CDMRP

VI. Peer Reviewed Medical Research Program

ENHANCING THE HEALTH OF OUR MILITARY

Vision

Find and fund the best medical research to protect, support, and advance the health and welfare of warfighters and all beneficiaries.

Mission

Support military health-related research of clear scientific merit.

Hendrick Ruck, Ph.D.
Human Effectiveness Directorate
Air Force Research Laboratory
FY06 Joint Programmatic Review Panel Chair

"It is an honor and a privilege to continue to lead the programmatic review of this program. Through careful scientific review, understanding of congressional intent, and addressing warfighter medical needs, the program is a shining example of dual-use science and technology development."

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 conditions of high military relevance in areas such as:

- **Military Operational Medicine:** Strategies to enhance our military's performance in operational and training environments
- **Combat Casualty Care:** Strategies to reduce head, spinal cord, and lung injuries; hemorrhage; musculoskeletal trauma; and other injuries experienced on the battlefield
- **Infectious Diseases:** Research to prevent, diagnose, and treat deadly infectious diseases such as malaria, leptospirosis, leishmaniasis, and hepatitis
- **Medical Biological and Chemical Defense:** Efforts to preserve combat effectiveness in response to biological and chemical warfare

 Enhancing the Health of Our Military

Program Background

The Department of Defense PRMRP was established in fiscal year 1999 (FY99) by Appropriations Conference Committee Report No. 105-746, which provided $19.5 million (M) 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 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 and approved by the Office of the Assistant Secretary of Defense (Health Affairs) (OASD[HA]). 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 Funding History). A total of 247 awards have been made through FY06 that already have yielded products and technologies aimed at enhancing the health and well-being of service personnel and their families.

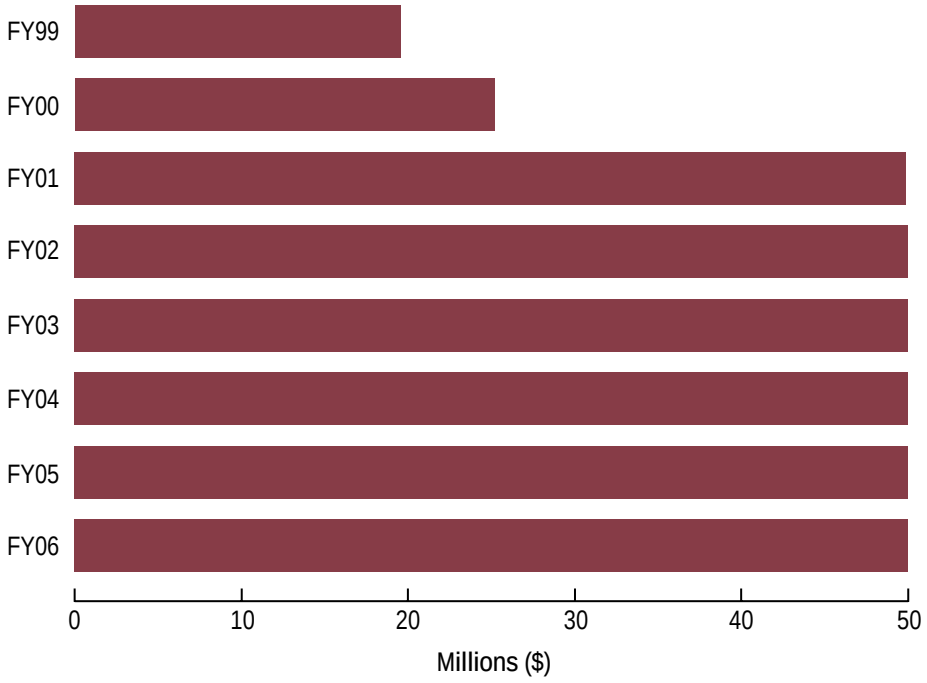

Figure VI-1. PRMRP Funding History

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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 PRMRP 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, Air Force 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, Army 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

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The Program Today

Fiscal Year 2006 Summary

A congressional appropriation of $50M was made 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 multiple focus areas added by the Office of the OASD[HA]. A total of 651 proposals was received across topic areas, and 51 awards were made as detailed in Table VI-1.

Although the PRMRP did not receive appropriations in FY07, the program continues to coordinate with other Department of Defense and Veterans Affairs agencies and support previously funded researchers by monitoring the progress of innovative products and technologies and disseminating these advancements on the PRMRP website. A summary of the program's funding history from FY99–06 is depicted in Table VI-2.

