CDMRP
Department of Defense

Congressionally Directed Medical Research Programs

2011 Annual Report

September 30, 2011

U.S. Army Medical Research and Materiel Command

Letter from the Director

I invite you to read the 2011 Annual Report for the Congressionally Directed Medical Research Programs (CDMRP). The CDMRP's vision is to provide hope by promoting innovative high-impact research, recognizing untapped opportunities, creating partnerships, and guarding the public trust. We believe in transparency and this report serves to continue that tradition. In the pages that follow, you will see our management models, highlights of our programs, and details of our financial accounting. This report represents the efforts of dedicated professionals who are committed to the CDMRP vision. I am humbled to work alongside such a talented and compassionate team. All of us at the CDMRP are eternally grateful for the opportunity to administer these critical research programs that you will read about. We would not be able to accomplish our goals without the efforts of Congress, consumer advocates, clinicians, and scientists who partner with the CDMRP to provide hope for those suffering.

Jeffrey C. Leggit, M.D.
Colonel, Medical Corps, U.S. Army
Director, CDMRP

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Department of Defense

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Congressionally Directed Medical Research Programs
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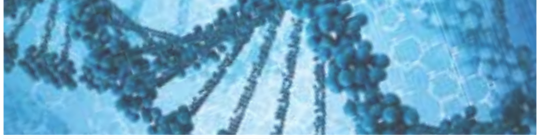

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Introduction: Who We Are and What We Do

A grassroots advocacy movement in the early 1990s campaigned for an increase in breast cancer research funding, and the U.S. Congress responded with an initial congressional appropriation in 1992 of $25 million (M) to be managed by the Department of Defense (DOD) U.S. Army Medical Research and Materiel Command (USAMRMC).[1] The following year, Congress appropriated $210M to the DOD for extramural, peer-reviewed breast cancer research. These appropriations marked the beginning of the CDMRP.

The success in managing the initial congressional appropriations in breast cancer research, combined with additional advocacy movements and the need for focused biomedical research, propelled the CDMRP into a global funding organization for cancer research, military medical research, and other disease-specific research. Through fiscal year 2011 (FY11) the CDMRP has been responsible for managing more than $6.5 billion (B) in appropriations (see Figure 1, CDMRP Funding History).

The CDMRP is a unique partnership among the U.S. Congress, the public, and the military supporting untapped research opportunities to encourage innovation and ingenuity in biomedical science. Hallmarks of the CDMRP include investing in groundbreaking research; supporting the next generation of researchers as well as established scientists; and funding clinical research to prevent, detect, diagnose, and treat diseases, conditions, and injuries. From small concept award investments to large consortia, the CDMRP strives to find and fund the best research for the benefit of the warfighter and the American public.

This Annual Report highlights the CDMRP's business practices, individual programs, and the financial accounting for FY10–FY11. Additional information about specific research programs can be found on the CDMRP website, requested by phone (301-619-7071), or through e-mail (CDMRP.PublicAffairs@amedd.army.mil).

Vision

Find and fund the best research to eradicate diseases and support the warfighter for the benefit of the American public

Mission

Provide hope by promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust

[1]Known as the U.S. Army Medical Research and Development Command prior to 1995.

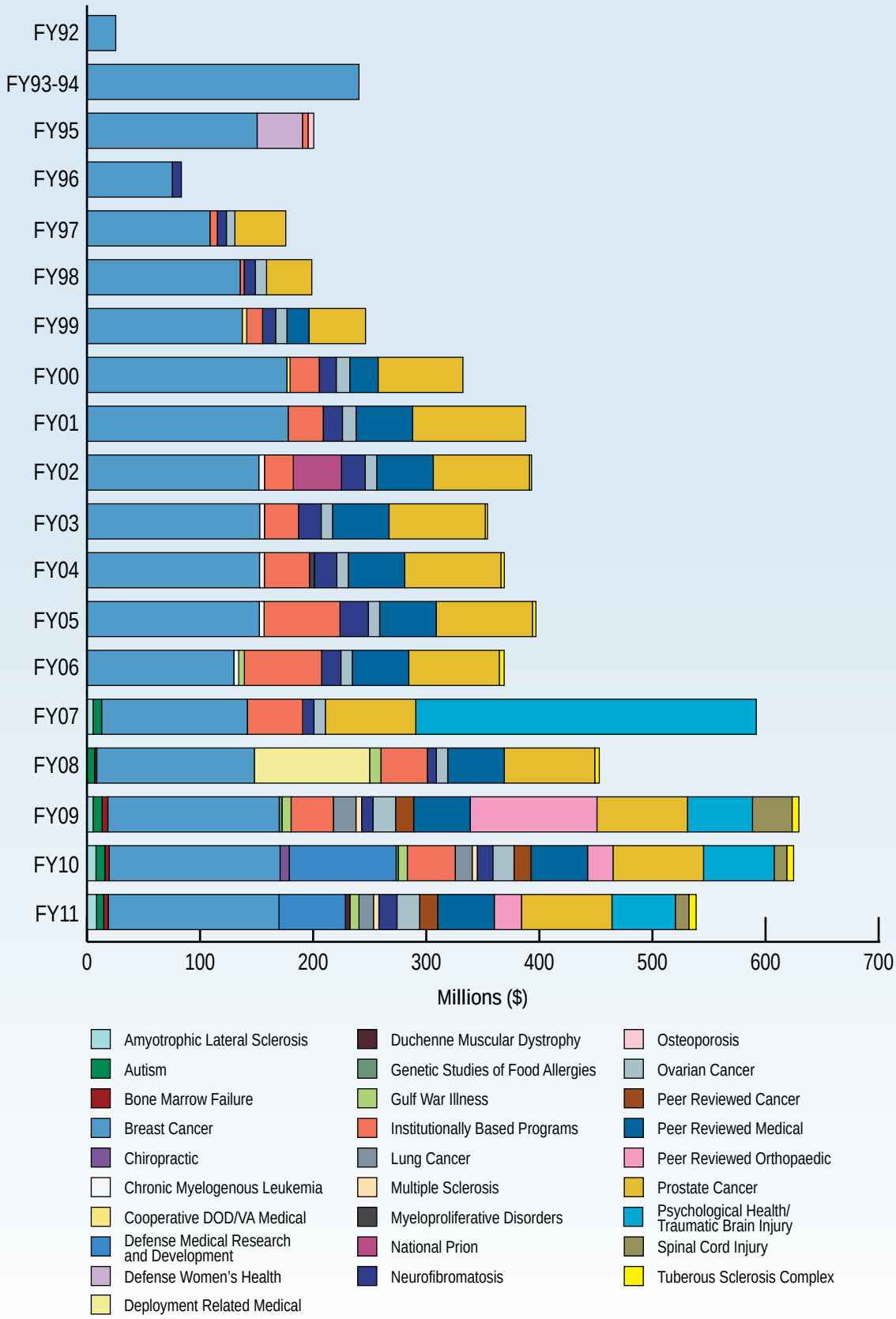


*Figure 1. CDMRP Funding History**

***Data as of September 30, 2011.**
Investment of FY11 funds will be complete as of September 30, 2012.

Our Management Cycle

The CDMRP employs a flexible management cycle to maintain the individuality of each program while also meeting the needs of Congress, the DOD, the research and advocacy communities, and the public at large. This management cycle begins with a congressional appropriation and ends with the completion of the funded research. Each step in the execution and management cycle is depicted in Figure 2 followed by descriptions of each milestone.

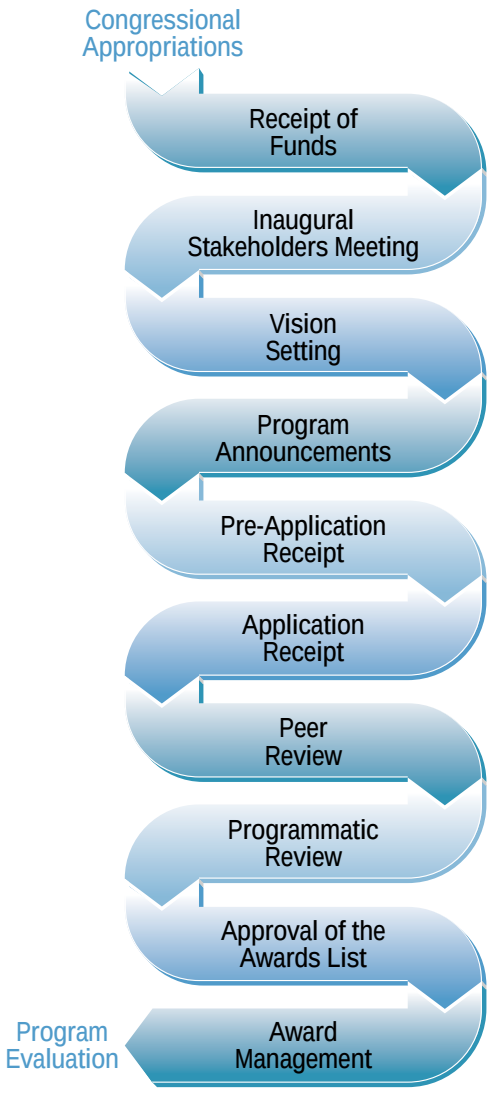
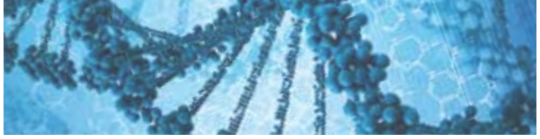


Figure 2. Execution and Management Cycle



Congressional Appropriation and Receipt of Funds

Programs assigned for complete life-cycle management to the CDMRP exist because of yearly, individual congressional appropriations. These funds are not in the President's budget; Congress adds them annually to the DOD appropriation to fund new programs or continue existing programs.

Stakeholders Meeting

For new programs, a stakeholders meeting is held within the first months after receipt of funds. The goal of stakeholders meeting is to survey the research landscape and identify gaps in both the scientific and consumer interest areas. Stakeholders are world-renowned scientists, clinicians, and consumer advocates[2] (additional information about consumer advocates can be found on page 11). Recommendations from the stakeholders meeting are then used to facilitate vision setting. In FY11, there was one stakeholders meeting held for the new CDMRP program, Duchenne Muscular Dystrophy Research Program (DMDRP).

Vision Setting

A vision setting meeting is held annually after a congressional appropriation to define an annual investment strategy (or initially after the inaugural stakeholders meeting). The development of an annual investment strategy was recommended by the National Academy of Sciences Institute of Medicine.[3] The CDMRP adopted this recommendation. Through the work of each program's Integration Panel (IP), which consist of the most visionary scientists, clinicians, and consumer advocates, individualized investment strategies are developed. Members of the IP recommend the annual investment strategy to identify underfunded and underrepresented areas of research and encourage research in those areas that are considered the most critical to patients, scientists, clinicians, and consumer advocates. The annual investment strategy provides a high degree of flexibility and the necessary structure to most effectively obligate each congressional appropriation while avoiding unnecessary duplication with other funding agencies. In FY11, there were 16 vision setting meetings held for the CDMRP.

Program Announcements

The product of vision setting is an annual investment strategy that develops the framework for specific award mechanisms to achieve the program's vision. Award mechanisms represent the pressing needs of the research, advocacy, and military communities for each program and are released after vision setting in the form of program announcements (PAs). Individual PAs, i.e., solicitations for applications, provide details about a particular award mechanism, criteria scores, the application process, and requirements for submitting applications, including pre-applications, if required for that award mechanism.

A central philosophy embraced by the CDMRP is innovation. The CDMRP fills research gaps by funding high-risk, high-gain research that other agencies may not venture to fund. While individual award mechanisms have different requirements, ultimately the mechanisms supported by the CDMRP share the common goal of advancing innovative ideas, creative solutions, patient care, or breakthrough technologies and resources.

The CDMRP released 71 award mechanisms across 17 programs.

[2]**Consumers are patients, survivors, family members, or caregivers of people living with a disease, injury, or condition and are representatives of consumer advocacy, support, or military organizations.**

[3]**Institute of Medicine, *Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command*, The National Academies Press, 1993.**

Application Submission and Receipt

Application submission requires a two-step process consisting of a pre-application submission (which includes a letter of intent, preproposal, and/or nomination) followed by a full application submission. For those mechanisms that require a preproposal, the preproposal process was instituted for many of the funding opportunities offered by the CDMRP in response to the rising number of full applications received. As the number of full applications exponentially escalated during the past several years, management costs to administratively process, scientifically peer review, and programmatically review the applications also increased. Additionally, applicants were burdened with the compilation of a complex full application package submission when chances of being funded were significantly decreased. To mitigate the financial burden on the programs and on the time and effort required by applicants to submit, a preproposal step has been added to the program review cycle for many of the award mechanisms.

Through the use of the preproposal screening process, the CDMRP has successfully decreased the number of full applications to be administratively processed, scientifically peer and programmatically reviewed. The preproposal is an abbreviated response, usually one to three pages, detailing the research aims, strategy and methods, innovation, and/or impact of the project. The applicant prepares it with guidance based on individual PA requirements.

Following the submission of the preproposal, the application is screened by the IP or a peer review panel, based on the requirements described in each PA. The final product of the screening is a recommended list of invited applicants. All applicants are informed of their status and the invited applicants complete the requirements for a full application package submission. The preproposal screening process ensures a greater understanding of the intent of the award mechanism while decreasing management costs and saving funds for research investment. In FY11, the CDMRP held 19 preproposal screening meetings.

As summarized in Table 1, in FY11, the CDMRP received 5,428 preproposals and nominations that, after screening and invitation, resulted in 1,473 full applications received as of the date of this report. In addition, the CDMRP received 2,096 full applications from mechanisms that did not require preproposals or nominations for a total of 3,569 full applications received to date.

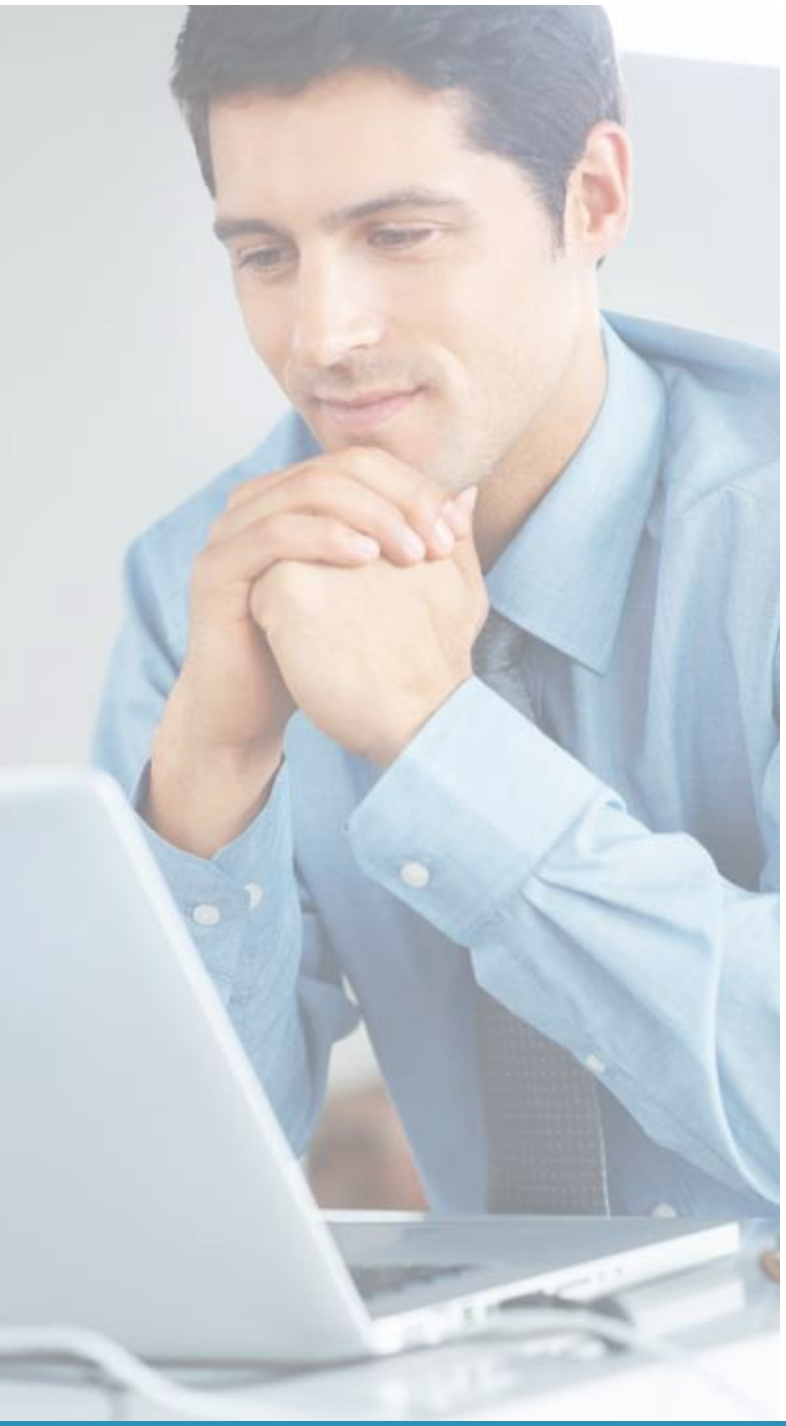
Table 1. Number of Submissions Received from October 1, 2010 to September 30, 2011 Across FY10–FY11 Programs

Mechanism Submissions	
Preproposals or nominations screened	5,428
Letters of intent received	3,015
Total pre-applications received	**8,443**
Full Application Submissions	
Full applications from invitations only	1,473
Full applications from letter of intent	2,096
Total full applications received	**3,569**

Review

The CDMRP adopted the recommendations set forth in 1993 by the National Academy of Sciences Institute of Medicine committee, which concluded that the CDMRP would be best served by a two-tier review process to reflect the traditional strengths of scientific review but can be tailored to accommodate individual program goals. Although the two tiers of review have different goals, they are complementary.

All reviewers for the CDMRP must uphold the highest standards of conduct to ensure the credibility of the programs and the processes. Additional details about the two tiers of review can also be accessed on the CDMRP website at http://cdmrp.army.mil/about/fundingprocess.



Peer Review

Peer review is conducted after application receipt. It is a criteria-based process where applications are evaluated based on their scientific and technical merit. Peer review is performed by external panels. Applications are categorized by scientific discipline, specialty area, and/or award mechanism and evaluated by both scientific and consumer peer reviewers. The CDMRP strives to give every application a fair and balanced review, taking steps to ensure conflict of interest does not influence the process. The products of peer review include the summary statements with final scores. From October 1, 2010 through September 30, 2011, a total of 85 peer review panels were held.

Programmatic Review

After applications have been scientifically peer reviewed, they undergo programmatic review resulting in a recommended-for-funding list. The IP that recommended the annual investment strategy for each program at vision setting performs this review. At programmatic review, the IP reviews each application based on the criteria published in the PA with a focus on not only scientific merit but also programmatic relevance, relative innovation, program portfolio composition and adherence to the intent of the award mechanism. Members of the IP recommend funding the best applications to fulfill the review criteria and answer the vision and mission of each program. From October 1, 2010 through September 30, 2011, a total of 20 programmatic review meetings were held.

Approval of the Awards List

The final product of programmatic review is the recommended-for-funding list that is reviewed and approved by the Commanding General, USAMRMC. For certain programs, approval is also attained from the Director of the Defense Medical Research and Development Program (DMRDP) Office within the Office of the Assistant Secretary of Defense for Health Affairs. Upon approval, electronic notification letters are sent to program applicants to inform them of their funding status.

In rare instances (less than 1%), applicants voice objections regarding the scientific peer review or programmatic review of their applications. The CDMRP established an Inquiry Review Panel to address applicant queries. These appeals must be based on the occurrence of factual or procedural errors at receipt, peer review, or programmatic review. If a factual or procedural error is identified, the application will be sent for re-review at the appropriate level (peer and/or programmatic review).

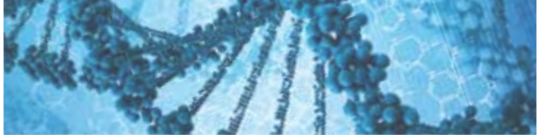
Award Management

The negotiation and management of awards are a major focus of the CDMRP. Approximately 600 to 700 new awards are made each fiscal year, totaling 10,719 awards throughout the CDMRP funding history (as of September 30, 2011). Life-cycle management is an active process from the recommended for funding through the closeout of the award. To ensure success, award management encompasses a partnership among many offices within USAMRMC including the CDMRP, the U.S. Army Medical Research Acquisition Activity (USAMRAA), the Office of Research Protections (ORP), the Office of Surety, Safety, and Environment, and Staff Judge Advocate.

Following award notification, USAMRAA initiates negotiations with the performing institute. Formalized analysis of the budget with respect to the scope of work to be done is performed through detailed discussions among the CDMRP, USAMRAA, the institute, and the researchers to ensure cost sharing when possible and avoidance of overlap in research funding with other funding agencies. In addition, the CDMRP facilitates regulatory review of each research project. The ORP manages and provides oversight on human subject protection review and animal welfare review for all the CDMRP-funded research. Once all aspects of negotiation are completed, an award is signed by USAMRAA. Awards are made in the form of grants, contracts, or cooperative agreements no later than 24 months after congressional appropriation.

The life-cycle management of awards continues throughout the period of performance with monitoring of the technical progress, financial reporting, and regulatory review. Awards are assigned a Science Officer (SO) to ensure a broad knowledge of each grant, communication among all parties involved, and the most comprehensive assistance possible to the Principal Investigator (PI). At a minimum, all PIs are required to submit annual progress reports and quarterly financial reports. Investigators with awards that include clinical trials or clinical research are required to submit a quarterly report to the SO and USAMRAA. These awards are monitored for approval of the clinical protocols, accrual of patients, and any adverse events. When the SO identifies issues such as slow recruitment to clinical trials, the entire management team (including the CDMRP, ORP, and USAMRAA) works with the PI to resolve the issue. The progress of large grants and consortia may also be monitored through external advisory boards, site visits, teleconferences, and other meetings throughout the entire period of performance.

CDMRP...
currently manages 10,719 awards.



Programs

Through FY11, The CDMRP has managed 106 award programs primarily focused on specific diseases, injuries, or conditions. Since inception of the CDMRP, congressional appropriation directed toward these research programs totals more than $6.5B. From FY92 through FY10 appropriations, the CDMRP has managed 10,719 research grants, contracts, and cooperative agreements.

The CDMRP completed execution of the FY10 appropriations that resulted in 786 new awards being processed. The CDMRP also initiated execution of appropriations for FY11, which totals more than $537M in funding across 18 programs. Table 2 depicts the FY10 and FY11 funding summary information for individual programs managed by the CDMRP while additional information about specific programs can be found on the two-page spread dedicated to each program starting on page 28. An overview of the appropriations and applications received and funded during FY92–FY10 can be found in Appendix A and the complete financial data for FY10–FY11 can be found in Appendix B.

As part of the DOD, the CDMRP works with a number of military partners to maximize the impact of its congressional special interest (CSI) programs on the health and welfare of our service members and their families. The Defense Medical Research and Development Program is the research arm of the Defense Health Program (DHP). The DMRDP has several major program areas, including Medical Simulation & Training and Health Information Technology, Military Infectious Diseases, Military Operational Medicine, Combat Casualty Care, Radiation Health Effects, and Clinical and Rehabilitative Medicine. Each DMRDP program area establishes key research topics and capability gaps through a Joint Program Committee (JPC), an advisory group consisting of tri-service military and non-military medical and programmatic experts. CSI programs managed by the CDMRP that align with the DMRDP program areas, such as the Peer Reviewed Orthopaedic Research Program (PRORP) and the Spinal Cord Injury Research Program (SCIRP), work closely with relevant JPCs during vision setting, programmatic review, and award management. The JPCs provide guidance on military-relevant research priorities for these CDMRP programs, and utilize their oversight of all core and CSI research efforts across the DOD services in their respective program areas to complement and leverage ongoing projects with CDMRP funding opportunities. Additional information about programs managed by the CDMRP that align with DMRDP program areas can be found on pages 38 and 39 of this Annual Report as well as on the CDMRP website at http://cdmrp.army.mil.

Table 2. CDMRP Programs, Appropriations, Applications Received and Awarded

Program	FY10			FY11[d]		
	Funds Received (in millions)	Proposals Received	Proposals Funded	Funds Received (in millions)	Proposals Received to Date	Proposals Funded to Date
Amyotrophic Lateral Sclerosis	$7.5	66	8	$8.0	60	
Autism	$8.0	203	15	$6.4		
Bone Marrow Failure	$3.8	81	10	$4.0	40	
Breast Cancer/Breast Cancer Research Semipostal	$151.0	3,251	268	$150.0	959	1
Defense Medical R&D[(a)]	$94.5	415	67	$58.7		
Defense Medical R&D (Chiropractic)[(a)]	$8.1	5	1			
Duchenne Muscular Dystrophy				$4.0		
Genetic Studies of Food Allergies	$1.9	48	5			
Gulf War Illness	$8.0	34	13	$8.0	38	
Institutionally-Based[(b)]	$42.3	25	25			
Lung Cancer	$15.0	4	1	$12.8		
Multiple Sclerosis	$4.5	210	14	$4.8	116	
Neurofibromatosis	$13.8	97	24	$16.0	85	
Ovarian Cancer	$18.8	138	23	$20.0	198	
Peer-Reviewed Cancer	$15.0	485	30	$16.0		
Peer-Reviewed Medical	$50.0	607	59	$50.0	712	
Peer-Reviewed Orthopaedic	$22.5	6	3	$24.0		
Prostate Cancer	$80.0	1,269	162	$80.0	1,314	
Psychological Health/Traumatic Brain Injury[(a)]	$11.6	41	6			
Psychological Health/Traumatic Brain Injury[(c)]	$50.8	n/a	26	$56.0		1
Spinal Cord Injury	$11.3	78	17	$12.0		
Tuberous Sclerosis	$6.0	51	9	$6.4	47	
Total	**$624.2**	**7,114**	**786**	**$537.1**	**3,569**	**2**

Data as of September 30, 2011
(a) The CDMRP assisted with full life-cycle management of this portion of a larger appropriation(s).
(b) Institutionally Based Programs include 26 separate research programs in FY09–FY10.
(c) The CDMRP provided only research award negotiation and management for this portion of a larger appropriation.
(d) FY11 cycle is pending and should be completed by September 30, 2012.

Vital Partnerships

The CDMRP attributes its success to partnerships with individuals and organizations, including the military, scientists, clinicians, consumer advocates, minority and underserved populations, professional organizations, and policy makers. Highlights of some of the central partnerships within the CDMRP are described on the following pages.

CDMRP...

recognizes that progress is made through partnerships, team science, and synergistic research.

USAMRMC

There are several offices within USAMRMC that the CDMRP works with to execute its research programs, as shown in Figure 3. Partners work collaboratively to ensure that congressional appropriations are used for the benefit of the American public and the warfighter.

