons producing walking patterns. How do these pathways excite the spinal locomotor neurons? They do so by releasing specific chemicals, neurotransmitters, which are sensed by the locomotor neurons. Neurotransmitters are chemicals that relay, amplify, and modulate signals between nerve cells. Two of the neurotransmitters released by these pathways are the powerful neuromodulators called Serotonin and Norepinephrine.

After spinal cord injury, the MLR-to-brainstem pathway remains intact and functional, but the brainstem-to-spinal cord pathways get disrupted. However, in most human injuries there are spared nerve fibers that are still connected above and below the injury even though there may be partial or complete paralysis below the injury. Also important is the fact that spinal cord cells below the injury site remain alive. So as long as the spinal cord injury is above the thoracolumbar area, the locomotion circuitry will remain intact. These factors are important and Dr. Noga has figured out how to take advantage of them with an existing treatment called deep brain stimulation.

Deep brain stimulation is approved for use in humans by the FDA for many purposes, including the treatment of movement disorders in persons with Parkinson’s disease where medications do not work to restore movement. This is good news for the spinal cord injury field because deep brain stimulation techniques already have a proven record of safety and efficacy. Dr. Noga has been investigating this method in spinal cord injury models by stimulating the MLR and measuring the release of neurotransmitters

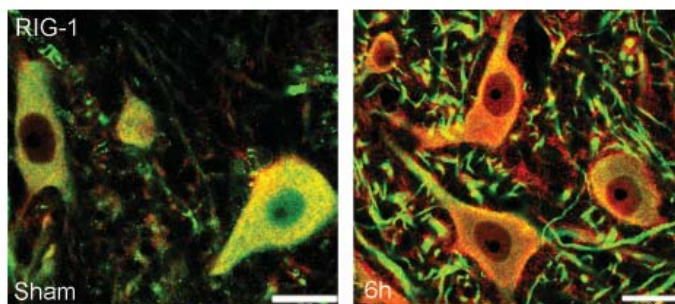


around the locomotion circuitry within the spinal cord. He has shown that cells activated by MLR stimulation include those important cells that release serotonin and norepinephrine in the spinal cord, which both help to stimulate locomotion. He has also demonstrated that many of the spinal locomotor-activated neurons have receptors which are sensitive to these neurotransmitters, thus providing a basis for their powerful neuromodulatory effects. The ability to enhance the activity of cells (and their release of neurotransmitters) that normally excite locomotor processes by the use of deep brain stimulation opens up the possibility of facilitating walking in persons with partial spinal cord injury. In accordance with this possibility, Dr. Noga has recently been awarded grants from the Christopher and Dana Reeve Foundation, the Craig Neilsen Foundation, and the National Institutes of Health to explore the therapeutic efficacy of deep brain stimulation over a variety of spinal cord injury types. 

Hot Topics

A highlight of research studies that have been accepted for publication recently in very high profile journals.

Dr. Juan Pablo de Rivero Vaccari led 2 studies evaluating different aspects of the innate immune system after experimental spinal cord injury. The first study was published in the journal *Glia* and discovered a novel mechanism involved in activating astrocytes after injury. Activated astrocytes go on to produce inflammatory mediators, which can contribute to causing secondary tissue damage. These findings are important because this mechanism is responsible for activating many different inflammatory events that are deleterious after injury. Thus, current research is focusing on understanding activation of this mechanism in neurons and in identifying inhibitors of this pathway that can be used as an anti-inflammatory treatment after spinal cord injury. The second study was published in the *Journal of Neuroscience* and expands his initial findings on neurons as cells of the innate immune response, which was initially published in the same journal back in 2008. This study identifies P2X4 as a therapeutic target to inhibit inflammation after injury. Therefore, future studies will test pharmacological blockers of P2X4 for their ability to improve function after spinal cord injury due to their anti-inflammatory properties.



Example of a protein (RIG-1) activated in astrocytes 6 hours after an experimental spinal cord injury, as indicated by the more orange colored cells on the right compared to the yellow cells on the left from a control spinal cord.

Glia (2011, Dec 7. doi: 10.1002/glia.22275) Astrogliosis Involves Activation of Retinoic Acid-Inducible Gene-Like Signaling in the Innate Immune Response After Spinal Cord Injury. **Juan Pablo de Rivero Vaccari**, Julia Minkiewicz, Xiaoling Wang, Juan Carlos De Rivero Vaccari, Ramon German, Alex E. Marcillo, **W. Dalton Dietrich**, **Robert W. Keane**.

Journal of Neuroscience (In Press) P2X4 Receptors Influence Inflammasome Activation Following Spinal Cord Injury. **Juan Pablo de Rivero Vaccari**, Dominic Bastien, Geoffrey Yurcisin, Isabelle Pineau, **W. Dalton Dietrich**, Yves De Koninck, **Robert W. Keane**, Steve Lacroix.

Dr. Kevin Park, and colleagues, recently published 2 studies evaluating different aspects of central nervous system axonal regeneration. The first study was published in the preeminent journal *Nature* and demonstrated that deleting two specific genes from neurons at the same time promotes continued and significant long-tract regeneration following injury to the axons. This study also showed that double deletion of these genes works synergistically to regulate activation and expression of several growth-related genes that improve axon regeneration. These findings are important in unlocking the mysteries of long distance regeneration. The second study was published in the journal *Neuron* and focused on the problem of neuronal death triggered by central nervous system axonal injury. They discovered, in their optic nerve injury model, that axon damage stimulates distinct regulation patterns of molecules involved in the unfolded protein response, which contribute to death of the neurons. This is important because it could lead to a potential neuroprotective strategies to prevent axonal injury associated cell death.

Nature (2011, 480:372-376) Sustained Axon Regeneration Induced by Co-deletion of PTEN and SOCS3. Fang Sun, **Kevin K. Park**, Stephane Belin, Dongqing Wang, Tao Lu, Gang Chen, Kang Zhang, Cecil Yeung, Guoping Feng, Bruce A. Yankner, Zhigang He.

Neuron (In Press) Differential Effects of Unfolded Protein Response Pathways on Axon Injury-induced Death of Retinal Ganglion Cells. Yang Hu, **Kevin K. Park**, Liu Yang, Xin Wei, Qiang Yang, Peter Thielen, Ann-Hwee Lee, Romain Cartoni, Laurie H. Glimcher, Dong Feng Chen, and Zhigang He.

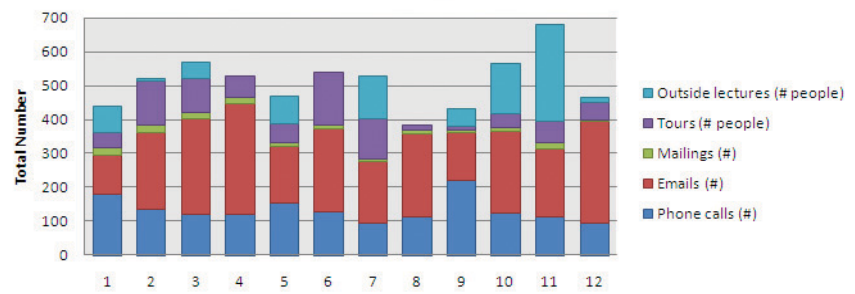
The “go to” source for information about spinal cord injury

If you are looking for information or have questions about spinal cord injury (SCI) and traumatic brain injury (TBI) research being conducted at The Miami Project and for updates describing continuing progress toward the goal of developing treatments for SCI and TBI, then the buck stops with the Education department. Headed up by Kim Anderson-Erisman, Ph.D., the little department that helps thousands of people each year is composed of Maria Chagoyen, Danielle Cilien, and Letitia Fisher. Aside from answering phone calls, and emails and giving numerous tours and lectures about our research, the Education department also answers many broader requests for information regarding injury prevention, clinical care referral, resources for living with paralysis, and advice about unproven therapies around the world. The graph shows the total number of people reached each month during outreach activities.



Drs. Green, Dietrich, Lynne, and Brackett at Open House 2011.

2011 Monthly Outreach



Dr. Rachel Cowan talking to a tour group during Open House 2011.

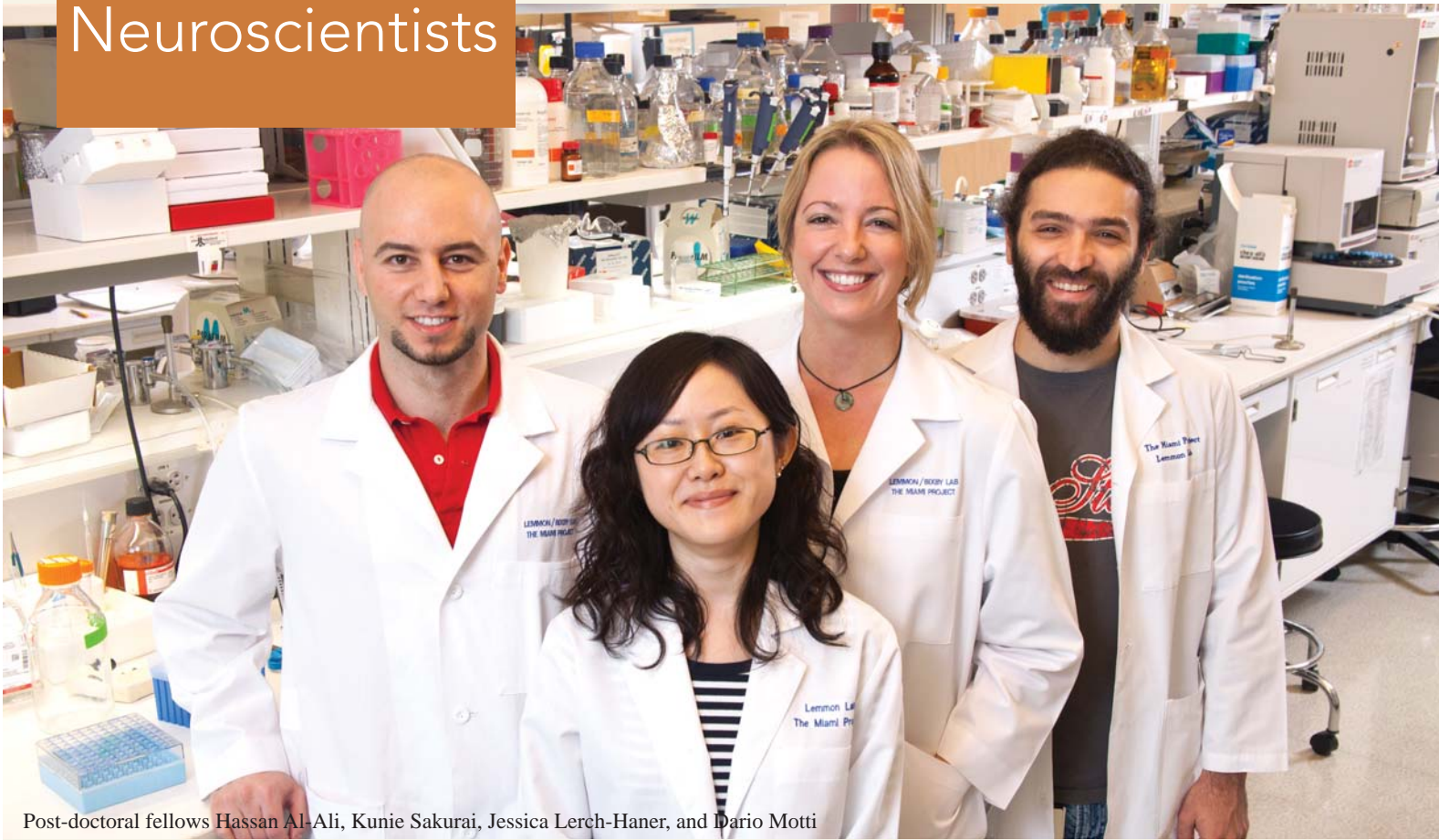
On February 26, 2011 the Education department hosted the 1st Miami Project Community Open House. We opened up our doors to the public for an afternoon packed full of information. The Miami Project Scientific Director, Dr. Dietrich, gave a detailed overview of discoveries that were accomplished by faculty members throughout the years. This was followed by an open discussion session stimulated by the audience regarding clinical trials, risk versus benefit, and how to tell the difference between proven and unproven therapies. The final component of the day was behind-the-scenes tours of five laboratories, including a cell culture lab, cell transplantation lab, regeneration lab, human exercise lab, and human motor training lab. There were over 100 community members in attendance and the event was a great success! The 2nd Annual Community Open House was February 18, 2012 and was an even greater success! The focus this year was on chronic spinal cord injury and talks covered scar tissue, cell replacement, regeneration, muscle spasticity, neuropathic pain, and Brain-Machine Interface technology.

