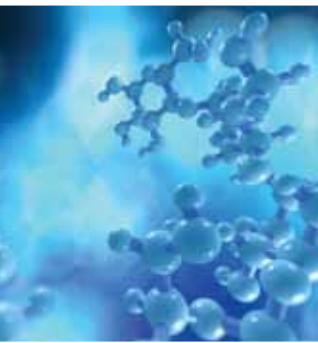


CDMRP



Department of Defense



2012

Congressionally Directed Medical Research Programs

Annual Report

September 30, 2012



U.S. Army Medical Research and Materiel Command

Letter from the Director

I am proud to introduce the 2012 Annual Report for the Congressionally Directed Medical Research Programs (CDMRP). For more than 20 years, the CDMRP has worked with consumers, scientists, and clinicians to identify and manage high-impact research and recognize untapped opportunities. We strive to be good stewards of both the funds and the trust placed on us by Congress and our stakeholders. We believe in transparency, and this report serves to continue that tradition.

The efforts of dedicated professionals who are committed to the CDMRP vision and mission are reflected throughout this 2012 Annual Report. I am humbled to work alongside such a talented and compassionate team, and everyone at the CDMRP is grateful for the opportunity to administer these critical research programs. Together, we will continue our efforts to provide hope for service members (past and present), their families, and the American public.

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

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Department of Defense

**U.S. Army Medical Research and Materiel Command
Congressionally Directed Medical Research Programs**

**Annual Report
September 30, 2012**

Congressionally Directed Medical Research Programs

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CDMRP

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Introduction

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.

Introduction

This annual report highlights the CDMRP as an organization, its individual programs, and the financial accounting for FY11–FY12. Additional information about specific research programs can be found on the CDMRP website, or requested by phone (301-619-7071) or through e-mail (CDMRP.PublicAffairs@amedd.army.mil).

Who We Are

The beginnings of the Congressionally Directed Medical Research Programs (CDMRP) can be traced to the early 1990s when a grassroots advocacy movement campaigned for an increase in breast cancer research funding. The U.S. Congress responded with an initial appropriation of \$25 million (M) in 1992 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 establishment of the CDMRP.

The CDMRP evolved into a global funding organization for biomedical research that spans different areas (i.e. cancer, neurologic, and orthopedic) due in part to the success in managing the initial congressional appropriations for breast cancer research. Since 1992, the CDMRP has grown in size and scope, and through fiscal year 2012 (FY12), we have been responsible for managing nearly \$7 billion (B) in appropriations (see Figure 1, CDMRP Funding History).

What We Do

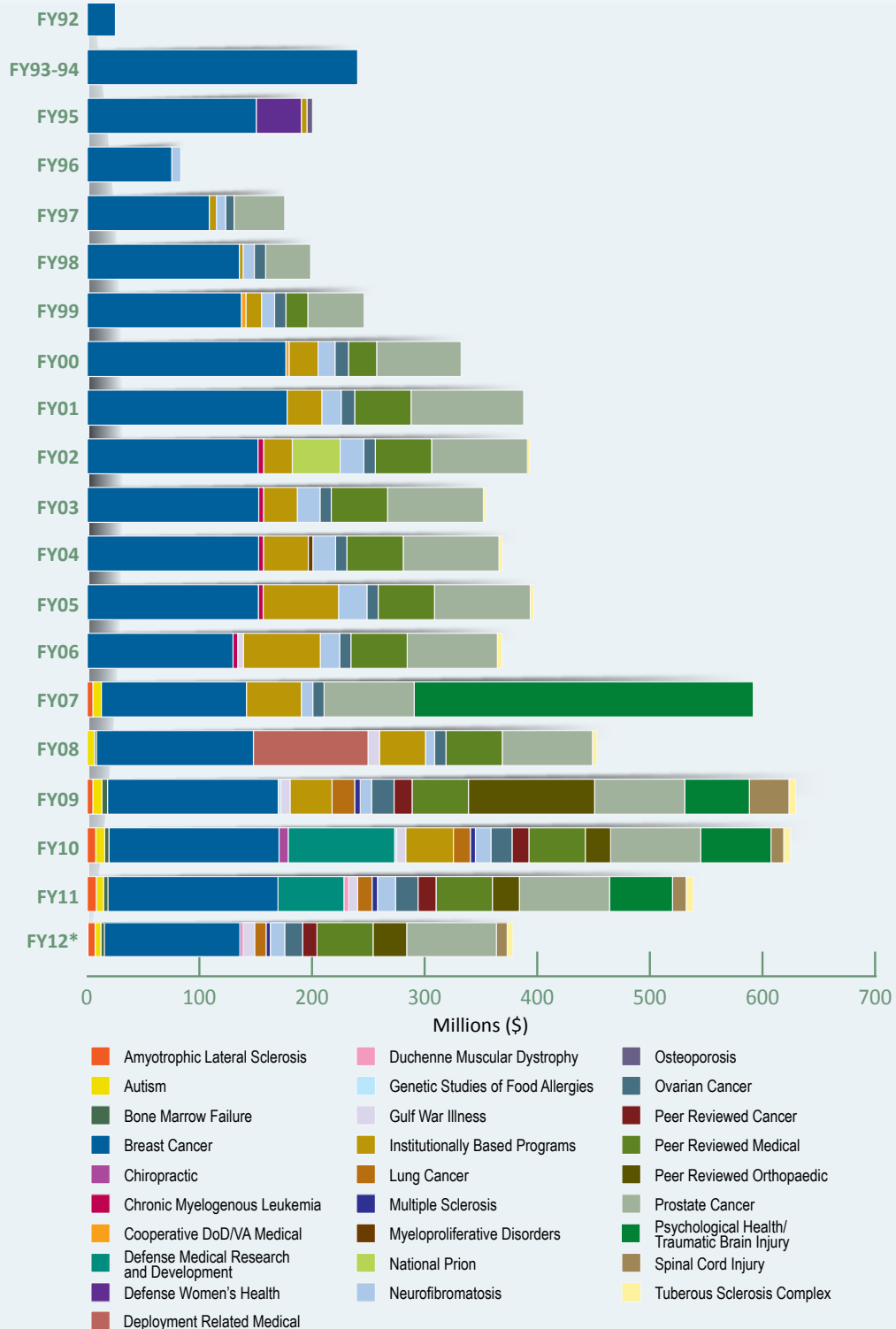
The CDMRP strives to tap research opportunities that encourage innovation and ingenuity in the biomedical sciences in response to the expressed needs of our stakeholders—Congress, the American public, and the military. Hallmarks of the CDMRP include investing in groundbreaking research; supporting the next generation of researchers as well as established scientists; and funding clinical research to prevent, detect, diagnose, and treat diseases, conditions, and injuries. The CDMRP fills research gaps by funding high-risk, high-gain projects that other agencies may not venture to fund. While individual programs are unique in their focus, all of the programs managed by the CDMRP share the common goal of advancing innovative ideas, creative solutions, patient care, or breakthrough technologies and resources. 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.



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

CDMRP Funding History

Figure 1. CDMRP Funding History



Data as of September 30, 2012. Investment of FY12 funds will be complete as of September 30, 2013.

*Does not include amounts of DHP Core and PH/TBI funding executed on behalf of the JPCs that is currently estimated at \$100M.

Introduction

Programs

Since the inception of the CDMRP, congressional appropriations directed toward the different research programs or funds directed to the CDMRP for execution totaled \$6.998B.

The CDMRP has managed and/or executed 107 biomedical research programs resulting in funding for 11,315 assistant agreements (consisting of grants and cooperative agreements) and contracts. For an overview by program, please see Appendix A.

As detailed in Table 1, in FY12, CDMRP completed the execution of the FY11 appropriations by processing 595 new awards across 19 programs and initiated the management of \$378.9M across 16 programs as well as execution of another 3 programs on the behalf of others. For FY11–FY12 financial data, please reference Appendix B. For more information on programs, please see page 45.

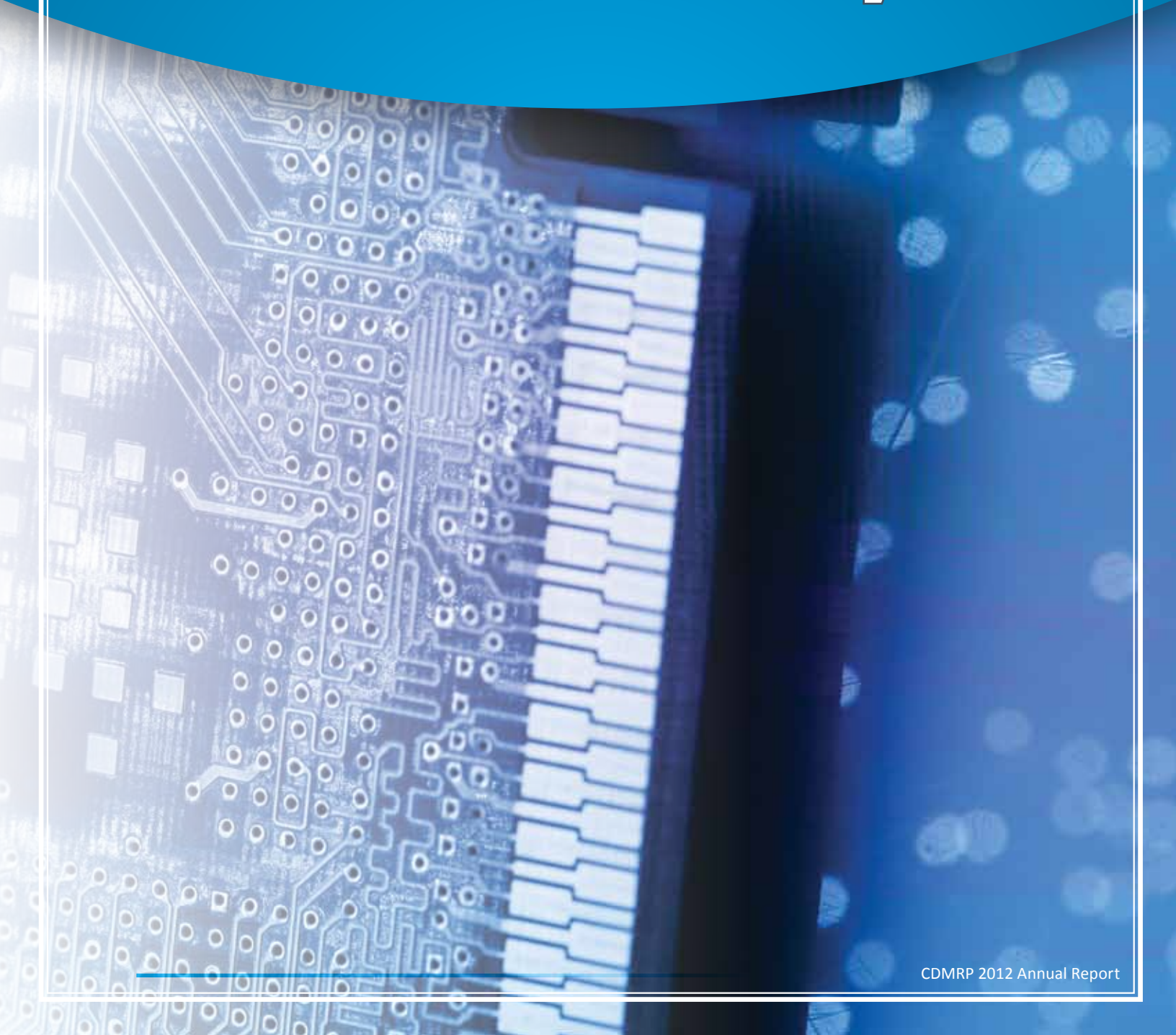
Table 1. CDMRP Programs, Appropriations, and Applications Received and Awarded

Programs Managed by CDMRP (a)	FY11			FY12 ^a	
	Funds Received (in millions)	Applications Received	Applications Funded	Funds Received (in millions)	Applications Received to Date
Amyotrophic Lateral Sclerosis	\$8.00	60	6	\$6.40	51
Autism	\$6.40	119	16	\$5.10	119
Bone Marrow Failure	\$4.00	40	7	\$3.20	35
Breast Cancer/Breast Cancer Research Semipostal	\$150.90	1,006	87	\$120.70	780
Duchenne Muscular Dystrophy	\$4.00	26	4	\$3.20	-
Gulf War Illness	\$8.00	38	8	\$10.00	33
Lung Cancer	\$12.80	292	31	\$10.20	375
Multiple Sclerosis	\$4.80	116	10	\$3.80	37
Neurofibromatosis	\$16.00	85	13	\$12.80	89
Ovarian Cancer	\$20.00	198	29	\$16.00	211
Peer Reviewed Cancer	\$16.00	852	44	\$12.80	167
Peer Reviewed Medical	\$50.00	712	55	\$50.00	720
Peer Reviewed Orthopaedic	\$24.00	112	23	\$30.00	144
Prostate Cancer	\$80.00	1,314	170	\$80.00	1,139
Spinal Cord Injury	\$12.00	79	17	\$9.60	-
Tuberous Sclerosis	\$6.40	47	10	\$5.10	54
Programs Executed on Behalf of Others (b)					
Army Rapid Innovation Fund	\$13.57	n/a	5	TBD	TBD
Defense Medical R&D	\$58.76	160	31	TBD	TBD
Psychological Health/Traumatic Brain Injury	\$61.43	261	29	TBD	TBD
Total	\$557.06	5,517	595	\$378.90	3,954

(a) CDMRP executed and managed the full appropriation.

(b) CDMRP assisted with execution of the specified portion of a larger appropriation(s).

Our Management Cycle



Our Management Cycle

The CDMRP employs a flexible and responsive management cycle to maintain the individuality of each program while also meeting the needs of Congress, DoD, research and advocacy communities, and the public at large. This management cycle, described in detail on the following pages, 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 3.

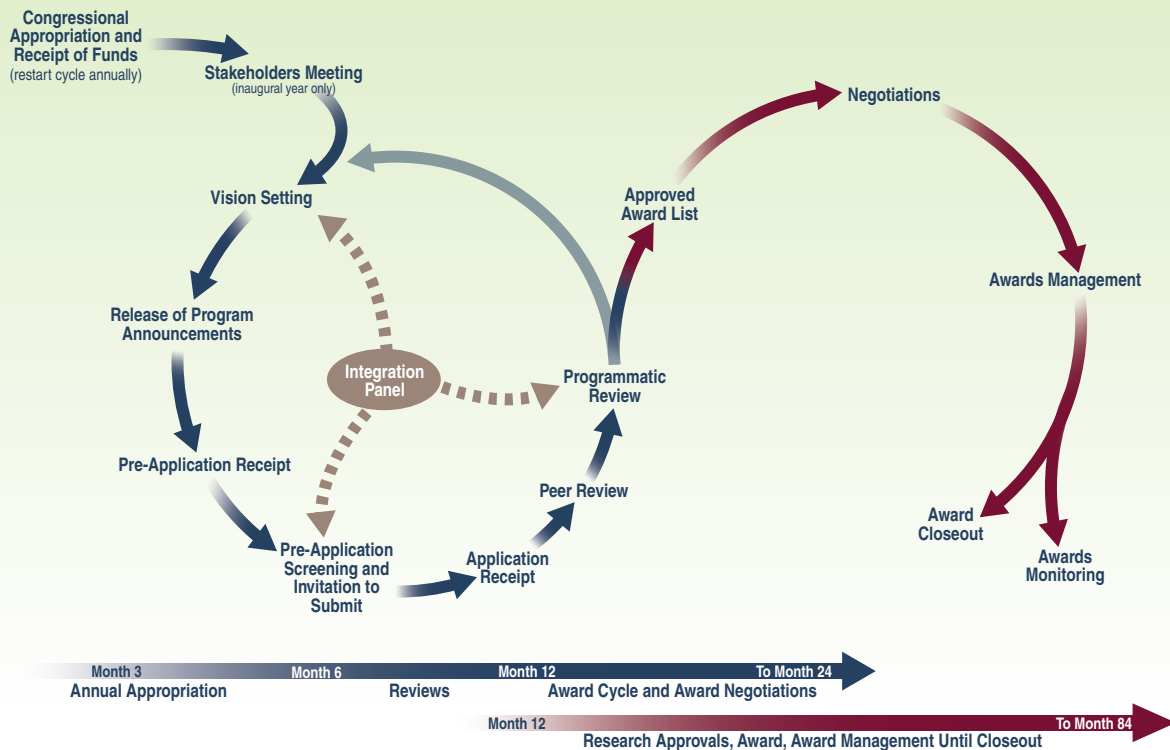


Figure 3. Execution and Management Cycle

Congressional Appropriation and Receipt of Funds

The management cycle begins with a congressional appropriation for targeted biomedical research to be managed by the CDMRP. The programs assigned to the CDMRP for complete life-cycle management exist because of annual, 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 the stakeholders meeting is to survey the research landscape and identify gaps in both the scientific and consumer interest areas. Stakeholders are world-renowned consumers, scientists, and clinicians. The CDMRP defines consumers as 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 (additional information about consumers can be found on page 14). Recommendations from the stakeholders meeting are then used to facilitate vision setting.

Vision Setting

A vision setting meeting is held to define an annual investment strategy for a given program (see Figure 3). The development of an annual investment strategy was recommended by the National Academy of Sciences Institute of Medicine (IOM).² The CDMRP adopted this recommendation in the administration of its programs. Through the work of each program's Integration Panel (IP), consisting of consumers, scientists, and clinicians, individualized investment strategies are developed. Members of the IP recommend the annual investment strategy to encourage research in underfunded and underrepresented areas that are considered most critical to consumers, scientists, and clinicians. To ensure impartiality and the integrity of the process, IP members are prohibited from applying for funds for the fiscal year in which they participated in vision setting. The annual investment strategy provides a high degree of flexibility and the necessary structure to most effectively obligate congressional appropriations while avoiding unnecessary duplication with other funding agencies. In total, 26 vision setting meetings were held for the CDMRP in FY12.

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. Dissemination strategies to alert the research communities when new PAs are released are wide ranging and include mass e-mails, targeted advertising, telephone contacts, and face-to-face interactions. Examples include:

- E-mailing more than 900 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 80 professional associations
- Notifying more than 300 VA facilities and military research laboratories
- 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 68,000 unique recipients
- Distributing electronic news items to nearly 575 consumer advocate groups
- Presenting the CDMRP display and funding opportunities at national scientific meetings
- Providing research institutions with award details for news releases

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. The preproposal process was instituted for some award mechanisms 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 associated with each full application 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 full application package, a preproposal process was added to the pre-application submission for many award mechanisms. The preproposal is an abbreviated process, consisting of one to three pages,

² 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.

Our Management Cycle

detailing the research aims, strategy and methods, innovation, and/or impact of the project. Through the use of the preproposal screening process, the number of full applications to be administratively processed and scientifically peer and programmatically reviewed has significantly decreased; this ensures a greater understanding of the intent of the award mechanism and decreases management costs and saves funds for research investment.

Following the submission of the preproposal, the pre-application is screened by either 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. In FY12, the CDMRP held 57 preproposal screening meetings.

As summarized in Table 2, in FY12, the CDMRP received 8,974 preproposals and nominations that, after screening and invitation, resulted in 3,131 full applications received as of the date of this report. In addition, the CDMRP received 2,689 full applications from mechanisms that did not require preproposals or nominations for a total of 5,820 full applications received to date.

Table 2. Number of Submissions Received from October 1, 2011 to September 30, 2012 Across FY11–FY12 Programs

Mechanism Submissions	
Preproposals or nominations screened	8,974
Letters of intent received	3,134
Total pre-applications received	12,108
Full Application Submissions	
Full applications from invitations only	3,131
Full applications from letter of intent	2,689
Total full applications received	5,820

Review Process

Critical to the success of the CDMRP is the two-tier review process that was adopted from the recommendations set forth in 1993 by the National Academy of Sciences IOM committee. The IOM concluded that the CDMRP would be best served by a two-tier review process that reflects 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.

Reviewers for each tier for the CDMRP must uphold the highest standards of conduct to ensure the credibility of the programs and the processes.



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 product of a peer review is a summary statement with final scores. There were 188 peer review panels held from October 1, 2011 through September 30, 2012.

Programmatic Review

After applications have been scientifically peer reviewed, they are programmatically reviewed by members of the program's IP, the same panel that recommended the annual investment strategy. At the programmatic review level, the IP considers each summary statement 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. The IP recommends a list of applications to be funded that best fulfills the review criteria and reflects the vision and mission of each program. There were 26 programmatic review meetings held from October 1, 2011 through September 30, 2012.

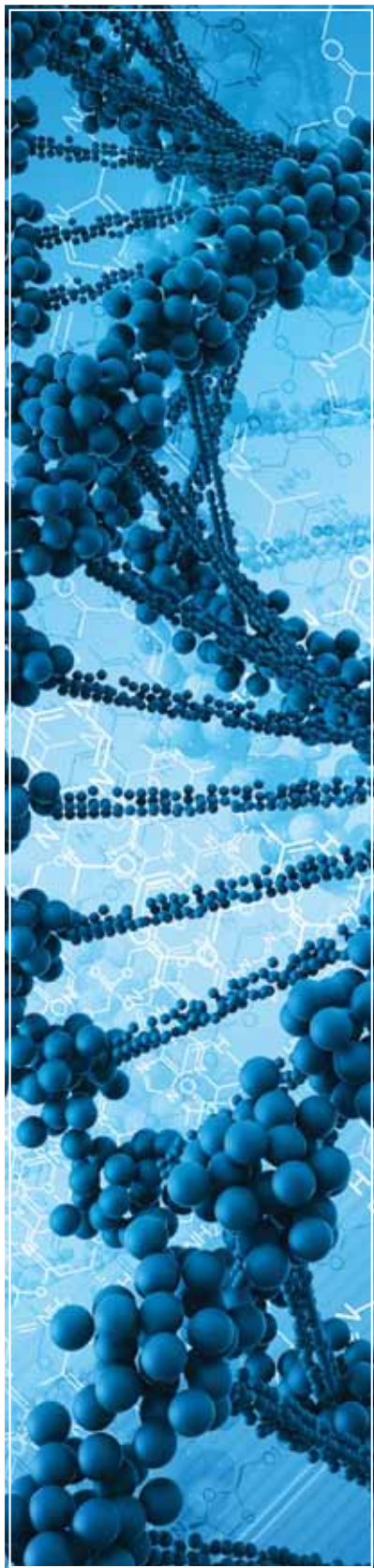
Additional details about the two tiers of review can also be accessed on the CDMRP website at <http://cdmrp.army.mil/about/fundingprocess>.

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 granted from the Director of the Defense Medical Research and Development Program (DMRDP) within the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]). 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).





Negotiations and 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. Awards have performance periods of up to 5 years, and during this time, the CDMRP actively manages and monitors progress. As of September 30, 2012, the CDMRP has managed 11,315 awards throughout its funding history.

Life-cycle management is an active process from the recommended-for-funding point through the closeout stages 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. Formal analysis of the budget with respect to the scope of work to be performed is completed through detailed discussions between 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 CDMRP-funded research. Once all aspects of negotiation are complete, an award is signed by USAMRAA.

The life-cycle management of awards continues throughout the period of performance with monitoring of the technical progress, financial reporting, and regulatory review. Each award is assigned a Science Officer (SO) with broad knowledge of the assistance agreement (AA) to ensure effective communication among all parties involved and provided 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 progress 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 an issue, 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 AAs and consortia may also be monitored through external advisory boards, site visits, teleconferences, and other meetings throughout the entire period of performance.

Award Monitoring

Program Evaluation

The CDMRP is constantly assessing research relevance, productivity, and accomplishments of its funded research. For example, each award funded by the CDMRP is monitored at least annually for progress. During each review, research outcomes are identified and captured continuously throughout the life of each award. The CDMRP strives to improve processes and enhance its response to stakeholders by continually reviewing award mechanisms and funding opportunities to ensure the needs of the research and consumer communities are met. Often, research highlights are developed by individual programs to convey the importance of research outcomes and findings supported by the program and then disseminated to the public (see below, Research News and Reports).

Research News and Reports

The CDMRP remains transparent to the public and utilizes varied communication processes and media techniques to communicate with its many stakeholders and audiences. Abstracts for all awards are available on the CDMRP website. Information on the progress of awards can be found on Defense Technical Information Center (DTIC) at <http://www.dtic.mil/dtic/>. The following public relations efforts

highlight CDMRP initiatives to disseminate timely, accurate, understandable, and credible research news and information to consumers, military, scientists, clinicians, Congress, and the public at large.

Public Relations

The CDMRP website remains a central mode of communication to the public. The dynamic website features facts and news about the CDMRP, individual research programs, funding opportunities, and consumer involvement. The media center has been a popular feature of the website, offering visitors a unique experience as they access videos, press releases, research highlights, consumer stories, program books, and annual reports.

