

CHRISTOPHER REEVE PARALYSIS FOUNDATION 2003 Annual Report



PERSISTENCE

THE CHRISTOPHER REEVE PARALYSIS FOUNDATION (CRPF) IS COMMITTED TO FUNDING RESEARCH THAT DEVELOPS TREATMENTS AND CURES FOR PARALYSIS CAUSED BY SPINAL CORD INJURY AND OTHER CENTRAL NERVOUS SYSTEM DISORDERS. THE FOUNDATION ALSO VIGOROUSLY WORKS TO IMPROVE THE QUALITY OF LIFE FOR PEOPLE LIVING WITH DISABILITIES THROUGH ITS GRANTS PROGRAM, PARALYSIS RESOURCE CENTER, AND ADVOCACY EFFORTS.

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CHAIRMAN'S MESSAGE

COLLABORATIVE SPIRIT, EXHAUSTIVE RESEARCH

LAST YEAR, I BEGAN TO BREATHE ON MY OWN, regain my sense of smell, and speak normally. No one could have predicted these milestones when I injured my spinal cord and became paralyzed from the neck down in 1995. But they are not miracles.

In February 2003, surgeons at University Hospitals in Cleveland implanted an experimental device that activates my diaphragm, allowing me to breathe



CHRISTOPHER REEVE
Chairman of the Board

without a respirator. Developed by a team of doctors and biomedical engineers, the device – an investigative diaphragm pacing system – reflects how far researchers have come in finding treatments for paralysis. Although CRPF did not finance the particular project that produced the device, its development clearly demonstrates the value of scientific collaboration and validates one of CRPF's most important goals: promoting collaborative, interdisciplinary research.

Our Research Consortium on Spinal Cord Injury has taken just that approach since it began nine years ago. The Consortium harnesses the collective energy of seven renowned scientists with wide-ranging skills and a willingness to pool their efforts. These senior investigators also are nurturing the next generation of spinal cord researchers, gifted young scientists who “graduate” from the Consortium and start their own spinal cord laboratories.

With your support, our efforts are paying off in other ways as well. In May 2003, the Christopher Reeve Paralysis Act was introduced in Congress. If enacted, this unprecedented bill would expand research, rehabilitation, and quality of life programs

at the National Institutes of Health, the Centers for Disease Control and Prevention, the National Center for Rehabilitation Research, and the Department of Veterans Affairs. CRPF's Action Network (featured on www.ChristopherReeve.org) has been instrumental in gathering supporters and linking them to members of Congress. The Action Network enables the public to become informed advocates, giving ordinary citizens the information they need to make the case for increased government funding for spinal cord research. Together, our voices can and will make a difference.

In September 2003, I was honored to receive the Mary Woodard Lasker Public Service Award. It pays tribute to individuals whose support of medical research and the health sciences leads to advances in medical care. This award would not have been possible without the countless scientists who devote their lives to finding treatments for spinal cord injuries and other disabilities. The Lasker award was a public acknowledgment of the importance of their work, which is supported by your contributions to CRPF.

In 2003, I experienced first hand how much scientists and doctors can accomplish when they have adequate funding and a collaborative spirit. Your generosity to CRPF is critical to moving promising discoveries in the laboratory into human trials in the clinic. With your continued commitment, the day will come when many more of us will not only breathe more easily, but actually will be able to stand up and walk into a future that is now transforming from a dream into a reality.

SCIENTIFIC PERSISTENCE, RENEWED DETERMINATION

THE HOPE THAT SOME DAY A SINGLE DISCOVERY would cure spinal cord injuries has given way to the conviction that it will take a series of carefully timed interventions that draw on research from many disciplines.

The first line of attack must halt the cascade of cell destruction that begins soon after the injury and can last for weeks, causing secondary damage far beyond the original insult. Next, doctors will need techniques to reverse paralysis and restore functions like bowel and bladder control and respiration. These interventions may include treatments to rebuild lost nerve circuitry and to maximize the ability of surviving nerve pathways to assume new roles. Novel approaches to rehabilitation will be essential, and bioengineering may even play a role.



OSWALD STEWARD, PH.D.
Chairman,
Science Advisory Council

In the last 18 months, the Christopher Reeve Paralysis Foundation (CRPF) has devoted more resources than ever before to jumpstart this multi-tiered line of attack and move promising research into clinical trials. A new \$5 million *Translational Research Fund* enables CRPF to support scientists who have made critical discoveries and have developed well-designed plans to move these discoveries from the laboratory to the threshold of human trials. In recognition of the challenges inherent to this process, Fund grants are larger than those CRPF makes through its Individual Grants Program. The Foundation has also organized the *CRPF North American Clinical Trials Network for the Treatment of Spinal Cord Injury*, a partnership among six academic centers with strong spinal cord neurosurgical and rehabilitation programs. These initial members of the Network are collaborating with a similar group of research centers in Europe to pool data, develop more sensitive outcome measures, and establish common protocols for safely testing new treatments.

These programs are designed to help move fundamental scientific discoveries into therapies that help paralyzed people. Already, neuroscientists from around the world have made major advances toward this overarching goal. Some of the milestones achieved in 2003 are summarized below.

PREVENTING SECONDARY DAMAGE. Following a spinal cord injury, immune cells respond to the injury site to clear debris, defend against infection, and encourage healing. Unfortunately, this process also causes harmful inflammation, which destroys more spinal cord tissue. Scientists moved closer to understanding how to manipulate the immune response to an injury in order to control damage and promote repair. For example:

– **Promoting repair:** Scientists continued to explore ways to enhance the benefits of the immune response. In an initial clinical trial in Israel, doctors injected activated macrophages, the large immune cells that devour debris and foreign pathogens, into the injured spinal cord to test the safety of this approach. Study participants appeared to have suffered no ill effects, so a second trial involving multiple centers in the United States was recently launched.

– **Controlling inflammation:** Other researchers focused on taming the destructive power of inflammation by harnessing signaling molecules that direct the immune response. When researchers injected chemical mediators or antibodies into the spinal cord soon after an injury, they found they could short-circuit the inflammatory response, reduce secondary injury, and promote repair of spinal tissue.

REGENERATING NERVE CELLS AND CIRCUITS. Major findings in 2003 advanced our understanding of how axons, the thread-like extensions on nerve cells that carry nerve impulses, grow and form connections with other neurons in early development. These findings raise hope that developmental processes might be recapitulated after an injury to induce axons to regrow over great distances and form new connections. Several developments in 2003 are particularly noteworthy:

– **Blocking growth inhibitors:** Naturally occurring substances that prevent the regrowth of injured axons increase in concentration following a spinal cord injury. Last year, we learned more about how to block some of these growth inhibitors, particularly those in myelin, the fatty insulation that surrounds axons. Myelin contains

molecules called Nogo, which activate receptors on nerve cells that inhibit axon growth. Three teams of scientists each bred genetically modified mice that lacked Nogo, but only one of the mutant mouse strains experienced a dramatic improvement in axon regeneration following spinal cord injury. Pinpointing precisely how that strain differed from the others could lead to new targets for treatments. In follow-up studies, researchers synthesized small molecules that prevented Nogo from activating its receptors and promoted axon regeneration when injected into animals with spinal cord injuries. Based on these promising results, scientists are working to move this technique into clinical trials. Finally, in an entirely different approach, scientists demonstrated that immunizing animals against the molecules that impede axon growth stimulated regeneration and recovery of function. Although the animals in this project were immunized before an injury, potential human treatments would involve administering antibodies after an injury.