The education department continued its “Neurotrauma Lecture Series” curriculum for high school students in Virginia. As part of the curriculum, several faculty members gave lectures that were transmitted via telecommunication to students at two campuses in Virginia. The education department also participated in the 2nd 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.

Clockwise from top right: Dr. Dietrich speaks to guest at Open House 2011; Brain Fair 2011 activities; Open House 2012 audience listening to research update; Take your child to work day; Open House 2012 participants.



The Next Generation of Neuroscientists



Post-doctoral fellows Hassan Al-Ali, Kunie Sakurai, Jessica Lerch-Haner, and Dario Motti

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 a cure. Our long-term educational goal is to increase the number of scientists and laboratories working on paralysis research and central nervous system disorders around the world. Students and young scientists beginning their careers gain skills from The Miami Project's state-of-the-art comprehensive research and academic environment. During 2011, the faculty members of The Miami Project were actively training almost 200 students of various levels (high school, undergraduate, graduate, medical) in their laboratories.

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 2011, the following students were awarded this fellowship:

- Christina Baker – Sanchez lab
- Jesse Bryant – Nash lab
- David Douriez – Hentall lab
- Jessica Johnson – Widerström-Noga lab
- Jose Ramos – Lee lab
- Luis Montoya – Thomas lab
- Yoelkys Morales – Sagen lab
- Anthony Martin – Brambilla lab



Students presenting their research at the National Neurotrauma meeting public event.

The University of Miami Citizens Board also funded a summer research fellowship for one outstanding University of Miami undergraduate student working in a Miami Project laboratory. In 2011, that student was:

Cecilia Perez – Sagen lab

Drs. John Bixby, Dalton Dietrich, and Vance Lemmon received supplemental funding from the American Recovery and Reinvestment Act to fund 9 summer students during 2011, and those students were:

| | |
|------------------------|---|
| Marisa Adhikusuma - | Tsoufas lab collaboration w/ Bixby lab |
| Daniel Cabrera - | Lemmon-Bixby lab |
| "JJ" Joaquin Jimenez - | Lemmon-Bixby lab |
| Michelle LeBlanc - | Pearse lab collaboration w/ Dietrich lab |
| Emily Packard - | Bramlett lab collaboration w/ Dietrich lab |
| Lindsey Salay - | Lemmon-Bixby lab |
| Christina Sedaghat - | Atkins & Vaccari labs collaboration w/ Dietrich |
| Alex Torres - | Lemmon-Bixby lab |
| Alexandria Wick - | Dietrich lab |

Two particularly motivated students volunteered full-time for the summer working in Miami Project laboratories, and they were:

Giselle Fontela – Thomas lab
Natalie Torrente – Park lab

All 20 of these exceptional students wrote an abstract about their specific research project and presented a poster at the 1st Miami Project Summer Student Research Session on August 5, 2011.

Summer Student Research Projects:

Development of a Method for Determining Effects of LTP and Cortical Spreading Depression: Recording Evoked Potentials In Vivo. Alexandra Wick, Thomas Sick, Amade Bregy, Justin Sick, W. Dalton Dietrich.

Evaluation of Myelinated Axon Profiles in the Spinal Cord Following Experimental Autoimmune Encephalomyelitis. Anthony Martin, Roberta Brambilla.

Brain-Computer Interfaces, Functional Electrical Stimulation and Their Roles in Neurological Rehabilitation for Paralysis Patients. Christina Baker, Scott Roset, Zoe Englander, Edelle Field-Fote, Justin C. Sanchez.

Discovering Neurite Growth-Promoting Protein Kinase Inhibitors. Daniel Cabrera, Jon Alexander Torres, Hassan Al-Ali, Vance Lemmon, John Bixby.

NRM Recordings in SCI Model. David Douriez, Ian Hentall.

β -Amyloid Precursor Protein Expression Following Polytrauma. Emily Packard, Helen Bramlett.

Passive Muscle Stretch Leads to Lasting H-Reflex Depression in Humans with Chronic Spinal Cord Injury. Giselle Fontela, Katie Gant, Luis Montoya, Lena Habash, Christine K. Thomas.

Effects of Increased Physiological Demands on Wheelchair Propulsion Mechanics. Jesse Bryant, Mark S. Nash, Rachel E. Cowan.

Impact of Prescription Pain Medication on Dorsal Column and Spinothalamic-Mediated Functions in Persons with



Miami Project Summer Student Research Day 2011

SCI-Related Neuropathic Pain. Jessica Johnson, Yenisel Cruz-Almeida, Letitia Fisher, Jim Adcock, Elizabeth Felix, Eva Widerström-Noga.

Developing a Bioluminescent Marker System for Probing Gene Expression Changes in Reactive Astrocytes. J. Jimenez, SR Beckerman, E. Hunt, T. Slepak, S. Deo, S. Daunert, JL Bixby, VP Lemmon.

Meningeal Fibroblast Invasion Following Penetrative Spinal Cord Injury. Jose Ramos, Cynthia Soderblom, Jae Lee.

DYRK Family Kinases Regulate Neuronal Morphology by Affecting the Phosphorylation Status of Doublecortin. LD Salay, TI Slepak, VP Lemmon, JL Bixby.

Muscle Activity Produced by Repeated, Sustained Passive Stretch in SCI and Uninjured Subjects. Luis Montoya, Katie Gant, Giselle Fontela, Lena Habash, Christine K. Thomas.

Rab27b May Play a Role in the Anterograde Transport of Trk and p75NTR Receptors in Non-Neuronal and Neuronal Cells. Marisa Adhikusuma, Pantelis Tsoulfas.

Gene Delivery of Brain Derived Neurotrophic Factor (BDNF) Following Spinal Cord Injury and Schwann Cell Implantation. Michelle E. LeBlanc, Mousumi Ghosh, Betsy Jullienne, Damien D. Pearse.

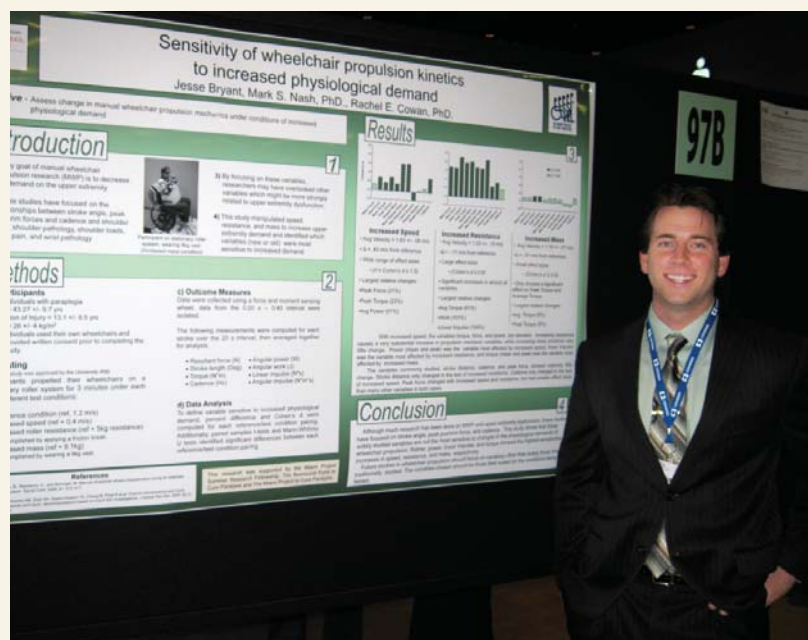
Examination of Signaling Pathways Involved in KRAS Activation-Induced Optic Nerve Regeneration. Natalie Torrente, Kevin Park.

Innate Immune Response Proteins as Biomarkers of Presymptomatic Alzheimer's Disease. Christina Sedaghat, Juan Pablo de Rivero Vaccari.

Developing the Natural Analgesic Conopeptide μ -SIIIA as a Candidate for Neuropathic Pain Gene Therapy to Repress $Na_v1.8$ Mediated Neuropathic Pain. Yoelkys Morales, Krystyna Simon, Shyam Gajavelli, Stanislava Jergova, Blake H Priddy, Jacqueline Sagen.

Taking it to the next level

One Miami Project Summer Student Research Fellow, University of Miami senior Jesse Bryant, continued on with his research project into the Fall semester. He submitted an abstract on his research to the Biomedical Engineering



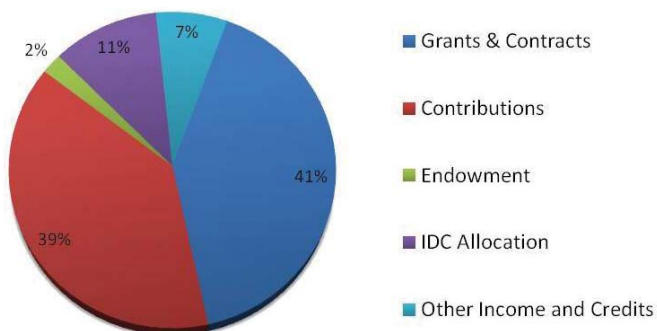
Student Jesse Bryant with his poster at the Biomedical Engineering Society meeting.

Society and it was accepted for poster presentation. Congratulations! The title of his poster was “Sensitivity of wheelchair propulsion kinetics to increased physiological demands” and he presented it at the Biomedical Engineering Society 2011 Annual Meeting in Hartford, CT.

