

CONGRESSIONALLY DIRECTED
MEDICAL RESEARCH PROGRAMS:
PARTNERING FOR A CURE

VI. Peer Reviewed Medical Research Program





Vision

Find and fund the best medical research to protect and support the warfighter and their beneficiaries and to eradicate diseases that impact these populations.

Mission

Provide support for military health-related research of clear scientific merit.



In their efforts to protect our country, members of the military are subjected to a variety of diseases and injuries that are not commonly encountered by civilians. Research sponsored by the Peer Reviewed Medical Research Program (PRMRP) aims to preserve the health of our military forces by targeting these and other conditions of high military relevance including:

- ❖ Hearing loss due to the extremely loud noises generated by military equipment and explosives;
- ❖ Musculoskeletal trauma experienced in times of war and during training exercises;
- ❖ Exposure to deadly infectious diseases such as malaria, leptospirosis, leishmania, and hepatitis while deployed in developing countries; and
- ❖ Acute lung injury and respiratory complications in members of the military who operate armored vehicles due to intermittent, high-level exposures to toxic gases (e.g., carbon monoxide, sulfur dioxide, ammonia, and nitrogen oxides) from engine exhaust and the firing of weapons.





Program Background

The Department of Defense (DOD) PRMRP was established in fiscal year 1999 (FY99) by Appropriations Conference Committee Report No. 105-746, which provided \$19.5 million (M) to DOD to establish a medical research program that focused on issues pertinent to U.S. military forces. Congress directed the Deputy Secretary of Defense to work with the Surgeons General of the Services to establish a program to select medical research projects of clear scientific merit and direct relevance to military health. The U.S. Army Medical Research and Materiel Command (USAMRMC) became the Executive Agent for this new program through Joint Services coordination and the specific recommendation of the Armed Services Biomedical Research Evaluation and Management (ASBREM) Committee. The USAMRMC instituted the plan recommended by the ASBREM Committee. From FY99 through FY06, Congress appropriated a total of \$344.5M through the PRMRP to fund peer-reviewed research focused on military health (see Figure VI-1 – PRMRP History). A total of 196 awards have been made through FY05 that already have yielded products and technologies aimed at enhancing the health and readiness of service personnel and their families.

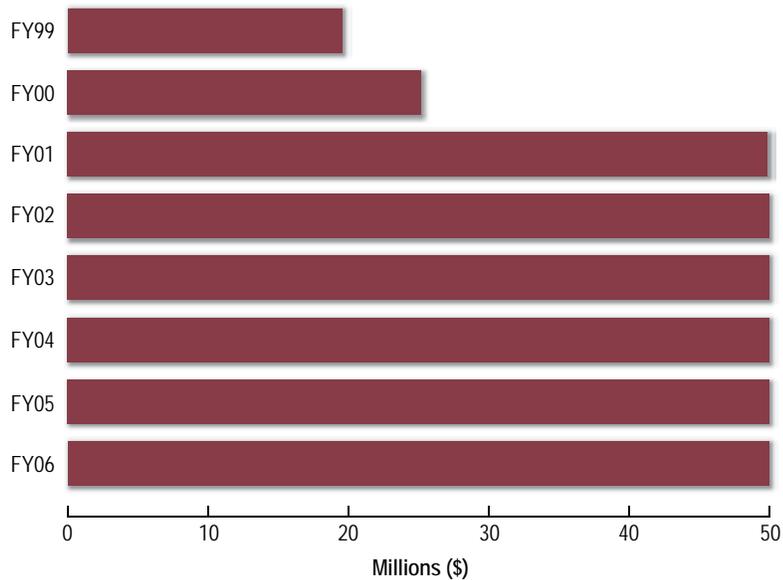


Figure VI-1. PRMRP History

The Program Today

Fiscal Year 2005 Summary

Congress appropriated \$50M to continue the PRMRP in FY05. The PRMRP requested proposals in four award mechanisms spanning 23 topic areas: 21 recommended by Congress (Conference Committee Report No. 108-622, pp. 365–366) and 2 additional topic areas with high military relevance added by the Office of the

Assistant Secretary of Defense (Health Affairs) (OASD[HA]). A total of 492 proposals were received across topic areas, and 40 awards were made. Table VI-1 provides a summary of the FY05 PRMRP topic areas in terms of proposals received, number of awards, and dollars invested.

