The Miami Project to Cure Paralysis is housed in the Lois Pope LIFE Center, a unique state-of-the-art facility designed to accelerate cutting-edge neurological research.

Founded in 1985 through the vision and dedicated efforts of Barth Green, M.D., an internationally recognized expert in the field of spinal cord injury, this Center of Excellence at the University of Miami Leonard M. Miller School of Medicine has assembled an international team of scientists and clinicians whose expertise relates directly to the problem of spinal cord injury.

In 1985, national attention focused on The Miami Project following the injury of NFL Hall of Fame linebacker Nick Buoniconti’s son, Marc. Together the family founded the Buoniconti Fund to Cure Paralysis, which raises awareness of and funds for spinal cord injury research at The Miami Project.

The Miami Project’s multidisciplinary research team, led by Scientific Director W. Dalton Dietrich, Ph.D., works cooperatively and synergistically to discover new treatments and ultimately apply them to people with spinal cord injury.
The Miami Project to Cure Paralysis, drawing on expertise in cell biology, electrophysiology, pharmacology, molecular biology, transplantation and surgical interventions, focuses its research in the following areas: Regeneration, Neuroprotection, Rehabilitation and Quality of Life. The Project is also committed to the Education and Training of young scientists entering the field of spinal cord injury research.

**REGENERATION RESEARCH**

Regeneration research is one of the most exciting areas of work underway at The Miami Project and the area that offers the greatest potential for finding a cure for spinal cord injury.

To reverse paralysis, scientists are developing new regeneration and repair treatments that will replace damaged nerves, promote and guide nerve regrowth, and establish reconnection of nerve fibers.

Promising treatment approaches are now emerging that show potential to be tested in clinical trials. The Miami Project has embarked on a Clinical Trials Initiative that is focused on taking pre-clinical discoveries made in Miami Project laboratories and carefully translating them into clinical trials.

The Miami Project takes a multifaceted approach to discover and develop regeneration treatments incorporating:

- **Cell Replacement strategies** that use embryonic, fetal, and adult (stem) cells and tissues for transplantation
- **Regrowth strategies** that use adult human cells for auto-transplantation (Schwann cells, olfactory ensheathing glia and oligodendrocytes)
- **Guidance and Reconnection strategies** to steer nerve fibers and help them establish functional connections.

By exploring new ways to promote the regrowth of injured nerves and repair the nerve pathways that carry information in the spinal cord, regeneration researchers hope to restore communication between the brain and paralyzed regions of the body.

**NEUROPROTECTION RESEARCH**

Neuroprotection researchers focus on understanding the damage that occurs during the hours and days after traumatic injury. With a better understanding of the early injury processes,
Miami Project scientists are designing and testing specific therapies to prevent damage, rescue neurons, and preserve nerve function. This new knowledge also influences the design of repair strategies.

Neuroprotective hypothermia treatments developed by University of Miami and Miami Project scientists are already revolutionalizing the way the medical community treats neurological disorders and heart attacks. While further research on drug and gene therapies is still needed, the practical application of new discoveries may mean that emergency paramedics will have new tools to limit the damage caused by traumatic injury, even at the scene of an accident.

**QUALITY OF LIFE**

People with spinal cord injury contend with many ongoing injury related problems that profoundly impact their quality of life. In addition to paralysis, issues such as pain, sexual function and fertility are also of interest to the investigative team.

Although not fully understood, abnormal pain sensations occur in as many as 70% of people with spinal cord injury. Miami Project scientists are developing new cell therapies and testing pharmacological agents to treat pain. Another important quality of life issue concerns fertility problems in men with SCI. While only 1% can father children naturally, Miami Project investigators have been extremely successful in developing treatment approaches that allow more men with SCI to become biological fathers.

**REHABILITATION RESEARCH**

Rehabilitation research is aimed at developing and evaluating new therapies and devices to improve muscle strength and function in people with spinal cord injury. While these rehabilitation therapies do not cure the injury, exercise programs and electrical stimulation assisted walking systems tested at The Miami Project have been shown to significantly enhance muscle strength and cardiovascular health.

Besides research efforts that promote health and wellness, Miami Project scientists are evaluating new therapies such as body weight support and treadmill training to determine their ability to help retrain the nervous system and improve walking function.

**EDUCATION AND TRAINING**

In addition to the various research focuses, a major function of The Miami Project is to provide education and training for the next generation of neuroscientists. Students and young scientists beginning their careers gain skills in the very specialized area of spinal cord research. Hundreds of researchers have trained at The Miami Project’s state-of-the-art center that offers an innovative and comprehensive research environment to answer the important questions in the quest for a cure for spinal cord injury.