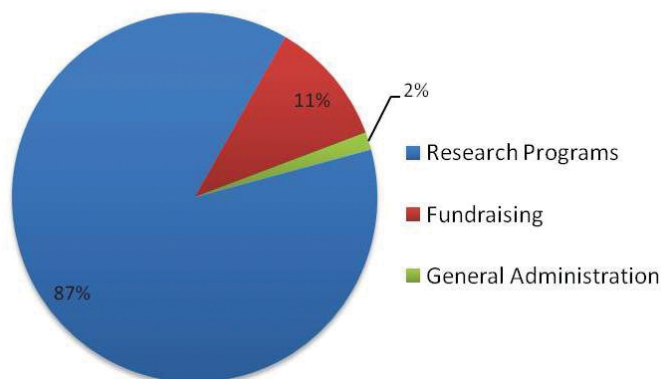
Bryant measured the response of several propulsion variables (force, torque, power, etc.) to the increased physical demands of increased speed, increased surface resistance, and increased wheelchair weight. The results showed that the widely studied propulsion variables (stroke angle, max force, and cadence) are not the most sensitive to changes in the physiological demands of wheelchair propulsion. The less commonly studied variables such as power, linear impulse, and torque actually showed the highest sensitivities to increases in speed, resistance, and mass, respectively, and thus, the variables chosen for future studies should be those best suited for the conditions being tested.

Jesse will be graduating from UM in May 2012 and is currently applying to graduate schools so he can begin pursuing a Ph.D. in biomedical engineering.

INCOME



EXPENSES



Abramson Foundation

Dr. Pantelis Tsoulfas (P.I.)
-Neural Stem Cells for Spinal Cord Injury

Christopher & Dana Reeve Foundation

Dr. Mary Bartlett Bunge (P.I.)
-Studies of Schwann Cell Transplantation

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

Dr. Brian Noga (P.I.)
Dr. Ian Hentall (Co-I.)
-Therapeutic Potential of DBS for Improving Walking Following Incomplete Spinal Cord Injury

Craig H. Neilsen Foundation

Dr. John Bethea (P.I.)
Dr. Roberta Brambilla (Co-I.)
-The Role of Astroglial-NF-kappaB in Regenerative Sprouting and Neuroprotection

Dr. Nancy Brackett (P.I.)
-Inflammasome Signaling and Sperm Cell Function

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 2011.

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. Mark S. 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. 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 C. Sanchez (P.I.)
-Tissue, Electrical, and Material Responses in Electrode Failure

-Creating the Synthetic Brain Through Hybrid Computational and Biological Systems: Repairing and Replacing Neural Networks

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

Dr. Mark S. Nash (P.I.)

-Obesity/Overweight in Persons with Early and Chronic SCI: A Randomized, Multicenter, Controlled Lifestyle Intervention

Dr. Damien Pearse (P.I.)

Dr. Mary Bartlett Bunge (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. Damien Pearse (P.I.)

-Site-directed Nanotherapeutics to Abrogate Relapsing/Remitting Multiple Sclerosis and Promote Remyelination Repair

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. 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 K. Park (P.I.)

-Novel Combinatorial Approaches to Enhance Retinal Ganglion Cell Survival and Axon Regeneration after Optic Nerve Injury

Fa Bene Foundation

Dr. Damien Pearse (P.I.)

-Cellular Therapies for Chronic Spinal Cord Injury Repair

Florida Department of Health Bureau of Emergency Medical Services

Dr. Gillian Hotz (P.I.)

-WalkSafe Florida State Implementation

Florida Department of Transportation

Dr. Gillian Hotz (P.I.)

-Safe Route to School-WalkSafe County Program

-WalkSafe Miami-Dade

-WalkSafe Tool Kit

-BikeSafe Program

International Spinal Research Trust

Dr. James Guest (Center P.I.)

-Comparison of Schwann Cells and Skin-derived Precursor Cells for Repair of Demyelination in the Primate Corticospinal Tract

Ironwood Pharmaceuticals, Inc.

Dr. Jacqueline Sagen (P.I.)

-Testing Analgesic Effects of FAAH Inhibitors in a Rat Spinal Cord Injury Pain Model

Medtronic Spinal and Biologics

Dr. Allan Levi (P.I.)

Dr. Barth Green (Co-I.)

Dr. Steven Vanni (Co-I.)

-Pivotal IDE Study of the Bryan Cervical Disc Prosthesis in the Treatment of Degenerative Disc Disease

Miami-Dade County Health Department via Center of Disease Control

Dr. Gillian Hotz (P.I.)

-Community Putting Prevention to Work – Safe Routes to School

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 Heart, Lung, and Blood Institute

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

Dr. Stephan Schürer (P.I.)
 Dr. Vance Lemmon (Co-I.)
 -LINCS Information Framework (LIFE) to integrate and Analyze Diverse Data Sets

National Human Genome Research Institute

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

National Institute of Child Health & Human Development

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

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

National Institute of Disability & Rehabilitation Research

Dr. Diana Cardenas (P.I.)
 Dr. Mark S. Nash (Co-I.)
 -Spinal Cord Injury Model Systems

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

Dr. Suzanne Groah (P.I.)
 Dr. Mark S. 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 (P.I.)
 Dr. Paula Monje (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- κ B 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. John Bixby (P.I.)
 -Predoctoral Training in the Neurosciences

Dr. Jesse Brodtkin (P.I.)
 Dr. Jacqueline Sagen (Sub-contractor for Small Business Innovation Research award)
 -Using a Multi-touch Screen to Automate Pain Assessment

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

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

Dr. W. Dalton Dietrich (P.I.)
 Dr. Helen Bramlett (Co-I.)
 -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.)
 -Cellular Transplantation Strategies Following Traumatic Brain Injury
 -The Importance of Temperature on Inflammation after TBI

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

Dr. John Harris (P.I.)
 Dr. Justin C. Sanchez (Co-I.)
 -An Ultra-Low Power Wireless Neural Recording Implant Based on a Novel Pulse Representation

Dr. Robert Keane (P.I.)

-Inflammasome Regulation After Spinal Cord Injury

Dr. Daniel Liebl (P.I.)

-Ephrins Regulate Stem Cell Proliferation following

Traumatic Brain Injury

-Regulation of Synaptic Formation & Efficacy Following

Traumatic Brain Injury

Dr. Allan Levi (P.I.)

-Transplantation of Autologous Schwann Cells for the

Repair of Segmental Peripheral Nerve Defects

Dr. Andrew Maudsley (P.I.)

Dr. Eva Widerström-Noga (Co-I.)

-Volumetric MRSI Evaluation of Traumatic Brain Injury

Dr. Brian Noga (P.I.)

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. Jacqueline Sagen (P.I.)

-Potent Analgesic Conopeptides for Treatment of Chronic Spinal Cord Injury Pain

Dr. Justin C. 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

Paralyzed Veterans of America Education Foundation

Dr. Rachel Cowan (P.I. – Post-doctoral Fellowship)

Dr. Mark S. Nash (Sponsor)

-From Research into the Clinic: The Manual Wheelchair Propulsion Database

Ralph C. Wilson Jr. Medical Research Foundation

Dr. Jacqueline Sagen (P.I.)

-Cell and Gene Therapy Strategies for Delivery of Novel Marine Snail Peptides in Chronic Spinal Cord Injury Pain

State of Florida James and Esther King Biomedical Research Program

Dr. John Bixby (P.I.)

Dr. Murray Blackmore (Co-I.)

Dr. Vance Lemmon (Co-I.)

-Combination Therapy in SCI: Proof of Concept for New Compounds and Candidate Genes

The Karl Kirchgessner Foundation

Dr. Kevin K. Park (P.I.)

-Developing PTEN shRNA-mediated Combinatorial Approaches to Improve Optic Nerve Regeneration

University of Miami Interdisciplinary Research Development Initiative

Dr. Ian Hentall (P.I.)

-Whole Body Pharmacological Profiling and Imaging of FAST Probes

University of Miami Stanley J. Glaser Foundation

Dr. Coleen Atkins (P.I.)

-Rehabilitation Strategies for Cognitive Disabilities after Traumatic Brain Injury

Veterans Administration Biological Laboratory Research and Development

Dr. Helen Bramlett (P.I.)

-Novel Treatment Strategies for Targeting Post-traumatic Epilepsy

Veterans Administration Rehabilitation Research and Development

Dr. Robert Jackson (P.I.)

Dr. Diana Cardenas (Co-I.)

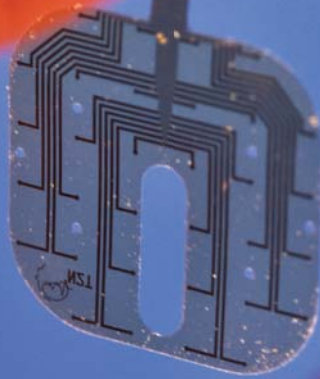
-Rehabilitation of IPF patients: Effects of Exercise and Oxidant Stress


Wings for Life Foundation

Dr. Damien Pearse (P.I.)

-Transcriptional Activation of Endogenous and Exogenous Neural Precursor cells for SCI Repair

Neuroprosthetics - The Merging of Technology and Biology to Enhance Function





When you mix neuroscience and biomedical engineering with the goal of developing devices targeting the restoration of function(s) lost as a result of disease or injury to the nervous system, you get the research field referred to as neuroprosthetics. This “young” field has exploded in the last decade and produced life-changing neural devices such as the cochlear implant to restore hearing, deep brain stimulators to reduce muscle tremors in Parkinson’s disease, and the spinal cord stimulator targeting neuropathic pain. What if they could create a device that was able to read your brain and trigger the appropriate movement? Science fiction you say? No, it’s the reality of the future – the very near future.

To use the **brain** to **restore** movement to **paralyzed limbs**.

You may have heard about monkeys being able to control a cursor on a computer screen with their thoughts. This has already been translated to humans with a system called BrainGate and BrainGate2. Already in clinical trials for people with high cervical injury, advanced Lou Gehrig’s disease, and locked-in syndrome, the BrainGate neuroprosthetics enable humans, who have no arm movement, to use their thoughts to control a computer cursor. This is an amazing feat and it is restoring the control of communication to individuals who are trapped inside their body due to severe neurologic disease. But wouldn’t it be great to take this technology one step further? To use the brain to restore movement to paralyzed limbs. The Miami Project is leaping into this field thanks to the excitement, intelligence, and drive of a biomedical engineer, Dr. Justin Sanchez.

Dr. Sanchez was recruited to the University of Miami department of Biomedical Engineering in 2010 and shortly thereafter was invited to become a faculty member of The Miami Project. Dr. Sanchez’s research specializes in the Brain Machine Interface (BMI) arena of neuroprosthetics and addresses 4 key issues:

1. Can we get signals out of the brain?
2. Can we decode those signals appropriately?
3. Can we build a fully implantable, i.e. invisible, BMI system?
4. Can we use that BMI system for rehabilitation and to restore functions that improve independence?

Can we get signals out of the brain?

