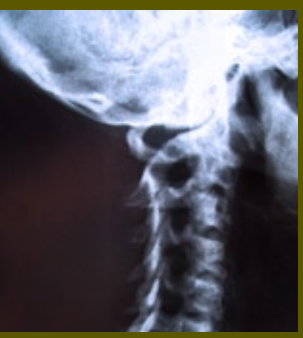
CDMRP

Department of Defense

Spinal Cord Injury Research Program





U.S. Army Medical Research and Materiel Command

Congressionally Directed Medical Research Programs

"Although relatively low in prevalence, spinal cord injury is devastating in effect. Thus, the SCIRP helps address a critical need for our nation's warfighters. Indeed, this CDMRP initiative has helped focus attention on this critical issue for the nation as a whole, attracting a very diverse pool of researchers to address this problem. The program is well organized to effectively meet its goals."

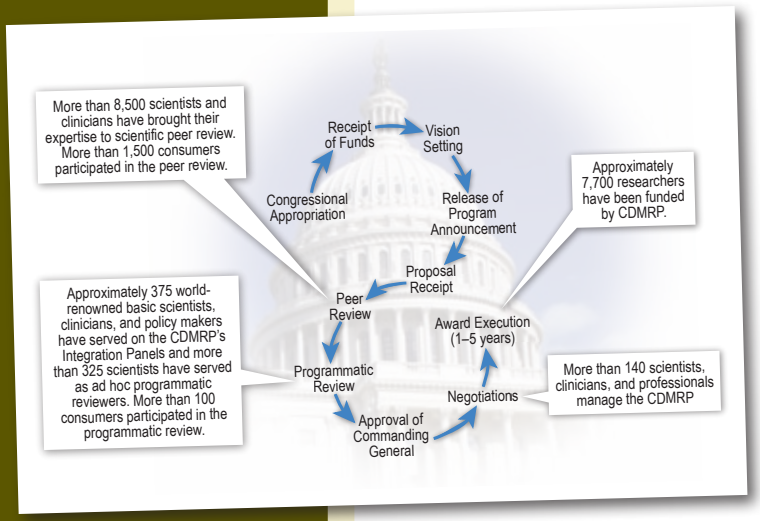
Arthur Sherwood, Ph.D.
Integration Panel Member

History

The Congressionally Directed Medical Research Programs (CDMRP) was born from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. The CDMRP was created as an office within the U.S. Army Medical Research and Materiel Command in fiscal year 1993 (FY93) to manage these funds, initiating a unique partnership among the public, Congress, and the military. Having grown to encompass multiple targeted research programs, the CDMRP has received more than $6 billion in appropriations since its inception in FY93 through FY10. Funds for the CDMRP are added by Congress to the Department of Defense budget annually, where support for individual research programs such as the Spinal Cord Injury Research Program (SCIRP) is allocated via specific guidance from Congress.

Proposal Review Process

The CDMRP program management cycle includes a two-tier review process recommended by the National Academy of Sciences' Institute of Medicine. Each level of review is conducted by panels composed of scientists and clinicians—subject matter experts—and consumers. The first tier of evaluation is an external scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review conducted by members of the Integration Panel who compare submissions and make funding recommendations based on relative 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 program priorities, reviewing proposals, and making funding recommendations. From a unique perspective gained through personal experience—as someone with a spinal cord injury—the consumer brings a sense of urgency and focus to all levels of decision making. Consumers evaluate proposals based on the potential impact and benefit to the patient population, encouraging funding recommendations that reflect the concerns of patients, their families, and the clinicians who treat them.

Spinal Cord Injury Research Program

Spinal cord injuries (SCIs) are serious and complex neurotraumatic wounds affecting military service members serving 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. The congressional appropriation for FY10 is $11.25M. 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 as well as their caregivers, families, and the American public.

Areas of research encouragement for the FY10 SCIRP include:

- Prevention, alleviation, or acute care of medical complications from SCI (e.g., autonomic dysreflexia, spasticity, sensory function, pain, skin care issues, bladder and bowel dysfunction, sexual dysfunction, and adjustment to disability)

Of particular interest within the areas of encouragement are:

- Implementation Research
- Clinical Practice Guidelines

FY10 Investment Strategy

Clinical Trial Award – Rehabilitation: With a focus on rehabilitation, this award mechanism supports the rapid implementation of Phase 0, I, and II clinical trials. Partnerships are sought between clinicians and bioengineers, and collaborations with new investigators are also encouraged.

Investigator-Initiated Research Award: Targeting independent investigators, this award mechanism supports projects that make an original and important contribution to SCI research and/or patient care. To promote collaborative research, a higher level of funding is available to projects that include a qualified collaborator.