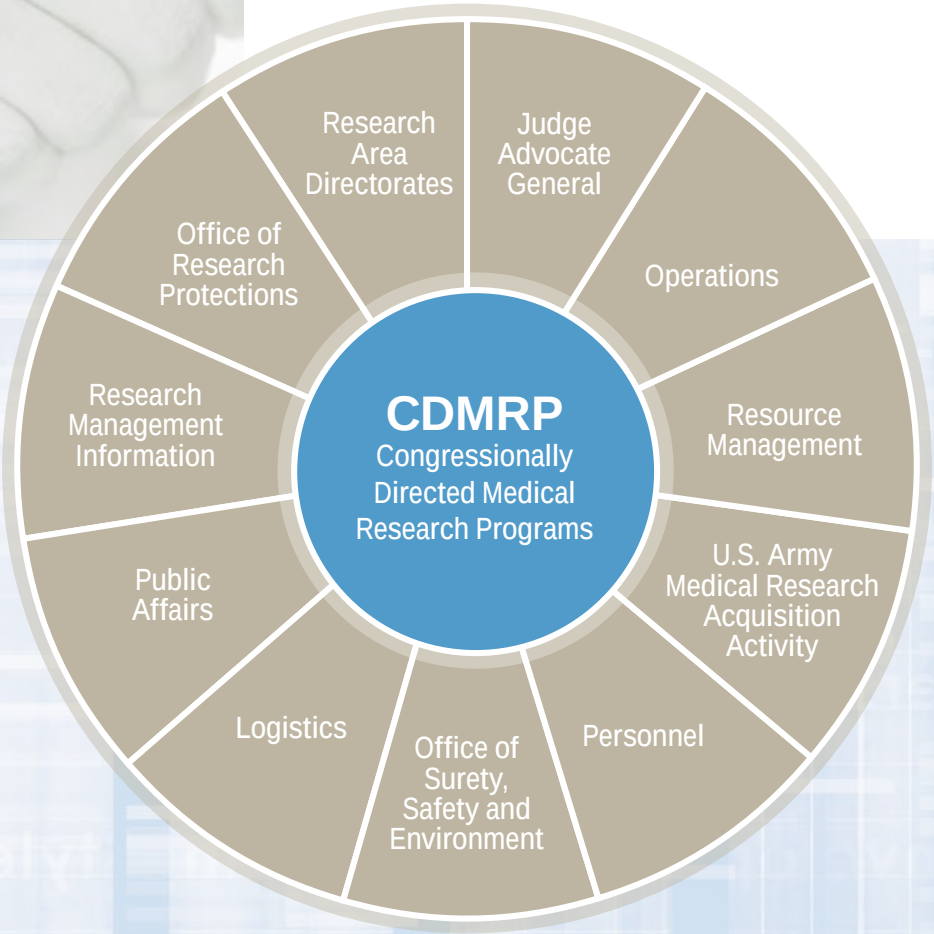


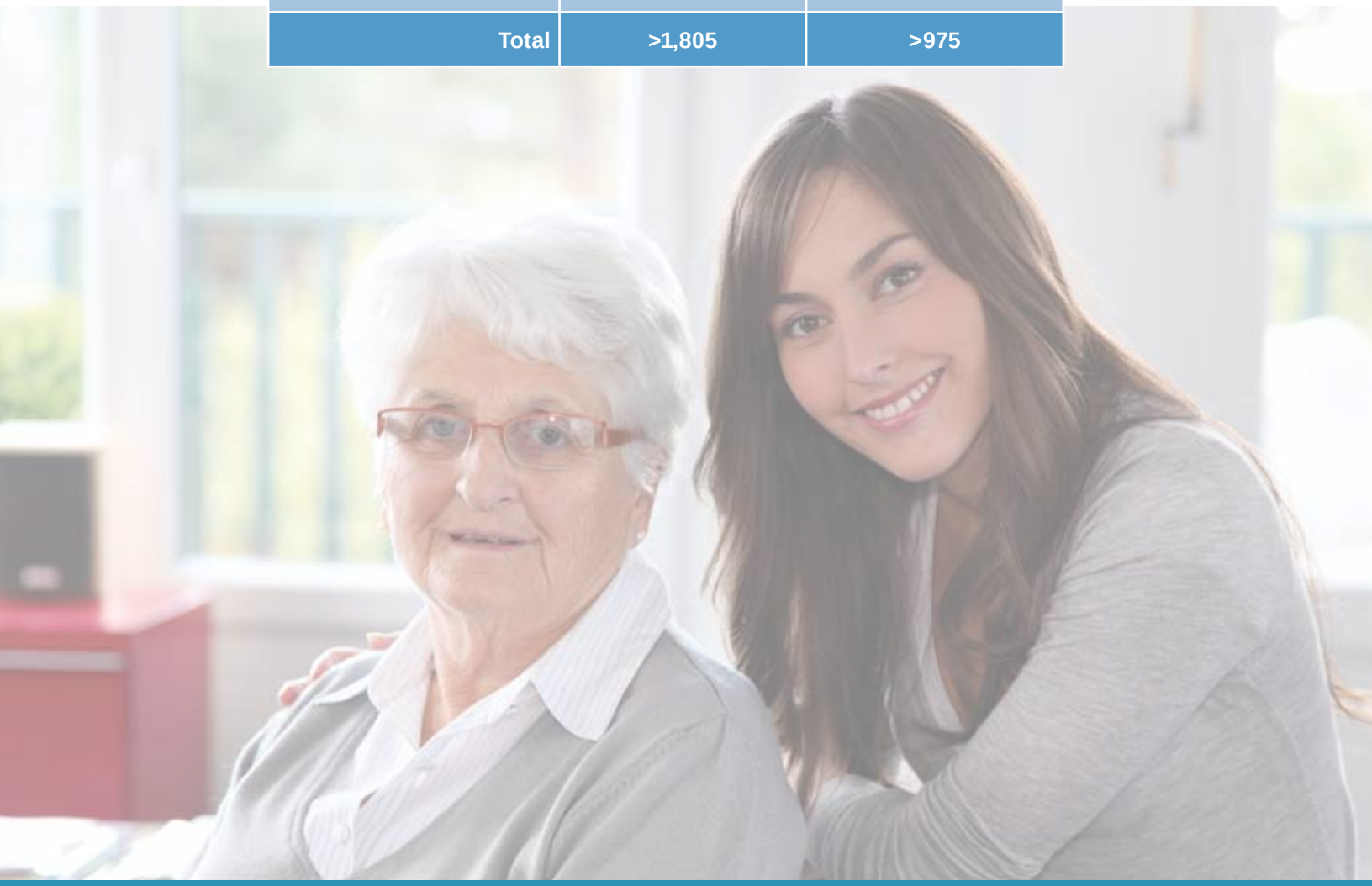
Figure 3. The USAMRMC Team

Consumer Advocates

Consistent with the CDMRP's founding principle of consumer involvement, consumer advocates are included in every aspect of program execution. Consumer advocates for the CDMRP are patients, survivors, family members, or caregivers of people living with a disease, injury, or condition and are representatives of consumer advocacy, support, or military organizations. Consumers continue to play an essential role in the establishment and growth of programs within the CDMRP. The value of consumer involvement is derived from each individual's firsthand experience with the disease, injury, or condition. This adds perspective, passion, and a sense of urgency that ensures the human dimension is incorporated in the program policy, investment strategy, and research focus. Since 1992, more than 1,805 consumers have represented their communities in the peer and programmatic review of applications. For more information on consumer involvement, see the consumer involvement pages on the CDMRP website (http://cdmrp.army.mil).

Table 3. Consumer Involvement in the CDMRP Since 1992

	Consumers	Consumer Organizations
Peer Reviewers	>1,675	>890
Programmatic Reviewers	>130	>85
Total	**>1,805**	**>975**



The Scientific Community

The growth and magnitude of the CDMRP can be attributed in part to the scientific community. The fulfillment of program goals requires cooperation, communication, and integration across multiple scientific and clinical disciplines. To date, more than 8,500 scientists and clinicians have provided the necessary subject matter expertise on peer review panels. In FY11, 357 scientists and clinicians served as IP or Joint Programmatic Review members, and more than 165 ad hoc reviewers were recruited to these panels. At the CDMRP, more than 140 scientists, clinicians, and professionals are currently involved in the day-to-day program execution and science management. Finally, approximately 8,086 researchers have been funded by the CDMRP in an effort to tackle the complex causes of diseases, conditions, and injuries and translate this knowledge to improved prevention, treatment interventions, patient survival, and quality of life.

Breast Cancer Research Semipostal Program

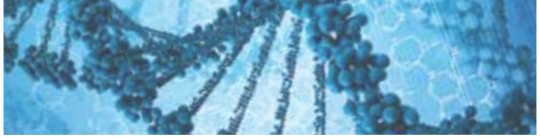
As a result of the Stamp Out Breast Cancer Act (Public Law 105-41 [H.R. 1585]), the National Institutes of Health and the DOD Breast Cancer Research Program (BCRP) are the designated recipients of revenues (70% and 30%, respectively) from sales of the U.S. Postal Service's Breast Cancer Research Semipostal (BCRS). The Stamp Out Breast Cancer Act resulted from the work of advocates for breast cancer research. This legislation led to the U.S. Postal Service's issuance of a new first-class breast cancer stamp, which costs 55¢, and can be purchased by the public. Since the stamp was first offered for sale in 1998, the monies received by the CDMRP from the BCRS through FY10 have been used to fully or partially fund 45 BCRP Idea Awards and 3 Synergistic Idea Awards. Both award mechanisms support highly innovative, high-risk, high-reward research that could lead to critical discoveries in breast cancer. As with all BCRP awards, proposals funded through the BCRS program are reviewed according to the two-tiered review system. The administration of funds from the Breast Cancer Research Semipostal Program represents a unique partnership between the DOD, advocates, and the public. A list of all awards supported by the BCRS can be found in Appendix C.

Military Partnerships

Fundamental to the success of the CDMRP is the coordination of efforts to advance research for the health of our service members and their families. USAMRMC executes and manages the Research Area Directorates (RADs). The RADs within USAMRMC execute and manage research that focuses specifically on military infectious diseases, combat casualty care, military operational medicine, and military clinical and rehabilitative medicine. By partnering with the USAMRMC RADs, the CDMRP facilitates the alignment of award portfolios and RAD mission relevance. Awards within the CDMRP portfolio with results critical to the military are highlighted for briefing to the Commanding General and the DOD Health Affairs office. Additional information about programs managed by the CDMRP that span military medical health can be found under the Programs section on page 8, as well as in the corresponding program pages in this report, which include DMRDP, PRORP, Psychological Health and Traumatic Brain Injury (PH/TBI) Research Program, and SCIRP.

DOD Small Business Innovation Research and Small Business Technology Transfer Programs

The CDMRP participates in the DOD Small Business Innovation Research and Small Business Technology Transfer (SBIR and STTR) programs. The SBIR and STTR programs are congressionally mandated, government-wide programs that are designed to harness the innovative talents of U.S. small businesses for our country's military and economic strength. These are technology- and product-driven programs intended to develop goods and services that the government can potentially use and the small business can continue to commercialize outside the SBIR and STTR programs.



Addressing Health Disparity

In 1998, the CDMRP established the Minority and Underserved Populations Program to provide focus to initiatives aimed at addressing health disparity. The primary function of the program is to promote execution strategies to eliminate the unequal burden of disease among minority and medically underserved populations, as appropriate across the research programs managed by the CDMRP. Program execution includes:

- Surveillance of disease impact on populations
- Solicitation of health disparity-focused research (based upon target disease incidence and mortality among populations)
- Outreach with information about specific funding mechanisms for minority serving institutions[4]
- Collaboration with other funding agencies on assessment of portfolio overlap and complementation
- Exchange of information with public and private advocacy and research organizations, including data on trends and standard of care relevant to disease disparity among minority and medically underserved populations

[4]For the purposes of minority institutions, the CDMRP uses the list compiled by the United States Department of Education, which can be accessed at http://www2.ed.gov/about/offices/list/ocr/edliteminorityinst-list

International Cancer Research Partners: One Voice, One Vision

In 2000, the CDMRP joined the National Cancer Institute and the National Cancer Research Institute of the United Kingdom to form the International Cancer Research (ICR) Partners in an effort to maximize the global investment in cancer research. The mission of the ICR Partners is to enhance the impact of research to benefit all individuals affected by cancer through global collaboration and strategic coordination of research.

Today, the ICR Partners include 52 cancer funding organizations from the United States, Canada, United Kingdom, and the Netherlands that have come together to classify their respective research portfolios using a common coding scheme (called the Common Scientific Outline). The most recent member to join was the Dutch Cancer Society. The ICR Partners are currently involved in discussions with other interested cancer research funding organizations in the United States, Europe, and elsewhere to join the partnership, expanding the efforts toward a global strategic mission to eradicate cancer. Additional information about the ICR Partners and research supported by its members can be found at http://www.cancerportfolio.org/.

Information Dissemination

A core philosophy of the CDMRP is transparency with respect to public awareness of how congressional funds are used and managed. The CDMRP employs many different modes to share information about research supported by the CDMRP, which are highlighted as follows.

The CDMRP Website

The CDMRP website is an important means to disseminate information to the public and scientific community. The recently redesigned website features facts and news about the CDMRP, individual research programs, funding opportunities, and consumer involvement with an animated media center that highlights press releases, research highlights, consumer stories, program books, annual reports, and videos.

http://cdmrp.army.mil/

Research Highlights

Research highlights inform the public about innovative research being conducted by investigators supported by funds from the CDMRP. They are typically developed by each program to focus on important research advances, implications for quality of life, and future research directions. Research highlights are posted and archived on the CDMRP website as well as published in individual program books. A total of 39 new research highlights were posted on the CDMRP website this fiscal year.

Program Announcement Outreach

Program Announcements describe the funding opportunities and application process for specific mechanisms within each program. Dissemination strategies are wide and include the following:

- Alerting more than 800 research administrators of upcoming award opportunities
- Posting PAs to the CDMRP website and Grants.gov
- Notifying websites that specialize in biomedical grant notification
- Notifying more than 60 professional associations, 300 Veterans Affairs facilities and military and medical research laboratories, and 6 federal agencies
- Advertising in professional journals and on federal business websites
- Targeted e-mails and advertising for specific award mechanisms and outreach
- Maintaining an e-mail distribution list of more than 26,000
- Distributing electronic news items to more than 200 consumer advocacy groups
- Exhibiting the CDMRP display and presenting funding opportunities at national scientific meetings, including the Annual Meeting of the American Association for Cancer Research
- Providing research institutions with award details for news releases

20 Years of Research Management Excellence

Significant initiatives, milestones, and research accomplishments attained by the CDMRP and its funded investigators over the past 20 years are highlighted over the next few pages.

CDMRP...

invests in groundbreaking research to prevent, detect, diagnose, and treat diseases, conditions, and injuries.

$25M appropriated to the BCRP for research on breast cancer screening and diagnosis for military women and their family members

1992

Dr. Dennis Slamon develops Herceptin® (trastuzumab), a monoclonal antibody against the HER-2/neu receptor in breast cancer

Dr. Michael Wigler conducts research that contributes to the discovery of the tumor suppressor gene phosphatase and tensin homolog (PTEN), which is mutated in breast cancer, prostate cancer, and glioblastomas

Dr. Richard Peto conducts Adjuvant Tamoxifen Longer Against Shorter (ATLAS) clinical trial, the largest breast cancer treatment trial ever undertaken, examining the optimal duration of adjuvant tamoxifen in early-stage breast cancer

1993

Grassroots efforts influenced public policy leading to a congressional appropriation of $210M for peer-reviewed breast cancer research

The National Academy of Sciences published a report, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, to guide the $210M appropriation for breast cancer research

Dr. Constantin Ioannides conducts studies on the characterization of immunodominant epitopes in breast cancer that leads to the development of NeuVax™(E75), a peptide-based vaccine to prevent recurrences; now entering a Phase 3 clinical trial

The USAMRMC asked the Institute of Medicine to review the implementation and progress of the BCRP; a report was subsequently published in 1997, A Review of the Department of Defense's Program for Breast Cancer Research

Consumers were integrated into the scientific peer review process

1995

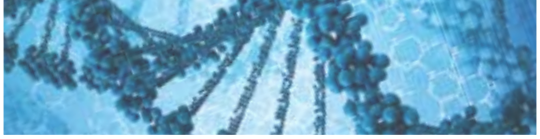
Dr. David Goldgar discovers the founder BRCA2 617delT mutation in Ashkenazi Jews

Dr. Susan Love develops a minimally invasive diagnostic procedure for detecting precancerous and cancerous breast cells in fluid from the breast ducts

Dr. Mary Daly establishes a high-risk breast cancer registry, which evolved into a program that now serves a large urban area with a range of risk assessment, screening, and preventive services

The Neurofibromatosis Research Program (NFRP) was established by an $8M appropriation

1996



The PCRP was established by a $45M appropriation

The Ovarian Cancer Research Program (OCRP) was established by a $7.5M appropriation

The BCRP sponsored its first Era of Hope conference

The Institute of Medicine issued a favorable report of the implementation and progress of the BCRP entitled A Review of the Department of Defense's Program for Breast Cancer Research

1997

Dr. Kathryn Verbanac conducts clinical studies testing the validity and accuracy of sentinel lymph node biopsy, the current standard of care for disease staging in breast cancer

Dr. Nicole Urban develops assays to measure HE4 and MSLN in serum; HE4 assay was licensed to Fujirebio Diagnostics, Inc., which partnered with Abbott and was approved by the U.S. Food and Drug Administration (FDA) as a new diagnostic test to monitor recurrence or progression of ovarian cancer

Dr. Bruce Korf establishes volumetric magnetic resonance imaging (MRI) as the standard approach for measurement of plexiform neurofibroma growth in clinical trials

Dr. Glenn Prestwich develops novel hyaluronic acid (HA)-targeted drugs, now in Phase 3 clinical trials, which bind HA receptors to breast cancer cells for enhanced delivery of anticancer agents

The BCRP was the recipient of 30% of the funds raised by the issuance of our nation's first semipostal stamp, the Breast Cancer Research Stamp

The CDMRP website was launched

The CDMRP published "Perspective from the Department of Defense Breast Cancer Research Program," Breast Disease (1998) 10: 33–45

Dr. Sundaram Ramakrishnan develops anginex, a potent anti-angiogenic and anticancer peptide (produced by ActiPep Biotechnology) and shows efficacy in combating ovarian cancer

Dr. Kimlin Ashing-Giwa develops a predictive model for the identification of sociocultural mediators and their role in breast cancer survivorship among different ethnic populations to improve health-related quality of life

1998

The Peer Reviewed Medical Research Program (PRMRP) was established by a $19.5M appropriation

Dr. Gregory Belenky develops an unobtrusive, wrist-worn actigraph with an embedded mathematical performance prediction algorithm for tracking activity and sleep periods

Dr. Richard Pietras develops and patents treatment of ovarian cancer with squalamine in combination with other anticancer agents/ modalities (in Phase 2 clinical trials through Genaera Pharmaceuticals)

Drs. Gregory Hannon and **Stephen Elledge** develop gene silencing and genetic screening strategies to identify new potential therapeutic targets

1999

Dr. Kathryn North observes that cognitive ability does not improve as children with NF1 age, despite decreases in the number, size, and intensity of T2 hyperintensities. She also identifies high comorbidity of attention deficit hyperactivity disorder and specific learning disabilities in children with NF1

Dr. Mary Daly publishes first resource book for high-risk women considering prophylactic oophorectomy, *Ovarian Cancer Risk-Reducing Surgery: A Decision-Making Resource*

The first electronic proposal submission was offered

The BCRP sponsored its second Era of Hope conference

Dr. Eldon Jupe examines the risk association between BRCA1, BRCA2, prohibitin T allele, and breast cancer, which leads to the development of OncoVue, a risk assessment test approved by the FDA that is commercially available

2000

Dr. David Bowtell discovers that the Asn372His genotype of BRCA2 significantly increases the risk of ovarian cancer. Additionally Dr. Bowtell identifies differences in epidemiological risk factors between ovarian, fallopian, and primary peritoneal cancer

Dr. Brigitte Widemann conducts a Phase 2 trial of the farnesyltransferase inhibitor R115777 in pediatric patients with NF1 and demonstrates that the compound is well tolerated with only mild toxicities

Dr. Kai Thomenius develops components for an ultrasound imager suited to remote emergency medicine such as imaging associated with combat casualty care Dr. David Getty conducts a Phase 3 clinical trial demonstrating that stereo mammography is more accurate than standard mammography in detecting true lesions in breast cancer screening

Dr. David Getty conducts a Phase 3 clinical trial demonstrating that stereo mammography is more accurate than standard mammography in detecting true lesions in breast cancer screening

Dr. Roger Packer conducts Phase 1 studies of pirfenidone in children with NF1 and progressive plexiform neurofibromas (PNF) and determines the optimal dose of pirfenidone for treatment. Recruitment initiatives for a Phase 2 clinical trial assessing the efficacy of pirfenidone in treating NF1 and PNF have been completed

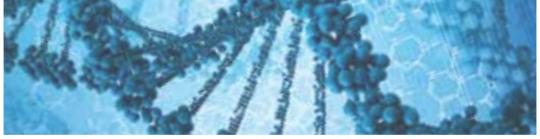
2001

Dr. Jeffrey Mason develops a liposome polymerase chain reaction assay to detect cholera toxin beta subunit in human urine

The 13 Cancer Centers in the **Prostate Cancer Clinical Trials Consortium (PCCTC)** (www.pcctc.org) headed by Dr. Howard Scher accrue more than 2,000 prostate cancer patients to 68 Phase 1 and Phase 2 clinical trials since 2006. The PCCTC advances five therapeutic candidates, including abiraterone acetate, docetaxel plus dasatinib, ipilimumab, MDV3100, and OGX-011, to Phase 3 study. The Phase 1/2 study of OGX-011 was funded by a PCRP award to Dr. Kim Chi

Drs. Santo Nicosia and **Jin Cheng** discover API-2/triciribine (now in Phase 1 clinical trials as VQD-002), as a putative inhibitor of Akt-activated cancers, which includes over 40% of ovarian tumors

Dr. Kevin Shannon develops mouse models of malignant peripheral nerve sheath tumors (MPNSTs), PNF, astrocytomas, and ependymomas for assessing the mutagenic potential of NF1 tumor therapies



Dr. David Gutmann demonstrates that NF1+/- mice lacking NF1 in astrocytes develop optic gliomas that result from axonal disorganization and damage and culminates in retinal ganglion cell death

Dr. Gordon Mills identifies lysophosphatidic acids in serum and develops humanized monoclonal antibodies that have been shown to reduce tumor volume and metastasis in preclinical studies; now in Phase 1 clinical trials for the treatment of solid tumors

Dr. Elizabeth Henske demonstrates that hamartin and tuberin play critical roles in amino acid sensing, uptake, and metabolism and tuberous sclerosis symptoms may be linked to defects in those key cellular functions

Dr. Raymond Mattingly demonstrates that a novel farnesyltransferase inhibitor combined with lovastatin reduces proliferation and induces apoptosis of malignant peripheral nerve sheet (MPNST) cells and is a potential treatment for NF1 MPNSTs

2002

The Chronic Myelogenous Research Program was established by a $5M appropriation

The Tuberous Sclerosis Complex Research Program (TSCRP) was established by a $1M appropriation

The National Prion Research Program was established by a $42.5M appropriation

The BCRP sponsored its third Era of Hope conference

The Electronic Grant System was launched, enabling electronic submission and real-time electronic management of CDMRP awards

The CDMRP published "Benefits and drawbacks of including consumer reviewers in the scientific merit review of breast cancer research," *Journal of Women's Health & Gender-Based Medicine*, 11(2), 119-136

The CDMRP published "Department of Defense Congressionally Directed Medical Research Program: Innovations in the federal funding of biomedical research," *Clinical Cancer Research*, 8(4), 957-962

The CDMRP published "Quantitative impact of including consumers in the scientific review of breast cancer research proposals," *Journal of Women's Health & Gender-Based Medicine*, 11(4), 379-388

Dr. Zhen Zhang, in collaboration with Vermillion, Inc., develops OVA1TM, the first IVDMIA (in vitro diagnostic multivariate index assay) of proteomic biomarkers cleared by the FDA to help physicians identify ovarian cancer patients whose surgeries should be referred to a gynecologic oncologist

Dr. Nancy Ratner identifies a 159-gene molecular signature distinguishing MPNST cell lines from normal Schwann cells

2003

Dr. Bernardo Sabatini conducts studies that show that the tuberous sclerosis complex (TSC) pathway regulates neuron soma size, the density and size of dendritic spines, and the properties of excitatory synapses in hippocampal pyramidal neurons both in cell culture and animal models

Dr. Vera Krymskaya identifies that a complex formation between TSC types 1 and 2 (TSC1 and TSC2) regulates cell adhesion and motility and that dysregulation of the complex formation may contribute to the pathogenesis of TSC

Dr. Robert Martuza develops an herpes simplex virus vector therapy for NF2 that reduces schwannoma tumor volume in an NF2 mouse model

Dr. Yoel Kloog generates a new class of Ras inhibitors for NF1

The PRMRP sponsored its first Military Health Research Forum

Dr. David Sabatini uses the CellProfiler, the first free, open-source system designed for flexible, high-throughput cell image analysis, as part of a high-throughput screen to identify new drug targets for treating TSC

Dr. Karen Cichowski demonstrates that NF1 is inactivated in sporadic gliomas via two mechanisms: excessive proteasomal degradation by PKC hyperactivation and homozygous NF1 loss when p53 is inactivated

2004

Dr. Jeffrey Peterson identifies Pak1 inhibitors as a treatment for NF2

Dr. Marianne Sadar discovers an extract from marine sponges that blocks activation of androgen receptors. A synthetic analog of the extract, EPI-001, shrank prostate tumors to 20% of their normal size with no toxicity in animal models

Dr. Karen Cichowski identifies a negative-feedback signaling pathway that underlies oncogene-induced senescence, a mechanism that protects benign lesions from becoming malignant in patients with NF

Dr. Steven Sparagana develops a comprehensive clinical database of TSC cases that documents the natural history and variability of TSC over the lifespan of individuals with the disease

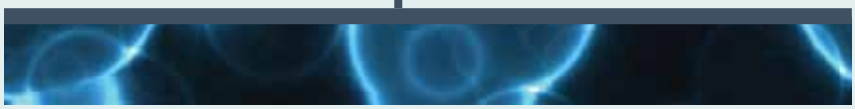
Dr. Allan Belzberg develops the tibial neuroma transposition animal model of neuroma pain to evaluate preventive strategies

Dr. Joseph Kissil shows that Pak1 is hyperactive in primary schwannomas isolated from NF2 patients and suppression of Paks 1-3 via shRNAs reduces the ability of NF2 mutant cells to grow in vitro and form tumors in a xenograft model of NF2. Long-term Pak1 inhibition via shRNA is restored through a methylation-dependent mechanism

Dr. Xiaoyuan Chen develops multimeric arginine-glycine-aspartic acid peptides with high alpha-v-beta-3 integrin affinity for positron emission tomography (PET) imaging of ovarian cancer, receives an exploratory Investigational New Drug (IND), and initiates Phase 0 studies for the peptide tracer having the greatest tumor targeting efficacy in vivo

Dr. Martin McIntosh discovers that MMP7 is elevated in serum up to 3 years prior to diagnosis of ovarian cancer

2005



Dr. Martin Pomper develops a series of PET radiotracers that target PMSA (prostate membrane-specific antigen), a protein that is made on the surface of prostate cells. The radiotracers were further developed commercially and have now moved to Phase 1 clinical trials to significantly improve imaging for patients with either newly diagnosed or recurrent prostate cancer

Dr. Cynthia Menard develops an MRI table to allow needle placement for prostate cancer patients lying on their backs (rather than side or stomach) to improve prostate gland stability during prostate biopsies, visualization of local prostate cancer recurrence after radiation treatment, and treatment to areas of recurrent tumor growth after radiotherapy

Drs. Victor-Felix Mautner and **Samuel Rabkin** demonstrate that imatinib mesylate (Gleevec®) inhibits Schwann cell viability and reduces the size of PNF in a xenograft model and reduces tumor volume of PNF fragments obtained from NF1 patients

Dr. Janet Sawicki develops a targeted treatment using nanoparticles to deliver diphtheria toxin-encoding deoxyribonucleic acid (DNA) to ovarian cancer cells, leaving healthy cells unaffected

Dr. Tin Tin Su develops a quantitative Drosophila-based assay to screen compounds and test their ability to rescue the larval lethality of TSC1 homozygous mutants

Dr. Ai Lin optimizes imidazolidinedione derivatives that are orally active with potential curative and prophylactic activity against the parasite that causes malaria

Dr. Patrick Kochanek initiates development of a resuscitation fluid for TBI incorporating colloidal polynitroxylated, pegylated hemoglobin (PNPH), offering reduced fluid volume while maintaining effective arterial pressure and neuroprotection compared to lactated Ringer's or hypertonic saline solutions

The Gulf War Illness Research Program (GWIRP) was established by a $5M appropriation

Dr. Mark Nellist identifies three regions essential for TSC1 or TSC2 function as well as a region of TSC1 required for maintaining TSC1 at sufficient levels in the cell to form a stable TSC1–TSC2 complex and inhibit mammalian target of rapamycin (mTOR)

Dr. Patricia Kruk demonstrates elevated urinary Bcl-2 as a biomarker in women at risk for ovarian cancer, and through a licensing agreement, Geopharma is developing a urinary detection device

The PRMRP sponsored the second Military Health Research Forum

2006

Dr. Fazlul Sarkar identifies a compound from cruciferous vegetables (e.g., broccoli, cauliflower, brussels sprouts, and cabbage) that inhibits prostate cancer cell growth. Dr. K.M. Rahman later shows that this compound, 3,3'-diindolylmethane (DIM), in combination with Taxotere, inhibits tumor growth by 80% in animal models. DIM has now moved into Phase 1 clinical trials

Dr. Julia Golier conducts a randomized cross-over trial of mifepristone (a glucocorticoid receptor antagonist) to determine its efficacy in improving general health and cognitive functioning in ill Gulf War veterans

Dr. Joseph Rizzo develops a retinal prosthesis that may be used to treat several forms of retinal blindness that are currently untreatable, including blindness caused by battlefield laser injury to the retina and military-related, blast-induced blindness

Dr. He Li shows that administration of corticosterone prior to or following intense, repeated stress prevents traumatic memory retrieval in an animal model of post-traumatic stress disorder (PTSD)

Dr. Jeffrey Pyne develops a virtual reality stress inoculation biofeedback training as a pre-deployment intervention to reduce PTSD development and related mental health problems

2007

The Amyotrophic Lateral Sclerosis Research Program (ALSRP) was established by $5M from the Army Research, Development, Test, and Evaluation funding

The Autism Research Program (ARP) was established by a $7.5M appropriation

The PH/TBI Research Program was established by a $301M appropriation

The PCRP sponsored its first IMPaCT conference

Dr. Liying Zhang develops an idealized three-dimensional (3D) human head model to examine the blast phenomena and determines that the maximum peak pressure transmitted to the scalp, skull, and brain was higher than the blast pressure received by the head

Dr. Robert Vogt shows that higher levels of nerve tissue antigen-specific IgG antibodies in archived dried blood spots of newborns were associated with a reduced risk of autism spectrum disorder (ASD) compared to matched controls

Dr. Paul Kizakevich develops an easy-to-use Personal Health Monitor for longitudinal data collection to study signs, symptoms, triggers, and behaviors in PTSD and mild traumatic brain injury (mTBI) patients. The device allows for the collection of comprehensive physical and physiological data while minimizing subject burden

Dr. Karen Cichowski discovers a mechanism for the development of prostate cancer metastasis whereby nuclear factor kB (NF-kB), a protein known to play a critical role in prostate cancer progression, is constitutively activated via loss of disabled homolog 2 interacting protein (DAB2IP). DAB2IP expression and subsequent activity, which control cell signaling to NF-kB, are blocked by the EZH2 protein, which has long been implicated in prostate cancer metastasis

2007 (cont.)