The first step in any BMI system is to access signals from the brain. Changes in intent and behavior are produced by signals both on the surface of the brain as well as deep inside the brain. These signals could be related to motor, sensory, or goal information. The ability to sample activity from the brain depends heavily on electrodes



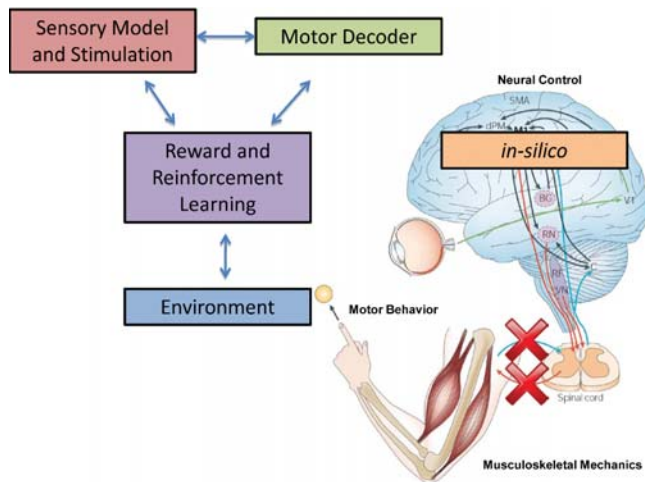
Dr. Justin Sanchez

since the nervous system communicates via electricity. An electrode is a medium for conducting an electrical current from the body to some kind of physiologic monitoring equipment. Electrodes come in many sizes and shapes that are tailored to accessing the information of interest. *Microelectrodes* (diameter of a human hair) can access the activity of *single* neurons. Typically, hundreds of these electrodes can access hundreds of neurons. These are the only electrodes that can access activity in the upper layers of the brain (cortex) and deep brain structures. In order to access the activity of *thousands* of neuronal assemblies, an *electrocorticogram* (ECoG) grid of electrodes is used, which can only sit on the surface of the brain. Finally, the *electroencephalogram* (EEG) has electrodes that sit on the scalp rather than on the surface of the brain and these can access *very large scale* activity in the brain related to behavior and cognition.

Can we decode those signals appropriately?

Once signals are out of the brain the next step is to decode them (i.e. interpret a user's intent). The process of

decoding in neuroprosthetics refers to the transformation of the signals recorded with electrodes into meaningful behavior for the user. If you'd like, you can think of decoding as the mysterious black box that magically takes thought and converts it to action. However, Dr. Sanchez makes it his business to remove the mystery from decoding. The process of decoding is very difficult because the activity of thousands or millions of neurons needs to be mapped to unique behaviors. These behaviors and the brain can also change over time or can be affected by experience and learning. Decoding brain signals falls into the domain of computational neuroscience and signal processing. Typically, engineering and signal processing do not contend well with scenarios that change over time (as is often encountered in biological systems) and much research is ongoing to develop innovative new approaches. Simple decoding approaches just match a change in a brain state to one behavior. More sophisticated decoders have the ability to adapt in synergy with their users and can learn through experience with their users. The great news is that advances in understanding the adaptation of

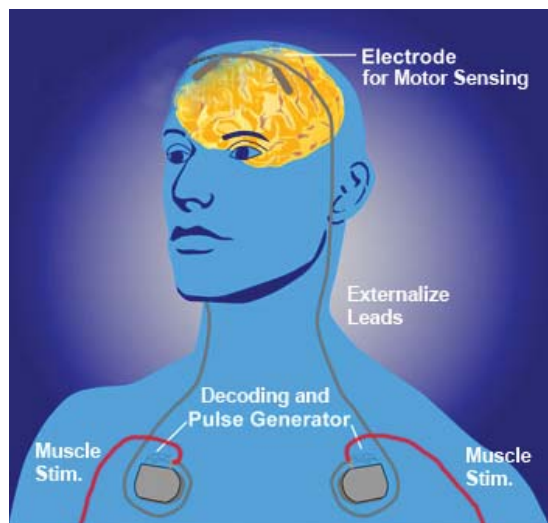


The components necessary for the ideal Brain-Machine Interface targeting functional recovery for SCI.

the brain and decoder is opening new perspectives in how the nervous system works and is influencing new medical device design.

Can we build a fully implantable, i.e. invisible, system?

So we can record thoughts and decode them into action, but who wants to have electrodes and wires sticking out of their head drawing more attention to the devices you use rather than who you are? Cosmesis, how it makes you look, is a significant issue for any therapy and plays a critical role when developing devices for persons living with spinal cord injury. Ultimately, the best neuroprosthesis will allow users to appear as any other individual without anyone being able to tell the difference. This is enabled with implantable electronics; information from the brain will be sampled, decoded, and control delivered to the body in a completely internalized manner. The design of fully implantable neuroprosthetics is difficult because of power, processing, and bandwidth issues. The activity




Proposed fully implantable BMI to be tested in people living with chronic C5 or C6 spinal cord injury.

of millions of neurons can create gigabytes of activity in very short periods of time. The ability to process all of that activity on the timescale of normal behavior requires fast processors. Ultimately, these implantable devices need to be powered for the lifetime of the users. The development of technology that addresses all of these requirements is on the cutting edge of what is currently possible with even the best electronics, but without a doubt all of those hurdles will be overcome in the near future. In fact, Dr. Sanchez and Dr. Jonathan Jagid (functional neurosurgery) are working to bring a leading edge technology that overcomes these issues to humans living with spinal cord injury. In a new effort led by Dr. Sanchez, a multidisciplinary team of Miami Project faculty members are seeking federal grant funding to perform feasibility testing of a brand new fully implantable BMI for individuals with motor complete, C5 or C6, chronic spinal cord injury. Expect to see more news about these developments later in 2012.

Can we use that system for rehabilitation and to restore functions that improve independence?

While the convergence of technology and neuroscience is providing the enablers for neuroprosthetics, the field will have limited impact if it does not effectively empower the user. The melding of rehabilitation with neuroprosthetics can provide the right combination of technology and function to enhance one's ability to perform activities of daily living with more independence. Reconnecting the brain with the body is the key to unlocking the expression of intent and communication with the world. Rehabilitating those new connections and strengthening them through practice could offer new, more effective functions that increase independence and improve overall quality of life. We ultimately envision a battery of combined therapies (BMI with rehabilitation, cell therapy, regeneration drugs, assistive devices such as exoskeletons, etc.) to create customized treatments that are tailored to each individual's needs.

These are exciting times indeed for people living with spinal cord injury! Technology is advancing as is our understanding of the nervous system after injury and how it responds to various inputs. The broad utilization of "neurotechnology" invokes the vision that neural interfaces, cell therapies, and neurorehabilitation can all be used together in a powerful way to repair and restore function to the damaged nervous system. By embracing technology we have found a new window through which we can learn how to enhance the reparative effects of neurotherapeutics and elicit the greatest amount of functional recovery for all the different variations of paralysis. 

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



W. DALTON DIETRICH, PH.D.

Scientific Director

Kinetic Concepts Distinguished Chair in Neurosurgery

Senior Associate Dean for Discovery Science

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

Neuroprotection and Improved Recovery of Function following CNS Trauma

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



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

Co-Founder

Professor and Chairman, Department of Neurological Surgery

Translational Interventions

Over the recent years my research efforts have mainly involved taking the cutting edge basic neuroscience work product and data created by our Miami Project team from the bench to our UM affiliated clinics and hospitals. A good example of such translational research efforts has included the use of modest hypothermia for neuroprotection both in cases of acute spinal cord injury and for use in the operating room for patients undergoing high risk spinal cord surgery. I am also privileged to be able to collaborate with The Miami Project cellular transplantation programs and have been working on projects involving adult mesenchymal stem cells as well as being part of the major effort transforming our successful Schwann cell laboratory model into human 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 involve 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 spinal cord injury (SCI). To improve regeneration of axons, we are investigating reducing the accumulation of proteoglycans (molecules that inhibit axonal growth), improving survival of transplanted Schwann cells (SCs), and genetically engineering SCs before transplantation to improve their 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 spinal cord injury (SCI) and diseases of the nervous system such as Multiple Sclerosis (MS) to try to understand the cellular and molecular mechanisms that contribute to astrogliosis and secondary neuronal cell death. To this end, my laboratory has two main research objectives. First, we are studying the neuro-inflammatory response that occurs following SCI and secondly, we are developing novel therapies for SCI and diseases of the central nervous system.



JOHN BIXBY, PH.D.

Professor, Departments of Molecular & Cellular Pharmacology and Neurological Surgery

Senior Associate Dean for Graduate & Postdoctoral Studies

VANCE LEMMON, PH.D.

Walter G. Ross Distinguished Chair in Developmental Neuroscience

Professor, Department of Neurological Surgery

High Content Screening and Functional Genomics of the Nervous System



Our laboratory has developed methods to test 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 to screen a novel chemical compound library to identify compounds that can overcome the regeneration-inhibitory effects of the injured CNS (collaboration with Dr. Goldberg and Prof. Young-Tae Chang, National University of Singapore). In 2011, this project was selected to be part of the NIH Neuroscience Blueprint Initiative to develop drugs to promote axonal regeneration.



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

Professor, Department of Neurological Surgery

Director, Clinical Neurotrauma

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

We have recently obtained two year funding from the Department of Defense to evaluate the neuroprotective effect of Perfluorocarbons in four rodent models of traumatic brain injury (penetrating brain injury, closed traumatic brain injury with secondary hypoxia, tissue culture with stretch injury, and mechanistic and safety studies). These oxygen carriers have shown benefit in previous studies involving fluid percussion injury and subdural hematoma models. We are also evaluating hypothermia neuroprotection, in humans and animals, using novel biomarkers 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 of the brain and spinal cord and applied neurophysiology related to neuroplasticity and motor learning. We want to understand which interventions best promote recovery of function. Some of the rehabilitation studies focus on recovery of hand and arm function, while others are aimed at walking function.

ROBERT W. KEANE, PH.D.

Professor, Department of Physiology & Biophysics

Regulation of Innate Immunity after CNS Trauma

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





ALLAN D. LEVI, M.D., PH.D., 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 Spinal Cord Injury

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

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

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

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

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

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



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

Professor, Department of Neurological Surgery

Cellular Implants for the Alleviation of Chronic Pain and CNS Injury

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

CHRISTINE K. THOMAS, PH.D.

Professor, Department of Neurological Surgery

Neuromuscular Weakness, Fatigue, Spasms, and Regeneration

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





PATRICK M. WOOD, PH.D.

Research Professor, Department of Neurological Surgery

Changes in the Molecular and Biological Properties of Human Schwann Cells

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

HELEN M. BRAMLETT, PH.D.

