

2011 Military Health System Conference

Clinical and Rehabilitative Medicine Research Program Overview

The Quadruple Aim: Working Together, Achieving Success

COL Janet R. Harris RN PhD

26 January 2011



US Army Medical Research and Materiel Command

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USAMRMC

Mission and Vision



MISSION



Responsively and responsibly create and deliver medical information and products for the warfighting family.



VISION



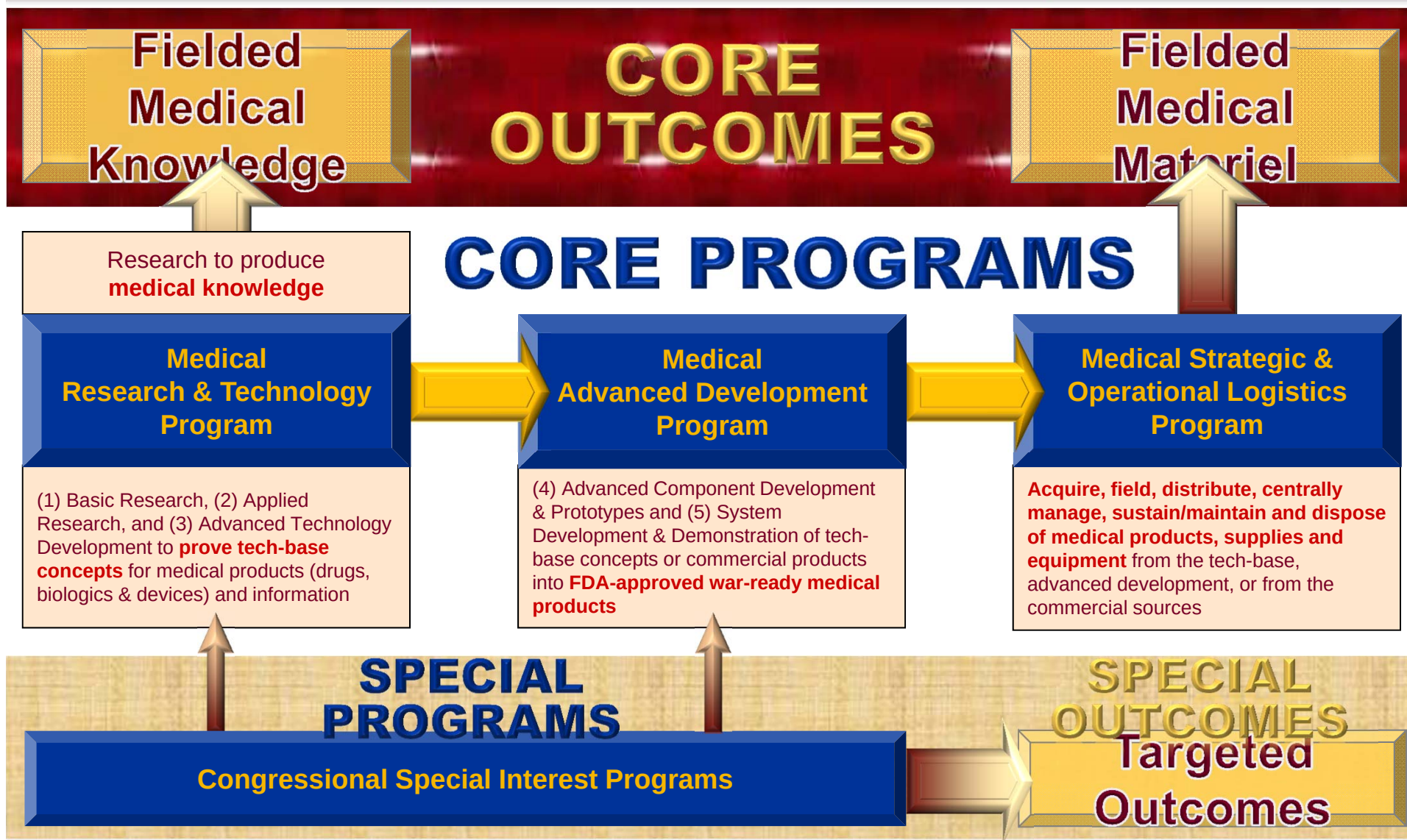
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USAMRMC



Customer-Focused Programs & Outcomes



CHANGE DRIVERS FOR THE MILITARY MEDICAL RDA MISSION



Emphasis on Contemporary Health Threats and Joint Programs

Secretary of Defense Guidance



June 26, 2008

Secretary Gates Memorandum *Caring for Our Wounded Personnel and Their Families*

"I request the development of a tailored plan to provide R&D investments that advance state of the art solutions for world class medical care with an emphasis on Post Traumatic Stress Disorder, Traumatic Brain Injury, prosthetics, Restoration Sight Eye-Care, and other conditions directly relevant to the injuries our soldiers are currently receiving on the battlefield."



April 6, 2009

Secretary Gates News Conference *Details New Pentagon Priorities*

FY2010 Defense Budget: "Continue the steady growth in medical research and development by requesting \$400 million more than last year."



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Secretary of the Army Imperatives

SUSTAIN

- ✦ Sustain Soldiers, Civilians and Families, through recruiting and improving quality of life
- ✦ Taking care of wounded Soldiers
- ✦ Rehabilitate Soldiers and get them back into the fight

PREPARE

- ✦ To continue to prepare Soldiers for success in the current conflict
- ✦ Continue to adapt its training and equipment to keep ahead of an adaptive enemy
- ✦ Training leaders and Soldiers

RESET

- ✦ Continue to reset units and to rebuild the readiness consumed in operations, to prepare them for deployments and future contingencies
- ✦ Reset for the future, not the past

TRANSFORM

- ✦ Transform the Army to meet the demands of the 21st century
- ✦ Continually modernize our forces and put our Cold War formations and systems behind us
- ✦ Future Combat Systems research and development is currently the Army's largest effort to modernize



CHANGE DRIVERS



What is driving change in the military R&D environment?

