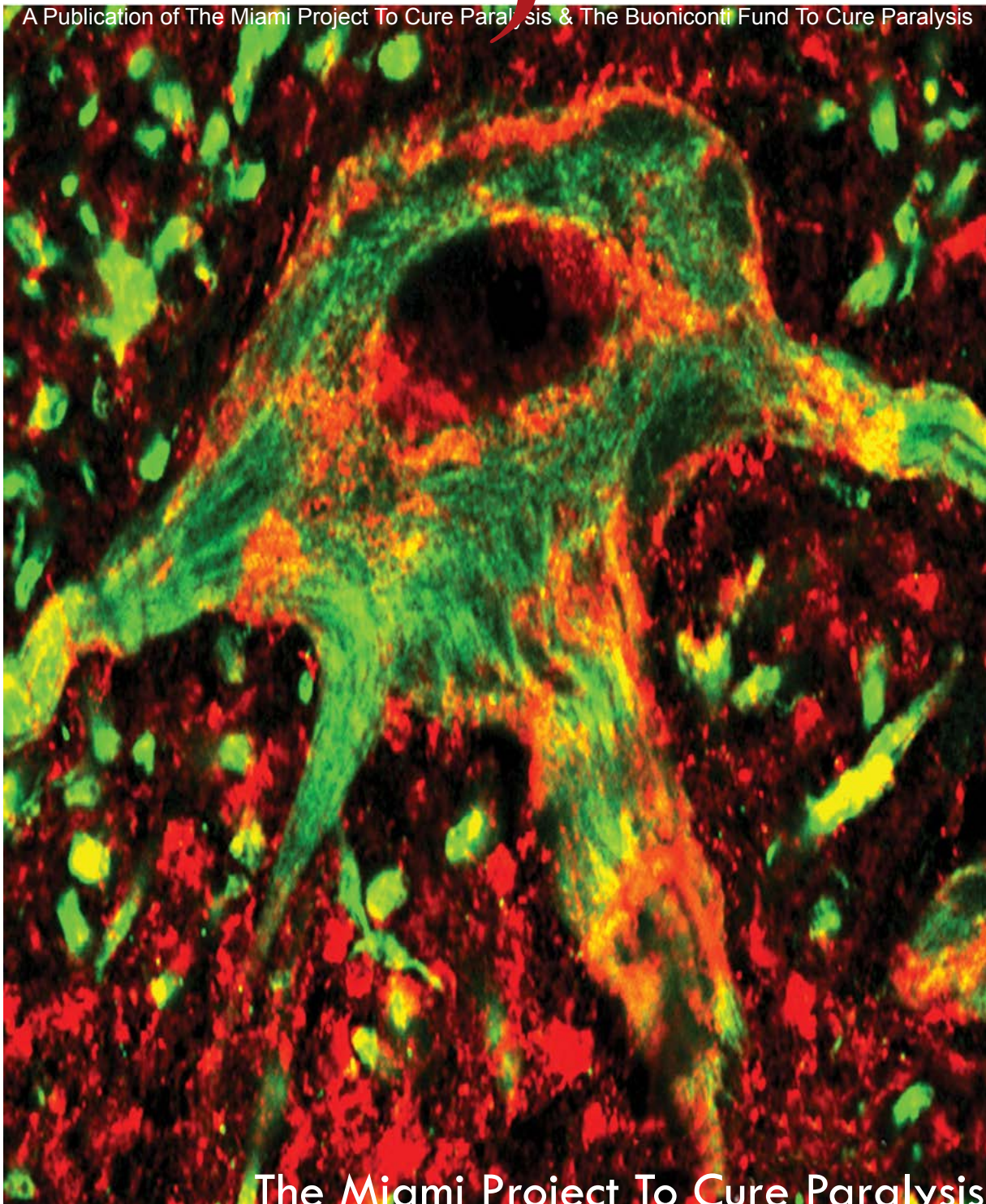


# THE PROJECT

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



The Miami Project To Cure Paralysis  
Research Review

2013



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.

The Miami Project to Cure Paralysis was established in 1985 to investigate mechanisms responsible for the detrimental consequences of spinal cord injury and to develop novel therapies to improve function in these individuals. Today, The Miami Project is an internationally recognized research institute that utilizes a multidisciplinary approach to target the devastating consequences of central nervous system injury and repair. Over the last several years, our discoveries have been successfully translated to people and in some instances have changed the way we provide care for individuals living with brain and spinal cord injuries. Our organization is unique in that it continues to concentrate on each critical stage of medical research including discovery, translational as well as clinical studies and trials. Our educational outreach programs help train the next generation of scientist clinicians and provide an important resource to the public for information regarding research and treatments.

This year has been the most exciting to date in the history of The Miami Project to Cure Paralysis. We have now successfully obtained four FDA-approved clinical trials

targeting spinal cord injury. Our Phase 1 Safety Trial to evaluate autologous human Schwann cell transplantation in subjects with subacute spinal cord injury is ongoing. We have successfully transplanted millions of Schwann cells into the injured spinal cord with no adverse effects. We are continuing to recruit additional subjects to evaluate the safety of this exciting experimental therapy. Future clinical investigations will evolve into the use of this therapy in subjects with incomplete injuries and in chronically injured individuals, which represent a significant population of subjects who could benefit from Schwann cell therapies.

[Another FDA approved trial](#) using Schwann cells targets peripheral nerve injury. This year, we received FDA approval to test autologous Schwann cells in combination with bridging strategies to promote regeneration after peripheral nerve injury which occurs following various types of trauma. Deep brain stimulation which is effective in patients with degenerative diseases such as Parkinson's disease is now being evaluated to target neuropathic pain in spinal cord injured subjects. This FDA approved program which is being conducted in concert with the Veterans Administration Hospital will hopefully provide new strategies for targeting this major quality of life consequence of spinal cord injury. Finally, our brain-machine interface program is generating excitement in the field whereby the merging of biological and biomedical fields will hopefully allow individuals to move their upper extremities which will enhance their independence. In this FDA approved trial, the ability to bypass gaps in the spinal cord with impulses coming from the brain to simulate muscle contraction is being led by our scientists and collaborators.

We continue to investigate the role of therapeutic hypothermia and temperature management in our patient populations with brain and spinal cord injury. In the area of spinal cord injury, treated individuals are being evaluated to determine safety and efficacy of this promising treatment in a proposed multicenter trial. For traumatic brain injury, therapeutic hypothermia also continues to be an important approach to limiting secondary injury mechanisms. Our scientists have identified a specific group of severe TBI subjects that may benefit most from early cooling. These particular clinical programs are an excellent example of how basic and translational studies have been successfully translated to the clinic.



In addition to these mentioned clinical studies, various clinical programs are actively investigating other aspects of spinal cord and brain injury that can hopefully improve function in patients. Our Miami Project Boot Camp is combining several neurorehabilitation modalities to promote function in people living with chronic spinal cord injury. Our ultimate goal is to combine state-of-the-art neurorehabilitation and conditioning strategies with cell therapies and other regenerative approaches to promote functional recovery. These types of combination approaches, important to the field of reparative medicine, are providing new possibilities to maximize cellular therapies and other rehabilitation protocols. In addition to motor function, studies continue to target neuropathic pain, male fertility, spasticity, bladder inflammation and other consequences of spinal cord injury that are becoming more common as our spinal cord injury community ages. Indeed, The Project is focusing on various factors associated with aging that will reduce comorbidities such as cardiovascular disease and diabetes or detect accelerated aging. The Miami Project is committed to developing whole life strategies that can maximize quality of life and good health in our research participants as our scientists continue to strive to develop new therapeutic interventions.

Discovery research, which fuels our clinical programs, also continues to prosper within The Miami Project to Cure Paralysis. Our scientific community is made up of outstanding researchers who are discovering new molecular and cellular mechanisms underlying cell death, axonal regeneration, and circuit repair. Ultimately, this new knowledge will be combined with our current therapeutic interventions to maximize protection and repair to promote functional recovery. The opportunity to clarify critical gaps in our knowledge regarding axonal regeneration and circuit plasticity can only improve our chances of developing cures for paralysis.

Each year Miami Project scientists compete for foundation and federal grants to support their laboratory investigations. Over the past year, our scientists have received numerous grants from the National Institutes for Health as well as the Department of Defense. These studies are helping to promote all phases of our research mission targeting brain and spinal cord injury. In addition, foundation funding from various spinal cord injury agencies is providing important support for our interdisciplinary programs. In combination with funds being generated by The Buoniconti Fund as well as The Miami Project, this important funding allows us to push forward the boundaries of our knowledge regarding paralysis and moving our discoveries into the clinic. The new, to be built, Christine Lynn Rehabilitation Hospital will allow for state-of-the-art neurorehabilitation strategies discovered in the research laboratory to be more efficiently translated into a large patient population undergoing clinical rehabilitation targeting a variety of acute and chronic human disorders.

These are indeed exciting times within The Miami Project and we thank our friends, colleagues, and research participants for their long-term support and commitment to our research. 2014 will definitely be another outstanding year for our research programs, and we thank everyone for their interest and contribution to our program.

Sincerely,

Barth A. Green, M.D., F.A.C.S.  
Co-Founder and Chairman, The Miami Project  
Professor and Chairman, Department of Neurological Surgery  
Professor, Departments of Orthopaedics  
and Rehabilitation Medicine  
University of Miami Miller School of Medicine

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Scientific Director, The Miami Project  
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	A Leader by Example Dr. Barth A. Green  6
	10 Faculty Spotlight Daniel Liebl, Ph.D.
	Dr. Mary Bunge Elected to The Institute of Medicine  11
	16 Staying Healthy After Spinal Cord Injury
	STTR Inflammation Business Grant  22

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## Research Review 2013

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

### RESEARCH HIGHLIGHTS

- 6 A Leader by Example Dr. Barth A. Green
- 8 Therapeutic Potential of Autologous Schwann Cell Transplantation
- 10 Faculty Highlight Daneil Liebl, Ph.D.
- 11 Dr. Mary Bunge
- 12 Active Clinical Studies and Trials
- 14 Education Outreach
- 16 Staying Healthy After SCI
- 18 Research Funding

### FEATURE ARTICLE

- 22 STTR Inflammation Business Grant
- 24 Faculty Profiles
- 34 Gail F. Beach Memorial Lecture Series
- 35 John R. Bethea, Ph.D.
- 36 Summer Student Research
- 37 Scientific Research Publications 2012
- 43 Aisha Khan

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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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Tim Saltsman  
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Maria Serna  
Jacqueline Tommasino

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Post-doctoral Fellows 14  
Graduate Students 20  
Medical/Residents/Observorships 16  
Undergraduate Students 55  
Volunteers 22  
Other students 11  
Research Staff 76

# A LEADER by EXAMPLE



Dr. Barth A. Green has never been one to shy away from situations others deem impossible. It is his true humanity and unwavering commitment that contribute to his success, and his passion for helping others.

