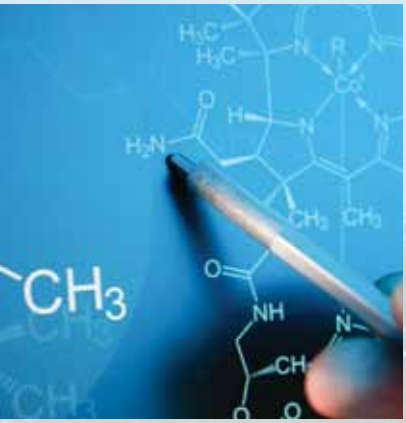
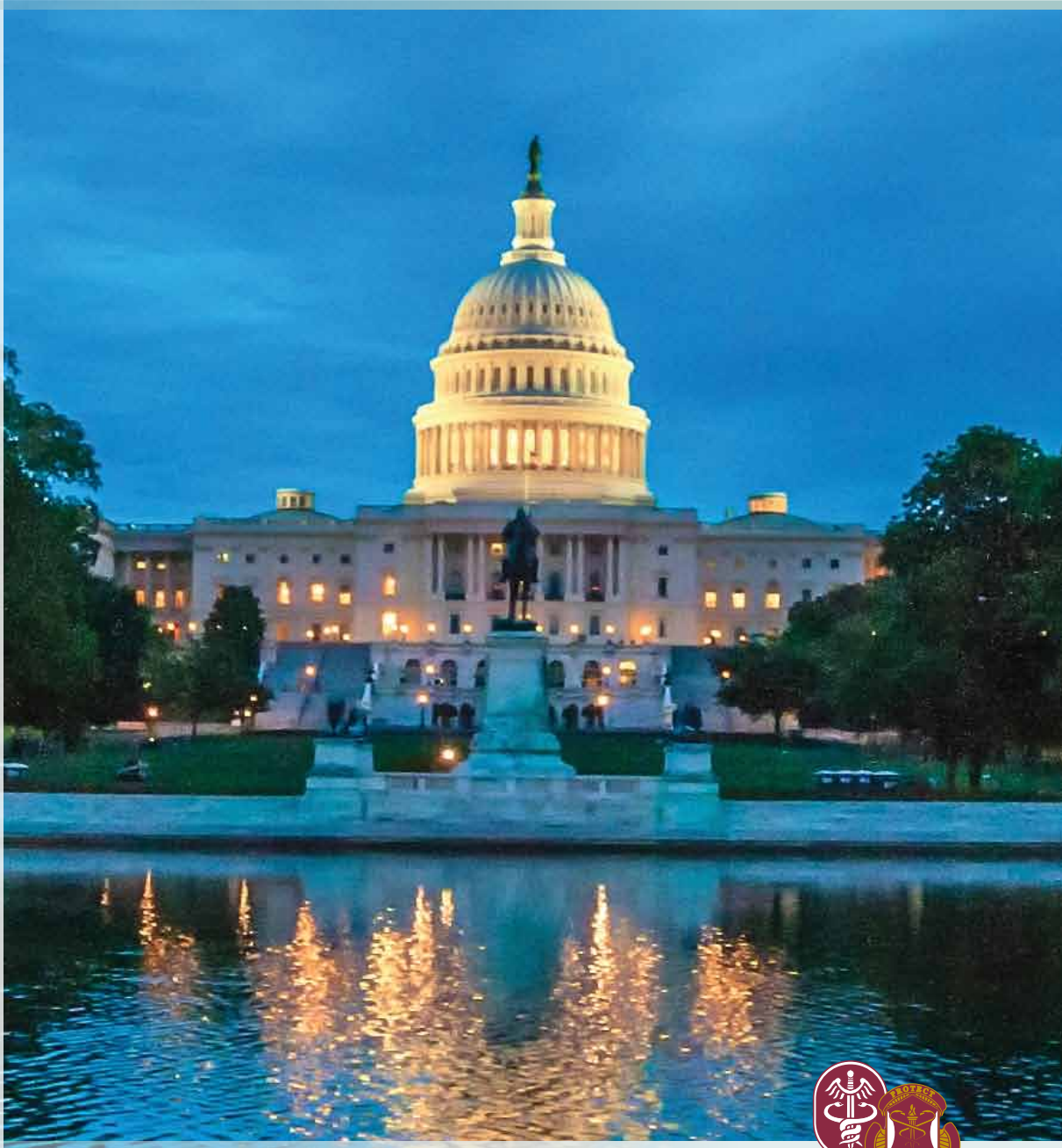


CDMRP
Department of Defense

Congressionally Directed Medical Research Programs

Annual Report
September 30, 2013



U.S. Army Medical Research and Materiel Command

Letter from the Director

I invite you to read the 2013 Annual Report for the Congressionally Directed Medical Research Programs (CDMRP). Despite the numerous challenges imposed this year, such as the sequester and the federal furlough, the CDMRP has remained true to its purpose and mission – to find and fund the best research...for the benefit of the American public.

