CDMRP

Department of Defense

Defense Health Program

Spinal Cord Injury Research Program





U.S. Army Medical Research and Materiel Command

"The SCIRP has given the Department of Defense the unique opportunity to invest in important and militarily relevant areas of spinal cord injury research. While SCI is a relatively 'infrequent' injury—some 11,000–12,000 cases per year in the U.S.—it is obviously devastating to the victim and their families both functionally and financially. The scale of this devastation in terms of lost productivity, quality of life, and other costs makes SCI a highly important area to focus our research efforts. It is also important because what we learn in SCI may inform us on mechanisms and potential therapies that may be applicable to traumatic brain injury and vice versa."

Kenneth Curley, M.D.
FY11–FY12 Integration Panel Chair

Congressionally Directed Medical Research Programs

History of the CDMRP

The Office of the Congressionally Directed Medical Research Programs (CDMRP) was created in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. This initiated a unique partnership among the public, Congress, and the military. The success in managing the initial congressional appropriations in breast cancer research combined with additional advocacy movements and the need for focused biomedical research catapulted the CDMRP into a global funding organization for cancer research, military medical research, and other disease-specific research. The CDMRP has grown to encompass multiple targeted programs and has received nearly $7 billion in appropriations from its inception through fiscal year 2012 (FY12). Funds for the CDMRP are added to the Department of Defense (DoD) budget in which support for individual programs, such as the Spinal Cord Injury Research Program (SCIRP), is allocated via specific guidance from Congress.

Application Review Process

The CDMRP uses a two-tier review process for application evaluation with both steps involving dynamic interaction between scientists and clinicians—subject matter experts—and consumers. The first tier of evaluation is a scientific peer review of applications measured against established criteria for determining scientific merit. The second tier is a programmatic review, conducted by the Integration Panel, which compares applications to each other and makes funding recommendations based on scientific merit, portfolio balance, and relevance to program goals.

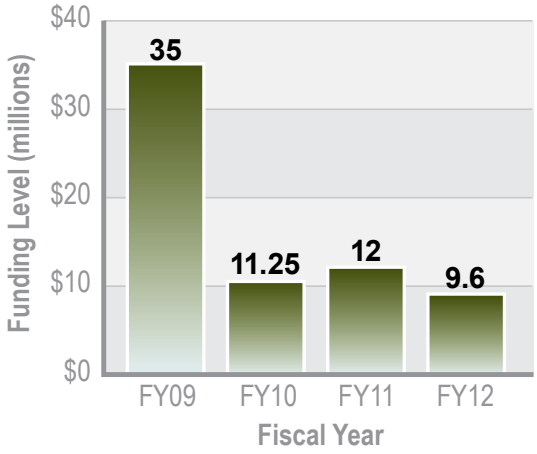
Consumer Advocacy Participation

A unique aspect of the CDMRP is the active participation of consumer advocates or patient/survivor representatives throughout the program's annual cycle. Consumers work collaboratively with leading scientists and clinicians in setting the SCIRP's vision and mission, reviewing applications, and making final funding recommendations. From the unique perspective gained through personal experience the consumer brings a sense of urgency and focus to all levels of decision making. Consumers evaluate applications based on the potential impact and benefit to the patient population, encouraging funding recommendations that reflect the concerns and needs of the spinal cord injury (SCI) population, their families and caregivers, and the clinicians who treat them.

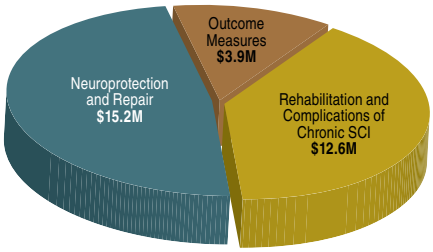
Spinal Cord Injury Research Program

History of the DoD SCIRP

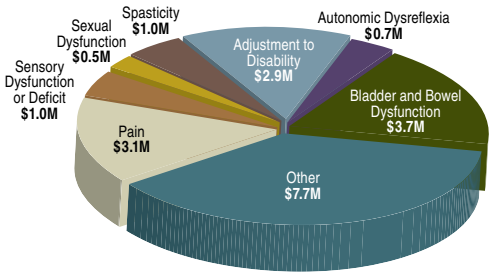
SCIs are serious and complex neurotraumatic wounds affecting military Service members and Veterans who served in the recent conflicts in Iraq and Afghanistan. The SCIRP was established by Congress in FY09 with a $35 million (M) appropriation to support research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies. Since then, a total of $67.85M has been appropriated to the program. The SCIRP focuses its funding on innovative projects that have the potential to make a significant impact on improving the function, wellness, and overall quality of life for military Service members, Veterans, and other individuals living with SCI. The program's current portfolio includes 87 awards spanning basic, translational, clinical, and qualitative research.