**D**r. Green has been a true champion for spinal cord injury (SCI) research. He completed his Bachelor's degree and Medical degree at Indiana University in the late 1960's, then went on to Northwestern University in Chicago to complete his neurological surgery residency training. He performed laboratory research while at both universities and his first research publication was in 1971. It was about the swelling (edema) that occurs inside the spinal cord immediately after injury. In 1973 he published some of the earliest research demonstrating the beneficial effects of local hypothermia in an animal model of SCI. Other topics in his early research were evaluating blood flow and tissue oxygenation in a rat model of SCI and scar tissue formation in a primate model of SCI. During his entire career he has published over 70 book chapters and over 190 peer-reviewed research articles!






Dr. Barth Green in the Army Reserves (left), Haiti (center), and Jackson Memorial Hospital (right).

Dr. Green was recruited to Miami in 1975 as a junior faculty member in the University of Miami Miller School of Medicine Department of Neurological Surgery. At the same time he joined the neurosurgery service at Jackson Memorial Hospital and the Miami Veterans Administration Hospital Medical Center. He established long-term clinical and research collaborations with the Departments of Orthopaedics and Rehabilitation, Neurology, and Radiology. He worked tirelessly providing clinical care to those who suffered spinal cord damage. In 1978 he helped establish and co-direct the first South Florida Regional Spinal Cord Injury Model System of Care. He and his colleagues were working to continually improve early, comprehensive care to achieve the best outcome for individuals with SCI. He also participated in the early methylprednisolone clinical trials for SCI in the 1980's. By 1985 he had become a full professor, and a perfect storm was brewing.

Dr. Green wanted to create a new way of thinking about spinal cord injury research. He wanted to develop a model that spurred research efforts and inspired hope, much like the Manhattan Project in the early 1940's. The main goal was to increase the number of research laboratories studying all aspects of SCI, basic and clinical, by recruiting premier scientists with diverse expertise and by training students who would go on to establish new SCI research laboratories throughout the world. The ultimate goal – to develop cures for SCI. The Miami Project was founded in 1985 by Dr. Green and 3 individuals who had recently sustained spinal cord trauma – Donald Misner, Beth Roscoe, and Marc Buoniconti and their families who began fundraising and raising awareness for SCI research, and Dr. Green began building.

Now, The Miami Project is the world's most comprehensive SCI research center and has been the model by which many other research centers have been built. The Miami Project has made a multitude of advances on all fronts including injury prevention, neuroprotection, cell replacement, regeneration, scar manipulation, rehabilitation, exercise conditioning, muscle spasticity, pain, and male fertility. The Miami Project has entered the era of translating our knowledge into clinical trials and more will be developed every year. And all along Dr. Green was a believer, and a leader.

Dr. Green's passion and leadership spread beyond The Miami Project. He served in the U.S. Army Reserves Medical Corps from 1965-2002, when he retired as a Lieutenant Colonel. He volunteered with the U.S. Coast Guard Auxiliary from 1985-1990. He also co-founded Shake-A-Leg with Harry Horgan, an adaptive water sports and education program serving thousands of children and adults annually who have physical, developmental, and financial challenges. And in 1996 he and Dr. Arthur Fournier co-founded Project Medishare for Haiti. Project Medishare is a volunteer organization that provides medical care for over 180,000 people annually. After the devastating earthquake in 2010, Project Medishare mobilized the first medical team on ground within 12 hours and has continued ever since. Dr. Green still spends several weeks each year working hands-on in Haiti.

For almost 50 years now Dr. Green's passion and unyielding commitment for helping others has made him a leader, the kind of leader people really follow – one who leads by example. 

# Expanding the Therapeutic Potential of Autologous Schwann Cell Transplantation to Peripheral Nerve Repair

*“We felt it was extremely important to literally utilize everything in our toolbox to make an effort to give this young lady a chance at recovering some function and sensation in her leg.”*

Dr. Allan Levi, Professor and senior faculty member at The Miami Project to Cure Paralysis, Chief of Neurospine service at Jackson Memorial Hospital, and Chief of Neurosurgery at University of Miami Hospital recently performed the world’s first peripheral nerve graft augmented by autologous Schwann cells in an attempt to repair a severely injured sciatic nerve. [The FDA approved](#) study took place at the University of Miami/Jackson Memorial Hospital.

The patient, Danielle Press, suffered life-threatening injuries in a boating accident off the coast of Key Biscayne on September 14, 2013. She was rushed to Ryder Trauma Center at the University of Miami/Jackson Memorial Medical Center with several deep, lacerating injuries to her upper leg. Trauma surgeons immediately operated on the young woman, to save her life and leg, and discovered that the sciatic nerve in her left leg, which controls the majority of movement and sensation in the leg, had been completely cut and separated. At that point, [Dr. Levi](#) was called in because of his expertise in peripheral nerve surgery.

Repairing the sciatic nerve - the largest nerve in the human body - presents one of the most difficult challenges in nerve surgery, particularly when a significant gap exists, as was the case with this patient. One of the major limiting factors in the repair of this nerve is the absence or lack of sufficient donor nerve material. Even in cases in which a relatively small gap exists, the donor sural nerves, which are the typical nerves that are harvested to perform this



Dr. Allan Levi (right) during a follow-up evaluation with Danielle Press (center) and research coordinator Dr. Marine Dididze (left).


repair, are insufficient because the cross-sectional area of the sciatic nerve is at least 15 to 20 times the width of the donor sural nerve. This means that only a fraction of the damaged axons have a nerve substrate to grow into. Insufficient donor material reduces the chance of successful regeneration through a segmental defect.

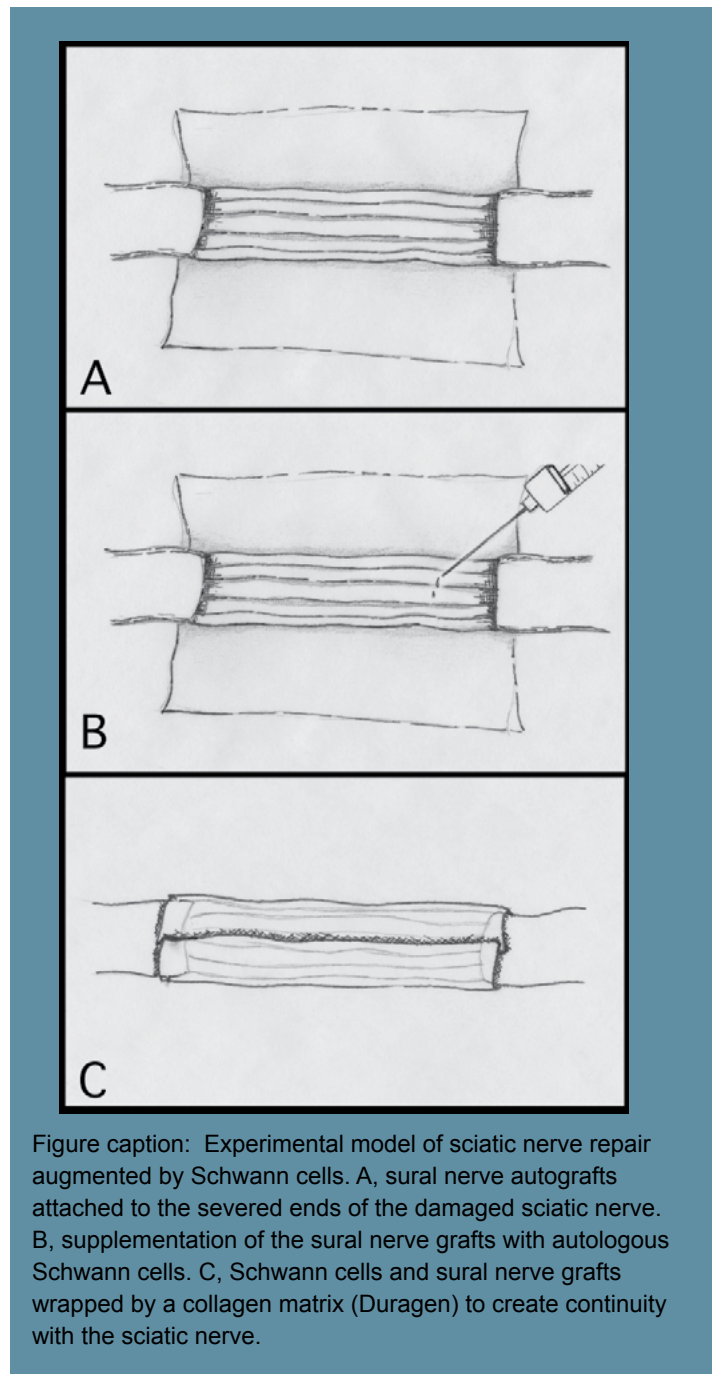


Dr. Levi, who specializes in the field of spine and peripheral nerve surgery, considered traditional nerve grafting, but felt that a better outcome might be obtained if the nerve graft was augmented with autologous Schwann cells, expanded in number using cell culture techniques. Schwann cells are involved in many important aspects of peripheral nerve biology including the conduction of nervous impulses along axons, nerve development, and regeneration. Dr. Levi and his team are already leading an FDA approved Phase I clinical trial testing the safety of autologous Schwann cell transplantation for acute spinal cord injuries. Pre-clinical work suggested that the use of Schwann cells could also be beneficial in unique cases of severe peripheral nerve injury.