In the pages that follow, you will see our promise of transparency in management of the precious financial resources Congress has entrusted to the CDMRP. You will see how we partner with all stakeholders to ensure an equal voice is given to accomplish the stated mission.

As my tenure as the Director for the CDMRP concludes, I would like to extend a sincere thank you to the staff of the CDMRP. It is a privilege to work alongside professionals that want to make a difference and believe in helping others. I want to challenge the clinicians and scientists to never accept the status quo; we can and should do better for our patients. And finally, to the advocates, you inspire each and every one of us every day. You are the reason we do what we do. Together, we will continue the fight until the battle is won.

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

Department of Defense

U.S. Army Medical Research and Materiel Command

Congressionally Directed Medical Research Programs

Annual Report

September 30, 2013

Congressionally Directed Medical Research Programs
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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 Congressionally Directed Medical Research Programs (CDMRP) as an organization, its individual programs, and the financial accounting for fiscal years 2012–2013 (FY12–FY13). Additional information about specific research programs can be found on the CDMRP website (http://cdmrp.army.mil), or requested by phone (301-619-7071) or e-mail (usarmy.detrick.medcom-cdmrp.mbx.cdmrp-public-affairs@mail.mil).

Who We Are

In the early 1990s, a grassroots advocacy movement campaigned for an increase in breast cancer research funding resulting in an 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 beginning of the CDMRP. Since then, the CDMRP has grown in scope and size, funding research that spans the biomedical field. From 1992 through FY13, the CDMRP has been responsible for managing more than $7.5 billion (B) in congressional appropriations across biomedical research programs (see **Figure 1**, CDMRP Funding History). With these monies, the CDMRP has funded 11,802 assistant agreements (consisting of grants and cooperative agreements) and contracts through FY12.

What We Do

The CDMRP originated within an environment that necessitated and fostered novel approaches to biomedical research in response to the expressed needs of its 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.