Associate Professor, Department of Neurological Surgery

The Pathophysiology and Treatment of CNS Injury

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



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

Associate Professor, Department of Neurological Surgery

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

The lab is engaged in translational research designed to develop useful models to test key questions of efficacy and safety in large animal models. The emphasis is on conducting testing of therapeutics to emulate human application as fully as possible; we use histological, behavioral, electrophysiologic, MRI, and ultrasound techniques. We design devices to deliver cells and therapeutics in a minimally injurious manner. Currently, we transplant Schwann cells and skin-derived precursor cells to repair tracts of the injured spinal cord. Other areas of research include studies of human post-mortem spinal cord tissue, intra-operative human spinal cord conduction studies, research design for human clinical trials, and active participation in human clinical trials.

DANIEL J. LIEBL, PH.D.

Associate Professor, Department of Neurological Surgery

Director, Neuroscience Graduate Program

Function of Growth and Guidance Molecules in the Developing and Regenerating Nervous Systems

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



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

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

JUSTIN C. SANCHEZ, PH.D.**Associate Professor, Department of Biomedical Engineering****Director, Neuroprosthetics Research Group****Neuroprosthetics and Neural Engineering**

The goals of my research are to develop brain-machine interfaces (BMI) to restore communication and 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 control for specific actions, 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.

**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 (SCI) 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 spinal cord injury (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
Translational Investigations for Chronic Spinal Cord Injury**

My research focuses on translational investigations and bridging the gap between basic science, clinical science, and the public community living with spinal cord injury. I recently completed a multi-center clinical study evaluating the reliability and validity of the Spinal Cord Independence Measure in the US healthcare setting and am currently focusing on issues specific to chronic injury.

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

**Research Associate Professor, Departments of Urology and Neurological Surgery
Male Fertility following Spinal Cord Injury**

Our research is focused on understanding and improving impairments to male fertility which occur following spinal cord injury (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 (1) how these brainstem (raphé) neurons respond during injury; (2) how raphé activity influences restorative molecular mechanisms in damaged regions; and (3) how recovery from traumatic spinal cord or brain injury is improved by prolonged electrical stimulation of these nuclei, a procedure with potential for treating acute injury in man.

GILLIAN A. HOTZ, PH.D.

**Research Associate Professor, Department of Neurological Surgery
Director, KiDZ Neuroscience Center
Director, Concussion, WalkSafe™ & BikeSafe™ Programs**

As a behavioral neuroscientist my clinical interests have always been investigating the neurocognitive deficits of those individuals that have sustained a traumatic and acquired brain injury. I have co-authored two neurocognitive tests, The Brief Test of Head Injury for Adults and the Pediatric Test of Brain Injury for Children. My research has also focused on injury prevention, preventing brain and spinal cord injuries in children, and I have developed the WalkSafe program, which has been shown to decrease the number of elementary school age children that get hit by cars, and now the BikeSafe program to educate middle school age children on bicycle safety skills. As the Director of the Concussion Program we have a comprehensive program including neurologic evaluation, neuroimaging, neuropharmacological management, and neuropsychological testing using ImPACT, a computerized neurocognitive screening measure.





ALBERTO MARTINEZ-ARIZALA, M.D.

Clinical Associate Professor, Departments of Neurology, Neurological Surgery, and Orthopaedics & Rehabilitation

Pathophysiology and Treatment of Secondary Complications in Spinal Cord Injury

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

BRIAN R. NOGA, PH.D.

Research Associate Professor, Department of Neurological Surgery

Brain and Spinal Mechanisms Controlling Walking

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

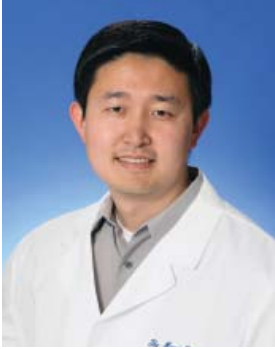
COLEEN ATKINS, PH.D.

Assistant Professor, Department of Neurological Surgery

Developing Novel Therapies for Traumatic Brain Injury and Spinal Cord Injury

The research in my laboratory focuses on developing novel therapeutic interventions for traumatic brain injury (TBI) and spinal cord injury (SCI). The research goal of my laboratory is to enhance rehabilitation and recovery by manipulating synaptic plasticity at specific levels of the neuroaxis following TBI and SCI. We have found that specific synaptic plasticity signaling pathways are altered after TBI and we are currently using pharmacotherapies to target those pathways to improve behavioral recovery after TBI.





JAE K. LEE, PH.D.

Assistant Professor, Department of Neurological Surgery

Neutralizing inhibitors of axon regeneration; stimulating plasticity

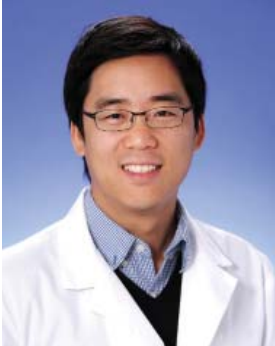
The long term research goal in my laboratory is to elucidate the mechanisms of cellular interactions in the injured adult spinal cord that creates an environment inhibitory to axonal growth. Currently, we know which cells can produce what types of inhibitory molecules, but we need a better understanding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

HOWARD B. LEVENE, M.D., PH.D.

Assistant Professor, Department of Neurological Surgery

Schwann Cell Transplantation after SCI

One proposed therapy for spinal cord injury is to introduce cells to the injury site to help repair, restore, or support existing neurons. 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 central nervous system (CNS). Previously, I and others have identified several key proteins that block axon regeneration, which are present in mature CNS neurons. In my current research, I will further extend my findings in order to better understand the mechanisms governing robust axon regeneration and also to explore the potential of developing therapeutic strategies for spinal cord injury and other neurodegenerative conditions.

ROBERTA BRAMBILLA, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Modulation of the immune response in neurologic disease

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





JUAN PABLO DE RIVERO VACCARI, PH.D.

Research Assistant Professor, Department of Neurological Surgery

Underlying mechanisms of the innate immune response and contributions to various CNS diseases

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

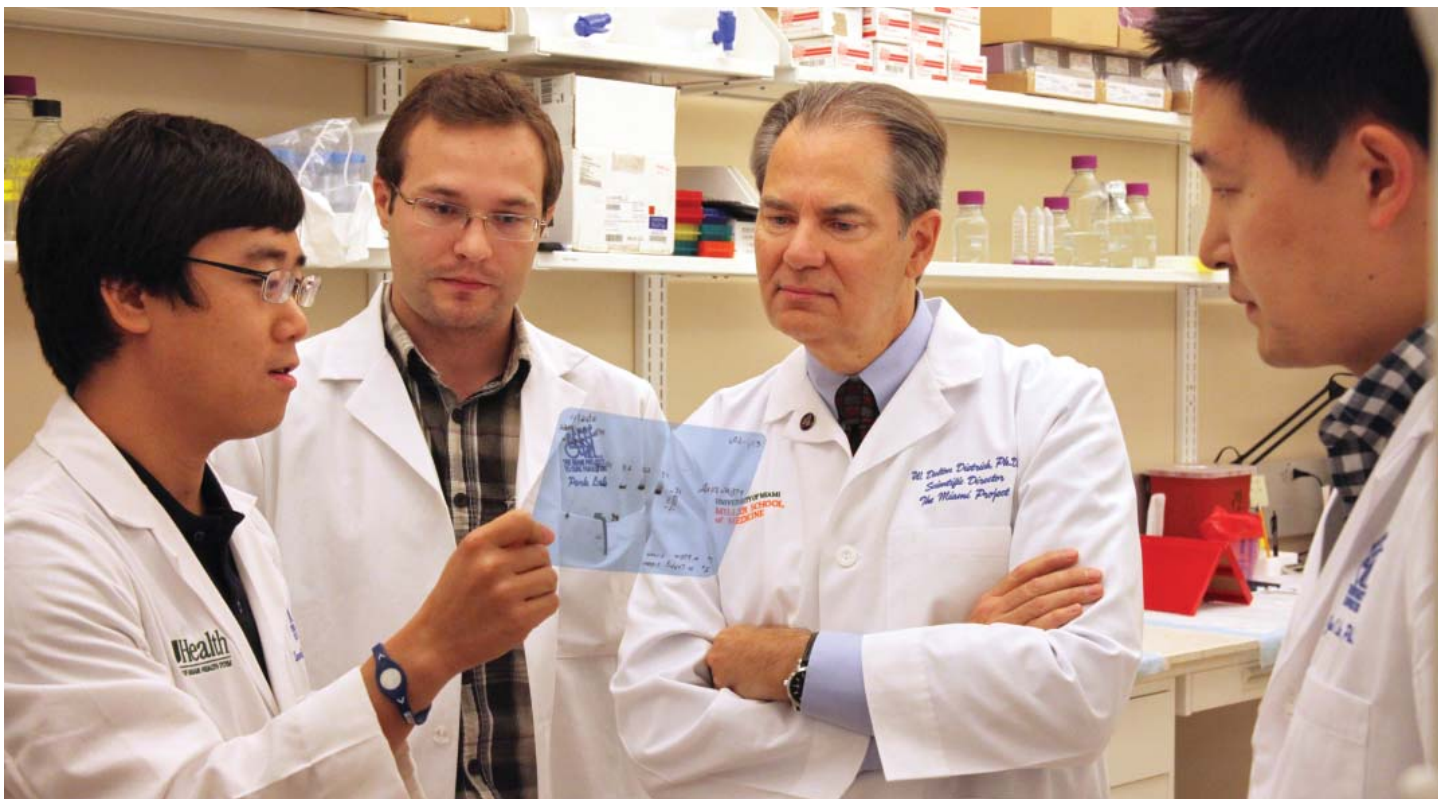
PAULA V. MONJE, PH.D.

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 central nervous system 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.



Dr. Dietrich discusses research with colleagues

Gail F. Beach Memorial Lecture Series

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

September 7, 2011

Qiufu Ma, Ph.D.

Harvard Clinical and Translational Science Center, Harvard University Medical School

"Generation of Sensory Neuron Diversity and Populating Coding of Pain Versus Itch"

November 2, 2011

Bente K. Pedersen, M.D., DMSc

Centre of Inflammation and Metabolism, University of Copenhagen

"Skeletal Muscle as an Endocrine Organ with Focus on IL-6"



Dr. Bente Pedersen, center, with Dr. Bethea and Dr. Nash

December 7, 2011

Christine E. Schmidt, Ph.D.

Department of Biomedical Engineering, University of Texas
"Engineering Novel Biomaterials for Axonal Regeneration"

January 4, 2012

Eva L. Feldman, M.D., Ph.D., FAAN

A. Alfred Taubman Medical Research Institute, University of Michigan

"Intraspinal Stem Cell Therapy for ALS: Challenges and Opportunities"



Guest lecturer Dr. Eva Feldman with Dr. Allan Levi

February 3, 2012

David Hovda, Ph.D.

UCLA Brain Injury Research Center, David Geffen School of Medicine at UCLA

"Cerebral Effort In Terms of Traumatic Brain Injury and Recovery of Function"



Dr. David Hovda, center, with Dr. Bramlett and Dr. Dietrich

March 7, 2012

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

University of Texas Southwestern Medical School

"In Vivo Discovery of Pharmacologic Agents for Neuropsychiatric Disease"

April 4, 2012

Patrizia Casaccia, MD, PhD

Icahn Medical Institute, Mount Sinai School of Medicine

"Protein Acetylation in Multiple Sclerosis"

June 6, 2012

Alvaro Pascual-Leone, MD, PhD

Beth Israel Hospital, Harvard University Medical School

"TBA"

Scientific Publications

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



Published studies that have passed the test of peer review are the benchmark of scientific progress. Listed here are the 2011 research publications by Miami Project scientists and colleagues.