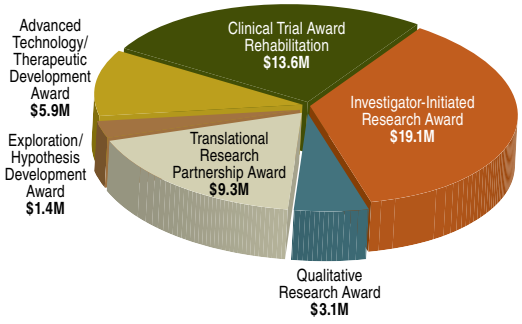
SCIRP Appropriations, FY09–FY12



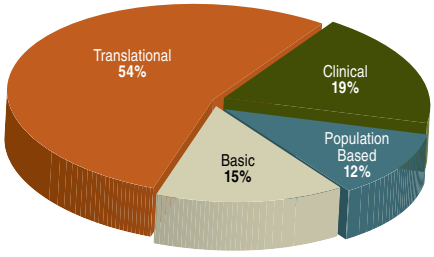
FY09 Investment by Area of Encouragement



FY10–FY11 Investment by Area of Encouragement



FY09–FY11 Investment by Mechanism



FY09–FY11 Research Phase

VISION

Advance the treatment and understanding of spinal cord injury and ameliorate its consequences relevant to injured Service members.

MISSION

To fund innovative and interdisciplinary research and foster collaborative environments for the development and translation of more effective strategies to improve the health and well-being of military Service members, Veterans, and other individuals living with spinal cord injury.

Key Priorities of the SCIRP

- Accelerating the movement of promising ideas in SCI research into clinical applications
- Fostering multidisciplinary collaborations
- Implementation research
- Innovative, high-impact research
- Qualitative research
- Rehabilitation studies

Research Highlights

Developing Treatment and Rehabilitation Strategies for Individuals with both Spinal Cord Injury and Traumatic Brain Injury

Michael Beattie, Ph.D. (top) and Geoffrey Manley, M.D., Ph.D. (middle), University of California, San Francisco; Graham Creasey, MB, ChB., FRSCEd. (bottom), VA Health Care System, Palo Alto, California

SCI is often accompanied by traumatic brain injury (TBI), which complicates treatment in both the critical care and rehabilitation settings. Validated treatment approaches for this dual diagnosis, however, are lacking. Drs. Michael Beattie, Geoffrey Manley, and Graham Creasey received an FY09 Translational Research Partnership Award to initiate a bedside-to-bench-to-bedside strategy for improving the clinical care of individuals with SCI/TBI dual injury. They queried the clinical community, including participants at the Santa Clara Valley Brain Injury Conference, to gather information on the current treatment strategies for SCI/TBI dual injury and to determine what they feel are the greatest needs for this population. Survey responses revealed that a majority of clinicians feel that there is a strong need for more research to improve the care of individuals with SCI/TBI dual injury and that animal models of hand function may motivate changes in clinical practice. Additional clinical information is being gathered from several national and local databases of SCI and TBI clinical care and patient outcomes to identify factors that may affect recovery, including type and extent of injury, medical complications, Functional Independence Measure, and other factors that affect recovery. All of this information will help to inform the development and characterization of SCI/TBI animal models. To establish a baseline for future models, the investigators utilized currently available protocols to create rat models of incomplete SCI plus mild and moderate TBI. A battery of tests of hand and forelimb function in these rats (e.g., ability to manipulate a piece of cereal and to walk along a runway) shows that rats with both TBI and SCI recover function more slowly than rats with SCI alone. The development of additional models will be based on the needs of the clinical community and will be used to evaluate clinic-driven hypotheses for new critical care and rehabilitation strategies for SCI/TBI dual injury. To bring the project full circle, data derived from the animal studies will be used to propose improved guidelines for clinical treatment. This partnership has fostered a community of researchers and clinicians working together to improve the care and treatment of individuals with SCI and TBI.