– *Controlling intracellular signaling:* Researchers continued to study the intracellular signaling molecules that guide growing axons to form appropriate connections. We know, for example, that certain receptors on the leading edge of the axons act as attractants to facilitate axonal growth while others repel growth. In 2003, scientists confirmed and extended the major discoveries made in 2002 about two critical signaling pathways called cyclic AMP (cAMP) and Rho. Researchers also started a new round of experiments to determine whether drugs that affect cAMP and Rho could help people with spinal cord injuries.

– *Transplanting cells:* Spinal cord trauma wipes out nerve cells and their support cells (“glia”) near the injury site, and both must be restored for full recovery to occur. The transplantation of two types of replacement cells received much attention last year:

Stem cells: Researchers made important technological breakthroughs in prompting these primitive cells to differentiate into more specialized cells that could be used in therapies. Several research groups began to assess whether different types of human stem cells could promote repair after spinal cord injury, and the results of these experiments should be available soon.

Olfactory ensheathing cells, or OEGs: Another promising candidate for transplant therapy is a special glial cell found in the olfactory nerves in the nose. These olfactory ensheathing cells, or OEGs, enable growing axons to penetrate the “do-not-enter” zone that separates the brain and the spinal cord from the rest of the body (called the “blood-brain barrier”). Previously, scientists had shown that transplanted OEGs could enhance nerve regeneration across a spinal cord injury. In 2003, new studies reproduced those findings and demonstrated that transplanted

OEGs could stimulate new growth, even when introduced weeks after the injury. In a Phase I clinical trial in Australia, a small group of people with spinal cord injuries have received OEGs, but the results are not due for three years. So far, no adverse effects have been reported.

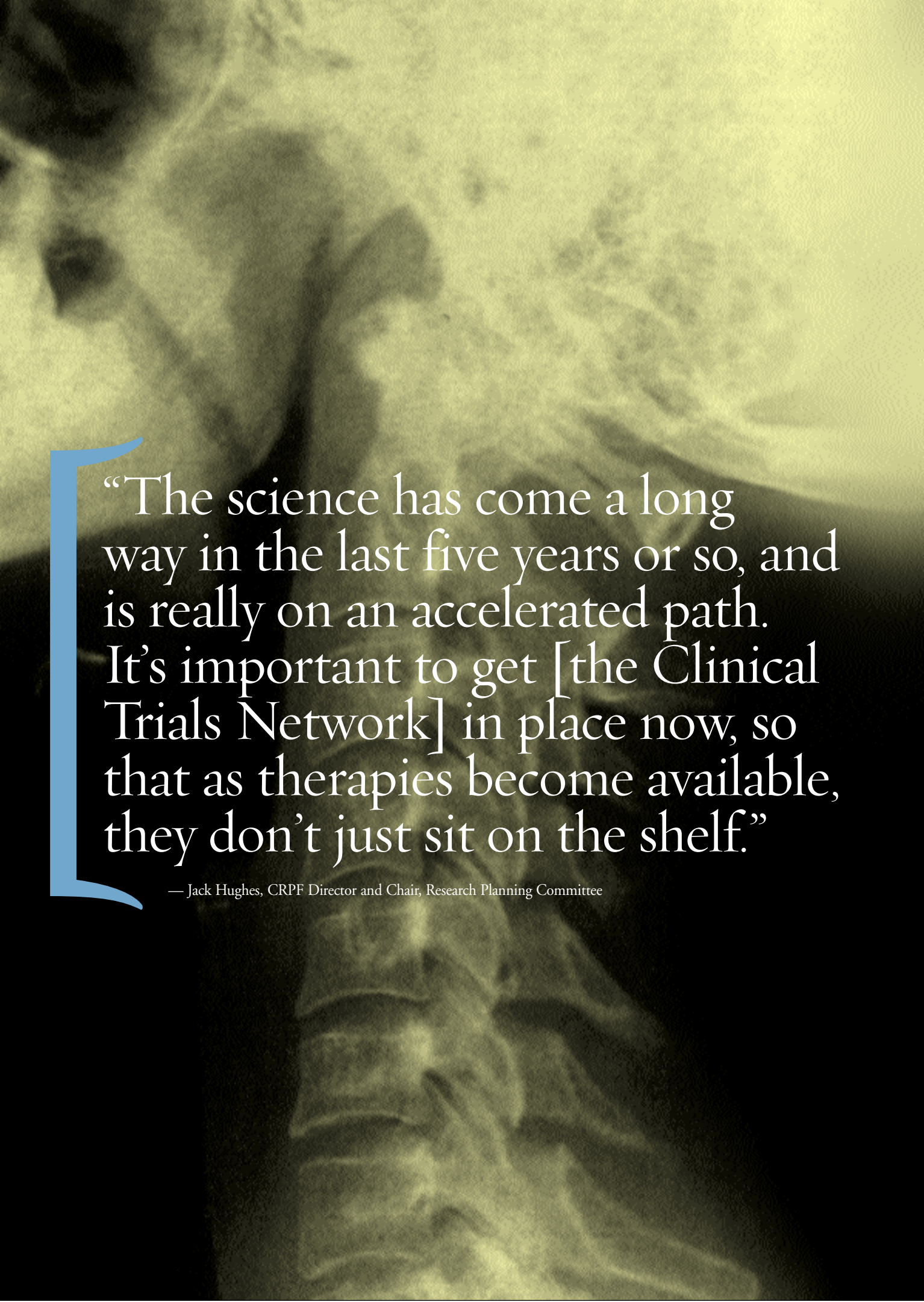
Meanwhile, in China and Portugal, doctors have transplanted cells from the nose into people with spinal cord injuries, but these experiments lack the controls of rigorous clinical trials, and little data is available on the people being treated.

– *Stimulating the generation of new neurons:* Last year brought a better understanding about the production of new neurons that occurs naturally throughout life, to a limited degree, in certain brain areas. Scientists became more familiar with the conditions that trigger cell division in these neuron-birthing zones, findings that may one day enable doctors to stimulate this process to re-establish critical communication channels between the brain and spinal cord.