Adelson PD, Pineda J, Bell MJ, Abend NS, Berger RP, Giza CC, Hotz G, Wainwright MS (In press) Common Data Elements for Pediatric Traumatic Brain Injury: Recommendations from the Working Group on Demographics and Clinical Assessment. *J Neurotrauma*.

Anderson KD, Acuff ME, Arp BG, Backus D, Chun S, Fisher K, Fjerstad JE, Graves DE, Greenwald K, Groah SL, Harkema SJ, Horton JA 3rd, Huang MN, Jennings M, Kelley KS, Kessler SM, Kirshblum S, Koltenuk S, Linke M, Ljungberg I, Nagy J, Nicolini L, Roach MJ, Salles S, Scelza WM, Read MS, Reeves RK, Scott MD, Tansey KE, Theis JL, Tolfo CZ, Whitney M, Williams CD, Winter

CM, Zanca JM (2011) United States (US) Multi-Center Study to Assess the Validity and Reliability of the Spinal Cord Independence Measure (SCIM III). *Spinal Cord*. 49:880-885.

Atkins CM (2011) Decoding Hippocampal Signaling Deficits After Traumatic Brain Injury. *Trans. Stroke Res*. 2:546-555.

Bagale SM, Brown AS, Carballosa Gonzalez MM, Vitores A, Micotto TL, Saleesh Kumar NS, Hentall ID, Wilson JN (2011) Fluorescent Reporters of Monoamine Transporter Distribution and Function. *Bioorg Med Chem Lett*. 21:7387-7391.

Bao Y, Bramlett HM, Atkins CM, Truettner JS, Lotocki G, Alonso OF, Dietrich WD (2011) Post-traumatic Seizures Exacerbate Histopathological Damage After Fluid-Percussion Brain Injury. *J Neurotrauma*. 28:35-42.

Bao F, Fleming JC, Golshani R, Pearse DD, Kasabov L, Brown A, Weaver LC (2011) A Selective Phosphodiesterase-4 Inhibitor Reduces Leukocyte Infiltration, Oxidative Processes, and Tissue Damage After Spinal Cord Injury. *J Neurotrauma*. 28:1035-1049.

Bates ML, Puzis R, Bunge MB (2011) Preparation of Spinal Cord Injured Tissue for Light and Electron Microscopy Including Preparation for Immunostaining. Conventional Animal Models of Movement Disorders (E.L. Lane, S.B. Dunnett, eds), Springer Humana, N.Y., *Neuromethods*. 62: 381-399.

Benglis DM Jr., Trimble B, Bullock R (2011) Past, Present and Future Developments of Intracranial Monitoring in Traumatic Brain Injury. Injury in Le Roux. *Neurocritical care*. Blackwell.

Brackett NL, Lynne CM, Sønksen J, Ohi DA (2011) Penile Vibratory Stimulation. In: *Surgical and Medical Management of Male Infertility*. M Goldstein, PN Schlegel eds. Cambridge University Press, Cambridge. 115-126.

Brambilla R, Ashbaugh JJ, Magliozzi R, Dellarole A, Karmally S, Szymkowski DE, Bethea JR (2011) Inhibition of Soluble Tumor Necrosis Factor is Therapeutic in Experimental Autoimmune Encephalomyelitis and Promotes Axon Preservation and Remyelination. *Brain*. 134:2736-2754.

Bregy A, Nixon R, Lotocki G, Alonso OF, Atkins CM, Tsoulfas P, Bramlett HM, Dietrich WD (In press) Posttraumatic Hypothermia Increases Doublecortin Expressing Neurons in the Dentate Gyrus After Traumatic Brain Injury in the Rat. *Exp. Neurol*.

Brophy G, Gillman C, Bullock R (In press) Pharmacokinetics of Cyclosporin A in Adults with Traumatic Brain Injury. *Pharmacology*.

Bryce TN, Biering-Sørensen F, Finnerup NB, Cardenas DD, Defrin R, Lundberg T, Norrbrink C, Richards JS, Siddall P, Stripling T, Treede RD, Waxman SG, Widerström-Noga E, Yezierski RP, Dijkers M (In press) International Spinal Cord Injury Pain Classification: Part I. Background and Description. *Spinal Cord*.

Bunge MB, Pearse DD (In press) Response to the report, "A Re-Assessment of a Combinatorial Treatment Involving Schwann Cell Transplants and Elevation of cyclic AMP on Recovery of Motor Function Following Thoracic Spinal Cord Injury in Rats" by Sharp et al. *Exp Neurol*.

Bunge MB, Wood PM (2011) Realizing the Maximum Potential of Schwann Cells to Promote Recovery From Spinal Cord Injury. Chapter 34 in *Handbook of Clinical Neurology, Spinal Cord Trauma, 3rd Edition* (J Verhaagen, JW McDonald, eds), Elsevier, N.Y.

Burns PB, Kressler J, Nash MS (In press) Physiological Responses to 'Exergaming' After Spinal Cord Injury. *Top Spinal Cord Inj Rehabil*.

Cahill KS, Green BA (2011) Commentary: Surgical Management of Thoracolumbar Neurologic Injuries. *Spine J*. 11:893-894.

Candiotti KA, Yang Z, Morris R, Yang J, Crescimone NA, Sanchez GC, Bird V, Leveillee R, Rodriguez Y, Liu H, Zhang YD, Bethea JR, Gitlin MC (2011) Polymorphism in the Interleukin-1 Receptor Antagonist Gene is Associated with Serum Interleukin-1 Receptor Antagonist Concentrations and Postoperative Opioid Consumption. *Anesthesiology*. 114: 1162-1168.

Cardenas DD, Moore KN, Dannels-McClure A, Scelza WM, Graves DE, Brooks M, Busch AK (2011) Intermittent Catheterization with a Hydrophilic-Coated Catheter Delays Urinary Tract Infections in Acute Spinal Cord Injury: A Prospective, Randomized, Multicenter Trial. *PM&R*. 3:408-417.

Carvajal JA, Cuartas E, Qadir R, Levi AD, Temple HT (2011) Peripheral Nerve Sheath Tumors of the Foot and Ankle. *Foot Ankle Int*. 32:163-167.

Cowan RE, Nash MS, de Groot S, van der Woude LH (2011) Adapted Manual Wheelchair Circuit: Test-Retest Reliability and Discriminative Validity in Persons with Spinal Cord Injury. *Arch Phys Med Rehabil*. 92:1270-1280.

Cowan RE, Ginnity KL, Kressler J, Nash MS (In press) Assessment of the 'Talk Test' and RPE for Exercise Intensity Prescription in Persons with Paraplegia. *Topics in Spinal Cord Injury Rehabilitation*.

Craciun S, Cheney D, Gugel K, Sanchez JC, Principe JC (2011) Wireless Transmission of Neural Signals Using

Entropy and Mutual Information Compression. *IEE Trans Neural Syst Rehabil Eng.* 19:35-44.

Cummock MD, Vanni S, Levi AD, Yu Y, Wang MY (2011) An Analysis of Postoperative Thigh Symptoms After Minimally Invasive Transpsoas Lumbar Interbody Fusion. *J Neurosurg Spine.* 15:11-18.

Daftarian P, Chowdhury R, Ames P, Wei C, King AD, de Rivero Vaccari JP, Dillon L, Price J, Leung H, Ashlock B, Mesri E, Perez V, Züchner S, Reiser J, Lemmon V, Keane RW (2011) In Vivo Electroporation and Non-Protein Based Screening Assays to Identify Antibodies Against Native Protein Conformations. *Hybridoma (Larchmt).* 30:409-418.

Daftarian P, Kaifer AE, Li W, Blomberg BB, Frasca D, Roth F, Chowdhury R, Berg EA, Fishman JB, Al Sayegh HA, Blackwelder P, Inverardi L, Perez VL, Lemmon V, Serafini P (2011) Vaccine Platform to Target Antigen-Presenting Cells Peptide-Conjugated PAMAM Dendrimer as a Universal DNA. *Cancer Res.* 71:7452-7462.

de Fazio M, Rammo R, Bullock R (In press) Management of Migrating Intracranial Bullets: Lessons Learned from an AK Bullet Through the Brainstem. *World Neurosurgery.*

de Fazio M, Rammo R, O'Phelan K, Bullock MR (2011) Alterations in Cerebral Oxidative Metabolism Following Traumatic Brain Injury. *Neurocrit.* 14:91-96.

de Rivero Vaccari JP, Minkiewicz J, Wang X, De Rivero Vaccari JC, German R, Marcillo AE, Dietrich WD, Keane RW (2011) Astroglial Involvement Involves Activation of Retinoic Acid-Inducible Gene-Like Signaling in the Innate Immune Response After Spinal Cord Injury. *Glia.* Dec7.doi:10.1002/glia.22275.

de Rivero Vaccari JP, Sawaya ME, Brand III F, Nusbaum BP, Bauman AJ, Bramlett HM, Dietrich WD, Keane RW (In press) Caspase-1 is Increased in the Scalp in Androgenetic Alopecia. *Derm Surgery.*

del Valle K, Theus MH, Bethea JR, Liebl DJ, Ricard J (2011) Neural Progenitors Proliferation is Inhibited by EphB3 in the Developing Subventricular Zone. *Int J Dev Neurosci.* 29:9-14.

Dietrich WD, Cappuccino A, Cappuccino H (2011) Systemic Hypothermia for the Treatment of Acute Cervical Spinal Cord Injury in Sports. *Curr Sports Med Rep.* 10:50-54.

Dietrich WD, Levi AD, Wang M, Green BA (2011) Hypothermic Treatment for Acute Spinal Cord Injury. *Neurotherapeutics.* 8:229-239.

Dulski TM, Basavaraju SV, Hotz GA, Xu L, Selent MU, DeGennaro VA, Andrews D, Ford H, Coronado VG, Ginzburg E (2011) Factors Associated with Inpatient Mortality in a Field Hospital Following the Haiti Earthquake. *American Journal of Disaster Medicine.* 6:275-284.

Eaton MJ, Widerström-Noga E, Wolfe SQ (2011) Subarachnoid Transplant of the Human Neuronal hNT2.19 Serotonergic Cell Line Attenuates Behavioral Hypersensitivity Without Affecting Motor Dysfunction After Severe Contusive Spinal Cord Injury. *Neurol Res Int.* doi:10.1155/2011/891605.

Farhat HI, Elhammady MS, Levi AD, Aziz-Sultan MA (2011) Cervical Subarachnoid Catheter Placement for Continuous Cerebrospinal Fluid Drainage: A Safe and Efficacious Alternative to the Classic Lumbar Cistern Drain. *Neurosurgery.* 68:52-56.