Functional tests, such as the ability to walk along a runway or manipulate a piece of cereal, have demonstrated that addition of a mild TBI can retard recovery of forelimb function from SCI.

Schwann Cell Implantation for SCI Repair

Damien D. Pearse, Ph.D. (right); Mary Bartlett Bunge, Ph.D. (middle); and James Guest, M.D., Ph.D. (left), University of Miami School of Medicine

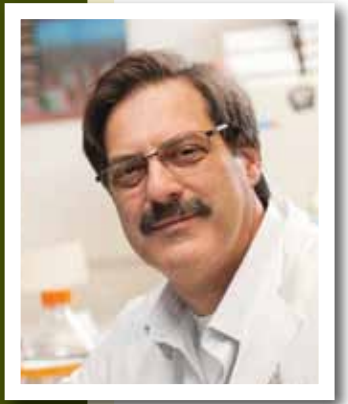
Individuals with SCI endure lifelong complications from their injuries. New strategies to repair the injured spinal cord and effectively restore function following SCI are greatly needed. Schwann cells, a key component of the peripheral nervous system, have been shown to be effective in promoting axon growth, remyelination, and functional recovery in many SCI models and may serve as effective cell therapy in humans. To avoid the need for immune suppression, Schwann cells can be derived in large numbers from an individual with SCI, expanded and purified in culture, and then implanted in the same individual. Drs. Damien Pearse, Mary Bunge, and James Guest received an FY09 Advanced Technology/Therapeutic Development Award to perform dosage, safety, and toxicity studies of Schwann cell implantation in animal models of SCI in preparation for human clinical trials. Optimal dose was obtained in a thoracic contusion (T8) rat model based on functional recovery over a course of 12 weeks after implantation. The investigators demonstrated that transplanted human Schwann cells survived for up to 6 months, the longest time examined, and were not associated with tumor formation, additional tissue damage, scarring, or adverse immune responses. The extent of axon growth into the spinal cord lesion correlated with the number of persisting human Schwann cells present in the animals. Importantly, locomotor function was significantly improved in injured rats treated with Schwann cells compared to injured controls. The team recently received approval from the U.S. Food and Drug Administration to evaluate the safety of human Schwann cell transplantation in individuals with SCI in a Phase 1 clinical trial.

1. The initiation of a Phase 1 clinical trial to evaluate the safety of using autologous Schwann cell transplantation following subacute SCI in man. 2. Schwann cells will be harvested from the individual's own sural nerve. 3. Schwann cells will be purified and expanded in culture. 4. Prior to transplantation, Schwann cells will be loaded into the injection syringe. 5. The spinal cord at the level of the injury will be surgically exposed. 6. Schwann cells will be injected into the injury site, forming a cellular bridge upon which axons can regrow. The transplanted Schwann cells can also remyelinate those axons surrounding the lesion that have been demyelinated after injury.

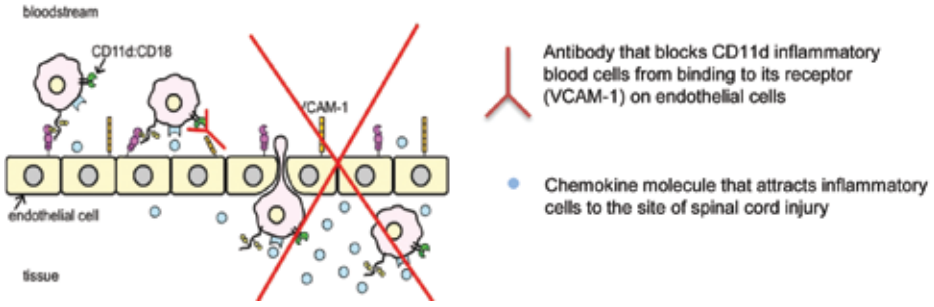
Research Highlights

New Anti-Inflammatory Treatment to Improve Neuroprotection

Gregory Dekaban, Ph.D. (top) and Arthur Brown, Ph.D. (bottom), University of Western Ontario