Contemporary War Casualties

- Current war casualties are driving changes in healthcare needs and therefore changes in R&D
- Specific types of casualties driving changes:
 - Traumatic Brain Injury (TBI)
 - Blast Injuries

	% Body Area	WWII	Korea	Vietnam	OIF/OEF
Head & Neck ↑	12%	21%	21%	16%	29%
Chest ↓	16%	14%	10%	13%	6%
Abdomen	11%	8%	8%	9%	11%
Extremities	61%	58%	60%	61%	54%

Owens, J Trauma FEB 2008

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TBI Suffered in Iraq



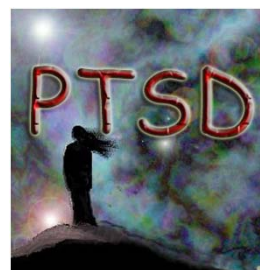
Trauma Team at Kirkuk Air Base in Iraq



Workshop at the Walter Reed Amputee Center



Blast Injury from Exploding Ordnance



RESETTING WOUNDED WARRIORS



R&D to Help Reset the Force

Evidence-based
return-to-duty
standards and
evaluation criteria



Redeployment

Medical
Evacuation

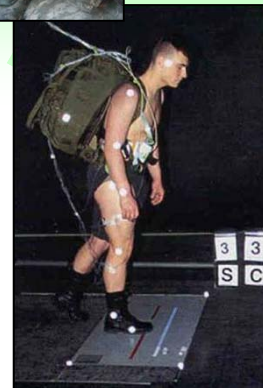
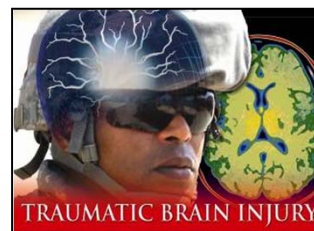
Reorientation
and Reunion

Warrior Transition Units
(Army)

Transitional Reentry Sites
(Defense and Veterans Brain Injury Center
(DVBIC))

Return to
Duty

Return to
Civilian
Life



CRMRP MISSION, FUNCTIONS, AND PARTNERS



Mission

Focus on definitive and rehabilitative care innovations required to reset our wounded warriors, both in terms of duty performance and quality of life

Functions

- Manage a core research program consisting of intramural and extramural efforts
- Leverage the congressional special interest research programs administered by USAMRMC, and research efforts in other federal laboratories, universities and industry.
- Coordinate the CRMRP research program with complimentary programs

Scientific Steering Committees, a Joint Program Committee, and a Joint Technology Coordinating Group were established to advise CRMRP on program direction and priorities

Coordinating Partners



- † DoD laboratories and medical centers
- † DoD Congressional special interest programs
- † National Institutes of Health
- † Defense Advanced Research Projects Agency
- † Department of Veterans Affairs

CRMRP PROGRAM AREAS



Neuromusculoskeletal Injury: (Incl. Amputee)

- Address psycho-social recovery aspects
- Improve rehabilitation for limb salvage and spinal injury patients
- Exercise and fitness systems and strategies
- Improved orthotics, prosthetics, robotics to improve extremity function
- Incorporate neural interface/feedback



Regenerative Medicine and Transplants:

- Improve speed of healing and decrease scarring
- Regenerate missing tissue and repair nerve gaps
- Improve functionality and appearance following craniofacial repair
- Develop architecture to integrate created tissue
- Reduce need for tissue rejection therapy
- Improve surgical approaches and limb/tissue function



Pain Management: (Acute/Chronic/Battlefield)

- Improve management of battlefield, acute and chronic pain
- Establish safety margins for individual prescriptions
- Identify and treat pain generators
- Develop strategies to empower patient in managing pain



Sensory Systems: (Vision/Hearing/Balance)

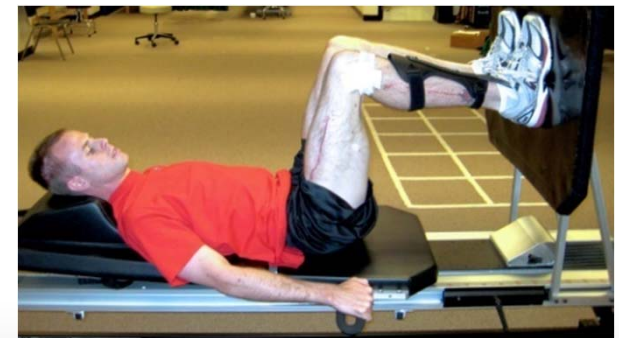
- Repair damage to the eye and visual system
- Restore hearing
- Treat tinnitus
- Improve diagnostics
- Rehabilitate TBI-associated sensory dysfunction



REHABILITATION



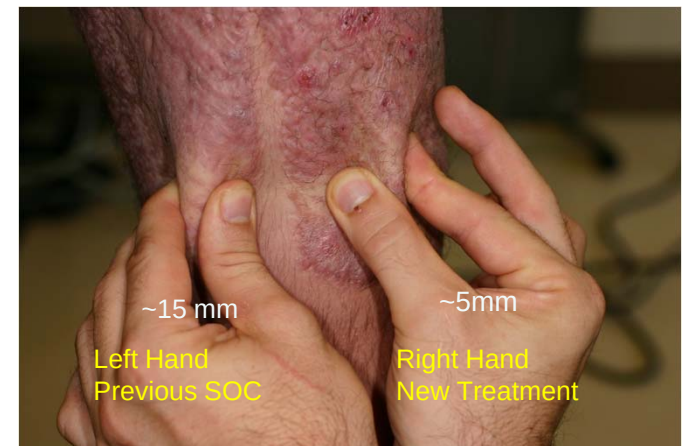
- Focuses on the rehabilitation of neuromusculoskeletal injuries, including amputee care and prosthetics
- Coordinating with the Center of Excellence for Extremity Injury and Amputation
- Major Initiatives:
 - Military Amputee Research Program
 - Prosthetics
 - Leveraging Orthopaedic Congressional funding (Peer-Reviewed Orthopaedic Research Program)
 - Major Extremity Trauma Research Consortium
 - Orthopaedic Rehabilitation Clinical Consortium



