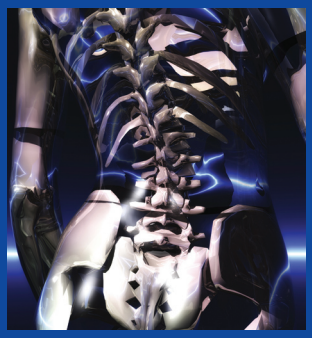
CDMRP

Department of Defense

# Peer Reviewed Orthopaedic Research Program

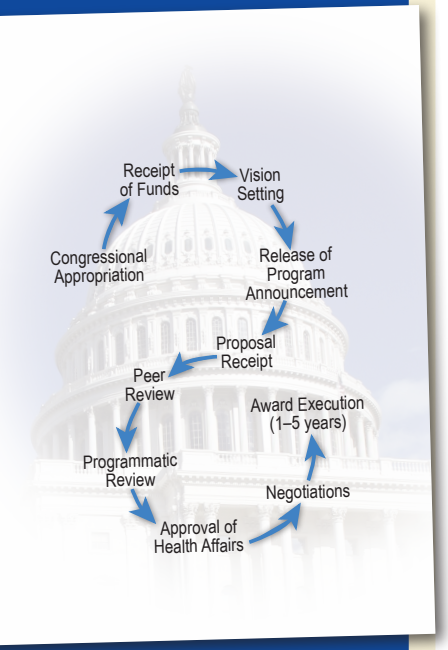


*U.S. Army Medical Research and Materiel Command*

# Congressionally Directed Medical Research Programs

## History

The Congressionally Directed Medical Research Programs (CDMRP) stemmed from an 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 (USAMRMC) in fiscal year 1993 (FY93) to manage these funds, initiating a unique partnership between the public, Congress, and the military. The CDMRP has grown to encompass multiple targeted research programs, managing over $6 billion in appropriations since its inception in FY93 through FY10. Funds for the CDMRP are added by Congress to the Department of Defense (DOD) budget annually, where support for individual research programs such as the Peer Reviewed Orthopaedic Research Program (PRORP) is allocated via specific guidance from Congress.




## Proposal Review

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 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 an orthopaedic injury or as someone providing direct supportive care to the injured—a 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.

When I was offered the opportunity to be a consumer reviewer for the DOD Congressionally Directed Medical Research Programs, I was excited to be part of this process, which was completely new to me. After sitting on the board with the scientists and other consumers and reviewing a number of proposals, I was amazed at the wealth of knowledge that goes into evaluating these proposals, all of which lead to improving the lives of service members.

***MSgt William "Spanky" Gibson***
***Office of the Assistant Secretary of the Navy (Manpower and Reserve Affairs)***
***PRORP Peer Reviewer FY09***

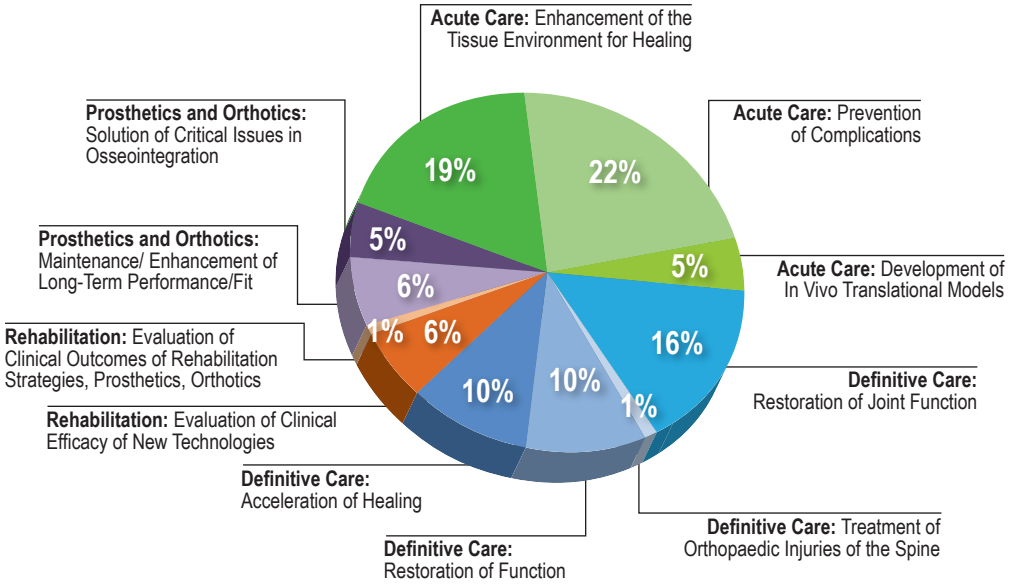
# Peer Reviewed Orthopaedic Research Program

## History

Understanding how to treat and facilitate rapid recovery from orthopaedic injuries is a priority within the military health system. A majority of the injuries sustained by military personnel in U.S. war efforts involve soft tissue wounds and bone fractures, pointing to a need for orthopaedic research that will provide superior medical care and treatment options for injured service members. The DOD PRORP was established by Congress in FY09 with appropriations totaling $112 million (M) to support military-relevant, peer-reviewed orthopaedic research. The program was continued in FY10 with a congressional appropriation of $22.5M.