*For further details about research efforts and findings at The Miami Project, please see the enclosed annual Research Review and biannual magazine, The Project.*
The broad scope of research carried out at The Miami Project has focused on answering questions that help define human spinal cord injury and reveal strategies for the repair of damaged spinal tissue. The team has also made advances in knowledge that have improved the current care of people with SCI. Over the last two decades, The Miami Project has made claim to several scientific achievements.

- **Pioneered** the concept of a multidisciplinary approach to SCI research; assembled the most comprehensive team of researchers to address the multifaceted problems of spinal cord injury.

- **First** to build a state-of-the-art SCI research facility that under one roof houses the tools and technology that in the hands of researchers will provide advances to find a cure.

- **Established** the largest collection of postmortem human spinal cord tissue in the Western Hemisphere. Pioneering anatomical observations and physiological recordings have revolutionized the understanding of human injury.

- **Designed** novel experimental strategies including mild lowering of body temperature (hypothermia) to limit secondary damage following SCI. Promising effects with Interleukin-10, and the inactivation of NFkappaB are also under investigation.

- **First** to demonstrate that adult human central nervous system neurons can regenerate when provided with a supportive cellular environment.

- **Discovered** that the adult nervous system has a remarkable capacity to accept and integrate transplants of neuronal cell lines. Demonstrated that embryonic neurons can reconnect to muscle and restore its function in animals.

- **Initiated** studies to explore whether neural precursor cells or stem cells can be developed and stimulated to mature into different types of nervous system cells.

- **First** to establish optimal laboratory methods to isolate and expand human Schwann cells in culture from adult peripheral nerves – which represent critical steps for the use of autologous Schwann cells grafts for neural repair.

- **First** to demonstrate remarkable improvement in walking function in animals using an innovative treatment that combined Schwann cell grafts with the administration of a cell messenger molecule (cyclic AMP) and the drug, rolipram.

- **First** to conceive and develop a novel intraoperative monitoring technique that makes spine surgery safer. The technique is now used nationwide and reduces the risk of paralysis during pedicle screw placement surgery.

- **First** to provide evidence that humans possess specialized nerve circuitry that influences walking and could possibly be enhanced by rehabilitation training. These observations contributed to the development of body weight support gait training. Miami Project investigators are currently adding to the body of knowledge regarding the effectiveness of this rehabilitative training.

- **First** to show that grip strength and sensory/motor function can be improved in people with chronic SCI by using a task-practice based therapy that influences the neural circuitry for controlling arms and hands.

- **Completed** extensive testing of a computer-driven Parastep® 1 assisted-walking system. Showed its ability to enhance cardiovascular and conditioning effects and provided supporting evidence for approval by Medicare to reimburse for the device.

- **Provided** evidence that electrically-stimulated exercise positively influences cardiopulmonary function and strengthens the immune system in paralyzed people.

- **First** to offer proof that poor sperm motility in men with SCI is a result of organ dysfunction. New knowledge and assistive reproductive procedures have afforded the opportunity for men with SCI to father biological children. Recent Miami Project findings reveal the possibility of a rational treatment for the infertility.

- **Created** bioengineered cell line transplants that show promise in the treatment of chronic SCI pain.

- **Developed** new strategies for the multidisciplinary evaluation of SCI pain. The comprehensive state-of-the-art approach targets pathological, physiological, psychological and social aspects of pain in order to tailor individual treatment strategies. This combination of methods will be useful in evaluating the outcomes of spinal cord injury clinical trials.
The Miami Project To Cure Paralysis

A Center of Excellence
At the University of Miami Miller School of Medicine

Research Participation

Post Office Box 016960 (R-48), Miami, Florida 33101-6960, (305) 243-7108, (305) 243-3913 (fax)
mpinfo@med.miami.edu, www.themiamiproject.org
CLINICAL RESEARCH

Investigators rely on individuals with SCI to serve as volunteers for specific clinical research. Studies are designed to answer questions about some aspect of SCI or the effectiveness of a particular treatment.

Clinical research at The Miami Project allows investigators to understand and develop better treatments for the complications associated with SCI. It also allows researchers to test treatments to promote maximal recovery.

All clinical studies have guidelines about how the experiment will be conducted (the protocol) and who can participate (the criteria.) These guidelines help ensure that researchers will be able to answer the questions they plan to study.

The protocol specifies the length of the study, the schedule of tests or interventions, how the results are to be measured, and the inclusion criteria. The criteria define the type of people included or excluded in the study and are based on such factors as age, gender, the type of injury and time since injury.