Table VI-1. Funding Summary for the FY05 PRMRP

Topic Areas	Proposals Received	Awards	Investment
Acellular Human Tissue Matrix Research	6	1	\$999,744
Alcoholism Research	23	2	\$1,539,498
Amyotrophic Lateral Sclerosis	28	2	\$1,979,313
Anti-radiation Drug Development	15	2	\$1,656,841
Autism	35	0	0
Autoimmune Diseases such as Scleroderma and Sjögren's Syndrome	29	1	\$1,003,600
Blood-related Cancer Research	29	2	\$2,563,046
Childhood Asthma	5	1	\$1,000,000
Chronic Pain Research	19	1	\$1,008,426
Conjugate Vaccines to Prevent Shigellosis	2	1	\$1,003,866
Diabetes Research	34	1	\$987,156
Duchenne's Disease Research	2	0	0
Epilepsy Research	8	0	0
Interstitial Dystitis	6	1	\$987,145
Lung Cancer Screening*	4	1	\$994,087
Lupus and Lupus-biomarker Research	29	2	\$2,273,452
Military Relevant Disease Management*	72	9	\$12,510,223
Orthopaedic Extremity Trauma Research	45	5	\$6,786,666
Osteoporosis and Bone-related Diseases Research	60	4	\$3,569,671
Paget's Disease	2	0	0
Post-traumatic Stress Disorder	33	3	\$3,006,343
Social Work Research	4	1	\$1,010,021
Volume Angio CAT (VAC) Research	2	0	0
TOTAL	492	40	\$44,879,098

Fiscal Year
2005
 492 Proposals Received
 \$50M in Appropriations
 40 Awards

* Topic area added by the OASD(HA)

VI-5



A Sampling of FY05 PRMRP-funded Projects

Combat Casualty Care

- ❖ Bisphosphonate-Ciprofloxacin Carried by or Tethered to Micron or Nanosized Hydroxyapatite Particles as a Prototype for Local Antibiotic Delivery to Injured Bone (Thomas Buxton, Investigator-Initiated Award)
- ❖ The Role of the Pseudopterosins and Their Analogs in Wound Healing (Raymond Little, Program Project Award)
- ❖ Development of Osseointegrated Implants for Soldier Amputees Following Orthopaedic Extremity Trauma (Roy Bloebaum, Advanced Technology Award)

Military Operational Medicine

- ❖ Efficacy of Adjunct Sleep Interventions for PTSD (EASI-PTSD) (Anne Germain, Investigator-Initiated Award)
- ❖ Biomarkers for Amyotrophic Lateral Sclerosis in Active Duty Military—BALSAM (David Millhorn, Investigator-Initiated Award)
- ❖ Family Maltreatment, Substance Problems, and Suicidality: Randomized Prevention Effectiveness Trial (Richard Heyman, Investigator-Initiated Award)

Infectious Disease

- ❖ Effect of Morphine and Trauma on *Acinetobacter baumannii* Infection in a Murine Model (Toby Eisenstein, Investigator-Initiated Award)
- ❖ Molecular Identification of Human Fungal Pathogens (Brian Wickes, Investigator-Initiated Award)

Lung Research

- ❖ Integration of Anatomic and Pathogenetic Bases for Early Lung Cancer Diagnosis (Wei Qian, Investigator-Initiated Award)

Fiscal Year 2006 Summary

Congress appropriated \$50M to continue the PRMRP in FY06. The PRMRP requested proposals in 5 award mechanisms spanning 22 topic areas: 21 recommended by Congress (Conference Committee Report No. 108-622, pp. 365–366) and 1 additional topic area with high military relevance added by the OASD(HA). A total of 651 proposals were received across topic areas, as detailed in Table VI-2, and approximately 48 awards are anticipated.

