

Fall 2017

THE PROJECT

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



UNIVERSITY OF MIAMI
MILLER SCHOOL
of MEDICINE



"Thank you Dad for everything you have done for me! You are an incredible man and my hero! I can only hope that in your eyes, I have earned your respect and am deserving of all the hard work that you have put into making my life better. I love you so much and I am so proud to be your son!" Together, we will find a cure for paralysis.

Dear Miami Project and Buoniconti Fund friends and supporters:

I'm proud to announce that The Miami Project and The Buoniconti Fund are on track to exceed all fundraising and research goals. Our clinical trials are proceeding at a great pace, and are demonstrating significant advances in both sensory and motor function. Our team has never been more focused and optimistic about the future of our research and the real potential for all those who are paralyzed to walk again.

It is with tremendous gratitude that I send out a BIG THANK YOU to all of our donors who have helped us to get to these exciting times in our history. Of course, I am always reminded of our humble beginnings when a simple promise from a father to his son ignited a scientific revolution. It is only because of my father, that The Miami Project and spinal cord injury research is as advanced as it is today.

As many of you may know, my father Nick Buoniconti has been struggling with his own health difficulties this past year. Now is a momentous time to acknowledge his greatness and recognize his tremendous efforts on behalf of the spinal cord injured community. While he has lived a Hall of Fame life with many achievements in sports, business, television and much more, his greatest accomplishments have been in the area of neuroscience and the vital role it will play in curing paralysis. "Thank you Dad for everything you have done for me! You are an incredible man and my hero! I can only hope that in your eyes, I have earned your respect and am deserving of all the hard work that you have put into making my life better. I love you so much and I am so proud to be your son!" Together, we will find a cure for paralysis.

Marc

A handwritten signature in black ink, appearing to read "Marc Buoniconti". The signature is stylized with a large, looped "M" and a cursive "Buoniconti".

Marc A. Buoniconti, President
The Buoniconti Fund and
The Miami Project

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

This year, several neuroscience discoveries are providing new treatment strategies for successfully treating people with neurological disorders.



Exciting progress is being made daily at The Miami Project to Cure Paralysis, a Center of Excellence at the University of Miami Miller School of Medicine. Over 200 scientists and investigators are conducting innovative basic science research, translational and clinical investigations targeting brain and spinal cord injury. This year, several neuroscience discoveries are providing new treatment strategies for successfully treating people with neurological disorders.

This success results from a proven bench-to-bedside approach that promotes the successful advancement of novel ideas and experimental treatments. Miami Project initiated clinical trials are underway showing safety and efficacy using neuroprotective and reparative approaches. A new multicenter therapeutic hypothermia clinical trial will treat acutely injured patients with severe spinal cord injury. This trial, which is based on research done at the Miami Project and the Department of Neurological Surgery, could provide the necessary data to establish new medical guide lines for the use of targeted temperature management in all patients with acute spinal cord injury.

In the area of reparative medicine and axonal regeneration, trials utilizing cellular therapies combined with innovative neurorehabilitation strategies and robotic devices to improve function are underway. Our initial human Schwann cell trial has been completed and published in a leading scientific journal for all investigators to read. A new trial that targets chronic spinal cord injury is currently evaluating Schwann cell transplantation in combination with an extensive rehabilitation protocol. The devastating consequences of peripheral nerve injury are also being treated with a combinational bridging and cell therapy strategy that is producing real benefits in injured individuals. It is important to emphasize The Miami Project's total commitment to develop and refine new treatment protocols based on reproducible data to maximize recovery.

Another critical mission of The Miami Project is to obtain new information on the cellular and molecular mechanisms underlying cell death and axonal regeneration. New knowledge is required to help fuel future clinical investigations and enhance innovative research projects. In addition to collaborating with academic investigators, the Miami Project researchers are collaborating with industry to help test novel therapeutic agents to help move new treatments forward. Our critical Educational and Outreach programs continue to reach out to individuals throughout the United States and abroad. Importantly, we acknowledge and thank our spinal cord injured community for their important contributions to the success of our clinical research programs.

With the future completion of the new Christine E. Lynn Rehabilitation Center for The Miami Project to Cure Paralysis at UHealth/Jackson, our programs will continue to grow and help many more individuals with injury-induced disabilities and quality of life issues. We remain excited about the future as we continue to collaborate with scientists worldwide to test new technologies and approaches for improving functional outcomes. These are extraordinary times at The Miami Project and we greatly appreciate the critical support from our friends and colleagues.

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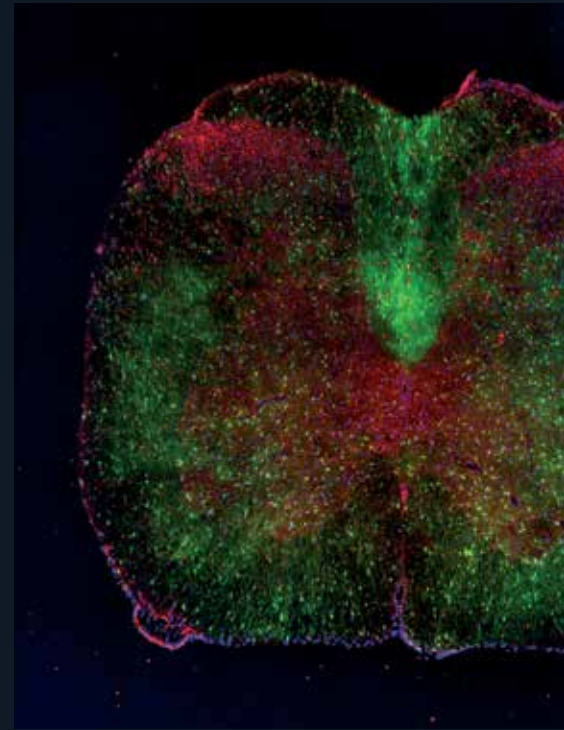
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On the cover:
Thoracic spinal cord section taken from a PLP-EGFP transgenic mouse in which oligodendrocytes are genetically labeled with green fluorescent protein. Oligodendrocyte progenitor cells are labeled in red with an antibody against NG2 and cell nuclei are labeled in blue with DAPI.

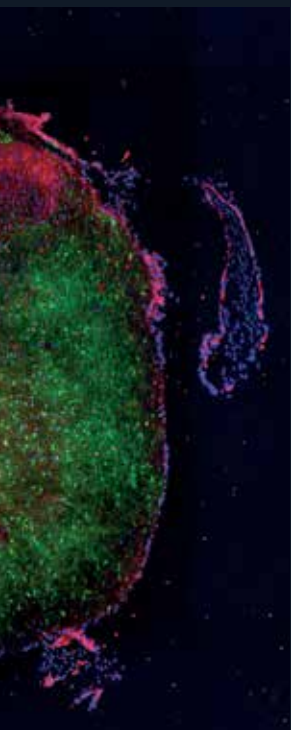


In Our Words

- 2 Message from the President, Marc Buoniconti
- 4 Message from Drs. Barth A. Green, W. Dalton Dietrich and Allan D. Levi

Research Journal Features

- 8 Living with Chronic Pain
- 10 Reducing Damage after Spinal Cord Injury
- 12 Male Fertility after Spinal Cord Injury
- 14 A Lifestyle Intervention Diabetes Prevention Program for Spinal Cord Injury
- 16 New Therapy in Development to Reduce Disability After Stroke
- 18 Releasing the Brakes to Stimulate Axon Regeneration



8

Living with
Chronic Pain



12

Male Fertility after
Spinal Cord Injury



20

31st Annual Great
Sports Legends
Dinner



24

Jack Nicklaus 15th
Annual Celebrity
Golf Invitational

Events to Benefit The Miami Project

- 20 31st Annual Great Sports Legends Dinner
- 24 Jack Nicklaus 15th Annual Buoniconti Fund
Celebrity Golf Invitational
- 26 Poker4Life
- 27 Ricky Palermo Golf Invitational
- 28 The Buoniconti Fund National Chapters
- 30 Darrell Gwynn Quality of Life Chapter of The Buoniconti Fund
- 32 In Memoriam - Don Misner
- 33 In Memoriam - Stanley Whitman
- 34 In Memoriam - Joe Fragnito
- 35 The Buoniconti Fund Board of Directors

LIVING WITH CHRONIC PAIN:

WHAT DO PEOPLE SAY?