Fraxellated CO2 Laser for Scar Contracture and Reduction



- **Problem**
 - Range of motion is reduced by burn scar contractures from thermal or chemical burns
- **Description**
 - Fraxellated laser: delivers independent, controlled patterns and depths of ablative and/or coagulative damage
 - Intent is to permit expansion of the skin and thereby reduce tension in scars
- **Studies**
 - Wilford Hall Medical Center
 - Initial studies conducted by Air Force
 - Study expansion being supported by DHP
 - Treatments were applied to burn scar contractures
 - ❖ Perioral and axillary regions
 - ❖ 5 treatments over 8-12 weeks
 - Assessed: range of motion, thickness, compliance and aesthetics (erythema and pigmentation)
- **Results:**
 - Immediate reduction in scar bulk
 - Smoothing of surface irregularities
 - Increased pliability
 - Pigmentation improvement
 - New production of scar collagen
 - Remodeling of scar

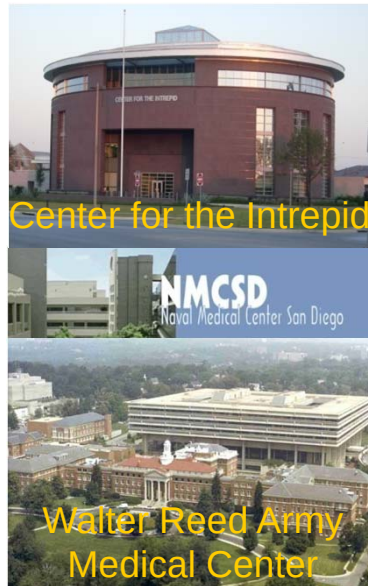


REHABILITATION



Investment Highlights

- **Military Amputee Research Program:** Congressional funding
 - Research embedded within military treatment facilities
 - Government, university and industry research
 - o Advanced prosthetics
 - o Rehabilitation
 - o Outcomes and program assessment
 - o Clinical management
 - o Database development/management

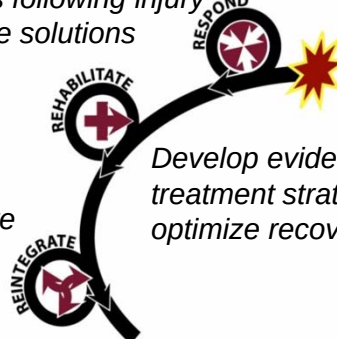


Respond to the acute care needs of wounded warriors following injury through innovative solutions

Post injury event

Develop evidence-based treatment strategies to optimize recovery of function

Return to a full and productive life, to include return to duty, competitive sports, or a new vocation



REHABILITATION



Investment Highlights

- **Prosthetics:**

- Lower Extremity: USAMRMC Managed Congressional funding
 - o C-Leg Generation 2 – Microprocessor powered knee (Commercialization NOV 2010)
 - o C-Leg Generation 3 – Ruggedized microprocessor controlled knee
 - o iWalk PowerFoot – Active plantar flexion push off
- Upper Extremity: VA-DARPA-USAMRMC Collaboration
 - o DEKA Arm – strap-and-go technology, foot-based control
 - o APL Arm – improved functionality, intended for targeted motor reinnervation
 - o Clinical trials for DEKA arm are planned to begin in Spring 2011, and APL arm studies are being developed



REHABILITATION



Coordinated Defense R&D - Prosthetics



- Revolutionizing Prosthetics Program
- Focused on upper extremity



- National Institute of Child Health and Human Development

White House Office of
S&T Policy has
requested a 10-year
plan for prosthetics



- USAMRMC Clinical and Rehabilitative Medicine Research Program
- USAMRMC Telemedicine and Advanced Technology Research Center (TATRC) - Advanced Prosthetics and Human Performance Portfolio
- Military Amputee Research Program
- Transition partner for clinical trials – active duty population



- VA Prosthetics and Sensory Aids Service (PSAS)
- Prosthetics, orthotics, and assistive device research
- Transition partner for clinical trials – veteran population

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REHABILITATION



The Major Extremity Trauma Research Consortium

- Johns Hopkins University led
- Consortium consists of orthopaedic researchers from U.S.
- Consortium aims include:
 - Improved outcomes and decreased fasciotomy in patients at risk for compartment syndrome by optimized clinical assessment, objective monitoring and tissue ultrafiltration
 - Outcomes following severe distal tibia, ankle and/or foot trauma: comparison of limb salvage versus trans-tibial amputation
 - Improving pain management in high energy orthopaedic trauma
 - Improving activity and quality of life following lower extremity trauma
- Funding amount to consortium: \$40 million (September 2010 – September 2015)



REHABILITATION



Orthopaedic Rehabilitation Clinical Consortium

- Award pending
- University-led consortium will collaborate with the following MTFs:
 - San Antonio Military Medical Center (SAMMC)
 - Walter Reed National Military Medical Center (WRNMMC)
 - Naval Medical Center Portsmouth (NMCP)
 - Naval Medical Center San Diego (NMCSD)
- The goal of the Consortium is to improve rehabilitation of combat and combat-related neuromusculoskeletal injuries (including spine injuries, burns, and contractures, and excluding spinal cord injury [SCI])
- Funding amount for consortium: \$19.5 million over 5 years