Appendix B, Table B-5, outlines the directions from Congress for the PRMRP appropriations and the investment strategy executed by the PRMRP for FY06.

Fiscal Year 2006

651 Proposals Received

$50M in Appropriations

51 Awards

John P. Foreyt, Ph.D.
Baylor College of Medicine
FY01 Investigator-Initiated Award Recipient

"Our minimal intervention approach using the Internet allows for widespread delivery and dissemination of evidence-based weight management programs that require less personnel time compared to more traditional approaches. This type of minimal contact intervention may be especially beneficial for weight gain prevention, which is increasingly being recognized as an important intervention target. Weight gain prevention approaches, like the one supported by the PRMRP, may help alter the overweight and obesity epidemic increases in the U.S. population."

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Table VI-1. Funding Summary for the FY06 PRMRP

Topic Areas	Proposals Received	Awards	Investment
Advanced Proteomics	11	3	$2.7M
Alcoholism Research	21	2	$1.9M
Autism	12	1	$0.9M
Autoimmune Diseases such as Scleroderma and Sjögren's Syndrome	32	4	$3.7M
Blood-Related Cancer Research such as Leukemia, Lymphoma, and Multiple Myeloma	25	3	$2.4M
Childhood Asthma	5	0	N/A
Childhood Cancer Research	19	2	$1.6M
Chronic Pain and Fatigue Research	25	5	$3.8M
Diabetes Research	99	5	$4.6M
Duchenne's Disease Research	3	1	$0.8M
Eye and Vision Research	52	8	$7.5M
Fibromyalgia	3	1	$0.9M
Interstitial Cystitis Syndrome	4	0	N/A
Kidney Cancer Research	14	1	$0.9M
Lupus Research	16	3	$2.8M
Military Relevant Disease Management[a]	179	0	N/A
Osteoporosis and Bone-Related Diseases Research	57	4	$3.6M
Paget's Disease	0	0	N/A
Polycystic Kidney Disease	17	1	$0.9M
Post-Traumatic Stress Disorder	46	5	$3.7M
Pulmonary Hypertension	8	1	$0.9M
Social Work Research	3	1	$1.0M
Total	651	51	$44.6M

[a] Topic area added by the OASD(HA).

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Table VI-2. Funding Summary for the FY99–06 PRMRP

Topic Areas	Awards	Investment
Acellular Matrix Research for Military Orthopedic Trauma	2	$1.7M
Acute Lung Injury/Lung Research	8	$8.1M
Advanced Proteomics	3	$2.7M
Advanced Soft Tissue Modeling	2	$3.8M
Alcoholism/Alcohol Abuse Prevention Research	18	$15.7
Amyotrophic Lateral Sclerosis	5	$5.9M
Anti-Diarrhea Supplement	1	$3.7M
Anti-Radiation Drug Development	2	$1.7M
Army Nutrition	1	$0.6M
Arthropod-Transmitted Infectious Diseases	4	$4.4M
Autism	1	$0.9M
Autoimmune Diseases such as Scleroderma and Sjögren's Syndrome	5	$4.7M
Biological Hazard Detection System/Bio-Sensor Microchip	1	$0.4M
Blood-Related Cancer Research	7	$8.2M
Bone-Related Disease Research (including Osteoporosis)	12	$12.2M
Casualty Care Research Center	2	$1.6M
Cell Response to Anti-Cancer Agents	1	$1.5M
Chemical Weapons Treatment	1	$1.3M
Chemo-Preventative Approaches to Smoking-Related Illnesses	1	$1.3M
Childhood Asthma/Pediatric Asthma	9	$8.0M
Childhood Cancer	2	$1.6M
Chronic Pain Research	7	$6.6M
Closed-Loop Frozen Blood Processing Systems	1	$1.5M
Conjugate Vaccines to Prevent Shigellosis	1	$1.0M
Defense and Veterans Head Injury Program	2	$3.1M
Dengue Fever Vaccine	2	$1.5M
Diabetes Research	6	$5.6M
Digital Mammography Imaging	1	$1.7M
Duchenne's Disease	1	$0.8M
Epilepsy	2	$3.2M
Eye and Vision Research	8	$7.5M
Fibromyalgia	1	$0.9M
Geneware Rapid Vaccine Development	1	$0.4M
Gulf War Illnesses	5	$4.0M

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Table VI-2. Funding Summary for the FY99–06 PRMRP (cont.)