Various informational materials are produced and distributed each year by the CDMRP. Whether it is a program book detailing the vision, goals, funding history, and research highlights of a specific program or a general brochure summarizing the application process, outreach materials are developed each year to disseminate information to constituencies. These informational materials are communicated to the public via the CDMRP website, e-mail distribution, and in person at scientific conferences and meetings. In FY12, 13 program books were created or updated, 2 brochures were produced, 31 research highlights were generated, and 5 exhibits and/or program banners were developed.





Vital Partnerships



The CDMRP carries out its mission by partnering with various external constituencies, including consumers, military, scientists, clinicians, 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.

Consumers

Since its founding, the CDMRP has included consumers (patients, survivors, family members, and/or caregivers) in both peer and programmatic review panels. Nearly 2,000 consumers have represented their communities and advocacy organizations since 1992, and their role continues to be vital. Their knowledge of a disease, condition, or injury comes from their personal experience as a patient, survivor, spouse, parent, or caregiver.

Consumers are nominated to peer review panels by the advocacy organizations for whom they serve. They are selected following an application process that includes an essay, telephone interview, and a discussion of their willingness and ability to fairly evaluate research applications in a specific field. Consumers serve on peer review panels with scientists, clinicians, and leading experts and have an equal voice in deliberations. Consumers also use their experiences to offer a fresh, new perspective and insight that other panel members may not have and bring a sense of urgency to the discussions.

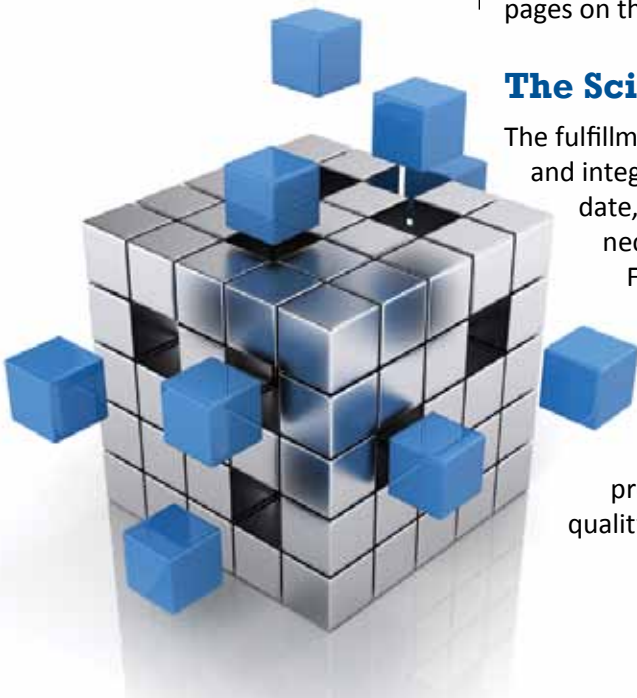
Similar to peer review panels, IPs of the CDMRP are composed of consumers, scientists, and clinicians. Consumer members of the IPs are vital partners in balancing the portfolio of each program to ensure a representation of the needs of the consumer community. All members, including consumers, at the programmatic review level have an equal voice and vote to select applications to be placed on the recommended-for-funding list.

In both the peer review and programmatic review processes, consumers bring passion and a true appreciation of how different research applications can impact the human dimension of science. For more information on consumer involvement, see the consumer involvement pages on the CDMRP website (<http://cdmrp.army.mil>).

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 necessary subject matter expertise on peer review panels. In

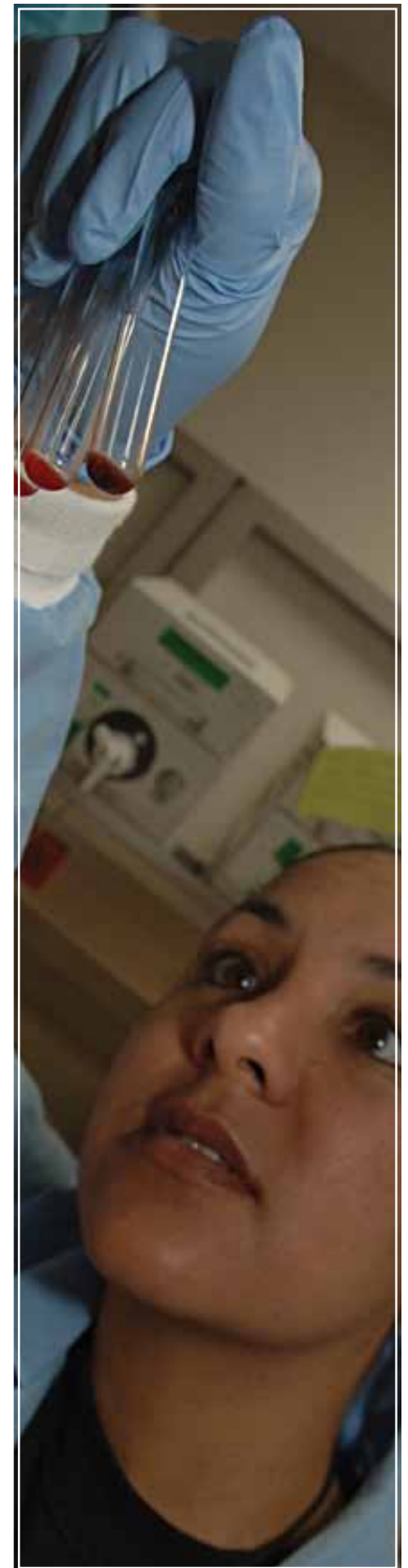
FY12, more than 250 scientists and clinicians served as IP or Joint Programmatic Review members, and over 75 ad hoc reviewers were recruited to these panels. Finally, approximately 8,450 researchers have been funded by the CDMRP in an effort to tackle the complex causes of diseases, conditions, and injuries and translate this knowledge into improved prevention, treatment interventions, patient survival, and quality of life.



Military Partnerships

U.S. Army Medical Research and Materiel Command

The CDMRP is located within the USAMRMC, the Army's medical materiel developer. There are several offices within the USAMRMC that the CDMRP works with to execute its research programs, as shown in Figure 2. The CDMRP works in synergy with partners in the USAMRMC to ensure that budgetary funds and congressional appropriations are used to the benefit of service members, their families, and the American public. For example, the CDMRP works closely with Research Area Directorates (RADs) within the USAMRMC. The RADs manage research activities related to military infectious diseases, combat casualty care, military operational medicine, and clinical and rehabilitative medicine. Awards within the CDMRP portfolio are aligned with the RADs to ensure that critical results benefit the overarching mission of the USAMRMC. In addition, the CDMRP's program management expertise is leveraged to support the mission of the RADs. The CDMRP also managed research projects under the Army's Rapid Innovation Fund.



Joint Program Committees

The DMRDP is the research arm of the Defense Health Program within the OASD(HA). The DMRDP focuses on advancing the state of medical science as it relates to conditions directly relevant to battlefield injuries and other ailments that affect both service members and their families (for additional information about the DMRDP, please see pages 56–57). Joint Program Committees (JPCs) are advisory bodies composed of medical and military experts that provide funding recommendations and program management support for DMRDP-funded research.

The CDMRP works with the JPCs to execute a number of extramural programs. The combined effort leverages the CDMRP's expertise in research program administration with the JPCs' expertise in technical areas for the advancement of the DMRDP mission to expedite the delivery of products and solutions that address challenges related to service members and their families. In FY12, the CDMRP assisted with program execution in the areas of neurotrauma, in-home and integrated mental health services, basic and applied psychological health, post-traumatic stress disorder (PTSD), traumatic brain injury (TBI), prosthetics, restoration of eye sight, and other conditions related to battlefield injury and military service.

This partnership supports the CDMRP's vision of finding and funding the best research to support the warfighter and the American public.

Department of Veterans Affairs

In support of the August 31, 2012 Presidential Executive Order 13625, the DoD and the Department of Veterans Affairs (VA) are combining more than \$100M to fund two new consortia aimed at improving diagnosis and treatment of mild traumatic brain injury (mTBI) and PTSD. The Consortium to Alleviate PTSD (CAP) and the Chronics Effects Neurotrauma Consortium (CENC) will be jointly managed by the VA and the CDMRP. Through this collaborative effort, the goals of PTSD prevention strategies, interventions, improved treatments, and understanding the after effects of mTBI as well as comorbidity with other conditions will be studied.

In addition, the CDRMP coordinates with the VA to enrich projects within the Gulf War Illness Research Program (GWIRP). The GWIRP is collaborating with the VA to make the best possible use of available resources in support of high-quality veteran-focused research on Gulf War Illness (GWI) (please refer to pages 60–61 for additional details on the GWIRP). VA scientists and clinicians serve on both peer and programmatic review panels for GWIRP to inform and help make funding recommendations, as well as provide valuable resources and expertise as investigators on many GWIRP-funded awards.





Interagency Collaborations

The CDMRP staff serves and participates on multiple federal and non-federal committees to compare research portfolios, identify gaps in research funding, and improve existing research efforts. In addition, the CDMRP encourages reciprocity by engaging individuals from federal and non-federal committees to participate in the peer and programmatic review of applications, as well as serve on review boards to monitor and oversee the progress of awards. These interagency collaborations strive toward synergy with other agencies, diversification of research portfolios funded, and underscore the importance of research coordination efforts. Examples of interagency collaborations with the CDMRP include:

- **Advisory Committee on Breast Cancer in Young Women**, a Centers for Disease Control and Prevention (CDC)-led body focused on evidence-based activities designed to prevent breast cancer, particularly among those at heightened risk, as well as promote the early detection of breast cancer and support of young women who develop the disease
- **Center to Reduce Cancer Health Disparities Working Group**, a center within the National

Cancer Institute (NCI) whose mission is to reduce the unequal burden of cancer and train the next generation of competitive researchers in cancer and cancer health disparities research

- **Federal Interagency Traumatic Brain Injury Research Working Group**, an NIH-sponsored group whose mission is to enhance communication, coordination, and collaboration in the field of traumatic brain injury across agencies
- **Gynecologic Cancer Foundation Allied Support Group**, a group of national ovarian cancer advocacy organizations that work together to promote collaboration and cooperation among the advocacy groups
- **Interagency Autism Coordinating Committee**, a federal advisory committee that coordinates efforts within the Department of Health and Human Services related to autism spectrum disorders (ASDs). Federal and non-federal members are included on the committee to ensure that a wide range of ideas and perspectives pertaining to ASDs are represented and discussed in a public forum

Vital Partnerships

- **Interagency Breast Cancer and Environmental Research Coordinating Committee**, a congressionally mandated group established by the National Institute of Environmental Health Sciences in collaboration with the NCI to review federal research efforts concerning the environmental and genomic factors related to breast cancer
- **Interagency Urology Coordinating Committee**, a federal advisory committee, facilitated by the National Institute of Diabetes and Digestive and Kidney Disorders of the Department of Health and Human Services, that coordinates the research activities of all national research institutes relating to urologic diseases to ensure their adequacy and technical soundness and to provide for the exchange of information necessary to maintain adequate coordination
- **International Cancer Research Partners**, a group of 56 cancer funding organizations that work together to enhance the impact of research to benefit all individuals affected by cancer through global collaboration and strategic coordination of research
- **Muscular Dystrophy Coordinating Committee**, an NIH-established committee to foster collaboration among federal health programs and activities relevant to the various forms of muscular dystrophy
- **National Urology Research Agenda**, an initiative launched by the American Urological Association to define national research priorities for the field of urology
- **Strategic Plan on Gulf War Illness Research**, a VA-led initiative to improve the health and well-being of Gulf War veterans and to utilize emerging knowledge to prevent similar war-related illnesses in the future
- **Trans-Agency Early Life Exposures and Cancer Working Group**, a working group composed of representatives from National Institutes of Health (NIH), CDC, and the CDMRP. The group's goals include (1) stimulating and facilitating research on early-life events/exposures and cancer within the context of the missions of the federal agencies; (2) planning and hosting lecture series to foster awareness, stimulate new scientific interest, and generate transdisciplinary collaborations among intramural and extramural research communities; and (3) conducting portfolio analysis to address current research funding portfolios on early-life events/exposures and cancer and to determine gaps and future needs
- **Trans-NIH Neurofibromatosis Working Group**, an NIH-sponsored group that meets to enhance communication and collaboration about the state of the science and progress on funded awards
- **Tuberous Sclerosis Alliance**, a group dedicated to finding a cure for tuberous sclerosis complex while improving the lives of those affected



Breast Cancer Research Semipostal Program

Grassroots efforts of breast cancer advocates led to the Stamp Out Breast Cancer Act (Public Law 105-41 [H.R. 1585]). This legislation resulted in the U.S. Postal Service's Breast Cancer Research Semipostal (BCRS) and the issuance of a new, 55¢ first-class breast cancer stamp that can be purchased voluntarily by the public. Since the stamp was first offered for sale in 1998, the monies received through FY12 by the CDMRP from the BCRS total \$22,505,375.91 and have been used to fully or partially fund 48 Breast Cancer Research Program (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, applications funded through the BCRS program are reviewed according to the two-tiered review system. The administration of funds from the BCRS represents a unique partnership among consumers, the DoD, and the general public. A list of all awards supported by the BCRS can be found in Appendix C.

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 of the SBIR and STTR programs.

Addressing Health Disparity

In 1998, the CDMRP established the Minority and Underserved Populations Program to focus on 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
- Collaboration with other funding agencies on assessment of portfolio overlap and complementary efforts
- 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





Milestones and Scientific Discoveries



Milestones and Scientific Discoveries

Each year, programs within the CDMRP assess scientific opportunities to advance research in specific areas. The investigators supported by individual programs are making significant advances against targeted diseases, conditions, and injuries. Highlights of CDMRP milestones and scientific discoveries are showcased on the following time line.



1992

CDMRP Milestone

- *\$25M appropriated to the Breast Cancer Research Program for research on breast cancer screening and diagnosis for military women and their family members*

1993

CDMRP Milestones

- *Grassroots efforts influence public policy, resulting in a congressional appropriation of \$210M for peer-reviewed breast cancer research*
- *The National Academy of Sciences publishes 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 including a two-tiered review process*

BCRP Advances

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



1995

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

CDMRP Milestones

- **The USAMRMC asks the IOM 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 are integrated into the scientific peer review process**

Milestones and Scientific Discoveries



1996

CDMRP Milestone

- *The Neurofibromatosis Research Program (NFRP) is established by an \$8M appropriation*

1997

CDMRP Milestones

- *The Prostate Cancer Research Program (PCRP) is established by a \$45M appropriation*
- *The Ovarian Cancer Research Program (OCRP) is established by a \$7.5M appropriation*
- *The BCRP sponsors its first Era of Hope conference*
- *The USAMRMC asks the IOM to review the implementation and progress of the BCRP; a report was published entitled "A Review of the Department of Defense's Program for Breast Cancer Research" which finds the two-tier review process meritorious*

BCRP Advance

- *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*

NFRP Advance

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

OCRP Advance

- *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*

PCRP Advance

- *Dr. George Wilding determines the mechanism by which androgen induces reactive oxygen species (ROS) in prostate cancer cells. The discovery leads to the development of APC-100, an antioxidant moiety of Vitamin E that blocks ROS and delays prostate cancer progression. Clinical trials of APC-110 begin in 2011*



1998

CDMRP Milestones

- *The BCRP is selected to receive 30% of the funds raised by the issuance of our nation's first semipostal stamp, the Breast Cancer Research Stamp*
- *The CDMRP launches its public website*
- *The CDMRP publishes "Perspective from the Department of Defense Breast Cancer Research Program," Breast Disease (1998) 10: 33–45*

BCRP Advance

- *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*

OCRP Advance

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

1999

CDMRP Milestone

- *The Peer Reviewed Medical Research Program (PRMRP) is established by a \$19.5M appropriation*

BCRP Advances

- *Dr. Lawrence Lum develops HER2 Bi-Armed Activated T Cells, which stimulate an immune response against HER2; now in Phase 2 clinical trials*
- *Dr. Gregory Adams develops ErbB2/ErbB3 bispecific scFv antibodies, now licensed by Merrimack Laboratories and currently in Phase 1 clinical trials*

NFRP Advance

- *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. (T2H represents a biologic marker of cognitive dysfunction.) She also identifies high comorbidity of attention deficit hyperactivity disorder and specific learning disabilities in children with NF1*

1999 continued on next page.

Milestones and Scientific Discoveries



1999 cont.

OCRP Advances

- **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 Corporation)
- **Dr. Mary Daly** publishes first resource book for high-risk women considering prophylactic oophorectomy, *Ovarian Cancer Risk-Reducing Surgery: A Decision-Making Resource*
- **Dr. Martin Cannon** demonstrates that enhancing the CD8+ T cell response to ovarian cancer reduces the size of tumors in 75% of cases without surgery or chemotherapy
- **Dr. Patricia Kruk** finds that inhibiting telomerase in cisplatin-resistant cells increased sensitivity to cisplatin treatment. Her research was among the first to indicate novel, extra-telomeric functions of telomerase

PCR Advance

- **Dr. Samuel Denmeade** develops plant-based agent thapsigargin as a pro-drug that can be cleaved into an active form after binding to prostate cancer cells and results in specific, localized cell killing. The agent is now in clinical trials for advanced prostate cancer

PRMRP Advances

- **Dr. Gregory Belenky** develops an unobtrusive, wrist-worn actigraph with an embedded mathematical performance prediction algorithm for tracking activity and sleep periods
- **Dr. Michael Roy** conducts a clinical trial showing that short-term combination exposure to pyridostigmine, diethyltouamide, and permethrin bromide, suggested as a cause of Gulf War Illness, does not adversely impact physical or cognitive performance



2000

CDMRP Milestones

- *The CDMRP offers the first electronic application submission*
- *The BCRP sponsors its second Era of Hope conference*
- *The OCRP sponsors the DoD Ovarian Cancer Investigators' Forum*

BCRP Advances

- *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*
- *Dr. Silvia Formenti conducts a clinical trial showing that breast radiation therapy in the prone, rather than the supine, position greatly reduces unnecessary exposure to the heart and lungs*

NFRP Advance

- *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*

OCRP Advances

- *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. David Bowtell discovers that the +331A allele of the progesterone receptor (PR) gene is significantly associated with protection against endometrioid ovarian cancer*

Milestones and Scientific Discoveries



2001

BCRP Advances

- **Drs. Gregory Hannon and Stephen Elledge** develop gene silencing and genetic screening strategies to identify new potential therapeutic targets
- **Dr. Mina Bissell** develops three-dimensional culture systems, contributing to understanding the complexity of the tumor microenvironment

NFRP Advances

- **Dr. Roger Packer** conducts Phase 1 studies of pirfenidone in children with NF1 and progressive PNF and determines the optimal dose of pirfenidone for treatment. A Phase 2 clinical trial assessing the efficacy of pirfenidone in treating NF1 and PNF has been completed
- **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

OCRP Advances

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

- **Dr. Andrew Berchuck** establishes the International Ovarian Cancer Association Consortium (OCAC)

PCRP Advances

- **Dr. Eugene Kwon** begins clinical testing of ipilimumab, an antibody to stimulate the immune response to prostate cancer by targeting the protein CTLA-4. Androgen deprivation plus ipilimumab results in 70%–100% response in some patients and advances to Phase 3 clinical trials for advanced prostate cancer
- **Dr. Kim Chi** develops an agent that targets the protein clusterin and results in death of prostate cancer cells. The agent has now progressed to Phase 3 clinical trials

PRMRP Advances

- **Dr. Kai Thomenius** develops components for an ultrasound imager suited to remote emergency medical conditions for use in combat casualty care
- **Dr. Jeffrey Mason** develops a field-deployable liposome polymerase chain reaction assay to detect botulinum, cholera, and tetanus toxins in environmental and biological specimens



2002

CDMRP Milestones

- *The National Prion Research Program is established by a \$42.5M appropriation*
- *The Chronic Myelogenous Research Program is established by a \$5M appropriation*
- *The Tuberous Sclerosis Complex Research Program (TSCRCP) is established by a \$1M appropriation*
- *The BCRP sponsors its third Era of Hope conference*
- *The CDMRP launches the Electronic Grant System, enabling real-time electronic management of awards*
- *The CDMRP publishes "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 publishes "Department of Defense Congressionally Directed Medical Research Programs: Innovations in the federal funding of biomedical research," *Clinical Cancer Research*, 8(4), 957-962*
- *The CDMRP publishes "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*

BCRP Advances

- *A Breast Cancer Center of Excellence Award to Dr. Laura Esserman contributes to development of a website, *BreastCancerTrials.org*, that educates patients about clinical trials and matches them with appropriate trials*
- *Dr. George Prendergast conducts preclinical studies on inhibitors of the IDO enzyme, leading to discovery of D-1MT, which is entering Phase 2 clinical trials*

NFRP Advances

- *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. Raymond Mattingly demonstrates that a novel farnesyltransferase inhibitor combined with lovastatin reduces proliferation and induces apoptosis of MPNST cells and is a potential treatment for NF1 MPNSTs*

OCRP Advance

- *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*

2002 continued on next page.

Milestones and Scientific Discoveries



2002 cont.

PCR Advancements

- **Dr. Evan Keller** demonstrates that blocking the activity of RANKL slows the progression of prostate cancer growth in bone. The monoclonal antibody against RANKL, denosumab, is later synthesized and in 2010 attains FDA approval as XGEVA and becomes the standard of care for the treatment of bone-related events in advanced prostate cancer
- The **North Carolina - Louisiana Prostate Cancer Project (PCaP)** is initiated as a landmark collaboration to study racial disparities in prostate cancer and recruiting over 2,000 Caucasian and African American men. After surviving major setbacks due to Hurricane Katrina in 2005, the study concludes in 2010 with key discoveries related to health care access and other socioeconomic factors

PRMRP Advancements

- **Dr. Barbara Soller** creates a portable sensor system for noninvasive measurement of muscle pH, oxygen, and hematocrit and demonstrates muscle oxygen levels may be an early indicator of hemorrhage
- **Dr. David Sahn** develops a method for the reliable and rapid assessment of newborn infants at risk for heart disease at remote health care facilities via teleradiology

TSCR Advancement

- **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



2003

NFRP Advances

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

OCRP Advances

- **Dr. Zhen Zhang**, in collaboration with Vermillion, Inc., develops OVA1™, the first 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. Sandra Orsulic** develops a novel mouse ovarian cancer model and mouse cell lines that lack the BRAC1 gene for studying the initiation and progression of hereditary ovarian cancer

PCRP Advance

- **Dr. Michael Karin** discovers that a mechanism for the development of castrations recurrent prostate cancer results from an inflammatory response involving lymphotoxin and NF- κ B, opening new opportunities for targeting this process for therapy

PRMRP Advance

- **Dr. Stephen Savarino** conducts a clinical trial demonstrating that orally administered bovine milk immunoglobulin collected from cows immunized with enterotoxigenic E. coli antigens provides protection against traveler's diarrhea

TSCR Advances

- **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, formed between TSC1 and TSC2 regulates cell adhesion and motility and that dysregulation of the complex formation may contribute to the pathogenesis of TSC

Milestones and Scientific Discoveries



2004

CDMRP Milestone

- *The PRMRP sponsors its first Military Health Research Forum*

NFRP Advances

- *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. Jeffrey Peterson develops a high-throughput screen to identify Pak1 inhibitors and evaluate them as a potential novel treatment for NF2*

OCRP Advance

- *Dr. Igor Jurisica creates OPHID/I2D, online databases of known and predicted protein-protein interactions, and NAViGaTOR, a software package for visualizing and analyzing PPI networks*

PCRP Advance

- *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*

TSCRP Advances

- *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. 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*



2005

CDMRP Milestone

- *The BCRP sponsors its fourth Era of Hope conference*

NFRP Advances

- *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*
- *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*

OCRP Advances

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

- *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 (matrix metalloproteinase 7) is elevated in serum up to 3 years prior to diagnosis of ovarian cancer*
- *Dr. George Coukos identifies nine candidate proteins for specific expression in ovarian cancer tumor blood vessels that have potential use as therapy targets or imaging targets (patent pending for this set of markers). He also confirms in a mouse model that the tumor endothelial marker 1 (TEM1) is a valid candidate for targeting cells in tumor blood vessels, and that the antibody MORAb-004 inhibits the establishment of tumor vasculature that expresses TEM1—an excellent example of public and private support of promising research as Morphotek is currently supporting multiple Phase 1 trials testing this antibody (MORAb-004) in a variety of cancers*

2005 continued on next page.

Milestones and Scientific Discoveries



2005 cont.