Fiscal Year
2006
 651 Proposals Received
 \$50M in Appropriations
 ~48 Awards

Table VI-2. Topic Areas Offered and Proposals Received for the FY06 PRMRP

Topic Areas	Proposals Received
Advanced Proteomics	11
Alcoholism Research	21
Autism	12
Autoimmune Diseases such as Scleroderma and Sjögren's Syndrome	32
Blood-related Cancer Research	25
Childhood Asthma	5
Childhood Cancer Research	19
Chronic Pain and Fatigue Research	25
Diabetes Research	99
Duchenne's Disease Research	3
Eye and Vision Research	52
Fibromyalgia	3
Interstitial Cystitis Syndrome	4
Kidney Cancer Research	14
Lupus Research	16
Military Relevant Disease Management*	179
Osteoporosis and Bone-related Diseases Research	57
Paget's Disease	0
Polycystic Kidney Disease	17
Post-traumatic Stress Disorder	46
Pulmonary Hypertension	8
Social Work Research	3
TOTAL	651

* Topic area added by the OASD(HA)



As shown in Figure VI-2, FY06 PRMRP award mechanisms span basic and clinical military-relevant health research as well as the development of advanced technology. Appendix B, Table B-5, summarizes the directions from Congress for the PRMRP appropriations and the investment strategy executed by the PRMRP for FY05 through FY06.