Armed Forces Institute of Regenerative Medicine

- Two consortia working together with the US Army Institute of Surgical Research (230 scientists)
 - Wake Forest – Pittsburgh University Consortium
 - Rutgers University – Cleveland Clinic Consortium
 - 28 Universities
 - 114 investigators – 30% of which are clinicians
 - 46 graduate students
 - 70 post-docs
- Total 5 yr funding of >\$270M
 - \$100M US Government funding from Army, Navy, Air Force, VA, and NIH
 - \$68M Matching funds from state governments and participating universities
 - \$109M in pre-existing research projects directly related to the deliverables of the AFIRM from NIH, DARPA, Congressional funding, NSF, philanthropy
 - DHP has supplemented \$19.8M for clinical trials since 2008



Cranio-Facial
Reconstruction



Healing Without
Scarring



Compartment
Syndrome



Limb and Digit Salvage
and Reconstruction



Burn Repair

<http://www.afirm.mil/>

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REGENERATIVE MEDICINE



Investment Highlights

- **Clinical trials initiated in multiple areas:**

- Hand/face transplants with and without strategies for safer immunomodulation
- Engineered Skin Substitutes to treat >50% TBSA burns (both autologous and allogenic)
- Skin graft stretching to expand the size of autologous skin samples for grafting
- Autologous skin cell spraying to treat burn injuries with less scarring
- Bandage for Improved healing and scar reduction
- Autologous fat injections (alone and also enriched with stem cells) to reduce severity of burn scarring
- Use of porcine extracellular matrix to regenerate limb muscle form and function
- Segmental nerve gap regeneration using a novel nerve scaffold biomaterial
- 510k scale up of polymeric, resorbable bone scaffolds and soft tissue scaffolds



PAIN MANAGEMENT



Pain Management Task Force

- 2010 NDAA (Sec. 711) tasked the Secretary of Defense to develop and implement a comprehensive policy on pain management by the military health care system
- Army SG convened a multi-agency Task Force to define strategic needs for improving pain management, including research
- R&D recommendations
 - Develop collaborative pain research strategies that advance Warrior pain care and rapid translation
 - Validate pain research needs
 - Expand telemedicine capabilities to incorporate pain management initiatives
 - Improve military pain research strategic communications

TASK FORCE RECOMMENDATION

A Standardized DoD and VHA Vision and Approach to Pain Management to Optimize the Care for Warriors and their Families

1	Focus on the Warrior and Family - Sustaining the Force
2	Synchronize a Culture of Pain Awareness, Education, and Proactive Intervention (Medical Staff, Patients and Leaders)
3	Provide Tools and Infrastructure that Support and Encourage Practice and Research Advancements in Pain Management
4	Build a Full Spectrum of Best Practices for the Continuum of Acute and Chronic Pain, Based on a Foundation of Best Available Evidence

PAIN MANAGEMENT



Capability Gaps

- Acute and chronic pain management in the battlefield/remote locations and resource-limited environments
- Continuum of care from acute to chronic pain in a traditional environment
- Strategies to identify and treat pain generators
- Addressing psycho-social aspects of recovery (management of pain)
 - knowledge and treatment strategies / therapies for treating pain and co morbidities



PAIN MANAGEMENT



Regional Anesthesia and Pain Management Initiative



- Defense and Veterans Pain Management Initiative (DVPMI)
 - Conducts acute and chronic pain research
 - Capabilities for consultation, referral, policy development, publications, education and training
- Research
 - Regional anesthesia – validation conducted in deployed setting
 - Translational research – biological effects of regional anesthesia
 - Biomarkers for pain
 - Outcomes evaluation (RAMPOS, POWER)
 - Evidence based practice
- Funding
 - Established by CSI funding
 - Transitioning to DHP
- Value to the Warfighter
 - First ever deployed Acute Pain Service with British Coalition Forces, Camp Bastion, Afghanistan
 - SME to OTSG on Pain Task Force - driving force behind all pain initiatives
 - First research since WWII on pain immediately following wounding
 - Since 2003 all advancements in battlefield pain control from point of injury, through air evacuation, to CONUS have been a direct result of the DVPMI
 - 2009: Military Advanced Regional Anesthesia & Analgesia (MARAA) Handbook



Molecular Signatures of Chronic Pain Subtypes

Rehabilitation – Acute and Chronic Pain Management

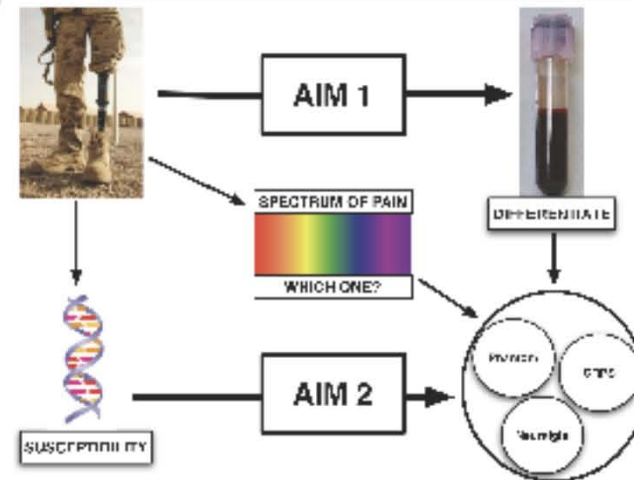
PI: Andrew Shaw MD

Org: Duke University Medical Center



Problem, Hypothesis and Military Relevance

- **Problem:** (1) There are no good tests to differentiate between different types of chronic amputation pain. (2) There are no good ways to measure susceptibility to chronic pain subtypes (phantom limb pain, neuralgia, CRPS).
- **Hypothesis:** (1) Plasma protein signatures can identify each type of amputation pain. (2) Sequencing the genes of these proteins can identify patients at risk for each type of pain.
- **Military Relevance:** New, objective tools facilitating the differential diagnosis and risk assessment of chronic pain states would allow more focused deployment of rehabilitation resources, and thus permit earlier return to functional status for injured warriors.