Qualitative Research Award: This award mechanism supports projects that specifically focus on qualitative research involving military personnel and combat veterans, their family members, and caregivers.

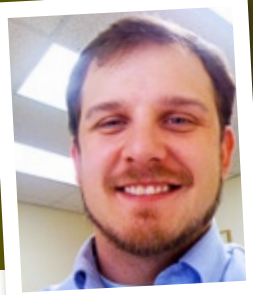
Translational Research Partnership Award: Designed to support the development of translational research through partnerships, this award mechanism seeks to fund multi-institutional, multidisciplinary partnerships among clinicians and laboratory scientists that accelerate the movement of promising ideas in SCI research into clinical applications. Collaborations with new investigators are encouraged.

VISION

Advance the understanding of spinal cord injury and ameliorate its consequences.

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 individuals with spinal cord injury.



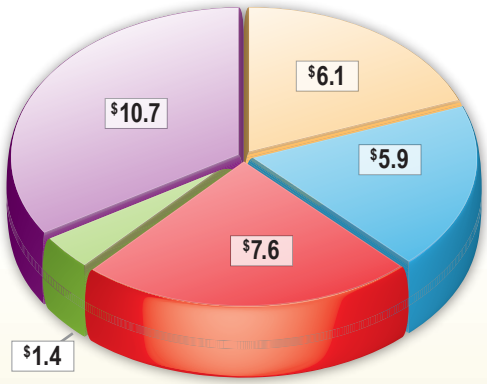
"I appreciated being included in the SCI review process. As a consumer, my comments were respected and welcomed both by the scientists and the staff."

Matthew Deans
Peer Review Consumer

Funding High-Impact Spinal Cord Injury Research

The SCIRP began in FY09 to promote research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies that offer real promise for enhancing long-term care of wounded Soldiers. Fifty-two awards encompassing 37 projects across five award mechanisms were funded for a total of more than $30M.

Total FY09 SCIRP Investment (Million)



FY09 SCIRP Funding by Research Area (Million)

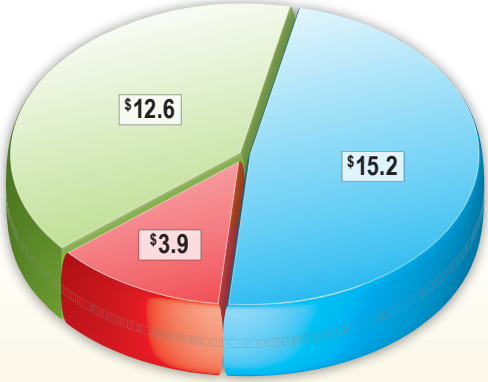


Photo of the Lokomat®Pro is courtesy of Hocoma©.

Advanced Technology and Therapeutic Development Award (ATTDA): The overall goal of the ATTDA is to accelerate the introduction of improved therapies, treatments, devices, or technologies for SCI into the clinical setting by supporting the generation of the preclinical data necessary to conduct clinical trials following award completion. The following three projects were funded under the ATTDA mechanism for a total of $5.9M:

- An anti-CD11d humanized antibody will be designed to prevent the acute infiltration of inflammatory cells into the injured spinal cord as a means to protect surrounding tissue, preserve neurological function, and improve outcome following SCI (Gregory Dekaban, Ph.D. and Arthur Brown, Ph.D.).
- Optimal dose, administration, and therapeutic window of small-molecule antagonists of the P2X7 class of adenosine triphosphate (ATP) receptors will be determined in animal models in an attempt to counteract the excess release of ATP at the injury site (Maiken Nedergaard, M.D., Ph.D. and Steven Goldman, M.D., Ph.D.).

- Sufficient preclinical data (e.g., optimal dose, central nervous system [CNS] distribution, toxicity, tumorigenicity, long-term persistence of recovery, association of treatment with aberrant sensation or pain) will be generated to move human Schwann cell transplantation, shown in experimental SCI models to improve functional recovery, into Phase I clinical trials for acute and chronic SCI patients (Damien Pearse, Ph.D.; Mary Bunge, Ph.D.; and James Guest, M.D., Ph.D.).

Photo is courtesy of the Miami Project to Cure Paralysis.