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

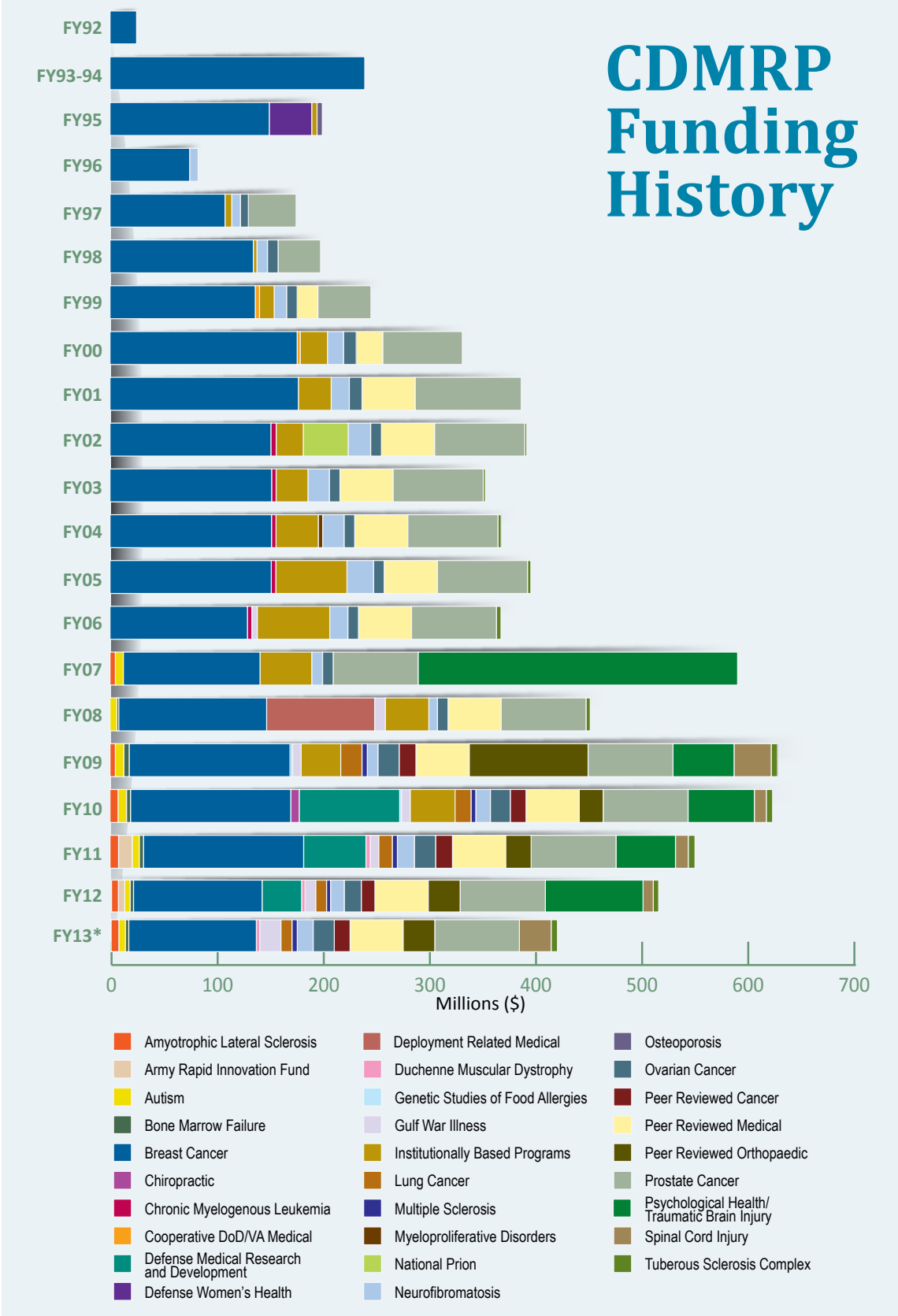


Figure 1. CDMRP Funding History

Data as of September 30, 2013. Investment of FY13 funds will be complete as of September 30, 2014.
** Does not include amounts of Defense Health Program Core and Psychological Health and Traumatic Brain Injury funding executed on behalf of the Joint Programmatic Committee that is currently estimated at $40M.*

Programs

Since its inception, the CDMRP has managed and/or executed 107 biomedical research programs totaling $7.5B. Highlights of current programs managed and/or executed by the CDMRP can be found within the program pages in this Annual Report beginning on page 37. As detailed in **Table 1**, in FY13 the CDMRP completed the execution of FY12 appropriations by processing 486 new awards across 19 programs.

In addition, in FY13, the CDMRP initiated the management of $422M across 16 programs as well as execution of another 3 programs on the behalf of other organizations. An overview of appropriations and applications received and funded since the CDMRP's inception can be found in Appendix A. For FY12–FY13 financial data by program, see Appendix B.

Table 1. CDMRP Programs, Appropriations, and Applications Received and Awarded in FY12–FY13

Programs Managed by the CDMRP[a]	FY12			FY13	
	Funds Received (in millions)	Applications Received	Applications Funded	Funds Received (in millions)	Applications Received to Date
Amyotrophic Lateral Sclerosis	$6.40	51	3	$7.50	61
Autism	$5.10	120	12	$6.00	-
Bone Marrow Failure	$3.20	35	9	$3.20	30
Breast Cancer/Breast Cancer Research Semipostal	$120.70	1,427	120	$120.60	853
Duchenne Muscular Dystrophy	$3.20	16	4	$3.20	-
Gulf War Illness	$10.00	33	6	$20.00	48
Lung Cancer	$10.20	375	20	$10.50	304
Multiple Sclerosis	$3.80	37	6	$5.00	35
Neurofibromatosis	$12.80	89	12	$15.00	89
Ovarian Cancer	$16.00	211	19	$20.00	157
Peer Reviewed Cancer	$12.80	167	27	$15.00	-
Peer Reviewed Medical	$50.00	720	56	$50.00	158
Peer Reviewed Orthopaedic	$30.00	145	38	$30.00	114
Prostate Cancer	$80.00	1,139	100	$80.00	626
Spinal Cord Injury	$9.60	55	11	$30.00	-
Tuberous Sclerosis	$5.10	54	9	$6.00	55
Programs Executed on Behalf of Others[b]					
Army Rapid Innovation Fund	$5.89	n/a	3	TBD	TBD
Defense Medical Research and Development	$37.05	n/a	15	TBD	TBD
Psychological Health/ Traumatic Brain Injury	$91.67	70	16	TBD	TBD
Total	**$513.51**	**4,744**	**486**	**$422.00**	**2,530**

[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

The CDMRP has always employed a flexible management cycle that is both responsive to the needs of the individual programs and to the requirements of the stakeholders for each program including Congress, the DoD, researchers, advocate communities, and the public. Each program follows the management cycle described in detail on the following pages, but does so with consideration to the requirements and needs of the program's stakeholders. Each step in the execution and management cycle is depicted in Figure 2.