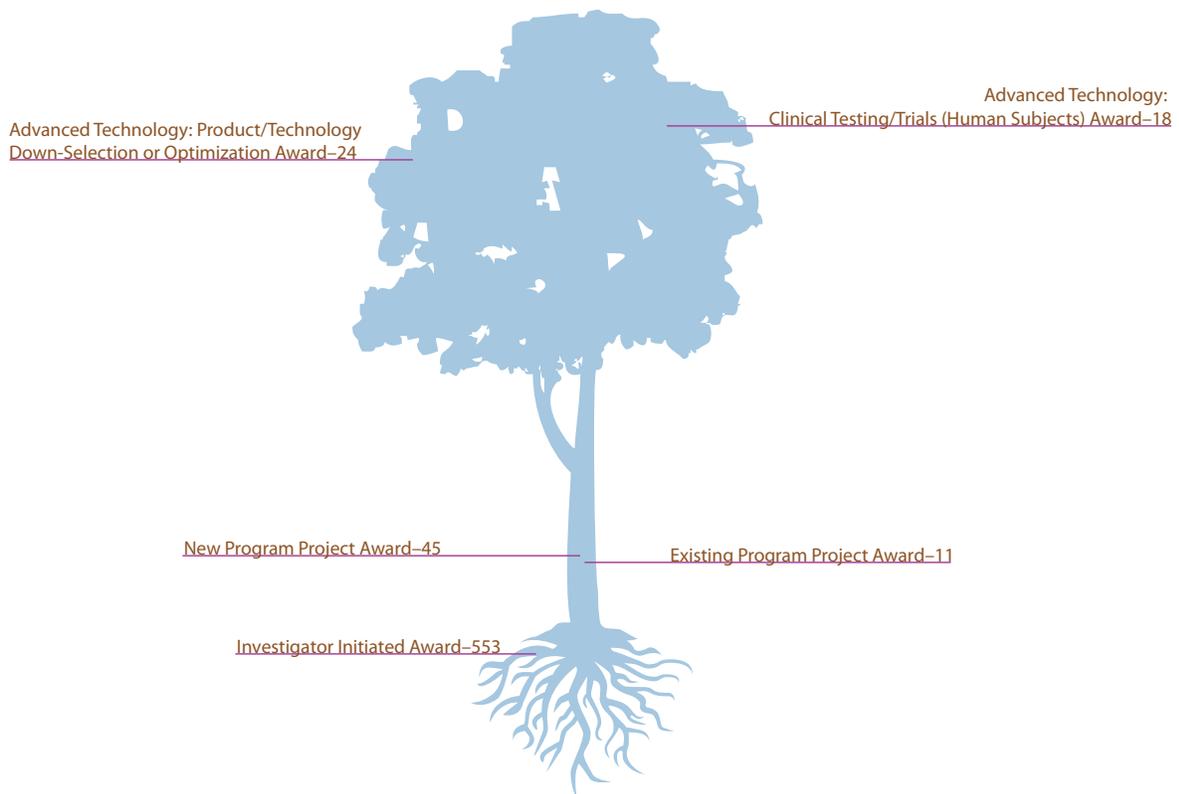


Figure VI-2. FY06 PRMRP Award Mechanisms

Joint Programmatic Review Panel

One aspect of the plan recommended by the ASBREM Committee required the formation of a Joint Programmatic Review Panel (JPRP) to determine programmatic priorities. The PRMRP JPRP is composed of representatives from the four military services, OASD(HA), and the Departments of Health and Human Services and Veterans Affairs. The JPRP provides programmatic and strategic direction for the PRMRP and serves as a recommending body to the USAMRMC Commanding General on final funding decisions.

FY06 JPRP Members

U.S. AIR FORCE REPRESENTATIVES

Hendrick Ruck, Ph.D. (JPRP Chair), Director, Human Effectiveness Directorate, Air Force Research Laboratory

Colonel James Riddle, D.V.M., M.P.H. (JPRP Alternate Chair), Chief, Biosciences and Protection, Human Effectiveness Directorate, Air Force Research Laboratory

Lieutenant Colonel Debra Malone, M.D., Chief, Formulation Branch, Modernization Directorate, Headquarters, U.S. Air Force Division of Science and Technology

Lieutenant Colonel Donnamarie Jones, R.Ph., Pharm.D., Chief, Biomedical Research and Compliance, Office of the Surgeon General

Major David G. Watson, Ph.D., Flight Commander, Laboratory Services

U.S. NAVY REPRESENTATIVES

Captain Doug Forcino, Ph.D., Program Director, Office of Naval Research

Captain Richard Haberberger, Ph.D., Executive Officer, Naval Medical Research Center

Captain David Neri, Ph.D., Deputy Director, Medical Research and Development, Navy Bureau of Medicine and Surgery

U.S. ARMY REPRESENTATIVES

Colonel James Lamiell, M.D., Chief, Clinical Investigation Regulatory Office, Army Medical Department Center and School

Colonel Bruno Petruccelli, M.D., M.P.H., Director, Epidemiology and Disease Surveillance, U.S. Army Center for Health Promotion and Preventive Medicine

Colonel Richard Schaefer, M.D., M.P.H., Associate Professor and Chief, Department of Surgery, Orthopaedic Surgery Service

U.S. MARINE CORPS REPRESENTATIVE

Lieutenant Commander Carl Manemeit, M.A., Expeditionary Medicine Project Officer, Marine Corps Warfighting Laboratory

DEPARTMENT OF HEALTH AND HUMAN SERVICES REPRESENTATIVE

Captain Patrick McNeilly, Ph.D., Administrative Officer, Department of Health and Human Services; Public Health Advisor, Office of Human Research Protections, Office of the Secretary, U.S. Public Health Service

DEPARTMENT OF VETERANS AFFAIRS REPRESENTATIVE

Brenda Cuccherini, Ph.D., Program Specialist, Office of Research and Development

OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE (HEALTH AFFAIRS) REPRESENTATIVES

Salvatore Cirone, D.V.M., M.P.V.M., Program Director, Health Science Policy

John Lucas, Sc.D., Senior Program Management Office



Military Health Research Forum

The PRMRP held its second biannual Military Health Research Forum May 1–4, 2006 in San Juan, Puerto Rico. The forum provided a means for investigators funded by the program to present their research findings, products, and technologies and develop future collaborations related to military health research. The forum was organized around five general research areas including Combat Casualty Care, Infectious Diseases, Military Operational Medicine, Wellness and Fitness, and Technology Development. A feature of the program was an interactive Technology Showcase where 13 products and technology developed and supported by PRMRP researchers were exhibited.

One of the highlights of this interactive session was a technology demonstration of a noninvasive sensor system to assess tissue perfusion and guide resuscitation.