Topic Areas	Awards	Investment
Healthcare Information Protection	1	$0.9M
High-Risk Infectious Disease	3	$3.7M
Infectious Disease Tracking System	1	$2.5M
Interstitial Cystitis Research	2	$2.0M
Kidney Cancer	1	$0.9M
Laser Eye Injury/Eye Cancer Research and Treatment	3	$2.9M
Limb Loss and Paralysis Research	2	$3.2M
Low Vision Research	1	$3.0M
Lung Cancer Screening	2	$1.6M
Lupus and Lupus-Biomarker Research	5	$5.1M
Malaria Vaccine Initiative (SBRI)[a]	1	$2.0M
Medical Surgery Technology	1	$1.2M
Medications for Fungal and Bacterial Infections such as Fungi Free	1	$0.3M
Metabolically Engineered Tissue for Trauma Care	1	$0.3M
Military Nutrition Research	2	$2.2M
Military Relevant Disease Management	47	$75.3M
Molecular Biology for Cancer Research	3	$2.5M
Muscle Function Research	2	$3.4M
Neuroscience Research	1	$1.0M
Obesity-Related Disease Prevention (esp. for minorities)	1	$1.0M
Orthopaedic Extremity Trauma Research	5	$6.8M
Paget's Disease	1	$1.0M
Polycystic Kidney Disease	1	$0.9M
Post-Traumatic Stress Disorder	9	$7.7M
Preclinical and Clinical Activities of the Novonex/Ex-Rad Drugs	1	$1.6M
Pulmonary Hypertension	1	$0.9M
Radiation Protection	1	$0.9M
Real-Time Heart Rate Variability	1	$0.9M
Remote Emergency Medicine Ultrasound	1	$2.0M
Reserve Component Medical Training Program	1	$2.0M
Respiratory Research	1	$2.2M
Sleep Management	4	$5.5M
Smoking Cessation	6	$9.1M
Social Work Research	4	$5.0M
Traumatic Brain Injury	3	$6.4M
Total	247	$295.7M

[a] Seattle Biomedical Research Institute

A Sampling of FY06 PRMRP-Funded Projects

On the following pages are exciting accomplishments supported by the PRMRP in the areas of:

- Vaccine Development
- Drug Validation
- Internet-Based Technology
- Technology Development

Major David G. Watson, Ph.D.
FY06 JPRP Member

"The members of the Joint Programmatic Review Panel take great pride in their efforts to select the best mix of basic, applied, and translational research across five separate award mechanisms in 22 topic areas, which we believe will have the greatest impact on the health of the members of our armed forces. I believe each panel member understands the tremendous responsibility that has been entrusted to them to make this happen."

PRMRP Vaccine Development

Diarrhea caused by enterotoxigenic *E. coli* (ETEC) infection is a significant health threat for military and civilian personnel traveling around the globe. Incidence rates as high as 50 percent occur where food and water sanitation is poor. ETEC elicits diarrhea in the small bowel by elaboration of secretogenic enterotoxins and expression of colonization factors that induce intestinal adherence. 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 decreased performance. While no licensed ETEC vaccine exists, Dr. Stephen Savarino, from the Naval Medical Research Center is using a promising approach to develop a new antidiarrheal vaccine. Dr. Savarino is investigating the protective efficacy of passive, oral immunoprophylaxis with hyperimmune antifimbrial bovine milk immunoglobulin (BIgG) against ETEC infection. Based on the studies of the ETEC surface structures involved in intestinal adherence, Dr. Savarino's main objective is to apply cutting-edge technology for the development of an antidiarrheal supplement that will prevent diarrhea by blocking the infectious ETEC adherence onto the intestinal surface. To accomplish this goal, the investigative team identified the highly conserved ETEC adhesive components, expressed the ETEC proteins using a recombinant technology, and prepared a stock of ETEC antigens to immunize cows (bovine) for the production of the highly specific antibodies. The colostrums of the immunized cows were processed to collect the enriched bovine antibodies against the ETEC antigens. These high-quality bovine milk antibodies showed significant antidiarrheal effects in a primate model challenged with the ETEC strain. Taken together, Dr. Savarino's studies hold a great promise for the antidiarrheal BIgG vaccine that is currently in Phase I clinical trials at Johns Hopkins University, Baltimore, Maryland.