Trauma to the central nervous system (CNS) initiates tissue responses that include swelling and inflammation. Inflammation, in turn, causes damage to surrounding tissues, resulting in secondary injury and increased loss of neurological function. It is critical, therefore, to treat for inflammation as soon as possible following SCI to protect undamaged neurological tissues and improve recovery and long-term functionality. Previous studies in animal models have shown that treatment with a monoclonal antibody against the immune cell protein CD11d reduces systemic inflammatory response after CNS trauma and improves recovery. Drs. Gregory Dekaban and Arthur Brown received an FY09 Advanced Technology/Therapeutic Development Award to advance a humanized anti-CD11d antibody into clinical trials. In the first year of this award, the team has developed assays to measure the serum concentration of anti-CD11d after treatment, to characterize the antibody's activity, and to determine the subject's biological response to this treatment. The team also compared the effectiveness of several anti-CD11d antibodies of increasing affinity in a rat model and identified the most effective antibody for reducing inflammation and improving neurological recovery. Experiments are in progress to optimize the dosing schedule for this antibody treatment in the rat SCI model. To aid in further analysis of this antibody, Drs. Dekaban and Brown are developing additional animal models for testing in different types and degrees of severity of SCI and new functional measurements, including behavioral scales for locomotion and treadmill training in a larger animal model of SCI. These preclinical studies of anti-CD11d antibodies in animal models of SCI will pave the way for translating this promising therapeutic for human use.

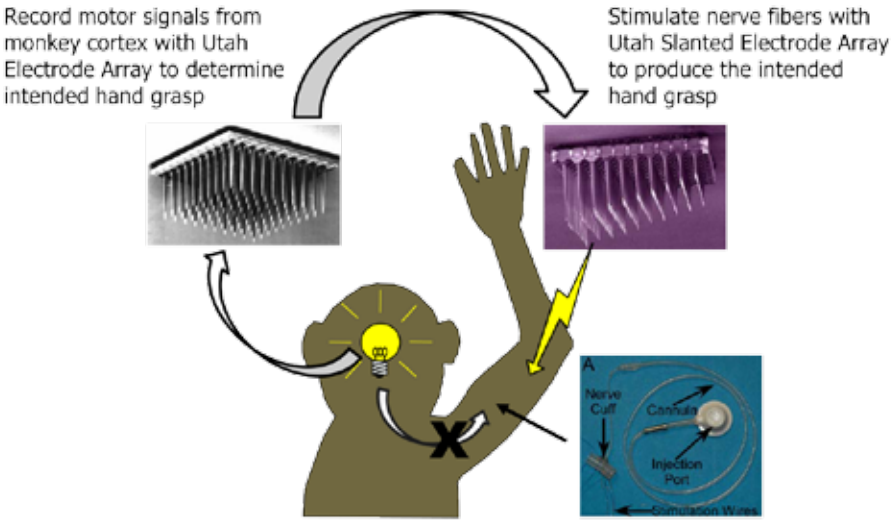


Antibody bound to CD11d present on the surface of neutrophils and monocyte/macrophages blocks their ability to infiltrate the spinal cord lesion thereby reducing inflammation. This results in an improved locomotor recovery and a reduction in pain often associated with SCI.

Restoring Coordinated Hand Function After Paralysis

Gregory A. Clark, Ph.D. (top), University of Utah, Salt Lake City, Utah
Lee E. Miller, Ph.D. (bottom), Northwestern University, Chicago, Illinois

The single most difficult injury to surmount for many individuals with SCI is the loss of hand function. Although some restoration of hand use has been obtained through functional electrical stimulation techniques, the resulting movements are limited, difficult to control, and fatigue muscles easily. In FY09, Dr. Gregory Clark received an Investigator-Initiated Research Award through the SCIRP to develop an improved approach to restoring coordinated hand function following paralysis. In collaboration with Dr. Lee Miller at Northwestern University School of Medicine, Dr. Clark will implant high-channel-count Utah Slanted Electrode Arrays (USEAs) into the peripheral forearm nerves of a large animal model to activate paralyzed muscles. The intrafascicular implantation of USEAs will facilitate the activation of motor units of multiple forearm, wrist, and hand muscles selectively and independently, leading to more coordinated and graded movements with a reduced risk of fatigue. Drs. Clark and Miller have performed the first-ever chronic implantation of USEAs into a large animal model with little initial adverse reaction. Three months following USEA implantation, compound action potentials were evoked in arm muscles following nerve stimulation by USEA electrodes. In future planned experiments, signals recorded directly from motor cortex with Utah Electrode Arrays will be used to drive the stimulation of the USEA to produce movement despite a temporary, nerve-block-induced paralysis of the forearm and hand. The performance on trained motor behaviors, such as individual digit flexions and grasp-and-placement tasks, will be used to evaluate performance of cortical control of the implanted USEA and will provide feedback for the researchers to fine-tune the system. If successful, this novel brain-machine interface will provide a means of restoring voluntary control of paralyzed muscles following SCI.