Drs. Levi, Anderson-Erisman, and Dididze immediately went to work to obtain special approval from the FDA and University of Miami Institutional Review Board for this single patient to combine standard nerve grafting with autologous human Schwann cells, with a goal of providing an opportunity to maximize nerve regeneration and restoration of function. On October 14, Dr. Levi performed a nerve graft on the now research participant using a combination of her own nerves and her own Schwann cells. This world's first procedure was done at Jackson Memorial Hospital. "At the University of Miami and Jackson Memorial Hospital we always provide not only the standard of care, but try to think outside the box in order to change the practice of medicine and better people's lives," Dr. Levi said. "We felt it was extremely important to literally utilize everything in our toolbox to make an effort to give this young lady a chance at recovering some function and sensation in her leg." Dr. Levi and his team believe that by combining standard nerve grafting with autologous human Schwann cells provides an opportunity to maximize nerve regeneration and restoration of function. This combination strategy for compassionate use is dictated by the severity of the current clinical case and forms the basis for this FDA approved single participant study. Enhancing the potential for nerve regeneration will potentially allow for motor and sensory recovery, including protective sensation. The medical team believed this approach, in which no viable alternative strategies exist to supplement repair, is the correct approach in implementing a new cellular strategy. Adapting the current, established FDA approved protocol of autologous human Schwann cell preparation for sub-acute thoracic SCI permitted the medical team to implement cell preparation relatively seamlessly and with considerable experience.

The research participant will continue to be followed for the next five years, during which time doctors will closely monitor her progress. As her condition improves, she will begin a long road of physical rehabilitation.

Dr. Levi and his team are now seeking funding from the Department of Defense for a full Phase I clinical trial testing this experimental combination. 




## Faculty Spotlight Dan Liebl, Ph.D.

**D**r. Dan Liebl is a Full Professor in the University of Miami department of Neurological Surgery and a faculty member of The Miami Project to Cure Paralysis. Dr. Liebl earned his Ph.D. at Kent State University in 1994 and went on to complete his post-doctoral training at the University of Texas Southwestern in Dallas in the laboratory of well-respected scientist Dr. Luis Parada. Dr. Liebl joined the faculty of The Miami Project in 2000.

The overarching goal of [Dr. Liebl's](#) research is to understand mechanisms that contribute to central nervous system (CNS) damage, which includes spinal cord injury (SCI) and traumatic brain injury (TBI), and develop new strategies aimed at minimizing damage and maximizing tissue repair. A few years ago Dr. Liebl's research team made an important discovery, in that, receptors critical for proper development of the CNS may negatively affect the injured adult CNS. These receptors have been termed "dependence receptors", which by definition requires dependence with their respective ligands (molecules that bind the receptor and cause it to change its properties) to induce positive signals (such as regulating axonal growth and guidance); however, following cellular stress and decreased ligand interactions these receptors undergo modifications to become death receptors. Interestingly, colleagues of Dr. Liebl first described dependence receptor roles in tumor/cancer progression, which led the way to Dr. Liebl's discoveries in the injured CNS. Dr. Liebl noted that "there are large amounts of similarities between cancer biology and the CNS injury field and new discoveries can be found by studying other fields of medicine." In the injured CNS, Dr. Liebl found that both neurons and oligodendrocytes, two of the most susceptible cells to traumatic injury, undergo dependence receptor-mediated cell death after injury. Dr. Liebl has also shown that these death signals can be blocked by reapplication of ligands through infusion techniques, which prevents neuron and oligodendrocytes cell death in animal models. In short, dependence receptors represent a new therapeutic strategy to reduce progressive injury known to occur for months and even years in humans after the initial trauma has occurred.

Dr. Liebl identified two additional roles for dependence receptors that could impact the recovery process. First, dependence receptors also regulate residential neural stem/progenitor cell (NSPC) survival, where NSPCs that reside in a specific region of the adult brain represent a potentially

important target for endogenous cell replacement strategies after CNS injury. In particular, Dr. Liebl discovered that NSPCs express certain dependence receptors and blocking their ligand-mediated cell death can enhance the overall NSPC population. Second, in the injured brain, NSPCs are believed to have the capacity to move to injured tissue areas, and expanding this population in neurogenic regions is the first step to generating a large enough population to alter injury progression and recovery. Furthermore, these findings have also led to the hypothesis that cell transplantation strategies may benefit from blocking dependence receptor functions, where a majority of stem cells from multiple sources are known to undergo dramatic cell death shortly after transplantation.

In parallel to conducting his research Dr. Liebl has trained multiple graduate students and post-doctoral fellows. He was also Director of the Neuroscience Graduate Program at the University of Miami from 2008-2013. His research has been extensively funded by the National Institutes of Health and he reviews grants for several agencies. 



# Dr. Mary Bartlett Bunge Elected to the Institute of Medicine

*“Ever since childhood I have wanted to make a difference and do something worthwhile - I hope that this honor helps confirm that I have achieved this goal.”*




In October 2013, Mary Bartlett Bunge, Ph.D., Professor, Cell Biology, Neurological Surgery and Neurology at the University of Miami Miller School of Medicine's Miami Project to Cure Paralysis was elected as a member Institute of Medicine (IOM). Election to the [IOM](#) is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service. “Dr. Bunge’s distinguished scientific career has spanned more than 50 years, a period during which she not only made numerous seminal discoveries but also helped advance the careers of many other distinguished scientists,” said Pascal J. Goldschmidt, M.D., Senior Vice President for Medical Affairs and Dean of the Miller School. “We are delighted that the IOM values her accomplishments, expertise, and service as much as we do. We are all extremely proud of Dr. Bunge.”

[Dr. Bunge](#) has worked for nearly four decades on a specific cell, the Schwann cell, found in the peripheral nervous system that she and her late husband, Richard Bunge, M.D., judged to be an important component to repairing the damaged spinal cord. Her work with Schwann cells has led to numerous discoveries, and is now central to an FDA approved Phase I clinical trial using autologous Schwann cells in subacute spinal cord injured individuals. This work will serve as a foundation for future cell replacement and regeneration trials at The Miami Project.

“I am very surprised but very deeply honored to have been selected to be a member of the IOM. Ever since childhood I have wanted to make a difference and do something worthwhile - I hope that this honor helps confirm that I have achieved this goal. Throughout my career I have had very exceptional mentors so I have been very fortunate in being able to fly on the wings of eagles,” said Bunge, the Christine E. Lynn Distinguished Professor in Neuroscience. True to her selfless style, Dr. Bunge shares this distinction with her deceased husband Dr. Richard Bunge, with whom she worked for nearly 40 years, and also [Dr. Patrick Wood](#) and numerous outstanding students and fellows who were trained in their laboratory.

“It is an honor to welcome our highly distinguished colleagues to the IOM,” said IOM President Harvey V. Fineberg. “These individuals have inspired us through their achievements in research, teaching, clinical work, and other contributions to the medical field. Their knowledge and skills will deeply enrich the IOM.” At its 43<sup>rd</sup> annual IOM meeting 70 new members and 10 foreign associates were added. New members are elected by current active members through a selective process that recognizes individuals who have made major contributions to the advancement of the medical sciences, health care, and public health. IOM’s charter ensures diversity of talent among the Institute’s membership by requiring at least a fourth of the members to be selected from fields outside the health professions, such as engineering, social sciences, law, and the humanities. The newly elected members raise IOM’s total active membership to 1,753 and the number of foreign associates to 120. With an additional 93 members holding emeritus status, IOM’s total membership is 1,966.

The IOM is unique in its structure as both an honorific membership organization and an advisory organization. Established in 1970 by the National Academy of Sciences, IOM has become recognized as a national resource for independent, scientifically informed analysis and recommendations on health issues. With their election, members make a commitment to volunteer their service on IOM committees, boards, and other activities. Projects during the past year include studies of environmental factors in breast cancer, health information technology and patient safety, nutrition rating systems and graphics on food packaging, the scientific necessity of chimpanzees in research, establishing crisis standards of care during catastrophic disasters, improving care for epilepsy, and treatment of post-traumatic stress disorder. 



Beginning 2014, The Miami Project clinical researchers currently have 18 research studies available for people who have had a spinal cord injury. They are investigating questions regarding exercise science, rehabilitation training, pain, male fertility, aging, and neuroprosthetics.

TOPIC	STUDIES	POPULATION
<b>Activity and Nutrient Modifying</b>	Cardiometabolic Risk, Obesity and Cardiovascular Disease in People with Spinal Cord Injury	C4-T12, motor complete
	Effect of an Omega-3 Supplement Intervention Program on Cardiometabolic Health in People with Spinal Cord Injury	C4-T12, motor complete
	Obesity/Overweight in Persons with Early and Chronic SCI: A Randomized Multi-Center Controlled Lifestyle Intervention	C5-L1, any severity
	New Walking Device (Bionic Exoskeleton) and Autonomic Dysreflexia in People with Spinal Cord Injury	C7-T6, any severity
	Clinically Meaningful Changes in Wheelchair Propulsion Stress	All levels, any severity
	Training Programs to Improve Outcomes for Individuals with Spinal Cord Injury	All levels, any severity
<b>Male Fertility</b>	Fertility Evaluation	All levels, any severity
	Treatment of Infertility	All levels, any severity
<b>Rehabilitation</b>	Influence of Sensory Input on Spasticity and Walking Function in Individuals with SCI	T12 or above, any severity
	Skilled Motor Training and tDCS to Improve Leg Function After SCI	T12 or above, motor incomplete
	Prospective, Randomized Controlled Trial for Shoulder Pathology and Pain in Chronic SCI	T1-T12, motor complete or mild incomplete
<b>Pain</b>	Experiences of living with persistent pain after a spinal cord injury	L1 or above, any severity
	International Spinal Cord Injury Basic Pain Data Set Survey for Self-Report Measure	All levels, any severity
<b>Brain Machine Interface</b>	Assessment of Candidates and Design Considerations for Neuroprosthetic Devices for Individuals with Chronic Spinal Cord Injury	C5-C6, motor complete
	Treatment of Pain and Autonomic Dysreflexia in Spinal Cord Injury with Deep Brain Stimulation	T6 or above, incomplete
<b>Aging</b>	Telomeres as an Aging and Health Biomarker in Persons with Spinal Cord Injury	All levels, any severity
	Muscle Weakness and Fatigue with Age after Spinal Cord Injury	C2-C8, any severity
	Pilot Study Investigating the Impact of Time Post-Spinal Cord Injury on the Bladder Inflammatory Profile	All levels, any severity

The Miami Project also has [11 clinical trials](#) ongoing or in the planning stages to test interventional repair or neuroprotective strategies for spinal cord injury or traumatic brain injury. There has never been a more exciting time!