Frequent outcomes and complications in amputated or salvaged limbs include infection, compartment syndrome, non-union, heterotopic ossification, and temporary or permanent muscle function loss, among others. The PRORP crafts investment strategies and funding portfolios to address these challenges, with the goal of helping injured service members achieve optimal recovery from combat-related orthopaedic injuries.

### The PRORP Funding Portfolio FY09




***PRORP FY09 Percentage of Funded Projects by Priority Research Area***

## VISION

Provide all Warriors affected by orthopaedic injuries sustained in the defense of our Constitution the opportunity for optimal recovery and restoration of function.

## MISSION

Address the leading burden of injury and loss of fitness for military duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat or combat-related activities.

The unprecedented team approach exemplified by the Peer Reviewed Orthopaedic Research Program reflects a unified effort to provide the best science-based medical and rehabilitation solutions for our injured warriors, their family members, and the health care providers who serve them. It has truly been a privilege and an honor to serve with the clinicians, academicians, researchers, consumers, and educators who have devoted their time, expertise, and research careers to this critical research mission."

***LTC(P) Rachel Evans, Center for the Intrepid, Brooke Army Medical Center***
***PRORP Integration Panel Member***
***FY09 and FY10***

# PRORP Program Highlights

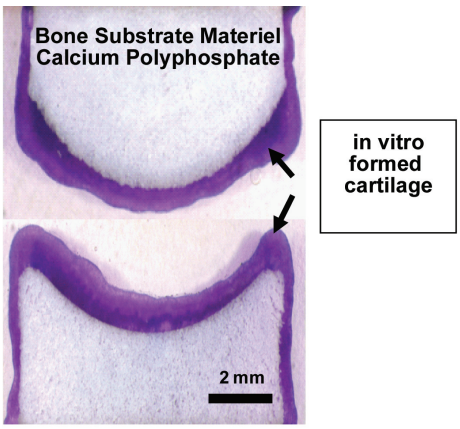
In FY09, the PRORP called for proposals in seven different funding mechanisms to create a broad research portfolio of basic, translational, and clinical studies, as noted in the diagram to the right. A selection of the 83 research projects chosen for funding are highlighted in the following pages to exemplify the research that has been initiated through PRORP support.

## Restoration of Joint Function Using a Biphasic, Biodegradable Implant

Rita Kandel, M.D., Mount Sinai Hospital, and Paul Zalzal, M.D., McMaster University
**Translational Research Partnership Award**

Dr. Rita Kandel and Dr. Paul Zalzal, recipients of an FY09 Peer Reviewed Orthopaedic Research Program Translational Research Partnership Award, hypothesize that large, anatomically correct joint implants composed of cartilage integrated to the surface of a porous, degradable bone substitute, may restore damaged articular joint surface, form, and function to a normal structural state. Current available treatments for intra-articular fractures are limited to arthroplasty (joint replacement), arthrodesis (joint fusion), or amputation, and often result in significant loss of bone and cartilage, leading to debilitation.

Dr. Kandel, Dr. Zalzal, and other investigators will collaborate to design and optimize the bone substitute, develop conditions to form cartilage on larger surfaces using human chondrocytes, and evaluate the joint implant in a preclinical model.

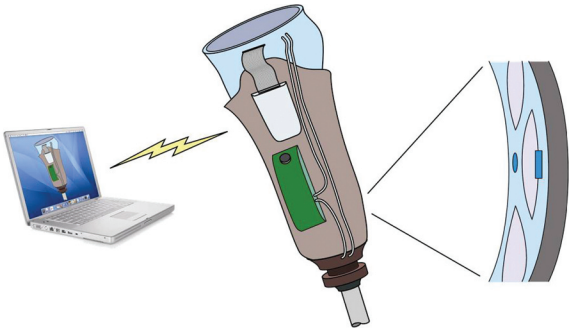


Appearance of Biological Implant

## High-Performance Prosthetic Socket with Proprioceptive Haptic Feedback and Prognostic Pressure Monitor

Jason Wheeler, Ph.D., Sandia National Laboratories
**Technology Development Award**

Current socket fit technologies pose significant problems to the effectiveness of an artificial limb. Dr. Jason Wheeler, recipient of a FY09 Peer Reviewed Orthopaedic Research Program Technology Development Award, is exploring new technologies that can monitor and adjust prosthesis socket fit to improve comfort and functionality for active individuals with lower limb amputations. Dr. Wheeler and his colleagues propose to develop and test socket technologies that allow chronic pressure and shear sensing, automatic fit adaptation to accommodate limb shape changes and activity levels of the users, and a system for tactile display of information from the prosthesis. The proposed socket incorporates a silicone liner fitted with multiple pressure sensors and discrete fluid-filled bladders whose volume can be individually regulated by the pressure sensors. Multiple systems to provide haptic feedback will also be tested for potential incorporation into the socket.