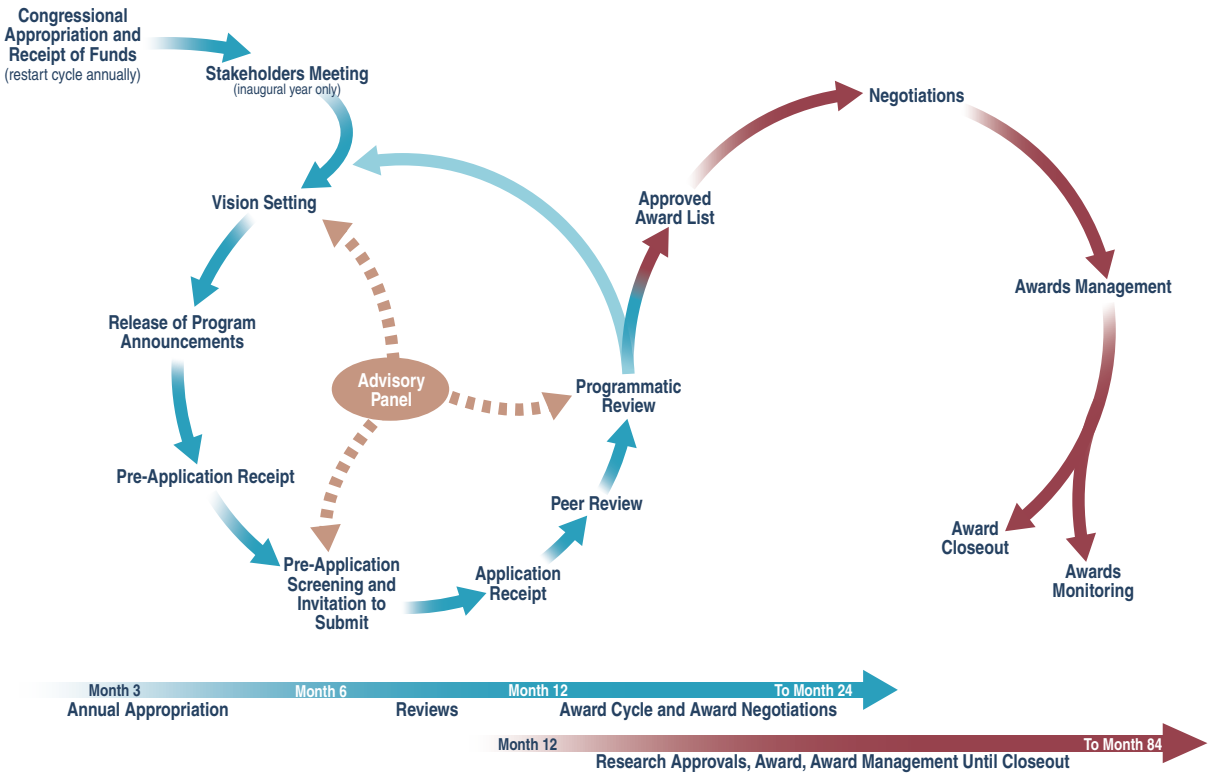


Figure 2. Execution and Management Cycle

Congressional Appropriation and Receipt of Funds

The management cycle begins with a congressional appropriation for targeted biomedical research to be managed by the CDMRP. These funds are not in the President's budget; Congress appropriates the funds annually to be managed by USAMRMC with the CDMRP as the execution agent. Program funds are appropriated in direct response to the needs of service members and their families, advocacy groups, research communities, and the public at large. These appropriations do not take away any monies to fund the warfighter, but the results of research are useful for the health care of service members, their families, and other military beneficiaries.

Stakeholders Meeting

For new programs, a stakeholders meeting is held to survey the research landscape and identify gaps in the scientific and consumer interest areas. Stakeholders are 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 13.) Recommendations from stakeholders meetings are then used to facilitate vision setting.

Vision Setting

Based on the recommendations of the National Academy of Sciences Institute of Medicine (IOM),[2] each research program holds an annual vision setting meeting to identify research gaps and define an individual investment strategy for the program year. Vision setting is conducted by an advisory panel specific to the individual program and consists of scientists, clinicians, military members, and consumers. The advisory panel, also called an Integration Panel (IP), a steering committee, or a Joint Programmatic Committee

(JPC) depending on the program, recommends an investment strategy that encourages research in underfunded and underrepresented areas that are considered (1) most critical to the program and (2) most critical to advance science and treatment of diseases, injuries, or conditions. 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. The advisory panel also recommends which award mechanisms to offer for the program year during vision setting. Award mechanisms are the vehicles to generate different types of research to meet varied programmatic goals. Some award mechanisms are intended to promote basic research (Idea Awards, Investigator-Initiated Research Awards) while others focus on clinical development (Translational Awards, Clinical Trial Awards). Sixteen vision setting meetings were held by the CDMRP in FY13.