TREATMENT	POPULATION	PRE-CLINICAL	PHASES	
			1	2
AUTOLOGOUS SCHWANN CELLS	Acute SCI	Ongoing	Enrolling	
	Chronic SCI			
	Severe peripheral nerve injury		Enrolling, limited	
BIOMARKERS	Acute SCI		Enrolling	
	Acute TBI		Enrolling	
NACTN	Acute SCI		Enrolling	
RILUZOLE	Acute SCI		Completed	Pending
THERAPEUTIC HYPOTHERMIA	Acute SCI		Enrolling	Pending
	Acute TBI		Enrolling	
COSBID	Acute TBI		Enrolling	
INTREPID	Acute, Moderate, or Severe TBI			Enrolling



Ekso bionic stepping device (left); Dr. Ross Bullock (top middle); Harvesting Schwann cells from peripheral nerve fascicles (bottom middle); Drs. Allan Levi and Jim Guest in the OR preparing for a transplant (top right); Graduate student Katie Gant recording brain activity to screen for the brain machine interface study (bottom right).

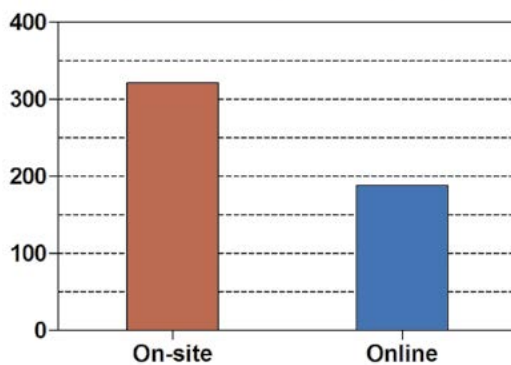
# Communication Education Outreach

## How to find the information you need

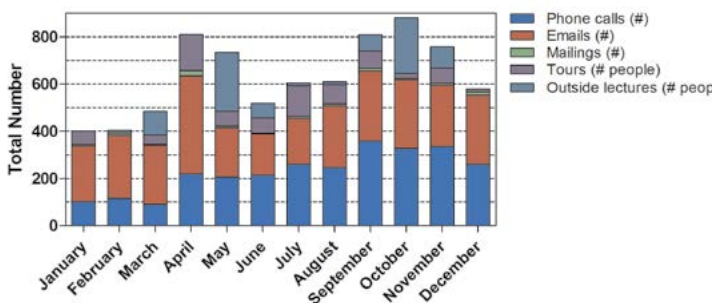


Activities during Open House 2013: Demonstration of brain stimulation (upper left), talking one-on-one with guests (lower left), open discussion between the audience and

2013 Research Participants



2013 Monthly Outreach



The Miami Project believes that an important component of developing treatments for paralysis involves communication with the community. The Education department, directed by [Kim Anderson-Erisman, Ph.D.](#), is responsible for helping thousands of our community members each year. The other valuable members of the department are Maria Chagoyen, Danielle Cilien, and Letitia Fisher. The department answers phone calls and emails to provide people with information about all of our research programs as well as provide information about injury prevention, clinical care referral, resources for living with paralysis, and advice about unproven therapies around the world. They conduct numerous tours and lectures about our research. The top graph shows the total number of people reached each month during 2013 outreach activities. The Education department also assists all of The Miami






t), community guests viewing cells through microscopes (upper right), faculty and faculty members (lower right).



Brain Fair March 2013 and Disability Mentoring Day October 2013

and plans for targeting chronically injured individuals in the future, neuroprotective interventions, including the hypothermia trial, and an upcoming trial using deep brain stimulation to attempt to reduce severe neuropathic pain were discussed. This was followed by a “Meet the Scientists” session in which the audience met 15 of our faculty, heard brief explanations of their current research, and had the opportunity to ask questions. The final component of the day was behind-the-scenes tours of four laboratories, including a cell culture lab, regeneration lab, neurotrauma injury model lab, and human rehabilitation lab. There were over 140 members in attendance and the event was a great success! The 4<sup>th</sup> Annual Community Open House is scheduled for April of 2014.

The Education department also participated in the 4<sup>th</sup> Annual Brain Fair and Take Your Child to Work Day, hosted Disability Mentoring Day for the 4<sup>th</sup> year in a row, and gave invited lectures to multiple SCI consumer groups. If you have questions, don’t hesitate to email [mpinfo@med.miami.edu](mailto:mpinfo@med.miami.edu) or call us at 305-243-7108. 

Project clinical research faculty with recruitment for their clinical studies. During 2013, 500 people were able to participate in our studies targeting chronic spinal cord injury (SCI). In addition, Dr. Anderson-Erisman maintains a comprehensive resource page on The Miami Project website to provide individuals with tools for staying healthy while living with paralysis -- [www.themiamiproject.org/stayinghealthy](http://www.themiamiproject.org/stayinghealthy). This includes information about stretching, exercising, diet, nutrition, and sports and leisure activities.

On April 20, 2013 the Education department hosted the 3<sup>rd</sup> Annual Miami Project Community Open House. We opened up our doors to the public for an afternoon packed full of information. The afternoon began with a discussion session about clinical trials. This included the current Schwann cell trial targeting newly injured individuals



## IS LIFTING WEIGHTS ENOUGH?

## Staying Healthy After Spinal Cord Injury (SCI)

Exercising and maintaining optimal health is difficult for anyone these days; add on the effects of SCI (muscle paralysis, fat accumulation, reduced metabolism, nutritional imbalances, increased time and effort to perform tasks, medication side effects, etc.) and it can easily become overwhelming! So then how should one go about trying to tackle this to best achieve and maintain a healthy life long into the future?

Dr. Mark Nash and his colleagues have been working on this theme in the Applied Physiology Research Laboratory at The Miami Project since 1986. Of course, one important component is exercise. After evaluating many different types of exercise, Dr. Nash has narrowed in on Circuit Resistance Training (CRT). CRT is a form of exercising or conditioning the body by performing resistance training and short bursts of high-intensity aerobic activity. In Dr. Nash's circuit, there are six resistance activities performed with the arms and

alternated with an aerobic activity such as arm ergometry (arm cycling). These activities alternate in a specific pattern and with very little rest time in between. The goal is to increase strength and endurance, as well as the important fitness characteristics of anaerobic power (maximal power generated during full-force, short-term physical effort). Dr. Nash has demonstrated that this CRT paradigm does indeed increase muscle strength, endurance, and anaerobic power in people with SCI, and has published follow-up work showing success in treating persons with SCI entering 'middle age'.

Another important component of the optimal health equation involves nutrition. Diet is important for the able-bodied population, so why wouldn't it be equally - if not more important for the SCI population? One of Dr. Nash's current grant studies is evaluating nutritional modification, combined with exercise in people living with chronic SCI. After SCI, the rate at which calories





Example of a high protein supplement that can be used to create a blended drink to consume before and after training.


are burned is typically reduced. This is partially because paralyzed muscles begin to accumulate fat deposits as lean muscle mass atrophies (is wasted away), and those muscles are not as efficient in utilizing calories taken in through the diet. The logical approach is to reduce calories taken in through the diet, but more importantly to improve the nutritional density of food to provide more nutrients while allowing you to feel full after eating. This approach is being tested in the current study.

In trying to achieve a better balance between caloric intake and caloric expenditure one approach being investigated involves trying to increase lean mass in muscles that are not paralyzed by SCI. Dr. Nash recently published a study evaluating this approach. The idea of protein supplementation to increase fitness comes from the body building arena. Protein supplementation used immediately after working out has been used for decades by body builders to bulk up lean muscle by increasing muscle protein synthesis and decreasing degradation. Can this work for people with SCI too?

The goal of the study was to determine if protein supplementation enhanced the effects of CRT in people with cervical SCI. Participants in the main experimental

group performed CRT three times per week for 6 months. The protein supplementation used in the study can be purchased at most health food stores, and was a blended drink containing 48grams of chocolate or vanilla-flavored whey protein supplement (Gold Standard Natural 100% Whey, ON, Sunrise, FL or Metabolic Whey, MRM, Vista, CA) containing 36-37 grams of protein, less than 8 grams of carbohydrates, and less than 4 grams of fat. The blended drink was split in half and consumed immediately before and immediately after each training session. A second experimental group drank the protein supplement on days when they did not exercise (“delayed” protein supplementation). The study demonstrated (1) that CRT is a very effective mode of exercise for people with cervical SCI and (2) that protein supplementation immediately before and after CRT training sessions further improved energy metabolism.

In 2014, Dr. Nash will be releasing a DVD of a multidisciplinary exercise program specifically for people with SCI that can be done in the community or at home. The DVD will cover resistance training, aerobic fitness, and tai chi (an ancient Chinese graceful form of exercise) with multiple routines for people to follow along. When ready, the DVD will also be posted on the Staying Healthy page of our website, [www.themiamiproject.org/stayinghealthy](http://www.themiamiproject.org/stayinghealthy).

So, it looks like lifting weights is an important aspect of improving and maintaining health after SCI, but a combination of nutritional balance and cross-training may be even better. Cheers! 



Filming for the multidisciplinary exercise DVD.



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 2013.

## Acorda Therapeutics, Incorporated

Dr. Corneliu Luca (P.I.), Dr. Edelle Field-Fote (Co-I.)

-A Randomized Trial to Evaluate Ampyra for Gait Impairment in Parkinson's Disease

## American Heart Association Scientific Development Grant

Dr. Juan Pablo De Rivero Vaccari (P.I.)

-Activation of Rig-like Receptor Signaling after Focal Cerebral Ischemia

## Center for Disease Control

Dr. Gillian Hotz (P.I.)

-Community Transformation

## Children's Tumor Foundation

Dr. Cristina Fernandez-Valle (P.I.), Dr. Paula Monje (Co-I.)

-Creation of Human Merlin-Null Schwann cells for NF2 Studies

## Christopher & Dana Reeve Foundation

Dr. James Guest (Center P.I.)

-North American Clinical Trials Network

## Craig H. Neilsen Foundation

Dr. Nancy Brackett (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)

-Improving Reproductive Function in Men with Spinal Cord Injury

Dr. Stanislava Jergova (P.I. – Post-doctoral Fellowship), Dr.

Jacqueline Sagen (Sponsor)

-Recombinant Stem Cell Therapy for Spinal Cord Injury Pain

Dr. Robert Keane (P.I.), Dr. Juan Pablo De Rivero Vaccari (Co-I.)

-Inflammasome Regulation Following Spinal Cord Injury

Dr. Daniel Liebl (P.I.)

-A Novel Eph Receptor-Mediated Mechanism of Cell Death Following Spinal Cord Injury

Dr. Mark Nash (P.I.)