# FY09 PRORP Funded Research

## The Major Extremity Trauma Research Consortium

Ellen MacKenzie, Ph.D., Johns Hopkins University
**Clinical Consortium Award**

Dr. Ellen MacKenzie, recipient of the FY09 Peer Reviewed Orthopaedic Research Program Clinical Consortium Award, will build on the existing Major Extremity Trauma Research Consortium (METRC) she and co-Principal Investigator Dr. Michael Bosse established with funding from the 2008 Orthopaedic Extremity Trauma Research Program. In addition to the data coordinating center at Johns Hopkins University, the original METRC consisted of 12 core clinical centers and 30 satellite centers; it was created to address major issues concerning early, acute treatment of combat-related limb injuries. PRORP funding will allow METRC to grow to 24 core civilian clinical centers and 39 satellite centers, to perform studies related to the definitive and rehabilitative care of wounded warriors with orthopaedic injuries, and to set up research infrastructure within four military treatment facilities (MTFs) that treat the majority of wounded warriors in the United States. The four MTFs will participate as additional core clinical sites under the expanded METRC organization. The overall structure and breadth of METRC and its planned research will help to eliminate the gaps in care and optimally manage the research areas that are pertinent both to the acute and definitive care of the wounded warrior.

METRC's ultimate goal is to provide evidence needed to establish better treatment guidelines for the optimal care of the wounded warrior and ultimately improve the clinical, functional, and quality of life outcomes of both service members and civilians who sustain high energy trauma to the extremities. Initial studies funded by the PRORP Clinical Consortium Award will focus on compartment syndrome monitoring, comparison of limb salvage versus transtibial amputation, perioperative pain management, and quality of life issues following lower extremity trauma.

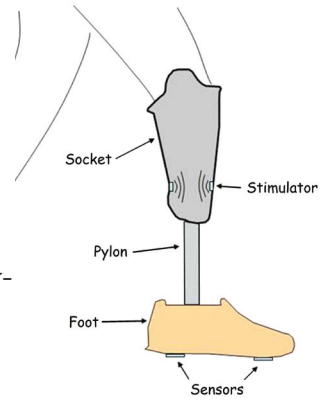
## Use of the TRPV1 Agonist Capsaicin to Provide Long-Term Analgesia in a Rat Limb Fracture/Open Repair, Internal Fixation Model

Michael Buys, Ph.D., Capt. (USAF), Wilford Hall Medical Center, Lackland Air Force Base
**Career Development Award**

Current methods of treatment for acute pain can be ineffective in traumatic orthopaedic injury or can result in long-term side effects that outweigh the short-term benefits. Dr. Michael Buys, recipient of an FY09 Peer Reviewed Orthopaedic Research Program Career Development Award, is exploring the inactivation of transient receptor potential vanilloid 1 (TRPV1) via local instillation of purified capsaicin into fracture sites and surrounding injured soft tissues during open repair of fracture to provide prolonged analgesia and decreased inflammation without affecting motor or sensory nerve function or impairing bone healing. During the study, Dr. Buys will develop a rat pain model for lower extremity fracture and open reduction internal fixation (ORIF) that will parallel battlefield injuries sustained by wounded warriors and mimic a normal time line of healing and inflammation. Additionally, Dr. Buys will examine the dose-response relationship of capsaicin infiltration of the soft tissue and fracture site to pain, inflammation, and fracture healing. The project will be carried out under the mentorship of Dr. Timothy Brennan of the University of Iowa, with the goal of providing Dr. Buys the training and experience necessary to establish a basic and translational research career focused on the treatment and prevention of acute and chronic pain from battlefield injuries.