Developing Products and Technology

Many projects funded by the PRMRP have begun to yield combat health support technologies and products in the areas of combat casualty care, military infectious diseases, military operational medicine, chronic disease management, and medical chemical and biological defense. Some of the therapeutic agents, devices, and procedures that have improved the overall readiness and well-being of military service personnel (at least in part) through funding by the PRMRP follow on the next two pages and are highlighted in Figure VI-3 – Notable PRMRP-supported Products.



HENDRICK RUCK, PH.D., FY06 JPRP CHAIR

"The Peer Reviewed Medical Research Program provides an exciting opportunity to support Department of Defense efforts to advance science and technology aimed at helping those people who really keep America safe."



COLONEL BRUNO PETRUCCELLI, M.D., M.P.H., FY06 JPRP MEMBER

"It is a great honor and source of gratification for me to take part in a process that directs resources from the public trust toward the kind of research that holds the most promise for the health and safety of troops, veterans, their families, and ultimately all of humanity."



A NEW CLASS OF NON- STEROIDAL ANTI- INFLAMMATORY DRUGS FOR THE TREATMENT/PREVENTION OF CHRONIC PAIN



With support from an FY04 Advanced Technology Award, Dr. Lenard Lichtenberger at the University of Texas Health Science Center–Houston is investigating the utility of a new class of nonsteroidal anti-inflammatory drugs (NSAIDs), which are coupled with phosphatidylcholine (PC), in the treatment and/or prevention of chronic neuropathic pain in people with spinal cord injury. Preliminary results in rodent model systems show that PC-NSAIDs have lower gastrointestinal toxicity and more enhanced therapeutic effectiveness than the parent NSAID in inhibiting fever, inflammation, and pain. Positive results in these preclinical studies should hasten the development of PC-NSAID formulations for parenteral and enteral use in patients suffering from chronic pain. It is intended that the research performed during this project will result in better treatment for military personnel immediately following battle and/or accidents to help prevent early inflammatory processes that lead to painful central nervous system injury.

SELF-OPERATED DEVICE TO TREAT PSEUDOFOLLICULITIS BARBAE

FY03 Advanced Technology Award recipient Dr. James Childs from Palomar Medical Technologies, Inc., is developing a self-operated, portable, low irradiance Pseudofolliculitis Barbae treatment device without physician supervision. The condition is marked by inflammation on the beard area that can compromise the ability to wear close-fitting, protective facial gear. Current protocols are in clinical trials at the Naval Medical Center in San Diego using a larger, physician-operated system. Further trials are planned with the Navy and Army for smaller units using self-treatment parameters. If successful, this device would not only be a great benefit to military service personnel but to the general public as well.



ELECTROPORATION-FACILITATED GENE THERAPY FOR WOUND HEALING



With funding from an FY02 Investigator-Initiated Research Award, Dr. John Harmon of Johns Hopkins University is using electroporation, in which an electric field passed through tissue opens small pores in cell membranes, to deliver DNA molecules into cells successfully. Dr. Harmon is using mouse models to study the effect of delivering the gene for keratinocyte growth factor (KGF) by electroporation. The technique improved the speed of closure in slow-healing wounds produced experimentally in mice. An additional benefit of this technique may be the treatment of slow wound healing in diabetics as observed in diabetic mice having KGF delivered into wounds by electroporation.

PORTABLE SENSOR SYSTEM TO MEASURE TISSUE PERFUSION



FY02 Investigator-Initiated Research Award recipient Dr. Babs Soller at the University of Massachusetts, in collaboration with the Luxtex Corporation and Nimbis Medical, is developing and testing a prototype, portable sensor system based on near infrared spectroscopy to noninvasively measure tissue perfusion. This system quickly and accurately measures muscle pH, muscle oxygen tension, and hematocrit from light reflected from the forearm muscle and will guide combat medical personnel in resuscitation care. The prototype devices are currently in ongoing clinical trials at the University of Massachusetts Memorial Medical Center and have been delivered to the USAMRMC's Core Combat Casualty Care Research Program for further field testing and evaluation.