Up to 80%
of people
living with SCI
experience
some form
of long-term
pain.

Unfortunately, living with chronic spinal cord injury (SCI) can also mean living with chronic pain. Up to 80% of people living with SCI experience some form of long-term pain. The two most common types of pain are muscle-related (musculoskeletal) and neurologic-related (neuropathic), and people can experience either, both, or a mixture of these kinds of pains in multiple areas of the body. Living with chronic pain can have a major impact on life, for example interfering with daily activities, mood, social interactions, and sleep. Effective treatment options are limited, particularly for neuropathic pain, and often come with unwanted side effects. In order to better optimize pain care, it is important to understand the perspective of people living with SCI and chronic pain and identify their priorities and expectations regarding pain management.

Dr. Widerstrom-Noga and colleagues were funded by the Department of Defense to gain this knowledge. First, they interviewed 35 people with SCI living with moderate to severe chronic pain. They identified multiple themes from these interviews and from the most frequently endorsed themes created 42 statements (21 barriers and 21 facilitators) about the experience of living with chronic pain. Second, they surveyed a larger population of people with SCI living with moderate to severe chronic pain (491) to determine how much they agreed or disagreed with the statements.

The results demonstrated that the most common facilitators to dealing with chronic pain were:

- Information regarding pain and treatments
- Resilience
- Coping
- Medication


and the most common barriers to dealing with chronic pain were:

- Poor health care communication
- Pain impact and limitations
- Poor communication about pain
- Difficult nature of pain
- Treatment concerns

“Yeah the pain... the pain takes a lot from my life. It really takes a lot from my life.”

People who have the greatest difficulty in dealing with their chronic pain are more likely to experience a combination of: (1) Pain that significantly impacts and limits their daily life activities (2) Pain that has a more difficult nature (e.g., more intense, more constant) (3) Having poor communication with their health care providers regarding their pain (4) Having lower resilience (e.g., lower personal ability to cope) (5) Using more pain medication (6) Being younger.

Overall, the findings from this study indicates that most participants view provider-patient communication and educational efforts regarding pain and pain management as priorities and critical needs. It also demonstrates that developing positive coping skills and building resilience are important intervention strategies.

If you are interested in reading this article please contact us at Paininfo@med.miami.edu 

Article – Eva Widerström-Noga, Kimberly D. Anderson, Salomé Perez, Judith P. Hunter, Alberto Martinez-Arizala, James P. Adcock, Maydelis Escalona. (2017). Living with chronic pain after spinal cord injury: A mixed-methods study. *Archives of Physical Medicine and Rehabilitation* 98:856-865.

Kim Anderson-Erisman, Ph.D.,
Eva Widerström-Noga, D.D.S., Ph.D.



Reducing Damage after Spinal Cord Injury is not so

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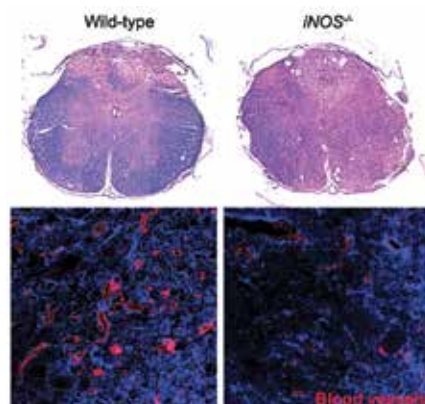
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The spinal cord can be injured in many ways. Car accidents, falls, violence, and sports are the four leading causes of traumatic spinal cord injury (SCI). Regardless of the cause, the resulting damage to the spinal cord develops in a similar way. The first phase is called the “primary injury” and is caused by the sudden blow that fractures, dislocates, or compresses the bones of the spine (vertebrae). Additional damage occurs due to bleeding, activation of the immune system (inflammation), and fluid accumulation in and around the spinal cord. This “second injury” can last for a period of time between several days to weeks. Decreased blood flow, inflammation, and increased production of destructive molecules (free radicals) leads to an environment of oxidative stress, which triggers a chain reaction resulting in more cell death in the spinal cord and ultimately more loss of function.

One particular enzyme that is expressed by cells in response to cell damage and inflammation is called inducible nitric oxide synthase (iNOS). iNOS contributes to a high production of nitric oxide (NO). NO, while being an important molecule involved in regulating many different processes in the body, when produced at high levels following injury leads to the formation of many free radicals and results in significant cell death. Researchers at The Miami Project hypothesized that blocking the action of iNOS after spinal cord injury would reduce levels of NO, and therefore result in less free radical production and cell death as well as better functional outcomes. Experiments confirmed that fewer cells died around the area of injury when animals were treated with iNOS-blocking drugs and that these animals performed better in some locomotor tests (Maggio et al., 2012). However, these experiments only blocked the action of iNOS for a few days, in the acute time period after spinal cord injury.

Drs. Pearse, Dietrich, Ghosh and their collaborators wondered whether a longer-term inhibition of iNOS would produce better results. Although iNOS and NO are involved in processes that cause cell death immediately after injury, they are also involved in the processes of wound healing and repair. In order to understand whether blocking iNOS for longer periods of time would lead to even greater recovery, the team designed new experiments.



Long-term removal of iNOS results in significantly less preserved brain tissue and blood vessels after spinal cord injury. Six weeks post-injury, control (wild-type) mice (left panel) had more healthy tissue and blood vessels than iNOS knockout (iNOS^{-/-}) mice (right panel)

A transgenic mouse model in which iNOS was “knocked out” was used; mice were specially bred to have a complete and permanent loss of the iNOS enzyme after spinal cord injury. Two weeks after injury, the iNOS knockout mice exhibited a more rapid and significant improvement in walking function, which continued until four weeks post-injury. However, six weeks after injury, the mice missing iNOS did not perform any better than regular “non-knockout”, control mice. In addition, the iNOS knockout mice actually had LESS preserved white and gray matter, and fewer axons and blood vessels compared to controls (Maggio et al., 2017).

So the process is not simply black and white. In the short term, blocking the actions of iNOS results in more preserved tissue and improved function. However, in the long term, knocking out iNOS seems to have negative

effects, by blocking protective or reparative processes that are important for the formation of new blood vessels and preserving tissue. These results will help scientists identify the optimal duration of time that iNOS should be blocked in order to produce the best outcomes after SCI. 🧪

Articles –

Dominic M. Maggio, Amanpreet Singh, J. Bryan Iorgulescu, Drew H. Bleicher, Mousumi Ghosh, Michael M. Lopez, Luis M. Tuesta, Govinder Flora, W. Dalton Dietrich, Damien D Pearse. (2017). Identifying the long-term role of inducible nitric oxide synthase after contusive spinal cord injury using a transgenic mouse model. *International Journal of Molecular Sciences* 18(2)

Dominic M. Maggio, Katina Chatzipanteli, Neil Masters, Samik P. Patel, W. Dalton Dietrich, Damien D. Pearse. (2012). Acute molecular perturbation of inducible nitric oxide synthase with an antisense approach enhances neuronal preservation and functional recovery after contusive spinal cord injury. *Journal of Neurotrauma* 29(12): 2244-2249



Dr. Mousumi Ghosh, one of the lead investigators of the study



Male Fertility after Spinal Cord Injury

After spinal cord injury (SCI), most men face obstacles when pursuing sexual activity and biologic fatherhood. Damage to the spinal cord contributes to sexual dysfunction and reduced semen quality. As a result, most men living with SCI experience erectile dysfunction, cannot ejaculate with sexual intercourse, and have poor semen quality. Sexual function can also be affected by low testosterone and premature symptoms of aging, which are both common after spinal cord injury.