## A Prosthesis to Train the Proprioceptive Capabilities of the Residual Limb of Military Personnel Recovering from Lower Limb Amputation

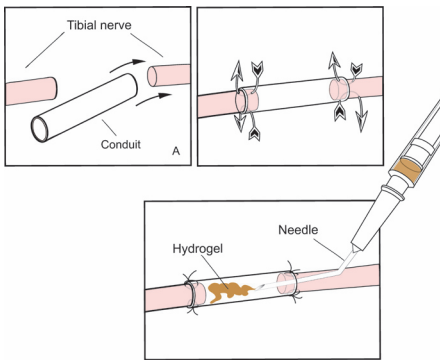
Dr. Brian Glaister, Ph.D., Empowering Engineering Technologies Corporation, Seattle, Washington
**Hypothesis Development Award**




Dr. Brian Glaister, a recipient of an FY09 Peer Reviewed Orthopaedic Research Program Hypothesis Development Award, is developing force-feedback sensory devices for lower limb prostheses, which will help overcome one of the major obstacles in early rehabilitation following an amputation. Amputees often rely on visual feedback to sense their body position, which is less effective than somatosensory feedback. The proposed device uses vibrotactile feedback to communicate biomechanical information, such as force intensity and spatiality, from the prostheses directly to the skin. Dr. Glaister anticipates that such a device may dramatically accelerate post-operative gait training in amputees by eliminating the need to rely on visual cues to walk.

## Multicenter Clinical Trial of Keratin Biomaterials for Peripheral Nerve Regeneration

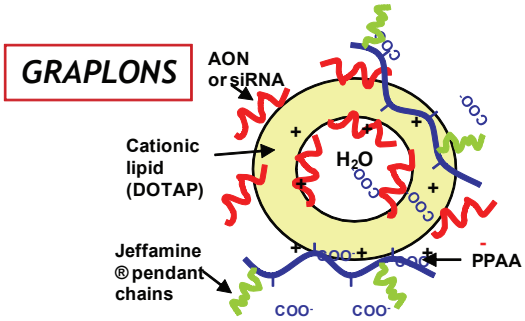
Zhongyu Li, M.D., Ph.D., Wake Forest University Health Sciences
**Clinical Trial Award**




Dr. Zhongyu Li, recipient of an FY09 Peer Reviewed Orthopaedic Research Program Clinical Trial Award, will conduct clinical trials to examine the safety and efficacy of a novel keratin hydrogel biomaterial as a luminal filler in nerve conduits. Early preclinical studies have shown promising results with the use of keratin hydrogel in promoting nerve regeneration. Dr. Li hypothesizes that the use of keratin hydrogel-filled nerve conduits should safely support nerve regeneration for patients who have suffered traumatic peripheral nerve transections. This technology may simplify surgical nerve repair by eliminating the need to harvest donor sensory nerve for autograft and the accompanying donor site morbidity.

## Integrated Proteomic Analysis and siRNA Therapy for Treatment of Heterotopic Ossification

Charles Roth, Ph.D., Rutgers University
**Idea Development Award**




Service members with injuries from high-energy blast explosions experience significant problems with heterotopic ossification (HO). Dr. Charles Roth received an FY09 Peer Reviewed Orthopaedic Research Program Idea Development Award to develop methods for preventing and treating HO by modifying the tissue microenvironment at the injury site. Specifically, Dr. Roth and colleagues from Daemen College and the U.S. Army Institute of Surgical Research plan to identify proteins involved in the initiation and development of HO by analyzing patient samples and designing short interfering RNAs (siRNA) to modulate their production. Moreover, a novel method of siRNA delivery, graft polyelectrolyte-liposome-oligonucleotide (Graplon) nanoparticle complexes, will be assessed to overcome some of the barriers that have limited the effectiveness of siRNA-mediated gene silencing. Dr. Roth anticipates that this study will result in a safe, nontoxic alternative to currently available treatments for HO that can be scaled up for preclinical testing.

# The Vision for FY10

The PRORP challenges the scientific community to design innovative research that will foster new directions for and address neglected issues in orthopaedic research and the treatment of combat-relevant orthopaedic injuries. In FY10, Congress continued the PRORP with an appropriation of $22.5M to the PRORP. Two award mechanisms addressing underfunded priorities were offered:

| Focus | Award Mechanism |
|---|---|
| **Clinical Research** | ***Orthopaedic Rehabilitation Clinical Consortium Award:*** Supports the development of a multi-institutional consortium to conduct clinical studies aimed at improving rehabilitation of combat and combat-related neuromusculoskeletal injuries. The intent of this award is to establish an infrastructure to rapidly execute clinical studies in a partnership of military and non-military clinical research centers. |
| **Training/Career Development** | ***Career Development Award:*** Supports active duty military researchers, physical therapists, occupational therapists or physician scientists at early career stages in gaining the experience necessary to pursue career opportunities at the forefront of orthopaedic and rehabilitation research, and in making significant contributions to combat-relevant orthopaedic research and/or clinical care. |

For more information, visit
***http://cdmrp.army.mil***
or contact us at:
***CDMRP.PublicAffairs@amedd.army.mil***
**(301) 619-7071**

10-2010