Dr. Mikulas Chavko determines that pressure detected in the rat brain following exposure to blast overpressure is contingent on the orientation to the blast direction, suggesting that pressure waves enter the protective tube and body by diffraction, moving in the opposite direction of the blast wave

Dr. Michael Vitek measures the safety and toxicity of COG1410 in rats and dogs to form the basis of an IND application to the FDA for the treatment of TBI. COG1410 is a mimetic of the wild-type apoE protein but it is very small and therefore crosses the blood-brain barrier and exerts anti-inflammatory and neuroprotective activities similar to wild-type apoE

Dr. Charles Levy leverages combat veterans' comfort and familiarity with communications technology and immersive environments to build a prototype virtual-world environment in which to conduct therapy for returning combat veterans with mTBI/PTSD

Dr. Serge Przedborski targets amyotrophic lateral sclerosis (ALS) drug development by examining differential gene expression in subpopulations of motor neurons that are prone to relatively different vulnerability to neurodegeneration with similar pathology and pattern in both forms of ALS, whether sporadic or familial

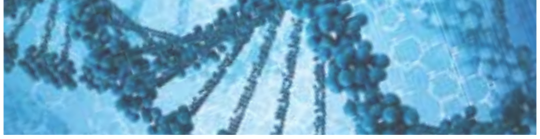
Dr. Nicholas Webster identifies the lead drug, 5E5, and 38 other promising compounds for the treatment of brain injury based on their ability to activate the TrkB receptor

Dr. Donald Stein develops a set of analogs specifically to maintain the neuroprotective properties of progesterone while increasing solubility following TBI

Dr. Peter Bergold determines that minocycline and N-acetylcysteine synergistically improve behavioral performance following moderate controlled brain injury in rats

Drs. James Tour and **Thomas Kent** of the Mission Connect Consortium synthesize potent antioxidant nanomaterials that use small carbon nanotubes to carry antioxidants for the treatment of oxidative stress following TBI, representing an entirely new class of treatment for TBI

Lt Col Jeffrey Cigrang, a STRONG STAR Consortium investigator, finds preliminary evidence through a pilot clinical trial that cognitive behavioral therapy may be successfully provided to service members in a primary care setting. Currently, a substantial number of veterans affected by PTSD do not receive the professional care they need due to the stigma associated with seeking help through a mental health clinic. This approach may help overcome this barrier to care and better meet the needs of service members



2008

The Bone Marrow Failure Research Program (BMFRP) was established by a $1M appropriation

The Deployment Related Medical Research Program (DRMRP) was established with ~$92M of the $273M appropriated in the Supplemental Appropriations Act of 2008 (Public Law 110-252)

The BCRP sponsored its fifth Era of Hope conference

Dr. Lisa Conboy investigates the effectiveness of acupuncture to address the multiple symptoms of Gulf War Illness (GWI), for which treatments can be tailored to individual needs

Dr. Vuk Stambolic implements real-time NMR to characterize the molecular mechanism of GTP catalysis by Rheb and the impact of the TSC2 GAP activity on this process. He also characterizes a series of TSC2 GAP domain mutants found in tuberous sclerosis patients and determines the molecular mechanism of action of the TSC2 GAP activity on Rheb. These studies may lead to the development of TSC2-mutation-specific therapeutic strategies

2009

More than 74,879 applications have been received to date

More than 8,086 scientists and clinicians have been funded through the CDMRP

More than 1,800 consumers have represented their communities within the CDMRP

The CDMRP provided pre- and post-award execution support for the DMRDP, the Research and Development (R&D) Arm for the Office of the Deputy Assistant Secretary of Defense for Health Affairs

The Genetic Studies of Food Allergies Research Program (GSFARP) was established by a $2.5M appropriation

The Lung Cancer Research Program (LCRP) was established by a $20M appropriation

The Multiple Sclerosis Research Program (MSRP) was established by a $5M appropriation

The Peer Reviewed Cancer Research Program (PRCRP) was established by a $16M appropriation

The PRORP was established by appropriations totaling $112M

The SCIRP was established by a $35M appropriation

2010

The PRMRP, GWIRP, and PH/TBI Research Program sponsored the third Military Health Research Forum

Dr. Ying-Hsui Su develops a padlock probe mediated DNA microarray method to detect colorectal cancer in urine samples

Dr. Peter Hammerman demonstrates discoidin domain receptor 2 (DDR2) mutations are present in 4% of squamous cell lung cancers, and DDR2 mutations are associated with sensitivity to dasatinib

2011

The BCRP sponsored its sixth Era of Hope conference

The PCRP sponsored its second IMPaCT conference

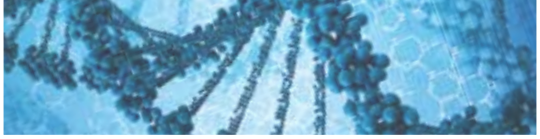
The DMDRP was established by a $4M appropriation

CDMRP Programs

The following pages highlight individual CDMRP programs, including the program's vision/mission and highlights of notable accomplishments supported by that research program. Additional information on individual programs can be found on the CDMRP website at http://cdmrp.army.mil.

CDMRP Programs	FY11 Appropriation
Amyotrophic Lateral Sclerosis	$8M
Autism	$6.4M
Bone Marrow Failure	$4.0M
Breast Cancer/Breast Cancer Research Semipostal	$150.0M
Defense Medical R&D[a]	$58.7M
Duchenne Muscular Dystrophy	$4.0M
Gulf War Illness	$8.0M
Lung Cancer	$12.8M
Multiple Sclerosis	$4.8M
Neurofibromatosis	$16.0M
Ovarian Cancer	$20.0M
Peer Reviewed Cancer	$16.0M
Peer Reviewed Medical	$50.0M
Peer Reviewed Orthopaedic	$24.0M
Prostate Cancer	$80.0M
Psychological Health/Traumatic Brain Injury[b]	$56.0M
Spinal Cord Injury	$12.0M
Tuberous Sclerosis	$6.4M

(a)The CDMRP assisted with full life-cycle management of this portion of a larger appropriation.
(b)The CDMRP provided only research award negotiation and management for this portion of a larger appropriation.



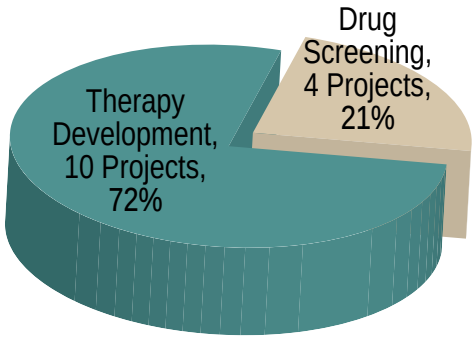
Amyotrophic Lateral Sclerosis Research Program

Vision

Improve treatment and find a cure for ALS

Mission

Fund innovative preclinical research to develop new treatments for ALS



*FY07–FY10 ALSRP Portfolio by Research Area**

***Includes FY08 in which no appropriation was made**

Program History

ALS, also known as "Lou Gehrig's disease," is an incurable, degenerative neurological disorder. For reasons that are not understood, the nerve cells of the brain and spinal cord that control voluntary muscle movement gradually deteriorate. ALS can prove difficult to diagnosis because the initial symptoms are both subtle and vague and can be attributed to a number of conditions. Average life expectancy after diagnosis ranges from 2–5 years, and about 10% of ALS patients live more than 10 years after diagnosis.[1] There are no known therapies to effectively halt the progression of ALS. Men and women who have served in the U.S. military are 60% more likely than civilians to develop a fatal muscle-wasting disease such as ALS.[2] In addition, 1990-1991 Gulf War veterans have been shown to be twice as likely to develop ALS as the general population, though the reasons for this incidence are not understood yet.

There are currently no known therapies to effectively halt the progression of ALS although one FDA-approved drug, riluzole, modestly slows progression. Several drug candidates are in clinical trials, and some show early promise. New focus areas, including transcript profiling and immune system modulation, are being investigated as novel approaches for ALS therapeutic interventions.

In June 2007, the DOD redirected $5M of FY07 Army Research, Development, Test, and Evaluation funding for the CDMRP to initiate the ALSRP as a broadly competed, peer-reviewed research program. The ALSRP has focused on supporting preclinical development of therapeutics for ALS, offering a Therapeutic Development Award in FY07 and FY09. Six awards have been made using these funds, holding the promise of improved therapies for ALS patients. For FY10, the ALSRP received a $7.5M appropriation from Congress and added a Therapeutic Idea Award to its portfolio to promote novel basic research related to therapeutics. This award mechanism proved so robust that the ALSRP is again offering both the Therapeutic Development Award and the Therapeutic Idea Award in FY11 following a new appropriation of $8M. The portfolio of research supported by the program is depicted to the left.

[1]**ALS Association.**

[2]**Weisskopf M, et al. 2004. Annual Meeting of the American Academy of Neurology, San Francisco, California.**

Protein Aggregation Inhibitors for ALS Therapy

Richard Silverman, Ph.D., Northwestern University

ALS is a clinically severe, fatal neurodegenerative disorder characterized by a progressive and irreversible loss of upper and lower motor neurons, muscle atrophy, and paralysis. Dr. Silverman, along with his collaborators, Dr. Donald R. Kirsch (Cambria Pharmaceuticals), Dr. Robert J. Ferrante (University of Pittsburgh), and Dr. Richard I. Morimoto (Northwestern University), received an ALSRP Therapeutic Development Award in 2010 to investigate protein aggregation inhibition as a potential therapeutic strategy for ameliorating disease progression in ALS. This research team performed high-throughput screens to identify compounds that protect cells against the toxic effects of SOD1 aggregation.

Dr. Silverman previously identified three lead chemotypes that protect cells from aggregated mutant SOD1: arylsulfanyl pyrazolones, pyrimidine-2,4,6-triones (PYT), and cyclohexane-1,3-diones. The investigators discovered that CMB-021805, a PYT analog, when administered at a dose of 20 mg/kg to G93A ALS mice (transgenic mice with mutant SOD1 gene at codon 93), improved survival and extended the life of the mice by 26%. Pathological findings in untreated G93A mice, including gross spinal cord atrophy and neuronal loss in the ventral horns from the lumbar spinal cord, were significantly reduced by CMB-021805 as compared to untreated ALS mice. Furthermore, when mice were treated with CMB-021805 at 10 mg/kg twice daily (BID), survival was extended by approximately 31% in the G93A mice, as compared to untreated ALS mice. The 10 mg/kg BID-treated mice also displayed a significant improvement in the gross loss of white and grey matter at 126 days by 26% and 28%, respectively, and a reduction of the loss of ventral horn neurons by 36% compared to untreated mice. Further studies showed that CMB-021805 reversed the effects of 3-nitropropionic acid, which inhibits the mitochondrial electron transport chain, suggesting that this may improve mitochondrial function. While additional experiments are needed, these findings may lead to a better understanding of the disease mechanisms that initiate ALS and help to identify targets for potential biomarkers and new therapies to combat ALS.

Preclinical Studies of Induced Pluripotent Stem Cell-Derived Astrocyte Transplantation in ALS

Nicholas Maragakis, M.D., Johns Hopkins University, Baltimore, Maryland

A recent development in stem cell technology involving induced pluripotent stem cells (iPSCs) is helping scientists more precisely understand the pathophysiology behind ALS. iPSCs start as skin cells harvested from an ALS patient that are re-programmed in culture (through exposure to certain transcription factors), first into stem cells that have the capacity to become any type of cell, and then differentiated into glial-restricted precursor cells (iPSC-GRPs). The iPSC-GRPs act like neural developmental stem cells and can become motor neurons, astrocytes, or oligodendrocytes in culture. Evidence suggests that astrocytes and other non-neuronal cell types play a role in the neurodegeneration of ALS. These iPSC-GRPs may ultimately be transplanted into patients to treat ALS. Replacement of astrocytes derived from iPSC-GRPs may offer a technically and biologically more feasible treatment modality for ALS patients compared with motor neuron transplantation.

Using funding from an FY09 ALSRP Therapeutic Development Award, Dr. Maragakis is initiating preclinical studies of iPSC-GRPs to assess their therapeutic potential. Dr. Maragakis will examine whether human iPSC-GRPs derived from either sporadic ALS (sALS), familial SOD1-mediated ALS (fALS), or normal control subjects have the same capacity for engraftment, survival, and neuroprotective qualities following transplantation. By comparing normal iPSC-GRPs with sALS iPSC-GRPs and fALS iPSC-GRPs, Dr. Maragakis will attempt to reveal inherent differences in astrocyte biology related to ALS, providing potential insight into ALS disease mechanisms and potential therapies.

Autism Research Program

Vision

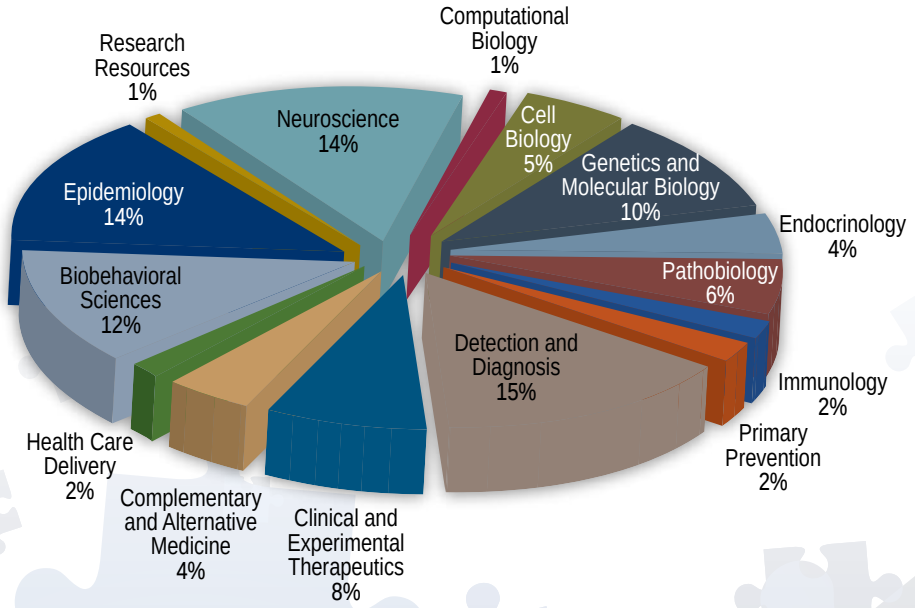
Improve the lives of individuals with autism spectrum disorders now

Mission

Promote innovative research that advances the understanding of autism spectrum disorders and leads to improved outcomes

Program History

To address the rising incidence of Autism Spectrum Disorders (ASD) in the United States where up to 1 in 110 children are diagnosed on the spectrum yearly, Congress appropriated $7.5M in FY07 to the ARP. Congressional appropriations to the ARP total $36.3M, including $6.4M in FY11. The immediacy of the program's vision has imparted a strong sense of action and steered the investment strategy of the ARP for the last 4 years. While the cause of ASD is unknown, the imperative to improve the lives of all individuals living with ASD and their families drives the ARP toward innovative, high-risk/high-gain research for the present and the future. Projects funded by this program span the basic, clinical, and population-based research, as shown below.



FY07–FY10 ARP Portfolio by Research Area

> *The Autism Research Program has worked diligently to stick to the initial vision to improve the lives of people with autism now and to maintain a diverse portfolio of research objectives. I have been with this program since the beginning and am very proud of the projects we have funded, which seek to do just that.*
>
> *Shelley Reynolds, FY11 IP Member*

> *It has been a great experience working with consumers on the ARP board. Our discussions guide the program to fund not only the best science, but the best science relevant to the needs of people with autism.*
>
> *Diane Chugani, Ph.D., FY11 IP Member*

From left to right: Iryna M. Ethell, Slawomir Sloniowski, Deirdre S. Davis and Monica J. Carson

Microglia as Biosensors and Effectors of Neurodysfunction

Monica J. Carson, Ph.D., University of California, Riverside

The symptoms of ASD appear several months to years after birth, following a period of normal growth and development. Defects in the formation of dendritic spines, and surface protrusions on neurons that receive excitatory input and play a role in cognitive development, have been observed in the brains of some individuals with ASD (i.e., individuals with Rett Syndrome). It has been hypothesized that systemic inflammation resulting from perinatal or early postnatal infections may be a reason for these deficits.

Dr. Carson received an FY08 Concept Award to characterize the effects of early postnatal inflammation in the hippocampus. Lipopolysaccharide (LPS), a component of some bacteria, was injected into non-pregnant adult mice, nursing dams, and mouse pups to mimic an infection. Systemic inflammation triggered a greater influx of proinflammatory macrophages into the developing brain than into the mature brain. The team demonstrated that the ratio of anti-inflammatory to proinflammatory receptors on microglia, the resident immune cell of the central nervous system (CNS), changes during normal development. Morphological analysis of dendritic spines in the hippocampus of pups treated with LPS revealed primarily age-associated increases in spine head and size and decreases in spine length. Pups injected with LPS on postnatal day 14 showed a pronounced reduction in excitatory synapses. Dr. Carson suggests that this outcome may be a neuroprotective response during hippocampal maturation, limiting the susceptibility of hippocampal neurons to cell death.

This study describes developmentally regulated changes in intrinsic immunity of the CNS and suggests that high levels of anti-inflammatory (neuroprotective) receptors on microglia may be required to sustain optimal brain function in infancy and childhood, when exposure to infections is common.

Ann and Philip Gibbons

A Consumer's Perspective: Ann Gibbons, ARP

Ann Gibbons, a Consumer Reviewer and IP member for the ARP tells the story of lives touched by ASD.

I often say I did not choose my mission; it was chosen for me. My happy baby boy, Philip, was 15 months old, and we went to a friend's house to play. Philip seemed different—at the front door he balked, refusing to enter the playroom filled with noisy toddlers. Just a few weeks earlier, he had toddled happily into this room. At home, he stopped stacking his wooden blocks; instead, he banged them on the coffee table. On our walks, he no longer talked about the animals we passed; instead, he began to drop sticks methodically into the storm drain, one after the other. Finally, at 27 months old, Philip was diagnosed with an autism spectrum disorder. It was 1990.

I am no hero; I'm just an ordinary person. Shakespeare once said, "Some men are born great…and others have greatness thrust upon them." I'm definitely not great. But I have tried to carry out the mission that was thrust upon me. I have tried to pursue the most scientifically based and effective treatments for my son. The prevalence of autism has apparently skyrocketed since Philip was diagnosed, but we still know so little about what causes it and what could prevent it.

Yet, I have hope. Philip is now 23 years old and, although he cannot go to work independently, he is a happy member of our household and has been greatly helped by behavioral therapy and medication to address his anxiety. I am gratified to see the increase in awareness and funding for autism and I am ever more confident that breakthroughs are within our reach.

Bone Marrow Failure Research Program

Vision

To understand and cure bone marrow failure disease

Mission

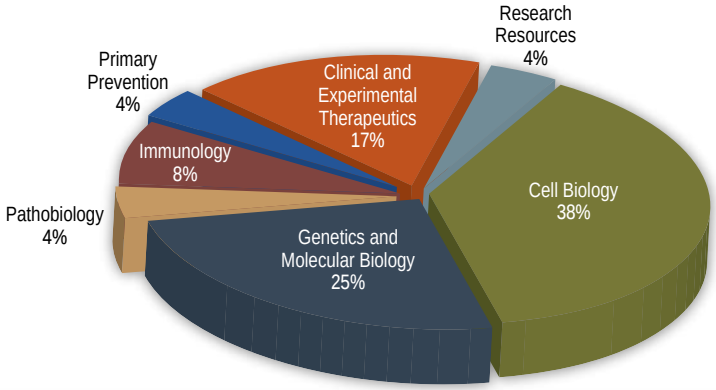
To encourage and support innovative research that is committed to advancing the understanding of inherited and acquired bone marrow failure disease, thereby improving the health of affected individuals, with the ultimate goals of prevention and cure

"Serving on the Integration Panel is a unique learning experience beyond any scientific peer review, from shaping the research agenda to strategic funding recommendations."

Peter Kurre, M.D.,
BMFRP FY11 IP Member

Program History

In FY08, Congress appropriated $1M to the BMFRP. Bone marrow failure is a term used to explain the outcome of several different diseases and conditions. Disorders of the bone marrow are critical and can lead to life-threatening diseases where the bone marrow does not function or produces abnormal cells of the blood system. Exposures to viruses, chemicals, and environmental toxins (a risk for service members) may lead to acquired bone marrow failure. Autoimmune responses can lead to bone marrow failure as well. Acquired bone marrow failure diseases include aplastic anemia, myelodysplasia, paroxysmal nocturnal hemoglobinuria, and pure red cell aplasia. There are inherited forms of bone marrow failure including Fanconi anemia (FA), dyskeratosis congenita, Shwachman-Diamond syndrome, and Diamond-Blackfan anemia. Since its inception, a total of $13.75M has been dedicated to the research of bone marrow failure through the BMFRP to study innovative research to advance the understanding of and cure bone marrow failure. The pie chart below reflects the BMFRP portfolio by research area.



FY08–FY10 BMFRP Portfolio by Research Area

Correction of Human Fanconi Anemia-Induced Pluripotent Cells by Homologous Recombination

Bruce Blazar, M.D., University of Minnesota, Twin Cities and J. Keith Joung, M.D., Ph.D., (pictured), Massachusetts General Hospital

FA is an inherited bone marrow failure disorder caused by genetic defects in certain DNA-repair proteins. The average survival rate for a patient with FA is approximately 20 years, and the current standard of care is a hematopoietic cell transplant from a donor. Unfortunately, due to defects in DNA repair, FA patients often suffer significant toxicities from the chemotherapy needed for this treatment.

Drs. Blazar and Joung were awarded an FY09 Synergistic Idea Award to develop a new, safer treatment for patients with FA that uses the patient's own cells. Using their combined expertise in zinc finger nuclease (ZFN)-mediated gene editing and somatic cell reprogramming, their long-term strategy is to extract cells from an FA patient, repair them, transplant the repaired cells back into the patient's bone marrow, and in the process avoid most of the pitfalls of traditional bone marrow transplantation and gene therapy. Dr. Joung will use his expertise with Oligomerized Pool Engineering (OPEN) to generate ZFNs that will accurately target FA defects for gene repair. OPEN, a technique developed by Dr. Joung, has been shown to generate engineered zinc finger arrays capable of binding to specified target DNA sequences with high activities. Additionally, rather than attempt to extract a patient's bone marrow cells, which are fragile and few in number at the time of diagnosis, Dr. Blazar will exploit recent advances in cellular re-programming to convert epithelial (skin) cells into iPSCs. Dr. Blazar will use episomal DNA, termed minicircles, to deliver re-programming genes. Using the ZFNs developed by Dr. Joung to target FA mutations and the minicircle technology for gene insertion, Dr. Blazar will repair the iPSCs, thereby creating a source of immature stem cells capable of differentiating into the blood-forming cells that the patient lacks. The integration of expertise and novel technologies from these two investigators will create a renewable source of patient-specific, gene-corrected hematopoietic cells that can be used to treat FA; this concept can be used in other bone marrow disorders.

A Consumer's Perspective: Lisa M. Minter, Ph.D., BMFRP IP Chair

I first heard of "aplastic anemia" as an undergraduate studying medical technology. The next time I encountered the term was in 1994, when my 12-year-old daughter, Stephanie Phakos, was diagnosed with the disease. After an initial response to immunosuppressive treatments, Stephanie relapsed and, ultimately, lost her courageous battle with this devastating illness. Like so many parents who have lost children, I was determined that from her loss something "positive" would emerge. With overwhelming support from my husband and our three sons, I entered graduate school and, in 2001, earned my doctorate in Animal Biotechnology and Biomedical Sciences at the University of Massachusetts, Amherst.

During the early stages of my research program, I looked for ways to make a broader impact on the field of bone marrow failure research. I found a critically important way of doing this was by serving on the CDMRP BMFRP Integration Panel. In 2009 I was invited to join the panel, and I assumed my present position as chair in 2011. In my 3 years serving on the panel, I have had the good fortune to work with exceptionally smart, talented, and dedicated professionals, each of whom brings a unique expertise and perspective to the panel. Unlike many scientific review panels, we are fortunate to have on the panel consumers who have past or ongoing direct and personal experience with bone marrow failure. Input from these individuals provides both a human face and a sense of urgency to our task of crafting funding mechanisms that will serve to advance our knowledge of underlying mechanisms of disease and innovative treatment options by supporting the best scientific proposals we can.

It has been nearly 16 years since I lost my daughter to aplastic anemia. Through participation in the BMFRP and my own research in bone marrow failure, I continue to hope that I can make something positive emerge.

Breast Cancer Research Program

Vision

To eradicate breast cancer by funding innovative, high-impact research through a partnership of scientists and consumers

Program Goals

Encourage innovation and stimulate creativity

Support research with high-impact potential

Foster new directions and fill important gaps

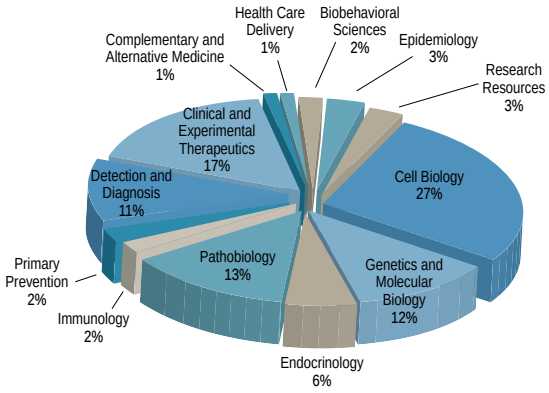
Facilitate multidisciplinary and synergistic collaborations

Bring new investigators into the breast cancer field

Train investigators early in their careers

Program History

The BCRP was established in 1992 as a result of the powerful efforts of breast cancer advocates. Their continued efforts, in concert with the program's successes, have resulted in more than $2.6B in congressional appropriations through FY11. The BCRP vision is adapted yearly to ensure that the program remains responsive to what is currently happening in the research community. Over the years, the BCRP has created and introduced unique mechanisms to support a broad portfolio of research and training awards that have transformed the breast cancer field. The BCRP challenges scientists to pursue high-risk, high-reward research that has the potential to make major leaps toward eradicating the disease. The program is committed to supporting new, innovative ideas that reflect the most recent discoveries in the field and could lead to breakthroughs. The BCRP also promotes synergistic collaborations across disciplines and integrates scientists and consumers in unique research partnerships. The BCRP training and early-career awards have provided the foundation for many of today's leading breast cancer researchers, and the program continues to invest in the future generation of breast cancer experts. Through its award mechanisms and innovative approaches, the BCRP plays a leading role in the breast cancer research community.