PCRP Advances

- The **Prostate Cancer Clinical Trials Consortium (PCCTC)** (www.pcctc.org) is initiated, bringing together 10 renowned cancer centers, led by Dr. Howard Scher, to speed up clinical testing of new drugs for prostate cancer. By 2008, the PCCTC grows to 13 members and by 2012, accrues more than 3,400 prostate cancer patients to 112 Phase 1 and Phase 2 clinical trials studying more than 50 new drugs. The PCCTC advances nine therapeutic candidates to Phase 3 clinical testing, including abiraterone acetate (ZYTIGA) and enzalutamide (XTANDI), both now FDA-approved and part of the standard of care for the treatment of advanced prostate cancer
- **Dr. Martin Pomper** develops a series of PET radiotracers that target 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

- **Dr. Arul Chinnaiyan** discovers that the protein SPINK1 is associated with the more aggressive forms of prostate cancer and later uses it as part of a panel of biomarkers in urine that can outperform PSA in the detection of prostate cancer
- **Dr. Douglas McNeel** develops an immunotherapy-based DNA vaccine to inhibit prostate cancer recurrence in patients after treatment for primary disease. The agent is later successful in Phase 1 clinical testing and enters Phase 2

PRMRP Advances

- **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

TSCR Advancement

- **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



2006

CDMRP Milestones

- *The Gulf War Illness Research Program (GWIRP), originally known as the Gulf War Veterans Illness Research Program, is co-managed for the first time with the USAMRMC's Military Operational Medicine Research Program with a \$5M appropriation*
- *The PRMRP sponsors the second Military Health Research Forum*

BCRP Advance

- *Dr. Carrie Hruska and colleagues at the Mayo Clinic show that molecular breast imaging (MBI) has greater sensitivity than mammography in women with dense breast tissue and is more cost-effective than magnetic resonance imaging; FDA-approved MBI units are now commercially available*

GWIRP Advance

- *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*

OCRPA Advance

- *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*

PCRPA Advance

- *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*

PRMRP Advance

- *Dr. Joseph Rizzo develops a prototype 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*

TSCRPA Advance

- *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)*

Milestones and Scientific Discoveries



2007

CDMRP Milestones

- *The Amyotrophic Lateral Sclerosis Research Program (ALSRP) is established by \$5M from the Army Research, Development, Test, and Evaluation Funding*
- *The Autism Research Program (ARP) is established by a \$7.5M appropriation*
- *The Psychological Health/Traumatic Brain Injury Research Program (PH/TBIRP) is established by a \$301M appropriation*
- *The PCRP sponsors its first IMPaCT conference*

ALSRP Advance

- *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*

ARP Advance

- *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 ASD compared to matched controls*

NFRP Advances

- *Dr. Bruce Korf and colleagues establish the NF Clinical Trials Consortium*
- *Dr. Feng-Chun Yang develops a mouse model of NF1 that displays similar skeletal manifestations as humans with NF1. This model can be used to study the mechanisms underlying the skeletal manifestations seen in NF1 and to test potential treatments*
- *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*

OCRP Advance

- *Drs. Gillian Mitchell and David Bowtell identify BRCA1/2 mutations in 14% of the 1,001 samples from women with invasive nonmucinous ovarian tumors. Moreover, they observe that a high proportion of women carrying BRCA1/2 mutations did not have a significant family history of breast or ovarian cancer, thereby challenging the current practice of offering genetic testing only to women with a positive family history for those two cancers*



2007

PCR/P Advances

- **Dr. Karen Cichowski** discovers a mechanism for the development of prostate cancer metastasis whereby nuclear factor κ B (NF- κ B), 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- κ B, are blocked by the EZH2 protein, which has long been implicated in prostate cancer metastasis
- **Dr. Michael Rosenfeld** discovers a mechanism involving androgen receptor recruitment to sites of chromosomal breakage that brings the *TMPRSS2* gene close to *ETS* family genes, enabling the gene fusion found to be common in prostate cancers. The discovery provides key strategies for the development of prostate cancer biomarkers and therapeutic agents.

PH/TBIRP Advances

- Two multidisciplinary research consortia, *Strong Star* and *Mission Connect*, were established to advance research in post-traumatic stress disorder, and another multidisciplinary research consortium called *INTRUST* was established to conduct clinical trials in the areas of post-traumatic stress disorder and traumatic brain injury

- **Dr. He Li** shows that administration of corticosterone prior to or following intense, repeated stress prevents traumatic memory retrieval in an animal model of PTSD
- **Dr. Jeffrey Pyne** develops a virtual reality stress inoculation biofeedback training as a predeployment intervention to reduce PTSD development and related mental health problems
- **Dr. Liying Zhang** develops an idealized three-dimensional 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. 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. 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

2007 continued on next page.

Milestones and Scientific Discoveries



2007 cont.

PH/TBIRP Advances cont.

- **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. 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

CDMRP Milestones

- *The Bone Marrow Failure Research Program (BMFRP) is established by a \$1M appropriation*
- *The GWIRP is re-established with a \$10M appropriation*
- *The Deployment Related Medical Research Program (DRMRP) was established with approximately \$92M of the \$273M appropriated in the Supplemental Appropriations Act of 2008 (Public Law 110-252)*
- *The BCRP sponsors its fifth Era of Hope conference*

GWIRP Advances

- *Dr. Lisa Conboy investigates the effectiveness of acupuncture to address the multiple symptoms of GWI, for which treatments can be tailored to individual needs*
- *Dr. William Meggs launches a crossover clinical trial of naltrexone and dextromethorphan to treat neuroinflammation and relieve GWI symptoms*

OCRP Advance

- *Dr. Christine Walsh observes that a natural dietary phytochemical, indole-3-carbinol, sensitized multiple ovarian cancer cell lines to bortezomib. This discovery has the potential to move bortezomib from the bench to the clinic as a treatment option for ovarian cancer*

PCRPA Advance

- *Dr. Lloyd Trotman discovers a new tumor suppressor gene, PHLPP1 ("flip 1"), that cooperates with the gene PTEN to prevent prostate cancer progression to aggressive disease, providing new insight for therapeutic targeting of this pathway*

TSCRPA Advance

- *Dr. Vuk Stambolic implements real-time NMR (nuclear magnetic resonance) 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 patients with tuberous sclerosis 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*

Milestones and Scientific Discoveries



2009

CDMRP Milestones

- *The Genetic Studies of Food Allergies Research Program (GSFARP) is established by a \$2.5M appropriation*
- *The Lung Cancer Research Program (LCRP) is established by a \$20M appropriation*
- *The Multiple Sclerosis Research Program (MSRP) is established by a \$5M appropriation*
- *The Peer Reviewed Cancer Research Program (PRCRP) is established by a \$16M appropriation*
- *The Peer Reviewed Orthopaedic Research Program (PRORP) is established by appropriations totaling \$112M*
- *The Spinal Cord Injury Research Program (SCIRP) is established by a \$35M appropriation*
- *The PRMRP, GWIRP, and PH/TBIRP sponsor the third Military Health Research Forum*

ALSRP Advance

- *Dr. Nicholas Maragakis initiates preclinical studies of induced pluripotent stem cell-derived astrocyte transplantation as a possible therapy for ALS*

BMFRP Advance

- *Dr. Charles Lin demonstrates the critical role of regulatory T cells in maintaining immune privilege mechanisms of the hematopoietic stem/progenitor cells (HSPC) niche. This work has established a novel concept of immune-privilege in the HSPC niche and uncovered its molecular and cellular mechanisms*

GWIRP Advances

- *Dr. Ashok Tuteja examines the probiotic Align® (*Bifidobacterium infantis* 35624) to improve global health and individual symptoms of irritable bowel syndrome in Gulf War Illness*
- *Dr. Anne-Louie Oaklander investigates small-fiber polyneuropathy as an underlying cause of symptoms associated with GWI*

LCRP Advances

- *Dr. Peter Hammerman demonstrates discoidin domain receptor 2 (DDR2) mutations are present in 4% of lung squamous cell carcinomas (SCC), and DDR2 mutations are associated with sensitivity to dasatinib. This work has led to the opening of a Phase 2 trial evaluating dasatinib in advanced SCC*
- *Dr. Chris Moskaluk and colleagues establish the first national early lung cancer biospecimen repository*

MSRP Advance

- *Dr. John Chen develops a myeloperoxidase-targeted MRI agent (myeloperoxidase-gadolinium) for the detection of early, preclinical, and subclinical disease activity (both with and without treatment) in an experimental autoimmune encephalomyelitis mouse model of multiple sclerosis*



2009

OCRP Advances

- **Dr. Rugang Zhang** observes that *Wnt5a* is expressed at lower levels in primary epithelial ovarian cancers; loss of *Wnt5a* correlates with a high cell proliferation index; and reconstituting *Wnt5a* in ovarian cancer cells causes cell senescence (irreversible cell growth arrest). These results suggest that targeting Wnt signaling is a novel strategy to induce senescence in epithelial ovarian cancer cells
- **Dr. David Bowtell** demonstrates that amplification of the 19q12 chromosomal locus is the most important chromosomal copy number change associated with primary treatment failure in ovarian cancer
- **Dr. Kathryn Terry** finds that dominant tumors (ovarian origin) are more strongly associated with multi-parity, tubal ligation, and endometriosis, whereas nondominant tumors (tubal origin) are more strongly associated with a family history of ovarian cancer and genetic variation in a telomere-associated protein, *TERT*

PCRPA Advance

- The **Prostate Cancer Biorepository Network (PCBN)** is initiated, bringing together Johns Hopkins University and New York University, to deliver high-quality biospecimens for wide usage by the research community. By 2012, the PCBN accumulates over 2,000 samples, resulting in the discovery of a link between the *SPARCL1* protein and aggressive prostate cancer

PH/TBI Advances

- **Drs. Gregory Gahm and Greg Reger** are conducting a randomized clinical trial comparing Virtual Reality Exposure Therapy to traditional Prolonged Exposure Therapy in the treatment of combat-related PTSD
- **Dr. Mikulas Chavko** uses a rat model of blast injury to reveal that pressure detected in the rat brain is contingent on the orientation to the blast direction

PRCRP Advance

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

PRORP Advances

- **Dr. Aaron Dollar** develops a body-powered prosthetic hand prototype that allows for a range of grasping positions and the ability to adapt passively to the shape of any object within its grasp.
- **Dr. Brian Glaister** develops a physical exotendon device to facilitate walking for individuals with significant mobility impairments.

TSCRPA Advances

- **Dr. Angeliqe Bordey** develops an animal model that will allow TSC researchers to study the development of cortical tuber lesions at specific time points during embryonic development
- **Dr. Francis McCormack** and colleagues establish the Lymphangioliomyomatosis (LAM) Clinical Research Network

Milestones and Scientific Discoveries



2010

CDMRP Milestone

- *The CDMRP provides pre- and post-award execution support for the Defense Medical Research and Development Program Execution (DMRDP)*

ALSRP Advance

- *Dr. James Connor investigates the infusion of an iron-binding protein, apo-ferritin, to sequester and redistribute the excess iron found in ALS, thus controlling the symptoms associated with ALS*

ARP Advance

- *Dr. Daniel Cox develops a virtual reality system to evaluate and enhance the driving skills of individuals with autism*

DMRDP Advances

- *Drs. Arthur Kuo and Glenn Klute aim to develop a prosthetic knee-ankle-foot system that actively coordinates the joints. A key innovation of the project is that the knee and ankle-foot prostheses will be computer-controlled but self-powered by harvesting energy from the user*
- *Dr. Crystal Jiang and colleagues are developing new tools that will, for the first time, produce a complete clinical wound profile by merging information on host response biomarkers with the identity of potentially dangerous microorganisms in combat wound*

GWIRP Advances

- *Dr. Yoshio Nakamura conducts an exploratory randomized clinical trial to evaluate how a sleep-focused mind-body program may enhance primary care for GWI and alleviate symptoms*
- *Dr. Brian Cooper investigates the synergistic actions of neurotoxicants pyridostigmine bromide and pesticides on pain receptors in muscle and blood tissues*

LCRP Advance

- *Dr. Avrum Spira, Dr. Peter Schnall, and colleagues establish the Detection of Early Lung Cancer Among Military Personnel clinical consortium seeking to improve the process of diagnosing individuals at high risk of developing lung cancer*

OCRP Advance

- *Dr. Robert Kurman's consortium developed and validated an inclusive scoring algorithm to assist pathologists in diagnosing STICs, the proposed precursor for most ovarian high-grade serous cancers*

PRORP Advance

- *Dr. Stephen Stanhope and colleagues establish the Bridging Advanced Developments for Exceptional Rehabilitation, or BADER, Consortium to conduct clinical research to optimize evidence-based orthopaedic rehabilitation care for wounded warriors*



2011

CDMRP Milestones

- *The CDMRP executes research projects under the Army's Rapid Innovation Fund*
- *The BCRP sponsors its sixth Era of Hope conference*
- *The PCRP sponsors its second IMPaCT conference*
- *The Duchenne Muscular Dystrophy Research Program (DMDRP) is established by a \$4M appropriation*

ALSRP Advance

- *Dr. Nicholas Cosford evaluates the effectiveness of enzyme inhibitors of apoptosis as novel treatments to halt the progression of ALS*

GWIRP Advances

- *Dr. Julia Golier evaluates the effects of daily intranasal insulin on cognitive and physical symptoms of GWI*
- *Dr. Alvin Terry examines the effects of organophosphate exposure on impairment of nerve cell transport in the brain, as a determinant of GWI symptoms*

2012

PH/TBIRP Advance

- *The DoD and the VA solicit two new consortia aimed at improving diagnosis and treatment of mild Traumatic Brain Injury and Post-Traumatic Stress Disorder. Once in place, these consortia called the Consortium to Alleviate PTSD and the Chronic Effects of Neurotrauma Consortium will be devoted to the health and welfare of our nation's service members, veterans, and their family members.*



Programs



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



Lucie Bruijn, Ph.D., Chief Scientist for The ALS Association and FY12 ALSRP IP Chair

“There is an urgent need for treatments for ALS, a devastating disease with no cure and only one FDA-approved treatment that slows progression of the disease by a few months.

The ALSRP is a very exciting program providing the opportunity for investigators from academia and industry to develop new treatment approaches for ALS. This important program funding translational research fills an enormous gap in the research pipeline to enable new treatments to move from the laboratory to the clinic.”

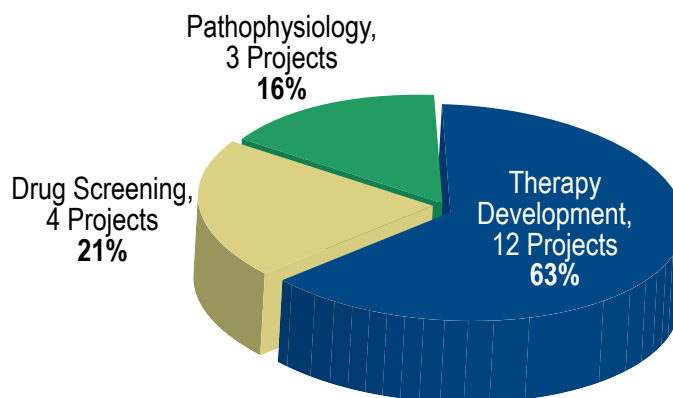
The ALSRP’s 20 awards made from FY07–FY11 focus on a variety of molecular targets that either protect neurons from neurotoxicity or contribute to disease progression.

Background and 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 diagnose 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 to 5 years⁴ and about 10% of patients with ALS live more than 10 years after diagnosis.⁵ 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. 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 yet understood.

There are currently no known therapies to effectively halt the progression of ALS, though one FDA-approved drug, riluzole, modestly slows ALS progression. Several drug candidates are now 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.

The Amyotrophic Lateral Sclerosis Research Program (ALSRP) was established by Congress in FY07 with a \$5M appropriation and a mission to support preclinical therapy development for ALS. Though not funded in FY08, the program has consistently been funded since FY09, with total appropriations of more than \$31M, including \$6.4M in FY12.



FY07–FY11 ALSRP Portfolio by Research Area

⁴ www.alsa.org

⁵ Weisskopf M, et al. 2004. Annual Meeting of the American Academy of Neurology, San Francisco, California.



Targeted Riluzole Delivery by Antioxidant Nanovectors for Treating Amyotrophic Lateral Sclerosis

Raymond Grill, Ph.D., University of Texas Health Science Center at Houston

Causes for ALS range from genetic to environmental factors to the unknown, but it has been suggested that similarities exist in the actual pathological events that contribute to the progressive neuronal degeneration that characterizes ALS. These pathological mechanisms include progressive oxidative and inflammatory conditions that destroy central nervous system (CNS) tissues. There is currently no cure for ALS. Riluzole (Rilutek®) is the only treatment for ALS approved by the FDA, though it only prolongs life by a few months. The bioavailability of riluzole, however, has been shown to be reduced during the progression of the disease in animal models of ALS. New therapeutic approaches need to be developed that can: (1) improve the bioavailability and efficacy of riluzole and (2) have novel efficacious properties that can work in tandem with riluzole.

Recently, the laboratory of James Tour, Ph.D. at Rice University has developed a novel nanoscale construct



composed of hydrophilic carbon clusters (HCCs). HCCs exhibit potent antioxidant characteristics that may target oxidative stress mechanisms in ALS. HCCs can be further functionalized through the chemical addition of polyethylene glycol (PEG) to serve as “carrier” molecules to enhance penetration of therapeutics into the CNS.

Using funds from an FY11 ALSRP Therapeutic Idea Award, Dr. Raymond Grill and Dr. Tour will test the efficacy of PEG-HCCs in a mouse model of ALS. The project will examine whether sustained intravenous administration of PEG-HCCs can reduce ALS-like behavioral symptomatology, promote motor neuron survival, and prolong life. They will also test whether a combination of riluzole and PEG-HCCs can enhance riluzole’s bioavailability and efficacy as an ALS therapeutic.

Inhibitors of TDP-43 Aggregation and Toxicity

Leonard Petrucelli, Ph.D., Mayo Clinic and Foundation, Jacksonville, Florida

Dr. Leonard Petrucelli’s laboratory has pioneered neuroscience research aiming to understand the underlying mechanisms of ALS and identify potential drug targets for its treatment. TAR DNA-binding protein-43 (TDP-43) has been found to go awry in approximately 90% of all ALS patients. Studies in yeast have revealed that C-terminal TDP-43 fragments are prone to aggregate and only TDP-43 species that form inclusions, which result from continued protein aggregation, are toxic to neurons. Dr. Petrucelli is using an FY09 ALSRP Therapeutic Development Award to identify compounds that prevent TDP-43 aggregation as potential neuroprotective agents for ALS.

Using a previously developed human neuroblastoma cell line (M17D3) that overexpresses green fluorescent protein (GFP)-tagged C-terminal TDP-43 truncation product, GFP-TDP220-414, Dr. Petrucelli has begun screening compounds that reduce TDP220-414



aggregation, which is expressed as an attenuation of the GFP fluorescence. More than half of the 58,000 compounds from a select, proprietary small-molecule library have been screened on the M17D3 cells, and to date, 2,141 compounds were found to attenuate GFP fluorescence (i.e., TDP fragment aggregation) by at least 30%.

Expression of another relevant truncation product, GFP-TDP208-414, which can be exploited in M17D3 and also causes neurotoxicity in primary cortical neuronal cultures, is also being examined.

Future experiments will include further screening of the most promising compounds on primary cortical neuronal cultures. Expression of lactate dehydrogenase released into culture media will be measured as an indicator of cytotoxicity to further validate the compounds as potential therapeutic agents.

ARP

AUTISM RESEARCH PROGRAM

Vision

Improve the lives of individuals with autism spectrum disorders now

Mission

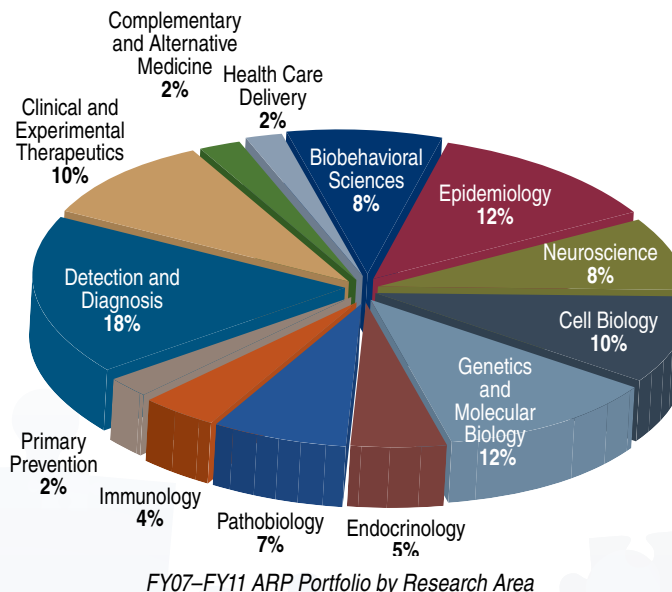
Promote innovative research that advances the understanding of autism spectrum disorders and leads to improved outcomes



Yolanda Cosby and her son Eric

Background and Program History

With the alarming rise of ASD in the United States, where 1 in 88 children and as many as 1 in 54 boys are diagnosed on the spectrum yearly, Congress has answered the call and appropriated funds to the DoD budget to execute and manage the Autism Research Program (ARP). The cause of ASD is unknown; however, progress is being made on several fronts and the answers related to ASD diagnosis and treatment will likely be multifaceted. The immediacy of the ARP vision, to improve the lives of individuals with autism now, has imparted a strong sense of action and has steered the investment strategy of the ARP for the past 5 years. 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 future. From its inception in FY07, appropriations of \$41.4M have been managed by the ARP to invest in the advancement of autism research to assist and improve the lives of individuals living with ASD.



A Consumer's Perspective: Yolanda Cosby, FY11 Consumer Peer Reviewer

From Denial to Acceptance and Beyond

Yolanda Cosby knew about autism. As a special education teacher, she had worked at a school for autistic children. She could see the signs; she knew the actions and reactions. It became familiar; it became routine. Perhaps too routine.

When her oldest son, Eric, was diagnosed with autism at 2 years of age, Yolanda refused to believe it. Following the path of the five stages of grief, Yolanda experienced denial, anger, bargaining, and depression before finally accepting her son's diagnosis. "After he was diagnosed with a developmental disability, I thought, 'Eric is fine—he just needs some speech services,'" said Yolanda. "I didn't even discuss it with my friends and family, because I thought it would clear up if he went to Early Intervention Services. Then I thought 'Why Me?', and then I tried to make a deal with God. I said I would go to church every Sunday if he would help Eric." Yolanda also blamed herself for Eric's diagnosis. It was her fault, she reasoned, because she did not take her daily vitamins during pregnancy, and also suffered from gestational diabetes. Once she experienced the final stage of grief—acceptance—Yolanda said her life, and Eric's, dramatically improved and came into focus. "When I finally realized that autism is here in



Technology-Enhanced Early Intensive Behavior Intervention Services for Children with Autism Spectrum Disorders in Military Families

Wayne Fisher, Ph.D., University of Nebraska Medical Center

ASD encompasses a range of developmental disorders that involve impairments in language, social relatedness, and repetitive behaviors. ASD affects approximately 13,000 children whose parents are active duty military service members. Early intensive behavior intervention (EIBI) has been demonstrated to improve long-term outcomes for children with ASD when started at 2 to 3 years of age and practiced at least 25 hours per week. Unfortunately, only 10% of military children are receiving this treatment because access to services and trained professionals is severely limited or lacking entirely in many areas where military families are stationed.



Dr. Wayne Fisher, of the University of Nebraska Medical Center and FY10 recipient of an ARP Clinical Trial Award, is leading an effort to greatly increase the availability of EIBI to military families anywhere in the world through web-based training curricula developed to educate paraprofessionals as EIBI tutors and instruct parents in the use of EIBI techniques in the home. These training curricula use slide-by-slide narration and video demonstrations, as well as scripted role-plays for practicing the techniques with other adults.

While trained paraprofessional tutors will help to implement the EIBI services locally, it will continue to

be important for children to receive care from one physician, with ASD expertise, who knows their medical history. Imperative to making EIBI available remotely, therefore, is the use of behavior capture systems and video conferencing. Parents will be able to record and annotate video clips of problem behavior from multiple cameras strategically

located throughout the home and store them on a secure server where they can be viewed by the child's physician, regardless of location. Similarly, video conferencing will allow the child to be cared for by a single physician, no matter where the military family is stationed or how frequently they relocate.

Dr. Fisher believes that this web-based training program will increase the number of trained EIBI tutors near military bases and other remote areas, provide long-lasting clinical benefits to children with ASD, reduce parental stress in military families, and eliminate geography as a barrier to effective EIBI treatment. The effectiveness of this technology-driven enhanced intervention will be evaluated in a randomized clinical trial with 50 paraprofessionals and 50 military parents along with their children who have been diagnosed with ASD.

my family to stay, I came to grips and asked myself, 'What can I do to help the situation?'" Yolanda said. "That is the point when advocacy became part of my life."