Proposed Solution

- **Aim 1a:** Describe the molecular (proteomic) signatures of phantom pain, neuralgia pain and Complex Regional Pain Syndrome (CRPS) in 450 war injured amputees.
- **Aim 1b:** Describe the biology of chronic amputation pain subtypes in terms of the peptides and proteins expressed in early and late blood samples from amputees
- **Aim 2a:** Generate list of candidate risk genes for each subtype of amputation pain.
- **Aim 2b:** Sequence genes of proteins from Aim 2a to find new polymorphisms associated with functional differences and risk of each pain subtype.

Timeline and Direct Cost

Activities	Year 1	Year 2	Year 3
Compliance and approval	■		
Recruit subjects		■	
Discovery Proteomics (Aim 1)		■	
Gene Sequencing (Aim 2)		■	
Validation studies (Aims 1 & 2)			■
Report preparation		■	■
Estimated Budget (\$K)	400K	400K	200K

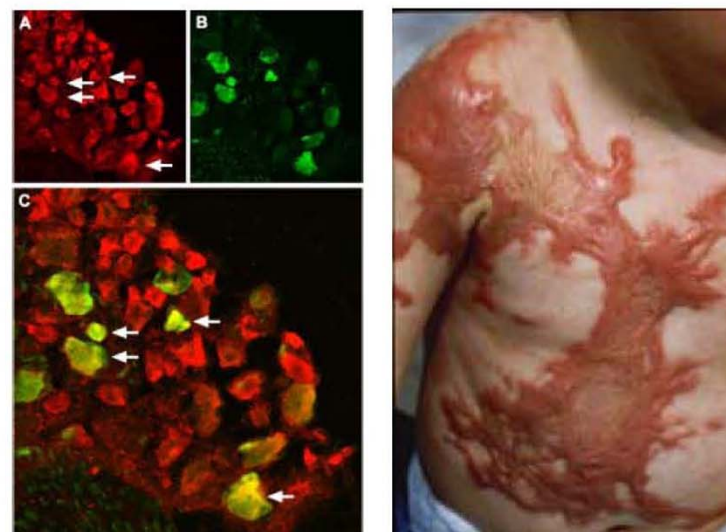
Role of endogenous agonist of TRPV1 in burn pain

PI: Laura McGhee

Org: US Army Institute of Surgical Research

Problem, Hypothesis and Military Relevance

- Problem: Management of acute pain after burn injury to prevent development of chronic pain
- Hypothesis: Burned skin releases oxidized linoleic acid metabolites (OLAMs) that function as endogenous TRPV1 agonist. Potential analgesics may be developed from compounds that block OLAM synthesis or action.
- Military Relevance: Since the beginning of OIF/OEF, the US Army Institute of Surgical Research has cared for over 800 soldiers injured in the conflict. Their pain management is often complex and difficult. Often the soldiers are on large amounts of opioids to manage their pain and still report high levels of pain.



Proposed Solution

- Specific Aim 1: Evaluate the analgesic efficacy of NDGA and anti-OLAM antibodies in a rat model of burn pain. This injury produces a third degree burn with thermal hyperalgesia that is still significant at 14 days after injury. The pharmacological studies will evaluate 3 P450 inhibitors and 3 combinations of anti-OLAM antibodies as compared to vehicle controls.
- Specific Aim 2: Evaluate the correlation between clinical scar tissue levels of OLAMs and patient reports of pain intensity using a 100mm VAS. Discarded burn tissue will be collected from the USAISR during OR procedures. The tissue will be assayed for OLAMs using immunoassay methods. Pain levels will be correlated to OLAM levels.

Timeline and Cost

Activities	FY	10	11	12
Evaluate the analgesic efficacy of OLAM synthesis inhibitors				
Evaluate the analgesic efficacy of anti-OLAM antibodies				
Collect scar tissue and assay for OLAM levels. Correlate OLAM levels and pain levels				
Estimated Budget (\$K)		250K	250K	250K

Exploration of a novel persistent reversal of pathological pain: mechanisms and mediators

Rehabilitation: Acute and Chronic Pain Management

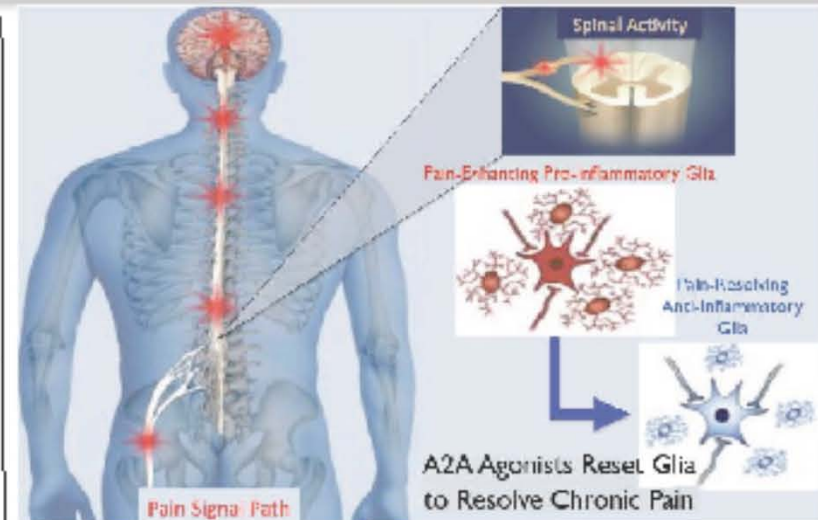
PI: Watkins, Linda R.

Org: University of Colorado at Boulder



Problem, Hypothesis and Military Relevance

- Due to the physical nature of their work, military personnel often suffer from nerve injury leading to chronic pain.
- Chronic pain is poorly managed by currently available therapeutics, which target neurons of the pain pathway.
- We believe that glial cells, immune-like cells in the spinal cord, are the true mediators of chronic pain.
- We have discovered a novel non-opioid, non-addictive therapeutic (Adenosine 2A [A_{2A}] agonists) which targets glia.
- A_{2A} agonists resolved pathological pain in an animal model for 4+ weeks after a single intrathecal injection, an unprecedented result of great promise.
- **Hypothesis:** Shifting spinal cord glia to a pain-resolving anti-inflammatory state using A_{2A} agonists could resolve chronic pain.