FY92–FY10 BCRP Portfolio by Research Area

FY11 Award Mechanisms	
Postdoctoral Fellowship Award	Supports the training of exceptionally talented recent doctoral graduates
Idea Award	Supports research that has extraordinary potential to lead to major advancements in breast cancer research
Era of Hope Scholar Award	Supports exceptionally talented early-career scientists who are the "best and brightest" in their fields
Innovator Award	Supports visionary individuals who have demonstrated creativity, innovative work, and leadership in any field
Transformative Vision Award	Supports a coordinated, translational research effort involving multiple PIs and advocates to answer a question of major importance in breast cancer prevention or treatment
Clinical Translational Research Award	Supports advanced translational research leading to a clinical trial, to significantly improve current approaches to breast cancer prevention and/or therapy
Impact Award	Supports unique research projects that could revolutionize the understanding, prevention, and/or treatment of breast cancer

Notable BCRP-supported products and outcomes

Making an Impact

Herceptin – Dennis Slamon
Provided early funding for research leading to the development of monoclonal antibodies against the HER-2/neu receptor

Sentinel Lymph Node Biopsy – Kathryn Verbanac and Lorraine Tafra
Supported a clinical trial testing the validity and accuracy of sentinel lymph node biopsy, the current standard of care for disease staging

PTEN Tumor Suppressor Gene – Michael Wigler
Funded the discovery of a homozygously deleted locus on chromosome 10, which identified the PTEN mutation found in many cancers

BRCA2 Mutation – David Goldgar and Susan Neuhausen
Funded the discovery of the founder BRCA2 617delT mutation in Ashkenazi Jews

OncoVue – Eldon Jupe
Supported early work leading to the development of a breast cancer risk assessment test that is now commercially available

ATLAS Clinical Trial – Richard Peto
Supported initiation of the largest breast cancer treatment trial ever undertaken, examining the optimal duration of adjuvant tamoxifen in early-stage breast cancer

shRNA Libraries – Gregory Hannon and Stephen Elledge
Supported the development of shRNA libraries for gene silencing and genetic screening strategies, now commercially available

Margaret Dyson Family Risk Assessment Program – Mary Daly
Supported the establishment of a high-risk breast cancer registry, which evolved into a program that now serves a large urban area with risk assessment, screening, and preventive services

Skp2 Expression – Michele Pagano
Supported the discovery that high Skp2 expression correlates with destabilization of p27 and poor survival; immunohistochemical analysis of Skp2 and p27 is now common practice in clinical pathology laboratories

In the Pipeline

Three-Dimensional Culture Systems – Mina Bissell
Supported the development of a 3D culture system and assay to study breast cancer heterogeneity and the role of tissue microenvironment

Disparity in Minority Populations – Funmi Olopade
Supported early studies on genetic risk factors that contribute to the high incidence and mortality from breast cancer in young African American women

E75, a HER2/neu-Derived Peptide Vaccine – Constantin Ioannides
Supported characterization of immunodominant epitopes that led to the development of an immunogenic peptide-based vaccine that is now entering Phase 3 clinical trials

Molecular Breast Imaging – Carrie Hruska
Supported clinical studies to determine if molecular breast imaging has comparable sensitivity and specificity to MRI and may be a more cost-effective alternative

Optical Spectroscopy – Nimmi Ramanujam
Supported the development and clinical testing of optical spectroscopy to better identify tumor margins during surgery

Homing Peptides – Erkki Ruoslahti
Funded the identification of homing peptides that specifically home to breast tumors and have potential to deliver therapeutics with higher efficacy and reduced side effects

HER2 Bi-Armed Activated T cells (HB-ATC) – Lawrence Lum
Supported early work leading to discovery that HB-ATC induce memory antigen-specific T cells directed at HER2/neu; currently in Phase 2 clinical trials

ALM, Bispecific scFv Molecule – Gregory Adams
Funded preliminary work leading to development of ALM, which co-targets HER2 and HER3; patented and commercially licensed, now in Phase 1 clinical trials

Breast Cancer Research Semipostal Program

Recent Awards

FY09

- **Peggy Reynolds, Cancer Prevention Institute of California**
  - "Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk"
- **John Wysolmerski, Yale University**
  - "Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer"

FY10

- **Pepper Schedin, University of Colorado, Denver**
  - "The Immune Modulatory Program of Post-Partum Involution Promotes Pregnancy-Associated Breast Cancer"
- **Anthony Leung, Johns Hopkins University**
  - "The Role of Poly(ADP-Ribose) in microRNA Activity in Breast Cancers"

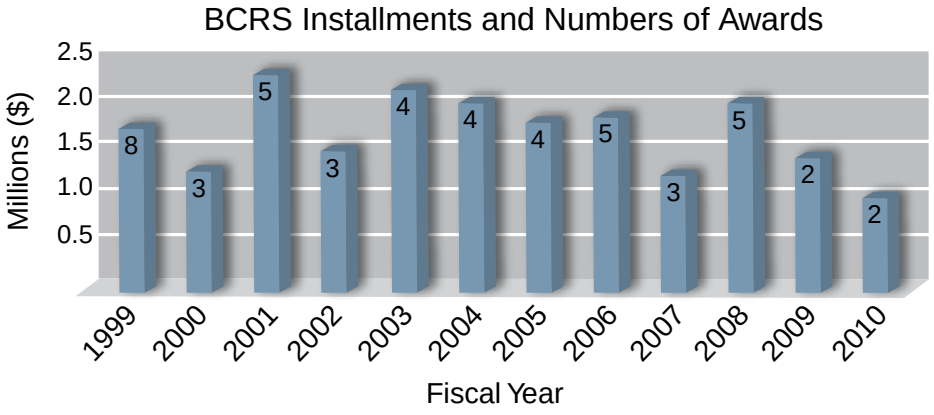
Program History

As a result of the efforts of breast cancer advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the U.S. Postal Service's issuance of a new first-class stamp, the BCRS. The stamp, which costs 55¢, can be purchased on a voluntary basis by the public. Net revenues from sales of the BCRS are provided to two designated funding agencies, the DOD BCRP and the National Institutes of Health, to support breast cancer research. Public Law 110-150 reauthorized the BCRS through December 31, 2011.

Research and Management Cost Allocations

Since the BCRS was first issued in 1998, the monies received by the BCRP through FY10 have been used to fully or partially fund 45 Idea Awards and 3 Synergistic Idea Awards. Both award mechanisms support highly innovative, high-risk, high-reward research that could lead to critical discoveries in breast cancer. As with all BCRP awards, applications funded through the BCRS program are reviewed according to the two-tiered review system.

Total Proceeds from BCRS	**$20,931,948.89**
Research	$19,943,757.11
Management Costs	$988,191.78



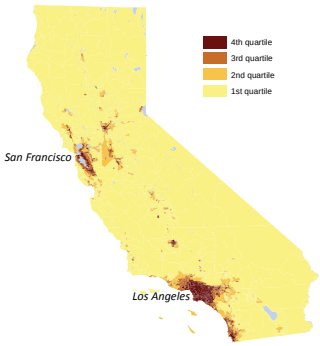
The impact of this method of drug therapy would lie not only in the selective targeting of breast cancer tumors, but also in the reduction of the side effects experienced by women undergoing conventional chemotherapy for breast cancer.

Exerpt from Dr. Youngjae You research project, see opposite page

Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk

Peggy Reynolds, Ph.D., M.P.H., Cancer Prevention Institute of California

The incidence rates of breast cancer have been known to vary dramatically based on geographic region, with higher rates found in industrialized and urban regions. This disparity led to the idea that these rates could be associated with higher exposure to environmental hazards. California has some of the highest rates of breast cancer worldwide, with higher concentrations of cases in the San Francisco and Los Angeles urban centers, which have high levels of hazardous air pollutants (HAPs). Dr. Reynolds received an FY09 Idea Award to evaluate the risk of developing breast cancer in association with the estimated exposure to HAPs through an analysis of the California Teachers Study (CTS). The CTS is the largest prospective cohort study to date that was specifically designed to study breast cancer. Approximately 125,000 women have taken part in this study and represent a geographically dispersed population of California. The focus of Dr. Reynolds' study is to analyze the identified cases of invasive breast cancer within this cohort, as obtained through the California Cancer Registry, along with data obtained from the Environmental Protection Agency (EPA) regarding the estimated outdoor concentrations of HAPs. The use of a geographic information system will allow for an assignment of the levels of specific HAP compounds or classes of compounds with the individual addresses of CTS participants. Analysis will include evaluating the importance of individual compounds and their effects on breast cancer risk, along with the collective risk of exposure to multiple HAPs. Currently, Dr. Reynolds has completed the necessary residential address geocoding and has focused on selecting the priority compounds and identifying the optimal strategy for using the EPA-modeled data. The overall impact of this study would come from the identification of specific air pollutants that increase the risk of developing breast cancer following exposure.

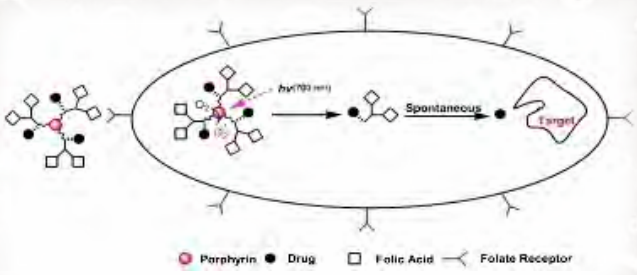


Modeled Benzene Concentrations California, 2002

Targeted Delivery and Remote-Controlled Release of Chemotherapeutic Agents

Youngjae You, Ph.D., University of Oklahoma Health Sciences Center

The systemic delivery of chemotherapy results in the death of both cancerous cells and fast-growing but otherwise healthy cells. Patients receiving this type of nonselective therapy unfortunately experience significant and undesirable side effects. Dr. You, recipient of an FY08 Idea Award, is addressing this problem by developing a novel drug delivery strategy involving the use of localized chemotherapy specifically engineered to target breast cancer cells, without affecting normal cells. Since breast cancer cells have been found to express a higher level of folate receptor over that of normal cells, Dr. You is developing a strategy that will capitalize on this difference by conjugating folic acid with a core-modified porphyrin and a linker tethered to the drug of choice. The addition of folic acid will allow for the specific targeting of breast cancer cells, while the linker will be cleavable during the irradiation of breast tissue. The release of drugs would then be controlled, thus minimizing the side effects seen with systemic delivery. Dr. You proposed the synthesis of the envisioned conjugated molecules using the drugs paclitaxel and topotecan and will conduct studies to measure not only the kinetics of the controlled release of these drugs, but also the mechanisms of folate receptor-mediated uptake. The impact of this method of drug therapy would lie not only in the selective targeting of breast cancer tumors, but also in the reduction of the side effects experienced by women undergoing conventional chemotherapy.



Defense Medical Research and Development Program Execution

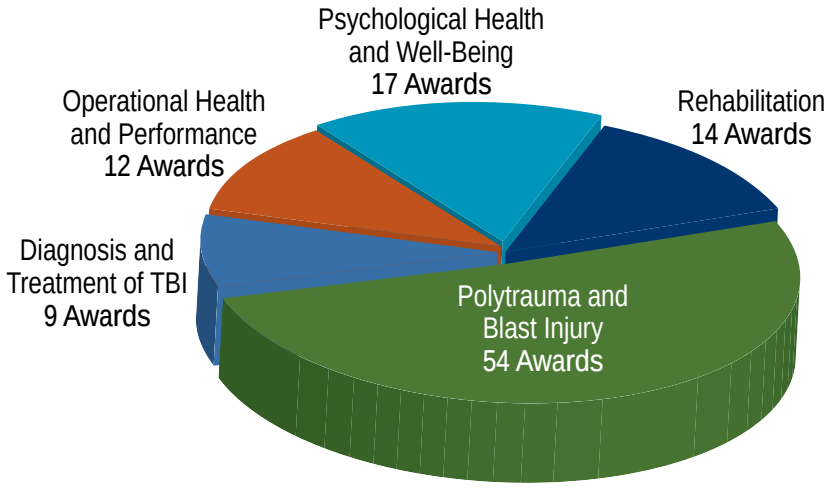
Vision

To provide outstanding pre- and post-award execution support to the Defense Health Program (DHP) DMRDP (http://dmrdp.fhpr.osd.mil/), in alignment with implementation of the research agenda for the DHP Medical Research and Development Office. These efforts will help to fulfill the priority to advance medical R&D for wounded warriors and to expedite the delivery of products and solutions to service members and their families.

FY10 Execution Support to the DMRDP

DMRDP execution responsibility was assigned to the USAMRMC in FY10 in four military-relevant focus areas aligned with four DOD Joint Program Committees (JPCs), for more information. see page 8), including Military Infectious Diseases (JPC-2), Military Operational Medicine (JPC-5), Combat Casualty Care (JPC-6), and Military Clinical and Rehabilitative Medicine (JPC-8). Key research gaps and emphasis areas were established by each JPC and proposals solicited accordingly. The JPCs consist of tri-service military and non-military medical and programmatic experts and representatives from the Departments of Veterans Affairs (VA) and Health and Human Services (HHS).

The CDMRP provided pre- and post-award execution support for approximately $1.1M of the FY10 DMRDP funds assigned to USAMRMC. Two extramural DMRDP Program Announcements (a Basic Research Award announcement and an Applied Research and Advanced Technology Development Award announcement) were utilized to target the initial DMRDP portfolio elements. These two solicitations resulted in 106 awards across JPCs 2, 5, 6, and 8; note details below.



Additional portfolio details are provided at http://cdmrp.army.mil/dmrdp/default

Chiropractic Research Program

In accordance with the FY10 National Defense Authorization Act, DMRDP R&D funds supported the establishment of the Chiropractic Clinical Trial Award for research on the outcomes of chiropractic treatment in the military health system. In partnership with JPC-8, CDMRP oversaw the review and award of a $7.5M grant to the RAND Corporation to carry out the proposal "Assessment of Chiropractic Treatment of Low Back Pain, Military Readiness, and Smoking Cessation in Military Active Duty Personnel," or ACT. Principal Investigator Ian Coulter, Ph.D. of RAND Corporation is joined by investigators at Samueli Institute and Palmer College of Chiropractic to conduct three clinical studies with active duty personnel from several military sites across the nation. The studies will: (1) compare pain and functional outcomes of chiropractic manipulation therapy plus standard care to standard care alone in a randomized, controlled trial of active duty military personnel with nonsurgical acute, subacute or chronic low back pain; (2) measure and compare changes in smoking behavior after participation in a smoking cessation program offered with chiropractic manipulation therapy plus standard care or with standard care alone; (3) assess the effect of chiropractic manipulation therapy on military readiness, by comparing pre- and post-treatment differences in reflexes and reaction times in Special Operation Forces; and (4) determine differences in strength, balance, and likelihood of reinjury between combat-ready troops receiving either chiropractic manipulation therapy or sham manipulation. Study results are expected to provide insight into risks and benefits of expanding chiropractic care within the military health system.

DMRDP Leverages CSI Programs for Portfolio Enhancement

In addition to execution support directly aligned with FY10 DMRDP funding, CDMRP has provided management support for CSI programs closely aligned with the program thrusts of the DHP DMRDP, including the Peer Reviewed Orthopaedic, Spinal Cord Injury, and Psychological Health/ Traumatic Brain Injury Research Programs. "Management of each of these programs in FY10 included coordination with relevant JPCs during vision setting, programmatic review, and award management. The JPCs provided guidance on military relevant research priorities and, through their knowledge and oversight of all core and CSI research efforts across the DOD, Veterans Affairs, and Health and Human Services identified opportunities to leverage DMRDP research gaps with CSI funding opportunities. This approach to coordination and leveraging across the DHP provides effective support to the research most directly relevant. These partnerships allow for a focus on supporting the research most directly relevant to the health of the warfighter while maintaining CDMRP's vision of finding and funding the best research possible to advance injury treatment and eradicate disease for the benefit of the general public.

Deployment Related Medical Research Program

Vision

To improve the health and/or mitigate injury of deployed military personnel and their family members by finding new solutions to the prevention, diagnosis, and treatment of deployment-related injuries and psychological challenges

Outcomes

To date, the 53 awards made by the DRMRP have resulted in:

17 **Publications**

6 **Patent applications**

1 **Additional grant obtained for further investigation**

Program History

The DRMRP was established in FY08 to support peer-reviewed research focused on emergent approaches and technologies critical to advancing the health and welfare of deployed military personnel and their families. Approximately $101.9M of the $273M provided in the Appropriations Act of 2008 (Public Law 110-252) was utilized to support the DRMRP. In subsequent years, biomedical research funding focusing on deployment related conditions and/or injuries has been funded through the Defense Medical Research and Development Program (see pages 36–37 for additional information).

To date, a total of 50 research projects have been funded through the DRMRP. These projects were funded across a variety of topic areas relevant to the health and welfare of deployed military personnel and their families, including:

- Blood safety and blood products
- Injury prevention
- Final development of medical devices for use in-theater (including portable suction machines and electrocardiograms for theater hospitals)
- Wound infection vaccines
- TBI and psychological health (including PTSD)
- Wound infection and healing
- Trauma treatment and rehabilitation (including face, visual/ocular, and nerve damage; dental; and auditory systems)

A Transportable Pathogen-Reduction System for Treatment of Whole Blood

Raymond Goodrich, Ph.D., CaridianBCT Biotechnologies, Lakewood, Colorado

During combat, fresh whole blood (FWB) is used to treat life-threatening blood loss resulting from traumatic injuries when screened blood components are unavailable. While FWB may be critical in saving the lives of injured warriors, it is often transfused without any donor screening, nor standard viral testing. Additionally, FWB is used without leukoreduction, which introduces a large number of viable white blood cells into severely injured patients, potentially increasing the rate of infections and other serious immunological complications.

Dr. Goodrich and his research group, recipients of an FY08 DRMRP Advanced Technology/Therapeutic Development Award,

aim to develop a portable, disposable device for pathogen reduction in FWB that will minimize the risk of infectious disease transmission as well as potential adverse immunological effects of bypassing leukoreduction. With the award, Dr. Goodrich and his team are developing a prototype for the device (named the Mirasol System for Whole Blood) that uses riboflavin (vitamin B2) and UV light to rapidly inactivate pathogens and leukocytes in whole blood. Validation and optimization studies are being conducted for the device's effectiveness against pathogens including bacteria, viruses, and parasites. Dr. Goodrich plans on assessing the quality and safety of FWB for use in patients following Mirasol System treatment under various storage conditions. When this phase of the study is complete, the Mirasol System will undergo operational testing in simulated combat environments.

Optimizing Biomechanical Analysis to Improve Running-Specific Prostheses

Jae Kun Shim, Ph.D., University of Maryland, College Park

Running is an ingrained part of military culture and a functional goal for many military amputees. Previous studies modeling amputee running have used erroneous methodology that has not been validated. This has likely resulted in large errors in biomechanic and kinetic calculations that are used in the design of prostheses. Furthermore, these studies have mostly been conducted in prostheses designed for walking and standing, rather than running. Dr. Shim received an award to develop and validate a new model for running-specific prostheses that could lead to improvements in current prosthetic designs.

Motion analysis will be conducted using a four-camera motion capture system that will collect 3D positional data of reflective markers placed along the running-specific prostheses. Forces will be applied to simulate running. Inverse dynamics analysis will be conducted to provide a precise estimate of the joint kinetics and energetics experienced while an amputee is running. From these data, optimal reflective marker sets that yield the smallest error will be identified.

To date Dr. Shim has set up an MTS machine and designed a protocol involving reflective marker and force transducer placement. Preliminary data from running prostheses have been generated.

Sealing Penetrating Eye Injuries Using Photoactivated Bonding

Irene E. Kochevar, Ph.D. and Col Anthony J. Johnson, M.D., Massachusetts General Hospital

Penetrating eye injuries from improvised explosive devices are not uncommon in current military conflicts. Lacerations to the cornea and sclera require immediate, waterproof closure to stabilize the wound and prevent endophthalmitis (infection of the intraocular cavity), which can cause permanent loss of vision or loss of the eye itself. Eye lacerations are generally treated with sutures or cyanoacrylate glue as a temporary stabilization technique when surgery is not immediately possible. While these methods are useful, applying sutures is a lengthy surgical procedure requiring a skilled ophthalmologist, and cyanoacrylate glue requires subsequent surgical intervention and can cause damage to the adjacent tissue during removal. Dr. Kochevar and Col Johnson received an award to assess an advanced technology called Photochemical Tissue Bonding (PTB) as a potential alternative for sutures or cyanoacrylate glue for treating ocular lacerations. In PTB, a green laser activates the immediate formation of molecular bridges between a layer of amniotic membrane and the surface of the eye without collateral damage, and the eye can heal without further intervention. Importantly, PTB may be quickly administered by physicians without extensive ophthalmologic training due to its simplicity, and it may more effectively preserve the vision of wounded warriors in combat.

Duchenne Muscular Dystrophy Research Program

Vision

To extend and improve the function, quality of life, and life span for all individuals diagnosed with DMD

Mission

To fund research to accelerate the development and clinical testing of new therapeutics and increase our understanding of successes and failures of therapeutics in clinical trials

Program History

Duchenne muscular dystrophy (DMD) affects approximately 1 of every 3,500 male infants (about 20,000 new cases a year). This form of muscular dystrophy results from a mutation in the dystrophin gene that leads to an absence of dystrophin in muscle cells, allowing these cells to be easily damaged. Boys living with DMD experience devastating muscle weakness that affects the skeletal muscles, heart, and respiratory muscles. Symptoms of DMD typically develop prior to age 5 and by age 12 most patients are confined to a wheelchair. Young men with DMD rarely live beyond their early 30s.

A much milder version of DMD is Becker muscular dystrophy (BMD). The onset of BMD usually occurs in the teens or in early adulthood, and the course of the disease is slower and less predictable than for DMD.

Currently there are many challenges that exist for the DMD research community to advance our knowledge and treat this disease. These challenges include:

- A better understanding of current animal models, muscle regeneration, dystrophin function, and the downstream effects of dystrophin deficiency
- Development of new in vitro and in vivo models, validated biomarkers, and clinical outcome measurements
- Further development of cell, gene, biologic, and small molecule therapies and repurposing FDA-approved therapeutics
- A substantial need to increase the workforce in DMD research

To address these challenges, Congress established the DMDRP in FY11 to promote the understanding, diagnosis, and treatment of DMD. The FY11 congressional appropriation to the DMDRP was $4M.

"This is an incredibly exciting time for patients and families living with Duchenne muscular dystrophy. Many promising and novel therapies are now being developed and tested. The CDMRP is at the forefront of supporting these critical efforts."

Justin Fallon, Ph.D., FY11 IP Member

Duchenne muscular dystrophy is the most common, lethal diagnosis of childhood. While some muscular dystrophy cases are predictable, Duchenne happens spontaneously. The incredible support of the DMDRP is expanding research and allowing us to inch that much closer to ending Duchenne. By supporting a rare disease like Duchenne so generously, the entire rare disease community stands to gain from the progress being made. There is no doubt that we will be victorious against Duchenne with DMDRP on our side.

Pat Furlong, FY11 IP Chair and Consumer Reviewer

FY11 DMDRP Funding Opportunities

The DMDRP will support research studies that contribute to our understanding of the mechanisms of initiation, progression, and/or improving patient care for DMD. The award mechanism offered by the DMDRP—the Investigator-Initiated Research Award—will promote translational research that will accelerate the movement of promising ideas into clinical applications. The DMDRP is interested in studies that address the following DMD research focus areas:

- Developing new biomarkers to improve evaluation of diagnosis, disease severity, disease progression, and/or response to treatment
- Assessment of clinical trial outcomes, such as:
  - Molecular, functional, imaging, etc.
  - Testing and validating surrogate markers
  - Evaluating potential composite scores for outcomes assessment
  - Patient outcomes, e.g., quality of life and activities of daily living
- Ancillary studies conducted in conjunction with clinical trials or observational studies
- Characterization of animal models and development of greater access to them
- Extension or expansion of preclinical data in support of the therapeutic development path. This could include preparation for IND and clinical trials

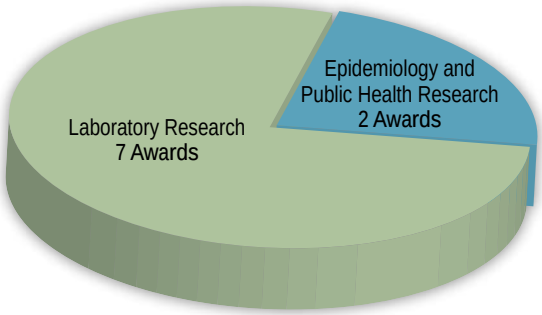
Genetic Studies of Food Allergies Research Program

Food allergy is an immune system reaction that occurs soon after eating a certain food. Ingestion of even a tiny amount of the allergy-causing food may trigger the sudden release of chemicals, including histamine, resulting in symptoms of an allergic reaction. The symptoms may be mild (rashes, hives, itching, swelling, etc.) or severe (trouble breathing, wheezing, loss of consciousness, etc.). A food allergy is potentially life-threatening and affects an estimated 6%–8% of children under age 4 and about 4% of adults. Currently, there is no cure for food allergies.

Program History

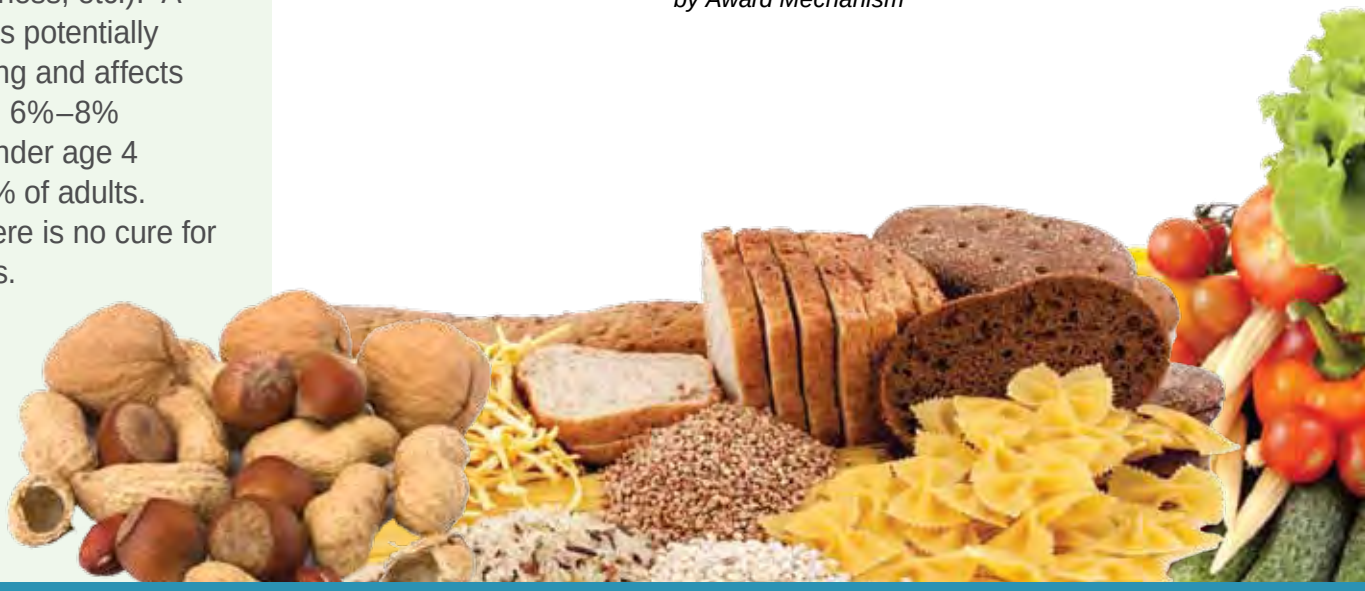
The GSFARP was established in FY09 with a $2.5M appropriation to provide support for scientifically meritorious genetic research focused on food allergies. The FY10 appropriation was $1.875M; there are no appropriations for FY11.

Through a variety of award mechanisms, the portfolio of funded research spans laboratory, epidemiology, and public health research, as shown below.



FY09–FY10 GSFARP Portfolio by Research Discipline

FY09–FY10 GSFARP Portfolio by Award Mechanism



The FY09 GSFARP offered an Investigator-Initiated Research Award intended to support genetic studies that make an important contribution to the field of food allergies research and/or patient care. Four awards were supported.

"Genes Associated with Food Allergy and Eosinophilic Esophagitis"

David Broide, M.D., University of California, San Diego

Objective: To identify genetic markers that reflect complications in eosinophilic esophagitis, such as esophageal remodeling and narrowing or tightening of the esophagus.

"Genetic and Epigenetic Predictors of Development, Persistence, and Remission of Sensitization and Food Allergy in a Prospective Infant Cohort"

Katrina Allen, M.D., Ph.D., Murdoch Childrens Research Institute, Australia

Objective: To identify genetic markers and epigenetic modifications that predict which infants are more likely to have food allergies.

"Genetics of Eosinophilic Esophagitis"

Marc Rothenberg, M.D., Ph.D., Cincinnati Children's Hospital

Objective: To identify genetic risk factors for eosinophilic esophagitis and to gain molecular insight into disease pathogenesis.

"Genetics, Epigenomics, and Food Allergy"

Xiaobin Wang, M.D., M.P.H., Sc.D., Children's Memorial Hospital, Chicago

Objective: To investigate epigenomics profiles and interplay of genetics and epigenomics in relation to the development of food allergies.

The FY10 GSFARP solicited research proposals through two award mechanisms—the Concept Award, intended to support the exploration of a highly innovative new concept or untested theory, and the Idea Award, designed to support innovative ideas and high-impact research approaches. Five awards were supported.

"Exploration into the Genetics of Food Allergy"

Jonathan Spergel, M.D., Ph.D., Children's Hospital, Philadelphia

Objective: To perform a whole genome scan to identify genes relevant to food allergies and explore their biological significance.

"TGF-Beta Gene Polymorphisms in Food Allergic versus Non-Food Allergic Eosinophilic Esophagitis"

David Broide, M.D., University of California, San Diego

Objective: To investigate whether interactions between TGF-b gene polymorphism and food sensitization contribute to increased complications, such as esophageal remodeling, in a subset of patients with eosinophilic esophagitis.

"Mechanisms of Oral Tolerance Breakdown in Food Allergy"

Talal Chatila, M.D., University of California, Los Angeles

Objective: To investigate how allergy-inducing and allergy-reducing genes interact to promote food allergy.

Toward Development of a Food-Based Genetic Approach to Overcoming Food Allergies

Jixun Zhan, Ph.D., Utah State University

Objective: To genetically engineer probiotic bacteria that produce anti-allergic agents in the human body that can effectively prevent food allergies.

Development of a Novel Treatment for Food Allergy Using a New, Genetically-Defined Mouse Model of the Disease

Pamela Guerrerio, Ph.D., M.D., Johns Hopkins University

Objective: To investigate whether the Loeys-Dietz Syndrome (LDS) contributes to food allergy and examine the efficacy of losartan in suppressing the severity of the LDS-mediated allergic disease.

Gulf War Illness Research Program

Vision

Improve the health and lives of veterans who have Gulf War Illness

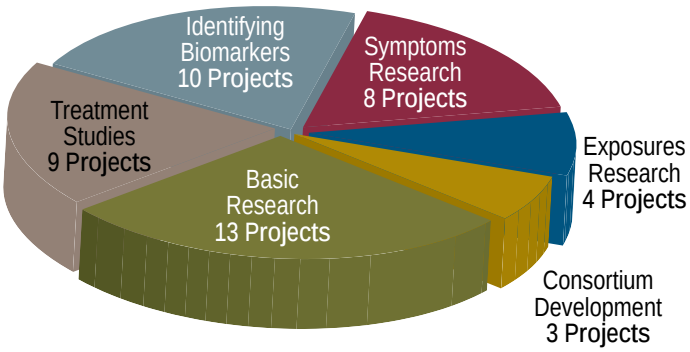
Mission

Fund innovative Gulf War Illness research to identify effective treatments, improve definition and diagnosis, and better understand pathobiology and symptoms

Program History

Gulf War Illness (GWI) is characterized by persistent symptoms such as chronic headache, widespread pain, cognitive difficulties, unexplained fatigue, gastrointestinal problems, respiratory symptoms, and other abnormalities that are not explained by traditional medical or psychiatric diagnoses. This complex set of chronic symptoms may affect as many as 200,000 veterans of the 1990–1991 Gulf War, of the nearly 700,000 deployed to that region.[1] The GWIRP focuses its funding on innovative projects that have the potential to make a significant impact on GWI, improving the health and lives of affected service members and their families.