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

Dr. Brian Noga (P.I.), Dr. Ian Hentall (Co-I.)

-Acute Facilitation of Walking After SCI Using Deep Brain Stimulation

Dr. Kevin Park (P.I.), Dr. Jae Lee (Co-I.)

-Novel Combinatorial Approaches to Promote Axon Regrowth After Chronic SCI

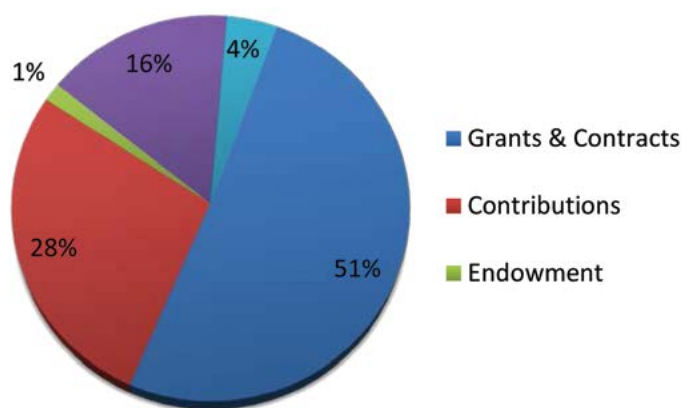
Dr. Urs Rutishauser (P.I.), Dr. Damien Pearse (Co-I.)

-Optimization of PST-Engineered Schwann Cells for SCI Repair

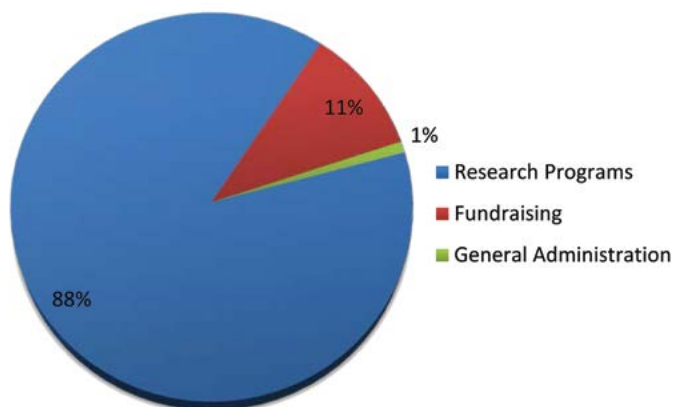
Dr. Jacqueline Sagen (P.I.)

-Utilizing Designer Genes to Alleviate Chronic SCI Pain

## Income



## Expenses



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

**Department of Defense (DOD) Defense Advanced Research Projects Agency (DARPA)**

Dr. Justin 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  
-Responsive NeuroRehabilitation using an Advanced Brain Monitoring BCI

Dr. Justin C. Sanchez (P.I.), Dr. Edelle Field-Fote (Co-I.)  
-Responsive Neurorehabilitation Using an Advanced Brain Monitoring BCI

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

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

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

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

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

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

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

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

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

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

**Department of Defense (DOD) Multiple Sclerosis Research Program of the Office of the Congressionally Directed Medical Research Programs**

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

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

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

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

Dr. M. Ross Bullock (Site-P.I.)  
-A Randomized, Double Blind, Placebo Controlled, Dose-Escalation Study of NNZ-2566 in Patients with Traumatic Brain Injury  
Dr. M. Ross Bullock (P.I.)  
-Clinical Phase IIB Trial of Oxycyte Perfluorocarbon in Severe Human Traumatic Brain Injury  
- Laboratory studies evaluating PFC in models of Penetrating, and closed TBI.

**E. Matilda Ziegler Foundation for the Blind**

Dr. Kevin Park (P.I.)  
-Novel Combinatorial Approaches to Enhance Retinal Ganglion Cell Survival and Axon Regeneration after Optic Nerve Injury

**FISM Fondazione Italiana Sclerosi Multipla (Italian Multiple Sclerosis Foundation)**

Dr. Roberta Brambilla (P.I.)  
-The Pro-Remyelination Effect of Transmembrane Tumor Necrosis Factor: Investigation Into the Role of Tumor Necrosis Factor Receptor 2

## Florida Department of Transportation

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

## 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  
 -Cellular Trials to Support Corticospinal Axon Regeneration in Non-Human Primates

## KiDZ Neuroscience Center

Dr. Gillian Hotz (P.I.)  
 -Accelerometer Concussion Study in College Football Players

## Medtronic Spinal and Biologics

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

Dr. Justin Sanchez (P.I.)  
 -Fully Implantable Brain-Machine Interface for Humans with Spinal Cord Injury

## National Eye Institute

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

## National Football League Charities Medical Research

Dr. Coleen Atkins (P.I.)  
 -The Effects of Mild Hyperthermia on Outcome after Mild Traumatic Brain Injury

## National Heart, Lung, and Blood Institute

Dr. David Fuller (P.I.), Dr. Justin 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 Nash (Co-I.)  
 -Improving Hand and Arm Function in Individuals with SCI

## National Institute of Disability & Rehabilitation Research

Dr. Diana Cardenas (P.I.), Dr. Rachel Cowan (Co-I.), Dr. Mark Nash (Co-I.)  
 -South Florida Spinal Cord Injury Model Systems

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

Dr. Mark Nash (P.I.), Dr. Kim Anderson-Erisman (Co-I.)  
 -Sleep Disordered Breathing in Persons with Chronic Tetraplegia: Characterization and Intervention

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

## National Institute of Neurological Disorders & Stroke

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

Dr. Kim Anderson-Erisman (Co-P.I.), Dr. W. Dalton Dietrich (Co-P.I.)  
 -NIH Neurotrauma Summer Research Experience Program

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

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

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

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

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

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



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

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

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

Dr. Jae Lee (P.I.)  
 -Role of Fibroblasts in Axon Regeneration After SCI  
 - Translational Profile of Perivascular Fibroblasts After Spinal Cord Injury

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

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

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

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

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

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

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

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

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

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

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

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

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

**University of Miami SAC Awards**  
 Dr. Ian Hentall (P.I.)  
 -Control of Brain Edema by Electrical Stimulation in Midbrain

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

Dr. Vance Lemmon (P.I.)  
 -A Novel Vaccine Strategy Targeting Cocaine

Dr. Daniel Liebl (P.I.)  
 -Remodeling Vascular Networks Following Traumatic Brain Injury

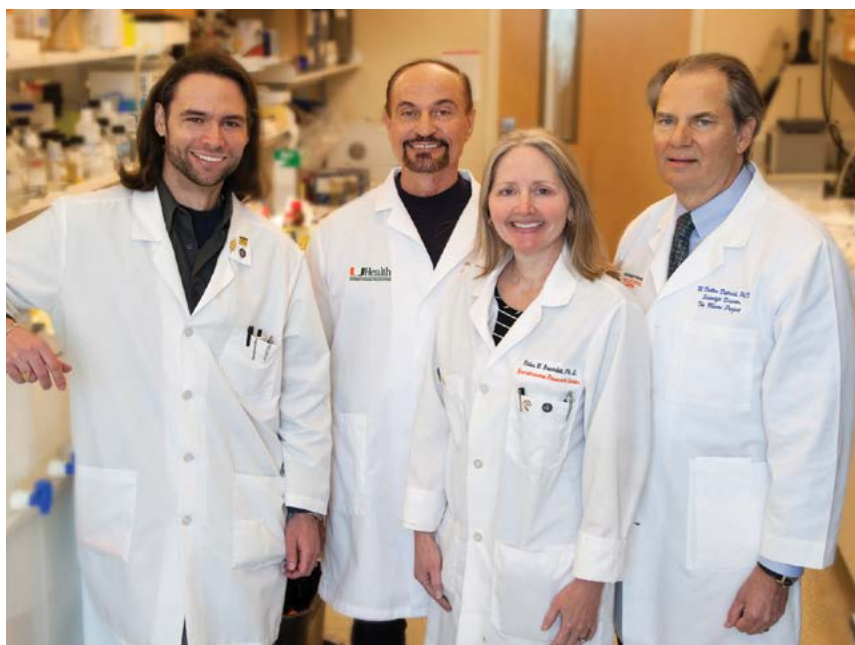
**Veterans Administration Biological Laboratory Research and Development**  
 Dr. Helen Bramlett (P.I.)  
 -Novel Treatment Strategies for Targeting Post-Traumatic Epilepsy

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

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

## Technology Advances on the Inflammasome Front

The inflammasome gets activated after SCI and TBI and is involved in signaling messages that cause more cells to die, which contributes to secondary tissue damage. Thus, if inflammasome activation can be neutralized to some degree, there may be tissue sparing, which results in greater functional recovery.

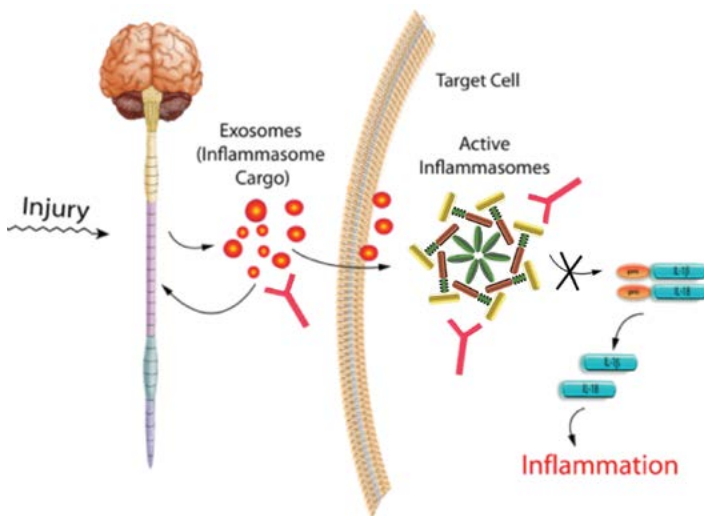


Drs. Juan Pablo de Rivero Vaccari, Robert W. Keane, Helen M. Bramlett, and W. Dalton Dietrich (left to right).

We have discussed in a previous article (*The Project 2011*) the importance of intellectual property and patenting of technology to the successful development of therapeutic interventions for spinal cord injury (SCI) and traumatic brain injury (TBI). We've also discussed the importance of targeting inflammation as a treatment component of SCI and TBI. One area that a group of Miami Project faculty has been advancing on involves regulating the inflammasome activity after injury.