Proposed Solution

- The proposed project explores basic science issues, ranging from behavioral studies to characterize the phenomenon to mechanistic studies to understand the unprecedented, enduring pain resolution induced by intrathecal A_{2A} agonists.
- Aim I tests A_{2A} agonist utility for: (a) treating long-standing neuropathic pain (chronic constriction injury; CCI), (b) treating neuropathic pain in other DoD relevant models (Chung, spinal cord injury), & (c) providing continuing pain resolution with repeated dosing over time (CCI).
- Aim II explores mechanisms underlying A_{2A} resolution of CCI-induced neuropathic pain by testing if pain resolution: (a) is due to A_{2A} -induced IL-10, (b) acts via protein kinase A or C, (c) acts by resetting glia into an alternatively activated state, or (d) is unique to the A_{2A} adenosine receptor subtype.

Timeline and Direct Cost

Activities	FY	10	11	12
Characterization Studies (Specific Aims IA, IB, & IC): efficacy if chronic pain; generalization to other pathological pain models of DoD relevance; efficacy with repeated treatment;				
Mechanistic Studies (Specific Aims IIA, IIB): role of IL-10 early & late; intracellular signaling pathways				
Mechanistic Studies (Specific Aims IIC, IID): glial alternative activation; adenosine receptor subtypes				
Estimated Budget (\$K)		333.3	333.3	333.3

SENSORY SYSTEMS



Capability Gaps

- Inadequate treatment of traumatic injuries, war-related injuries, and diseases to ocular structures, and the visual, vestibular or hearing system(s)
- Prevention, treatment, and mitigation of sensory dysfunction associated with traumatic brain injury (TBI) and war-related injuries
- Inadequate vision restoration
- Inadequate hearing restoration
- Population-based studies, epidemiology
- Inadequate ocular diagnostics
- Inadequate prevention strategies
- Inadequate rehabilitation strategies



SENSORY SYSTEMS



Investment Highlights

- New start program area in 2010
- Focused on restoration and rehabilitation of traumatic injury
- Coordinating with the Vision and Hearing Centers of Excellence
- Vision
 - Corneal wound repair
 - Novel therapeutics, including regenerative medicine
 - Rehabilitation of TBI-related visual dysfunction
- Hearing and Balance
 - Hearing restoration
 - Treatment of tinnitus
 - Rehabilitation of balance disorders

Preserving Vision After Traumatic Brain Injury

Diagnosis and Treatment of Brain Injury; Polytrauma and Blast Injury/Treatment of Sensory System
Traumatic Injury (Vision, Hearing, and Balance)

PI: Johnny Tang, M.D.

Org: University Hospitals Case Medical Center



Problem, Hypothesis and Military Relevance

- Traumatic brain injury (TBI) in military and civilian situations commonly results in significant vision loss or dysfunction, and this abnormality remains unexplained and untreatable.
- Our goal is to develop an animal model that reproduces the effects of TBI from munitions and improvised explosive devices (IEDs) and to develop therapies to inhibit damage from TBI.
- This work responds to needs in the FY10 DMRDP program, with particular focus on diagnosis and treatment of traumatic brain injury, and polytrauma and blast injury.

1. TBI injury causes visual dysfunction by 2 means:
animal studies of how and where defects arise



2. Development of therapies to inhibit TBI-induced visual dysfunction:
PARP inhibitor
iNOS inhibitor
local hypothermia

Proposed Solution

- We will create an animal model of TBI secondary to shockwave and blunt trauma to (1) investigate and characterize the functional and structural abnormalities that develop in the visual axis, (2) investigate where in the visual system the trauma-induced defects develop using a new and advanced functional imaging method (manganese-enhanced magnetic resonance imaging (MEMRI)), and (3) treat TBI pharmacologically using inhibitors of poly(ADP-ribose) polymerase (PARP), inducible isoform of nitric oxide synthase (iNOS), and local hypothermia.
- We have significant preliminary data that indicates the imminent feasibility in our plan.

Timeline and Direct Cost

Activities	FY	10	11	12
Development and Characterization of an animal model of TBI using fluidic percussion and shockwave injury.				
Identification of pathways/mechanisms using biochemical, electrophysiology and advanced neuroimaging studies.				
Development of treatment modalities for TBI/TON.				
Estimated Budget (\$K)		\$240	\$250	\$260



DMRDP

Photoreceptor loss stimulates retinal plasticity that causes visual dysfunction.

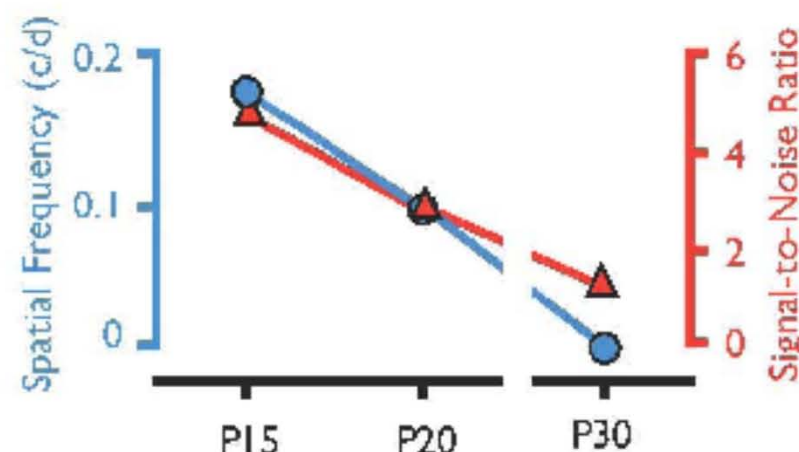
Polytrauma and Blast Injury: Treatment of Sensory System Traumatic Injury (Vision, Hearing, and Balance)