DOD-funded GWI research began in 1994 with the establishment of a Gulf War Veterans' Illnesses Research Program (GWVIRP) to study the health effects of service members deployed in the 1990–1991 Persian Gulf War. From FY94 to FY05, the GWVIRP was managed by the USAMRMC Military Operational Medicine Research Program (MOMRP). Research pertaining to GWI also was funded intermittently through the CDMRP's Peer Reviewed Medical Research Program, which supports military health-related research. The MOMRP shared management responsibility for the GWVIRP with the CDMRP in FY06 with separate $5M appropriations. Although the GWVIRP did not receive funding in FY07, a $10M appropriation renewed the program in FY08, renamed the GWIRP, to be managed fully by the CDMRP. The GWIRP has been continued in FY09, FY10, and FY11 with $8M appropriations each year. The program supports peer-reviewed research for treatment of the complex symptoms that comprise GWI, identification of objective markers (biomarkers) for the disease, and understanding the pathobiology underlying GWI. The pie chart below reflects the GWIRP portfolio by research area.



*FY06–FY10 GWIRP Portfolio by Research Area**
***Five projects fit into two different research topics**

[1] ***Gulf War Illness and the Health of Gulf War Veterans: Scientific Findings and Recommendations*, U.S. Department of Veterans Affairs, Research Advisory Committee on Gulf War Veterans' Illnesses, 2008.**

Structural MRI and Cognitive Correlates in Pest-Control Personnel from the Gulf War

Kimberly Sullivan, Ph.D. and Maxine Krengel, Ph.D., Boston University

Pesticides were widely used during the 1990–1991 Gulf War to protect troops from infectious disease-carrying insects. During their deployment, Gulf War veterans were exposed to pesticides where they worked, slept, and ate. One class of these pesticides, organophosphates, is known to produce chronic neurological symptoms over certain exposure levels by inhibiting the enzyme acetylcholinesterase. Drs. Sullivan and Krengel used an FY06 GWIRP Investigator-Initiated Research Award to follow up on their previous CDMRP-funded work that suggested MRI and morphometric analysis of pesticide applicator personnel who took pyridostigmine bromide (PB) tablets, could provide an objective biomarker for GWI. Based on this indication, the follow-on FY06 study compared high and low pesticide-exposed applicators in a pilot study to attempt to define a biomarker for brain pathology and associated neuroanatomical and cognitive effects.

The FY06 study found lower volumes of brain white matter in highly symptomatic Gulf War veteran pesticide applicators as compared to less symptomatic veterans. Specific pesticide exposures that showed significant differences with regard to brain volumetric correlations and cognitive functioning were the organophosphate dichlorvos (used in pest-strips) and the organochlorine lindane (a delouser). These particular exposures showed interactive effects when combined, resulting in significantly lower cerebral and cerebellar white matter and gray matter volumes.

Additional study results showed a significant interaction and lower hippocampal volumes, as well as lower scores in visual memory assessments, for combined high N,N-Diethyl-meta-toluamide (DEET) and PB exposure, suggesting both a structural and functional relationship. These results implicate pest strips (dichlorvos), delousers (lindane), insect repellents (DEET), and anti-nerve gas pills (PB) issued to almost all troops deployed to the Gulf War. Therefore, these findings could apply to the larger cohort of deployed Gulf War veterans and begin to explain the underlying physiological changes associated with GWI.

Biomarkers of Gulf War Veterans' Illnesses: Tissue Factor, Chronic Coagulopathy, and Inflammation

Ronald Bach, Ph.D., VA Medical Center, Minneapolis, Minnesota

Many veterans of the 1990–1991 Gulf War suffer from unexplained chronic and often debilitating health issues, including widespread pain, headaches, fatigue, cognitive deficits, and other symptoms. Preliminary evidence has indicated that a high percentage of ill Gulf War veterans may be in a hypercoagulable state, i.e., having an abnormally increased tendency toward blood clotting, the basis of which is unknown.[2] Dr. Bach is using funds from an FY08 GWIRP Investigator-Initiated Research Award to further explore this concept. Dr. Bach will examine the level of tissue factor (TF), the biological initiator of blood coagulation, in blood samples from ill Gulf War veterans and healthy controls. Overexpression of TF in the bloodstream can lead to disseminated intravascular coagulation (DIC) and impaired blood flow in the smallest of blood vessels. This restriction of microcirculation, applied chronically, can produce symptoms commonly associated with GWI.

In addition to TF, Dr. Bach will examine a panel of coagulation markers, including D-dimer, which indicates fibrin clot formation; thrombin-antithrombin III complex, to indicate ongoing coagulation activity; prothrombin fragment 1.2, a measure of ongoing thrombin generation; and TF-procoagulant activity, which can initiate DIC. Immune function will also be assessed by measuring levels of inflammatory markers in the blood samples. Together, these markers may indicate a possible state of chronic inflammation in ill veterans and thus support a connection between chronic coagulation and immune function, and ultimately, the symptoms of GWI.

[2]Hannan KL, Berg DE, Baumzweiger W, Harrison HH, Berg LH, Ramirez R, and Nichols D. 2000. Activation of the coagulation system in Gulf War Illness: A potential pathophysiologic link with chronic fatigue syndrome, a laboratory approach to diagnosis. *Blood Coagulation and Fibrinolysis* 11(7):673-678.

Lung Cancer Research Program

Vision

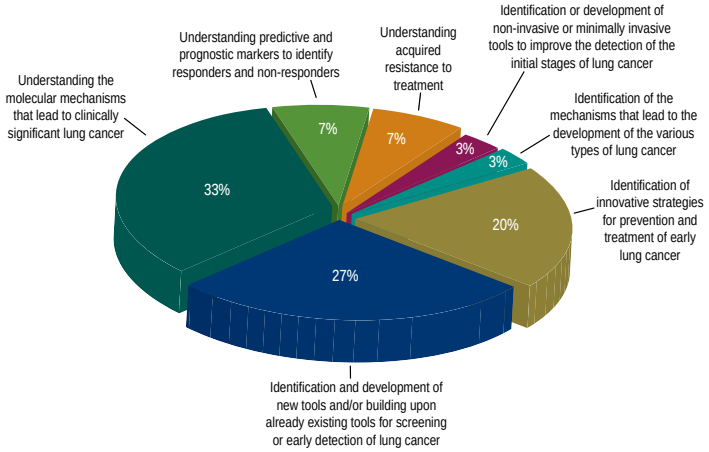
Eradicate deaths from lung cancer to better the health and welfare of the military and the American public

Mission

Support and integrate research from multiple disciplines for early detection, diagnosis, prevention, cure, and control of lung cancer

Program History

The LCRP was established by Congress in FY09 with an appropriation of $20M. The program was continued with congressional appropriations of $15M in FY10 and $12.8M in FY11. As the second most commonly diagnosed cancer among both men and women and among VA patients, lung cancer is the most lethal of all types of cancer, taking more lives each year than all other major cancers. In the United States alone, it is estimated that 222,520 new cases will be diagnosed and 157,300 deaths will occur due to lung cancer this year.



FY09–FY10 LCRP Portfolio by Research Area

Areas of Emphasis

The LCRP challenges the scientific community to design innovative research that will foster the development of integrated components to identify, treat, and manage early curable lung cancer. The LCRP specifically encourages applications that address critical needs of the lung cancer community and concentrate on any of the following areas:

- Identification or development of non-invasive or minimally invasive tools to improve the detection of the initial stages of lung cancer
- Identification, development, and/or building upon already existing tools for screening or early detection of lung cancer. Screening may include, but is not limited to, computed tomography scans, x-rays, other imaging biomarkers, genetics/genomics/proteomics, and assessment of risk factors
- Understanding the molecular mechanisms that lead to clinically significant lung cancer
- Identification of the mechanisms that lead to the development of the various types of lung cancer
- Identification of innovative strategies for the prevention and treatment of early lung cancer
- Understanding predictive and prognostic markers to identify responders and non-responders
- Understanding acquired resistance to treatment

Elucidation of the Mechanisms of Immune Reactivity in Small Cell Lung Cancer to Identify Targets for Detection, Imaging, and Treatment

Ite Laird-Offringa, Ph.D., University of Southern California

Small cell lung cancer (SCLC) is the most aggressive kind of lung cancer and accounts for about 15% of all lung cancer diagnoses. The majority of patients are diagnosed with disseminated disease and even with treatment have a median survival of only 6–12 months. Based on evidence that SCLC is associated with rare cancer-associated autoimmune diseases, Dr. Laird-Offringa hypothesizes that SCLC tumors cause a defined immune response in patients and that identifying the underlying molecular mechanisms of this response may lead to novel strategies for early detection and treatment of SCLC. With Ph.D. student Mario Pulido, Dr. Laird-Offringa is currently exploring whether post-translational modifications in proteins frequently misexpressed in SCLC tumors are responsible for SCLC-associated immune responses. Any unique immunogenic molecular alterations found will be assessed as potential molecular targets for detecting and treating SCLC.

Blood-Based Biomarkers for Lung Cancer Early Detection and Evaluation of CT-Based Lesions

Samir Hanash, M.D., Ph.D., Fred Hutchinson Cancer Center; Adi Gazdar, M.B.B.S., University of Texas Southwestern Medical Center at Dallas; Stephen Lam, M.D., British Columbia Cancer Agency; and David Gandara, M.D., University of California, Davis

Accurate and efficient early detection of lung cancer is crucial for improving patient prognoses. Currently available methods for detection and diagnosis (e.g., CT scans) are limited in their ability to detect small pulmonary nodules and cannot distinguish between malignant and benign lesions, leading to frequent misdiagnosis. Using a team approach that brings together a variety of expertise—including medicine, biology, genetics, biochemistry, pharmacology, epidemiology, and statistics—Drs. Hanash, Gazdar, Lam, and Gandara are working together with the goal to identify biomarkers that may be used to diagnose non-small cell lung cancer before the onset of symptoms in high-risk populations, and supplement current detection methodologies by distinguishing between benign and malignant disease via a simple blood test. The investigators are currently developing a preliminary panel of genomic, proteomic, and metabolic biomarkers, and plan to conduct several validation studies in biospecimens from patients with known clinical outcomes.

"The LCRP has been a wonderfully fulfilling experience. In my capacity as a co-founder of Lung Cancer Foundation of America (LCFA), I need to stay on top of the latest advances in lung cancer research in order to share that knowledge with the lung cancer community and to help fund the most promising lung cancer research. The LCRP fits perfectly with that role and allows me to contribute and enhance my knowledge as a lung cancer survivor and lung cancer patient advocate to both LCFA and LCRP."

Lori Monroe, FY11 IP Member

Multiple Sclerosis Research Program

Vision

To prevent the occurrence, cure, reverse, or slow the progression, and lessen the personal and societal impact of multiple sclerosis

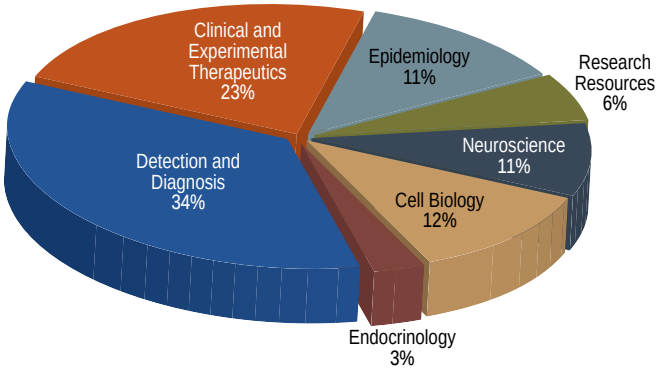
Mission

To support pioneering concepts and high-impact research relevant to the prevention, etiology, pathogenesis, assessment, and treatment of multiple sclerosis

Program History

In FY09, Congress appropriated $5M to the MSRP. The program was continued with a congressional appropriation of $4.5M in FY10 and $4.8M in FY11. Research supported by the MSRP explores pioneering concepts and high-impact research relevant to multiple sclerosis (MS). MS is considered an autoimmune disease because the body's immune system attacks myelin, a key substance that serves as a nerve insulator and helps in the transmission of nerve signals. While most common in young adults, particularly women between the ages of 20 and 40, individuals of all ages are diagnosed with this debilitating disease. However, the cause of MS is unknown; scientists believe that a combination of immunological, environmental, viral, and genetic factors may be involved.

The MSRP examines the research landscape and, knowing the funding gaps, utilizes its investment strategy for the greatest impact for the research community and the American public. The FY09–FY10 MSRP research portfolio is depicted below.



FY09–FY10 MSRP Portfolio by Research Area

A Consumer's Perspective: Scott Hanson

At first glance, Scott Hanson looks like a typical young man. He is married, the proud father of a 17-month-old boy, works as a labor policy research analyst, and is a fan of the Green Bay Packers. His life is not without challenges, however. Like 400,000 other Americans, Scott has been diagnosed with MS.

"Since my diagnosis, MS has affected virtually every facet of my life—from continued education to career direction to family planning to retirement planning to vacation planning," Scott said. He noted how his physical activity also has been impacted, explaining that he cannot run marathons because running elevates his body temperature, which may lead to worsening of symptoms. However, he still tries to ice skate—as pure a Wisconsin pastime as there can be—and he proudly admitted that he always gets up after he falls. Despite his diagnosis, Scott has been active in advocacy and education efforts for people with MS and their families. He works with the National Multiple Sclerosis Society (NMSS) and the Wisconsin Chapter of the NMSS, and for nearly 9 years, he has served on the Government Relations Committee of the Wisconsin Chapter of the NMSS.

"I have trained hundreds of volunteer advocates who speak to elected leaders to enact laws and policies to improve the lives of people living with MS," said Scott, who also served a 3-year term on the Federal Activism Committee of the NMSS.

Harnessing GPR17 Biology for Treating Demyelinating Disease

Nitin Karandikar, M.D., Ph.D. and Qing Lu, Ph.D., University of Texas Southwestern Medical Center at Dallas

The CNS and nerve cells throughout the body depend on the protective covering of the nerve fibers called the myelin sheath to amplify electrical signals conveyed through neural axons. MS is an inflammatory disorder of the CNS in which the myelin sheath is damaged. In the CNS, myelin is produced by oligodendrocytes. Oligodendrocytes and the myelin sheath are the major targets of the MS disease process. Loss of oligodendrocytes leads to loss of myelin sheath from around axons—a process called demyelination. The immediate consequence of demyelination is that axons become considerably less efficient at conducting electrical impulses. However, demyelination may be followed by a spontaneous regenerative process called remyelination in which myelin sheath is restored and the axons resume enhanced impulse conduction.

While several receptor-mediated signaling pathways have been found to play an important role in oligodendrocyte differentiation/myelination, the role of G-protein coupled receptor signaling remains elusive. Research teams led by Drs. Karandikar and Lu have been studying the mechanism of oligodendrocyte myelination. Previously, they identified a G-protein coupled receptor, GPR17, as a negative regulator of the process. The researchers found that GPR17 inhibits myelination and maturation of oligodendrocytes and that it is highly expressed in inflammatory demyelination, both in human MS and animal models.

Funded by an FY09 MSRP Synergistic Idea Award, the collaborating research teams are now working to determine whether GPR17 signaling activation results in blockade of remyelination in the damaged axons (neuroinflammatory lesions) and, thus, are looking to find an important target for promoting remyelination. Using animal models, they plan to delineate the role of GPR17 in demyelinating diseases and test the therapeutic potential for GPR17 agonists and antagonists in MS. If successful, this study may lead to the development of novel therapeutic strategies for demyelinating disease using GPR17 as a target.

His advocacy efforts attracted the attention of NMSS leadership, who nominated Scott as a consumer peer reviewer for the DOD MSRP. Scott expressed gratitude for the opportunity to serve as a reviewer, adding that he hopes the MSRP will make a difference in ending the disease. His service as a peer reviewer has spanned three program cycles from 2009 through 2011.

"I was humbled to be asked to serve with very smart individuals in the fields of science and medicine as they related to improving the lives of people like me living with MS," Scott said. "I appreciated never being talked down to as a consumer reviewer, and I was grateful for the interest of other panelists who were genuinely open to discussing topics at my level."

As research into MS continues, Scott said he is grateful for the efforts of scientists and clinicians in his home state and around the world.

"Where I live in Wisconsin, I see tremendous interest from the scientific community in the lives of people living with MS," Scott said. "Members of the medical community have described to me how they have been personally affected as participants running, walking, cross-country skiing, and riding bikes with people living with MS to raise money for research against the disease."

Now Scott roots for two teams – the Packers and MS researchers.

Neurofibromatosis Research Program

Vision

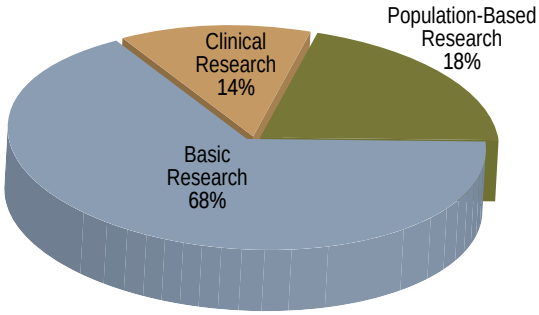
Decrease the clinical impact of neurofibromatosis

Mission

Promote research directed toward the understanding, diagnosis, and treatment of NF1, NF2, and schwannomatosis to enhance the quality of life for persons with those diseases

Program History

The NFRP was established in FY96 when the efforts of NF advocates led to a congressional appropriation of $8M. Since that time, $227M has been appropriated to the program, including $16M in FY11. Over its 15-year history, the NFRP has invested in key initiatives to support the development of critical resources, sponsor multidisciplinary collaborations, bring talented investigators into the field, and promote the translation of promising ideas into the clinic. The program's current portfolio includes 269 awards spanning basic, clinical, and population-based research as shown below.



FY96–FY10 NFRP Portfolio by Research Area

"The NFRP is truly one of the best—if not the best—neurofibromatosis research programs because of its funding-focused, innovative, and stringently reviewed research. Not only am I honoring my father, my brother, and the many friends who have lost their lifelong battles with NF; I am also shaping a brighter future for those living with NF by sharing my story, advocating for NF research, and participating as a consumer for NFRP."

Beverly Oberlander, NFRP FY08–FY09 and FY11 Consumer Peer Reviewer

Dr. David Stevenson, University of Utah

Anterolateral tibial bowing is a skeletal manifestation of NF1 that is observed in 5% of children with the disease. The majority of NF1 individuals with tibial bowing will sustain a fracture of that bone that will not heal properly (i.e., pseudarthrosis), resulting in multiple surgeries, poor limb function, and amputation. Dr. Stevenson received an FY10 NFRP Investigator-Initiated Research Award to identify clinical predictors of tibial pseudarthrosis and better understand its pathophysiology to inform the treatment of NF1 patients suffering from tibial bowing.

Dr. Vijaya Ramesh, Massachusetts General Hospital

NF2 is a genetic disorder resulting in loss of function of the protein merlin. The loss of functional merlin in NF2 may lead to overactive mTOR signaling and uncontrolled cell proliferation. Dr. Ramesh, recipient of an FY10 Investigator-Initiated Research Award, seeks to define the mechanism by which merlin regulates mTOR signaling. Additionally, she will test agents known to block abnormal mTOR activation in cell culture and mouse models.

Dr. Chie-Schin Shih, Indiana University

NF1-associated PNF are difficult to treat as these tumors are frequently located near vital structures including nerves, blood vessels, and the airway. Sutent (sunitinib), an oral medication currently used to treat other types of tumors, is a multireceptor tyrosine kinase inhibitor that has reduced the number and size of tumors in an NF1 mouse model. In this Phase 2 study, funded by an FY10 NFRP Clinical Trial Award, Dr. Shih will evaluate the efficacy of Sutent in individuals with clinically significant PNF.

Dr. Maura Cosetti, New York University School of Medicine

The Postdoctoral Traineeship Award was first offered in FY09 to enable doctoral-level scientists and recent medical school graduates to obtain the necessary experience to pursue an independent career in NF research. Dr. Cosetti, a neurology fellow at the New York University School of Medicine, received an FY10 Postdoctoral Traineeship Award to develop, refine, and validate a multidimensional metric to evaluate quality of life in NF2 patients. As the clinical management of NF2 can be complex and controversial, Dr. Cosetti's disease-specific, validated quality of life metric will be used to inform NF2 patient treatment, evaluate treatment outcomes, and standardize results across clinical trials.

Ovarian Cancer Research Program

Vision

Eliminate ovarian cancer

Mission

To support research to detect, diagnose, prevent, and control ovarian cancer

Key Initiatives

Leverage critical research resources

Challenge current thinking and approaches

Accelerate movement of promising ideas into clinical applications

Support partnerships between clinicians and laboratory scientists

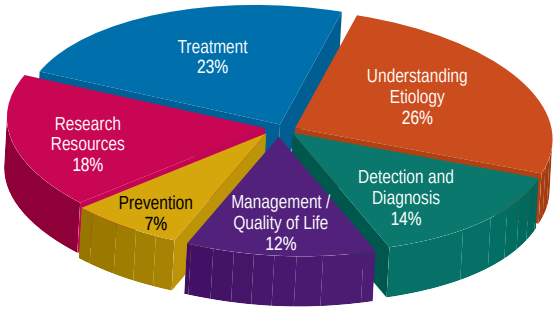
Facilitate multidisciplinary and nontraditional collaborations

Foster the next generation of ovarian cancer researchers

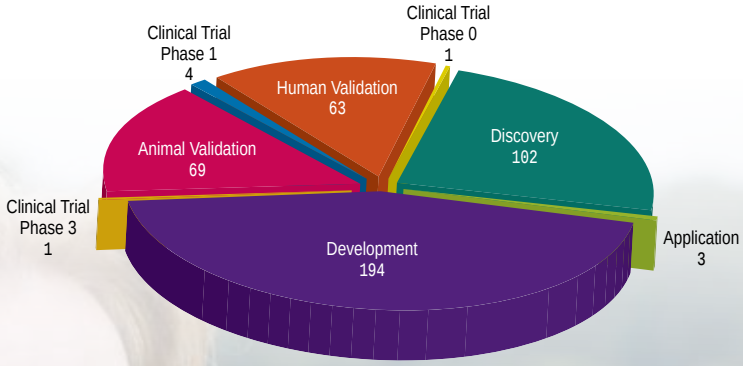
Program History

In FY97, the Congressional Appropriations Conference Committee Report No. 104-863 provided $7.5M to be administered by the DOD for ovarian cancer research. Since then, ovarian cancer survivors, scientists, and clinicians have advocated for increased public awareness, resulting in $20M in FY11 and a total appropriation of $180.45M to the OCRP. To target critical research and to be responsive to the needs of the ovarian cancer community, the OCRP evaluates and refines its goals annually.

The OCRP is always looking at new ways to drive scientific progress to impact ovarian cancer. As a leader in funding extramural ovarian cancer research, the OCRP is investing in high-impact, innovative research that continues to fulfill unmet needs and push the field of ovarian cancer research forward. A total of 236 awards were made through FY10.



FY97–FY10 OCRP Portfolio by Research Area



FY97–FY09 OCRP Research Phases

Achievements at a Glance: Making an Impact

Zhen Zhang, Ph.D. – OVA1TM Helps Determine Whether an Ovarian Mass Is Malignant

Developed OVA1TM, the first IVDMIA of proteomic biomarkers cleared by the FDA to help physicians determine if a pelvic mass is benign or malignant before it is removed. This information will help physicians identify patients who should be referred to a gynecologic oncologist.

Martin McIntosh, Ph.D. – MMP7 and Early Detection of Ovarian Cancer

Discovered that MMP7 is elevated in serum up to 3 years prior to diagnosis of ovarian cancer.

Janet Sawicki, Ph.D. – Nanoparticle Delivery of a Suicide Gene for Ovarian Cancer Treatment

Developed a targeted treatment using nanoparticles to deliver diphtheria toxin-encoding DNA to ovarian cancer cells, leaving healthy cells unaffected.

Nouri Neamati, Ph.D. – SC144, A Novel Anticancer Agent

Validated SC144 (small-molecule inducer) as a novel anticancer agent that could be used to develop combination therapies for drug-sensitive and drug-resistant ovarian cancer.

Santo Nicosia, M.D. and Jin Cheng, M.D., Ph.D. – API-2/Tricirbine Inhibits Akt-Activated Cancers

Discovered API-2/tricirbine (now in Phase 1 clinical trials as VQD-002), a compound that potentially inhibits Akt-activated cancers, which includes more than 40% of ovarian tumors.

Sundaram Ramakrishnan, Ph.D. – Anginex Inhibits Angiogenesis in Ovarian Cancer

Developed anginex, a potent antiangiogenic and anticancer peptide that shows efficacy in combating ovarian cancer. PepTx, Inc., founded by Dr. Ramakrishnan's program project collaborator, Dr. Kevin Mayo, produces anginex, which is marketed by Phoenix Pharmaceuticals.

Richard Pietras, M.D., Ph.D. – Squalamine Enhances the Effectiveness of Chemotherapy

Developed and patented treatment of ovarian cancer with squalamine in combination with other anticancer agents/modalities (now in Phase 2 clinical trials through Genaera Pharmaceuticals).

Martin Cannon, Ph.D. – Stimulating CD8+ T Cell Response Against Ovarian Tumor Antigens

Demonstrated that enhancing the CD8+ T cell response to ovarian cancer reduces the size of tumors in 75% of cases without surgery or chemotherapy.

Rebecca Liu, M.D. – Ovarian Cancer Cells Sensitive to Resveratrol

Showed that ovarian cancer cells are sensitive to glucose deprivation and resveratrol treatment when compared to control cells and that resveratrol can inhibit the PI3K/Akt/Tor pathway in ovarian cancer cells.

George Coukos, M.D., Ph.D. – Promising Panel of Biomarkers

Discovered a panel of nine tumor vascular biomarkers that are expressed in the tumor vasculature in vivo, indicating that they are candidates for imaging or therapeutic targeting (patent is pending for the tumor vascular markers and methods of use thereof). Now in Phase 1 clinical trials.

Andrew Berchuck, M.D. – Ovarian Cancer Genetic Association Study and International Ovarian Cancer Association Consortium

Founded the International Ovarian Cancer Association Consortium. Currently validating the finding from Dr. David Bowtell's program project that +331A allele of PR gene is significantly associated with protection against endometrioid ovarian cancer.

David Bowtell, Ph.D. – Valuable Population-Based Resources

Built a multicenter, population-based resource involving the collection of linked epidemiologic and clinical data and biospecimens from 2,003 cases and 1,073 matched controls (1,719 questionnaires, more than 1,600 blood samples, and 1,100 frozen tissue samples) to study ovarian cancer risk factors and biomarkers.

Igor Jurisica, Ph.D. – Computational Biology Technologies to Identify Biomarkers

Created OPHID/I2D, online databases of known and predicted protein-protein interactions (PPIs), and NAViGaTOR, a software package for visualizing and analyzing PPI networks.

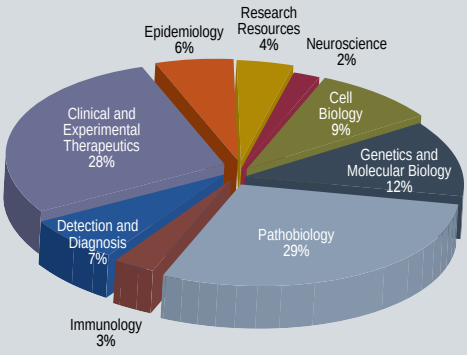
Peer Reviewed Cancer Research Program

Vision

To improve quality of life by decreasing the impact of cancer on service members, their families, and the American public

Mission

Fostering the next generation of cancer research by providing new investigators and their early career mentors opportunities to excel in groundbreaking cutting-edge research for the prevention, detection, and treatment of cancer



FY09–FY10 PRCRP Portfolio by Research Area

Program History

The PRCRP was initiated by Congress in FY09 to study cancers with respect to service members and their families. It has continued each year with total appropriations of $47M through FY11. Since the inaugural year of the PRCRP, the focus of cancers has broadened but the intent has remained the same—to fund the most innovative research with a relevance to military beneficiaries.

Multiple epidemiological studies have shown an increased incidence in several cancers within military populations as compared to non-military populations. The Veterans Health Administration acknowledged the toll on military service members and their families in its National Cancer Strategy in 2003.[1] In 2007, there were 355,442 military beneficiaries diagnosed with cancer, for a prevalence of 4.1%.[2] Both a healthy force and healthy family support unit allows the service member to focus on his or her role as a service member and facilitates the overarching military mission.

[1]*VHA-Directive* 2003-34. [2]Crawford et al. *Military Medicine* 172 (2007) 1084–88.

A Consumer's Perspective: Richard J. Spayde, Jr.

High-risk, high-gain research, with an emphasis on innovation and cutting-edge technology, was the key phrase that captured my attention about the CDMRP. As a survivor of acute myelogenous leukemia, I underwent two complete stem cell transplants within 40 days, the second transplant experimental, and know first-hand the importance of looking beyond the ordinary to achieve your highest goals. I witnessed first-hand the difference that people can make in other's lives. It is my turn to complete the cycle of giving and assist patients not only in need today, but those that have yet to be diagnosed.