Program Announcements

The award mechanisms recommended by each program's advisory panel at vision setting lead to the release of Program Announcements (PAs). PAs provide applicants details about a particular award mechanism, including the programmatic intent, a description of the type of studies

[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.

being requested, eligibility, and submission requirements, to include the application review criteria and processes. When new PAs are released by a program, research communities are alerted through a wide range of strategies including mass e-mails, tweets, targeted advertising, telephone contacts, and face-to-face interactions. Examples include:

- E-mailing 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 90 professional associations
- Notifying more than 50 U.S. Department of Veterans Affairs (VA) facilities and military research laboratories
- Maintaining an e-mail distribution list of more than 77,000 unique recipients
- Distributing electronic news items to nearly 450 consumer advocacy groups
- Presenting the CDMRP display and funding opportunities at national scientific meetings
- Providing research institutions with award details for news releases
- Using Twitter to alert the research communities when PAs are released

Application Submission and Receipt

Application submission requires a multi-step process consisting of a pre-application submission (which includes a letter of intent, preproposal, and/or nomination) followed by full application submission. The pre-application 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 application review also increased. Additionally, applicants were burdened with the submission of a complex, full application package when chances of being funded were significantly decreased. To mitigate the financial burden on the programs and the time and effort required by applicants to submit a full application package, a pre-application submission process was implemented for many award mechanisms. The pre-application is an abbreviated submission, consisting of one to three pages, outlining the research aims, strategy, and methods, innovation, and/or impact of the project. Through the use of the pre-application screening process, the number of full applications to be administratively processed and scientifically peer and programmatically reviewed has significantly decreased. This process allows for a more focused review of higher-grade applications that decreases management costs and saves funds for research investment.

Pre-applications are screened by either the program's advisory panel 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 can complete the requirements for a full application package submission. In FY13, the CDMRP held 17 pre-application screening meetings.




As summarized in **Table 2**, in FY13, the CDMRP received 8,879 pre-applications and nominations that, after screening and invitation, resulted in 3,945 full applications received as of the date of this report. In addition, the CDMRP received 3,237 full applications from mechanisms that did not require pre-applications or nominations for a total of 7,182 full applications received to date.

Two-Tier Review Process

The CDMRP utilizes a two-tier review of applications that is based on the recommendations set forth by the IOM committee in 1993. The two tiers of review are peer review and programmatic review. Although the two tiers have different goals, they are complementary.

Table 2. Number of Submissions Received from October 1, 2012, to September 30, 2013, Across FY12–FY14 Programs

Mechanism Submissions	
Pre-applications or nominations screened	8,879
Letters of intent received	2,023
Total pre-applications received	**10,902**
Full Application Submissions	
Full applications from invitations only	3,945
Full applications from letter of intent	3,237
Total full applications received	**7,182**

Reviewers for each tier for the CDMRP must uphold the highest standards of conduct to ensure the credibility of the programs and the processes. The CDMRP strives to give every application a fair and balanced review, taking steps to ensure that conflicts of interest do not influence the process.

Peer Review

Peer review is a criteria-based process where applications are evaluated based on their scientific and technical merit. Applications are categorized by scientific discipline, specialty area, and/or type of PA (i.e., award mechanism) to be assessed by external panels consisting of both scientific and consumer peer reviewers. The peer review panel evaluates each application based on the review criteria outlined in the PA and rates the various criteria numerically. Each application is evaluated for its own merit independent of other applications. The product of peer review is a summary statement, which describes the strengths and weaknesses of the application in accordance with the published review criteria, and an overall peer review score. There were 171 peer review panels held from October 1, 2012, through September 30, 2013.

Programmatic Review

After applications have been scientifically peer reviewed, they are programmatically reviewed by members of a program's advisory panel (IP, steering committee, or JPC), the same panel that recommended the annual investment strategy. At the programmatic review level, the advisory panel considers each peer review summary statement based on the criteria published in the PA with a focus on not only scientific merit but also programmatic relevance, relative impact and innovation, program portfolio composition, and adherence to the intent of the award mechanism. Applications are compared to each other to find those that best fit the vision and mission of the program. The advisory panel recommends a list of applications to be funded that best fulfills the vision and mission of each program. To ensure impartiality and the

integrity of the process, peer and advisory panel members are prohibited from applying for funds for the fiscal year in which they participated in vision setting. There were 29 programmatic review meetings held from October 1, 2012, through September 30, 2013.

Additional details about the two tiers of review can 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 some 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 errors at receipt, peer review, or programmatic review. If an error is identified, the application will be sent for re-review at the appropriate level (peer and/or programmatic review).