– *Retraining and rewiring the injured spinal cord:* Rehabilitation is critical following spinal cord injury, and some forms of exercise may help surviving nerve circuits compensate for those destroyed by an injury – but no one knows yet which approaches work best. Last year, a major clinical study compared step training on a treadmill to traditional rehabilitation. The results have not yet been published. At the same time, scientists identified genes that are turned on by exercise, an indication that certain types of exercise may do more than maintain muscle strength and cardiovascular fitness in people with spinal cord injuries. Research is continuing to identify the best training techniques and how they affect biological systems, including the skeletal and the immune systems.

– *Applying bioengineering and robotics:* Loss of function following spinal cord injury occurs when nerve connections between the brain and the body are severed. New developments in bioengineering and robotics have raised hope that brain signals might be intercepted and used to control robotic devices, like artificial hands or legs. Last year, researchers harnessed nerve signals recorded from monkeys’ brains and successfully trained the monkeys to move a computer cursor with thoughts alone. This remarkable project could lead to new technologies that enable individuals with spinal cord injuries to use their thoughts to turn lights on and off, answer the phone, or potentially, execute even more complicated tasks.

These advances demonstrate how scientific persistence toward a goal – no matter how challenging the goal might be – can pay off with real advances. Each new piece of the spinal cord puzzle takes us one vital step closer to new therapies.



“The science has come a long way in the last five years or so, and is really on an accelerated path. It’s important to get [the Clinical Trials Network] in place now, so that as therapies become available, they don’t just sit on the shelf.”

— Jack Hughes, CRPF Director and Chair, Research Planning Committee

PROMISING THERAPIES, PRIORITY CLINICAL TRIALS

SPINAL CORD RESEARCH is at a critical crossroads. Dozens of promising therapies aimed at regenerating function out of the injured cord are in the pipeline, and moving them into clinical use is the highest priority.

Yet, despite the increasing traffic on the path to clinical progress, the roadway is still largely under construction. A number of fundamental scientific questions remain unanswered, both about the immense natural variability of spinal cord injury and how best to measure therapeutic efficacy. Such questions require large studies, and large studies require multiple centers using the same examination criteria and treatment protocols. At the same time, there is a notable lack of infrastructure in place for sharing data and standardizing treatment protocols across North American research centers – in part because there has been little need to. Until now, that is.

With spinal cord clinical trials already underway in the U.S. and many more to come in the next few years, there is an urgent need to build bridges among researchers and pave the way for accelerated progress.

“We’ve learned from head injury and stroke trials that you really need to lay the groundwork and do your homework in order to get interpretable data from a clinical trial,” says Susan Howley, CRPF Executive Vice President and Director of Research.

Toward that end, the Foundation has brought together five leading clinical research centers and a biostatistical center to create the CRPF North American Clinical Trials Network for the Treatment of Spinal Cord Injury. The Network’s singular focus is to bring promising therapies out of the laboratory and into their proper place

CRPF NORTH AMERICAN CLINICAL TRIALS NETWORK FOR THE TREATMENT OF SPINAL CORD INJURY	
<i>Institution</i>	<i>Principal Investigators</i>
Baylor College of Medicine, Houston	Robert G. Grossman, M.D. Shankar Gopinath, M.D.
Northwestern University, Rehabilitation Institute of Chicago	William Zev Rymer, M.D., Ph.D. Lisa-Ann Wuermsler, M.D. David Chen, M.D.
University of Texas Health Science Center, Houston	Guy Clifton, M.D. Andrew C. Papanicolaou, Ph.D.
University of Toronto, Toronto	Charles Tator, M.D. Michael G. Fehlings, M.D., Ph.D.
University of Virginia, Charlottesville	John Jane, M.D., Ph.D.
University of Texas School of Public Health, Houston*	Ralph Frankowski, Ph.D.

*Biostatistics and Data Management Center

in the quest for a cure, in a manner that provides incontrovertible evidence of effectiveness and safety. Led by principal investigator Robert Grossman, M.D., a neurosurgeon at Baylor College of Medicine, the team is collaborating with a similar-minded European consortium to define the “natural history” of spinal cord injury and refine outcome measures for treatment. In the process, the groups are building the foundation for a global cross-collaboration that will help speed therapeutic development and get useful therapies to people who need them.

“The science has come a long way in the last five years or so, and is really on an accelerated path,” says CRPF Director Jack Hughes. “It’s important to get [the Clinical Trials Network] in place now, so that as therapies become available, they don’t just sit on the shelf.”

‘Jumpstarting’ Clinical Testing

Hughes, who heads the Board’s Research Planning Committee, sees the Network as an opportunity for the Foundation to “jumpstart” the process of moving therapies into clinical trials. “To push research to a level where there are real expectations for therapies, there has to be a certain level of infrastructure in place and standard measures for efficacy and status,” he says. “By taking the lead on this initiative, the Foundation can help get therapies all the way through the testing process, something individual researchers may not have the resources to do. An important part of this is to make researchers’ jobs easier, so they don’t have to think about how to set up this whole infrastructure as part of a therapy trial.”

“The goal downstream is to be ready to go when the stream of

anticipated viable interventions reaches clinical trial stage,” says Howley. The Network plans to seek funding within two to three years from the National Institutes of Health for specific therapeutic or combination trials, according to Grossman. He and the Foundation have had initial meetings with program officers at the National Institute of Neurological Disorders and Stroke (NINDS) to discuss the study group design and parameters for outcome measures.



L-R: Martin E. Schwab, Ph.D., Ralph Frankowski, Ph.D., Volker Dietz, M.D., Susan P. Howley, Claudia Link, Ruediger Rupp, and Bernard Bussel at a meeting of the North American and European Networks.

“It’s important to have a lot of preliminary questions answered before moving into the ‘gold standard’ of a phase 3 efficacy trial,” says Naomi Kleitman, Ph.D., NINDS program director for spinal cord injury and peripheral nerve repair. In particular, she says, “It’s very important to look at the clinical measures that have been

developed and ask whether they’ll be sensitive enough to pick up any anticipated functional change that an intervention might produce.”

SCI Poses Special Challenges

By its nature, spinal cord injury presents special challenges to therapeutic development. For one thing, it is clear that initial spinal trauma produces a series of degenerative and regenerative steps. Therapeutic strategies under investigation target individual steps along the complicated pathway to recovery, from limiting secondary inflammation immediately after an injury, to preventing scar formation and stimulating axons to re-grow, to using stem cells to replace dead or damaged nerve cells.

“When you have a process as complicated and multifactorial as spinal cord injury, it’s pretty unlikely that any one therapy is going to have much effect,” says Grossman. “The trick will be in combining the therapies.” Gaining useful, well-powered data about which therapy to use when, and in what combinations, relies largely on having measures in place that are able to detect subtle but meaningful changes in a person’s status.

“It’s generally accepted that unless you have a miracle drug, you’re going to need a very large number of patients to demonstrate that the results you see aren’t just chance,” says Grossman.

Right now, points out Howley, outcomes measures that are currently used

in evaluating spinal cord therapy are “very crude,” and not likely to pick up the small changes that are expected from early regenerative therapies, for example.