After Eric's fifth birthday, Yolanda was still coming to grips with his autism and getting suggestions from doctors, family members, and friends. She needed a foundation upon which to begin her advocacy efforts and began volunteering her time with Autism Speaks. "I got so much advice when he was diagnosed, my head was spinning," Yolanda said. "I had two children 17 months apart, and I needed some support. I wanted to bond with a group that understood what was going on with me. Advocacy has provided me a sort of therapy by helping other families that have loved ones with autism." Six years after Eric's diagnosis, and 5 years after she plunged into the world of advocacy, Yolanda said she is right where she wants to be. She continues to work with Autism Speaks, as well as with the Interactive Autism Network (IAN), and recently served as a peer reviewer for the DoD ARP. In future years, she said she hopes to learn more about autism to help families struggling to accept the diagnosis.

"Today, I am strong, thanks to Autism Speaks, the IAN Project, and the Autism Research Program," Yolanda said. "I feel like I am working to assist with funding the cause for autism. I know that I am making a difference for the future."

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

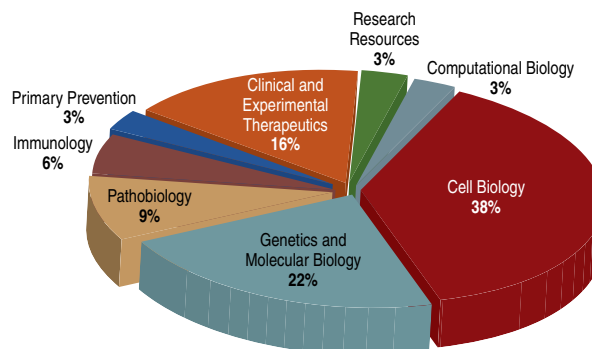


**David Fiaschetti,
D.D.S., FY12 IP
Member**

“The continued opportunity to participate in the BMFRP Integration Panel enables me to directly interact with researchers, medical providers, and consumers, all with the same goal of enhancing treatment for bone marrow failure. I believe it is only through research that the day will come when a diagnosis of ‘bone marrow failure’ no longer means potential early death.”

Background and Program History

In FY08, Congress appropriated \$1M to the DoD budget for the study of bone marrow failure (BMF), and the Bone Marrow Failure Research Program (BMFRP) has been managed by the CDMRP since its inception. From its inception in FY08, appropriations of \$16.95M have been managed by the BMFRP to invest in the advancement of innovative research to understand and cure BMF. Bone marrow, the sponge-like tissue found inside bones, contains blood-forming stem cells that develop into red blood cells, white blood cells, and platelets. Disorders of the bone marrow are critical and can lead to life-threatening diseases where the bone marrow either does not function or produces abnormal blood cells. These diseases are classified into two major categories: inherited or acquired BMF. Exposures to viruses, chemicals, and environmental toxins (a risk for service members) may lead to acquired BMF. Many forms of BMF lead to the development of cancers such as leukemia. Treatment of BMF is determined by the cause and severity of the illness; for some patients, the currently available treatment options may not be appropriate or feasible.



FY08–FY11 BMFRP Portfolio by Research Area



A Consumer’s Perspective: Neil Horikoshi, J.D., FY12 Integration Panel Member

On Wednesday, February 29, 2012, Neil Horikoshi observed the 12th anniversary of his diagnosis of a blood disorder ultimately identified as aplastic anemia.

Luck and fate have defined my journey as a person with BMF disease, from the first appearance of symptoms, including shortness of breath and fatigue, to the diagnosis of aplastic anemia, an acquired BMF disease, in February 2000. I was living in Japan at the time and had planned a trip to India. But for the luck of securing the last available appointment for a physical before leaving for India, I probably would not be here to write this story. The words “99% chance of leukemia” were life-changing: I received an infusion of red blood cells and platelets, took the last flight out of Tokyo, and flew overnight to Honolulu. I arrived early in the morning, and



Myelodysplastic Syndromes

Amit Verma, M.B.B.S., Albert Einstein College of Medicine of Yeshiva University, Bronx, New York

Myelodysplastic syndromes (MDS) are a group of incurable diseases that lead to BMF, with one-third of cases ultimately advancing to leukemia. Research into the causes of MDS has been hampered by a lack of cells lines and relevant mouse models, and sufficient patient samples are difficult to obtain. In FY11, the BMFRP offered the Resource Development Award to support the development of research resources that could be shared by the BMF research community. Although microarray technology provides a wealth of gene expression (GE) data for the investigation of biological and medical processes, variability in experimental conditions and microarray platforms has limited the utility of these data. Dr. Amit Verma was awarded an FY11 Resource Development Award to use his newly developed meta-analytical approach to integrate data from the National Center for Biotechnology Information's Gene Expression Omnibus database. Using samples from individual investigators, Dr. Verma's team will create a large MDS GE database. In preliminary studies, Dr. Verma's team demonstrated



the feasibility of this approach when they integrated data from several different labs and generated using different platforms to develop an MDS GE database capable of distinguishing biologically distinct cell types despite the experimental variability of the samples. Employing the newly established database, they were able to elucidate the mechanism for TGF- β overactivation in MDS stem cells, a state that leads to BMF.

The database Dr. Verma proposes to develop with the support of the BMFRP Resource Development Award will represent one of the largest MDS GE databases. This resource will allow investigators to search MDS samples to identify expression patterns in genes of interest and subtypes of MDS patients that may benefit from targeted therapies. The development of this resource and its subsequent sharing with the BMF research community will support the efforts of researchers in understanding the causes of MDS and developing lifesaving treatments.

proceeded straight to a hematology appointment, where I had a bone marrow biopsy. Within a few days, I was diagnosed with aplastic anemia.

In 2000, the publicly available information provided a very grim assessment of high mortality and a limited probability of long-term survival. I put my affairs in order. I was distressed to learn that aplastic anemia was deemed an "orphan disease"—one that is mostly ignored by pharmaceutical companies because it does not promise much profit for the manufacturer. Because funding for research is limited, very few researchers or postdoctoral students pursue BMF research. Leading researchers who specialized in aplastic anemia and who had demonstrated relatively successful treatment in clinical studies were my only hope. Bone marrow transplant was not an option.

But through crisis comes opportunity. I became a member and later Chair of the Board of Directors of the Aplastic Anemia and MDS International Foundation. When I was later invited to join the BMFRP IP as a consumer reviewer, I came to understand how the BMFRP is supporting research and investment in this orphan disease. The BMFRP works to find cures for both acquired and hereditary BMF, and it is a joy to witness the work of researchers across the BMF spectrum. It is also most gratifying to hear the stories of other BMF consumers and peer reviewers, who reinforce the meaning of hope for all BMF patients. I am humbled by the talent and commitment of the IP members, who are experts in their respective fields. I thank all those doing research in BMF and all other orphan diseases. You are the angels providing hope to patients throughout the nation and around the world.

BCRP

BREAST CANCER RESEARCH PROGRAM

Vision

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



Maria Wetzel,
Michigan
Breast Cancer
Coalition,
BCRP
Consumer
Reviewer

"I am confident that the BCRP expects the funded research to truly make a difference in the mission to end breast cancer. We as reviewers have to be critical thinkers, ask continually if a proposal is simply more of the same and incremental, or if it holds the possibility of real progress."

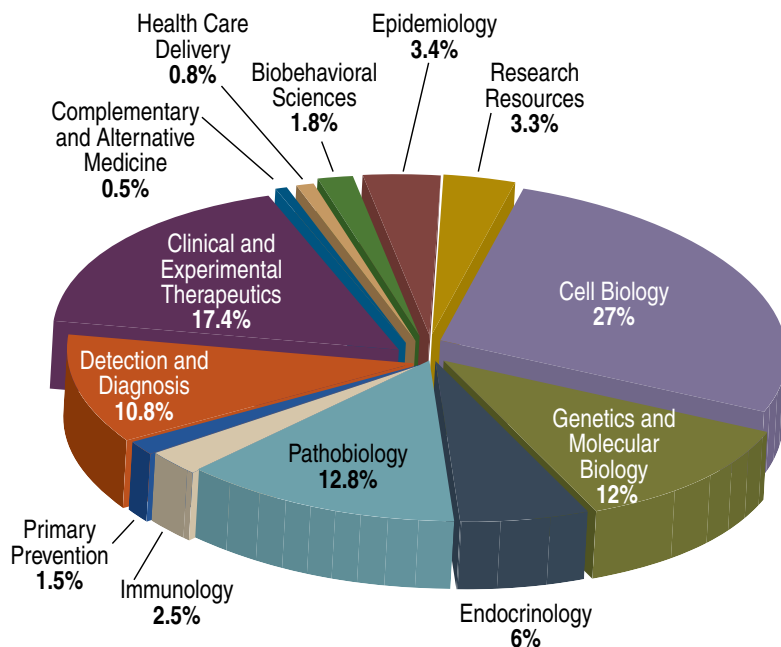


Background and Program History

The Breast Cancer Research Program (BCRP) plays a leading role in the fight against breast cancer through its innovative approaches and its focus on research that will bring an end to this disease. The BCRP was established in 1992 as a result of the passionate and dedicated efforts of breast cancer advocates. Their continued efforts, in concert with the program's successes, have resulted in more than \$2.7B in congressional appropriations through FY12 to support breast cancer research. Over the years, the BCRP has created unique award mechanisms that have transformed the breast cancer research field. The BCRP enables the scientific community to propose their best, innovative ideas that address the urgent need to end breast cancer. Scientists are challenged to pursue high-risk, high-reward research, set new paradigms that could lead to critical discoveries and breakthroughs, and make an unprecedented impact on breast cancer. The BCRP also promotes synergistic collaborations across disciplines and integrates scientists and consumers in unique and meaningful research partnerships. The BCRP's 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 "best and brightest" next generation of breast cancer experts and innovators.

Program Portfolio

From FY92–FY11, the BCRP funded more than 6,100 awards, covering early-stage ideas in basic research, translational and applied research, and clinical studies/trials involving breast cancer patients.



FY92–FY11 BCRP Portfolio



BCRP Achievements at a Glance

Awards supported by the BCRP have led to many products that have transformed breast cancer research and resulted in clinical breakthroughs for breast cancer patients. Many more innovations supported by the BCRP are in the pipeline. A sampling is shown below.

Products and Clinical Breakthroughs

Herceptin – Characterization of this monoclonal antibody led to its development into a standard-of-care treatment for HER2+ breast cancers. (PI: Dennis Slamon)

Sentinel Lymph Node Biopsy – Clinical trials testing this diagnostic/prognostic technique contributed to the current standard of care, which enables clinicians to perform tumor staging and determine if more extensive lymph node removal is necessary. (PI: Kathryn Verbanac)

PTEN Tumor Suppressor Gene – Discovery of this frequently mutated oncogene enabled development of a genetic test used for clinical diagnoses. (PI: Michael Wigler)

BRCA2 617delT mutation – Discovery of this gene mutation led to development of a commercialized genetic screening test for BRCA1/BRCA2 mutations. (PIs: David Goldgar and Susan Neuhausen)

Oncovue – Risk association studies led to development of this breast cancer risk assessment test that is now commercially available and offered at over 30 breast care centers in the U.S. (PI: Eldon Jupe)

Expression Arrest™ shRNA libraries – Development of this resource targeting over 30,000 genes provides rapid screening tests to study gene regulation and to identify new therapeutic targets. (PIs: Gregory Hannon and Stephen Elledge)

Margaret Dyson Family Risk Assessment Program – Establishment of a high-risk familial breast cancer registry evolved into this program, which provides individuals with risk assessment, screening, and preventive services. (PI: Mary Daly)

BreastCancerTrials.org – This online resource provides information to patients about breast cancer clinical trials and matches them with appropriate trials. (PI: Laura Esserman)

Molecular Breast Imaging (MBI) – A clinical study showed that this imaging technique has greater detection sensitivity than mammography in dense breast tissue and is more cost-effective than MRI; FDA-approved MBI units are now commercially available. (PI: Carrie Hruska)

ATLAS Clinical Trial – Preliminary analysis indicated that the rate of breast cancer recurrence was lower in women treated with tamoxifen for 10 years versus 5 years; currently in the follow-up phase until 2015. (PI: Richard Peto)

Innovations in the Clinical Pipeline

NeuVax™ – Characterization of the HER2 receptor led to development of this peptide vaccine, which is now in Phase 3 clinical trials. (PI: Constantine Ioannides)

HER2 Bi-Armed Activated T cells – Discovery that these cells stimulate an immune response against the HER2 receptor led to advancement of this immunotherapy to a current Phase 2 clinical trial. (PI: Lawrence Lum)

IDO Inhibitor – Identification of lead inhibitors of IDO, a protein that prevents an anti-tumor immune response, led to the discovery of an IDO inhibitor called D-1MT, which is now in Phase 2 clinical trials. (PI: George Prendergast)

Prone Radiotherapy – Clinical trials showed that breast radiation therapy in the prone, rather than the supine, position greatly reduces unnecessary exposure to the heart and lungs, making prone radiotherapy a potential standard choice in breast radiotherapy. (PI: Silvia Formenti)

Optical Spectroscopy – Development and clinical testing of novel optical tools show promise for real-time assessment of tumor margins and generation of molecular information about breast tissue to assist clinicians in making treatment decisions. (PI: Nimmi Ramanujam)

MM-111 Antibody – This bispecific antibody capable of simultaneously engaging both HER2 and HER2 receptors is in early phase clinical trials for HER2+ advanced breast cancer. (PI: Gregory Adams)

BREAST CANCER RESEARCH SEMIPOSTAL PROGRAM



Recent Awards

FY10

- ◆ Pepper Schedin, Ph.D., University of Colorado, Denver
The Immune Modulatory Program of Postpartum Involution Promotes Pregnancy-Associated Breast Cancer
- ◆ Anthony Leung, Ph.D., Johns Hopkins University
The Role of Poly (ADP-Ribose) in microRNA Activity in Breast Cancers

FY11

- ◆ Andy Minn, M.D., Ph.D., University of Pennsylvania; Partnering PI: Roger Greenberg, M.D., Ph.D.
Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements
- ◆ Xiaosong Wang, M.D., Ph.D., Baylor College of Medicine; Partnering PI: Rachel Schiff, Ph.D.
Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer
- ◆ Susana Gonzalo Hervas, Ph.D., St. Louis University
Stabilization of 53BP1 in Triple-Negative and BRCA-Deficient Breast Tumors: A Novel Therapeutic Strategy

Background and Program History

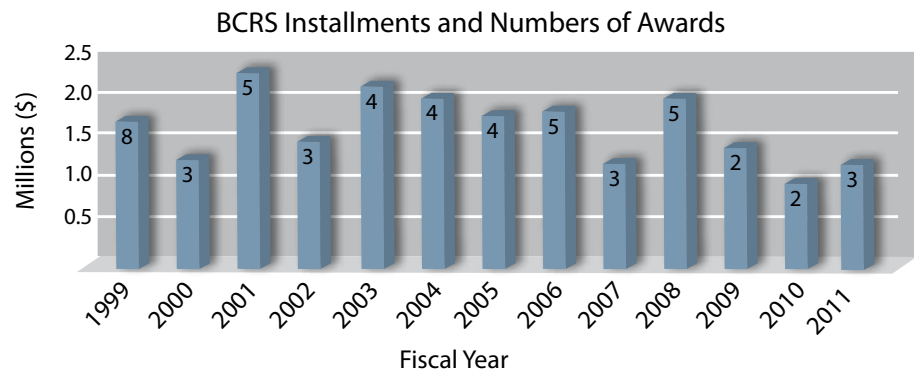
As a result of the efforts of breast cancer advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the U.S. Postal Service's issuance of a new first-class stamp, the Breast Cancer Research Semipostal (BCRS) in 1998. The stamp, which costs 55¢, can be purchased on a voluntary basis by the public. Net revenues from sales of the BCRS are provided to two designated funding agencies, the DoD BCRP and NIH, to support breast cancer research. Public Law 110-80 reauthorized the BCRS through December 31, 2015.

Research and Management Costs

Breast cancer stamp funding received by the BCRP has been used to fully or partially fund 48 Idea Awards and 3 Synergistic Idea Awards between FY99 and FY11. Both award mechanisms support innovative, high-risk, high-reward research that could lead to major advancements in breast cancer. Applications funded through the BCRS program were reviewed and recommended for funding according to the two-tier review system implemented by the DoD BCRP.

Total Proceeds from BCRS	\$22,505,375.91
Research	\$20,811,933.31
Management Costs	\$997,967.78

Note: Funds yet to be allocated—\$695,474.82



John Wysolmerski, M.D., Yale University

"With the help of the BCRP, we have defined important roles for PTHrP in normal development and lactation. The task now is to use this knowledge to understand how it influences breast cancer in patients and to determine whether this pathway can serve as a therapeutic target for treatment."

Pepper Schedin, Ph.D., University of Colorado, Denver

"Because of BCRP funding, postpartum breast cancer is now recognized in the field as a significant component of breast cancer deserving of research focused on targeted interventions."



Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer

John Wysolmerski, M.D., Yale University, New Haven, Connecticut

Parathyroid hormone-releasing protein (PTHrP) is secreted from breast epithelial cells to regulate mammary gland development and to promote calcium accumulation in the mammary gland for milk production during lactation. While many functions of PTHrP require it to be secreted from cells, a segment of the protein may be retained within a cell and enter the nucleus. Previous breast cancer studies have suggested that nuclear PTHrP may contribute to more aggressive tumors. Dr. John Wysolmerski received an FY09 BCRP Idea Award to investigate the role of nuclear PTHrP in mammary gland development, maintenance of mammary stem cells, and breast cancer prognosis. Elucidating the role of PTHrP may result in a novel target for breast cancer treatment.



Dr. Wysolmerski employed a genetically modified mouse model that has a shortened form of PTHrP that is unable to enter cell nuclei. Unexpectedly, Dr. Wysolmerski observed that loss of nuclear PTHrP

resulted in defective mammary ductal outgrowth in female mouse embryos. In addition, proteins that normally appear in the surrounding dense mammary mesenchymal tissue were absent or significantly reduced. These results led to a novel hypothesis of PTHrP action during embryonic mammary gland development: PTHrP is secreted from mammary epithelial cells and binds

to receptors on nearby mesenchymal cells where it is internalized and shuttled into the cell nucleus to mediate mammary gland development. Experiments are in progress to further validate these findings. Dr. Wysolmerski's preliminary analysis of more than 600 human breast tumor samples suggests that PTHrP expression may predict poor clinical outcome and be correlated with markers of aggressive breast cancer. Analysis of mortality data from this breast cancer cohort also indicated that PTHrP may be associated with increased risk of death.

The Immune Modulatory Program of Postpartum Involution Promotes Pregnancy-Associated Breast Cancer

Pepper Schedin, Ph.D., (shown left) and Virginia Borges, M.D. (shown right), University of Colorado Denver, Anschutz Medical Campus, Denver, Colorado

Breast cancer is the most common cancer among pregnant and postpartum women. Evidence suggests that women with postpartum breast cancer have a higher risk of metastases and death. Studies using mouse models of breast cancer indicate that postpartum breast involution—the return of the lactating mammary gland to its pre-pregnancy state—promotes tumor growth and metastasis. One theory is that involution results in suppression of the immune cells that target and kill tumor cells. Dr. Pepper Schedin received an FY10 BCRP Idea Award to investigate the role of immunosuppression in the involuting mammary gland in breast cancer. Dr. Schedin's group characterized the immune cell profile of the mammary gland throughout the entire reproductive cycle and confirmed that the postpartum involuting gland has an immune suppressive environment. They further

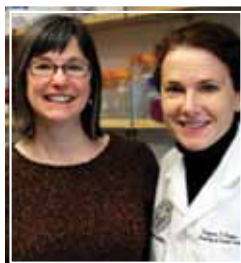


Photo courtesy of University of Denver

found that mammary tumor cells injected into postpartum mice during involution developed into significantly larger mammary tumors than in nulliparous mice (mice that never produced offspring). Characterization of their immune cell profiles confirmed that involution is correlated with immune suppression.

In collaboration with Dr. Virginia Borges, Dr. Schedin is also studying the immune profile of breast tumor tissue in women under 45 years of age. Preliminary analyses demonstrated an increase in immune cell infiltrate into pregnancy-associated breast tumors. Further analyses will determine whether these immune cells support an immunosuppressive phenotype. Increased understanding of the role of the immune system in breast involution may lead to potential targets to prevent and treat postpartum breast cancer.

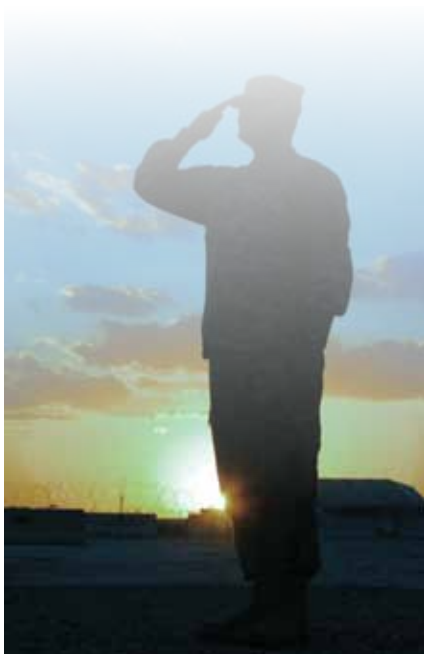
DEFENSE MEDICAL RESEARCH AND DEVELOPMENT PROGRAM EXECUTION

Mission

To provide full life-cycle operational management support to the Defense Medical Research and Development Program (DMRDP), a core Department of Defense research program within the Office of the Assistant Secretary of Defense for Health Affairs (OASD(HA)).

Dr. Rauch, the Director of Medical Research, Office of the Assistant Secretary of Defense (Health Affairs)

“The health and well-being of our service members, veterans, and their family members are of paramount concern to the Department of Defense (DoD). The research efforts supported by the DMRDP are critical to the goal of the DoD to provide excellence in health care solutions to these brave citizens.”



Background and Program History

The OASD(HA) Defense Medical Research and Development Program Execution (DMRDP) was established in FY10 and continues to date. The OASD(HA) assigned execution management responsibilities to the USAMRMC as one of several execution agents to provide strategic and operational management support. The DMRDP research areas of responsibility assigned to USAMRMC for strategic and operational management include:

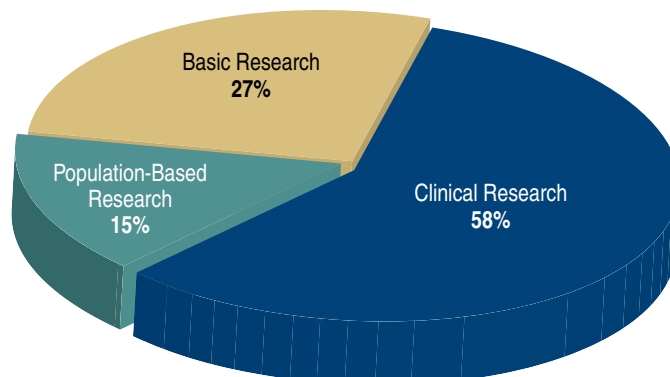
- Medical Training and Health Information Services
- Military Infectious Diseases
- Military Operational Medicine
- Combat Casualty Care
- Clinical and Rehabilitative Medicine

Strategic responsibility was assigned to JPCs aligned with these five research areas. Operational support responsibility was assigned to two primary execution agents, the CDMRP and the Telemedicine and Advanced Technology Research Center.

CDMRP Portfolio Execution Assignments

From FY10–FY11, the CDMRP has executed \$153.26M in support of the DMRDP, funding basic through translation research efforts. These projects are expected to yield critical prevention, detection, diagnosis, treatment, and rehabilitation and reintegration strategies for the nation’s service members, veterans, and their family members.

The primary research areas targeted by the DMRDP include TBI, psychological health, polytrauma and blast injury, wound infection, blood products and safety, operational health and performance, and device development.