The inflammasome is a group of proteins that are part of the innate immune response. The innate immune system is your body's first line of defense against infections; it is also activated after trauma. The inflammasome gets activated after SCI and TBI and is involved in signaling messages that cause more cells to die, which contributes to secondary tissue damage. Thus, if inflammasome activation can be neutralized to some degree, there may be tissue sparing, which results in greater functional recovery.

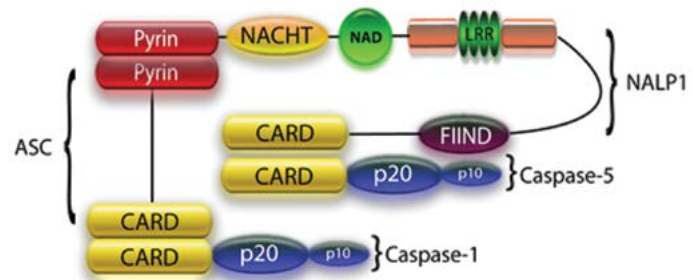
Drs. [Helen M. Bramlett](#), [Juan Pablo de Rivero Vaccari](#), [W. Dalton Dietrich](#), and [Robert W. Keane](#) have been investigating inflammasome activation and neutralization for several years in multiple experimental animal models. In 2009 they formed a small biotechnology company called InflamaCORE™, LLC (<http://inflamacore.com>) with the goal of “developing novel therapeutic interventions to target abnormal inflammation following central nervous system injury and repair”. With guidance from the University of Miami Technology Transfer Office,



Schematic of inflammasome activation after spinal cord injury. Injury induces secretion of exosomes containing inflammasome proteins that fuse with the plasma membrane of target cells in the spinal cord. Target cells activate the inflammasome to cleave pro-interleukin-1β (IL-1β). Antibodies against inflammasome proteins block exosome signaling and activation of the inflammasome in the target cells to inhibit inflammation.

they successfully received a patent on their intellectual property in late 2013. [*Modulating Inflammasome Activity and Inflammation in Central Nervous System Injury*. Robert W. Keane, Ph.D., W. Dalton Dietrich, Ph.D., Juan Pablo de Rivero Vaccari, Ph.D., Helen M. Bramlett, Ph.D. US Patent Application No. 12/182,886]

Another big advance they made in late 2013 was being awarded a Small Business Technology Transfer (STTR) grant from the National Institutes of Health (NIH) to begin work in 2014. The STTR program is an avenue by which small businesses can collaborate with research institutions and receive federal funding to promote commercialization of technology. The title of the project is “Therapeutic Neutralization of the Inflammasome after Spinal Cord Injury” and InflamaCORE™ will be collaborating with the University of Miami. The long-term goal of the project is to develop an anti-inflammatory therapy that improves outcomes after SCI in humans. This could potentially translate into the first FDA-approved biologic for the treatment of SCI. The 2 short-term goals of this specific grant are to 1) develop a humanized version of an antibody (to be called ICCN100) that stops inflammasome activation and 2) test the safety and efficacy of ICCN100 in our mini-pig model of SCI.



The NALP1 inflammasome is a multiprotein complex comprised of NALP1, caspase-1, caspase-5, and the adaptor protein ASC. Upon inflammasome activation, caspase-1 is cleaved, resulting in the maturation of interleukin-1 pro-inflammatory cytokines.

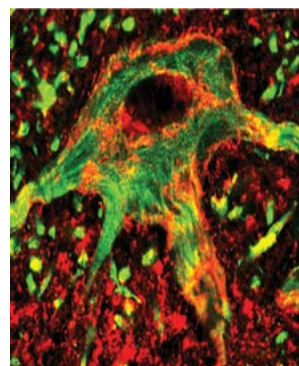
There are 3 milestones by which they will measure success:

**Milestone 1** – Determine the efficiency of ICCN100 in inhibiting inflammasome activation *in vitro* and *in vivo*.

**Milestone 2** – Determine the optimum dose of ICCN100 needed to decrease inflammation following SCI in mini-pigs, and to establish whether the optimum dose leads to improvements in functional and histopathological outcomes following SCI.

**Milestone 3** – Determine the pharmacokinetics and toxicity of ICCN100 treatment strategy in mini-pigs.

After these 3 milestones are met the next phase will consist of producing and scaling up a drug of clinical quality and an Investigational New Drug application for launching clinical trials regulated by the FDA. We will be keeping a close eye on this exciting program throughout the year and congratulations to the team. 🎉



#### On the cover:

Confocal image of a frozen section of the injured rat spinal cord that was double stained for motor neurons (green) and for the NALP1 inflammasome protein (red).



# The Miami Project To Cure Paralysis

## Faculty Profiles

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



### **W. DALTON DIETRICH, III, PH.D.**

**Scientific Director, The Miami Project**

**Kinetic Concepts Distinguished Chair in Neurosurgery**

**Senior Associate Dean for Discovery Science**

**Professor, Departments of Neurological Surgery, Neurology, and Cell Biology**

#### **Neuroprotection and Improved Recovery of Function following CNS Trauma**

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



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

**Co-Founder, The Miami Project**

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

#### **Translational Interventions**

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

**MARY BARTLETT BUNGE, PH.D.****Christine E. Lynn Distinguished Professor in Neuroscience****Professor, Departments of Cell Biology, Neurological Surgery, and Neurology****Development of Combination Strategies to Repair the Injured Spinal Cord**

The goal in my laboratory is to foster regeneration of axons across and beyond a 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  
Vice Provost for Research****VANCE LEMMON, PH.D.****Walter G. Ross Distinguished Chair in Developmental Neuroscience****Professor, Department of Neurological Surgery****High Content Screening and Functional Genomics of the Nervous System**

Our laboratory has developed methods to test thousands of genes or chemicals in hundreds of thousands of neurons each week and obtain quantitative information about cell morphology and gene expression. This “high throughput” capability allows us to tackle questions about development and regeneration using systems biology approaches. The Lemmon-Bixby lab has several ongoing projects related to axon regeneration. One project is to test the roles of known signaling proteins called protein kinases. In this screen we have tested hundreds of kinases by overexpression and have also tested more than 1500 kinase inhibitors, many of which strongly promote neurite growth in vitro. Using machine learning and cheminformatics (collaboration with Dr. Stephan Schürer) we can identify critical kinases and their signaling networks as well as potential lead therapeutic compounds. A second project is based on the observation that peripheral sensory neurons initiate a genetic program appropriate for axonal regeneration after injury. Our laboratory is combining next-generation sequencing with cell-based phenotypic screening to identify genes and microRNAs that are part of this genetic program. Finally, in collaboration with Dr. S. Schürer and Dr. Ubbo Visser, we are developing RegenBase, an information system that integrates diverse data on nerve regeneration after spinal cord injury with data from other information resources.





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

**Professor, Department of Neurological Surgery**

**Director, Clinical Neurotrauma**

**Preclinical Mechanistic and Neuroprotection Research in Traumatic Brain Injury (TBI) and Clinical Trials, and Neuromonitoring Techniques in the Injured Brain**

We are near completion of a two year grant from the Department of Defense to evaluate the neuroprotective effect of Perfluorocarbons in four rodent models of traumatic brain injury (penetrating brain injury, closed traumatic brain injury with secondary hypoxia, tissue culture with stretch injury, and mechanistic and safety studies). These oxygen carriers have shown benefit in previous studies involving fluid percussion injury and subdural hematoma models. We are also evaluating hypothermia neuroprotection, in humans and animals, using novel biomarkers. We are also obtaining pilot data with FDA approved Human stem cells, transplanted into the rat brain, as therapy for Penetrating TBI

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

**Professor and Chair, Department of Rehabilitation Medicine**

**Chief of Service & Medical Director, Department of Rehabilitation Medicine**

**Pain Interventions and Prevention of Urinary Tract Infections**

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



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

**Professor, Departments of Physical Therapy and Neurological Surgery**

**Motor Restoration after Spinal Cord Injury**

The studies in the Neuromotor Rehabilitation Research Laboratory cross the boundaries of basic neurophysiology and neurorehabilitation. We apply principles of neuroplasticity and motor learning to understand how interventions can be optimized and combined to promote best recovery of function. Some of our rehabilitation studies focus on recovery of hand and arm function, while others are aimed at walking function.

**ROBERT W. KEANE, PH.D.**

**Professor, Departments of Physiology & Biophysics, and Neurological Surgery**

**Regulation of Innate Immunity after CNS Trauma**

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







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

**Professor, Departments of Neurological Surgery, Orthopedics, and Rehabilitation Medicine  
Chief of Neurospine Service, Jackson Memorial Hospital/Chief of Neurosurgery, University of Miami Hospital**

**Cellular Transplantation Strategies after SCI/Systemic Hypothermia after Acute SCI**

My clinical research interests currently focus on developing cellular transplantation strategies to repair injuries within both the human central and peripheral nervous system. I am currently Co-PI on our clinical trial “Transplantation of Autologous Human Schwann Cells (SCs) to Repair the Injured Spinal Cord - Phase I - safety study”. This represents a first-in-man dose escalation study of autologous human SCs for patients with sub-acute thoracic SCI (T3 to T11). We are also very interested in the use of SCs for peripheral nerve injuries with long segmental defects and have performed such a transplantation in a patient with a significant acute sciatic nerve injury. Hypothermia continues to show promise in a variety of acute central nervous system injuries. There are various factors that need to be considered with systemic cooling of the SCI patient, including methods of cooling, window from injury to initiation, duration and depth of hypothermia, rate of re-warming, etc. While profound levels of hypothermia ( $T < 32^{\circ}\text{C}$ ) can be difficult to administer and are subject to increased complication rates, mild (modest) levels of hypothermia ( $T 32\text{--}34^{\circ}\text{C}$ ) have been shown to provide significant protection against traumatic and ischemic neuronal cell death. I am currently the PI of our institutional protocol studying systemic hypothermia induced via an intravascular catheter and continued for 48 hours after acute cervical SCI.