Kleitman uses the analogy of a hurdle race. “We’ve learned from prior experiences about the importance of not setting the hurdle too high.” Rather than trying to show a “huge primary effect,” she says experts have come to realize that “maybe a smaller or functionally significant effect in a subgroup of patients would be a very good thing. In fact, it might be worthwhile to design your trial to look at that,” she says, by stratifying the patients according to the location of injury or other parameters.

The CRPF Network investigators have compiled a long list of variables and measures of progress to enable multiple analyses of the data set – including everything from age and injury particulars, to the timing of any post-injury interventions, to results of imaging studies that check for hemorrhaging or other factors that could influence outcomes. Biostatistical experts at the University of Texas-Houston will then examine the data from many angles to sort out which treatment works best for which people.

“If we had a therapy that made people leap out of bed and walk around as if nothing happened, we wouldn’t need to worry about detecting clinical trial outcomes,” Kleitman points out. “But we’re looking at much more realistic scenarios than that.”

PROOF OF SUCCESS

In the highly competitive world of science, being published is a noteworthy accomplishment because it signifies that an investigator’s research has undergone vigorous peer review and is recognized for its novelty, merit and validity. It is also a defining achievement, the “work product” of a scientist and one of the measures by which his contributions to the field are tracked. And, being published is one of the most effective ways for an investigator to share his findings

with his colleagues in the broader scientific community and help facilitate their research.

In some ways, scientific publications are equally as important for organizations like CRPF. They are one of the measures we use to judge the quality of applicants to our research programs and an outcome measure by which we judge the success of our research grants. They are proof-positive to our donors and supporters that we have invested their gifts to the Foundation wisely and in ways that help drive us closer to effec-

tive treatments for spinal cord injury.

In 2003, 28 CRPF-funded individual research grant projects were completed, out of which 51 publications emerged. Also in 2003, the seven laboratories of the CRPF Research Consortium on Spinal Cord Injury accounted for 20 publications.**

For a copy of any of these publications, please contact CRPF at 800.225.0292

*** Numerous manuscripts from both programs were submitted to journals prior to December 31, 2003 but were accepted and published in 2004.*

STORIES OF APPRECIATION, WORDS OF ENCOURAGEMENT



WILDERNESS INQUIRY, MINNEAPOLIS, MN – QUALITY OF LIFE GRANT RECIPIENT

“I would like to thank you from the bottom of my heart for allowing me the opportunity to be associated with Wilderness Inquiry. I live on a fixed income and without your help would never be able to afford to go on these adventures. I have seen moose, deer, bald eagles, osprey and various wild animals all in their natural habitat because of Wilderness Inquiry. I have become a better man due to Wilderness Inquiry. It is almost as if I am not handicapped when I am on these adventures.”

SHAKE-A-LEG, NEWPORT, RI – QUALITY OF LIFE GRANT RECIPIENT

“CRPF generously awarded Shake-A-Leg \$25,000 to assist with operational costs for the educational and recreational components of our Body Awareness Therapy Program for adults and teenagers. These programs serve people with spinal cord injuries and related neurological disabilities ages 13 and up in a therapy environment that encourages physical and educational development that empowers participants to move beyond their disability.”

GREAT LAKES ADAPTIVE SPORTS ASSOCIATION, LAKE FOREST, IL –

QUALITY OF LIFE GRANT RECIPIENT

“The Great Lakes Adaptive Sports Association is grateful to the Christopher Reeve Paralysis Foundation for its Quality of Life Grant. The \$5,000 received has made a major impact on the lives it has touched through the various adaptive sports programs and services. In addition to providing education and opportunities regarding one’s leisure time these funds have provided new hope to those individuals with physical impairments as to the improvised quality of life. Thank you for helping in accomplishing our mission of ‘Let No One Sit on the Sidelines.’”

“Receipt of this award confirms CRPF’s dedication and vision to champion all aspects of scientific research related to spinal cord injury. These grants are regarded as very prestigious in the neuroscience community. As a post-doctoral fellow, this generous individual award will provide me both flexibility to pursue research goals that I choose and recognition of potential personal achievement. This grant will provide me with a clear advantage in securing future research commitments. I look forward to a fruitful relationship with the Foundation and am grateful for the opportunity to pursue my scientific interests.”

STEPHEN I. RYU, M.D.

CRPF Individual Research Grant Recipient
Stanford University
Department of Neurosurgery

“I feel very privileged to be the recipient of a CRPF grant award. I hope that my research, funded by the CRPF, will lead to the development of strategies for promoting neuronal regeneration in patients with damage to the central nervous system.”

WILLIAM A. BARTON, PH.D.

CRPF Individual Research Grant Recipient
Sloan Kettering Institute
Department of Structural Biology and Neuroscience

“The CRPF grant is an exceptional chance for me and the support is going to have a huge impact on the continuity of my scientific work. The grant from the CRPF offers me the opportunity to continue on with my experiments that are now entering the most difficult and all important in vivo stage of analysis. Additionally, to be part of the scientific society of the CRPF, gives me the possibility to meet other scientists from the field of spinal cord regeneration and exchange scientific ideas. For me this is a great honor. Such meetings and exchanges are very important as we continue to strive for a treatment that will stimulate regeneration in spinal cord injury patients.”

BARBARA GRIMPE, PH.D.

CRPF Individual Research Grant Recipient
Case Western Reserve University
Department of Neurosciences

2003 INDIVIDUAL RESEARCH GRANTS

\$4,070,350

Bruce Appel, Ph.D.

Vanderbilt University, Nashville, TN
Analysis of oligodendrocyte precursor migration in zebrafish
\$150,000 (2)

William A. Barton, Ph.D.

Sloan Kettering Institute, New York, NY
Structural study of Nogo, NogoR, and p75NTR
\$74,250 (1)

Armin Blesch, Ph.D.

University of California, San Diego La Jolla, CA
Controlled gene therapy for spinal cord injury
\$74,800 (1)

Jose M. Carmena, Ph.D.

Duke University Medical Center Durham, NC
Closed-loop brain-controlled prosthesis for recovery of upper-limb functionality in subjects with spinal cord injuries.
\$120,000 (2)

Stefan Clemens, Ph.D.

Emory University, Atlanta, GA
Dopaminergic control of spinal cord function
\$67,859 (1)

Felicia Cosman, M.D.

Helen Hayes Hospital West Haverstraw, NY
Acute spinal cord injury: a randomized controlled trial to prevent bone loss.
\$149,616 (2)

Gerald R. Crabtree, M.D.

Stanford University School of Medicine Stanford, CA
Understanding and recapturing patterns of embryonic neurite outgrowth
\$149,964 (2)

Corinna Jane Darian-Smith, Ph.D.

Stanford University School of Medicine Stanford, CA
Cervical dorsal root lesions in monkey: impairment of dexterity and plasticity of primary sensory neurons
\$149,398 (2)

Michael D. Ehlers, M.D., Ph.D.