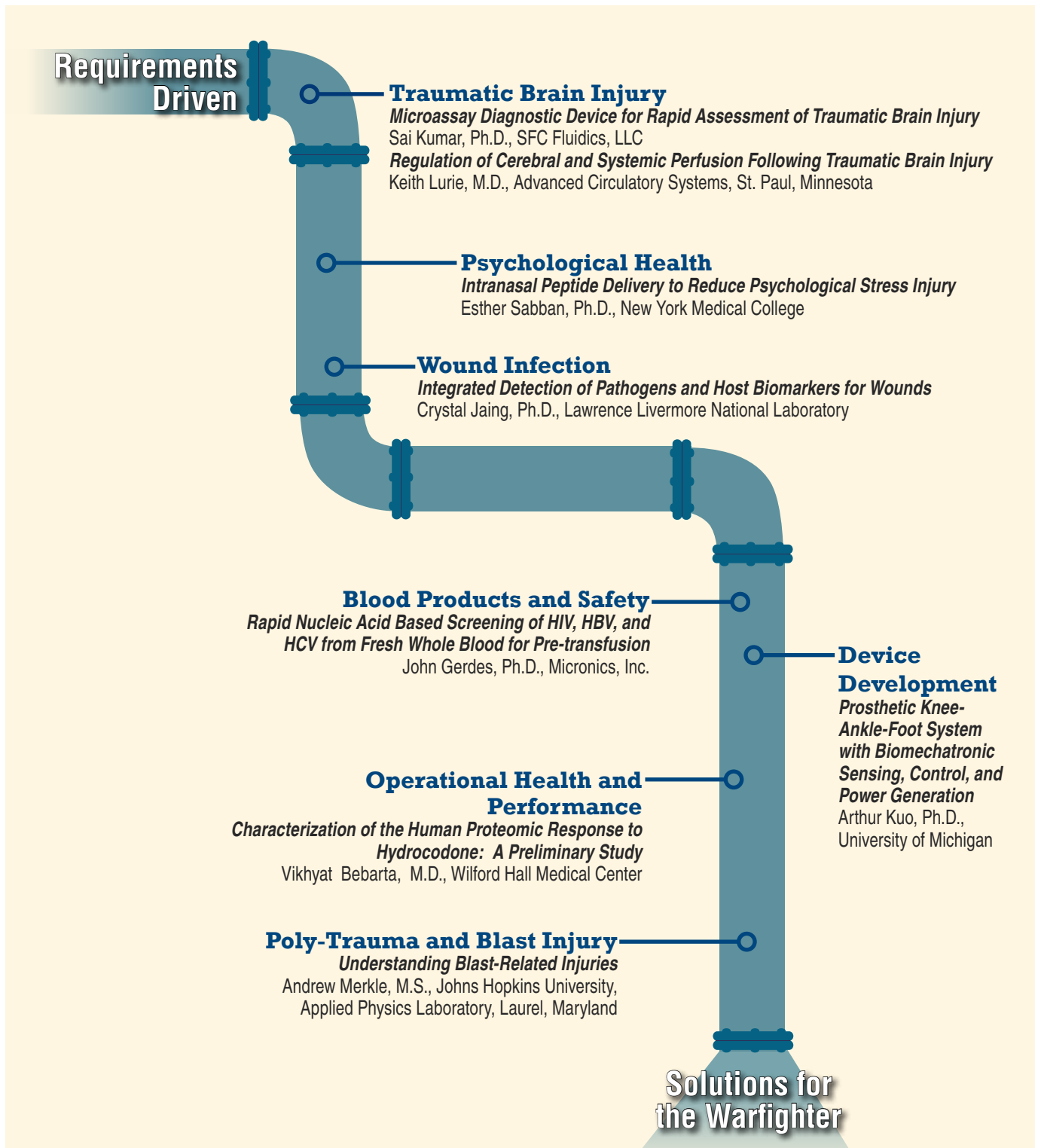


DMRDP FY10-FY11 Portfolio by Research Area



DMRDP Pipeline at a Glance

Awards supported by the DMRDP have the potential to yield critical prevention, detection, diagnosis, treatment, and rehabilitation and reintegration strategies for the nation's service members, veterans, and their family members. The following are examples by key research areas.



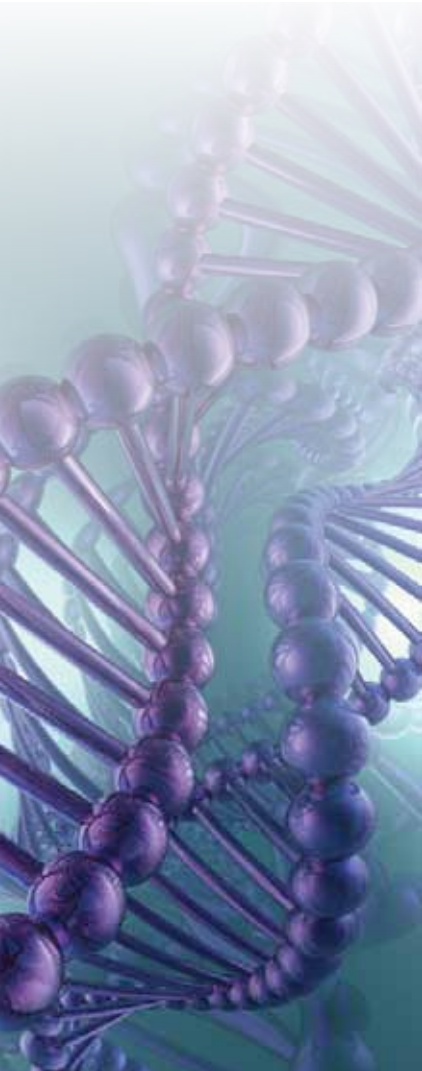
DUCHENNE MUSCULAR DYSTROPHY RESEARCH PROGRAM

Vision

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

Mission

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



Background and Program History

Duchenne muscular dystrophy (DMD) affects approximately 1 out of every 3,500 male infants (about 20,000 new cases per year). This form of muscular dystrophy results from mutations in the dystrophin gene that lead 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 DMD.

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

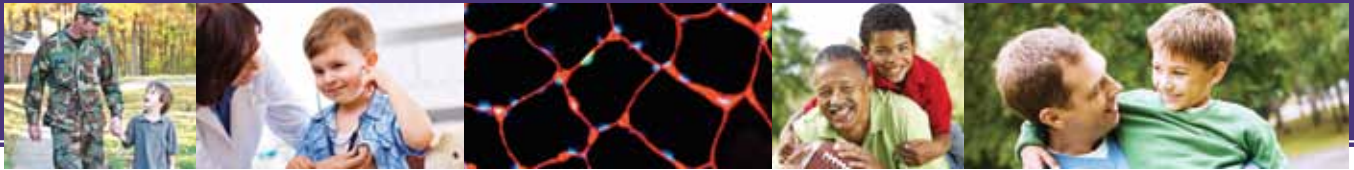
- A better understanding of current animal models, muscle regeneration, dystrophin function, and the downstream effects of dystrophin deficiency
- Development of new in vitro and in vivo models, validated biomarkers, and clinical outcome measurements
- Further development of cell, gene, biologic, and 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 Duchenne Muscular Dystrophy Research Program (DMDRP) in FY11 with a \$4M appropriation to promote the understanding, diagnosis, and treatment of DMD. This program was continued with a congressional appropriation of \$3.2M in FY12.



Tim Revell
FY11 DMDRP Consumer Reviewer

“Peer review showed me there is hope out there and that telling the story of Duchenne is more important now than ever. Thanks to my peer review experience, I learned more about some of the details of research than I had ever known before....We have met some of the most amazing people and we know now that there is hope for a cure to Duchenne. It is just a matter of time, money, and the right investment into research.”



FY11 Award Highlights



**Gail Thomas, Ph.D.,
Cedars-Sinai Medical
Center**
*A COX-Inhibiting Nitric Oxide
Donor to Counteract Functional
Muscle Ischemia in Duchenne/
Becker Muscular Dystrophy:*

Translational Research from Mice to Men

Objective: Determine whether short-term treatment with nitric oxide (NO)-donating drug naproxinod improves muscle blood flow regulation, as well as improves heart function, by restoring NO signaling in mdx mice. In addition, we will determine if the short-term benefits of naproxinod persist during long-term treatment without the development of untoward side effects.

Long-term goal: Establish naproxinod as a therapeutic to arrest muscular dystrophy disease progression, improve quality of life, and extend life.



Glenn Walter, Ph.D., University of Florida
*Optical Imaging of Dystrophic and
Damaged Muscle*

Objective: Evaluate a novel near infrared (NIR) imaging technique for imaging damaged muscle, quantifying drug delivery, and measuring tissue correction using NIR blood pool contrast agents such as indocyanine green.

Long-term goal: Establish NIR imaging, a low-cost nonionizing imaging technology, as a tool for monitoring muscle permeability and therapeutic agent delivery along with providing clinically useful information for diagnostic and prognostic purposes in patients with neuromuscular diseases.



**Avital Cnaan, Ph.D.,
Children's Research
Institute at Children's
National Medical Center**
*Establishing Minimal Clinically
Important Differences for
Current Clinical Trial Endpoints*

and Composite Outcome Measures in Duchenne Muscular Dystrophy via Extension of a Multicenter Natural History

Objective: Determine the minimally important differences (MIDs) of outcome measures by assessing the relationship between longitudinal changes in measured outcomes relating to motor abilities and functional outcomes as well as person-reported outcomes. In addition, we will demonstrate that MIDs are able to discriminate between different states of the disease and are sensitive to change.

Long-term goal: Develop practical and easily administered outcome measures that are sensitive and responsive to changes produced by treatments in children and adults with muscular dystrophies and other neuromuscular diseases across the lifespan and stages of disease severity.



**Paul Martin, Ph.D.,
Research Institute
at Nationwide
Children's Hospital**
*Translational Studies of GALGT2
Gene Therapy for Duchenne
Muscular Dystrophy*

Objective: Evaluate two gene therapy vectors AAV-(MCK and MHCK7)-GALGT2 for treatment of DMD in the mdx and Cmah^{-/-} mouse models. Will determine their dose response curves for physiological correction of mdx and Cmah^{-/-} mdx muscle and determine if AAV-MHCK7-GALGT2 can prevent cardiomyopathy.

Long-term goal: Develop a systemic treatment, e.g., GALGT2 gene therapy, for all the muscles of a DMD patient.

GWIRP

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



Dr. Roberta F. White, FY12 IP Chair

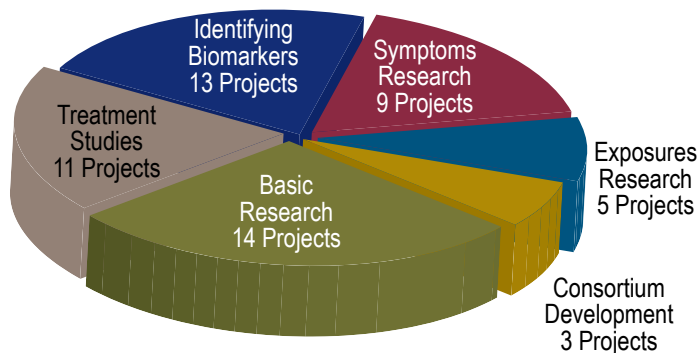
“The CDMRP program on Gulf War Illness is a highly innovative effort designed to develop new approaches to the understanding and treatment of Gulf War Illness. Like other CDMRP research programs, it utilizes specialized grant mechanisms to attract the kinds of research that can address this challenging health problem. CDMRP draws on the experience of Gulf War veterans and the expertise of scientists and clinicians who have worked extensively with this population to inform the development of award mechanisms and review of proposals.”



Background and Program History

GWIRP 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 more than 700,000 deployed to that region.⁶ The Gulf War Illness Research Program (GWIRP) focuses its funding on innovative projects that have the potential to make a significant impact on GWIRP, improving the health and lives of affected service members and their families.

DoD-funded GWIRP research began in 1994 with the establishment of the 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 GWIRP also was funded intermittently through the CDMRP’s PRMRP, 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 Gulf War Illness Research Program, to be managed fully by the CDMRP. The GWIRP has been continued with \$8M in appropriations in FY09, FY10, and FY11, and \$10M in FY12. The program is directed to support peer-reviewed research of treatments for the complex of symptoms that comprise GWIRP, identification of objective markers (biomarkers) for the disease, and understanding the pathobiology underlying GWIRP.



FY06–FY11 GWIRP Portfolio by Research Area
(6 projects fit into 2 different Research Areas)

⁶ 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.



Q10 for Gulf War Illness

Beatrice Golomb, M.D., Ph.D., University of California, San Diego

Coenzyme Q10 (Q10) is a vitamin-like antioxidant, naturally produced in human cells and important for cellular energy production. Unfortunately, natural Q10 levels can be inadequate to meet the needs of those with increased oxidative stress, a build-up of free oxygen radicals, or impaired energy production. This condition could describe thousands of veterans who served in the 1990–1991 Persian Gulf War and are now suffering with GWI.



Dr. Beatrice Golomb recently completed a 3.5-year study involving veterans with GWI that examined the benefits of daily Q10 administration. Two dose levels (100 mg/day and 300 mg/day) were compared to each other and against placebo treatment, and self-rated responses for overall health and symptom-based questionnaires were used as study outcome measures. The first 3-month treatment period of the study represented a randomized, double-blind, placebo-

controlled parallel design study and showed that Q10 at 100 mg led to significant benefit to Gulf War symptoms as well as improved physical function compared to placebo. Study outcomes were assessed by examining effects from the 20 health symptoms most commonly reported by study participants. These symptoms spanned categories including fatigue, mood, cognition, muscle function, pain, skin, and autonomic symptoms, with each included symptom present in at least half of the veterans. Not only was benefit to the summed score significant with Q10 at 100 mg, but the direction of difference for Q10 at 100 mg versus placebo was favorable for every one of the 20 symptoms.

These findings provide important preliminary validation for Q10 at 100 mg that could inform a larger clinical trial to show benefit to global self-rated health and affirm benefits to Gulf War symptoms.

FY11 Awards	
PI Name/Organization	Award Title
Dr. Yin Fang , Cleveland Clinic Foundation	Effectiveness of Acupressure Treatment for Pain Management and Fatigue Relief in Gulf War Veterans
Dr. Julia Golier , Bronx Veterans Medical Research Foundation, Inc./VA Medical Center, Bronx, NY	Intranasal Insulin: A Novel Treatment for Gulf War Multisymptom Illness
Dr. Richard Briggs , University of Texas, Southwestern Medical Center at Dallas	Abnormalities in Human Brain Creatine Metabolism in Gulf War Illness Probed with MRS
Dr. Terry Alvin , Georgia Health Sciences University	Organophosphate-Related Alterations in Myelin and Axonal Transport in the Living Mammalian Brain
Dr. Jarred Younger , Stanford University	Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach
Dr. Lea Steele , Baylor University	Establishing a 1991 Veterans Research Network To Improve Characterization of Gulf War Illness and Provide a National Resource for Veterans and Investigators
Dr. Lea Steele , Baylor University	Biomarker Discovery in Gulf War Veterans: Development of a War Illness Diagnostic Panel
Dr. Beatrice Golomb , University of California at San Diego	Efficacy of Treatments Tried: A Survey of Gulf War Veterans

LCRIP

LUNG CANCER RESEARCH PROGRAM

Vision

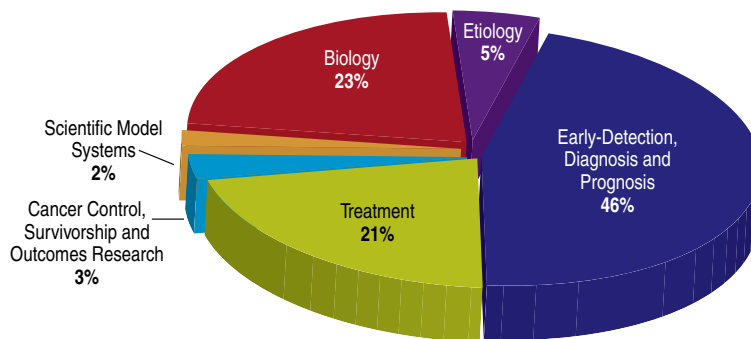
Eradicate deaths from lung cancer to better the health and welfare of the military and the American public

Mission

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

Background and Program History

The Lung Cancer Research Program (LCRP) was established by Congress in FY09 with an appropriation of \$20M to promote innovative and competitive research focused on the development of integrated components to identify, treat, and manage early curable lung cancer. Since its inception, the LCRP has received \$58M in congressional appropriations, including \$10.2M in FY12. As the second most commonly diagnosed cancer among men and women as well as 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 226,160 new cases will be diagnosed and 160,340 deaths will occur due to lung cancer this year.



FY09-FY11 LCRP Portfolio by Research Area



Stephanie Dunn-Haney FY11 Consumer reviewer

"I believe sharing my experience has informed the ideas and work of the other scientific reviewers. The scientists and medical professionals who are part of the process look to us for our passion, our perspective, and

our common sense. And the very bottom line is we keep them honest—they remember what and who they are there for!"



Spotlight on Clinical Consortia - Detection of Early Lung Cancer Among Military Personnel (DECAMP)

Avrum Spira, M.D., Boston University

Early detection of malignant lung lesions in their potentially curable stages is essential to improving the prognosis and long-term survival of lung cancer patients. Each year, lung cancer takes more lives than all other cancers combined, due in part to the fact that patients often lack signs and symptoms, and thus they are generally diagnosed at an advanced, incurable stage. Currently, low-dose computed tomography (LD-CT) scans are one of the primary imaging modalities for detecting pulmonary nodules. While LD-CT scans

are invaluable in detecting lung cancer, their inability to distinguish between benign and malignant disease result in high false positive rates, which can lead to unnecessary, invasive follow-up procedures and surgery. Therefore, there is a critical need for effective tools that can identify high-risk individuals who may benefit from more intense lung cancer screening, and differentiate benign radiographic abnormalities from malignant lesions. Such tools would greatly benefit both the American public and military personnel, who are at a higher risk of developing lung cancer due to increased rates of smoking (up to 50% higher than the general population) and increased exposure to environmental toxins during deployment and routine military duties.

The LCRP supports high-impact translational research through multiple award mechanisms. Most notably, the LCRP granted a \$13.5M Lung Cancer Early Detection Clinical Consortium Award in FY10 to the DECAMP Consortium—led by Dr. Avrum Spira at Boston University and co-investigator Dr. Peter Schnall at the American College of Radiology Imaging Network—to develop improved methods for early detection of lung cancer. In partnership with the four largest military medical treatment facilities* in the US, seven Department of Veterans Affairs hospitals, and additional clinical sites, the investigators aim to develop and validate both new and existing noninvasive biomarkers that can identify high-risk individuals who need additional lung cancer screening (i.e., LD-CT scans), and distinguish between benign and malignant lesions found during screening.

In support, Dr. Spira's team will first evaluate whether four existing airway and blood-based biomarkers can differentiate between benign and malignant lesions in 500 veterans with indeterminate lung nodules found on LD-CT scans. Dr. Spira hypothesizes that lung cancer affects the molecular profiles of tissues distal to the sites of disease (i.e., the field of injury effect) and that these changes can be measured in relatively noninvasive samples, such as in the blood or the nasal epithelium, even before lung cancer occurs. The investigators will evaluate the predictive value of these four biomarkers in combination with routine clinical tests and imaging data to develop the most robust predictor of developing lung cancer.

Concurrently, the investigators will study a cohort of 1,000 high-risk, former smoking military personnel and veterans to discover biomarkers that can distinguish individuals who will develop lung cancer—independent from other risk factors—from those who will remain disease-free. The patients will receive annual follow-ups for up to 4 years, where they will be assessed for the development of lung cancer. The serum and nasal epithelial cell samples collected during the followup visits will be used to identify any biomarkers that differentiate individuals who develop cancer from those who do not. If successful, these biomarkers may be used to identify high-risk individuals who may benefit from additional lung cancer screening.

The success of this two-part study may lead to sensitive, specific, and noninvasive tools for early detection of lung cancer. The goal is that the early detection of malignant lesions will lead to earlier diagnosis and improved outcomes for individuals at high risk for lung cancer and the reduction of lung cancer-related deaths.

**Naval Medical Center Portsmouth, Naval Medical Center San Diego, San Antonio Military Medical Center, and Walter Reed National Military Medical Center*

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



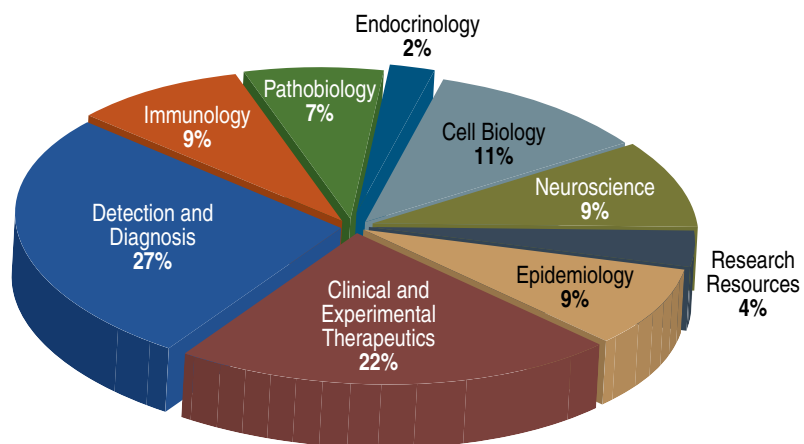
Murali Ramanathan, Ph.D.

“We appreciate the funding from the Congressionally Directed Multiple Sclerosis Research Program. It has enabled us to undertake multidisciplinary synergistic research that are not easily funded by other agencies.”

Background and Program History

MS is a degenerative, chronic inflammatory disease of the CNS that leads to cumulative neurologic disability over several years. Although MS affects over 400,000 individuals in the United States and about 2.1 million individuals worldwide, its etiology and pathogenesis are largely unknown. Moreover, the progression, severity, and specific symptoms of MS are unpredictable and vary from one person to another. While individuals of all ages are affected by MS, it is more commonly diagnosed in young adults, particularly women, between the ages of 20 and 40. Currently, there is no cure for MS.

From its inception in FY09, appropriations of \$18M have been managed by the MSRP for the advancing innovative and impactful research that addresses fundamental issues and gaps. The mission of the MSRP is to identify and fund promising research projects that are relevant to the prevention, etiology, pathogenesis, assessment, and treatment of MS and to ultimately lessen its personal and societal impact.



FY09-FY11 MSRP Portfolio by Research Area



From Doctor to Patient to Advocate

Phil Posner, Ph.D.

Knowing about MS and some of its symptoms is one thing. Being diagnosed with MS is completely different—and leads to a new awareness of the illness, along with a newfound respect of learning. Phil Posner, a neuroscience instructor who has a Ph.D. in medical sciences, is intimately aware of the differences.

“I had book knowledge of multiple sclerosis and also had three friends with relapsing/remitting multiple sclerosis. I tried to stay abreast of MS issues in order to help my friends.” He first noticed possible MS symptoms in

1986, but the neurologist who examined him in England did not seem concerned. His symptoms were atypical of MS patients. Once the diagnosis of MS was confirmed, two aspects of his life did not change: Phil’s dedication to advocacy work and his commitment to other MS patients. Having worked with organizations for many years,

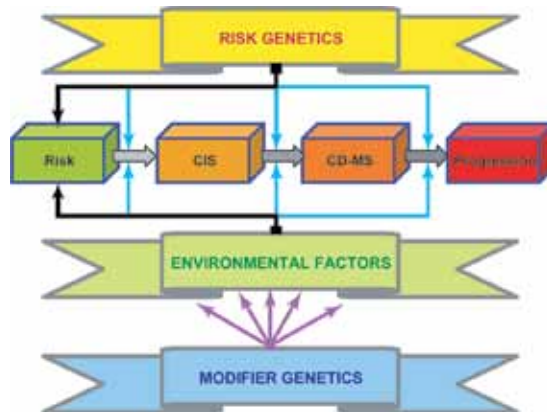


Gene-Environmental Interactions in Progression of Multiple Sclerosis

Murali Ramanathan, Ph.D., Jun Qu, Ph.D., Bianca Weinstein-Guttman, M.D., and Robert Zivadinov, M.D., Ph.D., State University of New York, Buffalo, New York

MS is a degenerative, chronic inflammatory disease of the CNS that causes demyelination of the axons, sclerotic plaque formation, and CNS atrophy. Although its etiology and pathogenesis are largely unknown, it is thought that interactions between MS susceptibility genes and diverse environmental factors significantly impact disease progression and clinical outcomes by promoting inflammation, injury, and degeneration of the CNS. Currently, these complex interactions between multiple genetic variations and numerous environmental factors and their potential clinical impact are largely uncharacterized due to the lack of analytical tools.

Recently, Dr. Murali Ramanathan, a recipient of an FY09 MSRP Synergistic Idea Award, developed an innovative, quantitative technique called AMBROSIA for analyzing gene-environmental interactions associated with disease outcomes. Using these tools, Dr. Ramanathan and collaborators, Drs. Qu,



Weinstein-Guttman, and Zivadinov, are analyzing the gene-environmental interactions that impact MS progression in two cohorts. Specifically, the investigators are assessing whether Epstein Barr virus infection, cigarette smoking, or the lack of vitamin D—environmental factors shown to be associated with MS risk and progression—interact with specific genetic variations to affect the clinical progression of

MS in cohorts that represent patients presenting with the first clinical demyelinating event (Clinically Isolated Symptom patients) as well as patients with longer disease duration (Clinically Definite MS patients).