SUPPLEMENT THAT PREVENTS TRAVELER'S DIARRHEA



With support from an FY03 New Program Project Award, CAPT Stephen J. Savarino at the Naval Medical Research Center, in collaboration with Johns Hopkins University and ImmuCell Corporation, is developing an anti-diarrheal supplement against travelers' diarrhea made from bovine milk immunoglobulins (BlgG). Enterotoxigenic *Escherichia coli* (ETEC) is the predominant cause of travelers' diarrhea in military and civilians alike. The breakthrough that paved the way for this research was the discovery by CAPT Savarino's group of a conserved group of proteins (called adhesins) that are required for ETEC to cause disease. In purified form, these proteins were used to generate anti-adhesin milk IgG by cow immunization. Diarrhea is a significant health threat for travelers to developing countries. Incidence rates as high as 50 percent occur where food and water sanitation is poor. The military requirement for solutions in this area is becoming more acute. Since the inception of the war on terrorism, the global commitment of U.S. fighting forces has been concentrated increasingly in developing areas of the world. Rehydration and antibiotic treatment are the cornerstones of disease management, but even with early institution of appropriate therapy, diarrheal diseases exact a cost in terms of lost duty and effectiveness. There is no licensed drug or biologic that provides a safe, effective mode of prevention, leaving an important deficiency in military and travel medicine. This investigational treatment has shown proof of principle as a safe, food-based anti-diarrheal supplement. In 2006, the first of two clinical trials was completed under this project, showing that anti-adhesin BlgG antibodies afford significant protection against ETEC. Three additional clinical trials to be conducted during 2007–2008 are expected to solidify the foundation for further development of a multivalent BlgG product suitable for field testing.



2001



Field-deployable ultrasensitive portable immunoassay system for detection of biological toxins (Jeffrey Mason, Ph.D., Armed Forces Institute of Pathology)

Spherical robot for combat casualty care. Mini-robot design for military telesurgery in the battlefield: Breaking the size barrier for surgical manipulators (Blake Hannaford, Ph.D., University of Washington)

2002



Blood processing system for forward medical treatment facilities (Thomas Robinson, Ph.D., Mission Medical)



Noninvasive sensor system to determine tissue perfusion and guide resuscitation (Babs Soller, Ph.D., University of Massachusetts Medical School)



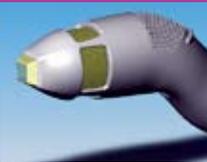
Temporary, implantable sensor biochip for monitoring lactate and glucose during hemorrhage (Anthony Guiseppi-Elie, Ph.D., formerly of Virginia Commonwealth University)



Telemedicine-based ultrasound for detecting heart disease in newborns at remote military health care facilities (David Sahn, M.D., Oregon Health & Science University)



Figure VI-3. Notable PRMRP-supported Products

		2003		2004		
						
<p>Development of an orthopaedic nail to prevent bone infections (Irving Shapiro, Ph.D., Thomas Jefferson University)</p>		<p>Portable light-based self-treatment for Pseudofolliculitis Barbae (James Childs, Ph.D., Palomar Inc.)</p>	<p>Development of a bovine milk immunoglobulin supplement that prevents traveler's diarrhea (CAPT Stephen Savarino, M.D., M.Ph., Naval Medical Research Center)</p>	<p>Development of safe, simple, and rapidly produced vaccines against malaria using a DNA-based technology (CAPT Thomas Richie, M.D., Ph.D., Naval Medical Research Center)</p>	<p>A hybrid neuroprosthesis for mobility after paralysis from spinal cord injury (Ronald Triolo, Ph.D., Case Western Reserve University)</p>	<p>Nucleic acid testing device for use at battalion aid stations (Tom Peterson, IQuum, Inc.)</p>



Bottom Line

Since 1999, the PRMRP has been responsible for managing \$344.5M in congressional appropriations. The program has supported 196 exciting medical research projects in 60 military relevant topic areas through FY05 that have direct relevance to the health of members of the active duty military forces, retirees, and their beneficiaries.