Farhat HI, Hood B, Vanni S, Levi AD (2011) Minimally invasive repair of spontaneous intracranial hypotension. *JNeurosurg.* 114:505-509.

Field-Fote EC, Roach KE (2011) Influence of a Locomotor Training Approach on Walking Speed and Distance in People with Chronic Spinal Cord Injury: A Randomized Clinical Trial. *Phys Ther.* 91:48-60.

Fode M, Krogh-Jespersen S, Brackett NL, Ohl DA, Lynne CM, Sønksen J (2011) Male Sexual Dysfunction and Infertility Associated with Neurological Disorders. *Asian J Androl.* Dec 5. doi:10.1038/aja.2011.70.

Fulk G, Field-Fote EC (2011) Measures of Evidence in Evidence-Based Practice. *J Neurol Phys Ther.* 35:55-56.

Ghosh M, Jährling N, Henao MC, Dodt H-U, Pearse DD (In press) The utility of 3D Ultramicroscopy for Evaluating Cellular Therapies After Spinal Cord Injury. *Top Spinal Cord Inj Rehabil.*

Goldstein MS, Scalzitti DA, Bohmert JA, Brennan GP, Craik RL, Delitto A, Field-Fote EC, Magistro CM, Powers CM, Shields RK (2011) Vitalizing Practice Through Research and Research Through Practice: The Outcomes of a Conference to Enhance the Delivery of Care. *Phys Ther.* 91:1275-1284.

Groah SL, Hosier H, Ward EA, Nash MS, Libin A, Taylor AJ (2011) Cardiometabolic Risk Clustering and Atherosclerosis: Is There a Link in Spinal Cord Injury? *Top Spinal Cord Inj Rehabil*. 16:1-13.

Groah SL, Nash MS, Ward EA, Libin A, Mendez AJ, Burns P, Elrod M, Hamm LF (2011) Cardiometabolic risk in community-dwelling persons with chronic spinal cord injury. *J Cardiopulm Rehabil Prev*. 31:73-80.

Guest J, Benavides F, Padgett K, Mendez E, Tovar D (2011) Technical Aspects of Spinal Cord Injections for Cell Transplantation. Clinical and Translational Considerations. *Brain Res Bull*. 84:267-279.

Hartings JA, Bullock MR, Okonkwo DO, Murray LS, Murray GD, Fabricius M, Maas AI, Woitzik J, Sakowitz O, Mathern B, Roozenbeek B, Lingsma H, Dreier JP, Puccio AM, Shutter LA, Pahl C, Strong AJ; Co-Operative Study on Brain Injury Depolarisations (2011) Spreading Depolarisations and Outcome After traumatic brain injury: a prospective observational study. *Lancet Neurol*. 10:1058-1064.

Hartings JA, Watanabe T, Bullock MR, Okonkwo DO, Fabricius M, Woitzik J, Dreier JP, Puccio A, Shutter LA, Pahl C, Strong AJ; Co-Operative Study on Brain Injury Depolarizations (2011) Spreading Depolarizations have Prolonged Direct Current Shifts and are Associated with Poor Outcome in Brain Trauma. *Brain*. 134:1529-1540.

Hama AT, Broadhead A, Lorrain DS, Sagen J (In press) The Antinociceptive Effect of the Asthma Drug Ibudilast in Rat Models of Peripheral and Central Neuropathic Pain. *J Neurotrauma*.

Hama A, Sagen J (2011) Activation of Spinal and Supraspinal Cannabinoid-1 Receptors Leads to Antinociception in a Rat Model of Neuropathic Spinal Cord Injury Pain. *Brain Res*. 1412:44-54.

Hama A, Sagen J (2011) Antinociceptive Effect of Riluzole in Rats with Neuropathic Spinal Cord Injury Pain. *J Neurotrauma*. 28:127-134.

Hama A, Sagen J (2011) Centrally Mediated Antinociceptive Effects of Cannabinoid Receptor Ligands in Rat Models of Nociception. *Pharmacol Biochem Behav*. 100:340-346.

Hellal F, Hurtado A, Ruschel J, Flynn KC, Laskowski CJ, Umlauf M, Kapitein LC, Strikis D, Lemmon V, Bixby J, Hoogenraad CC, Bradke F (2011) Microtubule Stabilization Reduces Scarring and Causes Axon Regeneration After Spinal Cord Injury. *Science*. 331:928-931.

Hentall ID, Carballosa Gonzalez MM (In press) Promotion of Recovery From Thoracic Spinal Cord Contusion in Rats by Stimulation of Medullary Raphe or its Midbrain Input. *Neurorehabil Neural Repair*.

Hood B, Benglis DM, Levi AD, Vanni S (In press) Occiput to Thoracic Fusion After Surgical Resection of Desmoid Tumor. *World Neurosurgery*.

Hu Y, Park KK, Yang L, Wei Xin, Yang Q, Thielen P, Lee AH, Cartoni R, Glimcher LH, Chen DF, He Z (In press) Differential Effects of Unfolded Protein Response Pathways on Axon Injury-Induced Death of Retinal Ganglion Cells. *Neuron*.

Hunanyan AS, Alessi V, Patel S, Pearse DD, Matthews G, Arvanian VL (2011) Alterations of Action Potentials and the Localization of Nav1.6 Sodium Channels in Spared Axons After Hemisection Injury of the Spinal Cord in Adult Rats. *J Neurophysiol*. 105:1033-1044.

Iremashvili V, Brackett NL, Ibrahim E, Aballa TC, Lynne CM (2011) The Choice of Assisted Ejaculation Method is Relevant for the Diagnosis of Azoospermia in Men with Spinal Cord Injuries. *Spinal Cord*. 49: 55-59.

Jagid J, Harris L, Bullock R (In press) Chapter #185 Traumatic Intraparenchyma Hematoma-Lobectomy. *Neurosurgical Tricks of the Trade*. Elsevier.

Jayakumar AR, Bethea JR, Tong XY, Gomez J, Norenberg MD (2011) NF- κ B in the Mechanism of Brain Edema in Acute Liver Failure: Studies in Transgenic Mice. *Neurobiol Dis*. 41:498-507.

Jergova S, Hentall ID, Gajavelli S, Varghese MS, Sagen J (In press) Intraspinal Transplantation of GABAergic Neural Progenitors Attenuates Neuropathic Pain in Rats: A Pharmacologic and Neurophysiological Evaluation. *Exp Neurol*.

Kathiresan AS, Ibrahim E, Aballa TC, Attia GR, Lynne CM, Brackett NL (In press) Anejaculatory infertility due to multiple sclerosis. *Andrologia*. doi: 10.1111/j.1439-0272.2011.01208.

- Kathiresan AS, Ibrahim E, Aballa TC, Attia GR, Lynne CM, Brackett NL (2011) Pregnancy Outcomes by Intravaginal and Intrauterine Insemination in 82 Couples with Male Factor Infertility Due to Spinal Cord Injuries. *Fertil Steril*. 96:328-331.
- Kathiresan ASQ, Ibrahim E, Aballa TC, Attia GR, Ory SJ, Hoffman DI, Maxson WS, Barrionuevo MJ, Lynne CM, Brackett NL (2011) Comparison of IVF/ICSI Outcomes in Male Factor Infertility Patients with and without Spinal Cord Injuries. *Fertil Steril*. 96:562-566.
- Kochanek PM, Bramlett H, Dietrich WD, Dixon CE, Hayes RL, Povlishock J, Tortella FC, Wang KK (2011) A Novel Multicenter Preclinical Drug Screening and Biomarker Consortium for Experimental Traumatic Brain Injury: Operation Brain Trauma Therapy. *J Trauma*. 71:S15-24.
- Kressler J, Cowan R, Ginnity K, Nash MS (In press) Subjective Measures of Exercise Intensity to Gauge Substrate Partitioning in Persons with Paraplegia. *Topics in Spinal Cord Injury Rehabilitation*.
- Kwon BK, Okon EB, Tsai E, Beattie MS, Bresnahan JC, Magnuson DK, Reier PJ, McTigue DM, Popovich PG, Blight AR, Oudega M, Guest JD, Weaver LC, Fehlings MG, Tetzlaff W (2011) A Grading System to Evaluate Objectively the Strength of Pre-Clinical Data of Acute Neuroprotective Therapies for Clinical Translation in Spinal Cord Injury. *J Neurotrauma*. 28:1525-1543.
- Lee JK, Zheng B (In press) Role of Myelin-Associated Inhibitors in Axonal Repair After Spinal Cord Injury. *Exp Neurol*.
- Lemmon VP, Jia Y, Shi Y, Holbrook SD, Bixby JL, Buchser W (2011) Challenges in Small Screening Laboratories: Implementing an On-Demand Laboratory Information Management System. *Combo Chem*. 14:42-48.
- Lerch JK, Bixby JL, Lemmon VP (In press) Isoform Diversity and its Importance for Axon Regeneration. *Neuropathology*. Dec 13. doi:10.1111/j.1440-1789.2011.01280
- Lerch JK, Kuo F, Motti D, Morris R, Bixby JL, Lemmon VP (In press). Isoform Diversity and regulation in peripheral and central neurons revealed through RNA-Seq. *PLoS One*.
- Li L, Park I, Seth S, Sanchez JC, Principe JC (In press) Functional Connectivity Dynamics Among Cortical Neurons: a Dependence Analysis. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*.
- Liu K, Tedeschi A, Park KK, He Z (2011) Neuronal Intrinsic Mechanisms of Axon Regeneration. *Annu Rev Neurosci*. 34:131-152.
- Lotocki G, de Rivero Vaccari JP, Alonso O, Molano JS, Nixon R, Safavi P, Dietrich WD, Bramlett HM (2011) Oligodendrocyte Vulnerability Following Traumatic Brain Injury in Rats. *Neurosci Lett*. 499:143-148.
- Maas AI, Harrison-Felix CL, Menon D, Adelson PD, Balkin T, Bullock R, Engel DC, Gordon W, Langlois-Orman J, Lew HL, Robertson C, Temkin N, Valadka A, Verfaellie M, Wainwright M, Wright DW, Schwab K (2011) Standardizing Data Collection in Traumatic Brain Injury. *J Neurotrauma*. 28:177-187.
- Mahmoudi B, Sanchez JC (2011) A Symbiotic Brain-Machine Interface Through Value-Based Decision Making. *PLoS One* 14:e14760.
- Manzano GR, Casella G, Wang MY, Levi AD (In press) A Prospective, Randomized Trial Comparing Expansile Cervical Laminoplasty Versus Cervical Laminectomy and Fusion for Multi-Level Cervical Myelopathy. *Neurosurgery*.
- Marcillo A, Frydel B, Bramlett HM, Dietrich WD (In press) A Reassessment of P2X7 Receptor Inhibition as a Neuroprotective Strategy in Rat Models of Contusion Injury. *Exp Neurol*.
- Marrero E, Rossi SG, Darr A, Tsoulfas P, Rotundo RL (2011) Translational Regulation of Acetylcholinesterase by the RNA Binding Protein Pumilio-2 at the Neuromuscular Synapse. *J Bio Chem*. 286:36492-36499.
- Mawhinney LJ, de Rivero Vaccari JP, Alonso OF, Jimenez CA, Furones C, Moreno WJ, Lewis MC, Dietrich WD, Bramlett HM (In press) Isoflurane/Nitrous Oxide Anesthesia Induces Increases in NMDA Receptor Subunit NR2B Protein Expression in the Aged Rat Brain. *Brain Res*.
- Mawhinney LJ, de Rivero Vaccari JP, Dale GA, Keane RW, Bramlett HM (In press) Heightened Inflammation Activation is Linked to Age-Related Cognitive Impairment in Fischer 344 rats. *BMC Neurosci*.