With all of these challenges, it seems like the deck is stacked against men with spinal cord injuries who want to enjoy a healthy sex life or biologically conceive a child. Fortunately, researchers in the lab of Dr. Nancy Brackett at The Miami Project have been working hard for many years to understand the factors contributing to these issues and develop solutions for men living with SCI. They published a management algorithm for ejaculatory dysfunction that allows for semen retrieval, non-surgically, in 97% of men with SCI (Sinha et al., 2017).

The first step of evaluating the fertility potential of men with SCI involves obtaining a semen sample. Since very few men are able to ejaculate via masturbation or sexual intercourse, medical assistance is required to obtain sperm for assisted conception procedures. The choice of assisted conception depends largely on the number of healthy sperm that can be obtained from the man. Higher numbers of healthy sperm allow for the possibility of less invasive, less costly assisted conception procedures, such as intrauterine insemination, or even intravaginal insemination at home. Lower numbers of healthy sperm often require more expensive and invasive assisted conception procedures to achieve pregnancy, such as in vitro fertilization and intracytoplasmic sperm injection. A medical procedure called “penile vibratory stimulation” (PVS) usually results in the highest number of healthy sperm relative to other methods of semen retrieval in men with SCI who are unable to father children naturally.

A recent study (Chong et al., 2017) published by researchers in the lab of Dr. Brackett investigated three different methods of PVS in the same group of men with SCI to determine which one was optimal for achieving ejaculation. Clinical recommendations of attempting PVS with one device first are made based on the results. The findings of this study will help guide clinicians and patients toward the optimal method of PVS, and thereby, toward the optimal method of assisted conception.

After a sample is obtained, the next step is to evaluate the quality of the semen, which is often abnormal in men after spinal cord injury. Although sperm numbers are often normal, sperm motility (how well they move) is typically very low. This condition contributes to infertility. Previous research from Dr. Brackett’s lab has shown that inflammatory factors in the semen contribute to low sperm motility in men with SCI. They hypothesized that semen quality could be improved by a medication that interferes with the formation of some of these factors. The results of the study (Ibrahim et al., 2017), recently published in the *Journal of Spinal Cord Medicine*, showed that men with spinal cord injury had improved sperm motility after taking an oral medication (a pill) called probenecid for four weeks. This is the first study to report improved sperm motility after oral medication in men with SCI. Further research will determine the optimal dosage regimen. This treatment holds promise for improving reproductive options in men with spinal cord injury. 🇺🇸

Articles –

Varsha Sinha, Stacy Elliot, Emad Ibrahim, Charles M. Lynne, Nancy L. Brackett. (2017). Reproductive health of men with spinal cord injury. *Topics in Spinal Cord Injury Rehabilitation* 23(1):31-41

William Chong, Emad Ibrahim, Teodoro C. Aballa, Charles M. Lynne, Nancy L. Brackett. (2017). Comparison of three methods of penile vibratory stimulation for semen retrieval in men with spinal cord injury. *Spinal Cord* May 30 (epub)

Emad Ibrahim, Teodoro C. Aballa, Charles M. Lynne, Nancy L. Brackett. (2017). Oral probenecid improves sperm motility in men with spinal cord injury. *Journal of Spinal Cord Medicine* May 2:1-4

Everyone knows that being overweight poses risks for heart disease and diabetes. However, anyone who's tried to lose weight knows it's no easy task. **There is no miracle pill for losing weight.**

A Lifestyle Intervention Diabetes Prevention Program for Spinal Cord Injury

Of course, there are all kinds of fad diets and supplements, but it's pretty important that weight loss occurs healthily and that typically involves some combination of exercise, diet, will power, and perseverance. Now let's add spinal cord injury (SCI) into the equation. Obviously, one of the biggest consequences of SCI is muscle paralysis, and the higher the level of injury the more muscles are paralyzed. This is problematic in two ways: 1) fat is easily deposited in muscles that are not moving, which increases the amount of fat mass in the body, and 2) it's hard to exercise paralyzed muscles, which makes it more difficult to lose weight by exercise alone. Other consequences of SCI may be less obvious; for example, SCI alters the way your body controls the metabolism of food, which can lead to unhealthy levels of sugars and lipids circulating in your blood. This can lead to an even greater risk of developing heart disease and diabetes. On top of all of that, it takes more effort and more time to do everything while living with SCI. What to do?!?

A few years ago, the National Institutes of Health (NIH) funded a large multicenter trial comparing a diabetes Prevention Program to a standard of care medication therapy for non-disabled people at risk of developing type-2 Diabetes. That trial was so effective it was stopped early, which almost never happens in clinical trials unless the benefit of treatment is so substantial that NIH wants to fast-track the treatment for widespread use! Dr. Mark Nash and colleagues were recently funded by the Department of Defense to test a modified version of this Diabetes Prevention Program in people living with SCI. We'll call it a Lifestyle Intervention Program for SCI.

Components of the Lifestyle Intervention Program:

First 6 months
<ul style="list-style-type: none"> • Supervised exercise intervention <ul style="list-style-type: none"> ○ An upper extremity circuit resistance training program performed 3 days each week
<ul style="list-style-type: none"> • Nutritional intervention <ul style="list-style-type: none"> ○ A calorie-restricted Mediterranean-style diet
<ul style="list-style-type: none"> • Behavioral intervention <ul style="list-style-type: none"> ○ A 16-session protocol targeting behavioral changes through education, problem-solving skills, and cognitive restructuring
Second 6 months
<ul style="list-style-type: none"> • Self-care (unsupervised) extension phase maintenance program

Behavioral intervention topics:

Session	
1	Introduction to lifestyle intervention. Explain study goals.
2	Introduce self-monitoring of weight at home.
3	Teach three ways to eat less fat.
4	Educate about healthy eating. Recommend alternate foods.
5	Introduce physical activity modules.
6	Tailor physical activity regimen to needs of the individual.
7	Teach principles of energy balance between calories and exercise. Teach principles of health maintenance from exercise.
8	Introduce principles of stimulus control as a method to prevent unhealthy eating. Introduce principles of stimulus control as a method to maintain exercise adherence.
9	Present five-step model of problem-solving.
10	Introduce basic skills for eating and exercising away from home.
11	Practice identifying negative thoughts and how to counter them.
12	Introduce concept that slips are part of lifestyle change and provide tips for behavioral change maintenance.
13	Introduce principles of aerobic fitness and coping with boredom.
14	Provide strategies for managing social cues, both stressful and supportive.
15	Summarize stress management principles presented over the course of the intervention.
16	Focus on enhancing motivation and maintaining behavioral change post-lifestyle intervention.

The team recently published results from three of the participants (Bigford et al., 2017), all men with chronic paraplegia who were overweight. All three of the participants experienced a greater than 7% reduction in body mass, which was the primary study goal, and were able to maintain that loss in the maintenance phase of the program. This benefit was associated with a reduction in fasting sugar and triglyceride levels in the blood. These are all important factors to reduce regarding the risk of developing diabetes. Furthermore, the exercise program was able to increase upper extremity strength and improve cardiorespiratory fitness – important for reducing fatigue and accomplishing activities of daily living. More data on a larger population will be forthcoming, but these initial results are very encouraging, and the first to show that people with SCI could substantially reduce their risk for diabetes! 🇺🇸

Article – Gregory E. Bigford, Armando J. Mendez, Luisa Betancourt, Patricia Burns-Drecq, Deborah Backus, and Mark S. Nash. (2017). A lifestyle intervention program for successfully addressing major cardiometabolic risks in persons with SCI: a three-subject case series. *Spinal Cord Series and Cases* 3, 17007; doi:10.1038/scsandc.2017.7.