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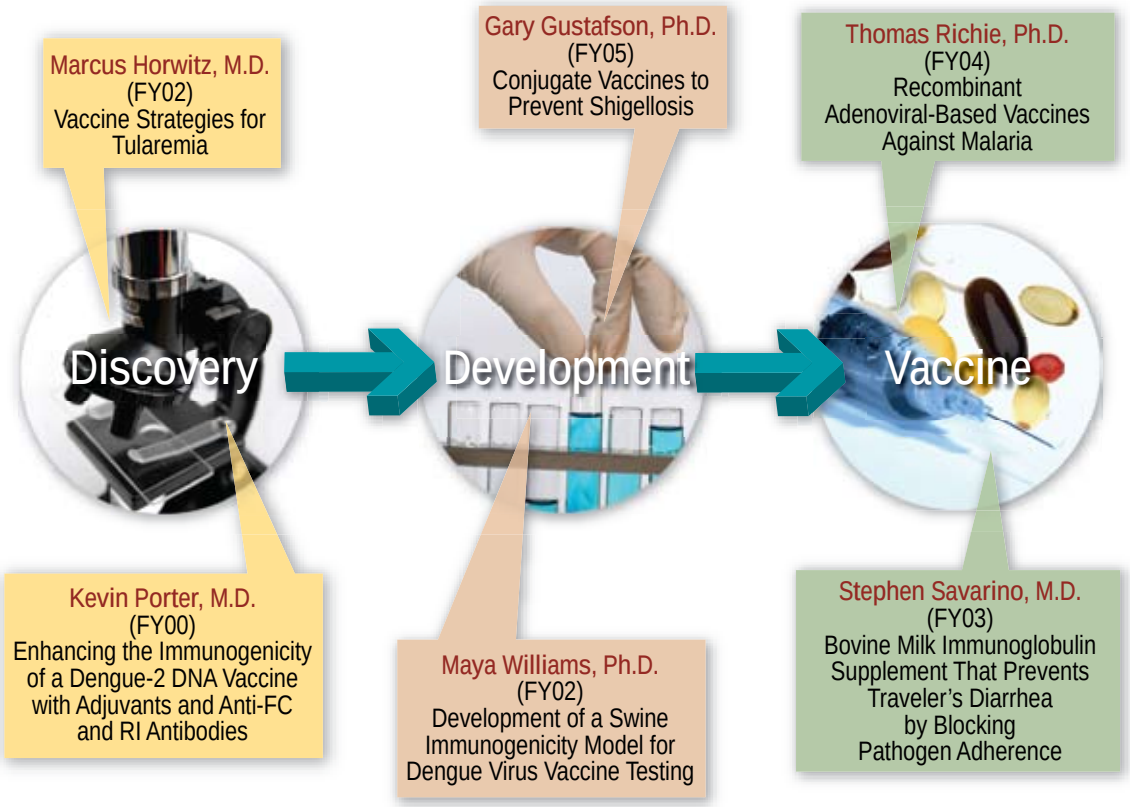
Marcus Horwitz, M.D.
(FY02)
Vaccine Strategies for Tularemia
Gary Gustafson, Ph.D.
(FY05)
Conjugate Vaccines to Prevent Shigellosis
Thomas Richie, Ph.D.
(FY04)
Recombinant Adenoviral-Based Vaccines Against Malaria
Discovery
Development
Vaccine
Kevin Porter, M.D.
(FY00)
Enhancing the Immunogenicity of a Dengue-2 DNA Vaccine with Adjuvants and Anti-FC and RI Antibodies
Maya Williams, Ph.D.
(FY02)
Development of a Swine Immunogenicity Model for Dengue Virus Vaccine Testing
Stephen Savarino, M.D.
(FY03)
Bovine Milk Immunoglobulin Supplement That Prevents Traveler's Diarrhea by Blocking Pathogen Adherence