Duke University Medical Center Durham, NC
Spatial regulation of endocytosis during growth cone migration and collapse
\$150,000 (2)

Abdeljabbar El Manira, Ph.D.

Karolinska Institutet Stockholm, Sweden
Awaking locomotor networks by activation of endogenous modulatory receptors
\$150,000 (2)

David D. Fuller, Ph.D.

University of Florida, Gainesville, FL
Plasticity in spinal respiratory pathways following treadmill exercise
\$150,000 (2)

K. Christopher Garcia, Ph.D.

Stanford University School of Medicine Stanford, CA
Structural biology of Nogo receptor-ligand interactions
\$150,000 (2)

Francis John Golder, DVM, Ph.D., DACVA

University of Wisconsin, Madison, WI
Respiratory functional recovery after cervical spinal cord injury: strengthening existing synaptic pathways
\$149,600 (2)

Sten Erik Grillner, Ph.D.

Karolinska Institutet Stockholm, Sweden
Mechanisms of modulation of the locomotor CPG – a synaptic, cellular and molecular analysis
\$150,000 (2)

Barbara Grimpe, Ph.D.

Case Western Reserve University Cleveland, OH
Down-regulation of the xylosyltransferase 1, the GAG-chain initiating enzyme, and the use of bridge-building Schwann cells to stimulate regeneration in the spinal cord
\$133,684 (2)

Chenghua Gu, Ph.D.

The Johns Hopkins University School of Medicine, Baltimore, MD
Semaphorin/neuropilin signaling during development and adult CNS regeneration
\$60,000 (1)

Bryan C. Hains, Ph.D.

Yale University School of Medicine New Haven, CT
Sodium channels and pain after spinal cord injury
\$46,109 (2)

Mark Henkemeyer, Ph.D.

UT Southwestern Medical Center Dallas, TX
Eph-Ephrin signaling in the growth cone
\$150,000 (2)

Carole Ho, M.D.

Stanford University School of Medicine Stanford, CA
Identification and characterization of neuronal regeneration associated genes induced by cAMP and laminin by expression profiling
\$136,180 (2)

John H. Martin, Ph.D.

Research Foundation for Mental Hygiene New York, NY
Engineering spinal connections to bypass spinal injury
\$148,616 (2)

Ana Martin-Villalba, M.D.

Deutsches Krebsforschungszentrum Heidelberg, Germany
Blocking of CD95-Ligand-induced cell death to treat spinal cord injured patients
\$150,000 (2)

Mehdi M. Mirbagheri, Ph.D.
Rehabilitation Institute of Chicago
Chicago, IL
Restoration of neuromuscular function in spinal cord injury
\$147,397 (2)

Sergei N. Prokopenko, Ph.D.
Emory University, Atlanta, GA
Signaling pathways of derailed axon guidance receptor controlling a choice of commissures in the central nervous system
\$75,000 (1)

Barbara Ranscht, Ph.D.
The Burnham Institute, La Jolla, CA
Cadherins in establishing connectivity in the spinal cord
\$150,000 (2)

Stephen I. Ryu, M.D.
Stanford University School of Medicine
Stanford, CA
Enhancing the performance of cortically controlled prosthetic arm systems
\$150,000 (2)

Cristina Lavinia Sadowsky, M.D.
Washington University in St. Louis
St. Louis, MO
Effects of an activity-based therapeutic program on physical health and quality of life in persons with spinal cord injuries
\$71,165 (1)

Rajeev Sivasankaran, M.D.
Children's Hospital Boston, Boston, MA
Investigating the role of protein kinase C in axon regeneration
\$150,000 (2)

Ernest F. Terwilliger, Ph.D.
Beth Israel Deaconess Medical Center
Boston, MA
Targeting therapeutic gene transfer to spinal cord motor neurons
\$75,000 (1)

Mark H. Tuszynski, M.D., Ph.D.
University of California, San Diego
La Jolla, CA
Nerve guidance channels for spinal cord injury
\$75,000 (1)

Scott Whittemore, Ph.D.
University of Louisville, Louisville, KY
Stem cell repair of spinal cord injury
\$150,000 (2)

Sara Ivy Wilson, Ph.D.
Columbia University, New York, NY
Spinal commissural neurons: functional development and circuitry
\$120,000 (2)

Xiaorong Xu, Ph.D.
University of Rochester Medical Center
Rochester, NY
Assuring conduction in spinal motor neurons
\$97,738 (2)

Other awards: \$148,974

2003 CRPF RESEARCH CONSORTIUM ON SPINAL CORD INJURY

\$2,403,688

Mary B. Bunge, Ph.D.
University of Miami
Miami, FL
\$260,000

Carl W. Cotman, Ph.D.
University of California at Irvine
Irvine, CA
\$260,000

V. Reggie Edgerton, Ph.D.
University of California, Los Angeles
Los Angeles, CA
\$260,000

Fred H. Gage, Ph.D.
The Salk Institute for Biological Studies
La Jolla, CA
\$260,000

Lorne M. Mendell, Ph.D.
State University of New York
Stony Brook, NY
\$260,000

Luis F. Parada, Ph.D.
UT Southwestern Medical Center
Dallas, TX
\$260,000

Martin E. Schwab, Ph.D.
University of Zurich
Zurich, Switzerland
\$260,000

Animal Core Laboratory
University of California at Irvine
Irvine, CA
\$383,688

Microarray Core Laboratory
The Salk Institute for Biological Studies
La Jolla, CA
\$200,000

CRPF Consortium Advisory Panel

ALBERT J. AGUAYO, M.D.
Center for Research in Neuroscience
Montreal General Hospital
Montreal, Canada

ROBERT G. GROSSMAN, M.D.
Department of Neurosurgery
Baylor College of Medicine
Houston, TX

GUY M. MCKHANN, M.D.
The Zanvyl Krieger Mind/Brain
Institute
The Johns Hopkins University
Baltimore, MD

ERIC M. SHOOTER, PH.D.
Department of Neurobiology
Stanford University
School of Medicine
Stanford, CA

2003: PERSISTENCE PERSONIFIED



SOMEWHERE IN TIME

The Orange County (California) Guild, a west coast chapter of CRPF, raised more than \$100,000 for the Foundation at its 16th annual black-tie dinner and silent auction. Christopher Reeve attended the event, which was held in Monarch Beach, California on May 10, 2003. "Somewhere in Time," the theme for this enchanting evening, was reminiscent of the 1980 film starring Christopher and Jane Seymour.

RACING TO RECOVERY

Ever since racecar driver Sam Schmidt was rendered quadriplegic in an accident several years ago, he's been working to find a cure for paralysis. He established the Sam Schmidt Paralysis Foundation and Sam Schmidt Motorsports. On May 12, 2003 Christopher Reeve addressed the crowd at Sam's fundraiser titled "Racing to Recovery: An Evening with Christopher Reeve," which was timed to coincide with the Indianapolis 500. Sam split the proceeds among the Sam Schmidt Paralysis Foundation, the Rehabilitation Hospital of Indiana, and CRPF. In addition to generously giving \$40,000 directly to CRPF, Sam donated \$150,000 to fund one of CRPF's individual research grants for two years.