New Therapy in Development to Reduce Disability After Stroke

Do you know the signs of stroke?

If not, just remember the acronym “FAST”, which stands for:

Facial drooping

Arm weakness

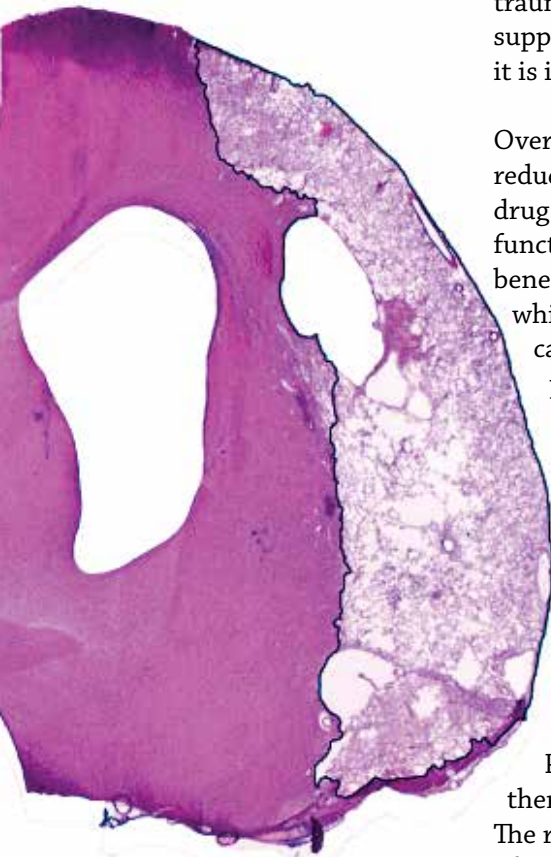
Speech difficulties

Time to act

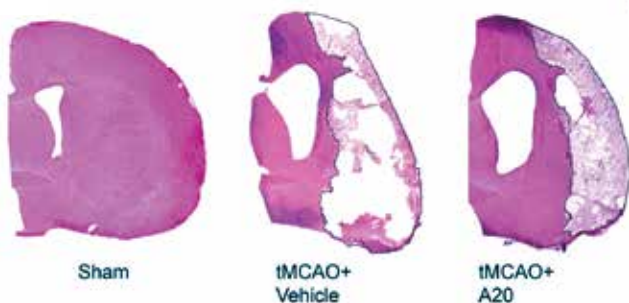
A stroke occurs when a blood vessel that supplies the brain gets blocked or ruptures. When an area of the brain is deprived of oxygen and nutrients, which are carried by the blood, brain cells begin to die. This also happens after a traumatic brain injury and to spinal cells after a traumatic spinal cord injury. As more and more time passes without an oxygen supply, additional brain cells can die and recovery outcomes are worse. This is why it is important to act “FAST” if stroke is suspected.

Over the last decade, extraordinary advances in acute therapies have been made to reduce the mortality rate after stroke. However, currently only one FDA approved drug, tissue plasminogen activator, is used in the clinic to improve neurological function in acute stroke patients. Unfortunately, only a small number of patients benefit from this therapy because of the limited time window after stroke during which it can be given and still have a positive effect. The effects of stroke can vary, but common problems include memory loss, muscle weakness or paralysis, and problems with speech. More than 2/3 of people who experience a stroke are left with some disability, and stroke is the leading cause of adult long-term disability worldwide. Therefore, additional research is required to develop and test new therapies that protect the brain from irreversible injury and produce improved outcomes.

Dr. W. Dalton Dietrich, Scientific Director of The Miami Project, and his team of researchers recently evaluated the effects of a new compound P7C3-A20 that has been reported in some pre-clinical studies to be protective of nerve cells (neurons) and to enhance the formation of new adult neurons (i.e., neurogenesis). This study involved treating animals with P7C3-A20 that had been given an experimental stroke to determine whether there were any potential benefits on long-term behavior and brain tissue damage. The researchers including Zachary Loris, a Neuroscience Graduate Student who successfully defended his Thesis Dissertation in August, also conducted




The scientists hypothesized that early treatment after experimental stroke would protect adult neurons from irreversible damage, while also promoting the formation of new neurons; both of which would contribute to better functional outcomes.



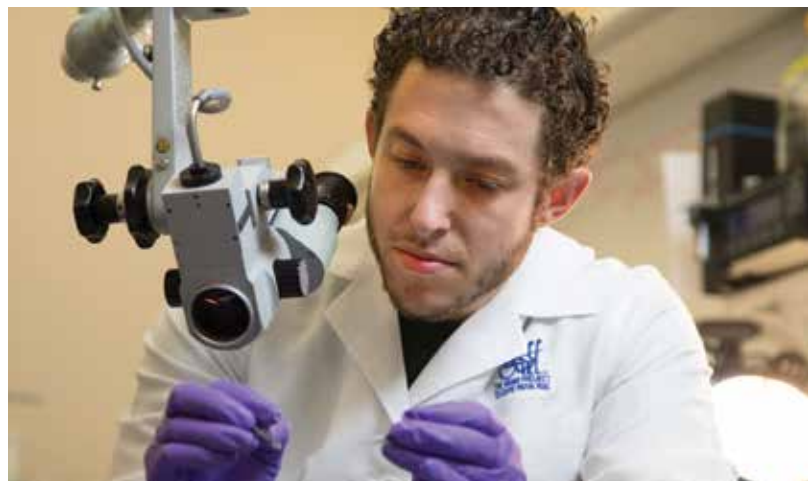
Treatment with P7C3-A20 reduces atrophy after stroke. Animals treated with P7C3-A20 (tMCAO+ A20) had increased brain tissue volume compared with controls (tMCAO+ Vehicle) after experimental stroke. A representation from an uninjured (sham) animal is also shown

experiments to determine whether the treatment improved adult neurogenesis in specific brain regions which are known to have the potential to produce new neurons in the adult. The scientists hypothesized that early treatment after experimental stroke would protect adult neurons from irreversible damage, while also promoting the formation of new neurons; both of which would contribute to better functional outcomes.

The results of their investigation were recently published in the journal of Experimental Neurology. Dr. Dietrich and colleagues found that P7C3-A20 treatment significantly improved behavioral outcomes including motor tasks and memory function compared to stroke animals not treated with the experimental compound. Analyses of the brain lesions also showed that the treatment reduced the size of the lesion. Finally, P7C3-A20 treatment increased the number

of newly formed adult neurons in two specific brain regions. This study provides the first data showing that the compound P7C3-A20 is beneficial in experimental stroke and leads to improvements in long-term function. Dr. Dietrich emphasized that new compounds like P7C3-A20 that are currently targeted for drug development may potentially be translated into the clinic to protect against secondary injury mechanisms after brain or spinal cord injury, as well as enhance reparative strategies leading to clinically relevant behavioral recovery. 

Article – Zachary B. Loris, Andrew A. Pieper, W. Dalton Dietrich. (2017). The neuroprotective compound P7C3-A20 promotes neurogenesis and improves cognitive function after ischemic stroke. *Experimental Neurology* 290:63-73.