The four collaborators of this award bring together expertise in neurology, systems pharmacology and computational genomics, neuroimaging, and bioanalytical chemistry to tackle this important research question. The study results may facilitate the development of preventive and therapeutic interventions for MS that disrupt harmful interactions between genetic and environmental factors.

Phil got a new opportunity in 2006, when he and his wife moved to Northern Virginia. He attended a regional health fair, met officials from the National Capital Chapter of the MS Society, volunteered to help, and has not looked back.

In 2011, Phil was nominated as a peer reviewer for the DoD MSRP. He was familiar with research review panels because of his background, and he quickly found the interest and energy to examine and discuss many different proposals. “There is an amazing dialogue that takes place integrating the science with the practicality of the problems faced by the consumer reviewers,” Phil said. “Both the scientists and the consumer reviewers learn from each other. I personally have learned much valuable information from the proposals we review as well as from the other panel members with MS and the scientists on the panel.”

“When I meet other people who have MS, I always listen to their stories,” Phil said. “Everyone is different. I have learned that there are a lot of people, young and old, who need help with various life issues. I have learned how rewarding it is to be able to help, and I have learned how much a little support for someone can add to the quality of his or her life.”

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



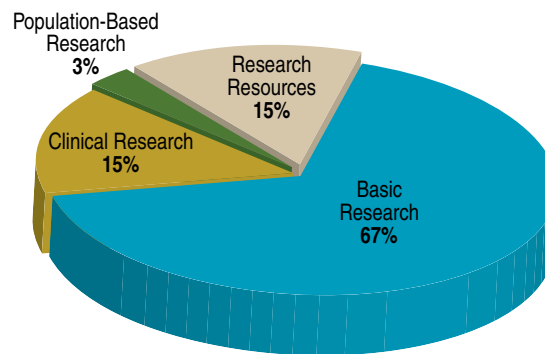
Barbara Franklin, NFRP Consumer Reviewer

"Consumers bring a unique perspective, whether it is as a person with NF or as a family member. Frequently, we are thanked by the scientists, who say our stories remind them why they're in the lab and why it is urgent to accomplish their goals quickly. Listening to their thoughtful analyses of the proposals assures me that the best science is awarded each year."



Background and Program History

The Neurofibromatosis Research Program (NFRP) was established in FY96 when the efforts of NF advocates led to a congressional appropriation of \$8M. Since initial appropriation, more than \$234M has been appropriated to the program, including \$12.8M in FY12. Over its 16-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 282 awards spanning basic, clinical, and population-based research, as shown below.



FY96-FY11 NFRP Portfolio by Research Area



Neurofibromatosis Clinical Consortium

Bruce Korf, M.D., Ph.D., University of Alabama at Birmingham

The severity of NF-related complications in affected individuals is extremely variable, and current therapies are unable to eradicate symptoms. Therefore, the identification of effective NF therapies is greatly needed. The Neurofibromatosis Clinical Trials Consortium (NFCTC) was established in 2006 to accelerate clinical trials for children and adults with significant complications of NF. Over the last 5 years, with funding from the NFRP, the NFCTC has conducted clinical trials investigating treatments for NF1 complications including PNF, cognitive disorders, low-grade gliomas, and MPNST. With support from the NFRP in FY11, the NFCTC will continue its mission. The Consortium has expanded to include 13 member sites as well as four additional collaborating sites to improve geographical coverage and inclusion of adults and children with all forms of NF. In addition, the NFCTC will broaden its focus to include NF2 and schwannomatosis alongside NF1 in performing clinical trials.



David Gutmann, M.D., Ph.D., Washington University in St. Louis, School of Medicine

Approximately two-thirds of children affected with NF1 experience learning disabilities and attention-deficit disorder (ADD), limiting their performance in school. Dr. David Gutmann, a recipient of an FY09 Investigator-Initiated Research Award, is exploring NF1-associated learning disorders using a genetically engineered mouse model of NF1 in which the mice develop optic gliomas. He has demonstrated that dopamine levels can be detected noninvasively using PET in NF1 mutant mice. Treatment with the ADD medication methylphenidate or L-deprenyl corrected the attention deficit seen in NF1 mutant mice and returned dopamine levels, measured by PET, to those of normal mice. Dr. Gutmann's work suggests that there may be a subset of children with NF1-associated learning disabilities who may respond more favorably to dopamine-targeted therapies, and these children could be identified using noninvasive PET imaging techniques.



Nancy Ratner, Ph.D., Children's Hospital, Cincinnati

The majority of children with NF1 have T2 hyperintense lesions, visible by MRI, that are thought to be areas of myelination failure. Additionally, recent data suggest that thalamus T2 hyperintensities correlate with low IQ scores and learning deficiencies. Dr. Nancy Ratner hypothesized that oligodendrocytes, myelin-producing cells in the brain, are aberrant in NF1 patients, resulting in T2 hyperintensities and myelination defects that contribute to NF1-associated brain abnormalities and learning difficulties. Dr. Ratner's research team, with funding from an FY09 Investigator-Initiated Research Award, is utilizing a mouse model with a deletion of the NF1 gene exclusively in oligodendrocytes to investigate this hypothesis. Preliminary data suggest that loss of NF1 in oligodendrocytes results in myelination defects. Studies are currently under way to determine if these myelination abnormalities contribute to cognitive defects and tumor development.



Elizabeth Schorry, M.D., Children's Hospital, Cincinnati

Identification of genes or other factors that modify NF1 could enable clinicians to identify patients who are at an increased risk of serious complications from the disorder. Differences in clinical symptoms and severity have even been documented in twins with NF1, suggesting that noninherited factors are involved. Dr. Elizabeth Schorry, with funding from an FY09 Exploration-Hypothesis Development Award, is examining copy number variants (CNVs), genetic changes that may occur after conception, in identical twins with differing NF1 symptom severity. Ten pairs of identical twins have been enrolled in the study and analysis of CNVs within twin pairs is in progress. Dr. Schorry is also identifying genes found within the CNVs that may modify the clinical features of NF1. This study represents an important step in the identification of NF1 biomarkers and therapeutic targets.

OCRP

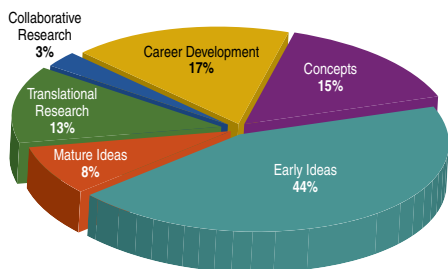
OVARIAN CANCER RESEARCH PROGRAM

Vision

Eliminate ovarian cancer

Mission

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



FY97-FY11 OCRP Portfolio by Research Phases



Program History and Background

The Ovarian Cancer Research Program (OCRP) was established in FY97 with a congressional appropriation of \$7.5M. Since then, dedicated efforts by ovarian cancer advocates to increase public awareness of this disease and federal funding for its research have resulted in a total appropriation of more than \$196M to the OCRP, including \$16M in FY12. Each year the OCRP vision is adapted in response to dynamic changes in the field, and an investment strategy is developed to ensure that funds are best directed toward the most critical needs and scientific gaps. The OCRP evaluates the funding landscape by comparing research portfolios and mechanisms of other federal and non-federal agencies and develops novel award mechanisms to target the areas that are most critically in need. The OCRP's annual investment strategy and associated award mechanisms provide the framework and direction necessary to most effectively invest the congressional appropriation in ovarian cancer research.

Throughout the history of the program, the OCRP has supported complementary approaches to answer questions that are vital to the advancement of science, exemplifying the innovative and focused nature of this program. The OCRP has focused on:

- Leveraging existing critical resources
- Accelerating promising strategies for prevention, detection, diagnosis, and treatment from discovery to the clinic
- Promoting collaborative partnerships to bring together the most talented scientists from different disciplines and different organizations to solve a problem
- Building a critical mass of dedicated career ovarian cancer researchers
- Fostering innovative, high-impact research that could ultimately lead to critical discoveries or major advancements

FY12 Award Mechanisms

FY12 Award	Mechanisms
Synergistic Translational Leverage Award	Supports a translational research effort involving multiple PIs who will leverage existing human resources to address a high-impact question in ovarian cancer
Outcomes Consortium Development Award	Supports a coordinated research effort involving multiple PIs and ovarian cancer consumers focusing on identifying and understanding predictors of disease outcomes, especially what is unique to long-term survivors
Teal Innovator Award	Supports visionary individuals to focus creativity, innovation, and leadership on ovarian cancer
Ovarian Cancer Academy Award	Supports additional early-career investigators to join the existing virtual Ovarian Cancer Academy, which provides intensive mentoring, networking, and a peer group in a collaborative and interactive environment
Pilot Award	Supports conceptually innovative, high-risk, high-reward research that will provide new paradigms, technologies, molecules, or applications



Achievements at a Glance: Making an Impact

OVA1™

Zhen Zhang, Ph.D.

Developed OVA1™, an FDA-approved panel of biomarkers, to assist physicians prior to surgery in determining if a pelvic mass is benign or malignant.

API-2/Triciribine

Santo Nicosia, M.D., and Jin Cheng, M.D., Ph.D.

Funded the discovery of API-2/triciribine that inhibits Akt-activated cancers that includes over 40% of ovarian tumors; moving into Phase 2 clinical trials as VQD-002.

Tumor Vasculature Markers

George Coukos, M.D., Ph.D.

Confirmed the validity of a specialized antibody against the protein TEM1 in a mouse model; Morphotek has Phase 1 trials testing this antibody (MORAb-004) in a variety of cancers.

Urinary Bcl-2 Levels

Patricia Kruk, Ph.D.

Demonstrated that Bcl-2 is elevated in urine samples of ovarian cancer patients, regardless of tumor grade, stage, size, and subtype; potentially a noninvasive and low-cost way to detect ovarian cancer.

Computational Biology to Identify Biomarkers

Igor Jurisica, Ph.D.

Developed the Online Predicted Human Interactive Database (OPHID), a publicly available tool that analyzes published datasets for differences in gene and protein expression; developed a companion program NAViGaTOR (Network Analysis, Visualization and Graphing Toronto) to help visualize these interactions.

CD8+ T Cell Response

Martin Cannon, Ph.D.

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

Sensitizing Ovarian Cancer Cells

Christine Walsh, M.D.

Demonstrated that indole-3-carbinol, a natural dietary phytochemical, sensitized multiple ovarian cancer cell

lines to bortezomib, an FDA-approved treatment for other cancers.

BRCA1/2 Mutations Without Family History

Gillian Mitchell, M.D. and David Bowtell, Ph.D.

Found that BRCA1/2 mutations were identified in 14% of 1,001 invasive nonmucinous ovarian tumors and nearly half of women carrying BRCA1/2 mutations did not have a family history of breast or ovarian cancer, challenging the current practice of offering genetic testing only to women with a positive family history.

Targeting Wnt Signaling

Rugang Zhang, Ph.D.

Observed that Wnt5a suppressed the growth of human ovarian cancer cells in both cell culture and mouse models and observed that reconstituting Wnt5a in ovarian cancer cells induced senescence (irreversible cell growth arrest), identifying a novel potential means and target for epithelial ovarian cancer treatment.

Precursor Evolution and Ovarian Cancer

Christopher Crum, M.D.

Demonstrated that patients with serous cancer have many more SCOUTs (secretory outgrowths) in their fallopian tubes compared to patients with benign lesions, suggesting that SCOUTs serve as surrogate precursors of ovarian cancer.

BRCAness

Panagiotis Konstantinopoulos, M.D., Ph.D.

Developed the BRCAness gene expression profile, which identifies tumors with the “BRCAness” phenotype (characterized by increased sensitivity to platinum analogues and PARP inhibitors as well as improved survival), and found that patients with BRCA-like tumors had improved overall survival compared to patients with non-BRCA-like tumors.

Premalignancy Gene Signature

Elizabeth Swisher, M.D. and Anton Krumm, Ph.D.

Identified a premalignant expression signature that may reflect early steps in BRCA1-mediated ovarian carcinogenesis.

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 and early-career investigators opportunities to excel in groundbreaking cutting-edge research for the prevention, detection, and treatment of cancer



Michael Katz, FY11 Consumer Reviewer, Multiple Myeloma Survivor and Colorectal Cancer Survivor

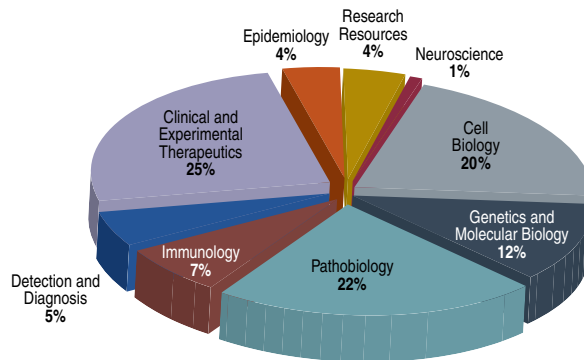
"I cannot begin to tell you how satisfying my advocacy work has been. It turns what is often a bad nightmare into a calling, a mission to help people work through what is often a frightening, paralyzing experience."



Background and History

The Peer Reviewed Cancer Research Program (PRCRP) was established in FY09 to support innovative and competitive research in cancers specifically designated by Congress as relevant to military service members and their families. Since its inception, Congress has appropriated \$47M to the PRCRP. Members of the military are exposed to hazardous environments due to the nature of their service and deployments and, thus, are at risk for the development of different types of cancers. The Veterans Health Administration acknowledged the toll of cancer on military service members and their families in its National Cancer Strategy in 2003 (VHA-Directive 2003-34). In 2007, there were 355,442 military beneficiaries diagnosed with cancer, for a prevalence of 4.1%, composed of over 60 different cancer types.⁷ Both a healthy force and healthy family support unit, free of serious illnesses, allows the service member to focus on his or her role as a service member and facilitates the overarching military mission.

The PRCRP's focus in FY12 is on support of exceptionally talented, early-career researchers and clinicians who have the potential to significantly advance the field of cancer research and deliver breakthroughs in the prevention, detection, and treatment of cancer to better the lives of service members, their families, and the American public.

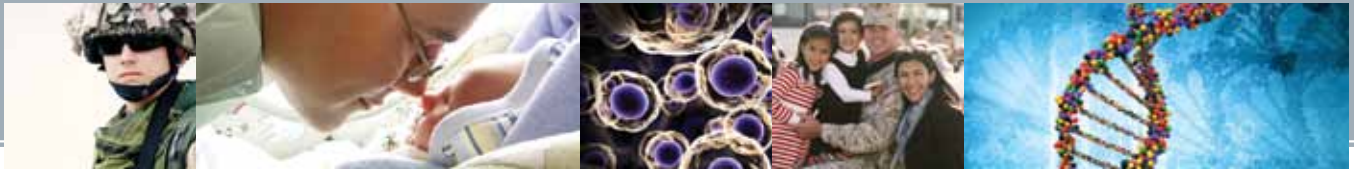


FY09–FY11 PRCRP Portfolio by Research Area

Lt. Col. Della Howell, M.D., FY12 Integration Panel Member

"I am so fortunate to have this opportunity to sit on the CDMRP IP as an active duty Air Force physician. The research that the CDMRP is funding will directly benefit our military members and their families. It has the distinction of being one of the few research programs that focuses on the 'underserved' cancer populations, such as children with cancer and adults with less common types of tumors. Since the panel consists of consumers, lab scientists, clinical experts, active duty military providers and cancer survivors, the discussions regarding the research proposals are excellent, resulting in what we hope will be exciting and innovative treatments for the cancer patient."

⁷ Crawford et al., *Military Medicine* 172 (2007) 1084-1088.



Role of Neuropeptide Y in Stress-Induced Cancer

Joanna Kitlinska, Ph.D. and Jason Tilan, Ph.D., Georgetown University

We all experience stressful events at different times in our lives. While acute stress can be beneficial in enhancing performance under extreme conditions, chronic stress has been implicated in the development of various diseases, including cancer. One of the sympathetic neurotransmitters, neuropeptide Y (NPY), is a potent feeding stimulant as well as regulator of energy usage, memory, and learning functions. Induction of NPY by chronic stress can augment conditions associated with tissue growth and angiogenesis. Although NPY is also implicated in modifying tumor growth, no direct link between stress-induced upregulation of NPY and acceleration of abnormal cell growth has been established.



Joanna Kitlinska



Jason Tilan

With funding from an FY09 PRCRP Concept Award, Dr. Joanna Kitlinska conducted studies focusing on unraveling the role of NPY in stress-induced cancer development and progression. An established 7,12 dimethylbenz[a]anthracene-induced carcinogen

murine model was utilized in these studies. In this model, both wild-type (NPY+/+) and NPY knockout (NPY-/-) animals developed various types of tumors, with leukemia/lymphoma and endometrial lesions among the most common. The animals were subjected to stress before and after appearance of the tumors to examine whether stress and NPY could affect tumor development and progression. The preliminary results suggested that NPY, alone or in combination with stress, could have a differential effect on cancer, depending on the cancer type. Lack of NPY inhibited development of leukemia/lymphoma independently of stress and completely prevented stress-induced advancement of malignant endometrial lesions. These exciting findings encouraged Dr. Kitlinska to pursue more comprehensive and mechanistic investigations of the effects of stress mediators on particular malignancies.

Learning to Advocate; Advocating to Learn

Stan Deden, FY11 Consumer Reviewer

Stan Deden, a nurse anesthetist with 20 years of experience when diagnosed with lymphoma, knew of the disease, but soon realized he had a lot more to learn. "Prior to my diagnosis, I knew relatively little about lymphoma," Stan said.

His treatment began and involved beam radiation to his chest, abdomen, and pelvis. He remained in remission for 9 years, and following a spontaneous remission in 2005, he continues in remission today. Stan credits the medical staff at the hospital where he worked and was treated for helping him understand the treatments. "After my initial therapy, my wife and I attended two national-level Patient Education Forums sponsored by the Lymphoma Research Foundation (LRF). At the forums, I interacted with other patients with the same diagnosis,



Stan Deden

and I learned that my diagnosis may not be as grim as I initially had thought."

Stan collected literature about lymphoma and continued to develop a knowledge and understanding about the illness. At a second LRF forum, he expressed an interest in a new chapter forming near his home; several months later he was recognized as a founding member of the LRF chapter in Minnesota. His ongoing work with the LRF led to his nomination as a consumer reviewer for the DoD PRCRP. "My background as a nurse, a Vietnam veteran with a military exposure-related cancer, and an advocate for lymphoma has allowed me to represent veterans and lymphoma patients on CDMRP panels in a unique way," Stan said. "My greatest hope is that one day a research proposal that I have reviewed leads to a standard-of-care procedure or treatment."

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



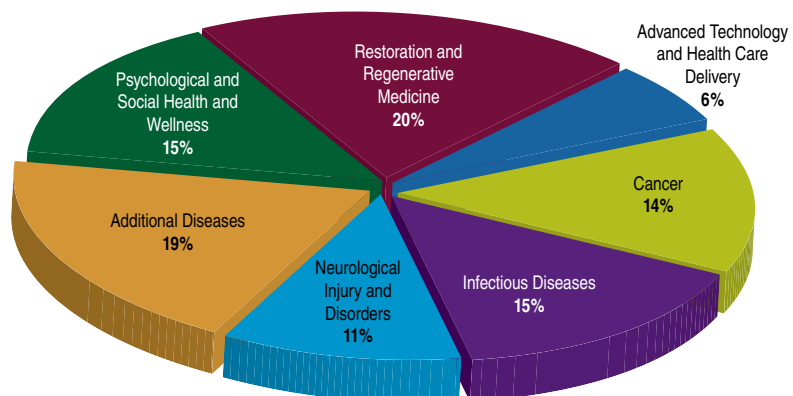
Background and History

Since 1999, the Peer Reviewed Medical Research Program (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 FY11 (excluding FY07, in which no appropriation was made), Congress has appropriated \$544.5M, supporting 437 research awards. The FY12 appropriation is \$50M. From its inception, PRMRP has funded research projects in more than 90 congressionally directed topic areas that address a wide range of fields of study including infectious diseases, cancer, neurological injury and disorders, psychological disorders, health and wellness, restoration and regenerative medicine, advanced technology, health care delivery, and a variety of disease conditions.

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.

FY11 PRMRP Topic Areas

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



FY99-FY10 PRMRP Award Portfolio by Category and Percentage of Total Funding



Research Highlights: A History of Accomplishments

The PRMRP has supported research that has led to many high-impact successes and products, including the following examples.

Dr. Babs Soller developed CareGuide™, a portable sensor system that noninvasively measures muscle pH, muscle oxygen, and hematocrit from light reflected on the forearm to assess tissue perfusion and guide treatment during resuscitation care.

Dr. James Childs developed a handheld device with a 1,060 nm diode laser and demonstrated safety and efficacy in the treatment of pseudofolliculitis barbae in a 20-subject clinical trial.

Dr. David Sahn combined ultrasound and telemedicine technologies to create a method for the reliable and rapid assessment of newborn infants at risk for heart disease at remote health care facilities via teliagnosis. The system allows geographically distant cardiology specialists to supervise real-time cardiac ultrasounds performed by physicians and nurses trained to operate a small, handheld ultrasound device.

Dr. Ronald Triolo developed a hybrid neuroprosthesis that combines external bracing with electrical stimulation of paralyzed muscles to allow for mobility after paralysis from spinal cord injury.

Dr. Anthony Guiseppi-Elie created and tested in small animals a biochip that can be temporarily implanted intramuscularly to telemetrically report local lactate and glucose levels to assess the potential for hemorrhagic shock during resuscitation and intensive care from traumatic injury.

Dr. Stephen Savarino showed that bovine milk immunoglobulin collected from cows immunized with enterotoxigenic *Escherichia coli* (ETEC) antigens and administered orally provided protection against ETEC challenge (traveler's diarrhea) in humans.

Dr. Ai Lin optimized imidazolidinedione derivatives and demonstrated in primates that they are orally active with potential curative and prophylactic activity against the parasite that causes malaria.

Dr. Patrick Kochanek developed a polynitroxilated, pegylated bovine cell-free hemoglobin (PNPH)-based, small volume resuscitation fluid for TBI combined with hemorrhagic shock that demonstrates potential as a neuroprotective agent.

Dr. Blake Hannaford developed a prototype field deployable surgical robot capable of telemanipulation that was successfully tested in a cross-Atlantic setting with simulated surgical tasks.

Dr. Mark Tommerdahl developed a novel, noninvasive prototype system for quantitative assessment of cerebral cortical health and demonstrated the ability to detect differences in cerebral cortical function between subjects with and without autism.

Dr. Joseph Rizzo developed a prototype, small animal model-scale retinal prosthesis with the potential 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.



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 most significant gaps in care for 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

CPT R. Clayton Hinchman, Military Officers Association of America

“The DoD Peer Review Orthopaedic Research Program was a fantastic experience for me as a transfemoral amputee and service-connected disabled veteran. I thoroughly appreciate the level of thought, expertise, and compassion displayed by the experts in orthopedic research. They will undoubtedly make a difference for future generations of orthopedic patients.”



Background and History

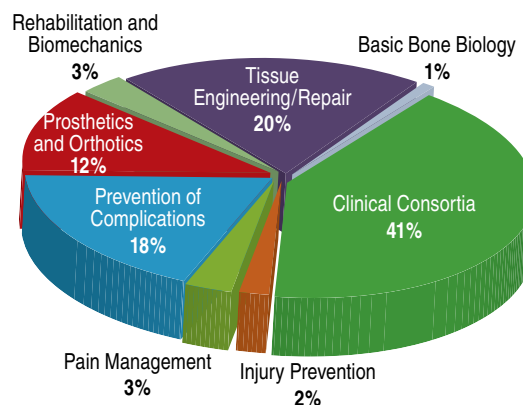
A large majority of the injuries sustained by military personnel in U.S. war efforts involve soft tissue wounds and skeletal fractures, pointing to an urgent need for orthopaedic research that will provide superior medical care and treatment options for injured service members. The Peer Reviewed Orthopaedic Research Program (PRORP) was established by Congress in FY09 to support military-relevant orthopaedic research. The program has been continued each year through FY12 with congressional appropriations totaling \$188.5M, including an appropriation of \$30M in FY12.

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.