- Mawhinney LJ, de Rivero Vaccari JP, Alonso O, Jimenez CA, Furones C, Moreno WJ, Lewis MC, Dietrich WD, Bramlett HM (In press) Isoflurane/Nitrous Oxide Anesthesia Induces Increases in NMDA Receptor Subunit NR2B Protein Expression in the Aged Rat Brain. *Brain Research*.
- Mondello S, Papa L, Buki A, Bullock MR, Czeiter E, Tortella FC, Wang KK, Hayes RL (2011) Neuronal and Glial Markers are Differently Associated with Computed Tomography Findings and Outcome in Patients with Severe Traumatic Brain Injury: A Case Control Study. *Crit Care*. 15: R156.
- Mummidisetty CK, Bohórquez J, Thomas CK (In press) Automatic Analysis of EMG During Clonus. *J Neurosci Methods*. 204:35-43.
- Nadeau S, Filali M, Zhang J, Kerr BJ, Rivest S, Soulet D, Iwakura Y, de Rivero Vaccari JP, Keane RW, Lacroix S (2011) Functional Recovery After Peripheral Nerve Injury is Dependent on the Pro-Inflammatory Cytokines IL-1 β and TNF: Implications for Neuropathic Pain. *J Neurosci*. 31:12533-12542.
- Naff N, Williams MA, Keyl PM, Tuhim S, Bullock MR, Mayer SA, Coplin W, Narayan R, Haines S, Cruz-Flores S, Zuccarello M, Brock D, Awad I, Ziai WC, Marmarou A, Rhoney D, McBee N, Lane K, Hanley DF Jr (2011) Low-Dose Recombinant Tissue-Type Plasminogen Activator Enhances Clot Resolution in Brain Hemorrhage: The Intraventricular Hemorrhage Thrombolysis Trial. *Stroke*. 42:3009-3016.
- Nance PW, Huff FJ, Martinez-Arizala A, Ayyoub Z, Chen D, Bian A, Stamler D (2011) Efficacy and Safety Study of Arbaclofen Placabil in Patients with Spasticity Due to Spinal Cord Injury. *Spinal Cord*. 49:974-980.
- Nash MS, Lewis JE, Dyson-Hudson TA, Szlachcic Y, Yee F, Mendez AJ, Spungen AM, Bauman WA (2011) Safety, Tolerance, and Efficacy of Extended-Release Niacin Monotherapy for Treating Dyslipidemia Risks in Persons with Chronic Tetraplegia: A Randomized Multicenter Controlled Trial. *Arch Phys Med Rehabil*. 92:399-410.
- Nash MS, Dalal KL, Martinez-Barrizonte J, Cardenas DD (2011) Suppression of Proatherogenic Inflammatory Cytokines as a Therapeutic Countermeasure to CVD Risks Accompanying SCI. *Top Spinal Cord Inj Rehabil*. 16:14-32.
- Noga BR, Johnson DM, Riesgo MI, Pinzon A (2011) Locomotor-Activated Neurons of the Cat. II. Noradrenergic Innervation and Colocalization with NE α 1a or NE α 2b Receptors in the Thoraco-Lumbar Spinal Cord. *J Neurophysiol*. 105:1835-1849.
- Noor NM, Steer DL, Wheaton BJ, Ek CJ, Truettner JS, Dietrich WD, Dziegielewska KM, Richardson SJ, Smith AI, Vandeberg JL, Saunders NR (2011) Age-Dependent Changes in the Proteome Following Complete Spinal Cord Transection in a Postnatal South American Opossum (monodelphis domestica). *PLoS One*. 6:e27465.
- Ohl DA, Quallich SA, Sonksen J, Brackett NL, Lynne CM (2011) Treatment of Ejaculatory Dysfunction. In: *Surgical and Medical Management of Male Infertility*. M Goldstein, PN Schlegel eds. Cambridge University Press, Cambridge, 127-132.
- Oliva AA Jr, Kang Y, Sanchez-Molano J, Furones C, Atkins CM (In press) STAT3 Signaling After Traumatic Brain Injury. *J Neurochem*.
- Oliva AA Jr, Kang Y, Truettner JS, Sanchez-Molano J, Furones C, Yool AJ, Atkins CM (2011) Fluid-Perfusion Brain Injury Induces Changes in Aquaporin Channel Expression. *Neuroscience*. 180: 272-279.
- Patrick E, Orazem ME, Sanchez JC, Nishida T (2011) Corrosion of Tungsten Microelectrodes Used in Neural Recording Applications. *J Neurosci Methods*. 198:158-171.
- Raval AP, Hirsch N, Dave KR, Yavagal DR, Bramlett H, Saul I (2011) Nicotine and Estrogen Synergistically Exacerbate Cerebral Ischemic Injury. *Neuroscience*. 181: 216-225.
- Ross AL, Panthaki Z, Levi AD (2011) Surgical Management of a Giant Plexiform Neurofibroma of the Lower Extremity. *World Neurosurg*. 75:754-757.
- Sakurai A, Atkins CM, Alonso OF, Bramlett HM, Dietrich WD (In press) Mild Hyperthermia Worsens the Neuropathological Damage Associated with Mild Traumatic Brain Injury in Rats. *J Neurotrauma*.
- Sanchez JC, Lytton WW, Carmena JM, Principe JC, Fortes J, Barbour R, Francis JT (In press) Hybrid Computational and Biological Tools for Dynamically Repairing and Replacing Neural Networks. *IEEE PULSE*.

Scheithauer BW, Amrami KK, Folpe AL, Silva AI, Edgar MA, Woodruff JM, Levi AD, Spinner RJ (2011) Synovial Sarcoma of Nerve. *Hum Pathol.* 42:568-577.

Schürer SC, Vempati U, Smith R, Southern M, Lemmon V (2011) Bioassay Ontology Annotations Facilitate Cross-Analysis of Diverse High-Throughput Screening Data Sets. *J Biomol Screen.* 16:415-426.

Smith RP, Lerch-Haner JK, Pardinas JR, Buchser WJ, Bixby JL, Lemmon VP (2011) Transcriptional Profiling of Intrinsic PNS Factors in the Postnatal Mouse. *Mol Cell Neurosci.* 46:32-44.

Steeves JD, Kramer JK, Fawcett JW, Cragg J, Lammertse DP, Blight AR, Marino RJ, Ditunno JF Jr, Coleman WP, Geisler FH, Guest J, Jones L, Burns S, Schubert M, van Hedel HJ, Curt A; EMSCI Study Group (2011) Extent of Spontaneous Motor Recovery After Traumatic Cervical Sensorimotor Complete Spinal Cord Injury. *Spinal Cord.* 49:257-265.

Steward O, Popovich PG, Dietrich WD, Kleitman N (In press) Replication and Reproducibility in Spinal Cord Injury Research. *Exp Neurol.*

Streit WJ, Xue QS, Prasad A, Sankar V, Knott E, Dyer A, Reynolds J, Nishida T, Zacharias DA, Shaw G, Sanchez JC (In press) Tissue, Electrical, and Material Responses in Electrode Failure. *IEEE PULSE.*

Sun F, Park KK, Belin S, Wang D, Lu T, Chen G, Zhang K, Yeung C, Feng G, Yankner BA, He Z (2011) Sustained Axon Regeneration Induced by Co-Deletion of PTEN and SOCS. *Nature.* 480:372-375.

Truettner JS, Alonso OF, Bramlett HM, Dietrich WD (2011) Therapeutic Hypothermia Alters MicroRNA Responses to Traumatic Brain Injury in Rats. *J Cereb Blood Flow Metab.* 31:1897-1907.

Tseng LA, Bixby JL (2011) Interaction of an Intracellular Pentraxin with a BTB Kelch Protein is Associated with Ubiquitylation, Aggregation, and Neuronal Apoptosis. *Mol Cell Neurosci.* 47:254-264.

Visser U, Abeyruwan S, Vempati U, Smith RP, Lemmon V, Schürer SC (2011) Bioassay Ontology (BAO): A Semantic Description of Bioassays and High-Throughput Screening Results. *BMC Bioinformatics.* 12:257.

Wallace DM, Ross BH, Thomas CK (In press) Characteristics of Lower Extremity Clonus After Human Cervical Spinal Cord Injury. *J Neurotrauma.*

Wahman K, Nash MS, Lewis JE, Seiger A, Levi R (2011) Cardiovascular Disease Risk and the Need for Prevention After Paraplegia Determined by Conventional Multifactorial Risk Models: The Stockholm Spinal Cord Injury Study. *J Rehabil Med.* 43:237-242.

Wang X, de Rivero Vaccari JP, Wang H, Diaz P, German R, Marcillo AE, Keane RW (In press) Activation of the Nuclear Factor E2-Related Factor 2/Antioxidant Response Element Pathway is Neuroprotective After Spinal Cord Injury. *J Neurotrauma.*

Widerström-Noga E (In press) *In Spinal Cord Medicine (2nd Edition*, Steven Kirschblum, Denise I. Campagnolo (Eds) Lippincott Williams & Wilkins.

Williams RR, Pearse DD, Tresco PA, Bunge MB (In press) The Assessment of Adeno-Associated Vectors as Potential Intrinsic Treatment for Brainstem Axon Regeneration. *J Gene Med.* doi:10.1002/jgm.1628.

Zariffa J, Kramer JL, Fawcett JW, Lammertse DP, Blight AR, Guest J, Jones L, Burns S, Schubert M, Bolliger M, Curt A, Steeves JD (2011) Characterization of Neurological Recovery Following Traumatic Sensorimotor Complete Thoracic Spinal Cord Injury. *Spinal Cord.* 49:463-471.

Zhang YP, Fu ES, Sagen J, Levitt RC, Candiotti KA, Bethea JR, Brambilla R (2011) Glial NF-kappa B Inhibition Alters Neuropeptide Expression After Sciatic Nerve Injury in Mice. *Brain Res.* 1385:38-46.

Zhuang Z, Huang J, Cepero ML, Liebl DJ (2011) Eph Signaling Regulates Gliotransmitter Release. *Commun Integr Biol.* 4:223-226.

Zijdewind I, Gant K, Bakels R, Thomas CK (In press) Do Additional Inputs Change Maximal Voluntary Motor Unit Firing Rates After Spinal Cord Injury? *Neurorehabil Neural Repair.*

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