AMERICAN IMAGE AWARDS

The American Apparel and Footwear Association held its 25th Annual American Image Awards in New York City on May 19, 2003. Christopher and Dana Reeve attended this black-tie gala, hosted by CNN's Paula Zahn. Dana was honored with the association's *Spirit of a Woman Award* for her humanitarian achievements as co-founder of the Christopher and Dana Reeve Paralysis Resource Center. The event raised \$320,000 for CRPF.

CELEBRATION OF THE HUMAN SPIRIT

A few weeks before starting his freshman year of college, Daniel Heumann was paralyzed in an automobile accident. For the past few years, his friends, who are an invaluable source of support to him, have held fundraisers for the Daniel Heumann Fund for Spinal Cord Research. This year, the organizers reached out to CRPF and asked us to be part of their event, called "Celebration of the Human Spirit." Christopher Reeve spoke at this very special gathering, which was held in Chicago on May 21, 2003 and hosted by actor Richard Kind. The *Human Spirit Award* was presented to Chicagoan Neal Goss, who was injured in high school and is now pursuing an accelerated MBA at the University of Pennsylvania. The event raised over \$400,000, netting nearly \$175,000 each for CRPF and the Daniel Heumann Fund.

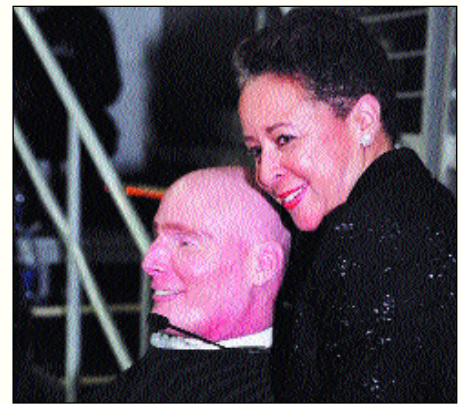


HEIDI'S DREAM BALL

The *Heidi Visionary Award* was presented to Christopher Reeve at the 2nd Annual "Heidi's Dream Ball," held in Dearborn, Michigan on October 4, 2003. This award is designed to honor extraordinary individuals or businesses that are responsible for opening doors of opportunities to the disabled. It is given in memory of Heidi Van Arnhem, a woman who was paralyzed at age 16 and went on to college, law school, and a life of activism dedicated to the disability community. Sponsored by Ford Mobility Motoring and P.I.N., an affiliate of J.D. Power and Associates, the black-tie gala raised more than \$100,000 for CRPF's research endeavors.

WASHINGTON INTERNATIONAL HORSE SHOW

The 45th Annual Washington International Horse Show (WIHS) was the venue for "Where the World Comes to Ride," a non-profit event benefiting CRPF and other charities. This gala was held on October 25, 2003, as part of the weeklong Olympic-level equestrian show-jumping competition. Christopher Reeve made a surprise appearance at the MCI Center in downtown Washington, D.C. When he was introduced by Sheila Johnson, Ph.D., WIHS's President, the crowd of 10,000 gave him a six-minute standing ovation. Dr. Johnson then presented Christopher with a \$150,000 donation to CRPF.



A MAGICAL EVENING

Hosted by actor John Lithgow, CRPF's 13th Annual "A Magical Evening" black-tie gala, held just days before Thanksgiving at the Marriott Marquis Hotel in New York City, truly lived up to its theme: *A Night to Give Thanks*. Raising almost \$1.8 million for CRPF, the evening marked Christopher's first public appearance without the help of a respirator.

The CRPF *Visionary Leadership Award* was given to renowned architect and designer Michael Graves, who was paralyzed in 2003 by a virus that attacked his spinal cord, and who has since helped to raise significant funds for SCI research. CRPF Director Francine LeFrak and her husband, Rick Friedberg, were honored with the CRPF *Human Spirit Award* for their longstanding dedication to the Foundation.

Dr. James Fawcett of Cambridge University and Dr. Jerry Silver of Case Western Reserve University both received the 2003 Reeve-Irvine Research Medal and shared the \$50,000 cash prize.

As always, the evening was another star-studded celebration. Wade Preston, star of the Tony Award winning production, *Movin' Out*, entertained with a piano performance of songs from the hit show. Among the other celebrities who helped to make the gala so memorable were magician David Blaine, journalists Diane Sawyer and Paula Zahn, director Mike Nichols, actor Richard Kind, and Miss USA, Susie Castillo.

QUALITY OF LIFE

REACHING THOUSANDS, ONE-OF-A-KIND HELP

IN 2003, THE CHRISTOPHER AND DANA REEVE Paralysis Resource Center (PRC) and our Quality of Life Grants program helped thousands of paralyzed people to enjoy fuller, healthier lives and to keep up with current research and treatment options.

Consider how many people the PRC reached in 2003, the first full year the center operated: The PRC Web site (www.paralysis.org) got nearly 2.3 million “hits”



DANA REEVE
Chair, Quality of Life
Committee

from more than 200,000 visitors, and some 7,000 people contacted the PRC by e-mail or phone with specific requests.

While these numbers validate the scope of the need for this valuable resource, it is the individual stories of people seeking and receiving help that prove to us how worthy this effort is. For

example, one of our information specialists helped the wife of an American serviceman to find rehabilitation services and obtain military benefits for her husband, who suffered a spinal cord injury in Iraq. Another specialist enabled a man in rural Australia to connect with other spinal cord injured people via Internet chat rooms. And we helped a gentleman who uses a wheelchair because of a stroke to understand his rights as an air traveler under the Americans with Disabilities Act so he could visit his family.

We are particularly proud of one accomplishment last year: the publication of the *Paralysis Resource Guide*, a 310-page book that serves as a user-friendly roadmap for people trying to navigate the complicated world of paralysis. Written by Sam Maddox, founder, former editor and publisher of *Spinal Network* and

creator of *New Mobility* magazine, this is the first guidebook of its kind to appear in many years. We began sending free single copies to individuals and organizations late last fall, and are heartened by the enthusiastic response we have received.

The PRC further extended its reach by joining an inter-library loan system that links us with thousands of libraries across the country. Thanks to this arrangement, visitors to our Web site can click on our Online Library Catalogue to browse through titles and pictures from our impressive collection of print and audio-visual materials, and, through their local libraries, borrow any items of interest.

In 2003, we also expanded aid to nonprofit organizations that enhance the day-to-day lives of adults and children with disabilities and their families, awarding \$1.3 million in Quality of Life Grants to 158 organizations in 13 different categories, including health promotion. One of our goals is to identify and support model programs that can be replicated elsewhere. For example, we funded a model program that promotes breast health for women with disabilities in Berkeley, California. Another is a summer internship program in Hopkins, Minnesota, that pairs disabled students with community businesses and educates employers about the needs and value of individuals with disabilities.