Many people with SCI wish to serve as research volunteers for SCI studies. Because research studies have specific criteria, not everyone with SCI is able to participate. A limited number of people meet the criteria and/or have the ability to make a commitment to participate in a particular study.

Through the commitment of relatively few volunteers, however, the knowledge gained and communicated ultimately benefits many people with SCI.

Choosing to participate in a research study is an important personal decision. To learn more about how clinical trials are carried out, where they are being conducted, and making informed decisions about research participation, see:

- Experimental Treatments for Spinal Cord Injury: What you should know (enclosed) provided by the International Campaign for Cures of spinal cord Paralysis (ICCP)
- www.Clinicaltrials.gov a service of U.S. National Institutes of Health
- www.CenterWatch.com a Clinical Trials Listing Service

BECOMING A PARTICIPANT AT THE MIAMI PROJECT

To be considered for current and future Miami Project research studies, complete the enclosed Intake Form. Information from the Intake Form will be maintained in The Miami Project's database as a resource for Miami Project researchers.

To be accepted in a research program, potential volunteers must:

- fit the criteria for a specific study
- be invited to participate by the investigator
- be able to commit the time and resources for the duration of the study

Specific Studies: Miami Project clinical researchers are conducting studies to improve current clinical and rehabilitative care. Presently, research participation is limited to people with disorders and injuries of the spinal cord. Enclosed is information that describes the purpose, criteria and duration of Active Studies underway at The Miami Project. If you feel you fit the criteria for a particular study and require further information, send an email to mpinfo@med.miami.edu or call the Miami Project Education Office at 305-243-7108.

Time Commitment: Depending on the study, the time commitment varies from two days to one year. Most studies require that the individual live in the Miami area for the duration of the study.

Costs: The Miami Project does not charge volunteers, nor generally provide compensation for participation in clinical trials. Expenses and arrangements for accommodations, meals, and medical care are the volunteer's responsibility for the duration of the study.
Frequently Asked Questions

When will there be a cure?
At the present time, neither Miami Project researchers nor any other scientist can predict when human trials to promote regeneration in the spinal cord will lead to a cure. The steps for moving a discovery from an idea in the laboratory to a treatment that can be tested in human trials are many. Researchers must gather sufficient proof of functional recovery in animal studies to justify the use of a treatment in human trials. They also need to demonstrate that the results can be repeated in independent laboratories and that the treatment works when tested in larger and chronically injured animals. In addition, to test a treatment in clinical trial, the proposed trial needs to be approved by regulatory agencies such as the Food and Drug Administration (FDA). The total process is incredibly time consuming and expensive, but it is essential to develop reliable cure therapies that can be used in the greatest number of people with predictable beneficial results.

Why haven’t you tested cell transplantations in a human yet?
First and foremost, patient safety is a real concern. Experimental cell grafting done before effectiveness and safety have been proven in pre-clinical testing could result in undesirable side effects such as chronic pain, further paralysis or even death. Experimental surgeries may lead to scarring and/or tethering of the spinal cord, which can produce further loss of function. In addition to these risks, there are many other considerations, including the high cost of surgical procedures, their inherent risk, and the potential for post-operative complications. All of these must be carefully considered so an experimental treatment is not taken to clinical trial prematurely, that is, prior to proving its potential benefit and understanding its potential risks via studies with animals.

Why is it taking so long to find a cure?
We understand that from the patient’s perspective scientific progress is painstakingly slow. What many people forget is that, up until the 1980s, spinal cord regeneration was believed by most researchers to be impossible. What many also forget is the spinal cord is incredibly complex and scientists are still making new discoveries about how the spinal cord functions. Encouragingly, since the early 1980s, the scope of SCI research has literally exploded as SCI researchers and their colleagues in related fields have achieved important scientific breakthroughs. These breakthroughs include a better understanding of spinal cord injuries themselves, drugs that can limit the amount of damage to the cord, the discovery of proteins that stimulate (or prevent) regeneration, and genetic-engineering and cell transplantation techniques that are being transformed into new therapeutic strategies. Investigators now are using multiple approaches and combination therapies to promote regeneration. They are testing a variety of potential treatments in different types of injuries in animals. It is also important to note that one step in testing new therapies is to conduct experiments with chronic injuries. These experiments require months of post-injury and post-grafting time in which to evaluate recovery. Until these treatment techniques are proven to work reliably, however, it would be premature and unsafe to test them clinically (see above).