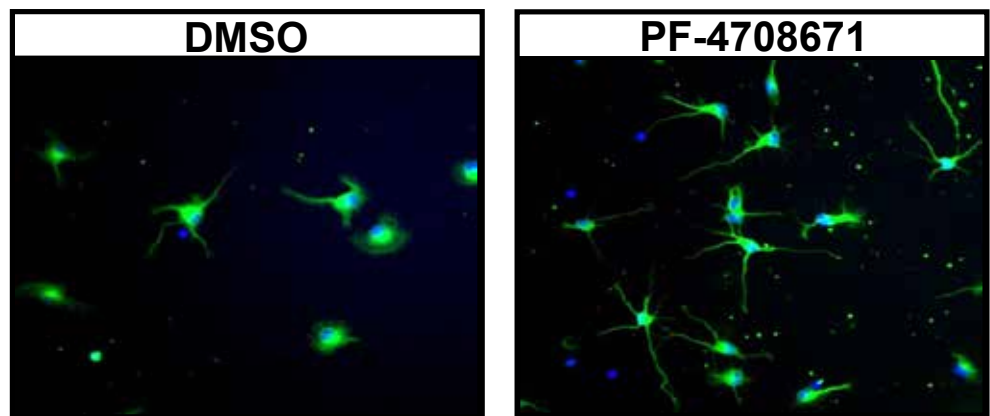
Zachary Loris, a graduate student in the Neuroscience Department, and lead author of this study

Releasing the Brakes to Stimulate Axon Regeneration

The results suggest that S6 kinase may be a useful target for drug therapy aimed at promoting regeneration and functional recovery after injury to the nervous system.

After injury, nerve cells in the adult brain and spinal cord are generally not able to regenerate the long cellular processes (axons) that connect distant areas of the nervous system. Inducing regeneration of these severed axons is one of the most difficult goals of spinal cord injury (SCI) research. A team of researchers at The Miami Project recently published findings in which they used a novel computational approach to identify a set of signaling proteins (kinases) that work together to “apply the brakes” to the growth of axons. Kinases can act in a positive or negative way; the negative way is called inhibitory. Surprisingly, one of the inhibitory kinases (S6 kinase) they found to “apply the brakes” was previously thought to serve exactly the opposite function—as part of a signaling pathway that “accelerates” axon growth and regeneration.

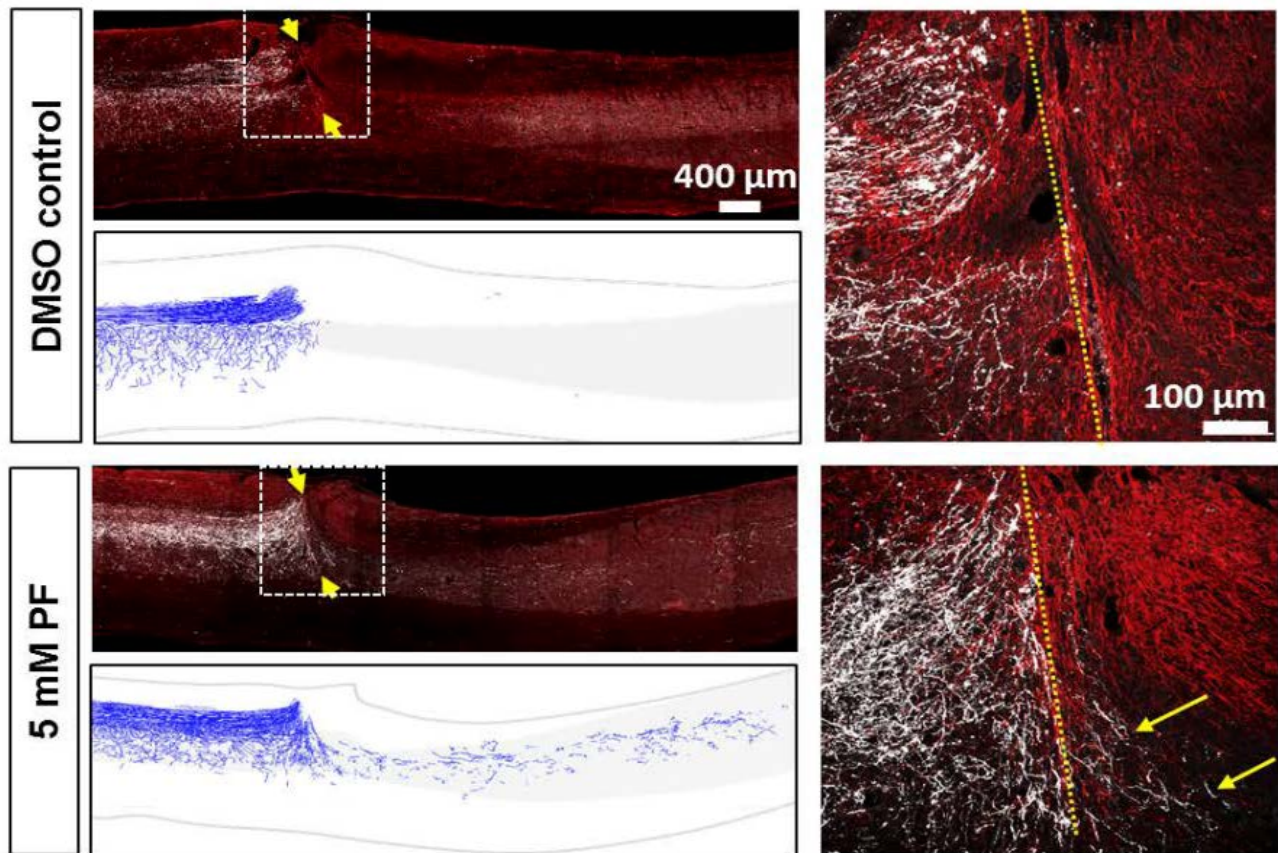
To test the idea that S6 kinase is a brake rather than an accelerator, they used neurons grown in dishes (cultured). They showed that when a specific inhibitor of S6 kinase (called PF) was added to the cultures, it strongly promoted axon growth from the neurons. They also demonstrated that specific signaling pathways in the neurons known to be important for axon growth were activated.



The S6 kinase inhibitor (PF-470861, right panel) results in increased axon growth compared to controls (DMSO, left panel)

To test whether S6 kinase acts as a brake on regeneration in adult animals, the researchers injected the inhibitor of S6 (PF) into the brains of mice whose spinal cords had been damaged in the neck region (cervical). They injected three different doses of PF into the brain regions controlling movement and sensation. Remarkably, injection of PF into the brain allowed regeneration of the injured axons in the spinal cord. The highest dose enabled large numbers of damaged

axons to regenerate into and beyond the lesion site for long distances. Those axons that regenerated past the lesion grew in the gray matter of the spinal cord instead of the white matter, which is more inhibitory and full of myelin. With these significant improvements in regeneration, they wanted to know if there were similar improvements in behavior (function). They found improvements in forelimb-hindlimb coordination and balance; motor, sensory, and proprioceptive ability; forelimb dexterity; and grasping ability.



Axons regenerate through and beyond the spinal cord lesion for long distances with the S6 kinase inhibitor (5 mM PF, bottom left), but not with DMSO control (top left). Higher magnification (right panels) shows that axons regenerate across the lesion gap (arrows) only after treatment with the S6 kinase inhibitor

The results suggest that S6 kinase may be a useful target for drug therapy aimed at promoting regeneration and functional recovery after injury to the nervous system. Importantly, drugs that inhibit S6 kinase already exist and are in large clinical trials for other diseases.

“We are very happy about this paper because it is a great validation that our computational strategies for analyzing in vitro data do translate appropriately to in vivo situations and that we have identified a very drugable target for SCI. Of course, we are testing it in several other models of regeneration now.” – Dr. Vance Lemmon

Article - Hassan Al-Ali, Ying Ding, Tatiana Slepak, Wei Wu, Yan Sun, Yania Martinez, Xiao-Ming Xu, VP Lemmon, and JL Bixby. (2017). The mTOR substrate S6 Kinase 1 (S6K1) is a negative regulator of axon regeneration and a potential drug target for Central Nervous System injury. *Journal of Neuroscience* 10.1523/JNEUROSCI.0931-17.2017.