The Paralysis Resource Center is truly becoming what Christopher and I dreamed it would: A one-of-a-kind information clearinghouse and a source of invaluable support for those who live with paralysis and the people – both at home and in the community – who care for them.

2003 QUALITY OF LIFE GRANTS

\$1,334,865

FIRST CYCLE

\$1,500	New Life Mobility Assistance Dogs, Inc. <i>Moravian Falls, North Carolina</i>	Disability Rights Education and Defense Fund (DREDF) <i>Berkeley, California</i>	Magee Rehabilitation Hospital <i>Philadelphia, Pennsylvania</i>
Easley High School <i>Easley, South Carolina</i>	Northern Kentucky University <i>Highland Heights, Kentucky</i>	Endeppence Center, Inc. <i>Norfolk, Virginia</i>	\$20,000
\$3,000	Shared Adventures <i>Santa Cruz, California</i>	Friends of Disabled Adults and Children, Too! Inc. <i>Stone Mountain, Georgia</i>	OSF Saint Francis Medical Center-Rehabilitation Services <i>Peoria, Illinois</i>
Artsbridge <i>Parkersburg, West Virginia</i>	Trail's Edge Camp <i>Ann Arbor, Michigan</i>	Habitat for Humanity/Metro Jackson, Inc. <i>Jackson, Mississippi</i>	Slippery Rock University of Pennsylvania <i>Slippery Rock, Pennsylvania</i>
The Luci Center <i>Shelbyville, Kentucky</i>	Vermont Studio Center <i>Johnson, Vermont</i>	Help Them Walk Again <i>Las Vegas, Nevada</i>	\$24,501
\$4,500	National Spinal Cord Injury Association (NSCIA) Northwest Ohio Chapter <i>Perrysburg, Ohio</i>	Lovelane Special Needs Horseback Riding Program <i>Lincoln, Massachusetts</i>	New York City Commission on Human Rights <i>New York, New York</i>
\$5,000	\$8,000 Donka, Incorporated <i>Wheaton, Illinois</i>	Millburn Regional Day School <i>Millburn, New Jersey</i>	\$25,000
Adaptive Dancing <i>Parker, Colorado</i>	\$8,433 National Lekotek Center <i>Evanston, Illinois</i>	The Stony Brook Foundation <i>Stony Brook, New York</i>	Advancing Independence: Modernizing Medicare and Medicaid (AIMMM) <i>Washington, DC</i>
Courage Center <i>Minneapolis, Minnesota</i>	\$10,000	TransAccess <i>San Jose, California</i>	American Syringomyelia Alliance Project, Inc. (ASAP) <i>Longview, Texas</i>
Freedom Wings International <i>Scotch Plains, New Jersey</i>	ALLTech <i>Gorham, Maine</i>	University of Washington <i>Seattle, Washington</i>	ARCH National Respite Network <i>Raleigh, North Carolina</i>
Giant Steps Therapeutic Equestrian Center <i>Petaluma, California</i>	Alta Bates Summit Foundation <i>Berkeley, California</i>	\$10,255 Cerebral Palsy Center <i>Hurffville, New Jersey</i>	Children's National Medical Center <i>Washington, DC</i>
Hawaii Centers for Independent Living <i>Honolulu, Hawaii</i>	Alternatives in Motion <i>Grand Rapids, Michigan</i>	\$10,780 California Polytechnic State University Foundation <i>San Luis Obispo, California</i>	University of Arizona Foundation <i>Tucson, Arizona</i>
Keene State College <i>Keene, New Hampshire</i>	The Bedford VA Research Corporation, Inc. (BRCI) <i>Bedford, Massachusetts</i>	\$12,500	University of California, San Francisco Department of Orthopedic Surgery <i>San Francisco, California</i>
The National Foundation for the Treatment of Pain <i>Monterey, California</i>	CalSTAR Intercollegiate Athletics and Recreational Sports <i>Berkeley, California</i>	Virginia Supportive Housing <i>Richmond, Virginia</i>	Virginia Housing Development Authority (VHDA) <i>Richmond, Virginia</i>
National Organization on Disability (NOD) <i>Washington, DC</i>	Central Coast Center for Independent Living <i>Salinas, California</i>	World T.E.A.M. Sports <i>Charlotte, North Carolina</i>	NEW YORK RANGERS QUALITY OF LIFE AWARD:
New Horizons Independent Living Center <i>Prescott Valley, Arizona</i>	Children's Emergency Medical Fund of New Jersey <i>Maplewood, New Jersey</i>	\$16,000	Achilles Track Club <i>New York, New York</i>
	The Disability Institute <i>Hopkins, Minnesota</i>	American Association of People with Disabilities (AAPD) <i>Washington, DC</i>	

SECOND CYCLE

\$1,675
University of Florida Dept. of Occupational Therapy
Gainesville, Florida

\$2,000
Oregon Disability Sports
Portland, Oregon
Sail-Habilitation
Island Heights, New Jersey