PRMRP Drug Validation

Patients with spinal cord injury (SCI) suffer from numerous (neurological, renal, and gastrointestinal [GI]) complications, and a majority experience chronic pain. Accordingly, many of these patients are on anti-inf ammatory, analgesic, and narcotic drugs, each with its own deleterious side effects. The use of nonsteroidal anti-inf ammatory drugs (NSAIDs), which have potent anti-inf ammatory and analgesic activity in patients with SCI, has been limited because of the drugs' GI side effects that result in peptic ulceration, hemorrhage, and anemia, which can be particularly devastating in a debilitated patient. Dr. Lenard Lichtenberger from the University of Texas Health Science Center at Houston is investigating the utility of a new class of NSAIDs, which are coupled with phosphatidylcholine (PC), in the treatment and/or prevention of chronic neuropathic pain associated with SCI. Preliminary results in rodent model systems show that PC-NSAIDs have lower GI toxicity and more enhanced therapeutic effectiveness than the parent NSAID to inhibit fever, inf ammation, and pain. Positive results in these preclinical studies should hasten the development of PC-NSAID formulations for parenteral and enteral use for improved treatment of patients suffering from Chronic Pain Syndrome. The research performed during this project is expected to result in better treatment for military personnel immediately following battle and/or accidents to help prevent early inf ammatory processes that lead to painful central nervous system injury.

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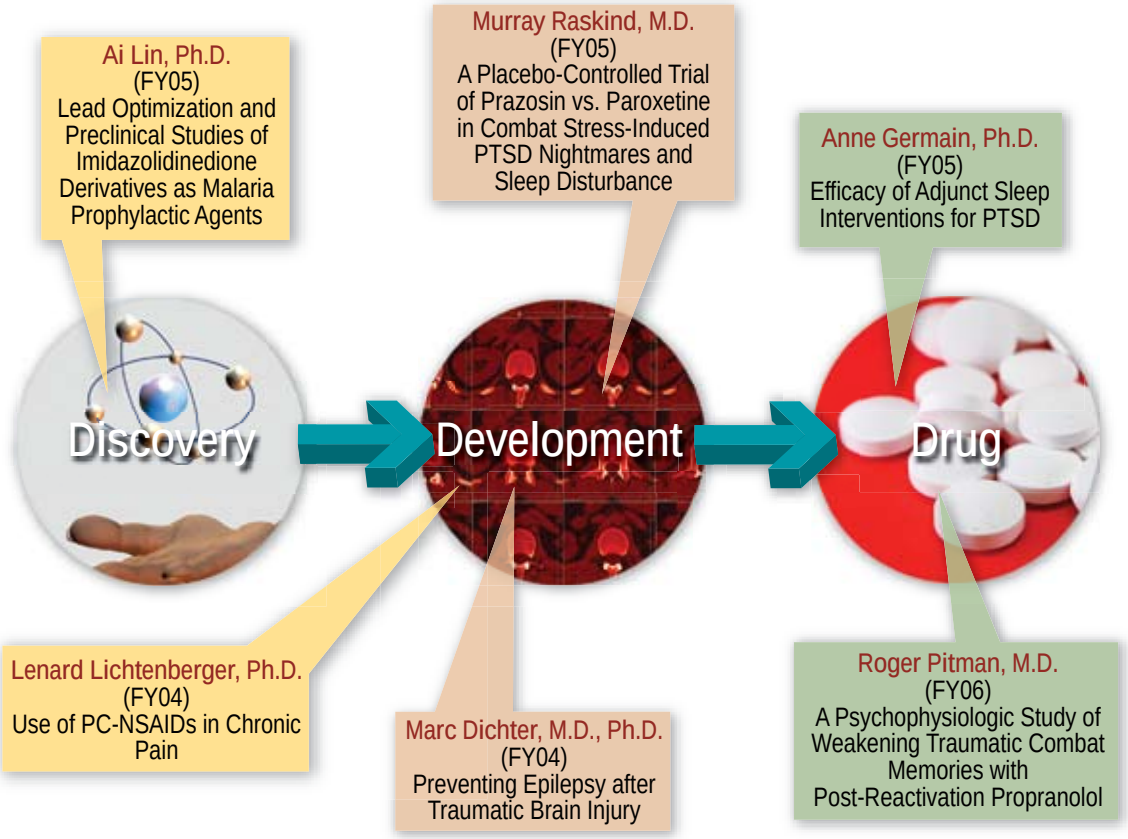
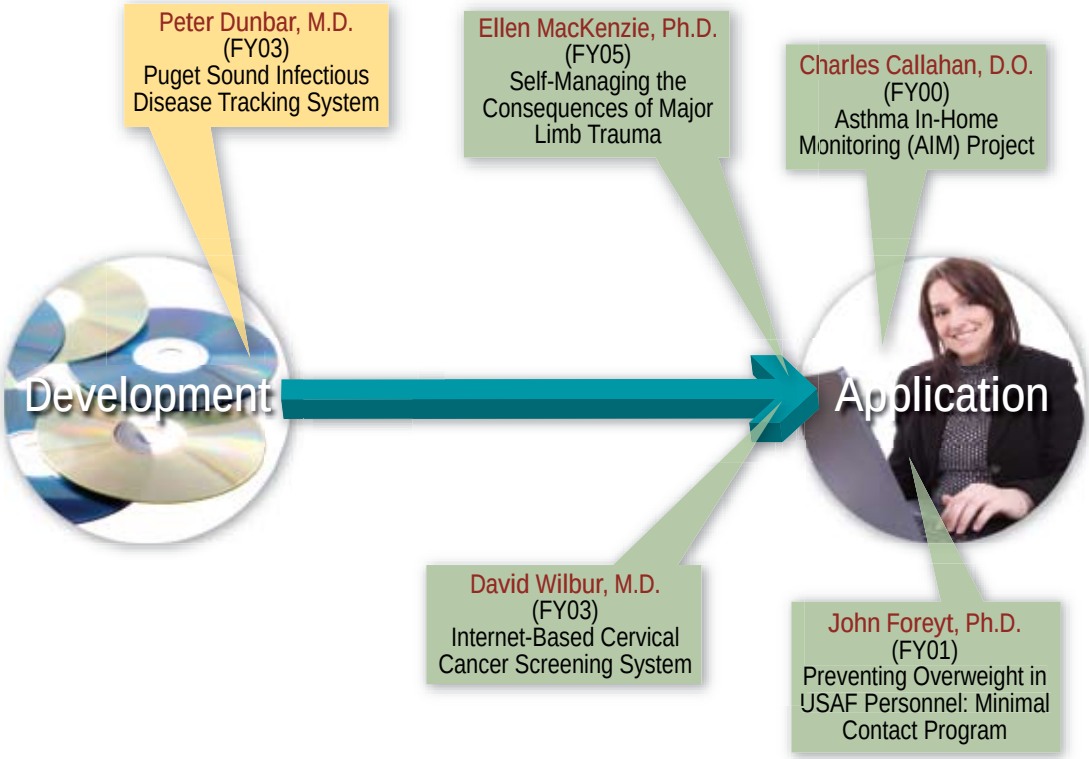