In FY11, PRORP focused its funding efforts in technology development, translational studies, and clinical trials in three areas of research of major impact to wounded warfighters:

- The prevention and treatment of post-traumatic osteoarthritis
- Improved outcomes of severe limb injuries through clinical studies to reduce or treat infection, therapies to heal large extremity nerve injuries, and novel rehabilitation interventions or orthoses
- Development of a modular, interoperable, three-degrees-of-freedom, externally-powered prosthetic wrist with a one-degree-of-freedom terminal device and control strategies

The FY11 program complements the existing PRORP award portfolio, which spans a spectrum of research areas and types:



FY09–FY11 PRORP Awards by Research Area and Dollar Amount



Use of Photodynamic Therapy Treatment to Promote Long Bone Fracture Healing

Margarete K. Akens, Dr. med. vet., Ph.D. Sunnybrook Research Institute

Dr. Margarete Akens, of the Sunnybrook Research Institute in Toronto, Canada, knows that when high-impact trauma is the cause of a long bone fracture, nothing is straightforward. This type of extremity combat injury is usually associated with complications such as lacerated soft tissue or an open wound, making the wound prone to infections that negatively impact bone healing. Even with the currently available treatments to enhance bone healing, these fractures can take up to a year to fully heal. Dr. Akens' strategy is to improve healing in complex skeletal injuries by using a drug-light therapy method called photodynamic therapy (PDT). In PDT, a photosensitizing drug is locally or intravenously administered and later activated at the site of the fracture with a laser light. One previous study with PDT showed that this approach could



rapidly improve vertebral bone strength, stiffness, and architecture, while another study showed that PDT could reduce bacterial growth within bone in a preclinical model of infected bone.

With funding from an FY09 Hypothesis Development Award, Dr. Akens has been able to test the treatment in fractured long bones in rats using the photosensitizer

Visudyne, at FDA-approved therapy for treating macular degeneration in the eye. Dr. Akens demonstrated an increase in bone and callus formation after PDT treatment, with best results when PDT is applied during the secondary stage of fracture healing. She hopes that if ongoing studies confirm the benefits of PDT treatment at the secondary stage of fracture healing, PDT could be applied to trauma patients expected to encounter impaired fracture healing.

Research Highlights

Dr. Aaron Dollar developed an anthropomorphic body-powered prosthetic hand prototype with 11 degrees of freedom to allow a range of grasping positions, and a finger coupling design that provides the ability to passively adapt to the shape of any object within its grasp.

Dr. Daniel Nelson successfully engineered the bacteriophage-derived protein PlyCB to bind integrins expressed by osteoblasts while also retaining the protein's natural ability to bind hydroxyapatite, a bone component used to coat orthopaedic implants, toward the goal of enhancing osseointegration.

Dr. Brian Glaister developed a prototype physical exotendon device to facilitate walking for individuals with significant mobility impairments.

MAJ Daniel Rhon initiated a clinical trial of active duty military personnel with low back pain to assess the value of early physical therapy as compared to a standard stepped-care approach without physical therapy.

Dr. Christopher Evans obtained preliminary results in a rat model demonstrating that modulating stiffness of an external fixator device can accelerate healing of segmental bone defects.

Mr. James Martin characterized the existence of a previously unknown set of chondrocyte precursor cells that migrate to sites of cartilage injury and have the potential to be modulated to heal cartilage damage and prevent the development of post-traumatic osteoarthritis.

Dr. Paul Weinhold found that low doses of the iron-chelating agent desferroxamine, when administered with demineralized bone matrix (DMB), enhanced healing of 2 mm tibial segmental bone defects in a rat model compared to DMB alone.

Dr. Keat Ong developed a vibrational layer of magnetoelastic material coated with a biocompatible film and demonstrated its ability to inhibit the adhesion of bacteria and fibroblasts, indicating the potential to prevent biofilm formation and soft tissue fibrosis at the surface of implanted devices.

PCRP

PROSTATE CANCER RESEARCH PROGRAM

Vision

Conquer prostate cancer

Mission

Fund research that will eliminate death and suffering from prostate cancer

Goals

Overarching Challenges

To ensure that critical needs of prostate cancer patients are being addressed by PCRP-funded research, all applicants are encouraged to focus research efforts in one of two key areas:

- Developing effective treatments for advanced prostate cancer
- Distinguishing aggressive from indolent disease

Focus Areas

To ensure a broad portfolio representing important areas of prostate cancer research, all PCRP-funded research must correspond with one of more of the following:

- Biomarker development
- Genetics
- Imaging
- Mechanisms of resistance*
- Survivorship and palliative care
- Therapy
- Tumor and microenvironment biology

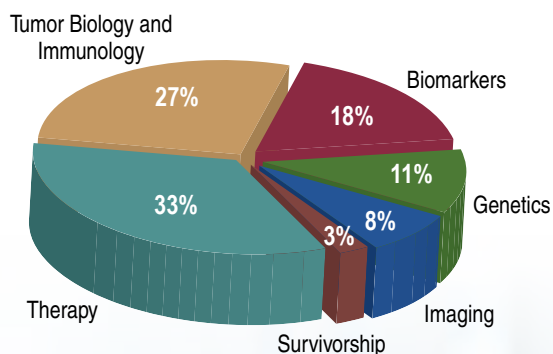
*New in FY12

Background and Program History

Since its inception in 1997 and over its 15-year history of congressional support totaling \$1.2B, the DoD Prostate Cancer Research Program (PCRP) has changed the landscape of biomedical research and energized 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 hundreds of thousands of prostate cancer patients and will ultimately conquer the disease.

Program Portfolio

From 1997–2011, the PCRP funded 2,504 research and training awards. The projects supported range from exploratory studies to generate cutting-edge ideas to providing for multi-institutional consortia designed to change how prostate cancer research is done. By getting to innovative solutions faster, PCRP-supported researchers can realize the goal of having a direct, positive impact on prostate cancer patients and their families. Since 2009, the PCRP has categorized the research it funds by focusing on the most critical needs for advancement. The chart (right) shows how the program has supported these areas through the FY09–FY11 awards.



FY09–FY11 Portfolio by PCRP Focus Area





Research Breakthroughs from PCRP-Funded Research

Key Discoveries	Moving Forward	Touching Patients
<p>Dr. Michael Karin discovered that a mechanism for castration-recurrent prostate cancer results from an inflammatory response involving lymphotoxin and NK-kB, opening new opportunities for targeting this process for therapy.</p> <p>Dr. Arul Chinnaiyan discovered that the gene SPINK1 is overexpressed in 10% of prostate cancers and that these cancers were found in patients with more aggressive disease, potentially identifying an important subtype of prostate cancer that may respond well to specific treatments.</p> <p>Dr. Lloyd Trotman discovered a new tumor suppressor gene, PHLPP1 (“flip one”), that cooperates with the gene PTEN to prevent prostate cancer progression to aggressive disease, providing new insight on therapeutic targeting of this pathway.</p>	<p>Dr. Martin Pomper developed PET radiotracers, specifically targeting prostate cancer cells through the peptide PMSA, that have been patented and are in Phase 1 clinical trials for enhanced imaging of metastatic prostate cancer</p> <p>Dr. Douglas McNeel developed an immunotherapy-based DNA vaccine, now in a Phase 2 clinical trial, to inhibit prostate cancer recurrence in patients after treatment for primary disease.</p> <p>Dr. Kim Chi developed a cytotoxic small molecule targeting the protein clusterin that increases prostate cancer cell killing and is now in Phase 3 trials of combination therapies.</p>	<p>ZYTIGA®, now available for treatment of advanced disease brought through clinical trials by the PCCTC.</p> <p>XGEVA®, now available for prevention of bone loss during androgen deprivation therapy, based on preclinical studies by Dr. Evan Keller who discovered that blocking the protein RANKL slows progression of prostate cancer skeletal metastases.</p>

National Research Resources Provided Through the PCRP

The PCRP has established three national resources that are able to support research across the nation and beyond. These include:



The Prostate Cancer Biorepository Network — Initiated in 2010, the PCBN provides high-quality prostate cancer biospecimens, protocols, and potential collaborations to enable research at multiple institutions (www.prostatebiorepository.org).



The Prostate Cancer Clinical Trials Consortium — Initiated in 2006, this collaboration of 13 major cancer centers tests novel drugs for the rapid development and utilization of effective treatments for patients. The PCCTC has tested over 70 drugs and brought 9 of them to Phase 3 trials with unprecedented speed (<http://pcctc.org>).



The Prostate Cancer Project — Initiated in 2003, PCaP investigates major factors associated with health disparity based on a robust repository of data and specimens also available to the wider research community (<http://www.ncla-pcap.org>).

New Approaches to Support High-Impact Research

The PCRP is focused on continuing to create new opportunities to support research most likely to make a rapid and meaningful impact for patients. For FY12, three new types of funding opportunities were developed:

- **Biomarker Development Award** — Supports high-impact research aimed at qualifying or validating diagnostic or prognostic biomarkers for rapid transition to prostate cancer clinical practice.
- **Clinical Exploration Award** — Supports the rapid execution of early phase, hypothesis-driven clinical trials and correlative studies that will have a major impact on prostate cancer management.
- **Transformative Impact Award** — Supports large, team-based research projects specifically designed to have a near-term, transformative impact on prostate cancer management.

PSYCHOLOGICAL HEALTH AND TRAUMATIC BRAIN INJURY RESEARCH PROGRAM EXECUTION

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

Eugene Swisher, Consumer Peer Reviewer

"It is an honor to be selected to represent the one million service members believed to have PTSD. I feel that the consumers in all the CDMRP panels make the difference in validating the research conducted."



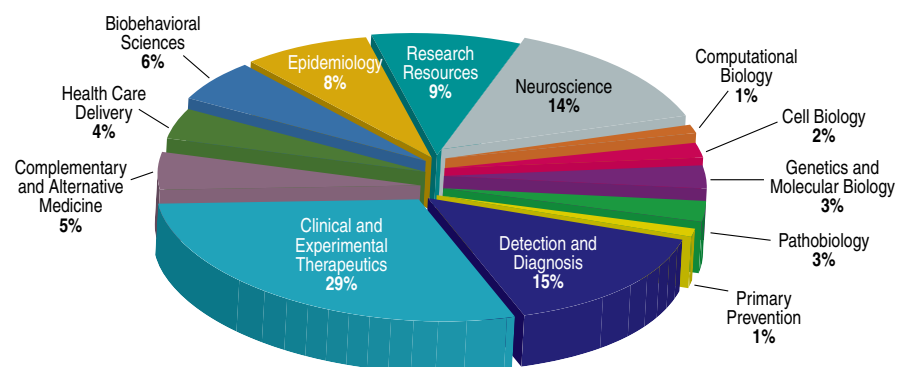
Background and History

The Psychological Health and Traumatic Brain Injury Research Program (PH/TBIRP) was established by Congress in FY07 in response to the devastating impact of TBI and psychological health (PH) issues, including PTSD, on our deployed service members in Iraq and Afghanistan. Appropriations totaling \$300M (\$150M each for TBI and PH (including PTSD) were assigned to the CDMRP for the purpose of soliciting and managing critical TBI- and PH-related research and development efforts to benefit service members, veterans, and other beneficiaries of the military health system.

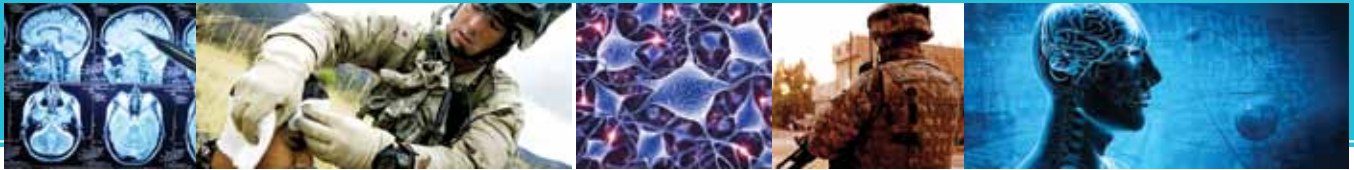
Additional congressional appropriations for the PH/TBIRP were assigned to USAMRMC between FY09 and FY11, totaling \$482.33M. Since FY09, a modified execution model was established, including assignment of program strategic oversight to USAMRMC-based JPC aligned with the OASD(HA). These JPCs provide recommendations to the OASD(HA) on research gaps, focus areas, and funding options. Operational execution management responsibilities, including actions ranging from crafting PAs, solicitation, and review of applications through full life-cycle management of awards, were assigned to multiple organizations, including the CDMRP. The modified process allows greater flexibility for leveraging congressional special interest funds to support core DoD research and development funding assigned to study PH and TBI. For more information on this execution model, see page 56 (DMRDP Execution).

The PH/TBIRP has supported 306 innovative projects since its inception, ranging from basic to translational research across a wide range of focus areas, including 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.

The application review process for the PH/TBIRP follows the traditional CDMRP two-tiered review process, where consumer involvement continues to be a hallmark. Our nation's wounded warriors serve in that capacity for the PH/TBIRP.



PH/TBI FY07, FY09-FY11 Portfolio by Research Area



PH/TBIRP Achievements at a Glance

Awards supported by the DoD PH/TBIRP are beginning to yield findings that will impact the standard of care for the nations' service members, veterans, and family members impacted by combat-related TBI and PH issues. The following are examples of projects funded across the research continuum (basic through translational).

Basic Research

Clinical Testing of a Noninvasive Brain Oxygenation Monitor, Donald S. Prough, M.D., University of Texas Medical Branch at Galveston, Galveston, Texas

Applied Research

Trauma Management Therapy for OEF and OIF Combat Veterans, Deborah Beidel, Ph.D., University of Central Florida

Translational Research/Team Science

- **TBI Multidisciplinary Research Consortium** combines the efforts of more than 20 TBI investigators dedicated to improving the diagnosis and treatment of mTBI.
- **PTSD Multidisciplinary Research Consortium**, also known as STRONG STAR (South Texas Research Organizational Network Guiding Studies on Trauma and Resilience), combines the efforts of approximately 100 military, civilian, and VA investigators and clinicians dedicated to the development and evaluation of the most effective interventions for the detection, prevention, and treatment for combat-related PTSD.
- **PTSD/TBI Clinical Consortium**, also known as INTRuST (Injury and Traumatic Stress), combines the efforts of the nation's leading investigators to bring to market novel treatments or interventions that will ultimately decrease the impact of military-related PH problems and TBI.

The Way Forward: Exciting New Targets for FY12

The strategic plan for execution in FY12 includes two collaborative efforts between the DoD and the VA. The first collaboration is called Chronic Effects of Neurotrauma Consortium (CENC) and its primary goal is to establish an understanding of the after effects of mTBI. Potential comorbidities will also be studied; that is, conditions that are associated with and worsen because of a neurotrauma. The second collaboration is called the Consortium to Alleviate PTSD (CAP), which will study potential indicators of the trauma, as well as prevention strategies, possible interventions, and improved treatments. Biomarker-based research will be a key factor for CAP studies.



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 living with spinal cord injury



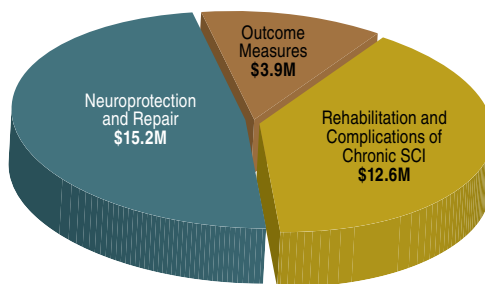
David Tharp, Psy.D., FY11 Consumer Reviewer

“The consumer reviewer brings an incredibly robust perspective to research that has direct impact on what is not only funded but can provide insight that only those who have been there can bring.”

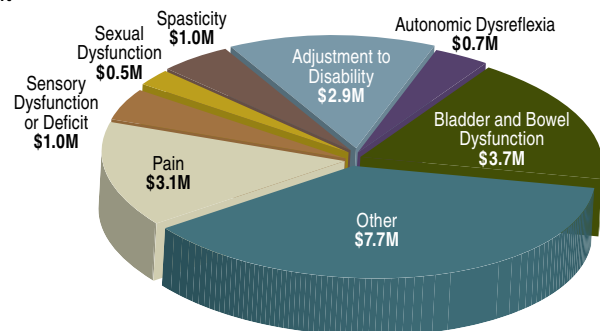


Background and Program History

The Spinal Cord Injury Research Program (SCIRP) was first funded by Congress in FY09 with a \$35M appropriation. Since the initial appropriation, an additional \$32.85M (FY10–FY12) has been appropriated for a cumulative total of \$67.85M. 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, veterans, and other individuals living with SCI. The program’s current portfolio includes 87 awards spanning basic, translational, clinical, and qualitative research, as shown below.



FY09 Investment by Area of Encouragement



FY10–FY11 Investment by Area of Encouragement



Restoring Hand Function After SCI Gregory Clark, Ph.D., University of Utah

Dr. Gregory Clark received an FY09 Investigator-Initiated Research Award to improve the restoration of coordinated hand function following paralysis. In collaboration with Dr. Lee Miller at Northwestern University School of Medicine, Dr. Clark has performed the first-ever chronic implantation of high-channel-count Utah Slanted Electrode Arrays (USEAs) into the peripheral forearm nerves in an animal model and recorded electrical activity in forearm muscles following USEA stimulation. Next, the investigators will attempt to induce the animals to perform specific motor tasks to evaluate brain stimulation of the USEAs. If successful, this novel brain-machine interface will provide a means of restoring voluntary control of paralyzed muscles following SCI.



Schwann Cell Implantation to Improve Functional Recovery After SCI

Damien D. Pearse, Ph.D. (shown right), Mary Bartlett Bunge, Ph.D. (shown middle), and James Guest, M.D., Ph.D. (shown left), University of Miami School of Medicine

Schwann cells (SCs), a key component of the peripheral nervous system, are effective in promoting axon growth, remyelination, and functional recovery in many SCI models. Drs. Pearse, Bunge, and Guest received an FY09 Advanced Technology/Therapeutic Development Award to perform dosage, safety, and toxicity studies of SC implantation in animal models with SCI. The investigators demonstrated that transplanted human SCs survive for up to 6 months in a rat model of SCI and were not associated with tumor formation, additional tissue damage, scarring, or adverse immune responses. Additionally, the extent of axon growth into the spinal cord lesion was correlated with the number of human SCs present in the rat model. These promising results allowed the team to submit an application to the FDA to begin a clinical safety trial in humans.



CD11d Antibody Therapy to Reduce Inflammation After SCI

Gregory Dekaban, Ph.D. (shown left) and Arthur Brown, Ph.D. (shown right), University of Western Ontario

Reducing the tissue inflammation that occurs following SCI may reduce neurological injury, leading to improved long-term functionality. Drs. Dekaban and Brown received an FY09 Advanced Technology/Therapeutic Development Award to develop an anti-inflammatory therapy for acute SCI using an antibody to the immune cell protein CD11d. The team has developed assays to measure and characterize the level of CD11d antibody present in immune cells following treatment. The team also compared the effectiveness of several anti-CD11d antibodies of increasing affinity in a rat model and identified the most effective antibody for reducing inflammation and improving neurological recovery. Additionally, they have developed behavioral scales for locomotion and treadmill training in a larger animal model of SCI. The preclinical studies of CD11d antibodies in animal models of SCI will pave the way for translating this promising therapeutic for human use.



Development of Treatment Strategies for Combined SCI and TBI

Michael Beattie, Ph.D. (shown left) and Geoffrey Manley, M.D., Ph.D. (shown middle), University of California, San Francisco, and Graham Creasey, M.B., Ch.B. (shown right), Palo Alto Institute for Research and Education

SCI is often accompanied by TBI; however, evidence-based approaches to the treatment of this dual diagnosis are lacking. The objective of the FY09 Translational Research Partnership Award received by Drs. Beattie, Manley, and Creasey is to gather information on the clinical treatment of SCI with TBI so that appropriate animal models can be developed for evaluating treatment strategies for this dual injury. Survey data revealed that the majority of clinicians indicated a strong need for more research into SCI/TBI dual injury and that models of hand function would be particularly helpful. The investigators are reviewing several national and local databases of SCI and TBI clinical care and outcomes. Characterization of rat models of SCI, TBI, or both is in progress to provide baseline data for future testing of clinical data-driven therapeutic hypotheses. This partnership has developed a community of researchers and clinicians working together to improve the care and treatment of individuals with both SCI and TBI.

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

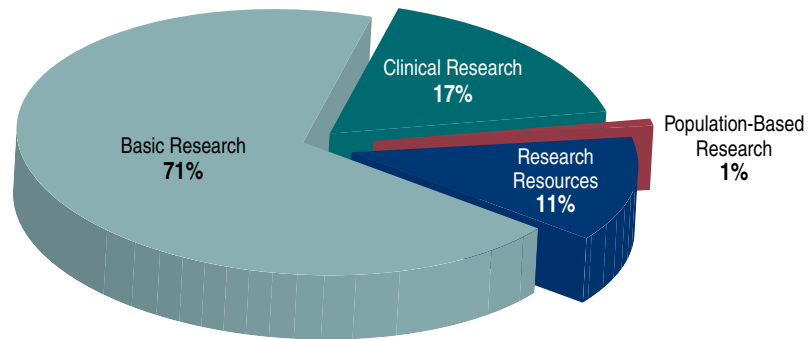


Ron Heffron,
TSCRP
Consumer
Reviewer

“From this experience [as a consumer 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.”

Background and Program History

The Tuberous Sclerosis Complex Research Program (TSCRP) was established in FY02 when the efforts of TSC advocates led to a congressional appropriation of \$1M. Since the initial appropriation, \$40M has been appropriated. Total appropriation through FY12 is \$41M. Today, the TSCRP is one of the leading sources of extramural TSC research funding in the United States. 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. In total, 88 awards have been made through FY11, bridging basic, clinical, and population-based research, as shown below.



FY02–FY11 TSCRP Portfolio by Research Area





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

In healthy cells, the TSC proteins function to modulate protein synthesis by suppressing mTOR signaling. Interestingly, maintenance

of synaptic plasticity, critical for learning, memory, and cognition, requires precise regulation of protein synthesis. Based on these observations, Dr. Mark Bear hypothesized that dysregulation of synaptic protein synthesis may contribute to TSC-associated learning and cognitive deficiencies. Dr. Bear's research team, with funding from an FY10 Idea Development Award, demonstrated that loss of TSC2 resulted in unregulated mTOR activity and suppressed hippocampal protein synthesis. In addition, treatment with mGluR5 positive allosteric modulator (PAM) restored hippocampal protein synthesis. Additionally, treatment with mGluR5 PAM also reversed hippocampal-dependent behavioral deficits in TSC2+/- mice. These exciting results suggest that mGluR5 PAM may be a novel therapeutic intervention for TSC-associated cognitive deficiencies.



**Francis McCormack,
M.D., University of
Cincinnati**

LAM, a life-threatening progressive lung manifestation of TSC, affects approximately 40% of women with TSC. Although a significant number

of molecular targets have been identified as potential therapeutics for LAM, clinical trials have been limited by the rare occurrence of the disease. Dr. Francis McCormack received an FY09 Clinical and Translational Research Award to develop a novel paradigm for conducting clinical trials in rare diseases by bringing clinical trials to local LAM treatment sites. He has established the LAM Clinical Research Network (LCRN), a collaboration of 24 LAM clinics throughout the United States. Preliminary results from one LCRN study suggest that serum vascular endothelial growth factor-D levels can be utilized to diagnosis LAM in women with TSC. Dr. McCormack and the LCRN are in a unique position to increase access to clinical trials for individuals with LAM and, in turn, facilitate the delivery of novel LAM treatment options to patients.



**Angelique Bordey,
Ph.D., Yale University**

Cortical tuber lesions that form during embryonic development are associated with the later development of seizures in persons with TSC. The mechanisms involved in

TSC lesion formation and seizure generation are not well understood and validated animal models for investigating the etiology or cause of TSC lesions and subsequent development of neurological disorders are currently unavailable. Through funding from an FY09 Idea Development Award, Dr. Angelique Bordey and her research team have developed and validated a mouse model of TSC that develops lesions containing many of the hallmark characteristics associated with human cortical tubers in TSC. This model will enable TSC researchers to study the development of cortical tuber lesions at specific time points during embryonic development.



**Tin Tin Su, Ph.D.,
University of Colorado,
Boulder**

The genes responsible for TSC, TSC1 and TSC2, normally act to suppress cellular growth, but loss of these proteins due to mutations can result

in excessive cell growth leading to tumor formation. *Drosophila melanaogaster* (fruit fly) models of TSC have been particularly useful in studying the function of normal and mutant TSC1/2. Dr. Tin Tin Su, with funding from an FY09 Exploration-Hypothesis Development Award, used the *Drosophila* model to screen for small molecules that may reverse the effects of TSC1/2 mutations. This work led to the identification of two small molecules that reliably inhibit the effects of mutant TSC1 in *Drosophila*. The next steps in this work involve validating the activity of these candidate small molecules using the *Drosophila* model and characterizing their mechanism of action.