I was honored to be chosen as a consumer reviewer where I could use my experience as a patient and survivor to evaluate the impact of proposed research projects on the cancer patient community. I must admit that I was a little skeptical, but my fears were soon relieved when my thoughts and ideas were not only welcomed but given equal consideration.

Being part of the review panel was an astonishing experience. I was in awe of the caliber of both the scientific reviewers and the research proposals submitted, and it gives me great comfort knowing that so many brilliant and passionate scientists are working together to find a cure. It is because of this world-class, cutting-edge research that I am alive today and my two little girls still have their Daddy to kiss them good night. I look forward to continuing my participation with the CDMRP in any way that I am needed, with the ultimate goal of seeing the day where my children and generations beyond will view cancer as a completely treatable or preventable disease.

Identifying Heritable and Environmental Cancer Risk Factors with Military Working Dogs

Carlos Alvarez, Ph.D., The Research Institute at Nationwide Children's Hospital and The Ohio State University, Columbus, Ohio and Guillermo Couto, D.V.M. and Kun Huang, Ph.D., The Ohio State University, Columbus, Ohio

Cancer is a complex disease mediated by genetic and epigenetic changes as well as environmental influences. Better understanding of molecular mechanisms and risk factors contributing to cancers can be achieved through collection and comprehensive analyses of genetic, molecular, epidemiological, and clinical data from a large and relatively homogenous population.

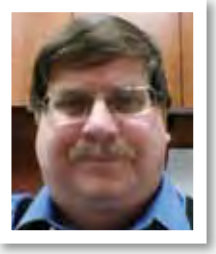
Funded by an FY10 PRCRP Idea with Collaborative Option Award, the scientific team of Drs. Couto, Huang, Leszek Rybaczyk, and Alvarez proposes to use military working dogs (MWD) in elucidating the genetic mechanisms that contribute to the development of complex diseases. MWDs are the ideal population for such study since they share with humans similar environmental and inherited disorders, including cancers. Importantly for MWDs, records about consistent veterinary care, well-documented pedigree, and living environments are available. As such, a canine longitudinal cohort registry composed of genetic, environmental, and clinical data will be established first. The team is planning to conduct a large-scale molecular characterization of genetic variations, combined with extensive analysis of clinical and environmental data components. Ultimately, the study may lead to the development of new effective treatments, thus improving the quality of patient care and quality of life.

XactMice – A Unique Model for Cancer Research

Antonio Jimeno, M.D., Ph.D., University of Colorado, Denver

The stroma or surrounding environment is critically important when studying cancer, its characteristics, and methods of treatment. The conventional models utilized in drug development include either cell lines, which lack the tissue environment, or animal models with implanted human cells surrounded by animal stroma. Although humanized chimeric mice were developed to address the issue related to the conventional models, this model is not very robust.

Dr. Jimeno received an FY09 PRCRP New Investigator Award to develop an ideal animal model for cancer research. Together with his study collaborator, Dr. Yosef Refaeli of the University of Colorado, Dr. Jimeno plans to generate XactMice, a fully humanized and individualized xenochimeric mouse model for head and neck squamous cell cancer. The elegant approach for this novel model comprises engrafting human tumor tissue in combination with conditionally immortalized human hematologic stem cells, both derived from the same patient, into an immune-deficient mouse. Drug efficacy studies will be conducted with both nude and XactMice models to further validate this innovative approach. The investigators believe that XactMice will be paradigm-changing in genetic cancer research.



"Being a member of the Integration Panel for the Peer Reviewed Cancer Research Program has been an enlightening and rewarding experience. By bringing together academicians, military professionals, and community advocates with a shared mission to alleviate the burden of cancer on military families, the PRCRP has been able to direct critical funding for novel and innovative cancer research."

John Kuttesch, M.D., Ph.D.,
FY11 IP Member

Peer Reviewed Medical Research Program

Vision

Improve the health and well-being of all military service members, veterans, and beneficiaries

Mission

Identify and select military health-related research of exceptional scientific merit

Outcomes

To date, the 382 awards made by the PRMRP have resulted in:

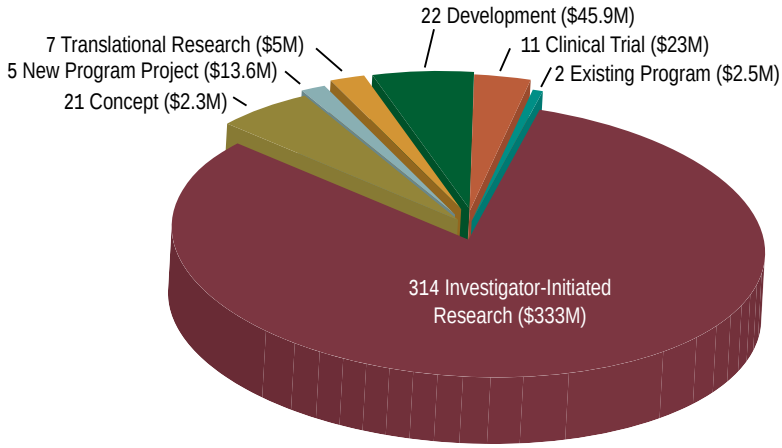
1,140 Publications

30 Granted patents

Program History

Since 1999, the PRMRP has supported research, under topic areas directed by Congress, with an underlying goal of enhancing the health and well-being of military service personnel, the veteran population, and their families. Through FY10 (excluding FY07, in which no appropriation was made), Congress has appropriated $494.5M, which has supported 382 research awards. From its inception, PRMRP has funded research projects in more than 80 congressionally directed topic areas that address a wide range of fields of study including infectious diseases, neurological diseases, psychological disorders, clinical management, health and wellness, research projects and technologies, restoration, regeneration, and robotics. The FY11 appropriation is $50M.

The PRMRP is committed to funding basic, translational, and clinical research that will strongly impact the development and implementation of devices, drugs, or clinical guidance that will change the face of diagnosis and treatment for a broad range of clinical applications. The program's research portfolio is depicted below.



FY99–FY10 PRMRP Portfolio by Funding Mechanisms/Categories

FY10 Peer Reviewed Medical Research Program Topic Areas

- Chronic migraine and post-traumatic headache
- Dystonia
- Drug abuse
- Epilepsy
- Fragile X syndrome
- Inflammatory bowel disease
- Interstitial cystitis
- Listeria vaccine for infectious disease
- Lupus
- Mesothelioma
- Neuroblastoma
- Osteoporosis and related bone disease
- Paget's disease
- Pheochromocytoma
- Polycystic kidney disease
- Post-traumatic osteoarthritis
- Scleroderma
- Social work research
- Tinnitus

Optogenetic Control of Epileptic Seizures

Anna Majewska, Ph.D., University of Rochester, Rochester, New York and Sydney Cash, M.D., Massachusetts General Hospital, Boston, Massachusetts

Epilepsy is currently treated with medication, surgery, and/or electrical stimulation. However, none of these therapeutic options is able to target specific neurons only during seizure episodes; consequently, they also affect seizure-free brain activity and, as such, have potential side effects. Drs. Majewska and Cash received FY08 Translational Research Awards through the PRMRP to test a new approach for treating seizures that will potentially overcome the limitations and side effects of current treatment options. These partnering PIs plan to combine optical and genetic approaches (optogenetics), in a rodent model, to alter the electrical activity of specific neurons during epileptic episodes using light activation to prevent the seizure from spreading. The ultimate goal is to create a treatment option that allows patients to be free of side effects.

Web-Based Visual Field Assessment and Diagnosis

Wolfgang Fink, Ph.D., California Institute of Technology, Pasadena, California

As critical as having an unrestricted visual field is to most people, it is essential for those individuals involved in military operations in theater. In addition to diseases and disorders that may cause visual field loss, trauma, either ocular or to the brain, may also cause critical visual impairments. There is a number of different automated visual field assessment equipment currently used; however, most of them have limited sensitivity, are bulky and not portable, limiting their use in geographically remote areas and/or military operational settings. Dr. Fink received an FY08 PRMRP Advanced Technology/Therapeutic Development Award to develop an advanced web-based system that will test the visual field with high spatial sensitivity and will rapidly and fully automatically analyze, characterize, store, and share the test data to aid in the diagnosis of visual field defects. This advanced visual field test and diagnosis system is easy to use and offers a new perspective for evaluating visual fields that includes computer-assisted diagnosis and telemedicine opportunities for individuals in geographically remote areas and/or military operational settings.

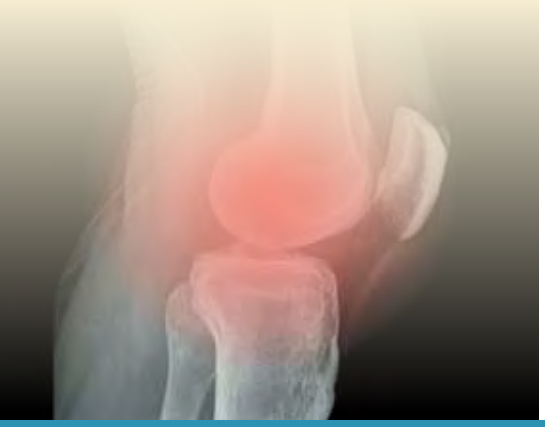
Peer Reviewed Orthopaedic Research Program

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

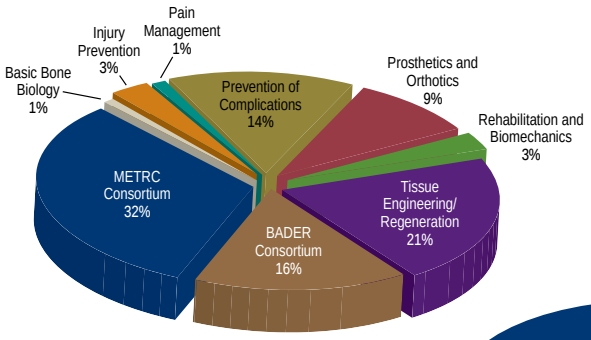
Address the leading burden of injury and loss of fitness for military duty by funding innovative, high-impact, clinically relevant research to advance optimal treatment and rehabilitation from musculoskeletal injuries sustained during combat or combat-related activities



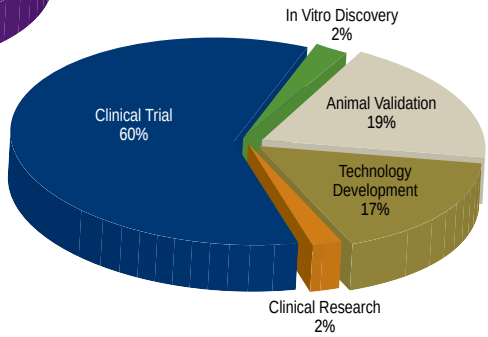
Program History

A large majority of the injuries sustained by military personnel in U.S. war efforts involve soft tissue wounds and skeletal fractures, pointing to an urgent need for orthopaedic research that will provide superior medical care and treatment options for injured service members. The PRORP was established by Congress in FY09 to support military-relevant orthopaedic research. The program has been continued each year through FY11 with congressional appropriations totaling $158.5M, including an appropriation of $24M in FY11.

Orthopaedic injuries sustained during combat-related activities tend to be very heterogeneous and complex in nature, typically involving multiple tissues such as skin, bone, muscle, cartilage, and nerves. Blast and other combat-related injuries frequently involve multiple limb traumas to an extent not seen in the civilian setting and are sustained in an environment where access to optimal acute care is limited. Frequent outcomes and complications include amputation, infection, compartment syndrome, non-union of the bone, heterotopic ossification, and temporary or permanent functional muscle 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.



FY09–FY10 PRORP Research Portfolio by Research Area



FY09–FY10 PRORP Portfolio by Research Type

Making an Impact: Spotlight on Clinical Consortia

The PRORP supports high-impact research through multiple mechanisms but perhaps most notably through the establishment of two complementary clinical consortia. The Major Extremity Trauma Research Consortium (METRC) was awarded a $38.7M Clinical Consortium Award by the PRORP in FY09 to conduct studies focused on the definitive care and surgical reconstruction of severe combat-related orthopaedic injuries. In FY10, the PRORP granted a $19.7M Orthopaedic Rehabilitation Clinical Consortium Award to

the Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium to conduct evidence-based rehabilitation research to optimize return to function for warfighters with orthopaedic injuries. These two clinical consortia represent a large-scale effort to provide new solutions along the continuum of care for wounded warriors with orthopaedic injuries.

As part of its strategy to make a difference now in the treatment and recovery for American service members injured in today's conflicts, the PRORP has established these consortia in partnership with four military medical treatment facilities (MTFs) that treat or serve the large majority of combat-injured from Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). In both consortia, investigators from Naval Medical Center Portsmouth, Naval Medical Center San Diego, San Antonio Military Medical Center, and Walter Reed National Military Medical Center are working with multiple civilian organizations to design and conduct clinical studies. These partnerships are designed to bring together military patients, researchers, and clinicians at the MTFs with the infrastructure, patient populations, and expertise of highly qualified civilian organizations to conduct studies with the potential to impact current clinical practice in military orthopaedic and rehabilitation medicine.

> *"The soldiers, sailors, airmen, and marines who protect our freedom with their selfless service in harm's way deserve the best care that this nation can deliver when they are injured. Often, the current available care meets their medical needs, but some conditions are so severe they require more than even the nation's best. Over 60% of those disabling problems are musculoskeletal in nature. The Peer Reviewed Orthopaedic Research Program seeks research on those unmet clinical needs for our nation's wounded warriors. One recently told us that he and his colleagues will do whatever it takes to protect us. We hope that the PRORP can also do whatever it takes to optimize their recovery and rehabilitation."*
>
> *BG Michael Yaszemski, FY11 IP Chair, and COL James Ficke, FY11 IP Chair Emeritus/ Co-Chair*

The METRC was established by the FY08 Orthopaedic Extremity Trauma Research Program and expanded by the FY09 PRORP Clinical Consortium Award. The consortium is led by Dr. Ellen MacKenzie at the Johns Hopkins University and Dr. Michael Bosse at the Carolinas Medical Center. In addition to the Coordinating Center at the Johns Hopkins University and the four collaborating MTFs, the METRC includes 24 core civilian study sites and over 30 satellite sites. METRC studies funded by the FY09 PRORP Clinical Consortium Award focus on novel technology for the diagnosis and treatment of compartment syndrome, a comparison of the outcomes of limb salvage versus transtibial amputation, multimodal perioperative pain management to reduce the use of addictive narcotics, and a collaborative care intervention to improve function outcomes and quality of life in lower extremity trauma patients.

The BADER Consortium was established by the FY10 PRORP Orthopaedic Rehabilitation Clinical Consortium Award and is led by Dr. Steven Stanhope at the University of Delaware and his co-investigators, Dr. Irene Davis at Spaulding Rehabilitation Hospital and Dr. Kenton Kaufman at the Mayo Clinic, Rochester, Minnesota. These three institutions and the designated MTFs are joined by core facilities at C-Motion, Inc., the Christiana Care Health System, the University of Texas at Austin, and the University of Michigan, as well as a number of scientific collaborators from 17 states, the District of Columbia, and Iceland. Clinical study design is ongoing, but initial studies are projected to focus on bone health, improving balance and stability, optimal walking using dynamic orthoses, and training to run to reduce injury risk, all in lower extremity injured patients.

Prostate Cancer Research Program

Vision

Conquer prostate cancer

Mission

Fund research that will eliminate death and suffering from prostate cancer

PCRP Research Goals

In FY10, the PCRP undertook a new initiative to focus on the two most critical issues in prostate cancer. The PCRP Overarching Challenges were established, and all applications for PCRP funding were required to address at least one of the following:

- developing effective treatments for advanced prostate cancer
- distinguishing aggressive from indolent disease

In addressing these two critical needs, researchers focus their studies on biomarkers, genetics, imaging, survivorship, therapy, or tumor biology and immunology.

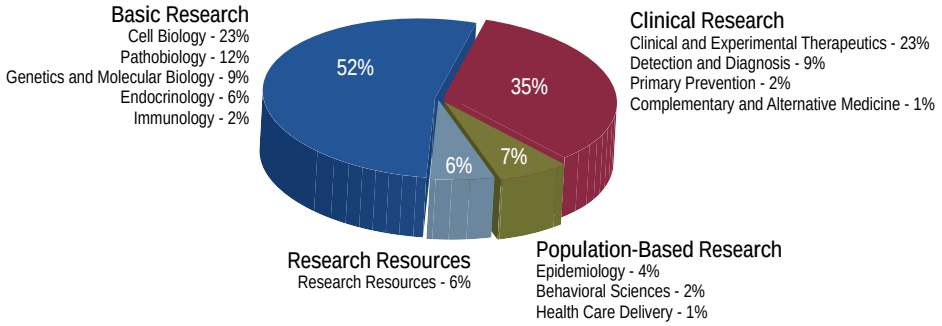
Program History

> *What a tremendous investment the PCRP has been for patients, scientists, clinicians, and the American people.*
>
> *Natasha Kyprianou, Ph.D.*
> *FY11 IP Chair*

The DOD PCRP started in 1997 when Congress provided its first appropriation directly targeted to support groundbreaking research toward the goal of eliminating prostate cancer. This initiative resulted from grassroots efforts by survivors and supporters dedicated to bringing hope to the more than 200,000 men diagnosed and more than 30,000 men dying from prostate cancer each year. From 1997–2011, these efforts resulted in the PCRP receiving over $1.1B in appropriations, including $80M in 2011. In that time, the program has changed the landscape of biomedical research, energizing the research community to conduct high-risk research that is more collaborative, innovative, and impactful on prostate cancer. The PCRP has played a major role in supporting the development of new treatments for advanced prostate cancer, has been the leading supporter of research toward understanding and resolving ethnic disparities in prostate cancer incidence and mortality, and has fostered the development of hundreds of new investigators who have become leaders in cutting-edge research that is making a difference for prostate cancer patients and will ultimately conquer the disease.

Program Portfolio

From 1997–2010, the PCRP funded more than 2,334 research projects. These projects range from exploratory studies to generate cutting-edge ideas to establishing multi-institutional consortia designed to change how science is done. By getting to answers faster, the PCRP researchers can realize their goal of having a direct, positive impact on prostate cancer patients and their families.



FY97–FY10 PCRP Portfolio by Research Categories

Research Breakthroughs Supported by the PCRP

- **Critical Role of the PCRP in FDA Approval of Abiraterone Acetate:** The PCCTC was critical to rapidly completing the Phase 1 and 2 clinical trials that helped move abiraterone acetate (ZYTIGA™) to FDA approval and drug availability for patients with the most lethal form of prostate cancer: metastatic, castration-resistant prostate cancer (CRPC). *PCCTC Awardees*
- **Discovery of New Drug Candidates for the Prevention of CRPC:** A novel small molecule inhibitor of the androgen receptor (AR) was isolated, characterized, and shown to block the growth of CRPC. Unlike current anti-androgen therapies, this inhibitor targets the amino terminal region of the AR and prevents protein-protein interactions that drive the gene expression that leads to uncontrolled growth of CRPC. *Dr. Marianne Sadar, British Columbia Cancer Agency*
- **Insight and Intervention for Prostate Cancer Skeletal Metastases:** In 2010 the FDA approved denosumab (XGEVA™) for treatment of bone loss during prostate cancer treatment based, in part, on PCRP-funded preclinical studies demonstrating that inhibiting a key regulator of bone resorption, RANKL (receptor activator of NF-kB ligand) can slow the progression of prostate cancer bone metastases. *Dr. Evan Keller, University of Michigan*
- **New Antibody Inhibits Prostate Cancer Growth, Metastasis, and Castration Resistance:** PCRP-funded studies identified and characterized an antibody that targets a protein, N-cadherin, present on the surface of metastatic prostate cancer cells. The antibody slows the progression of prostate cancer and prevents tumor invasion and metastasis. *Drs. Robert Reiter and Matthew Rettig, University of California, Los Angeles*

Advances on the horizon: PCRP-funded investigators are focusing great effort on a replacement for the invasive prostate cancer biopsy; circulating tumor cells could one day be used to diagnose prostate cancer through a simple blood draw.

> *"I have seen the PCRP provide opportunities for research like no other entity. The types of funding mechanisms they provide allow researchers to quickly change directions and follow new leads, moving innovative approaches into the clinic."*
>
> *Donna Peehl, Ph.D.*
> *Funded Investigator*

National Resources to Support Research

The PCRP has established three national resources to combat prostate cancer, including:

The Prostate Cancer Clinical Trials Consortium—tests novel drugs for the rapid development and utilization of effective treatments for PC patients (http://pcctc.org)

The Prostate Cancer Biorepository Network—provides high-quality prostate cancer biospecimens to researchers (www.prostatebiorepository.org)

The Prostate Cancer Project—investigates major factors associated with health disparity (http://www.ncla-pcap.org)

Looking Forward

As the PCRP moves forward, it will continue to push for innovative research that responds to critical needs in research and patient care. The program's funding opportunities are designed to address the PCRP overarching challenges, as shown by examples such as the ***Impact Award***, targeting the problem of overtreatment of primary prostate cancer, the ***Laboratory-Clinical Transition Award***, developing more effective treatments for advanced prostate cancer by funding the final stages of preclinical testing, and the ***Physician Research Training Award***, transitioning prostate cancer physicians into independent researchers best able to design innovative projects tailored to the needs of patients. These and other initiatives will move the PCRP closer to its vision of conquering prostate cancer.

Psychological Health and Traumatic Brain Injury Research Program

Vision

To prevent, mitigate, and treat the effects of traumatic stress and traumatic brain injury on function, wellness, and overall quality of life for service members as well as their caregivers and families

Mission

Establish, fund, and integrate both individual and multi-agency research efforts that will lead to improved prevention, detection, and treatment of PH/TBI

Outcomes

To date, the 289 awards made by the PH/TBI Research Program have resulted in:

142 Publications

11 Patents pending/ granted

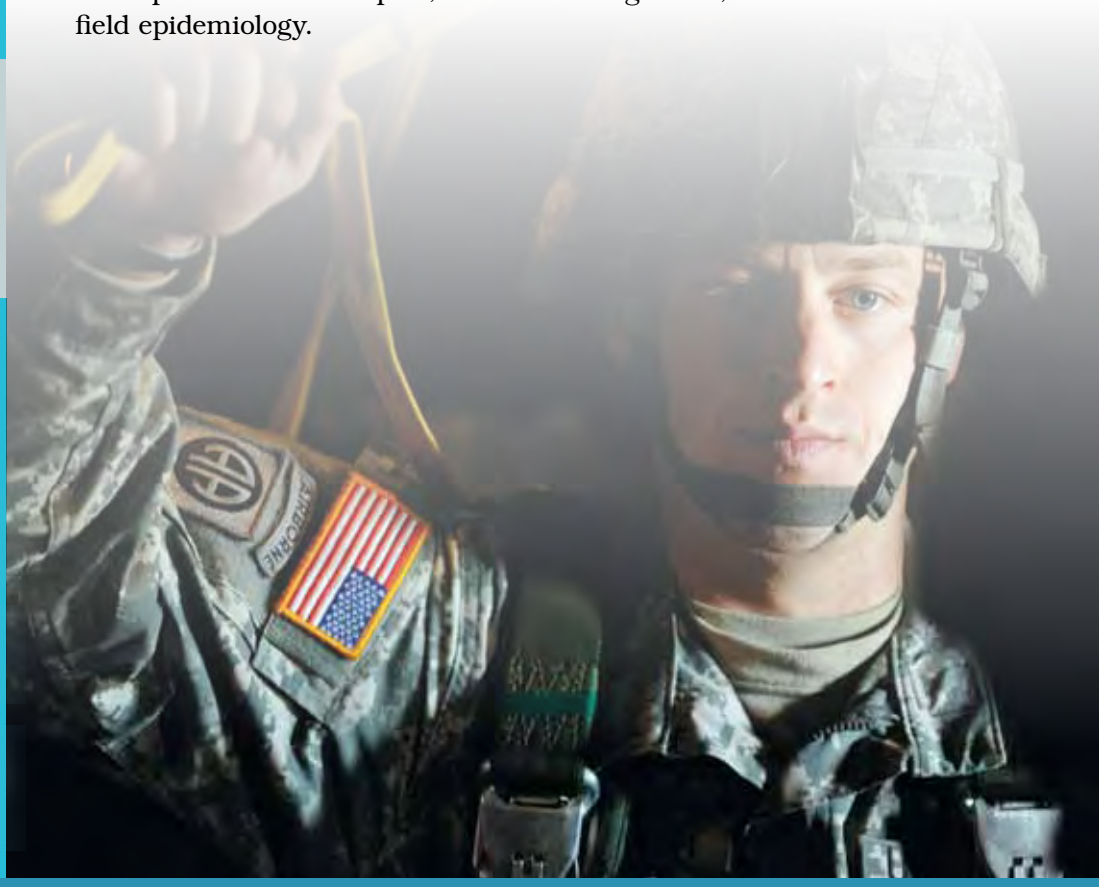
32 Additional grants obtained for further investigation

Program History

The PH/TBI Research Program was established in FY07 for the purpose of complementing ongoing DOD efforts toward promoting a better standard of care for PH (including PTSD) and TBI in the areas of prevention, detection, diagnosis, treatment, and rehabilitation. This includes research to benefit service members, their family members, veterans, and other beneficiaries of the military health system. A total of $586M, appropriated by Congress between FY07 and FY10 to support PH/TBI research, was assigned to the USAMRMC. The USAMRMC CDMRP was assigned management responsibility for $409.3M, which has supported 276 research awards.

Starting in FY10, the Program Management process was modified to include coordination with relevant USAMRMC JPCs during vision setting, programmatic review, and award management to leverage these CSI dollars in support of critical core DOD research priorities. For more information on the partnership and collaboration of the CDMRP with the JPCs including program execution and management, see pages 8 and 13.

The PH/TBI Research Program is committed to supporting our service members through innovative research addressing: screening, detection, diagnosis, treatment and intervention, neurobiology and genetics, prevention, families and caregivers, epidemiology, physics of blast, rehabilitation and reintegration, neuroprotection and repair, clinical management, and field epidemiology.



Making Major Advancements Through Collaboration

The PH/TBI Research Program is supporting innovative projects and multidisciplinary collaborations that have the potential to make a significant impact on the overall quality of life of service members and their families.

PTSD/TBI Clinical Consortium

The mission of the INTRuST (Injury & Traumatic Stress) Clinical Consortium is to improve functioning, wellness, and quality of life for U.S. service members, their families, and their caregivers by developing and evaluating novel treatments or interventions to ultimately decrease the impact of military-relevant PH problems and TBI. Dr. Murray Stein, at University of California, San Diego (UCSD), serves as Director of the INTRuST Clinical Consortium, which is a network composed of a clinical coordinating center at UCSD, 10 clinical sites, and 18 additional military treatment centers and VA medical centers that will participate in conducting 14 clinical trials as well as managing a biorepository and neuroimaging repository to decrease the impact of military-relevant PTSD and TBI. An external advisory board provides independent, expert advice regarding the progress of the INTRuST Consortium.

PTSD Multidisciplinary Research Consortium

The PTSD Multidisciplinary Research Consortium, STRONG STAR (South Texas Research Organizational Network Guiding Studies on Trauma and Resilience), is dedicated to the development and evaluation of the most effective interventions for the detection, prevention, and treatment for combat-related PTSD. The STRONG STAR team of approximately 100 military, civilian, and VA investigators and clinicians is led by Dr. Alan Peterson at University of Texas Health Science Center at San Antonio. This location is ideal as it includes the largest military medical complex in the DOD, the nation's largest concentration of OIF/OEF veterans, and is home to Fort Hood with more than 50,000 active duty personnel. The ultimate goal of the STRONG STAR consortium is to reduce or eliminate combat-related PTSD in active-duty military and recently discharged veterans, thereby contributing to the resilience and long-term health of our fighting forces. The STRONG STAR consortium is conducting 13 projects, including one animal study, retrospective data analyses, epidemiological studies, a data repository, a biorepository, and 10 clinical studies that are being conducted at seven sites.

TBI Multidisciplinary Research Consortium

The Mission Connect Mild TBI Research Consortium combines the efforts of more than 20 TBI investigators to improve the diagnosis and treatment of mild TBI through collaborative basic and clinical research. Led by Dr. James McCarthy (pictured left) at the University of Texas Health Science Center at Houston and Dr. Claudia Robertson (pictured right) at the Baylor College of Medicine, the Consortium approaches its goals by performing the spectrum of research from basic science through clinical trials. To date the Consortium has made notable progress on all projects, including the first complete characterization of acute cerebral effects of explosive blast injury in experimental animals and development of a novel antioxidant therapy for TBI using nanomaterials.

Spinal Cord Injury Research Program

Vision

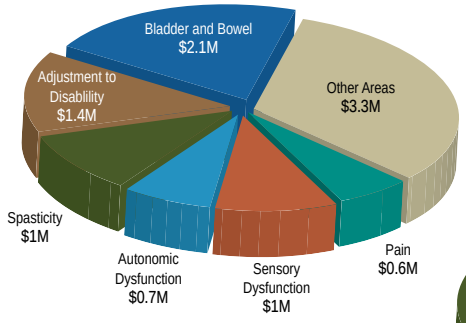
Advance the understanding of spinal cord injury and ameliorate its consequences

Mission

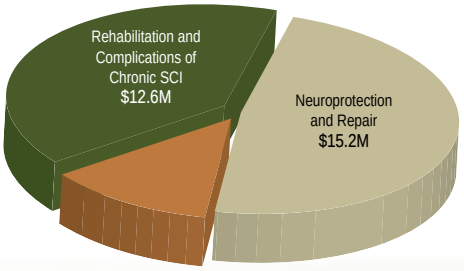
To fund innovative and interdisciplinary research and foster collaborative environments for the development and translation of more effective strategies to improve the health and well-being of individuals with spinal cord injury

Program History

The SCIRP was established by Congress in FY09 with a $35M appropriation to support research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies. Congress appropriated $11.25M in FY10 and $12M in FY11 to support this program. The SCIRP focuses its funding on innovative projects that have the potential to make a significant impact on improving the function, wellness, and overall quality of life for military service members and veterans as well as their caregivers, families, and the American public.