**DANIEL J. LIEBL, PH.D.**

**Professor, Department of Neurological Surgery  
Director, Neuroscience Graduate Program**

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

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

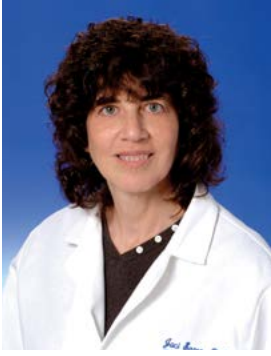


**MARK S. NASH, PH.D., F.A.C.S.M.**

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

**Physiological Assessment of Secondary Complications Following SCI: Electrical Stimulation, Cardiometabolic & Vascular Physiology, Cardioendocrine Pathology, and Exercise & Dietary Biochemistry**

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



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

**Professor, Department of Neurological Surgery**

**Cellular Implants for the Alleviation of Chronic Pain and CNS Injury**

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

**THOMAS J. SICK, PH.D.**

**Professor of Neurology and Physiology/Biophysics**

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

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



**CHRISTINE K. THOMAS, PH.D.**

**Professor, Department of Neurological Surgery**

**Neuromuscular Weakness, Fatigue, Spasms, and Regeneration**

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

**GILLIAN A. HOTZ, PH.D.**

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

**Neurocognitive Deficits and Injury Prevention**

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





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

**Associate Professor, Departments of Neurological Surgery and Rehabilitation Medicine  
Spinal Cord Injury Outcomes**

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

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

**Clinical Professor, Department of Neurological Surgery**

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

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



**ALBERTO MARTINEZ-ARIZALA, M.D.**

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

**Pathophysiology and Treatment of Secondary Complications in SCI**

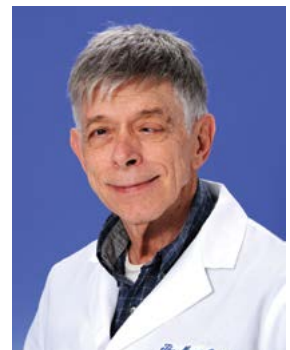
My research interests focus on common complications that are seen following spinal cord injury: pain, spasticity, syringomyelia, and tethered cord syndrome. My interests include investigating the basis for the development of the different spasticity and pain profiles in the spinal cord injured population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

**PATRICK M. WOOD, PH.D.**

**Research Professor, Department of Neurological Surgery**

**Changes in the Molecular and Biological Properties of Human Schwann Cells**

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







## **NAGI AYAD, PH.D.**

**Associate Professor, Department of Psychiatry and Behavioral Sciences**

**Cell Cycle Transitions in the Developing and Diseased Nervous Systems**

The research in my laboratory focuses on cell cycle transitions in the developing nervous system. My laboratory identified essential proteins required for controlling mitotic entry and exit and also demonstrated that cell cycle proteins are present and active in the developing nervous system and fully differentiated neurons. Specifically, the research group uncovered the mechanism through which the Anaphase Promoting Complex/Cyclosome (APC/C) and other cell cycle regulators such as Wee 1 control cell proliferation, cycle exit, and differentiation. These neural progenitor cell cycle proteins are kinases, ubiquitin ligases, and epigenetic enzymes that may be targets in cancer, spinal cord injury, and traumatic brain injury. Thus, my laboratory is searching for novel molecular

pathways that control neural development and are targets in multiple human maladies. This is accomplished using a multi-disciplinary approach that utilizes whole genome, siRNA, cDNA, and small molecule cell-based screens to develop therapies.

## **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.



## **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; Program Manager, Defense Advanced Research Projects Agency Neuroprosthetics and Neural Engineering**

The goals of my research are to develop brain-machine interfaces (BMI) to restore communication and movement control to people with neurological impairments. The approach is to use technology to directly interact with the central and peripheral nervous system, interpret the internal coding of brain activity for intent, and send commands to bionic devices to trigger movements. The laboratory uses electrophysiological and neural computational tools to seamlessly interface these devices with the nervous system. I am interested in developing combined therapies (technology with rehabilitation and repair) to personalize therapeutic approaches for people living with disabilities.





**PANTELIS TSOULFAS, M.D.**

**Associate Professor, Departments of Neurological Surgery and Cell Biology & Anatomy**  
**Neurotrophins: Specificity of Action**

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

**KIM ANDERSON-ERISMAN, PH.D.**

**Research Associate Professor, Department of Neurological Surgery**  
**Director of Education, The Miami Project to Cure Paralysis**

**Translational Investigations for Chronic SCI**

My research focuses on translational investigations and bridging the gap between basic science, clinical science, and the public community living with SCI. I recently completed a multi-center clinical study evaluating the reliability and validity of the Spinal Cord Independence Measure in the US healthcare setting. My current projects focus on 1) aging related changes in bladder health after SCI, 2) determining the minimum amount of exercise and locomotor training required for clinical trials targeting chronic SCI, and 3) identifying the facilitators and barriers to clinical trial participation from the SCI consumer perspective.



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

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

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

**IAN D. HENTALL, PH.D.**

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

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





**BRIAN R. NOGA, PH.D.**

**Research Associate Professor, Department of Neurological Surgery**

**Brain and Spinal Mechanisms Controlling Walking**

Our long-term goal is to develop and optimize treatments for spinal cord injury based on transmitter enhancement strategies that include deep brain stimulation, delivery of neurotransmitters or similarly acting drugs, or transplantation of cells secreting these substances. Of the many possible neurotransmitter candidates that could be used for this purpose, monoamines hold particular promise. We have concentrated our recent research effort on understanding the role monoamines play in the control of walking in 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 findings to treatments tailored to specific mechanisms. We are also examining the personal experiences of people living with chronic pain and SCI to increase our understanding about factors that help or hinder obtaining optimal pain relief. My research program is highly collaborative and includes extensive interdisciplinary protocols for a multimodal evaluation of self-reported pain symptoms and its psychosocial impact, quantitative assessment of neurological function, and biomarkers including non-invasive brain imaging and genetic polymorphism.



**COLEEN ATKINS, PH.D.**

**Assistant Professor, Department of Neurological Surgery**

**Developing Novel Therapies for TBI and SCI**

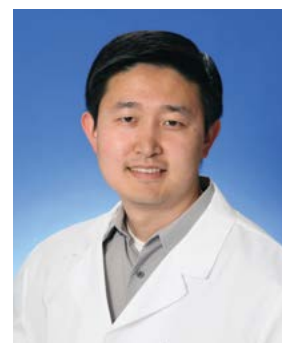
The research in my laboratory focuses on developing novel therapeutic interventions for traumatic brain injury (TBI) and spinal cord injury (SCI). The research goal of my laboratory is to enhance rehabilitation and recovery by manipulating synaptic plasticity at specific levels of the neuroaxis following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

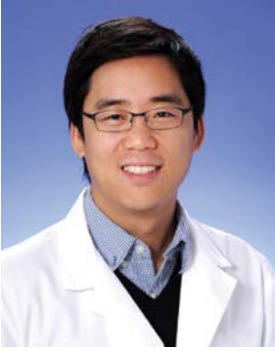
**Assistant Professor, Department of Neurological Surgery**

**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 SCI and related neurological disorders.






**KEVIN K. PARK, PH.D.**
**Assistant Professor, Department of Neurological Surgery**
**Intrinsic Mechanisms of Axon Regeneration**

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

**ROBERTA BRAMBILLA, PH.D.**
**Research Assistant Professor, Department of Neurological Surgery**
**Modulation of the Immune Response in Neurologic Disease**

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


**RACHEL E. COWAN, PH.D.**
**Research Assistant Professor, Department of Neurological Surgery**
**Enhancement and Preservation of Maximal Transfer and Wheelchair Propulsion Ability**

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

**JUAN PABLO DE RIVERO VACCARI, PH.D.**
**Research Assistant Professor, Department of Neurological Surgery**
**Underlying Mechanisms of the Innate Immune Response and Contributions to Various CNS Diseases**

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



**HOWARD B. LEVENE, M.D., PH.D.****Assistant Professor, Department of Neurological Surgery****Schwann Cell Transplantation after SCI**

One proposed therapy for spinal cord injury is to introduce cells to the injury site to help repair, restore, or support existing neurons. I work with my colleagues on a large animal model to study the effect and behavior of transplanted autologous Schwann cells. I have been involved in the refinement of this animal model. This approach allows for the scientific study of the behavior of implanted cells and generates the groundwork for clinical trials. Research utilizing this model is done in collaboration with clinicians and scientists at the Miami Project such as Drs. Guest, Solano, Pearse, Wood, Bunge, and many more.

**PAULA V. MONJE, PH.D.****Research Assistant Professor, Department of Neurological Surgery****Molecular Signals Controlling Schwann Cell Proliferation and Differentiation****In Vitro Methods to Enhance the Schwann Cell's Potency for CNS Repair**

My laboratory studies basic aspects of Schwann cell biology and their use in transplantation for CNS regeneration. Specifically, we are investigating the role of cAMP and growth factors in the reciprocal interactions between Schwann cells and neurons underlying the regulation of Schwann cell proliferation and myelination, as well as the initiation of Schwann cell dedifferentiation after injury. Our lab works intensively towards refining the use and developing new cell culture methods for the growth and assessment of function of both human and rodent Schwann cells. One important goal is to improve the quality of cultured adult Schwann cells for an intended use in clinical trials.



## Gail F. Beach Memorial Lecture Series

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

September 4, 2013

**Jonah R. Chan, Ph.D.**

University of California, San Francisco – San Francisco, CA

October 2, 2013

**Matthew N. Rasband, Ph.D.**

Baylor College of Medicine – Houston, TX

November 6, 2013

**Shawn Hochman, Ph.D.**

Emory University School of Medicine – Atlanta, GA



December 4, 2013

**Randy Trumbower, Ph.D.**

Emory University School of Medicine – Atlanta, GA

January 8, 2014

**Claire E. Hulsebosch, Ph.D.**

The University of Texas Medical Branch – Galveston, TX

February 24, 2014

**Robin Franklin, Ph.D.**

University of Cambridge – United Kingdom

March 5, 2014

**Timothy C. Cope, Ph.D.**

Wright State University – Fairborn, OH

April 2, 2014

**Leif A. Havton, M.D., Ph.D.**

University of California, Irvine – Irvine, CA

May 5, 2014

**Joseph El Khoury, M.D.**

Harvard Medical School – Boston, MA

## Longstanding Faculty Member

### John R. Bethea, Ph.D., Heads North




Dr. John Bethea when he joined The Miami Project faculty.

Dr. John Bethea has been a pillar of The Miami Project faculty since 1996. It is with mixed emotions that we wish him farewell in 2014 as he embarks on a new journey in his career. Dr. Bethea is now the Chair of the Department of Biology at Drexel University in Philadelphia, PA.