\$2,500
Access Information, Inc.
Boys, Maryland

Adaptive Ski Program
Santa Fe, New Mexico

Back Country Discovery
Fort Collins, Colorado

Bryn Mawr Rehabilitation Hospital
Malvern, Pennsylvania

Chautauqua County Youth Hockey Association
Jamestown, New York

Community Access Center
Riverside, California

Dancing Wheels
Cleveland, Ohio

Disabled Sports USA Far West
Citrus Heights, California

Fighting Back Scholarship Program, Inc.
Devon, Pennsylvania

Fishing Has No Boundaries, Inc.
Hayward, Wisconsin

Habitat for Humanity in the Roanoke Valley, Inc.
Roanoke, Virginia

Mobility Unlimited
Medford, Oregon

Police Athletic League
New York, New York

Rehabilitation Hospital of Indiana Sports Program
Indianapolis, Indiana

Sail Connecticut Access Program, Inc.
Cheshire, Connecticut

Soaringwords, Inc.
New York, New York

South Carolina Independent Living Center
Columbia, South Carolina

The Spina Bifida Association of the Delaware Valley
Media, Pennsylvania

Spirit Filled Riders, Inc.
Hackettstown, New Jersey

Tennessee Sled Hockey Association, Inc.
Franklin, Tennessee

World Institute on Disability
Oakland, California

YMCA of Greater Cincinnati-Campbell County
Cincinnati, Ohio

\$2,750
Wintergreen Adaptive Skiing
Afton, Virginia

\$3,000
Charles T. Sitrin Health Care Center
New Hartford, New York

Southeastern Utah District Health Department
Price, Utah

\$3,500
Spaulding Rehabilitation Hospital
Boston, Massachusetts

\$3,745
Baptist Healthplex
Clinton, Mississippi

\$3,750
Yachad, Inc.
Washington, DC

\$4,400
Muscular Dystrophy Association
Houston, Texas

\$4,500
Disability Resource Center of Southwestern Michigan
Kalamazoo, Michigan

\$5,000
Accessible Arts, Inc.
Kansas City, Kansas

Adaptive Health and Wellness Center, Inc.
Port Saint Lucie, Florida

The ALS Association- St. Louis Regional Chapter
Saint Louis, Missouri

American Stroke Foundation
Shawnee Mission, Kansas

Arc Southeastern Minnesota
Rochester, Minnesota

Camp S.T.A.R.
Hershey, Pennsylvania

Canine Companions for Independence
Santa Rosa, California

Canines Helping Independent People, Inc.
Canton, Ohio

Capital District Center for Independence, Inc.
Albany, New York

Center On Independent Living
San Antonio, Texas

Community Resources for Independence
Santa Rosa, California

Compassionate Care, Inc.
West Falmouth, Massachusetts

Disability Resource Center
Charleston, South Carolina

Double "H" Hole in the Woods Ranch
Lake Luzerne, New York

Easter Seals Arizona
Phoenix, Arizona

Easter Seals Rehabilitation Center of Greater Waterbury, Inc.
Waterbury, Connecticut

Employment Horizons Inc.
Cedar Knolls, New Jersey

Free Wheelchair Mission
Santa Ana, California

Greater Long Island Wheelchair Athletic Club
Lindenhurst, New York

Home Access Fund
Dallas, Texas

Jewish Hospital HealthCare Services, Inc.
Louisville, Kentucky

Kids Included Together, Inc.
San Diego, California

Memorial Foundation, Inc.
Hollywood, Florida

Michigan Paralyzed Veterans Association
Novi, Michigan

Mississippi Society for Disabilities, Inc.
Jackson, Mississippi

Multiple Sclerosis Service Society
Pittsburgh, Pennsylvania

Nacogdoches Treatment Center <i>Nacogdoches, Texas</i>	Society for Human Advancement through Rehabilitation Engineering Foundation (SHARE) <i>North Dartmouth, Massachusetts</i>	Southeast Alaska Independent Living, Inc. (SAIL) <i>Juneau, Alaska</i>	\$15,000
National Council on Spinal Cord Injury <i>Boston, Massachusetts</i>	\$8,000	Temple University Children's Medical Center <i>Philadelphia, Pennsylvania</i>	Creative Clay, Inc. <i>Saint Petersburg, Florida</i>
Pennsylvania State University <i>University Park, Pennsylvania</i>	Sam Schmidt Paralysis Foundation <i>Indianapolis, Indiana</i>	United States Adaptive Recreation Center <i>Big Bear Lake, California</i>	IMPACT Personal Safety <i>Santa Fe, New Mexico</i>
Shake-A- Leg, Inc. <i>Newport, Rhode Island</i>	\$10,000	U.S. Disabled Athletes Fund, Inc. <i>Atlanta, Georgia</i>	\$21,900
That Uppity Theatre Company <i>Saint Louis, Missouri</i>	American Stroke Association <i>Dallas, Texas</i>	Victory Gardens Theater <i>Chicago, Illinois</i>	Henry M. Jackson Foundation for the Advancement of Military Medicine <i>Rockville, Maryland</i>
Think First National Injury Prevention Foundation <i>Rolling Meadows, Illinois</i>	Breckenridge Outdoor Education <i>Breckenridge, Colorado</i>	\$11,176	\$25,000
Walton Foundation for Independence <i>Augusta, Georgia</i>	Dance in Education Fund, Inc. <i>White Plains, New York</i>	Wright State University <i>Dayton, Ohio</i>	Good Shepherd Rehabilitation Center <i>Allentown, Pennsylvania</i>
Wilderness Inquiry <i>Minneapolis, Minnesota</i>	Fort Sanders Foundation <i>Knoxville, Tennessee</i>	\$12,500	New England Spinal Cord Initiative/Travis Roy Foundation <i>Boston, Massachusetts</i>
WIRED International <i>Montara, California</i>	The Heuga Center <i>Edwards, Colorado</i>	Annie Sullivan Enterprises, Inc. <i>Lawrence, Kansas</i>	Rehabilitation Institute of Michigan <i>Detroit, Michigan</i>
\$6,000	JoJo's Hope <i>Metairie, Louisiana</i>	Arizona Spinal Cord Injury Association <i>Phoenix, Arizona</i>	Sharp HealthCare Foundation <i>San Diego, California</i>
Project Mobility: Cycles for Life <i>Saint Charles, Illinois</i>	Liberty Resources Inc. <i>Philadelphia, Pennsylvania</i>	Challenge Center, Inc. <i>La Mesa, California</i>	NEW YORK RANGERS QUALITY OF LIFE AWARD:
\$7,500	Los Amigos Research and Education Institute, Inc. <i>Downey, California</i>	The Good Grief Program at Boston Medical Center <i>Boston, Massachusetts</i>	Mount Sinai School of Rehabilitation Medicine <i>New York, New York</i>
Kostopoulos Dream Foundation <i>Salt Lake City, Utah</i>	National Sports Center for the Disabled <i>Evergreen, Colorado</i>	Independent Living Resource Center San Francisco <i>San Francisco, California</i>	
National Multiple Sclerosis Society Western NY/Northwestern PA Chapter <i>Buffalo, New York</i>	ShowMe Aquatics & Fitness <i>Saint Charles, Missouri</i>	Premier HealthCare, Inc. <i>New York, New York</i>	

FOR MORE INFORMATION ON CRPF'S QUALITY OF LIFE PROGRAM,
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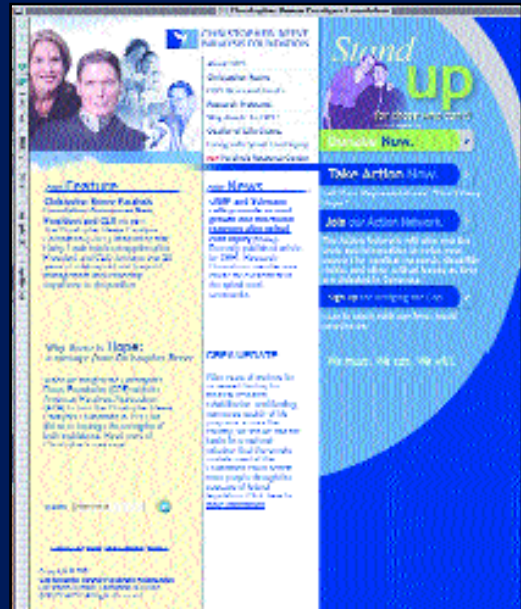
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**As of July 2004*

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- Directory of Research Programs
- Quality of Life Grants
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www.paralysis.org

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- News Updates
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For additional copies of this publication or further information about CRPF and its programs, contact:

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For a copy of CRPF's 2003 Financial Report, contact the Foundation.



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