Other countries are offering experimental treatments to people with SCI. Why are they farther ahead?
One may get the impression that other countries are ahead when clinicians offer experimental treatments without testing them in valid clinical trials or before the treatments have been carefully evaluated in pre-clinical testing. Preclinical testing is important to provide sufficient evidence of the treatment’s potential benefit and safety. Once this evidence is obtained, a valid clinical trial is necessary to determine whether any benefits to humans are associated with the treatment or whether they are a result of other factors. If a treatment is ever to be proven effective, preclinical testing and valid clinical trials will be essential. When a group offering an experimental treatment does not follow international guidelines for clinical trials in SCI, this may give the false impression that they are ahead.

One may also get this false impression when, based on the testimonies of people who have received experimental procedures, the clinicians claim the procedure is beneficial and safe. In clinical trials, anecdotal evidence (testimonials and case studies) is insufficient to prove benefit. Claims of benefit should be made only when data collected from participants in careful follow-up assessments in valid clinical trials show the benefit to be the result of the treatment.

Do you collaborate with other centers?
Yes, collaboration is very important to allow Miami Project scientists to stay at the cutting-edge and to accelerate overall progress in the field of SCI research. Though scientists at different centers are exploring different strategies, they communicate regularly through meetings, publications and private discussions. Often these communications lead to sharing of resources and ideas. Thus, no center can or should claim to be alone in their quest for a cure for SCI. Miami Project researchers are involved in many collaborations and are in communication with virtually all major SCI research groups. The Miami Project also has strong associations with other SCI advocacy groups and is a founding member of a collaborative effort called the International Campaign for Cures of Spinal Cord Injury Paralysis (ICCP).
Resources for Care

Receiving treatment for SCI is different than participating in research.

Facilities that offer treatment programs admit and evaluate a patient, and then design an individualized treatment plan for that person with the goal of maximizing recovery.

Facilities that conduct research focus on evaluating a treatment, not an individual. The goal is to evaluate the effectiveness of a new treatment. People with SCI serve as volunteers so researchers can collect information to understand more about SCI in general or about new treatments.

The Miami Project to Cure Paralysis is a research facility, not a patient care facility. Patient services such as inpatient care, outpatient evaluations or treatment are available from various clinical colleagues worldwide.

We offer information below about SCI clinical care at the University of Miami/Jackson Memorial Medical Center. The following may be useful in locating other clinical care facilities.

Choosing a High-Quality Rehabilitation Program
Available at http://www.bu.edu/hdr/products/choosing/choosing.pdf
From the Center for Health and Disability Research, 102 Irving Street, NW, Washington, DC 20010-2949 (866) 380-4344

Choosing an SCI Rehabilitation Facility
From the National Spinal Cord Injury Association (NSCIA), (800) 962-9629

SCI Clinical Care
at the University of Miami/Jackson Memorial and Miami VA Medical Centers

There are several clinical care programs available for people with spinal cord injury at the University of Miami/Jackson Memorial Medical Center. These programs are at the expense of the patient and are not Miami Project research programs. For assistance with coordinating a visit to the University of Miami, please call the Physician’s Referral Department at (305) 243-5757 or (800) 432-0191. International patients may contact the International Health Center at (305) 243-9100, fax (305) 243-9101.

UM Department of Rehabilitation Medicine
Inpatient and Outpatient services
For appointments with physicians or further information, call (305) 243-6605

UM Department of Urology
Urological Consultation
For appointments with physicians or further information, call (305) 243-6090

UM Department of Neurological Surgery/University of Miami Spine Institute
For appointments with physicians or further information, call, (305) 243-6946 or (800) 996-3783

Miami VA Medical Center SCI Service
Provides treatment for veterans with SCI.
For appointments with physicians or further information, call (305) 575-3174

Resources for SCI Information
For more about spinal cord injury information and resources, contact the following organizations.

National Spinal Cord Injury Association (NSCIA)
1 Church Street #600, Rockville, MD 20850
(800) 962-9629; (301) 214-4006
www.spinalcord.org E-mail: info@spinalcord.org

Christopher & Dana Reeve Paralysis Resource Center
636 Morris Turnpike, Suite #3A, Short Hills, NJ 07078
(800) 539-7309
www.paralysis.org E-mail: info@paralysis.org

United Spinal Association
75-20 Astoria Boulevard, Jackson Heights, NY 11370
(718) 803-3782
www.unitedspinal.org E-mail: info@unitedspinal.org

Paralyzed Veterans of America
801 Eighteenth Street, NW, Washington, DC 20006-3517
(800) 555-9140
www.pva.org Email: info@pva.org

SCI Information Network at www.spinalcord.uab.edu
University of Alabama Birmingham Model SCI System
619 19th Street South, SRC 529, Birmingham, AL 35249
(205) 934-3283 or Email: sciweb@uab.edu

Health Information on Spinal Cord Injuries/Diseases
From National Institutes of Health at http://health.nih.gov/