Actually, Dr. Bethea's relationship with The Miami Project goes back even further. In the mid-80's, after finishing his undergraduate training at Florida International University, he worked in the laboratory of Dr. Dietrich, our current Scientific Director. They published his first paper in 1987 evaluating changes in blood vessels immediately following experimental stroke lesions. [Dr. Bethea](#) moved away to earn his Ph.D. in Neuroscience at the University of Alabama at Birmingham, then up to Cleveland to complete post-doctoral fellowships at Case Western Reserve University in Neuroscience and the Cleveland Clinic in Immunology. Finally, in 1996 he found his way back to Miami to join the faculty of the Department of Neurological Surgery and The Miami Project. He worked his way up the ranks to full Professor by 2009.

Dr. Bethea has spent the last 20 years focusing his research on neuroimmunology in disease. Neuroimmunology is the evaluation of how the nervous system and immune system interact. He has focused primarily on the role of the immune system after spinal cord injury (SCI) and in multiple sclerosis (MS). His laboratory demonstrated that trauma-induced SCI triggers a very strong inflammatory response, both within the spinal cord and systemically. The trauma activates a signaling molecule, NF- $\kappa$ B, within multiple cell types (macrophages, microglia, endothelial cells, and neurons). NF- $\kappa$ B is a transcription factor that plays a pivotal role in regulating inflammation, and possibly programmed cell death pathways. His research team went on to generate experimental mice that do not express functionally active NF- $\kappa$ B in astrocytes and they demonstrated that those mice were significantly protected from SCI and MS-induced paralysis, inflammation, and myelin damage. His research will continue toward identifying and developing interventions targeting neuroprotection.

Dr. Bethea is internationally recognized for his research. He has served on multiple federal grant review study sections, published multiple peer-reviewed articles in high impact scientific journals, trained a host of students, and maintained consistent funding from the National Institutes of Health since 1999. Becoming the Chair of the Department of Biology at Drexel University is a significant advancement for Dr. Bethea. The department is already strong in molecular biology, cellular biology, ecology, paleobiology, and environmental science and has very strong undergraduate and graduate student training programs. Dr. Bethea will continue building a comprehensive program and will maintain a strong collaboration with The Miami Project as a Voluntary Professor. He will be greatly missed, but at the same time we wish him the best of luck. 



Long-time colleagues, Drs. Dalton Dietrich (left) and John Bethea (right).



# Summer Student Research

A major role of The Miami Project is to provide education and training for the next generation of neuroscientists. Our long-term educational goal is to increase the number of scientists and laboratories working on paralysis research and central nervous system disorders around the world. Students and young scientists beginning their careers gain skills from The Miami Project's state-of-the-art comprehensive research and academic environment.



The 2013 NIH summer students with Drs. Anderson-Erisman and Dietrich.

In 2013, Drs. Anderson-Erisman and Dietrich were awarded a 5-year NIH Summer Student Research Grant, which enables a handful of stellar undergraduate students the opportunity to work in the laboratory of a Miami Project faculty member for 10 weeks during the summer. Each week, the students attended 2 lectures and participated in 1 journal club, in addition to 37 hours of hands-on



3rd Miami Project Summer Student Research Session.

laboratory work (for a total of 40 hours each week). These 12 students wrote an abstract about their specific research project and presented a poster at the 3<sup>rd</sup> Miami Project Summer Student Research Session on August 9, 2013.

## Summer Students and their Research Projects:

Name	Summer mentor	Summer project
Crawford, Anna	Dr. E. Field-Fote	Effects of peripheral versus cortical stimulation on hand motor control in subjects with tetraplegia
Dabrowski, Katie*	Dr. C. Atkins	Mild Traumatic Brain Injury with Mild Hyperthermia Results in Spatial Learning and Memory Deficits and Contralateral Hippocampal Atrophy
Fritzie, Matthew	Dr. R. Cowan	Quantification of Clinically Significant Wheelchair Propulsion Stress Changes
Jain, Aakangsha	Dr. J. Sagen	Evaluation of Antinociceptive Effect of Novel Cannabinoid Receptor Agonists From <i>Conus</i> Venom in Neuropathic Pain
Lee, Jason	Dr. W.D. Dietrich	Elevated Brain Temperature during Mild Traumatic Brain Injury Exacerbates Cognitive Deficits but Reduces Cortical Neuronal Loss
Liu, Daniel	Dr. D. Pearse	The Development of an in situ hybridization Protocol to Monitor Schwann Cell Migration
Magee, Jesslyn*	Dr. D. Liebl	The effects of EphrinB3 and EphB3 knockout genes on blood vessel formation in the postnatal retinal mouse model
Mayo, Meagan*	Dr. C. Thomas	Electrophysiological measures of spasticity following spinal cord injury
Medina, Andres	Dr. B. Noga	Improvements of Locomotion Coordination with Deep Brain Stimulation of the Mesencephalic Locomotor Region in Animals with Spinal Contusion Injuries
Rangos, Nicole	Dr. K. Park	Assessing Tyrosine and Serine Phosphorylation of Retinal STAT3 in Response to Ciliary Neurotrophic Factor
Robinson, Talia	Dr. P. Monje	Study of Human Schwann Cells In Vitro: Interaction with axons and responses to mitogens and cAMP
Yacoel, Tamar	Dr. I. Hentall	Raphe Nuclei Electrical Stimulation Reduces Presence of Caspase-3 Following Traumatic Brain Injury

\*award winners of the poster session

# Scientific Publications

Published studies that have passed the test of peer review are the benchmark of scientific progress. Listed here are the 2013 research publications by Miami Project scientists and colleagues.

Adamczak SE, de Rivero Vaccari JP, Dale GA, Brand F III, Nonner D, Bullock R, Dahl G, Dietrich WD, Keane RW (In Press) Pyroptotic Neuronal Cell Death Mediated by the AIM2 Inflammasome. *J Cereb Blood Flow and Metab.*

Ahmad FU, Sidani C, Fourzali R, Wang MY (2013) Post-Operative Magnetic Resonance Imaging Artifact With Cobalt-Chrome Vs. Titanium Spinal Instrumentation. *Journal of Neurosurgery: Spine.* 19:629-636.

Ahmad F, Wang MY (2013) Spinal Deformity? There's an App for That! *World Neurosurg.* 80:446-447.

Ahmad F, Wang MY, Levi AD (2013) Hypothermia for Acute Spinal Cord Injury – A review – Invited Submission. *World Neurosurg.* S1878-8750(13)00015-6.

Al-Ali H, Blackmore M, Bixby JL, and Lemmon VP (2013) High content screening with primary neurons. In: Sittampalam GS, Gal-Edd N, Arkin M, Auld D, Austin C, Bejcek B, Glicksman M, Inglese J, Lemmon V, Li Z, McGee J, McManus O, Minor L, Napper A, Riss T, Trask OJ, Weidner J, editors. *Assay Guidance Manual* [Internet]. Bethesda (MD): Eli Lilly & Company and the National Center for Advancing Translational Sciences; 2004--2013 Oct 15. PMID: 24260776

Al-Ali H, Schuerer S, Lemmon VP, Bixby JL (2013) Chemical Interrogation of the neuronal kinome using a primary cell-based screening assay. *ACS Chem. Biol.* 8: 1027-1036.

Ashbaugh J, Brambilla R, Karmally SA, Cabello C, Malek TR, Bethea JR (2013) IL7R $\alpha$  Contributes to EAE Through Altered T Cell Responses and Non-Hematopoietic Cell Lineages. *J. Immunol.* 190:4525-4534.

Atkins CM, Cepero ML, Kang Y, Liebl DJ, Dietrich WD (2013) Effects of Early Rolipram Treatment on Histopathological Outcome After Controlled Cortical Impact Injury in Mice. *Neurosci Lett.* 532:1-6.

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## Resident Cell Manufacturing Expert

### Aisha Khan, M.S.C., M.B.A.



Aisha Khan


Since 2011, Ms. Aisha Khan, M.S.C., M.B.A. has been providing oversight for The Miami Project Schwann cell therapy cellular processing program. This is a critical component of the manufacturing of Schwann cells for human use. The manufacturing and control of human Schwann cell processing is subject to the US Food and Drug Administration (FDA) oversight. They require a step-by-step description of how Schwann cells are prepared in culture, after having been removed from humans in preparation for transplantation. Good Manufacturing Practices (GMP) must be followed and documented. With Ms. Khan's help we have developed several Master Batch Records and Standard Operating Procedures (SOPs) defining how Schwann cells are harvested, separated from the nerve, expanded in culture, purified, and prepared for transplantation. A list of product release criteria have been established, which must be met each time Schwann cells are prepared for transplantation into a research subject.



Cell processing for therapeutic intervention.

The cells have to be manufactured in a GMP facility. As a result we have been processing our cells at the University of Miami Diabetes Research Institute GMP Cell Processing Facility, which meets all of the FDA requirements. From 2002-2013, Ms. Khan was the Director of Operations for the GMP Cell Processing Facility. Recently, she became the Executive Director of Laboratory Operations for the Cell Processing Program at the University of Miami Interdisciplinary Stem Cell Institute (ISCI).

Ms. Khan has a wealth of experience in medical, manufacturing, quality assurance, regulatory, and service environments including several years of hands on experience in setting-up and managing GMP laboratories at world class research facilities in the US and abroad. She routinely provides guidance to other GMP facilities across the nation that are at various levels of maturity in their life cycles to become FDA compliant. She is an active member of the American Association of Blood Bank (AABB), the International Society of Cellular Therapy, the Regulatory Affairs Professional Society, and the Cell Transplant Society. She has also served as a member of the National Stem Cell Task Force and participated in the preparation of national protocols for Hematopoietic Cell Processing Laboratories and is currently the Co-Chair of the AABB Standards Committee for Cell Therapy Product Services and an inspector for the Foundation for Accreditation of Cellular Therapy (FACT) and AABB.

In her new role at ISCI, Ms. Khan is establishing a GMP compliant laboratory for cell therapies to be used in clinical trials. She continues to provide oversight for our Schwann cell manufacturing program and is continually running experiments to further improve our cell yield. Eventually, our human Schwann cell processing will be moved over to ISCI. 





We have

Discovered novel molecular targets to **promote axonal regeneration** to be translated to the **clinical setting**.

Developed new approaches to **reduce secondary complications** from spinal cord injury.

We are

Developing **new strategies** for endogenous repair after spinal cord and brain injury.

Currently conducting **four active FDA approved clinical trials**.

With your support

**We Will**

**Cure paralysis.**



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