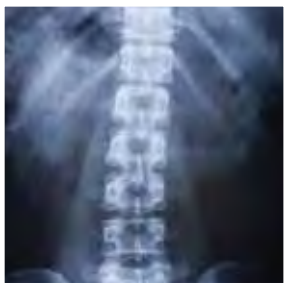
Total FY10 Investment by Area of Encouragement



Total FY09 Investment by Area of Encouragement

Clinical Trial Award – Rehabilitation

The Clinical Trial Award – Rehabilitation supports rapid implementation of rehabilitation-focused Phase 0, 1, or 2 clinical trials that have the potential for significant impact on the understanding of spinal cord injury (SCI) and amelioration of its consequences. Three of these projects were funded in FY10 for a total of $2.97M. One of these projects is a first-in-man study, led by Dr. Pierre Guertin of Nordic Life Science Pipeline, Inc., to test the safety and efficacy of a new drug called SPINALON for the induction of locomotor function in motor-complete SCI patients. This first-in-class drug is a central pattern generator-activating tritherapy that can be orally administered to elicit episodes of locomotion in an attempt to prevent or reverse secondary complications of SCI.



Investigator-Initiated Research Award

Targeting independent investigators, the Investigator-Initiated Research Award (IIRA) supports innovative projects that make an original and important contribution to SCI research and/or patient care. Six projects spanning a wide variety of research topics were awarded under the IIRA mechanism for a total of $4.72M in FY10. Dr. Linda Noble of the University of California, San Francisco, received one of these awards to investigate GM6001, a drug that blocks the activity of proteolytic enzymes called matrix metalloproteinases, which have been shown to impair neurologic recovery after SCI. This study will use mouse and dog models to determine the best time to administer GM6001 after SCI and measure its effectiveness for improving long-term neurologic and urologic recovery after moderate and severe SCI.

Qualitative Research Award

This mechanism supports qualitative research studies that will help researchers and clinicians better understand the experiences of individuals with SCI, and thereby identify the most effective paths for adjusting to disability and/or improving overall quality of life, health, and functional status after SCI. Two qualitative projects were awarded in FY10 for a total of $0.72M. Dr. Susan Charlifue of Craig Hospital is focusing her qualitative study on the health and well-being of family caregivers of veterans with SCI, since the well-being of the patient is directly related to the ability of the caregiver to cope with the challenges of caring for them. She plans to develop a tool for physicians to measure distress in SCI caregivers so that an appropriate support system can be made available to help them and ultimately improve the long-term outcomes for veterans with SCI.

Translational Research Partnership Award

The Translational Research Partnership Award is designed to support the development of translational research through multi-institutional, multidisciplinary partnerships among clinicians and basic research scientists to accelerate the movement of promising ideas in SCI research into clinical applications. Two of these projects were awarded in FY10 to 6 separate investigators for a total of $2.47M. Dr. Anthony Caggiano is heading up a team of three investigators to determine the potential of Glial Growth Factor 2 (GGF2) to promote anti-inflammatory and neuroprotective properties, as well as plasticity, when administered within the first 24–36 hours after injury. Rat and dog models will be used to determine optimal dose, route of administration, and therapeutic window, and establish tolerability and pharmacokinetics. The group expects that the results of this project will move GGF2, for which the group already holds an IND, into clinical trials and demonstrate improved functional recovery using the optimal treatment regimen they establish.

Tuberous Sclerosis Complex Research Program

Vision

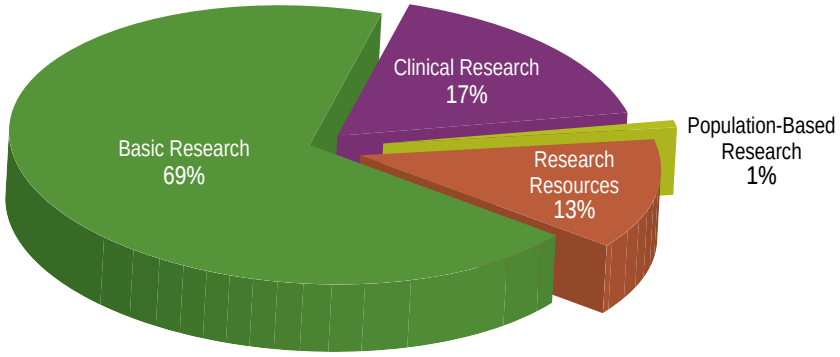
To lessen the impact of TSC

Mission

To encourage innovative research aimed at understanding the pathogenesis of TSC and to translate these findings to the care of individuals with TSC

Program History

The TSCRP was established in FY02 when the efforts of TSC advocates led to a congressional appropriation of $1M. Since then, a total of $35M has been appropriated to the program, including $6.4M in FY11. Today, the TSCRP is one of the leading sources of extramural TSC research funding in the United States. The TSCRP fills important gaps in TSC research not addressed by other funding agencies. The program's investment strategy is adapted yearly to facilitate rapid change and to better target funding to the most critical TSC research areas, thus ensuring that the program remains responsive to current needs and future opportunities. A total of 78 awards have been made through FY10, bridging basic, clinical, and population-based research, as shown below.



FY02–FY10 TSCRP Portfolio by Research Area

"From this experience [as a peer reviewer], I have learned to ask much smarter questions on behalf of the TS community and on behalf of [my son] Bao. I have also learned that this is the single most important thing I can do for my son and for those suffering from TSC."

Ron Heffron, TSCRP Consumer Peer Reviewer

Mary Koenig, M.D., University of Texas Health Science Center at Houston

Constitutive activation of the mTOR in TSC patients results in the overproduction of skin cells leading to the development of visible facial angiofibromas over time. Although rapamycin treatment inhibits the mTOR signaling pathway leading to the decrease in cell growth, this treatment results in multiple severe side effects.
Dr. Koenig hypothesized that topical rapamycin treatment would be effective in treating facial angiofibromas without causing the side effects observed upon systemic administration.
Dr. Koenig received an FY10 TSCRP Clinical Research Award to investigate the safety and efficacy of topical rapamycin for the treatment of facial angiofibromas in patients with TSC in a multicenter clinical trial.

Charles Nelson, Ph.D., Children's Hospital Boston

TSC patients often suffer from developmental delay, cognitive impairment, and ASDs. These neurodevelopmental disorders cause significant disabilities in TSC patients from early infancy through adulthood. The predictors and exact causes of neurodevelopmental disorders in TSC, however, are currently unknown. Therefore, Dr. Nelson, with funding from an FY10 TSCRP Clinical Research Award, will investigate and define predictors of ASD and cognitive impairment in infants with TSC to identify targets for early treatment intervention, which may improve neurodevelopmental outcomes for children with TSC.

Yu Li, Ph.D., Children's Hospital, Cincinnati

Renal angiomyolipomas are generally benign tumors that develop in the kidneys of 80% of TSC patients. The development of angiomyolipomas often leads to renal failure, which is the leading cause of death in adult TSC patients. Dr. Li, recipient of an FY10 TSCRP Exploration–Hypothesis Development Award, will investigate the efficacy of non-invasive thermal ablation using magnetic resonance (MR)-guided high intensity focused ultrasound (HIFU) for the treatment of renal angiomyolipomas in an animal model. This study will lay the foundation for future MR-guided HIFU clinical TSC research for the management of renal angiomyolipomas.

Mark Bear, Ph.D., Massachusetts Institute of Technology

TSC is a genetic disorder that results in the development of benign tumors and neurological impairments. It was previously determined that improper regulation of synaptic protein synthesis leads to cognitive impairment. Therefore, Dr. Bear hypothesizes that dysregulation of group 1 metabotropic glutamate receptors (mGluRs), involved in regulating synaptic protein synthesis, may be involved in the cognitive deficiencies associated with TSC.
Dr. Bear received an FY10 Idea Development Award to investigate the function of mGluRs in a TSC mouse model and evaluate mGluRs as therapeutic targets for the treatment of cognitive impairment in TSC.

Appendix A: FY92–FY10

Table A-1. *CDMRP Programs, Appropriations, Applications Received and Awarded*

Program	Fiscal Year	Appropriations Received (in millions)	Applications Received	Applications Funded
Amyotrophic Lateral Sclerosis	2007, 2009-2010	$17.5	130	14
Autism	2007-2010	$29.9	749	69
Bone Marrow Failure	2008-2010	$9.8	232	25
Breast Cancer	1992-2010	$2,532.3	45,226	6,107
Chiropractic Clinical Trials	2010	$8.1	5	1
Chronic Myelogenous Leukemia	2002-2006	$22.1	252	61
Defense Medical (DHPe)	2010	$94.5	415	67
Defense Women's Health	1995	$40.0	559	69
Deployment Related Medical	2008	$101.9	1,094	50
DOD/VA	1999-2000	$6.8	88	9
Genetic Studies of Food Allergies	2009-2010	$4.4	60	9
Gulf War Illness	2006, 2008-2010	$31.0	141	43
Institutionally Based Programs	1995-2010	$486.3	306	267
Lung Cancer	2009-2010	$35.0	525	30
Multiple Sclerosis	2009-2010	$9.5	336	35
Myeloproliferative Disorders	2004	$4.3	18	9
National Prion	2002	$42.5	136	38
Neurofibromatosis	1996-2010	$214.1	1,043	269
Osteoporosis	1995	$5.0	105	5
Ovarian Cancer	1997-2010	$160.5	2,344	236
Peer-Reviewed Cancer	2009-2010	$31.0	886	68
Peer-Reviewed Medical	1999-2006, 2008-2010	$494.5	4,604	382
Peer-Reviewed Orthopaedic	2009-2010	$134.5	363	98
Prostate Cancer	1997-2010	$1,050.0	11,861	2,334
Psychological Health/Traumatic Brain Injury	2007, 2009-2010	$420.9	2,681	276
Spinal Cord Injury	2009-2010	$46.3	376	70
Tuberous Sclerosis	2002-2006, 2008-2010	$29.5	344	78
Total		**$6,061.9**	**74,879**	**10,719**

Appendix B: FY10–FY11

Table B-1. *FY10–FY11 Amyotrophic Lateral Sclerosis (ALS) Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$7.5M for the ALS Research Program	Withholds[a] USAMRMC: $188,000 Management Costs[b] $616,257 (8.43%)	Research Therapeutic Development: $3,103,454 Therapeutic Idea: $3,592,289
	Total: $7.5M	Total: $804,257	Total: $6,695,743
2011	$8M for the ALS Research Program	Withholds[a] Congressional: $200,000 USAMRMC: $351,000 Budgeted Management Costs[b] $581,000 (7.8%)	Research Budgeted Peer-Reviewed Research: $6,868,000
	Total: $8M	Total: $1,132,000	Total: $6,868,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-2. *FY10–FY11 Autism Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$8M for the Autism Research Program	Withholds[a] USAMRMC: $200,000 Management Costs[b] $717,941 (9.2%)	Research Clinical Trial: $2,897,367 Exploration-Hypothesis: $468,839 Idea Development: $2,280,968 Idea Dev Multi PI: $1,216,937 Resource Development: $217,948
	Total: $8M	Total: $917,941	Total: $7,082,059
2011	$6.4M for the Autism Research Program	Withholds[a] Congressional: $160,000 USAMRMC: $281,000 Budgeted Management Costs[b] $414,000 (6.95%)	Research Budgeted Peer-Reviewed Research: $5,545,000
	Total: $6.4M	Total: $855,000	Total: $5,545,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

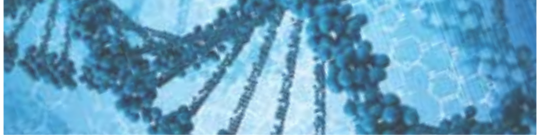


Table B-3. *FY10–FY11 Bone Marrow Failure Research Program Congressional Language and Appropriations, Withholds and Management Cost, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$3.75M for the Bone Marrow Failure Research Program	Withholds[a] USAMRMC: $94,000 Management Costs[b] $309,238 (8.46%)	Research Exploration-Hypothesis Development Award: $875,327 New Investigator Award: $2,471,435
	Total: $5M	Total: $403,238	Total: $3,346,762
2011	$4M for the Bone Marrow Failure Research Program	Withholds[a] Congressional: $100,000 USAMRMC: $175,000 Budgeted Management Costs[b] $300,000 (8.05%)	Research Budgeted Peer-Reviewed Research: $3,425,000
	Total: $4M	Total: $575,000	Total: $3,425,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-4. *FY10–FY11 Breast Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$150M for the Breast Cancer Research Program $1,004,833 in proceeds from the Stamp Out Breast Cancer Act	Withholds[a] USAMRMC: $3,750,000 Management Costs[b] $11,869,847 (8.12%)	Research Concept: $4,485,741 Era of Hope Scholar: $10,722,124 Era of Hope Scholar Expansion: $2,975,499 Transformative Vision: $7,883,980 Idea: $21,671,733 Idea Collaborative Option: $10,406,767 Idea Expansion: $6,949,163 Innovator: $22,278,299 Inter-Institutional Training: $3,998,141 Multi-Team: $15,109,880 Postdoctoral Fellowship: $18,616,896 Predoctoral Traineeships: $9,185,791 Communication $1,100,972
	Total: $151,004,833	Total: $15,619,847	Total: $135,384,986
2011	$150M for the Peer-Reviewed Breast Cancer Research Program	Withholds[a] Congressional: $3,750,000 USAMRMC: $6,581,000 Budgeted Management Costs[b] $11,169,000 (8.00%)	Research Budgeted Peer-Reviewed Research: $128,500,000
	Total: $150M	Total: $21,500,000	Total: $128,500,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-5. *FY10 Chiropractic Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$8,135,216 for Guidance for the Development of the Force	Management Costs[a] $635,509 (7.81%)	Research $7,499,707
	$8,135,216	Total: $635,509	Total: $7,499,707

[a]Percentage of management costs=management costs/(appropriation–withholds).

FY10 National Defense Authorization Act
SEC. 725. CHIROPRACTIC CLINICAL TRIALS.
(a) CLINICAL TRIALS REQUIRED.-The Secretary of Defense shall provide for the clinical trials described under subsection (b) to be conducted by the National Institutes of Health or an independent academic institution as the Secretary shall select for the purposes of conducting each trial. (b) CLINICAL TRIALS DESCRIBED.- (1) CONTROLLED TRIALS.-The clinical trials required by subsection (a) shall include controlled trials that, at a minimum, compare the outcomes of chiropractic treatment, used either exclusively or as an adjunct to other treatments, with conventional treatment on the following topics:
(A) Pain management.
(B) Orthopedic injuries or disorders that do not require surgery.
(C) Smoking cessation.
(2) INTERVENTIONAL TRIALS.-The clinical trials required by subsection (a) shall include interventional trials that, at a minimum, cover the following topics:
(A) The effect of chiropractic treatment on the reflexes and reaction times of special operation forces.
(B) The effect of chiropractic treatment on strength, balance, and injury prevention for members of the Armed Forces with combat specialties operating in a combat theater.
(c) SCHEDULE.-
(1) FIRST TRIAL.-The first clinical trial required by subsection
(a) shall begin not later than one year after the date of the enactment of this Act.
(2) FINAL TRIAL.-The final clinical trial required by subsection
(a) shall begin not later than two years after the date of the enactment of this Act.
(d) TRIAL PARTICIPANTS.-A participant of a clinical trial required by subsection (a) shall be a member of the Armed Forces on active duty.
(e) CHIROPRACTIC PROVIDERS.-Chiropractic treatment provided during a clinical trial required by subsection (a) shall be provided by a doctor of chiropractic who is licensed as a doctor of chiropractic, chiropractic physician, or chiropractor by a State, the District of Columbia, or a territory or possession of the United States, subject to credentialing requirements prescribed by the Secretary.
(f) REPORTS.-
(1) TRIAL PROTOCOL REPORTS.-Not later than 30 days before each clinical trial required by subsection (a) is scheduled to begin, the Secretary shall submit to the congressional defense committees a report on the protocol of such clinical trial.
(2) FINAL REPORTS.-Not later than one year after the completion of each clinical trial required by subsection (a), the Secretary shall submit to the congressional defense committees a report on such clinical trial, including any recommendations regarding chiropractic treatment for covered beneficiaries (as such term is defined in section 1072(5) of title 10, United States Code).

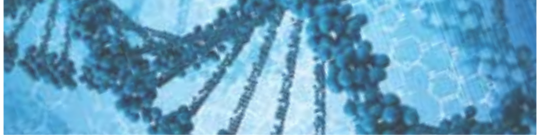


Table B-6. *FY10 Defense Medical Research and Development Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$94,530,311 for Guidance for the Development of the Force	Management Costs[a] $5,263,152 (5.64%)	Research Basic Research: $31,370,942 Applied Research and Advance Technology Development: $35,574,490 Intramural PTSD Advanced Technology/Therapeutic Development: $746,253 Advanced Technology/ Therapeutic: $440,000 DMRDP-IIRA Broad Agency Announcement (BAA): $17,148,433 Clinical Trial Award: $567,347 TBI New Investigator Award: $200,698 Cognitive Rehab Clinical Trial with Optional Partnering PI: $2,677,000 Applied Research and Advance Technology Development: $1,364,710 PH/TBI - IIRA BAA: $541,996
	Total: $94,530,311	Total: $5,263,152	Total: $89,267,159
2011	$59.9M for Guidance for the Development of the Force	Budgeted Management Costs[a] $1,225,000 (2.04%)	Research Budgeted Peer-Reviewed Research: $58,680,128
	Total: $59.9M	Total: $1,225,000	Total: $58,680,128

[a]Percentage of management costs=management costs/(appropriation–withholds).

FY10 Senate Report:
Military Medical Research-The Committee was pleased that the President's budget request included a substantial increase for military medical research. The additional $372,000,000 will address the numerous unique military medical areas of concern. The Committee understands that the Department of Defense is finalizing the capability gaps these resources will target and urges the Department to ensure the appropriate level of resources are devoted to address the following areas of research identified by the three Services: traumatic brain injury; psychological health (including suicide prevention, substance abuse, and family health and wellbeing); musculoskeletal injury; regenerative medicine for extremity injuries, burns, and craniofacial injuries; blast-related injury; infectious diseases; pain management; sensory dysfunction; respiratory disease; enroute care research (including studies on compartment syndrome, timing of transport, patient safety during transport, pain management); early recognition, diagnosis, and treatment of emerging threats (e.g., pandemic response, weaponized nanoparticles, etc.); operational medicine (including clinical patient safety studies and clinical medicine enhancements); human performance; wound management throughout the continuum of care; and undersea medicine, diving, and submarine medical research. The Committee recognizes that the while the Assistant Secretary of Defense for Health Affairs is the lead organization tasked with establishing the capability gaps, the Services all play a crucial role in developing the needs and executing the programs. In addition, there are various groups, institutions, and organizations that would like an opportunity to compete for these resources. Therefore, the Committee directs the Assistant Secretary of Defense for Health Affairs to report to the congressional defense committees by November 6, 2009 with a complete list of these capability gaps; a timeline and process for distributing and/or competing the resources; and a detailed description of how Health Affairs has integrated the Services into the development and execution process.

FY10 House Report:
GUIDANCE FOR THE DEVELOPMENT OF THE FORCE (2010-2015)
The fiscal year 2010 budget submission included $372,200,000 for traumatic brain injury, psychological health, eye injury, prosthetics, and other battlefield injuries research. The Committee has supported these types of research since 2007 and is encouraged that the Department has for the first time included funding for this type of research. The Committee urges the Department to utilize the established congressional directed medical research program and to work with the U.S. Army Medical Research and Materiel Command in finding the most efficient way of utilizing the unique and military relevant research available.

Table B-7. *FY11 Duchenne Muscular Dystrophy Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2011	$4M for the Duchenne Muscular Dystrophy Research Program	Withholds[a] Congressional: $100,000 USAMRMC: $175,000 Budgeted Management Costs[b] $300,000 (8.05%)	Budgeted Research $3,425,000
	Total: $4M	Total: $575,000	Total: $3,425,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-8. *FY10 Genetic Studies of Food Allergies Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$1.875M for the Genetic Studies of Food Allergies Research Program	Withholds[a] USAMRMC: $47,000 Budgeted Management Costs[b] $171,477 (9.38%)	Research Concept Award: $228,000 Idea Award: $1,428,523
	Total: $1.875M	Total: $218,477	Total: $1,656,523

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-9. *FY10–FY11 Gulf War Illness Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$8M for the Gulf War Illness Research Program	Withholds[a] USAMRMC: $200,000 Management Costs[b] $397,774 (5.1%)	Research Consortium Development: $767,822 Innovative Treatment Evaluation: $1,598,428 Investigator-Initiated Research: $5,035,976
	Total: $8M	Total: $597,774	Total: $7,402,226
2011	$8M for the Gulf War Illness Research Program	Withholds[a] Congressional: $200,000 USAMRMC: $351,000 Budgeted Management Costs[b] $599,000 (8.04%)	Research Budgeted Peer-Reviewed Research: $6,850,000
	Total: $8M	Total: $1,150,000	Total: $6,850,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

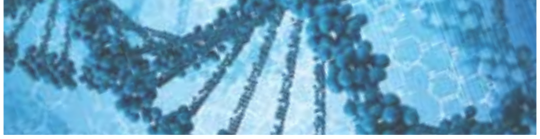


Table B-10. *FY10–FY11 Lung Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$15M for the Lung Cancer Research Program	Withholds[a] USAMRMC: $375,000 Management Costs[b] $944,013 (6.45%)	Research Lung Cancer Early Detection Clinical Consortium Award: $13,680,987
	Total: $15M	Total: $1,319,013	Total: $13,680,987
2011	$12.8M for the Lung Cancer Research Program	Withholds[a] Congressional: $320,000 USAMRMC: $562,000 Budgeted Management Costs[b] $953,000 (8%)	Research Budgeted Peer-Reviewed Research: $10,965,000
	Total: $12.8M	Total: $1,835,000	Total: $10,965,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

FY10 House Report:
PEER-REVIEWED LUNG CANCER RESEARCH
The Committee has included $15,000,000 for peer-reviewed lung cancer research. Lung cancer, continues to be the most lethal of all cancers, taking more lives annually than all other major cancers combined. The five year survival rate is only 15 percent and a major contributor is that 70 percent of the diagnoses are late stage. Furthermore, military personnel have increased exposure to lung cancer carcinogens and are thus more susceptible to lung cancer than the general population. These funds, in conjunction with the funds provided in fiscal year 2009, are primarily for an early detection program for military beneficiaries. It is expected that this early detection regimen will be initially implemented in Military Medical Treatment facilities in the National Capital Region.

Table B-11. *FY10–FY11 Multiple Sclerosis Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$4.5M for the Multiple Sclerosis Research Program	Withholds[a] USAMRMC: $113,000 Management Costs[b] $519,409 (11.84%)	Research Concept: $1,008,911 Idea: $2,858,680
	Total: $4.5M	Total: $632,409	Total: $3,867,591
2011	$4.8M for the Multiple Sclerosis Research Program	Withholds[a] Congressional: $120,000 USAMRMC: $211,000 Budgeted Management Costs[b] $359,000 (8.03%)	Research Budgeted Peer-Reviewed Research: $4,110,000
	Total: $4.8M	Total: $690,000	Total: $4,110,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-12. *FY10–FY11 Neurofibromatosis Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$13.75M for the Neurofibromatosis Research Program	Withholds[a] USAMRMC: $344,000 Management Costs[b] $982,761 (7.33%)	Research Clinical Trial: $1,308,192 Exploration - Hypothesis Development: $826,251 Investigator-Initiated Focused Research: $2,762,620 Investigator-Initiated Research: $4,002,309 New Investigator: $2,881,876 Postdoctoral Traineeship: $641,991
	Total: $13.75M	Total: $1,326,761	Total: $12,423,239
2011	$16M for the Neurofibromatosis Research Program	Withholds[a] Economic Assumptions: $81,000 FFRDC Reduction: $12,000 USAMRMC: $694,000 SBIR: $422,000 STTR: $55,000 Budgeted Management Costs[b] $1,176,000(7.98%)	Research Budgeted Peer-Reviewed Research: $13,560,000
	Total: $16M	Total: $2,410,000	Total: $13,560,000

[a]The following abbreviations are used for withholds: FFRDC, Federally Funded Research and Development Center; USAMRMC, U.S. Army Medical Research and Materiel Command; SBIR, Small Business Innovation Research; STTR, Small Business Technology Transfer.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-13. *FY10–FY11 Ovarian Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$18.75M for the Ovarian Cancer Research Program	Withholds[a] USAMRMC: $469,000 Management Costs[b] $1,411,000 (7.72%)	Research Pilot: $4,115,417 Translational Pilot: $3,052,835 Consortium: $9,701,748
	Total: $18.75M	Total: $1,880,000	Total: $16,870,000
2011	$20M for the Ovarian Cancer Research Program	Withholds[a] Congressional: $500,000 USAMRMC: $877,000 Budgeted Management Costs[b] $1,492,000 (8.01%)	Research Budgeted Peer-Reviewed Research: $17,131,000
	Total: $20M	Total: $2,869,000	Total: $17,131,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

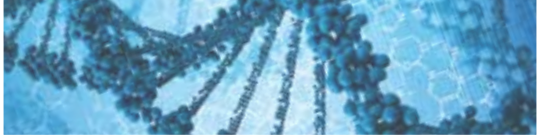


Table B-14. *FY10–FY11 Peer-Reviewed Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$15M for the Peer-Reviewed Cancer Research Program	Withholds[a] USAMRMC: $375,000 Management Costs[b] $1,363,714 (9.32%)	Research Blood Cancer: $2,059,253 Colorectal Cancer: $1,982,333 Genetic Cancer Research and Genomic Medicine: $2,862,226 Kidney Cancer: $1,776,990 Listeria Vaccine for Cancer: $543,200 Melanoma and Other Skin Cancers: $1,504,374 Pediatric Brain Tumor: $2,532,910
	Total: $15M	Total: $1,738,714	Total: $13,261,286
2011	$16M for the Peer-Reviewed Cancer Research Program	Withholds[a] Congressional: $400,000 USAMRMC: $702,000 Budgeted Management Costs[b] $1,130,486 (7.59%)	Research Budgeted Peer-Reviewed Research: $13,767,514
	Total: $16M	Total: $2,232,486	Total: $13,767,514

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command;

[b]Percentage of management costs=management costs/(appropriation–withholds).

FY10 Peer-Reviewed Cancer Research Program: The Committee provides $20,000,000 for a peer-reviewed cancer research program that would research cancers not addressed in the breast, prostate, lung and ovarian cancer research programs currently executed by the Department of Defense, and specifically the U.S. Army Medical Research and Materiel Command (USAMRMC). The funds provided are directed to be used to conduct research in the following areas: melanoma and other skin cancers, pediatric brain tumors within the field of childhood cancer research, genetic cancer research and genomic medicine, kidney cancer, blood cancer, colorectal cancer, listeria vaccine for infectious disease and cancer, and radiation protection utilizing nanotechnology. The funds provided under the Peer-Reviewed Cancer Research Program shall be used only for the purposes listed above. The Department of Defense is directed to provide a report by February 8, 2010, to the congressional defense committees on the status of the Peer-Reviewed Cancer Research Program as to the relevance of this type of research for service members and their families.

FY11 Peer-Reviewed Cancer Research Program: The recommendation provides $16,000,000 for a peer-reviewed cancer research program. The Department of Defense is directed to provide a report not later than 60 days after enactment of this Act to the congressional defense committees on the status of the peer-reviewed cancer reasearch programs. The funds provided are directed to be used to conduct research in the following areas: melanoma and other skin cancers, pediatric and childhood cancer research, genetic cancer research, pancreatic cancer, kidney cancer, blood cancer, colorectal cancer, mesothelioma, radiation protection utilising nanontechnology, and listeria vaccine for infectious disease and cancer. The funds provided under the Peer-Reviewed Cancer Research Program shall be used only for the puposes listed above.

The CDMRP requested Congressional guidance regarding topic area overlap between the PRCRP and the Peer Reviewed Medical Research Program (PRMRP). Both programs were directed to solicit proposals for the topics areas blood cancer, kidney cancer and melanoma with specific language appearing in the Joint Explanatory Statement and the House Appropriations Committee for Defense Report 111-230. Additionally, the CDMRP asked for guidance regarding the PRCRP directed topic area of Listeria vaccine for infectious disease and cancer research. The guidance received from the Congressional Liaison of the Office of the Surgeon General (OTSG) directed the three topic areas of blood cancer, kidney cancer, and melanoma to be included in the PRCRP solicitation for proposals but not PRMRP. Further guidance removed Listeria vaccine for infectious disease from the PRCRP topic area language and placed this topic area in PRMRP. Listeria vaccine for cancer remained in the PRCRP topic area list.