Great SPORTS Legends Dinner to Benefit The Buoniconti Fund

The Buoniconti Fund to Cure Paralysis honored an unparalleled group of Hall of Famers, Gold Medalists, World Champions and philanthropists in front of more than 1,300 supporters at the Waldorf Astoria in New York, raising millions for spinal cord injury research during the 31st Annual Great Sports Legends Dinner in 2016.


The benefit, hosted by NFL Hall of Famer **Nick Buoniconti** and his son **Marc**, was emceed by *NBC's Nightly News* anchor **Lester Holt** in front of a sold-out crowd, and Chaired by Buoniconti Fund Board Member Mark Dalton. The Buoniconti Fund 2016 Sports Legends honored New York Yankees great and World Series Champion **Mariano Rivera**, seven-time tennis Major winner and fashion designer **Venus Williams**, NFL Hall of Fame running back from the New York Jets **Curtis Martin**, New York Knicks legend and NBA Hall of Famer



2016 Legends and Honorees

Willis Reed, four-time IndyCar Series Champion **Dario Franchitti**, Olympic Gold Medalist **Tara Lipinski**, WNBA, NBA, and FIBA Hall of Fame basketball great **Cheryl Miller**, and record-setting long-distance swimmer **Diana Nyad**.

The evening featured the presentation of The Buoniconti Fund Award to Golden Globe Winner **Christian Slater**, The Humanitarian Award to Mr. Las Vegas **Wayne Newton**, The Buoniconti Fund's Outstanding Philanthropist Award, presented by Grammy Award winners **Gloria** and **Emilio Estefan**, to **James L. Nederlander**, President of The Nederlander Organization, The Great American Icon Award to legendary astronaut **Buzz Aldrin**, and The Christine E. Lynn Champion for a Cure Award to Sports Legend Dinner Event Chairman **Mark Dalton**. The Sports Legends Dinner also paid special tribute to Sports Legend Dinner past honoree **Muhammed Ali** and celebrated the 50th birthday of **Marc Buoniconti**.

The cast of the smash hit, Broadway musical, "**On Your Feet! – The Story of Gloria and Emilio Estefan**," dazzled the guests who sang along to the Estefan hits and danced around the ballroom. Since its inception in 1986, the Great Sports Legends Dinner has honored more than 300 sports legends and honorees and has raised millions for The Miami Project's spinal cord injury research programs. 



Christine E. Lynn and
Mark Dalton



Sergio Gonzalez, Dr. Julio Frenk and
Dr. Eugene Sayfie



Venus Williams and
Diana Nyad



Wayne Newton and Christian Slater



Lester Holt



Curtis Martin, Willis Reed and Cheryl Miller



Stephanie Sayfie Agaard, James L. Nederlander
and Suzie Sayfie



Justise Winslow and
Willis Reed



Wayne and Kathleen
Newton



Nick Boniconiti and Gloria Estefan



Tara Lipinski



Chip Ganassi, Mariano Rivera and
Dario Franchitti



Diana Nyad, Mariano Rivera, Marc Buoniconti, Emilio and Gloria Estefan, Nick Buoniconti and Dr. Barth Green



Wayne Newton with Terry and Marc Buoniconti



Delfina Blaquier, Ignacio "Nacho" Figueras with Gloria and Emilio Estefan



Ashleigh Johnson, Lynn Buoniconti, Chelsea Johnson and Cheryl Miller



Buzz Aldrin and Wayne Newton



Mariano Rivera with Marc Buoniconti and Cynthia Vijitakula



James L. Nederlander and Richard Gray




Golf Legend Jack Nicklaus Hosted 15th Annual Buoniconti Fund Celebrity Golf Invitational

Presented By Tudor Group

Jack Nicklaus, the greatest golfer who ever lived, along with NFL Hall of Famer **Nick Buoniconti** and his son **Marc** hosted the 15th Annual Buoniconti Fund Celebrity Golf Invitational Presented by **Tudor Group** at Nicklaus' home club and course, The Bear's Club in Jupiter, Florida. For the past 15 years, the two-day event, which included an inspirational Sunday night dinner was followed by the Monday golf tournament on the immaculate Bear's Club 18 holes. The tournament, has consistently brought together some of the world's top business leaders and celebrities to join forces to find a cure for spinal cord injuries. Since its inception, The Bear's Club event has raised millions to help fund spinal cord injury research programs at The Miami Project to Cure Paralysis at the University of Miami Miller School of Medicine.

Golfers and celebrities including Bon Jovi drummer **Tico Torres**, World Series Champion Pitcher **Scott Erickson**, three-time NBA Champion with the San Antonio Spurs **Bruce Bowen**, 1980 Olympic Ice Hockey Gold medalist and Team Captain **Mike Eruzione**, 2-Time NBA Champion with the Miami HEAT and NCAA Champion with Duke **Shane Battier**, NFL Hall of Fame Quarterback **Bob Griese**, 1972 Miami Dolphins Perfect Season member **Dick Anderson**, NY Yankee pitching great and AL Rookie of the Year **Stan Bahnsen**, former Dolphins Offensive lineman **Jeff Dellenbach**, former NY Giants Running back **Tucker Fredrickson**, Dallas Cowboys Super Bowl Champion **Thomas "Hollywood" Henderson**, three-Time Super Bowl Champion with San Francisco and Denver, cornerback **Tim McKeyer**, University of Miami Head Coach **Mark Richt**, Super Bowl MVP with the Washington Redskins **Mark Rypien**, Actor from All My Children, Single Ladies and Dancing with the Stars **Aiden Turner**, former NY Giants Linebacker **Brian Kelley**, former Dolphins Punter **John Kidd**, NHL Champion from the Colorado Avalanche **Alex Tanguay**, former Dolphins Receiver **Fred Banks**, former Dolphins Tight End **Jed Weaver** and many more enjoyed the Celebrity Dinner affair and an exciting day of golf on the prestigious golf course.

Special thanks to Tudor Group, PGA National Resort and Spa, Nicklaus Companies, Perry Ellis and more. 



Mark Dalton, Eric Dalton, Jack Nicklaus, Kurt Dalton and Dick Aldrich



Jack Nicklaus, Marc Buoniconti and Barbara Nicklaus



Aiden Turner



Bruce Bowen



Bob Griese, Nick Buoniconti with Barbara and Jack Nicklaus

12th Annual Poker4life™ Charity Poker Championship A Tremendous Success

Poker4Life™ (P4L) Charity Poker Championship Founders Jeremy Schwartz and Ethan Ruby celebrated another banner year at this year's tournament. More than 200 players enjoyed the electric atmosphere at NYC event space The Tunnel with a seat in the 2017 World Series of Poker Main event and the coveted P4L Bracelet up for grabs.

Congratulations to the 2017 Final Table Winners who were: 1st - Doug Bortner, 2nd - Anthony Tedesco, 3rd - Chris Gibson, 4th - Leszek Markowski, 5th - Marco Huijgen, 6th - Vincent Teutonico, 7th - Ben Jacobson, 8th - Nadav Gottesman, 9th - Scott Seamon, 10th - Tiffany Herlands, and to the 2017 "All-In" Award recipient Goumba Johnny Sialiano for all he does for the tournament and for being such a great supporter for over 10 years.

The P4L committee appreciates the support of all the guests, supporters and sponsors including ZYR Vodka, The Cosmopolitan Las Vegas, Sierra Nevada, Budweiser, NY Knicks, NY Rangers, NY Yankees, Pro




Ethan Ruby with Goumba Johnny Sialiano and Jeremy Schwartz



Ethan Ruby with winner Doug Bortner and runner up Anthony Tedesco

Poker Gear, Crazy Cups, Blast Billiards, PokerDivas, GoCharity, Poker Players Alliance, and many more. The event could not happen without their support.