Award Negotiations and Management

The negotiation and management of awards are a major focus of the administration processes at the CDMRP. During the period of performance for awards (which can be up to 5 years), the CDMRP actively manages and monitors progress. The awards management process is depicted in **Figure 3** and described in greater detail in the sections below. Approximately 500 to 600 new awards are made each fiscal year. As of September 30, 2013, the CDMRP has managed 11,802 awards throughout its funding history.

Execution of Assistance Agreements, Cooperative Agreements, or Contracts

After a funding recommendation is made, each award is assigned a Science Officer (SO). The SO serves as the technical representative for the lifetime of the award. To ensure success in the award negotiations process and regulatory oversight, the CDMRP partners with several offices within USAMRMC, including the U.S. Army Medical Research Acquisition Activity (USAMRAA); the Office of Research Protections (ORP); the Office of Surety, Safety,

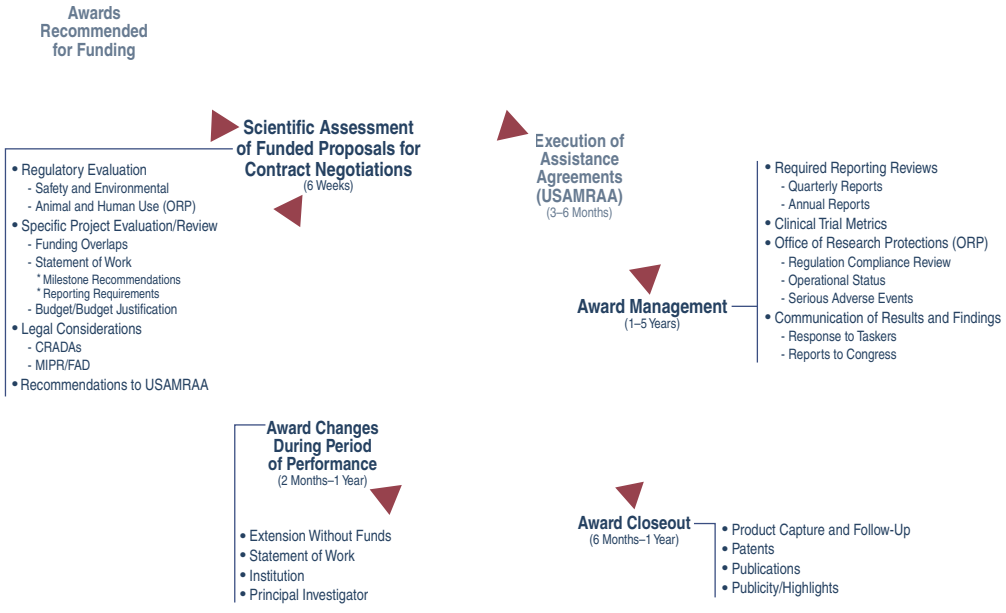


Figure 3. Execution and Management Cycle

and Environment (SSE); and Staff Judge Advocate (SJA). USAMRAA is the contracting element of USAMRMC. The ORP manages and provides oversight on human subject protection and animal welfare review for all of the CDMRP-funded research. Prior to receiving funding, research organizations receive a review from the SSE for compliance with Army safety regulations while the SJA provides legal advice and written opinions to CDMRP staff members when appropriate.

The SO also acts as a liaison, maintaining the proper flow of information between the awardee institution, the Principal Investigator (PI), the CDMRP program office, USAMRAA, and other offices within USAMRMC. Thus, the SO initially facilitates a regulatory review with ORP, a safety review with SSE, and a technical compliance review of the research project. USAMRAA initiates negotiations with the performing institution. Formal analysis of the budget with respect to the scope of work to be performed is completed through detailed discussions among the CDMRP, USAMRAA, the institution, and the researchers to ensure cost sharing when possible and avoidance of overlap in research funding with other funding agencies. Once all aspects of negotiation are complete, an award is signed by USAMRAA, and an assistance agreement (grant or cooperative agreement) or contract is issued.

Award Duplication and Overlap

The CDMRP uses multiple processes to minimize the likelihood of research duplication to ensure funded research is synergistic and harmonizes with health research projects undertaken by other agencies. The CDMRP's multi-step process to avoid award duplication and overlap spans application submission, peer and programmatic review, negotiation, and monitoring of funded awards as described below.