Clinical Trial Award – Rehabilitation (CTA-R): The CTA-R supports rapid implementation of rehabilitation-focused clinical trials that have the potential for significant impact on the understanding of SCI and amelioration of its consequences. Four projects were awarded under the CTA-R mechanism for a total of $7.6M:

- Zoledronic acid (to prevent bone loss) will be administered in combination with functional electrical stimulation rowing (to stimulate new bone formation) in male subjects with SCI (Leslie Morse, D.O.).
- A combination treatment consisting of parathyroid hormone (PTH) administration and directed vibration will be evaluated for increased bone mass and improved overall bone quality (Thomas Schnitzer, M.D., Ph.D.).
- A structured lifestyle intervention that includes circuit resistance training, calorie-matched Mediterranean-style diet, and behavioral support will be evaluated to combat the 66% higher rate of obesity found in persons with disabilities (Mark Nash, Ph.D.).
- The effectiveness of aquatic therapy will be compared with robotically assisted Lokomat training to evaluate the improvement of ambulatory capability and cardiovascular fitness of individuals with chronic motor incomplete SCI (Peter Gorman, M.D.).

Exploration – Hypothesis Development Award (EHDA): The EHDA supports the initial exploration of innovative, untested, high-risk, high-gain, and potentially groundbreaking concepts in SCI research. This award is designed to provide investigators with the opportunity to pursue serendipitous observations that, when explored, may provide the scientific rationale upon which a new hypothesis can be based. The following 10 projects were awarded under the EHDA mechanism for a total of $1.4M:

- Administration of PcTx1, an inhibitor of the acid-sensing ion channel 1a, will be explored as a potential mechanism to reduce secondary neuronal damage due to acidosis following SCI (Candice Askwith, Ph.D.).
- Copine VI, a neuron-specific, membrane-binding protein, will be tested in in vitro systems for its ability to repair the plasma membrane (Carl Creutz, Ph.D.).
- The effect of depression on functional recovery after SCI will be evaluated, and the antidepressant venlafaxine will be tested for its ability to improve both psychological health and the effectiveness of exercise rehabilitation in rats (Candace Floyd, Ph.D.).
- Biological and psychological factors will be examined for their influence on the vulnerability of SCI patients to pressure ulcers in an epidemiological study (Lisa Gould, M.D., Ph.D.).

"The SCIRP values consumer input in the peer review process, which is important because researchers and funding agencies need to listen to and respond to the needs of the population they serve."

Kim Anderson-Erisman, Ph.D.
Director of Education
The Miami Project to Cure Paralysis
Lois Pope Life Center

- Intensity-focused ultrasound will be evaluated for its effectiveness in mitigating bone loss after SCI (Sandra Poliachik, Ph.D.).
- Anabolic steroids, particularly nandrolone, a synthetic androgen, will be tested for their ability to block bone loss after SCI (Weiping Qin, M.D., Ph.D.).
- Valproic acid treatment, in combination with treadmill exercise, will be examined for enhanced structural and functional recovery in rats following SCI (John Redell, Ph.D.).
- Co-delivery of induced pluripotent stem cell-derived precursor cells and differentiation factors into the injured spinal cord tissue of rats will be investigated for the promotion of tissue repair (Molly Schoichet, Ph.D.).
- Loss of sleep after SCI will be studied to determine the underlying biological and molecular mechanisms (Gregory Holmes, Ph.D.).
- Isolated motor networks, disconnected from brain control centers due to SCI, will be evaluated for an altered response to neural stimuli, and the effects of reconnecting these isolated motor networks to their higher control systems will be assessed (David Schulz, Ph.D.).

Investigator-Initiated Research Award (IIRA): Targeting independent investigators, the IIRA supports projects that make an original and important contribution to SCI research and/or patient care. Fourteen projects spanning a wide variety of research topics were awarded under the IIRA mechanism for a total of $10.7M:

- A two-tiered early intervention approach will be tested in which rolipram will be administered within the first 4 hours after SCI to control inflammation, and bone marrow mononuclear cell grafts will be administered 12–72 hours later (Mark Tuszynski, M.D., Ph.D.).
- The dose of docosahexaenoic acid to be administered within 1 hour after SCI will be optimized for the preclinical studies necessary to move the drug to first-in-man studies (Adina Michael-Titus, D.Sc.).
- The balance of different types of fatty acids will be assessed in relation to SCI severity, and various formulations and concentrations of fenretinide will be tested for improvements to lipid balance in an SCI mouse model (Danuta Radzioch, Ph.D.).
- Chelation of excess iron, which occurs when red blood cells are carried into sites of SCI, will be balanced with the need for additional iron during endogenous cell replacement for tissue repair (Dana McTigue, Ph.D.).
- The formation of new intraspinal circuits will be promoted by “stretching” axons across SCI lesions with live axon bridges and encapsulating them in a collagen hydrogel (Douglas Smith, M.D.).
- The mechanism through which nerve transmission in surviving fibers after SCI is blocked by chondroitin sulfate proteoglycans (CSPGs) will be explored, and the potential neutralization of this effect by an antibody will be examined (Victor Arvanian, Ph.D., D.Sc.).
- ADAMTS-4, a neural aggrecanase, will be tested as a novel and more efficient method to digest inhibitory CSPGs (Diane Snow, Ph.D.).
- Digestion of scar tissue with an U.S. Food and Drug Administration-approved drug will be followed by the engineering of a complete vascular network to better support neuroregeneration (Ning Zhang, Ph.D.).
- Musculoskeletal modeling will assist in the development of a trunk stabilization device that will allow users to set seated positions at a variety of orientations (Musa Audu, Ph.D.).