APPENDIX A: FY92–FY11

Table A-1. Overview of Appropriations, Applications Received, and Awards Made for FY1992-2011

Programs Managed by CDMRP (a)	Fiscal Year	Appropriations Received (in millions)	Applications Received	Applications Funded
Amyotrophic Lateral Sclerosis	2007, 2009-2011	\$25.50	190	20
Autism	2007-2011	\$36.30	868	85
Bone Marrow Failure	2008-2011	\$13.75	272	32
Breast Cancer	1992-2011	\$2,683.20	46,232	6,194
Chronic Myelogenous Leukemia	2002-2006	\$22.05	252	61
Defense Women's Health	1995	\$40.00	559	69
Deployment Related Medical	2008	\$101.90	1,094	50
DOD/VA	1999-2000	\$6.79	88	9
Duchenne Muscular Dystrophy	2011	\$4.00	26	4
Genetic Studies of Food Allergies	2009-2010	\$4.38	60	9
Gulf War Illness	2006, 2008-2011	\$39.00	179	51
Institutionally Based Programs	1995-2010	\$486.31	306	267
Lung Cancer	2009-2011	\$47.80	817	61
Multiple Sclerosis	2009-2011	\$14.30	452	45
Myeloproliferative Disorders	2004	\$4.25	18	9
National Prion	2002	\$42.50	136	38
Neurofibromatosis	1996-2011	\$230.05	1,128	282
Osteoporosis	1995	\$5.00	105	5
Ovarian Cancer	1997-2011	\$180.45	2,542	265
Peer-Reviewed Cancer	2009-2011	\$47.00	2,200	112
Peer-Reviewed Medical	1999-2006, 2008-2011	\$544.50	5,316	437
Peer-Reviewed Orthopaedic	2009-2011	\$158.50	475	121
Prostate Cancer	1997-2011	\$1,130.00	13,175	2,504
Spinal Cord Injury	2009-2011	\$58.25	455	87
Tuberous Sclerosis	2002-2006, 2008-2011	\$35.90	391	88
Programs Executed on Behalf of Others (b)				
Army Rapid Innovation Fund	2011	\$13.57	n/a	5
Chiropractic Clinical Trials	2010	\$8.10	5	1
Defense Medical (DHPe)	2010-2011	\$153.26	575	98
Psychological Health/Traumatic Brain Injury	2007, 2009-2011	\$482.33	2,942	306
Total		\$6,618.94	80,858	11,315

(a) CDMRP executed and managed the full appropriation.

(b) CDMRP assisted with execution of the specified portion of a larger appropriation(s).

CDMRP APPENDIX B: FY11–FY12

Table B-1. FY11–FY12 Amyotrophic Lateral 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
2011	\$8M for ALS	Withholds Congressional: \$200,000 USAMRMC: \$351,000 Management Costs \$495,686 (6.7%)	Research Therapeutic Development: \$4,996,764 Therapeutic Idea: \$1,956,550
		Total: \$8M	Total: \$1,046,686
2012	\$6.4M for Peer-Reviewed ALS Research	Withholds USAMRMC: \$288,000 Budgeted Management Costs \$490,000 (8%)	Research Budgeted Peer-Reviewed Research: \$5,622,000
		Total: \$6.4M	Total: \$778,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-2. FY11–FY12 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
2011	\$6.4M for Autism Research	Withholds Congressional: \$160,000 USAMRMC: \$281,000 Management Costs \$359,704 (6%)	Research Clinical Trial: \$1,159,063 Idea Development: \$2,838,981 Idea Dev Multi PI: \$947,908 Pilot Award: \$653,344
		Total: \$6.4M	Total: \$800,704
2012	\$5.1M for Peer-Reviewed Autism Research	Withholds USAMRMC: \$229,000 Budgeted Management Costs \$389,500 (8%)	Research Budgeted Peer-Reviewed Research: \$4,481,500
		Total: \$5.1M	Total: \$618,500

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-3. FY11–FY12 Bone Marrow Failure 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 Bone Marrow Failure Disease Research Program	Withholds	Research Idea: \$1,413,105 Postdoctoral Fellowship: \$1,636,784 Resource Development: \$375,045
		Congressional: \$100,000 USAMRMC: \$175,000	
		Management Costs \$300,066 (8.1%)	
	Total: \$4M	Total: \$575,066	Total: \$3,424,934
2012	\$3.2M for Peer-Reviewed Bone Marrow Failure Disease Research Program	Withholds	Research Budgeted Peer-Reviewed Research: \$2,811,500
		USAMRMC: \$144,000	
		Budgeted Management Costs \$244,500 (8%)	
	Total: \$3.2M	Total: \$388,500	Total: \$2,811,500

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

**Table B-4. FY11–FY12 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
2011	\$150M for the Peer-Reviewed Breast Cancer Research Program	Withholds Congressional: \$3,750,000 USAMRMC: \$6,581,000	Research Clinical Translational Research Award: \$16,356,976 Collaborative Innovators Award: \$8,308,365 Collaborative Scholars and Innovators Award: \$3,543,901 Era of Hope Scholar Award: \$7,582,009 Era of Hope Scholar Expansion Award: \$6,115,730 Idea Award: \$12,480,513 Idea Award - Partnering PI Option: \$3,838,780 Idea Expansion Award: \$4,124,306 Idea Expansion Award: Collaborative Option: \$6,455,381 Impact Award: \$6,186,772 Innovator and Scholar Concept Award: \$2,285,395 Innovator Award: \$16,550,803 Innovator Expansion Award: \$6,680,000 Multi-team Award: \$3,906,161 Postdoctoral Fellowship Award: \$8,256,895 Transformative Vision Award: \$17,943,758
	\$877,952 in proceeds from the Stamp Out Breast Cancer Act	Management Costs \$9,051,519 (6.4%)	Communication \$879,688
	Total: \$150,877,952	Total: \$19,382,519	Total: \$131,495,433
2012	\$120M for the Peer-Reviewed Breast Cancer Research	Withholds USAMRMC: \$5,400,000	Research Budgeted Peer-Reviewed Research: \$106,075,475
	\$695,475 in proceeds from the Stamp Out Breast Cancer Act	Budgeted Management Costs \$9,220,000 (8%)	
	Total: \$120,695,475	Total: \$14,620,000	Total: \$106,075,475

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-5. FY11–FY12 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 Duchenne Muscular Dystrophy	Withholds Congressional: \$100,000 USAMRMC: \$175,000	Research Investigator Initiated Research: \$3,529,913
		Management Costs \$195,087 (5.2%)	
	Total: \$4M	Total: \$470,087	Total: \$3,529,913
2012	\$3.2M for Peer-Reviewed Duchenne Muscular Dystrophy Research	Withholds USAMRMC: \$144,000	Research Budgeted Peer-Reviewed Research: \$2,811,500
		Budgeted Management Costs \$244,500 (8%)	
	Total: \$3.2M	Total: \$388,500	Total: \$2,811,500

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-6. FY11–FY12 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
2011	\$8M for Gulf War Illness Peer-Reviewed Research Program	Withholds Congressional: \$200,000 USAMRMC: \$351,000	Research Clinical Trial: \$1,574,127 Innovative Treatment Evaluation: \$677,280 Investigator Initiated Research: \$4,764,071
		Management Costs \$433,522 (5.8%)	
	Total: \$8M	Total: \$984,522	Total: \$7,015,478
2012	\$10M for Peer-Reviewed Gulf War Illness Research	Withholds USAMRMC: \$450,000	Research Budgeted Peer-Reviewed Research: \$8,786,000
		Budgeted Management Costs \$764,000 (8%)	
	Total: \$10M	Total: \$1,214,000	Total: \$8,786,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-7. FY11–FY12 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
2011	\$12.8M for Peer-Reviewed Lung Cancer Research Program	Withholds Congressional: \$320,000 USAMRMC: \$562,000	Research Concept Award: \$1,725,132 Early Investigator Synergistic Idea: \$1,870,650 Investigator-Initiated Translational Research: \$5,783,502 Promising Clinician Award: \$1,761,913
		Management Costs \$776,803 (6.5%)	
	Total: \$12.8M	Total: \$1,658,803	Total: \$11,141,197
2012	\$10.2M for Peer-Reviewed Lung Cancer Research	Withholds USAMRMC: \$459,000	Research Budgeted Peer-Reviewed Research: \$8,961,500
		Budgeted Management Costs \$779,500 (8%)	
	Total: \$10.2M	Total: \$1,238,500	Total: \$8,961,500

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-8. FY11–FY12 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
2011	\$4.8M for Multiple Sclerosis	Withholds Congressional: \$120,000 USAMRMC: \$211,000	Research Concept Award: \$591,397 Idea Award: \$3,464,545
		Management Costs \$413,058 (9.2%)	
	Total: \$4.8M	Total: \$744,058	Total: \$4,055,942
2012	\$3.8M for Peer-Reviewed Multiple Sclerosis Research	Withholds USAMRMC: \$171,000	Research Budgeted Peer-Reviewed Research: \$3,338,700
		Budgeted Management Costs \$290,300 (8%)	
	Total: \$3.8M	Total: \$461,300	Total: \$3,338,700

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-9. FY11–FY12 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
2011	\$16M for Neurofibromatosis Research	Withholds Economic Assumptions: \$81,000 FFRDC Reduction: \$12,000 SBIR: \$422,000 STTR: \$55,000 USAMRMC: \$694,000 Management Costs \$1,005,109 (6.8%)	Research Clinical Trial: \$2,606,367 Clinical Consortium: \$5,000,000 Exploration - Hypothesis Development: \$327,500 Investigator-Initiated Focused Research-Optional Qualified Collaborator: \$2,037,990 Investigator-Initiated Research: \$1,580,250 Investigator-Initiated Research-Optional Qualified Collaborator: \$869,712 New Investigator: \$1,201,072 Postdoctoral Traineeship: \$108,000
		Total: \$16M	Total: \$2,269,109
2012	\$12.8M for Peer-Reviewed Neurofibromatosis Research Program	Withholds FFRDC Reduction: \$20,000 USAMRMC: \$575,000 Budgeted Management Costs \$977,000 (8%)	Research Budgeted Peer-Reviewed Research: \$11,228,000
		Total: \$12.8M	Total: \$1,572,000

The following abbreviations are used for withholds: FFRDC, Federally Funded Research and Development Center; SBIR, Small Business Innovation Research; STTR, Small Business Technology Transfer; USAMRMC, U.S. Army Medical Research and Materiel Command
 Percent of management costs=management costs/(appropriation-withholds).

Table B-10. FY11–FY12 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
2011	\$20M for Peer-Reviewed Ovarian Cancer Research Program	Withholds Congressional: \$500,000 USAMRMC: \$877,000 Management Costs \$1,259,229 (6.8%)	Research Clinical Consortium: \$2,298,252 Early Investigator Synergistic Idea Award: \$2,500 Pilot Award: \$3,175,769 Teal Expansion Award: \$2,529,066 Teal Innovator Award: \$3,328,893 Translational Leverage Award: \$3,463,471 Translational Pilot Award: \$2,565,820
		Total: \$20M	Total: \$2,636,229
2012	\$16M for Peer-Reviewed Ovarian Cancer Research	Withholds USAMRMC: \$720,000 Budgeted Management Costs \$1,223,000 (8%)	Research Budgeted Peer-Reviewed Research: \$14,057,000
		Total: \$16M	Total: \$1,943,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command.
 Percentage of management costs=management costs/(appropriation–withholds).

Table B-11. FY11–FY12 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
2011	\$16M for Peer-Reviewed Cancer Research Program	Withholds	Research
		Congressional: \$400,000 USAMRMC: \$702,000	Blood Cancer: \$1,795,508 Colorectal Cancer: \$1,316,840 Kidney Cancer: \$536,000 Listeria Vaccine for Cancer: \$296,000 Melanoma and Other Skin Cancers: \$3,619,650 Mesothelioma: \$1,188,720 Pancreatic Cancer: \$3,686,682 Pediatric Cancer: \$1,024,660
		Management Costs \$1,433,940 (9.6%)	
	Total: \$16M	Total: \$2,535,940	Total: \$13,464,060
2012	\$12.8M for Peer-Reviewed Cancer Research	Withholds	Research
		USAMRMC: \$576,000	Budgeted Peer-Reviewed Research: \$11,246,000
		Budgeted Management Costs \$978,000 (8%)	
	Total: \$12.8M	Total: \$1,554,000	Total: \$11,246,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

FY2011 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 research 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 utilizing nanotechnology, and Listeria Vaccine for infectious disease and cancer. The funds provided under the Peer-Reviewed Cancer Research Program shall be used only for the purposes listed above.

Note: The CDMRP requested Congressional guidance regarding topic area changes between the PRCRP and the PRMRP in FY2011 specifically shifting Listeria Vaccine for infectious diseases from PRCRP to PRMRP. Congressional staffers from the defense subcommittees for both the House and Senate Appropriations Committees approved this request in April 2011. Listeria Vaccine for cancer remained in the PRCRP topic area list.

FY2012 Peer-Reviewed Cancer Research Program: The conference agreement provides \$12,800,000 for a Peer-Reviewed Cancer Research Program that would research cancers not addressed in the breast, prostate, ovarian, and lung cancer research programs currently executed by the Department of Defense, and specifically by the U.S. Army Medical Research and Materiel Command. The funds provided are directed to be used to conduct research in the following areas: melanoma and other skin cancers, pediatric brain tumors, genetic cancer research, pancreatic cancer, kidney cancer, blood cancer, colorectal cancer, mesothelioma, and listeria vaccine for infectious disease and cancer. The funds provided under the Peer-Reviewed Cancer Research Program shall only be used for the purposes listed above. The Assistant Secretary of Defense (Health Affairs) 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 Research Program. For each research area, the report should include the funding amount awarded, the progress of the research, and the relevance of the research for servicemembers and their families.

Note: The CDMRP requested Congressional guidance regarding topic area changes between the PRCRP and the PRMRP again in FY2012 specifically shifting Listeria Vaccine for infectious diseases from PRCRP to PRMRP. Congressional staffers from the defense subcommittees for both the House and Senate Appropriations Committees approved this request in January 2012. Listeria Vaccine for cancer remained in the PRCRP topic area list.

Table B-12. FY11–FY12 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
2011	\$50M for Peer Reviewed Medical Research Program	Withholds Congressional: \$1,250,000 USAMRMC: \$2,194,000	Research Chronic Fatigue Syndrome: \$1,079,959 Chronic migraine & post-traumatic headache: \$1,095,083 Drug Abuse: \$3,850,620 Dystonia: \$216,192 Epidermolysis bullosa: \$1,118,720 Epilepsy: \$1,197,633 Fragile X Syndrome: \$1,589,195 Inflammatory bowel disease: \$3,332,852 Interstitial cystitis: \$1,644,093 Listeria vaccine for infectious disease: \$1,155,000 Lupus: \$206,144 Neuroblastoma: \$7,141,443 Osteoporosis & related bone disease: \$7,785,288 Paget's disease: \$903,196 Pancreatitis: \$2,498,233 Pheochromocytoma: \$1,092,778 Polycystic Kidney Disease: \$610,515 Post-traumatic osteoarthritis: \$4,248,780 Scleroderma: \$2,288,166
		Management Costs \$3,502,110 (7.5%)	
	Total: \$50M	Total: \$6,946,110	Total: \$43,053,890
2012	\$50M for Peer-Reviewed Medical Research	Withholds USAMRMC: \$2,250,000	Research Budgeted Peer-Reviewed Research: \$44,090,000
		Budgeted Management Costs \$3,660,000 (7.7%)	
	Total: \$50M	Total: \$5,910,000	Total: \$44,090,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

FY2011 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 Surgeons 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, posttraumatic 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.

Note: The CDMRP requested Congressional guidance regarding topic area changes between the PRCRP and the PRMRP in FY2011 specifically shifting Listeria Vaccine for infectious diseases from PRCRP to PRMRP. Congressional staffers from the defense subcommittees for both the House and Senate Appropriations Committees approved this request in April 2011. Listeria Vaccine for cancer remained in the PRCRP topic area list.

FY2012 Peer Reviewed Medical Research Program: The conference agreement provides \$50,000,000 for a Peer-Reviewed Medical Research Program. The conferees direct the Secretary of Defense, in conjunction with the Service Surgeons General, to select medical research projects of clear scientific merit and direct relevance to military health. Research areas considered under this funding are restricted to: arthritis, composite tissue transplantation, drug abuse, dystonia, epilepsy, food allergies, Fragile X syndrome, hereditary angioedema, inflammatory bowel disease, interstitial cystitis, lupus, malaria, nanomedicine for drug delivery science, neuroblastoma, osteoporosis and related bone disease, Paget's disease, polycystic kidney disease, post-traumatic osteoarthritis, scleroderma, tinnitus, and tuberculosis. The conferees emphasize that the additional funding provided under the Peer-Reviewed Medical Research Program shall be devoted only to the purposes listed above.

Note: The CDMRP requested Congressional guidance regarding topic area changes between the PRCRP and the PRMRP again in FY2012 specifically shifting Listeria Vaccine for infectious diseases from PRCRP to PRMRP. Congressional staffers from the defense subcommittees for both the House and Senate Appropriations Committees approved this request in January 2012. Listeria Vaccine for cancer remained in the PRCRP topic area list.

Table B-13. FY11–FY12 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
2011	\$24M for Peer-Reviewed Orthopedic Research Program	Withholds	Research
		Congressional: \$600,000 USAMRMC: \$1,053,000	Clinical Trial: \$11,578,841 Technology Development Award: \$2,300,000 Translational Research Partnership Award: \$6,372,825
	Management Costs \$2,095,334 (9.4%)	Total: \$3,748,334	Total: \$20,251,666
2012	\$30M for Peer-Reviewed Orthopedic Research	Withholds	Research
		USAMRMC: \$1,350,000	Budgeted Peer-Reviewed Research: \$26,360,000
	Budgeted Management Costs \$2,290,000 (8%)	Total: \$3,640,000	Total: \$26,360,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-14. FY11–FY12 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
2011	\$80M for Peer-Reviewed Prostate Cancer Research Program	Withholds	Research
		Congressional: \$2,000,000 USAMRMC: \$3,510,000	Clinical Consortium Award: \$949,734 Clinical Consortium Award - Clinical Research Site: \$6,781,279 Clinical Trial Award: \$1,120,013 Exploration-Hypothesis Development Award: \$4,419,302 HBCU Student Summer Training Program: \$1,195,068 Health Disparity Research Award: \$2,533,852 Health Disparity Training Award: \$1,642,072 Idea Development Award: \$28,361,342 Idea Development Award-Established Investigator: \$1,772,424 Impact Award: \$2,112,447 Laboratory-Clinical Transition Award: \$867,846 Physician Research Training Award: \$2,802,997 Population-Based Research Award: \$945,084 Postdoctoral Training Award: \$3,220,265 Synergistic Idea Development Award: \$10,453,055
		Management Costs \$5,252,177 (7%)	Communication \$61,043
	Total: \$80M	Total: \$10,762,177	Total: \$69,237,823
2012	\$80M for the Peer-Reviewed Prostate Cancer Research	Withholds	Research
		USAMRMC: \$3,600,000	Budgeted Peer-Reviewed Research: \$70,290,000
		Budgeted Management Costs \$6,110,000 (8%)	
	Total: \$80M	Total: \$9,710,000	Total: \$70,290,000

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-15. FY11–FY12 Spinal Cord 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	\$12M for Peer-Reviewed Spinal Cord Research Program	Withholds Congressional: \$300,000 USAMRMC: \$526,000	Research Clinical Trial-Rehabilitation: \$2,009,215 Clinical Trial-Rehabilitation-Nested New Investigator: \$414,123 Investigator-Initiated Research: \$4,204,760 Qualitative Research: \$2,365,459 Translational Research Partnership: \$1,005,137
		Management Costs \$1,175,306 (10.5%)	
	Total: \$12M	Total: \$2,001,306	Total: \$9,998,694
2012	\$9.6M for Peer-Reviewed Spinal Cord Research	Withholds USAMRMC: \$432,000	Research Budgeted Peer-Reviewed Research: \$8,439,200
		Budgeted Management Costs \$728,800 (7.95%)	
	Total: \$9.6M	Total: \$1,160,800	Total: \$8,439,200

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-16. FY11–FY12 Tuberos 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
2011	\$6.4M for Tuberos Sclerosis Complex (TSC)	Withholds Congressional: \$160,000 USAMRMC: \$281,000	Research Clinical Trial: \$1,678,542 Exploration-Hypothesis Development: \$745,499 Idea Development: \$1,452,336 Idea Development-Optional Qualified Collaborator: \$1,796,018
		Management Costs \$286,605 (4.8%)	
	Total: \$6.4M	Total: \$727,605	Total: \$5,672,395
2012	\$5.1M for Peer-Reviewed Tuberos Sclerosis Complex Research	Withholds USAMRMC: \$229,000	Research Budgeted Peer-Reviewed Research: \$4,481,500
		Budgeted Management Costs \$389,500 (8%)	
	Total: \$5.1M	Total: \$618,500	Total: \$4,481,500

The following abbreviations are used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command. Percentage of management costs=management costs/(appropriation–withholds).

Table B-17. FY11 Army Rapid Innovation Fund CDMRP-Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP-Executed Funds	Management Costs	Investment Strategy
2011	\$13,569,010	Management Costs \$38,190	Research Technology Development Award: \$13,530,820
	Total: \$13,569,010	Total: \$38,190	Total: \$13,530,820

Table B-18. FY11 Defense Medical Research and Development Program CDMRP-Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP-Executed Funds	Management Costs	Investment Strategy
2011	\$58,761,164	Management Costs \$5,726,517	Research Applied Research and Advanced Technology Development Award: \$10,258,193 Basic Research Award: \$2,281,662 Clinical Trial Award - Regenerative Medicine, Pain, Sensory System: \$4,587,938 Cognitive Rehabilitation Clinical Trial Award - Optional Partnering PI: \$2,167,703 DMRDP-IIRA-Broad Agency Announcement: \$5,135,192 Intramural TBI Investigator- Initiated Research Award: \$9,869 Military Infectious Diseases Applied Research Award: \$5,783,400 Military Infectious Diseases Basic Research Award: \$7,294,613 Military Infectious Diseases Clinical Trial Award: \$4,999,000 PH/TBI-IIRA-Broad Agency Announcement: \$251,628 Post-Traumatic Stress Disorder In-Home Therapy Clinical Trial Award: \$4,882,521 PTSD Multidisciplinary Research Consortium Award: \$5,382,928
	Total: \$58,761,164	Total: \$5,726,517	Total: \$53,034,647

Table B-19. FY11 Psychological Health/Traumatic Brain Injury Research Program CDMRP-Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP-Executed Funds	Management Costs	Investment Strategy
2011	\$61,432,853	Management Costs \$4,110,000	Research Applied Neurotrauma Research Award: \$18,580,690 Applied Psychological Health Award (without Clinical Trial): \$3,136,135 Applied Psychological Health Award with Clinical Trial - Partnering Option: \$6,374,081 Applied Research and Advanced Technology Development Award: \$2,816,190 Basic Psychological Health Award: \$767,717 Basic Psychological Health Award - Partnering Option: \$1,297,661 Basic Research Award: \$1,555,997 Basic/Applied Psychological Health Award (without Clinical Trial) - Partnering Option: \$4,775,626 Basic/Applied Psychological Health Award with Clinical Trial: \$3,221,461 DMRDP-IIRA-Broad Agency Announcement: \$4,776,784 Intramural PTSD Investigator-Initiated Research Award: \$349,201 Intramural TBI Investigator- Initiated Research Award: \$17,198 Investigator-Initiated Research Award: \$646,423 New Investigator Award: \$25,000 PH/TBI-IIRA-Broad Agency Announcement: \$8,937,689 PTSD/TBI Clinical Consortium Coordinating Center: \$45,000
	Total: \$61,432,853	Total: \$4,110,000	Total: \$57,322,853

APPENDIX C: BREAST CANCER RESEARCH SEMIPOSTAL AWARDS FY99–FY11

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

¹Total 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

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

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

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

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

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

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

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

⁹Total award amount was \$585,652; remaining funds were from the FY10 BCRP.

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY11	Andy Minn	\$399,942	University of Pennsylvania	Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements
	Xiaosong Wang	\$409,693	Baylor College of Medicine	Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer
	Susana Gonzalo Hervas	\$58,975 ¹⁰	St. Louis University	Stabilization of 53BP1 in Triple-Negative and BRCA-Deficient Breast Tumors: A Novel Therapeutic Strategy

¹⁰Total award amount was \$744,661; remaining funds were from the FY11 BCRP.



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September 30, 2012