Temporary anesthetic nerve block of motor signals from brain to hand mimics spinal cord injury

Consumer Highlights

Gary Linfoot

Chief Warrant Officer 5 (Ret.) Gary Linfoot was not just a helicopter pilot—he was a Night Stalker, a member of the 160th Special Operations Aviation Regiment (Airborne), home to the Army's best-qualified aviators and support Soldiers. On June 1, 2008, during his 19th combat tour in Iraq, Gary's AH-6 helicopter crashed in the aftermath of a catastrophic mechanical failure. Although Gary survived, he sustained a complete SCI in the lower thoracic (T10) region of the spinal cord, which left him paralyzed and without sensation below the waist. His wife, Mari, instantly threw herself into her new role as caregiver, advocating for Gary's physical needs, equipment, privacy, and benefits. "I heard the words, but it really took a long time for the paralysis part to register," said Mari, "although the circumstances were completely foreign to me, these new responsibilities came naturally."

Gary retired from the Army in July 2010 after 23 years of service, working now as a civilian mission simulator instructor, providing flight and mission instruction in the A/MH-6 "Little Bird" helicopter simulator to pilots in the 160th Special Operations Aviation Regiment, his former unit. His true heroism, however, lies in his work as a mentor, helping Soldiers who are suffering from SCIs, and serving as an advocate. Likewise, Mari has provided valuable support to caretakers, partners, and families in similar situations, using social networking sites and nonprofit organizations to share her experiences. She is an active participant in a Department of Veterans Affairs (VA) research program with the spouses of wounded warriors to assist in the reintegration of injured Soldiers as they return home.

In addition to their outreach endeavors, both Gary and Mari dedicate considerable time reading scientific literature about SCIs. As consumer peer reviewers for the SCIRP, they partnered with expert scientists and clinicians to help guide the direction of scientific research in hopes of finding treatments that will improve the quality of life for SCI patients. "I believe that when you put many good ideas together, you will usually get one great idea that serves the greater cause," said Gary of his new role. Mari added, "I am eager to learn more, help further spinal cord injury research and awareness, and continue to be a voice for my husband and other spinal cord injury patients."

Dr. David Tharp

As Dr. David Tharp prepared to serve in Afghanistan through the Air Force in a North Atlantic Treaty Organization (NATO) billet in Kandahar, the last thing he imagined for himself was being evacuated to Landstuhl Regional Medical Center (LRMC). Dr. Tharp, a clinical psychologist, served as a medical advisor to the Commander Kandahar Airfield (COMKAF). and acted as a liaison between the state-of-the-art medical facility that treats our most severely wounded Soldiers in the Regional Command South and COMKAF.

With 4 weeks remaining in theater, Dr. Tharp lost all feeling except numbness and tingling from below his chest to his toes making walking, running, and other movements quite challenging. "I never imagined that I would experience something so debilitating that it literally made it impossible to walk to work every day, let alone run from rocket attacks," he said. The neurologist stationed in Kandahar made the diagnosis of acute transverse myelitis, an inflammatory attack on the spinal cord, based on Dr. Tharp's symptoms. One month later, Dr. Tharp was transferred to LRMC, and then to the US Air Force Academy to finalize his treatment.

Following the return to his job at the VA, Dr. Tharp was asked to participate in the SCIRP peer review panel as a consumer reviewer (CR) . "When asked to do my part as a consumer reviewer to provide my insights into what research can and should focus on, it was an honor I could not refuse," he said. Dr. Tharp's experience working at the VISN 17 Center of Excellence for Research on Returning War Veterans and as an assistant professor at Texas A&M Health Science Center College of Medicine prepared him well for this role. "The CR brings an incredibly robust perspective to research that has direct impact on what is funded and can provide insight that only those who have been there can bring. Once again, as a CR, I am grateful that I got a chance to make an impact on something I never imagined!"

For more information, visit
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