PI: Dr. Glen Prusky

Org: Weill Cornell/ Burke Medical Research Institute

Problem, Hypothesis and Military Relevance

Retinal damage, including photoreceptor degeneration, is a common consequence of military action. Accumulating evidence suggests that such damage stimulates retinal plasticity that leads to maladaptive reorganization of surviving retinal circuits. Blocking such maladaptive changes would provide a novel target to maintain visual function following retinal damage, and reversing maladaptive retinal physiology could be an important route to stimulate recovery of visual function. Understanding the causal relationship between photoreceptor integrity, retinal physiology and visual function is the first step in identifying and targeting these processes. We hypothesize that the successful treatment of visual dysfunction resulting from retinal damage will depend ultimately on retinal interventions that stimulate or maintain retinal output that normally functions to maintain visual 'signals' above physiological 'noise'. To this end, we will investigate a causal role for retinal output in predicting visual function by quantifying visual behavior, photoreceptor integrity, and retinal ganglion cell (RGC) output, in animal models in which loss of visual function (experimental 'necessity'), and preservation of visual function (experimental 'sufficiency'), are independently assessed.



Proposed Solution

First, the spatial frequency threshold and contrast sensitivity of optokinetic tracking will be assessed in a given animal (~30 minutes). Animals will then be anesthetized and the physiological output of the retina will be evaluated with *in vivo* extracellular recordings of single RGCs - the output cells of the retina. Following this, the retina from one eye will be removed for slice electrophysiological assessment of synaptic components. Finally, the other eye will be excised and prepared for anatomical assessment. The results from each of these stages will be collated and group differences between degenerating animals, and non-degenerating, age-matched control animals will be quantified.

Timeline and Direct Cost

Activities	10	11	12
Salaries, maintenance of equipment, animal costs, "necessity" experiments	\$300,000		
Salaries, maintenance of equipment, animal costs, "sufficiency" experiments		\$300,000	
Salaries, maintenance of equipment, animal costs, anatomical experiments		\$300,000	
Estimated Budget (\$K)	300,000	300,000	300,000

Restoring vision after optic nerve injury

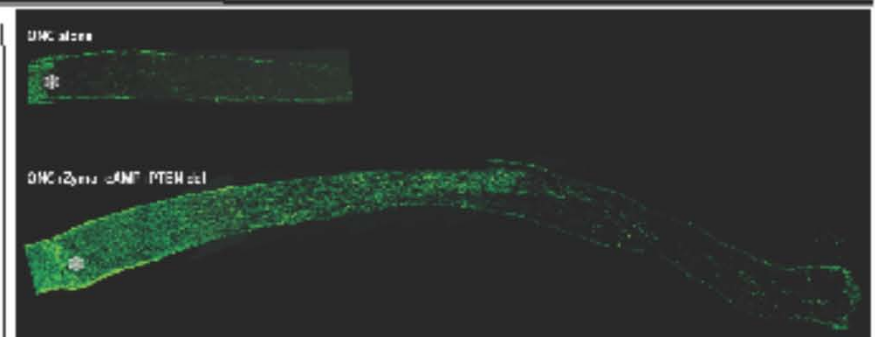
Polytrauma and Blast Injury: Treatment of Sensory System Traumatic Injury (Vision, Hearing, and Balance)

PI: Larry Benowitz, PhD Org: Children's Hospital Boston and Harvard Medical School



Problem, Hypothesis and Military Relevance

- The optic nerve does not regenerate if injured, leaving victims of traumatic nerve damage with lifelong losses in vision
- Regenerative failure is associated with the death of projection neurons (retinal ganglion cells, RGCs), an inability of RGCs to extend axons, and inhibitory signals in the extracellular environment
- Research is aimed at protecting RGCs from death, enabling these cells to regenerate axons to their central target areas, and restoring vision.
- Research addresses the Project and Task of Blast Injury and Protection/Restoration of sensory functions. May also be applicable to other instances of CNS injury, such as TBI.



Longitudinal sections through mouse optic nerves 2 weeks after optic nerve crush (injury site shown with asterisks on left). Regenerating fibers are visualized with antibodies to GAP-43. *Top*: Untreated mouse shows no regeneration. *Bottom*: Mouse treated with intraocular Zymosan, elevation of cyclic AMP, and deletion of the PTEN gene shows extensive regeneration.

Proposed Solution

- Investigate the mechanisms that underlie RGC death after nerve damage
- Develop strategies to promote RGC survival
- Continue developing strategies to enable RGCs to regenerate axons to their central target areas
- Combine the above approaches to maximize optic nerve regeneration
- Determine whether optic nerve regeneration restores visual functioning.

Timeline and Direct Cost

Activities	10	11	12
Identify causes of RGC death after axotomy,. Develop strategies to prevent cell death.			
Investigate combinatorial treatments to maximize RGC survival and promote axon regeneration.			
Investigate above treatments result in functional recovery. Write paper(s).			
Estimated Budget (\$K)	204,011	206,536	209,137

Rehabilitation of Visual and Perceptual Dysfunction after Severe Traumatic Brain Injury

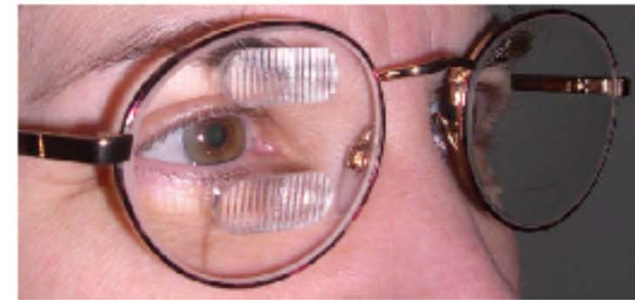


PI: Eliezer Peli

Org: Schepens Eye Research Institute, Harvard Med. School

Problem, Hypothesis and Military Relevance

- **Problem:** Severe TBI causes homonymous hemianopia and spatial neglect which impair detection of obstacles on the affected side, resulting in unsafe walking and driving. Peripheral prism (p-prism) glasses, an optical treatment we have developed, has shown great promise for hemianopia. Objects from the blind side appear to be on the seeing side, which can be helpful, but can also be confusing.
- **Hypothesis:** Perceptual-motor training will facilitate adaptation and correct perceived direction of obstacles when using p-prism glasses, resulting in improved mobility.
- **Military Relevance:** We address the Vision component of the *Restoration and Rehabilitation of Sensory System Traumatic* task in the *Rehabilitation* project.