- High-channel-count Utah Slanted Electrode Arrays will be developed and tested in vivo for intrafascicular stimulation of arm nerves to restore coordinated hand function (Gregory Clark, Ph.D.).
- Electrical stimulation of the motor cortex will be investigated in an animal model to elucidate the mechanism underlying this pain relief treatment so that procedures can be standardized for consistent clinical outcomes (Radi Masri, Ph.D.).
- Advanced magnetic resonance imaging (MRI) and diffusion tensor imaging will serve as noninvasive biomarkers for the stratification of type and severity of SCI at time of injury and the prediction of clinical outcomes (Adam Flanders, M.D.).
- A novel device will be developed specifically for SCI patients to help them monitor their physical activity level, set goals, and network with others for motivation (Dan Ding, Ph.D.).
- The underlying pathophysiology of SCI-induced autonomic dysreflexia, characterized by severe episodic high blood pressure as a result of overstimulation of the autonomic nervous system, will be explored (Keith Tansey, M.D., Ph.D.).

Translational Research Partnership Award (TRPA): Designed to support the development of translational research through partnerships, the TRPA funds multi-institutional, multidisciplinary partnerships among clinicians and laboratory scientists that accelerate the movement of promising ideas in SCI research into clinical applications. Six projects were awarded under the TRPA mechanism for a total of $6.1M:

- Advanced MRI methods will be used to improve the characterization of tissue damage following SCI, as well as the measurement of treatment responses (David Hackney, M.D.; Felix Wehrli, Ph.D.; and Alan Tessler, M.D.).
- Serum biomarkers predicting a positive response to glibencamide therapy will be identified in a rat model of SCI and validated in spinal cord injured patients in an effort to attenuate post-traumatic hemorrhagic necrosis and improve functional recovery (Phillip Popovich, Ph.D. and Marc Simard, M.D., Ph.D.).
- The Phase System, a novel SCI-specific outcome measure that assesses the ability to complete functional tasks, will be assessed for validity, reliability, and responsiveness as a measurement of functional recovery (Andrea Behrman, Ph.D.; D. Michele Basso, Ed.D.; and Craig Velozo, Ph.D.).
- Intermittent hypoxia therapy, previously shown to increase neural plasticity in the spinal cord, will be evaluated in combination with locomotor training to improve the restoration of limb motor function (Gordon Mitchell, Ph.D.; Gillain Muir, D.V.M., Ph.D.; and Randy Trumbower, Ph.D.).
- Growth factor-releasing nanofiber nerve guidance tubes will be surgically implanted in an animal model to act as a bridge between the damaged spinal cord and nerve roots, promoting axonal regeneration of SCI complicated by involvement of the conus medullaris and the cauda equina (Leif Havton, M.D., Ph.D.; Ahmet Höke, M.D., Ph.D.; and Kari Christe, D.V.M.).
- Current clinical practice evidence will be used to apply a "bedside to bench" approach for the development of a combined SCI–traumatic brain injury (TBI) model and improve treatment practices for patients with SCI and TBI (Michael Beattie, Ph.D.; Graham Creasey, M.B.Ch.B.; and Geoffrey Manley, M.D., Ph.D.).

"As a paralyzed veteran with a spinal cord injury, I have always been a strong supporter of SCI research! Therefore, it was a tremendous opportunity to once again have the opportunity to review proposals and provide consumer input on some of the leading-edge research from investigators around the world."

Michael Delaney, Past National President, Paralyzed Veterans of America (1980–82) and former Chair of the PVA Spinal Cord Research Foundation

"Serving the CDMRP SCIRP was the best opportunity I had to give back to the medical community that provided the critical care to keep me alive following my line-of-duty injury serving the United States Air Force. I can only hope to continue carrying the torch to help lead the next generation of responsible medical research so that my future brothers-in-arms and civilian counterparts have even better medical treatment options available to them should they need. Though treating spinal injuries and their secondary consequences is a broad focus, the proposals and initiatives this panel reviews clearly demonstrate a unified concern to better care for our nation's veterans and disabled citizens. It was an honor and a privilege to offer the voice of our community of spinal injured Americans in order to help medical researchers better understand the trials and tribulations we live with and concerns that are most pertinent to our health care."

Lt. Ian James Brown
Pilot and Pararescueman, United States Air Force (retired)

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