Ai Lin, Ph.D.
(FY05)
Lead Optimization and Preclinical Studies of Imidazolidinedione Derivatives as Malaria Prophylactic Agents
Murray Raskind, M.D.
(FY05)
A Placebo-Controlled Trial of Prazosin vs. Paroxetine in Combat Stress-Induced PTSD Nightmares and Sleep Disturbance
Anne Germain, Ph.D.
(FY05)
Efficacy of Adjunct Sleep Interventions for PTSD
Discovery
Development
Drug
Lenard Lichtenberger, Ph.D.
(FY04)
Use of PC-NSAIDs in Chronic Pain
Marc Dichter, M.D., Ph.D.
(FY04)
Preventing Epilepsy after Traumatic Brain Injury
Roger Pitman, M.D.
(FY06)
A Psychophysiologic Study of Weakening Traumatic Combat Memories with Post-Reactivation Propranolol

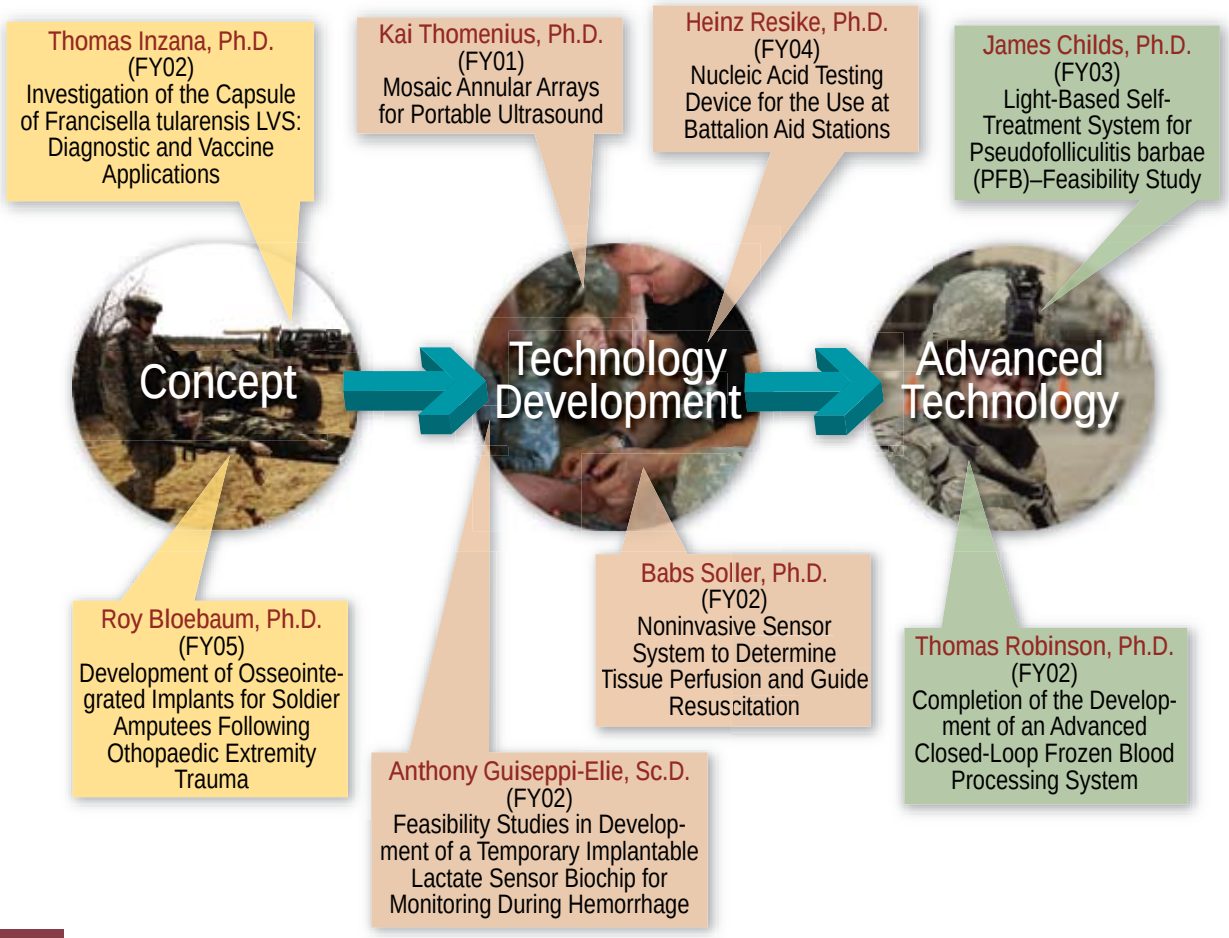
PRMRP Internet-Based Technology

As obesity reaches epidemic proportions in the United States, almost 20 percent of active duty military personnel are overweight. Currently, obesity is the main culprit for discharge. Dr. John P. Foreyt from Baylor College of Medicine is evaluating the effectiveness of minimal contact behavioral therapy (MCBT) plus usual care (UC) for controlling weight in U.S. Air Force personnel using a controlled experimental comparison between UC and MCBT. The MCBT therapy includes the use of a self-help book (the LEARN Program), an interactive Internet website, and motivational interviewing. Dr. Foreyt discovered that study participants assigned to the MCBT intervention group lost more weight than those assigned to the UC group. Additionally, 6-month and 12-month follow-up data showed that the MCBT condition maintained a significantly greater weight loss as compared to the UC group (who gained weight). These findings suggest that efficacy of a minimal contact and f exible Internet intervention and prevention for weight gain and loss can be used by the military to enhance troop health and readiness.



PRMRP Technology Development

Leishmaniasis is an infection transmitted by sand f ies that causes lesions of the skin, mucus membrane death, and if untreated, death. Leishmaniasis is common in tropical climates, such as Iraq and Afghanistan. Current detection and diagnosis of *Leishmania* takes weeks to months; therefore, early diagnosis is paramount. Dr. Heinz Reiske, of IQuum Inc. is developing the Liat™ *Leishmania* Assay, a fully automated sample-to-result nucleic acid test for leishmaniasis based on IQuum's Liat Analyzer. This device is designed to be deployable to the battlefield, easy enough to be used by nonspecialized personnel, fast enough to conduct tests in less than 1 hour, and cost-effective.

Dr. Heinz Reiske
IQuum Inc.

"We are very pleased to be applying our Liat system to this important application," said Dr. Reiske. "Our Liat Analyzer ideally addresses the need for rapid, easy-to-use, field-deployable nucleic acid testing, such as that for leishmaniasis."