Table B-15. *FY10–FY11 Peer-Reviewed Medical Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$50M for the Peer-Reviewed Medical Research Program	Withholds[a] USAMRMC: $1,250,000 Management Costs[b] $4,115,242 (8.44%)	Research Padget's Disease: $112,728 Osteoporosis and Related Bone Disease: $8,099,986 Interstitial Cystitis: $276,934 Lupus: $2,414,066 Drug Abuse: $4,546,494 Epilepsy: $2,929,235 Inflammatory Bowel Disease: $3,603,201 Mesothelioma: $2,992,742 Tinnitus: $1,238,878 Neuroblastoma: $2,369,606 Dystonia: $250,468 Fragile X Syndrome: $4,172,619 Pheochromocytoma: $1,131,106 Post Traumatic Osteoarthritis: $2,673,291 Chronic Migraine and Post-Traumatic Headache: $2,261,849 Scleroderma: $2,173,555 Social Work Research: $3,388,000
	Total: $50M	Total: $5,365,242	Total: $44,634,758
2011	$50M for the Peer-Reviewed Medical Research Program	Withholds[a] Congressional: $1,250,000 USAMRMC: $2,194,000 Budgeted Management Costs[b] $3,726,000 (8.0%)	Research Budgeted Peer-Reviewed Research: $42,830,000
	Total: $50M	Total: $7,170,000	Total: $42,830,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

FY10 Peer-Reviewed Medical Research Program: The recommendation provides $50,000,000 for a peer-reviewed medical research program. The Secretary of Defense, in conjunction with the Service Surgeon General, is directed to select medical research projects of clear scientific merit and direct relevance to military health. Research areas considered under this funding are restricted to: blood cancer, chronic migraine and post-traumatic headache, dystonia, drug abuse, epilepsy, fragile X syndrome, Inflammatory bowel disease, interstitial cystitis, kidney cancer, lupus, melanoma, meosthelioma, neuroblastoma, osteoporosis and related bone disease, Padget's disease, pheochromocytoma, polycystic kidney disease, post-traumatic osteoarthritis, scleroderma, social work research, and tinnitus. The recommendation emphasizes that the additional funding provided under the Peer-Reviewed Medical Research Program shall be devoted only to the purposes listed above.

FY11 Peer-Reviewed Medical Research Program: The recommendation provides $50,000,000 for a peer-reviewed medical research program and the Secretary of Defense, in conjunction with the Service Surgeon General, is directed to select medical research projects of clear scientific merit and direct relevance to military health. Research areas considered under this funding are restricted to: chronic fatigue syndrome, chronic migraine and post-traumatic headache, drug abuse, epidermolysis bullosa, epilepsy, fragile X syndrome, inflammatory bowel disease, interstitial cystitis, lupus, neuroblastoma, osteoporosis and related bone disease, Paget's disease, pancreatitis, pheochromocytoma, polycystic kidney disease, post-traumatic osteoarthritis, scleroderma, social work research, and tinnitus. The additional funding provided under the Peer-Reviewed Medical Research Program shall be devoted only to the purposes listed above.

The CDMRP requested Congressional guidance regarding topic area overlap between the PRCRP and the Peer Reviewed Medical Research Program (PRMRP). Both programs were directed to solicit proposals for the topics areas blood cancer, kidney cancer and melanoma with specific language appearing in the Joint Explanatory Statement and the House Appropriations Committee for Defense Report 111-230. Additionally, the CDMRP asked for guidance regarding the PRCRP directed topic area of Listeria vaccine for infectious disease and cancer research. The guidance received from the Congressional Liaison of the Office of the Surgeon General (OTSG) directed the three topic areas of blood cancer, kidney cancer, and melanoma to be included in the PRCRP solicitation for proposals but not PRMRP. Further guidance removed Listeria vaccine for infectious disease from the PRCRP topic area language and placed this topic area in PRMRP. Listeria vaccine for cancer remained in the PRCRP topic area list.

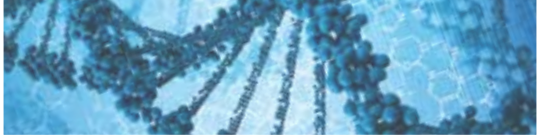


Table B-16. *FY10–FY11 Peer-Reviewed Orthopaedic Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$22.5M for the Peer-Reviewed Orthopaedic Research Program	Withholds[a] USAMRMC: $563,000 Management Costs[b] $1,716,678 (7.83%)	Research Orthopaedic Rehabilitation Clinical Consortium: $19,698,544 Career Development: $521,778
	Total: $22.5M	Total: $2,279,678	Total: $20,220,322
2011	$24M for the Peer-Reviewed Orthopaedic Research Program	Withholds[a] Congressional: $600,000 USAMRMC: $1,053,000 Budgeted Management Costs[b] $1,787,000 (8%)	Research Budgeted Peer-Reviewed Research: $20,560,000
	Total: $24M	Total: $3,440,000	Total: $20,560,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-17. *FY10–FY11 Prostate Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$80M for the Prostate Cancer Research Program	Withholds[a] USAMRMC: $2,000,000 Management Costs[b] $6,460,386 (8.28%)	Research Exploration-Hypothesis Development: $3,104,239 Health Disparity Research: $4,023,855 Health Disparity Training: $439,244 Idea Development-Established Investigator: $22,673,872 Idea Development-New Investigator: $13,549,901 Impact: $3,128,108 Laboratory-Clinical Transition: $3,194,841 Physician Research Training: $4,074,870 Population-Based Research: $1,872,759 Prostate Cancer Training: $4,608,425 Synergistic Idea: $6,992,728 Clinical Consortium-Clinical Research Site: $3,591,159 Communication $285,613
	Total: $80M	Total: $8,460,386	Total: $71,539,614
2011	$80M for the Prostate Cancer Research Program	Withholds[a] Congressional: $2,000,000 USAMRMC: $3,510,000 Budgeted Management Costs[b] $5,960,000 (8.00%)	Research Budgeted Peer-Reviewed Research: $68,530,000
	Total: $80M	Total: $11,470,000	Total: $68,530,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

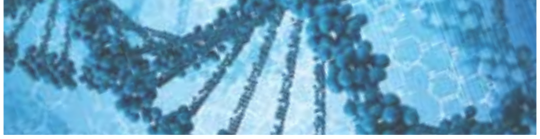


Table B-18. *FY10–FY11 Psychological Health/Traumatic Brain Injury Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$62,388,031 for the Psychological Health/ Traumatic Brain Injury Research Program	Management Costs[a] $3,552,637 (5.65%)	Research Advanced Technology/Therapeutic Development: $3,822,760 Applied Research and Advanced Technology Development: $9,961,910 Basic Research: $5,106,375 Cognitive Rehabilitation Clinical Trial Awards: $10,632,523 Concept Award: $663,490 Intramural PTSD Investigator-Initiated Research: $45,095 Investigator-Initiated Research: $3,867,915 PH/TBI Clinical Trial Award BAA: $2,499,948 PH/TBI IIRA BAA: $17,366,801 PTSD Multidisciplinary Research Consortium: $4,898,577
	Total (CDMRP): $50,685,508	Total: $3,552,637	Total: $58,865,394
2011	$60,160,769 for the Psychological Health/ Traumatic Brain Injury Research Program	Budgeted Management Costs[a] $4,110,000 (6.83%)	Research Budgeted Peer-Reviewed Research: $56,050,769
	Total (CDMRP): $60,160,769	Total: $4,110,000	Total: $56,050,769

[a]Percentage of management costs=management costs/(appropriation–withholds).

FY10 Joint Explanatory Statement: Traumatic Brain Injury and Psychological Health: The recommendation provides $120,000,000 for Traumatic Brain Injury (TBI) and Psychological Health research and treatment efforts. The fiscal year 2010 budget submission included $372,000,000 to address numerous unique military medical areas of concern including TBI and Psychological Health. The Department is encouraged to refer to the language in the House and Senate reports regarding gaps in research that need to be addressed within this funding to close those disparities.

FY10 House Report: TRAUMATIC BRAIN INJURY AND PSYCHOLOGICAL HEALTH

Traumatic Brain Injury (TBI) and psychological health issues have emerged as a significant cause of death to the warfighters in Iraq and Afghanistan. Whether mild, moderate or severe brain injury, the level of assessment and standard of care provided to the warfighter is in need of enhancement. Diagnosis, treatment, and rehabilitation must be at a level to ensure the best possible outcome. To this end, the bill includes $500,000,000, which is $127,800,000 above the budget request, to address all levels of brain injury and psychological health issues that servicemembers and their families experience.

The Department provides specialized treatment and rehabilitation for brain injured troops, but much more is needed. The Department is expected to continue to provide the necessary care and treatment to servicemembers and their families. The vast majority of disabled troops will ultimately return to their home communities, which may be far removed from specialized centers. Therefore, the identification of local services is crucial to an appropriate rehabilitation plan. The Department of Defense Military Centers and the Department of Veterans Affairs should coordinate with civilian centers to guarantee that optimal treatments and assistance are available throughout the country.

The Committee is aware of gaps within TBI and psychological treatment methods that need to be addressed. The Department is expected to continue working with the Department of Veterans Affairs, Department of Health and Human Services, academia and industry to focus on the research and treatment necessary to address the gaps that have been identified.

An area of particular interest is the provision of appropriate and accessible counseling to servicemembers and their families who live in locations that are not close to military treatment facilities, other Military Health System health facilities or TRICARE providers.

Funding provided in this bill is also to be used for the development and operation of the Defense Center of Excellance (DCoE) and the various centers, programs and initiatives that fall within its purview and resources to support the service medical departments as they continue to build and expand their TBI and psychological health capacity through initiatives and supportive programs. Other initiatives, such as telehealth, clinical standards supporting TBI and psychological health, and training and education outreach should also be included. Funding has also been provided to continue medical research and development on TBI and psychological health. The following research topics are recommended for consideration under this program: therapeutic drug discovery; optical imaging of blood flow; headache disorders; research into neural prothesis; studies of mental health disorders and Post Traumatic Stress Disorder (PTSD) to include neuropsychiatric studies, biochemical mechanisms that underlie human emotional reactions to combat stress and resulting clinical disorders, metrics for mental health assessment and methods to evaluate and improve PTSD rehabilitation efforts; studies of Traumatic Brain Injury (TBI) including basic research on neural injury treatments, cell replacement and regrowth strategies, specific therapies to prevent and reverse spinal cord and other neurotraumatic damage, pharmaceutical interventions to stimulate neural circuits, “activity-

based" physical therapy, and extended rehabilitation focused on impairments in vision and cognitive functioning; clinical research of blast-related cell damage and the resulting effects on neurological response; 3D models of IED blast waves to develop equipment to mitigate injury to service members; a fully automated, self contained, disposable chip to diagnose TBI at the point of onset; DA-EEG assessment and MRI quantization to allow an accurate assessment of TBI; computational approaches to integrate global transcriptomics and proteomics information to indentify the biological networks altered following TBI; studies of PTSD and/or TBI including basic research in neurorehabilitation, the integration of informatics, and advanced computational research to analyze brain tissue and activities, the use of advanced neuroimaging, behavioral and genetic information to develop biomarkers, diagnostics, and treatments for semi-acute and chronic injury stages. Funding provided for research and development shall incorporate all aspects of research in the areas of TBI and psychological health by conducting basic science and translational research for the purposes of understanding the etiology, developing preventive interventions and new treatments, and evaluating the outcomes to arrive at best-practice solutions. This requirement includes incorporating training, combat theater operations, post deployment evidence-based preventive and early intervention measures, practices, or procedures to reduce the likelihood that personnel in combat will develop PTSD or other stress-related conditions or sustain traumatic brain injuries.

Table B-19. *FY10–FY11 Spinal Cord Injury Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$11.25M for the Spinal Cord Injury Research Program	Withholds[a] USAMRMC: $281,000 Management Costs[b] $784,210 (7.15%)	Research Clinical Trial-Rehabilitation: $2,959,495 Investigator-Initiated Research: $4,326,548 Qualitative Research: $708,883 Translational Research Partnership: $2,189,864
	Total: $11.25M	Total: $1,065,210	Total: $10,184,790
2011	$12M for the Spinal Cord Injury Research Program	Withholds[a] Congressional: $300,000 USAMRMC: $526,000 Budgeted Management Costs[b] $893,000 (7.99%)	Research Budgeted Peer-Reviewed Research: $10,281,000
	Total: $12M	Total: $1,719,000	Total: $10,281,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

FY10 House Report: Spinal cord injuries are one of the many serious wounds resulting from conflicts in Iraq and Afghanistan that require many levels of research and treatment. Significant funding has been provided for research and treatment for neuro-traumatic wounds. However, given the complexity of these types of injuries and the steep learning curve associated with establishing effective treatment regimes, there is much more to be done. For the coming years, research into regenerating damaged spinal cords, arthritis research, and improving rehabilitation therapies offers real promise for enhancing the long-term care of wounded soldiers. Therefore, the Committee provides $15,000,000 to continue a competitive, peer-reviewed spinal cord injury research and treatment program. The Secretary of Defense is directed to submit a report to the congressional defense committees not later than 120 days after enactment of this Act on how these funds are to be allocated.

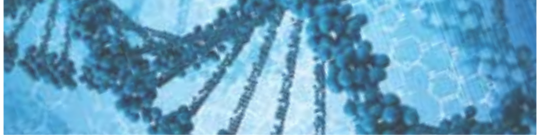


Table B-20. *FY10–FY11 Tuberous Sclerosis Complex Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
2010	$6M for the Tuberous Sclerosis Complex Research Program	Withholds[a] USAMRMC: $150,000 Management Costs[b] $463,706 (7.93%)	Research Clinical Research: $3,288,986 Exploration-Hypothesis Development: $709,412 Idea Development: $1,387,896
	Total: $6M	Total: $613,706	Total: $5,386,294
2011	$6.4M for the Tuberous Sclerosis Complex Research Program	Withholds[a] Congressional: $160,000 USAMRMC: $281,000 Budgeted Management Costs[b] $479,000 (8.04%)	Research Budgeted Peer-Reviewed Research: $5,480,000
	Total: $6.4M	Total: $920,000	Total: $5,480,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-21. *FY10 Institutionally Based Research Programs Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
ALS Therapy Development for Gulf War Illness Research			
2010	$1.6M for ALS Therapy Development for Gulf War Illness Research	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,000 (8%)	Research Peer-Reviewed Research: $1,430,000
	Total: $1.6M	Total: $170,000	Total: $1,430,000
Cancer Prevention Through Remote Biological Sensing Research			
2010	$1.6M for Cancer Prevention through Remote Biological Sensing Research	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,000 (8%)	Research Peer-Reviewed Research: $1,430,000
	Total: $1.6M	Total: $170,000	Total: $1,430,000
Center for Cancer Immunology Research			
2010	$1.6M for Center for Cancer Immunology Research	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,005 (7.86%)	Research Peer-Reviewed Research: $1,429,995
	Total: $1.6M	Total: $170,005	Total: $1,429,995
Center for Research on Minority Health Prostate Cancer			
2010	$0.8M for Minority Health Prostate Cancer Outreach Project	Withholds[a] USAMRMC: $20,000 Management Costs[b] $60,000 (7.69%)	Research Peer-Reviewed Research: $720,000
	Total: $0.8M	Total: $80,000	Total: $720,000
Childhood Cancer			
2010	$1.6M for Pediatric Cancer Research and Clinical Trials	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $158,489 (10.21%)	Research Peer-Reviewed Research: $1,393,511
	Total: $1.6M	Total: $206,489	Total: $1,393,511
Cold Springs Harbor Laboratory Women's Cancer Genomics Center			
2010	$2.4M for Women's Cancer Genomics Center Research	Withholds[a] Army: $13,000 USAMRMC: $60,000 Management Costs[b] $187,000 (8%)	Research Peer-Reviewed Research: $2,140,000
	Total: $2.4M	Total: $260,000	Total: $2,140,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

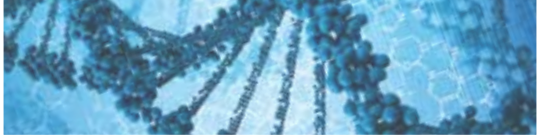


Table B-21 (cont.) *FY10 Institutionally Based Research Programs Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
Cooperative International Neuromuscular Research Group			
2010	$3.28M for Cooperative International Neuromuscular Research Group	Withholds[a] Army: $17,000 USAMRMC: $82,000 Management Costs[b] $258,421 (8%)	Research Peer-Reviewed Research: $2,922,579
	Total: $3.28M	Total: $357,421	Total: $2,922,579
Duchenne Muscular Dystrophy Research			
2010	$3.75M for Duchenne Muscular Dystrophy Research	Withholds[a] USAMRMC: $94,000 Management Costs[b] $291,000 (7.96%)	Research Peer-Reviewed Research: $3,365,000
	Total: $3.75M	Total: $385,000	Total: $3,365,000
Enhancing Wound Healing, Tissue Regeneration, and Biomarker Discovery			
2010	$2M for Enhancing Wound Healing, Tissue Regeneration, and Biomarker Discovery	Withholds[a] Army: $10,000 USAMRMC: $50,000 Management Costs[b] $155,000 (7.99%)	Research Peer-Reviewed Research: $1,785,000
	Total: $2M	Total: $215,000	Total: $1,785,000
Fighting Combat-Related Fatigue Research			
2010	$0.8M for Fighting Combat-Related Fatigue Research	Withholds[a] Army: $4,000 USAMRMC: $20,000 Management Costs[b] $61,000 (7.86%)	Research Peer-Reviewed Research: $715,000
	Total: $0.8M	Total: $85,000	Total: $715,000
Marty Driesler Lung Cancer Research			
2010	$1.6M for Marty Driesler Lung Cancer Research	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,000 (7.86%)	Research Peer-Reviewed Research: $1,430,000
	Total: $1.6M	Total: $170,000	Total: $1,430,000
Military Pediatric Training and Support			
2010	$4M for Military Pediatric Training and Support	Withholds[a] Army: $21,000 USAMRMC: $99,000 Management Costs[b] $310,008 (7.99%)	Research Peer-Reviewed Research: $3,569,992
	Total: $4M	Total: $430,008	Total: $3,569,992

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Table B-21 (cont.) *FY10 Institutionally Based Research Programs Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

Fiscal Year	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
Musculoskeletal Interdisciplinary Research Initiative			
2010	$1.6M for Musculoskeletal Interdisciplinary Research Initiative	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,000 (7.86%)	Research Peer-Reviewed Research: $1,430,000
	Total: $1.6M	Total: $170,000	Total: $1,430,000
Neutron/Hadron Particle Therapy and Proton Therapy Research			
2010	$1.6M for Hadron Particle Therapy $2.8M for Northern Illinois Proton Treatment and Research Center	Withholds[a] Army: $24,000 USAMRMC: $110,000 Management Costs[b] $416,000 (9.75%)	Research Peer-Reviewed Research: $3,850,000
	Total: $4.4M	Total: $550,000	Total: $3,850,000
Prader-Willi Syndrome			
2010	$1.6M for Prader-Willi Syndrome Research	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $140,282 (9.04%)	Research Peer-Reviewed Research: $1,411,718
	Total: $1.6M	Total: $188,282	Total: $1,411,718
Preventive Medicine Research Institute			
2010	$1.5M for Expanding Access to Proven Lifestyle Modification Treatments Focused on Preventing and Reversing Chronic Disease	Withholds[a] Army: $8,000 USAMRMC: $37,000 Management Costs[b] $105,001 (7.22%)	Research Peer-Reviewed Research: $1,349,999
	Total: $1.5M	Total: $150,001	Total: $1,349,999
Respiratory Biodefense Initiative Research			
2010	$2.4M for Center for Respiratory Biodefense	Withholds[a] Army: $13,000 USAMRMC: $60,000 Management Costs[b] $187,000 (8.04%)	Research Peer-Reviewed Research: $2,140,000
	Total: $2.4M	Total: $260,000	Total: $2,140,000

[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

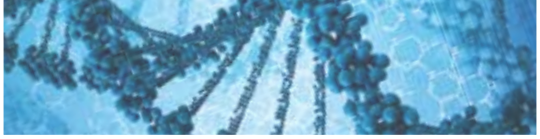


Table B-21 (cont.) *FY10 Institutionally Based Research Programs Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy*

	Congressional Appropriation	Withholds and Management Costs	Investment Strategy
Spinal Muscular Atrophy Research Program			
2010	$3M for Spinal Muscular Atrophy Research Program	Withholds[a] Army: $16,000 USAMRMC: $75,000 Management Costs[b] $199,001 (6.84%)	Research Peer-Reviewed Research: $2,709,999
	Total: $3M	Total: $290,001	Total: $2,709,999
Technology Solutions for Brain Cancer Detection and Treatment			
2010	$1.2M for Technology Solutions for Brain Cancer Detection and Treatment	Withholds[a] Army: $6,000 USAMRMC: $30,000 Management Costs[b] $89,000 (7.65%)	Research Peer-Reviewed Research: $1,075,000
	Total: $1.2M	Total: $125,000	Total: $1,075,000
Translational Research for Muscular Dystrophy			
2010	$1.6M for Translational Research for Muscular Dystrophy	Withholds[a] Army: $8,000 USAMRMC: $40,000 Management Costs[b] $122,000 (7.86%)	Research Peer-Reviewed Research: $1,430,000
	Total: $1.6M	Total: $170,000	Total: $1,430,000

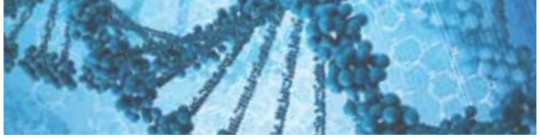
[a]The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.

[b]Percentage of management costs=management costs/(appropriation–withholds).

Appendix C: Breast Cancer Research Semipostal Awards

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY99	Daly	$283,649	Garvan Institute	Identification of Novel Prognostic Indicators for Breast Cancer Through Analysis of the EMS1/Cortactin Signaling Pathway
	Deuel	$5,000[1]	Scripps Institute	Novel Angiogenic Domains: Use in Identifying Unique Transforming and Tumor-Promoting Pathways in Human Breast Cancer
	Heyer	$111,444	University of California, Davis	In Vitro Recombination Activities of the Breast Cancer Predisposition Protein BRCA2
	Musgrove	$222,652	Garvan Institute	Role of Cyclin D1 and p27 in Steroidal Control of Cell Cycle Progression in the Mammary Gland in Vivo
	Shah	$279,000	University of Arkansas	Role of a Novel Matrix-Degrading Metalloproteinase in Breast Cancer Invasion
	Wang	$317,510	Texas A&M University	Scanning Microwave-Induced Acoustic Tomography
	White	$334,094	University of Texas Southwest Medical Center	Isolation of Factors That Disrupt Critical Protein/Protein Interactions Within the Telomerase Holoenzyme for Use in Breast Cancer Therapeutics
	Wreschner	$225,000	Tel Aviv University	Analysis of the Secreted Novel Breast Cancer-Associated MUC1/Zs Cytokine
FY00	Adamson	$578,183	Burnham Institute	Cripto: A Target for Breast Cancer Treatment
	Akporiaye	$454,500	University of Arizona	Tumor-Mediated Suppression of Dendritic Cell Vaccines
	Penn	$296,142	University of Toronto	Exploiting the Novel Repressed Transactivator Assay to Identify Protein Interactors and Peptide Inhibitors of the Myc Oncoprotein
FY01	Cai	$560,144	Vanderbilt University	Genetic Polymorphisms, Mitochondrial DNA Damage, and Breast Cancer Risk
	Carraway	$427,225	University of California, Davis	Identification of a Functional Human Homolog of Drosophila Kek1, an Inhibitor of Breast Tumor Cell Growth
	Chaudhary	$312,000	University of Texas Southwest Medical Center	The Role of Ectodysplasin A (EDA) and Its Receptors in the Pathogenesis of Breast Cancer
	Geahlen	$425,425	Purdue University	Characterization of Syk in Breast Carcinoma Cells
	Rosner	$454,181	St. Luke's-Roosevelt Hospital Center	Autocrine and Paracrine Control of Breast Cancer Growth by Sex Hormone-Binding Globulin
FY02	Dou	$491,999	University of South Florida	Synthetic Beta-Lactam Antibiotics as a Selective Breast Cancer Cell Apoptosis Inducer: Significance in Breast Cancer Prevention and Treatment
	Godwin	$504,000	Fox Chase Cancer Center	The Nuclear Death Domain Protein p84N5, a Candidate Breast Cancer Susceptibility Gene
	Perkins	$490,500	Yale University	Rapid Genomic Approach to Cancer Gene Discovery in Breast Cancer
FY03	Chung	$490,447	Yale University	Quantitative in Situ Assessment of the Somatostatin Receptor in Breast Cancer to Assess Response to Targeted Therapy with 111-in-Pentetreotide
	Kaaks	$367,639	International Agency for Cancer Research	Fatty Acid Synthesis Gene Variants and Breast Cancer Risk: A Study Within the European Prospective Investigation into Cancer and Nutrition (EPIC)
	Yaswen	$508,790	Lawrence Berkeley National Laboratory	Functional Analysis of BORIS, a Novel DNA-Binding Protein
	Ziv	$767,171	University of California, San Francisco	Admixture and Breast Cancer Risk Among Latinas

[1]Total award amount was $404,176; remaining funds were from the FY99 BCRP.



Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY04	Bissell	$386,569	Lawrence Berkeley National Laboratory	Use of HA-Metal Nanoparticles to Identify and Characterize Tumorigenic Progenitor Cell Subsets in Breast Tumors
	Clarke	$588,738	Northern California Cancer Center	The Hygiene Hypothesis and Breast Cancer: A Novel Application of an Etiologic Theory for Allergies, Asthma, and Other Immune Disorders
	Giorgio	$453,000	Vanderbilt University	Surface Functionalized Nanoparticles and Nanocrystals for Proximity-Modulated, Early Neoplasia Detection, Imaging, and Treatment of Breast Cancer
	Lemmon	$475,500	University of Pennsylvania	Harnessing Novel Secreted Inhibitors of EGF Receptor Signaling for Breast Cancer Treatment
FY05	Zinn[2]	$436,500	University of Alabama at Birmingham	Novel Screening and Precise Localization of Early Stage Breast Cancer in Animal Model
	Huang	$483,600	Cornell University, Weill Medical College	Migrastatin Analogues as Potent Inhibitors of Breast Cancer Metastasis
	Liu	$448,500	Ohio State University	Hunting for Novel X-Linked Breast Cancer Suppressor Genes in Mouse and Human
	Rao	$468,000	Stanford University	Ribozyme-Mediated Imaging of Oncogene Expression in Breast Tumor Cells
FY06	Devi	$155,085[3]	Duke University Medical Center	Modulation of Regulatory T Cells as a Novel Adjuvant for Breast Cancer Immunotherapy
	Lee	$489,000	University of Southern California	A New Mechanism for Estrogen-Starvation Resistance in Breast Cancer
	Li	$438,455	Baylor College of Medicine	The ER/PR Status of the Originating Cell of ER-Negative Breast Cancer
	Mousa	$377,620	Albany College of Pharmacy	Enhancing the Efficacy of Chemotherapeutic Breast Cancer Treatment with Non-Anticoagulant Heparins
	Rastinejad	$454,500	University of Virginia	Structural Characterization of the Interdomain Features of the Estrogen Receptor
FY07	Kuperwasser	$817,500	Tufts University	Mechanisms of Breast Cancer Associated with Obesity
	Kelly	$244,450[4]	University of Virginia	Genetically Encoded Targeted, Amplifiable, Imaging Agents for Early Detection of Breast Cancer
	Gerbi	$155,550[5]	Brown University	Hormonal Involvement in Breast Cancer Gene Amplification
FY08	Park	$111,663	North Dakota State University	In Utero Exposure to Dietary Methyl Nutrients and Breast Cancer Risk in Offspring
	Radosz	$528,939	University of Wyoming	Breast Cancer-Targeted Nuclear Drug Delivery Overcoming Drug Resistance for Breast Cancer Therapy
	Hill	$577,500	Oregon Health and Science University	Vaccine Vector for Sustained High-Level Antitumor CTL Response
	You	$503,666	University of Oklahoma Health Science Center	Targeted Delivery and Remote-Controlled Release of Chemotherapeutic Agents
	Seagroves	$166,667[6]	University of Tennessee Health Science Center	The Role of HIF-1 Alpha in Breast Cancer: A Positive Factor in Cancer Stem Cell Expansion via Notch?
FY09	Reynolds	$730,000[7]	Cancer Prevention Institute of California	Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk
	Wysolmerski	$620,626	Yale University	Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer
FY10	Schedin	$368,125[8]	University of Colorado, Denver	The Immune Modulatory Program of Post-Partum Involution Promotes Pregnancy-Associated Breast Cancer
	Leung	$556,875[9]	Johns Hopkins University	The Role of Poly(ADP-Ribose) in microRNA Activity in Breast Cancers

[2]The original Principal Investigator, Dr. Tandra Chaudhuri, is deceased.

[3]Total award amount was $461,933; remaining funds were from the FY06 BCRP.

[4]Total award amount was $687,397 remaining funds were from the FY06 BCRP.

[5]Total award amount was $787,325; remaining funds were from the FY06 and FY07 BCRP.

[6]Total award amount was $554,987; remaining funds were from the FY08 BCRP.

[7]Total award amount was $860,883; remaining funds were from the FY09 BCRP.

[8]Total award amount was $556,028; remaining funds were from the FY10 BCRP.

[9]Total award amount was $585,652; remaining funds were from the FY10 BCRP.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September 30, 2011