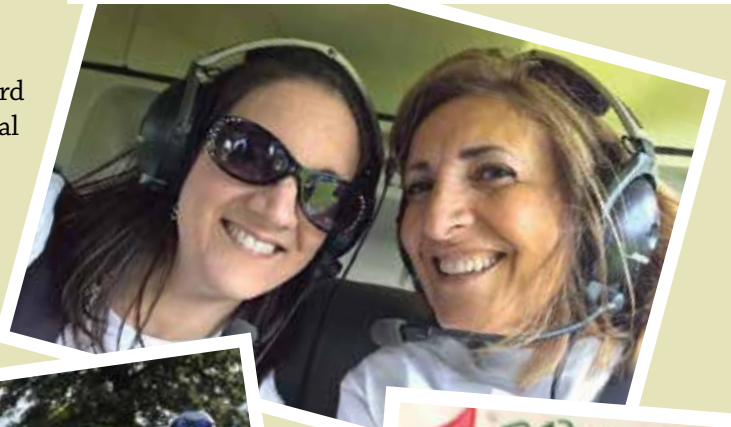
P4L would like to send a special thank you to Jewelry on 5th, Semper Capital, Marc Buoniconti, Suzie Sayfie, Tommy Crudup, Chef Jonathan Scinto, Courtney Culkin, Mary Gatchell, Jimmy Lee, Chris Murney and Tony's Di Napoli.

Because of the P4L supporters, we are proud to say that donations over the years have truly made it a difference in the advancement in paralysis research. The Buoniconti Fund and Miami Project are continuously making tremendous strides towards a cure as the result of this support. The 13th Annual Poker4Life™ Charity Poker Championship Event will again be held in spring of 2018. 

21st Annual Ricky Palermo Spinal Injury Golf Tournament

This year our friend Ricky Palermo and his family hosted The 21st Annual Ricky Palermo Spinal Injury Golf Tournament on August 5th at Terry Hills Golf Course with more than 200 golfers participating and 400 people attending the dinner that followed at Genesee Community College in Batavia, New York. The golf tournament has raised more than \$1.2 million over the past 21 years to help those suffering from the devastation of paralysis. Miami Project scientist Dr. Mark Nash spoke at the event.

One of the highlights of the event was a helicopter releasing “Golf Balls from Heaven” in memory of Joe Fragnito, Patty (Palermo) Fragnito’s husband. The ball closest to the pin won an amazing prize. Through the generosity of the Palermo’s friends and supporters, the tournament has been able to donate to programs that are involved in spinal cord injury research and care; United Memorial Medical Center in Batavia, Rochester’s Strong Memorial Hospital, Batavia’s YMCA functional electrical stimulation bike program to help people with challenges stay/get in shape and The Miami Project to Cure Paralysis’ research programs.



Top to Bottom:
Ricky Palermo with
Lena Ciszak and Luke
Peskor; Ricky Palermo;
Jamie Peskor and
Patty Fragnito; Jake
George, Tyler George,
Trey George and Trace
George; Picture of Joe
Fragnito on the Golf Balls
from Heaven poster

National Volunteer Chapters The BUONICONTI FUND

GOLF FOR A GREAT CAUSE

The **9th Annual Golf Tournament** to benefit the Tampa Chapter was held on October 29, 2016 at Westchase Golf Club. This tournament has been hosted by Rick Hart, with lead sponsorship from Invest Financial, since 2008 and raised more than \$250,000 to support the research at The Miami Project.



Rick Hart utilizes para golfer equipment to play



The Woody Foundation with Miami Chapter committee for check presentation

The Woody Foundation held its **6th Annual Golf Classic** on April 20 with nearly 100 golfers, sponsors and volunteers to support this great day of golf, community and spinal cord injury research awareness. The Woody Foundation has designated The Buoniconti Fund as an event beneficiary and partner for this tournament since 2012, raising more than \$200,000 to support the research at The Miami Project. The Woody Foundation, Inc. is a 501(c)(3) not for profit organization formed in 2011 to raise funds for the recovery of spinal cord injured persons. James “Woody” Beckham suffered his spinal cord injury making a rugby tackle in January 2011.



Adaptive team from Jackson Memorial Recreation Therapy

FIU SigEp Alumni and the Thomas B. Jelke Foundation teamed up to host the **Red Door Classic**. The mission was to have a golf tournament that attracted a crowd who cared about giving back to the community. The

Buoniconti Fund to Cure Paralysis was selected as one of the 3 event beneficiaries. The Miami Chapter has received more than \$20,000 in 2016-17 from the first two tournaments. The relationship began with FIU SigEp undergraduates, their philanthropic efforts raised \$25,000 since 2009.




Orlando Golf foursome

Hosting an annual golf tournament successfully for 20 years is a tremendous commitment. Nick Buoniconti and the Orlando Chapter have raised nearly \$1 million since 1999, and redefined the traditional tournament into a day of FUN for a good cause. Event partners and sponsors like Carrabba's Italian Grill, Coca-Cola and the community from industries such as law, construction and development, finance, restaurant and hospitality annually help raise much needed funds and awareness.



Pittsburgh Chapter Volunteer Director Jim Hoy and volunteers

The Pittsburgh Chapter hosted their **13th Annual Golf Tournament** on June 30 at Carmichaels Golf Course with another *sell out* crowd of golfers, volunteers and sponsors including Jeremie Synder Electrical. This annual tournament has raised \$200,000 to support The Miami Project to Cure Paralysis. 

Let us know if your community could benefit from a Volunteer Chapter which develops fundraising events and awareness campaigns to help us reach our goal of finding a cure for paralysis. There's no better time to create SCI awareness in your community! Email bfchapters@med.miami.edu or call **(305) 243-3863** to get started. Visit www.thebuonicontifund.com/chapters for the latest events and community outreach and join The Buoniconti Fund Chapters on Facebook.

CHAPTERS UPCOMING EVENTS

October 14-15 ~ Southeast Michigan Chapter ~ Detroit Marathon 'Run for a Reason' ~ Detroit, MI

October 20 ~ Miami Chapter ~ Corks & Forks at Morton's ~ Coral Gables, FL

November 17 ~ Darrell Gwynn Quality of Life Chapter ~ Hot Rods & Reels Charity Fishing Tournament ~ Homestead-Miami, FL

November 30 ~ Chicago Chapter – 19th annual Indulgence Night ~ Chicago, IL

January 13 ~ Miami Chapter ~ 9th annual Block Party presented by Hillstone Coral Gables ~ Miami, FL



Chapters Challenge is in its seventh year as a successful campaign that encourages our volunteers and supporters participating in local, national and international races to utilize our web-based program to raise funds and awareness on behalf of The Buoniconti Fund and The Miami Project to Cure Paralysis. Race participants can establish their own page, fundraising goals, contact friends and family, track their success, and make donations directly to The Buoniconti Fund. Our goal is to have our supporters walk, run, swim, bike or wheel their way across the finish line! <http://chapterschallenge.thebuonicontifund.com>



Darrell Gwynn with NASCAR drivers and Manny Martinez at HR&R Homestead-Miami 2016

Hot Rods & Reels Charity Fishing Tournaments

pair NASCAR drivers and legends with philanthropic supporters, executives and racing fans for a truly one of a kind, exciting day of fishing on the in-field lake during the Ford Ecoboost Weekend at Homestead-Miami Speedway and the Daytona 500 at Daytona International Speedway.


NASCAR drivers and legends team with NHRA Hall of Fame former drag racer Darrell Gwynn to raise awareness for spinal cord injury research and people living with paralysis. The Darrell Gwynn Quality of Life Chapter of The Buoniconti Fund to Cure Paralysis is the event host and benefiting charity.

Hot Rods & Reels participants, tournament sponsors, event partners and guests also have the unique opportunity to witness a special wheelchair presentation ceremony. Emmanuel "Manny" Martinez was the recipient of a custom wheelchair at Homestead-Miami Speedway in November 2016 and Greg DiGirolamo was the recipient at Daytona International Speedway in February 2017.