Peripheral prism (p-prism) glasses on right spectacle lens of a right hemianope. The glasses provide visual field expansion (up to 30°) on the blind side, which is helpful for obstacle avoidance when walking

Proposed Solution

- Extend our research to determine whether p-prism glasses improve function in TBI patients with neglect;
- Evaluate whether perceptual-motor training aids perceived direction adaptation when using p-prism glasses in TBI patients with hemianopia with and without neglect;
- Evaluate whether the training transfers and improves performance on other more "real world" tasks (collision judgments while walking in a virtual mall, and detections while driving in a simulator);
- Determine whether p-prism glasses are more effective than other treatments for hemianopia and neglect

Timeline and Cost

Activities	FY	10	11	12
Final development of the training tool and details of the training regimens		■		
Evaluations of improvements in function, direction adaptation and transfer to real-world tasks		■	■	
Evaluate whether p-prism glasses are more effective than other treatments			■	■
Estimated Total Budget (\$K)		\$675K	\$601K	\$696K

Wearable Visual Aid as Treatment for TBI Associated Visual Dysfunction



Product Status: FY09 VRP Awarded 16 SEP 10

USAMRMC Portfolio: Vision

Principal Investigator: James Weiland, PhD

Capability / Product Description

- Develop a simultaneous localization and mapping (SLAM) algorithm for use in multiple object detection and identification to assist in ambulation and navigation.
- Develop neurally inspired attention algorithms that detect important objects in an environment to assist in search tasks.
- Develop an algorithm for determining the gist of the user's environment to assist in the selection of the most suitable task-specific algorithmic aid.
- Implement a prototype wide-field, wide-dynamic-range camera for image capture and integrate it into a wearable system with a patient cueing interface, and test the portable system on visually impaired volunteers in real-world situations.

Clinical Development & Acquisition Phases

- Currently at TRL 4

Development Organizations

- University of Southern California

Benefits / ROI

This project addresses important issues of algorithm development and hardware implementation that have both specific and broad impact (i.e., individuals suffering from vision loss)

The completion of the study has a reasonable likelihood of leading to important advances and impacting patient care in the short term.

Key Risk(s) / Mitigation Strategy

- Possible lack of commercial interest

Funding

	FY09	FY10	FY11	FY12	FY13	FY14	FY15	FY16	FY17
Funded	\$1,997,191								
UFR									

2011 MHS Conference

Visual Information Restoration and Rehabilitation via Sensory Substitution Technology

PI: Dr. Aimee Arnoldussen

Org: Wicab, Inc.



Problem, Hypothesis and Military Relevance

- **Problem:** There is a need for new technologies for blinded service men and women that enhance safety, mobility and independence
- **Hypothesis:** The BrainPort vision device will improve activities of daily living, quality of life and rehabilitation for the blind
- **Military Relevance:** The BrainPort vision device is the only new technology likely available in the near term to address safety and mobility issues resulting from blinding injuries sustained in recent military conflicts. The military has historically been the leader in developing prosthetic devices.

Proposed Solution

- The BrainPort vision device is a visual prosthetic that enables perception of visual information using the tongue and camera system as a paired substitute for the eye
- Visual information is collected from a video camera and translated into gentle electrical stimulation patterns on the surface of the tongue
- With training users perceive shape, size, location and motion of objects in their environment
- The BrainPort vision device is immediately available for evaluation by wounded warriors and veterans

HOW THE DEVICE WORKS



Timeline and Cost

Activities	FY	10	11	12
BrainPort iterative user testing		■	■	■
Software enhancement development		■		
Implementing hardware and software improvements		■	■	■
Estimated Budget (\$2,241K)		748K	745K	748K

SUMMARY



- CRMRP is DoD's research program focused on resetting wounded warriors
- Collaboratively working with other government agencies
- Activities underway to develop the 10-year plan for prosthetics
- Leveraging of Congressional funding has significantly advanced the programs, especially prosthetics and rehabilitative medicine
- CRMRP is managing challenges; although policy drivers may be needed to realize full potential of these technologies

CRMRP POINTS OF CONTACT



COL Janet Harris

Director
301-619-8836
janet.harris@us.army.mil

MAJ Regina Davey

Interim Deputy Director
301-619-7255
regina.davey@us.army.mil

Dr. Brian Pfister

Strategic Portfolio Manager, Regenerative Medicine
301-619-8836
Brian.pfister@us.army.mil

Dr. Dettrick Stith

Strategic Portfolio Manager, Neuromusculoskeletal
Rehabilitation
301-619-9811
Dettrick.stith@us.army.mil

Dr. Tony Gover

Strategic Portfolio Manager, Pain Management
Strategic Portfolio Manager, Vision Restoration
301-619-9560
Tony.d.gover@us.army.mil

Mr. Joel Glover

Strategic Portfolio Manager, Hearing Restoration and
Rehabilitation
301-619-8836
Joel.glover@us.army.mil

Ms. Nancy Lingman

Strategic Portfolio Manager, Cognitive Rehabilitation
301-619-9430
Nancy.lingman@us.army.mil

Mr. Christian Walker

Commercialization Manager
301-619-8932
Christian.walker@us.army.mil

LEST WE FORGET WHY WE ARE HERE