- The first step in minimizing award duplication and overlap is the responsibility of the PI and institutional business official and is outlined in the Administrative and Cost Principles section of the General Application Instructions for every PA. For each research application, a comprehensive list of past, current, and pending funding support for the PI and all key personnel must be submitted to the CDMRP at the time of submission. Because overlap of research projects is difficult to assess from project titles and abstracts alone, the financial regulations guide recipient institutions to provide details regarding title, time commitments, supporting agency, name and address of the funding agency's procuring Contracting/Grants Officer, performance period, level of funding, brief description of the project's goals, and list of the specific aims. If applicable, places where the proposed project overlaps with other existing and pending research projects are to be clearly identified and, if there is no overlap, recipients must clearly state as such for each type of support listed. The instructions further state that an updated current and pending support document will be required during award negotiations.

CDMRP's multistep process to minimize award duplication and overlap

1. ***List of past, current, and pending funding support submitted by the PI at the time of application submission***
2. ***Identification of project innovation, research duplication, and overlap during the two-tier review process by peers in the field***
3. ***List of updated funding support at the time of award notification which is certified by the award recipient's Sponsored Programs Office***
4. ***Review of submitted documents and research program sites to assess pending and existing funding support during award negotiations***
5. ***Technical review of progress throughout the award period of performance which includes funding overlap and duplication***

Avoiding overlap and duplication to fund the best science...

- The second step is performed during scientific peer and programmatic reviews. During peer review, the reviewers, who have extensive knowledge of the subject, determine whether the research proposed has been done, is the subject of another application, or if the effort of the PI and all key personnel is appropriate. The peer reviewers consult the past, pending, and existing support documentation provided with the application to assist with this process. Their comments are captured in the peer review summary statement and also as administrative notes, both of which are reviewed by the CDMRP SO during award negotiations. During programmatic review, the advisory panel reviews whether the application has met the intent of the award mechanism and addresses whether the work appears to duplicate research funded elsewhere. From this two-tier process, the CDMRP does not depend on the knowledge of one subject matter expert but rather a panel of experts that discusses and evaluates the gaps and innovation of each project. Any areas for concern are captured as notes and are further investigated by SOs during award negotiations.
- The third step is the award notification letter. The funding letter requests updated details for all existing and pending support that differs from information submitted at the time of application. Updated support is required prior to the start of award negotiations and must be certified by the Sponsored Programs Office indicating that the information is current, accurate, and addresses any scientific or financial overlap.
- The fourth step is the award negotiations process conducted by USAMRAA. The SO provides technical assistance and performs a thorough review of the pending and existing support information and any notes from the peer and programmatic reviews. The SO also uses the CDMRP's internal grants management database, National Institutes of Health's (NIH's) Electronic Research Administration (eRA) Commons system, NIH Reporter, the International Cancer Research Partnership, and other appropriate research program websites to investigate potential overlap between the DoD award and other projects funded or submitted for funding to other federal or non-federal organizations. Search terms are tailored depending on the research focus and, if duplication or overlap is found, the SO coordinates with the CDMRP Program Manager and subsequently the PI to delete or modify duplicative tasks and reduce funding as appropriate. Any potential level of commitment overlap and/or research duplication must be resolved before finalizing the award. If the proposed research duplicates entirely another funded research project or is found to have overlap

or duplication that cannot be resolved, the recipient is required to withdraw the application from the DoD or relinquish the other funding.

- The fifth and final step occurs throughout the award period of performance. In accordance with the award agreement, technical progress reports are required, at a minimum, on an annual basis. These reports must adhere to USAMRMC technical reporting requirements and undergo a thorough review process by SOs and support staff. As part of the reporting requirements, PIs must report funding applied for and/or received during each reporting year. The SOs use this information as well as support acknowledged in publications or other outcomes resulting from the award to continually monitor research overlap. If overlap or duplication is identified, the SO and Program Manager will notify USAMRAA to stop funds until the suspected overlap has been resolved. If the issue cannot be resolved, USARMAA will terminate the award, and the money must be returned to the government.

Award Management

The life-cycle management of awards continues throughout the period of performance with monitoring of the technical progress, regulatory review, and financial reporting. At a minimum, all PIs are required to submit annual progress reports and quarterly financial reports. During the review of annual reports, research outcomes are identified and captured continuously throughout the life of each award. During evaluation of the progress of an award, the SO continues to update any potential overlap with other funding agencies to ensure the integrity of the process and good stewardship of federal monies. If overlap is found, the CDMRP and USAMRAA work with the awardee institution and the PI to resolve potential issues.

ORP staff communicates regularly with PIs to monitor compliance. PIs with awards that include clinical trials or clinical research are required to submit quarterly progress reports to their SOs and USAMRAA. These awards are monitored for approval of clinical protocols, accrual of patients, and any adverse events. When an 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 larger complex awards and consortia may also be monitored through external advisory boards, site visits, teleconferences, and other meetings throughout the entire period of performance. Information on the progress of awards can be found on the Defense Technical Information Center (DTIC) website at http://www.dtic.mil/dtic/. When required, CDMRP-funded research results and findings are summarized for inclusion in various congressional reports and Army-wide taskers.