Darrell Gwynn with NASCAR drivers and Greg DiGirolamo at HR&R Daytona 2017

In addition to raising funds for innovative spinal cord injury research at The Miami Project to Cure Paralysis, the Darrell Gwynn Quality of Life Chapter of The Buoniconti Fund uses high profile events like **Barrett-Jackson**, the world's greatest classic car auction, to provide the gift of mobility. Vehicles are generously donated to the Chapter from our incredible supporters. A portion of the proceeds from each vehicle is used to provide a new, customized wheelchair for a spinal cord injured individual.

A fully restored 1964 Ford Galaxie Custom Hardtop was donated by Frank Tiegs for Barrett-Jackson Scottsdale in January 2017, and a new wheelchair was presented to Derik Hanson. A 2007 Ford Mustang GT Custom Fastback was donated by John Miller as the Charity Vehicle for the Palm Beach auction in April 2017. This vehicle was #6 of only 50 hand crafted conversions by Sanderson. 



Darrell Gwynn with charity vehicle at Barrett-Jackson Palm Beach 2017

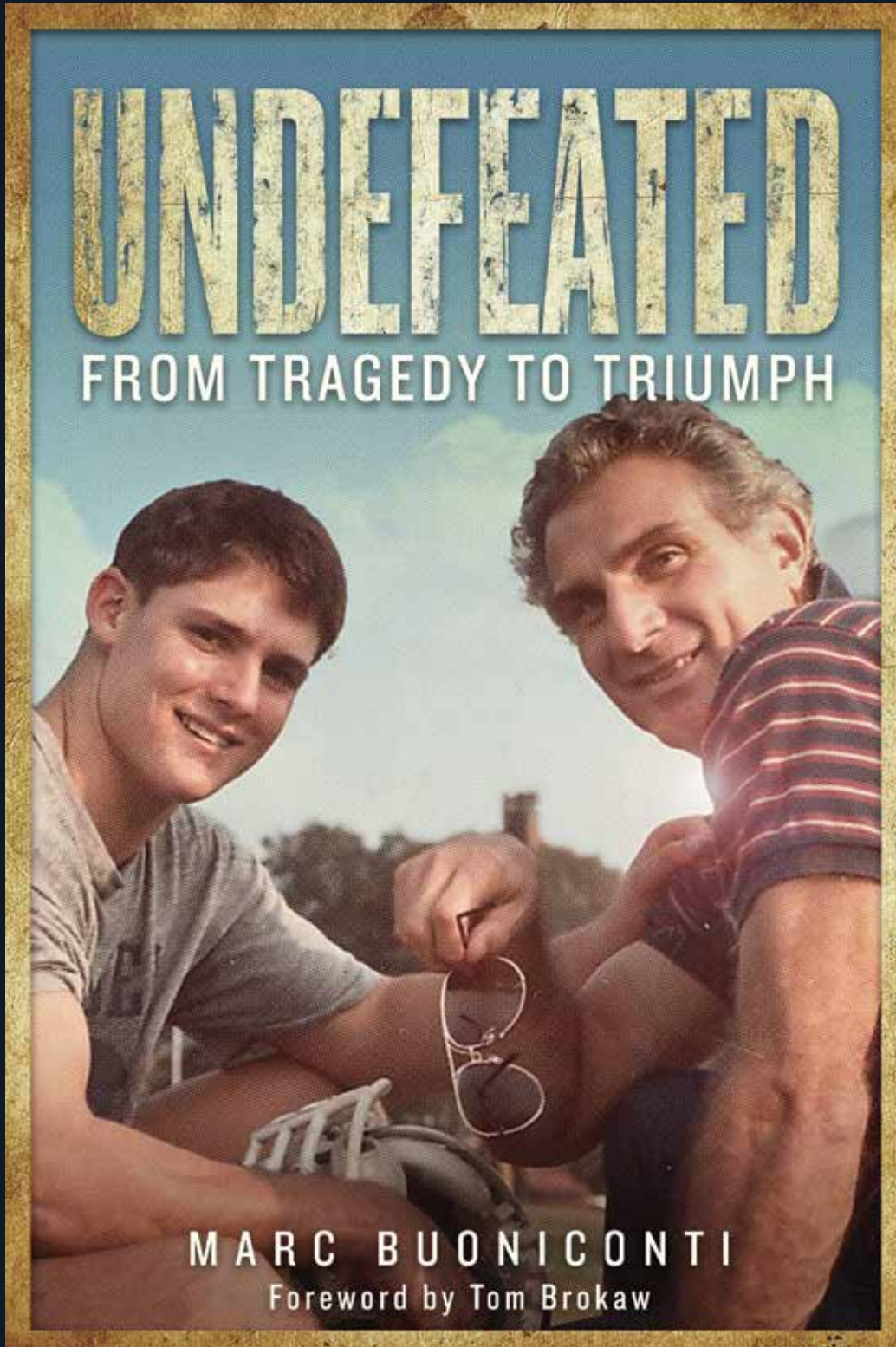


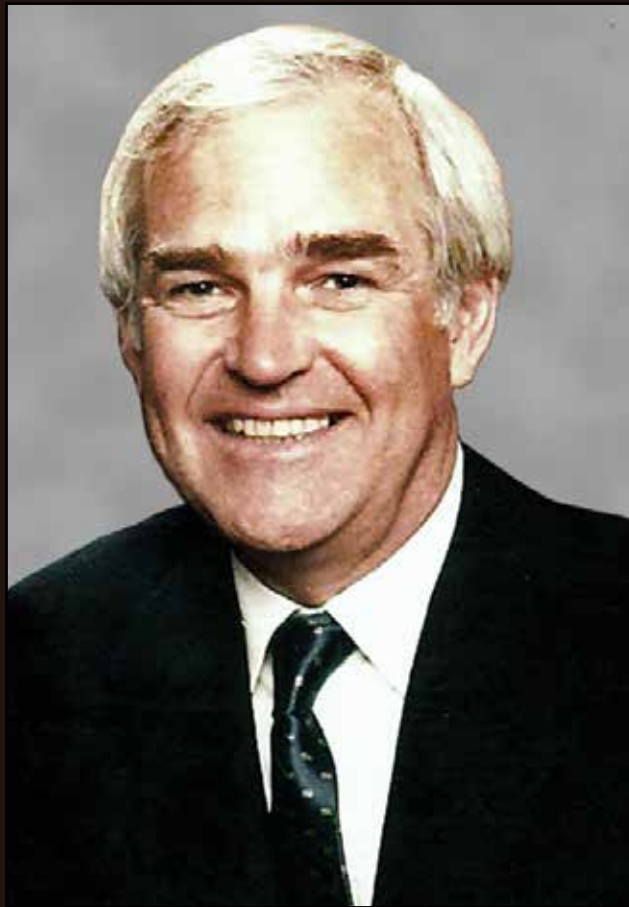
Darrell Gwynn with Derik Hanson at Barrett-Jackson Scottsdale 2017

Buy Marc's Newly Released Book Now!

Visit: www.TheBuonicontiFund.com/Undeclared

All proceeds benefit The Buoniconti Fund





Don Misner

1934 - 2017

Miami Project Co-Founder

Outstanding volunteer and donor

The Misner Foundation for Spinal Cord Injury
Research



Stanley Whitman

1918 - 2017

Major philanthropist and longtime Miami Project
and Buoniconti Fund supporter

Recipient of the 2009 Buoniconti Fund Award and
the 2016 Buoniconti Fund Humanitarian Award

Founder of Bal Harbour Shops



Joe Fragnito

1953 - 2017

Longtime friend of The Miami Project and
Buoniconti Fund

The Ricky Palermo Foundation

Thank you to our Buoniconti Fund Board of Directors



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September is National Spinal
Cord Injury Awareness Month

Help us create a National Conversation
in September and throughout the year
through Social Media. Follow us on
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#FacesOfParalysis



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