Award Closeout

Award closeout, which takes place at both USAMRAA and the CDMRP, is usually performed 6 months after the period of performance has expired. During this time, the CDMRP carefully monitors the final progress report and the patent report while USAMRAA reviews the final financial accounting. Actions regarding any patents, invention disclosures, publications, and follow-up funding are captured during award closeout. When significant discoveries are identified, the awards are flagged for further follow-up. Research products of particular scientific interest are also captured in the CDMRP products database and can be flagged for discussion and highlighted on the web or within individual program books.

Electronic Grants System

To assist in the negotiation and management of awards, the CDMRP designed an electronic business system called the Electronic Grants System (EGS) to consolidate, store, and retrieve data and files generated for each award from negotiations, regulatory review, and award management through award closeout. EGS enables real-time, electronic workflow and transfer of data among offices within USAMRMC. Thus, multiple users are able to input data, download reports, and manage daily administrative tasks associated with grant processing in a central, secure location. During the management of awards, research

outcomes and findings are entered and categorized in EGS and then subsequently analyzed by CDMRP staff for program evaluation efforts (see Program Evaluation), interacting with funded investigators, and reporting to stakeholders. Finally, the CDMRP website is connected to EGS, which enables end users to retrieve publically available, up-to-date information on funded awards. These electronic processes have increased efficiency in data management, saving time and money throughout the administration of awards. As a result of the success of EGS, other offices within USAMRMC are utilizing the system to help streamline their processes and centralization of research data.

Program Evaluation

The CDMRP is constantly assessing research relevance, productivity, outcomes, and accomplishments of its funded research. Each award funded by the CDMRP is monitored at least annually for progress based on an annual progress report submitted by the PI. During each review, research outcomes, such as tools or new models for research, drugs, or devices for clinical care, are identified and captured throughout the life of each award and even beyond the period of performance. In addition, 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. More than 55 research highlights were published and disseminated on the CDMRP website, in individual program books, and in the CDMRP Annual Report between October 1, 2012, and September 30, 2013. In addition, some research programs post CDMRP-funded scientific resources/tools on the CDMRP website for the greater scientific community to use. By encouraging investigators to share their resources with the scientific community, research is accelerated and new collaborations are formed.

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 the DTIC website at http://www.dtic.mil/dtic/.

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 delivered to the public via the CDMRP website, e-mail distribution, and in person at scientific conferences and meetings. Between October 1, 2012, and September 30, 2013, 11 program books were created or updated, more than 55 research highlights were generated, and 3 exhibits and/or program banners were developed.

Additionally, in FY13, the CDMRP began using social media as another means to expand its information dissemination strategies. The CDMRP implemented the use of YouTube in February 2013 to improve and encourage the public's ability to access videos about its publically funded research programs and investigators. The public is encouraged to visit the CDMRP on YouTube at http://www.youtube.com/user/CDMRP. Further, the CDMRP began using Twitter in April 2013 to exchange information about current news and happenings within the organization. Twitter users can subscribe or follow CDMRP tweets at https://twitter.com/CDMRP.

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.

Throughout the years, the CDMRP has earned the trust of the scientific, consumer, and military communities to continue to fund innovative and impactful research areas and gaps within each program's portfolio. To maintain the uniqueness of the CDMRP's award portfolio, several practices are utilized. By employing external experts in the program cycle, the CDMRP brings the most current and up-to-date knowledge to the table when research strategy and field gaps are reviewed during vision setting (see page 5). The CDMRP works to avoid award overlap with other agencies (see Award Negotiations and Management, page 8) and to remain vital to the funding arena by continually assessing the research-funding landscape. The CDMRP strives to remain unique and not duplicate the efforts of other funding agencies. The following sections discuss how the CDMRP interacts and partners with its stakeholders and other federal and non-federal agencies as well as how the CDMRP is integral to meeting the needs of the military's medical research.

Consumers

Since its founding, the CDMRP has included consumers (patients, survivors, family members, and/or caregivers) in both peer and programmatic review panels as full voting members. Their knowledge of a disease, condition, or injury comes from their personal experience as a patient, survivor, spouse, parent, or caregiver.

Nearly 2,000 consumers have represented their communities and advocacy organizations at least once since 1992, and their role continues to be vital. Consumers are nominated to peer review panels by the advocacy organizations for which 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. Similar to peer review panels, consumers also serve on the advisory boards of the CDMRP. Consumers serve on peer review panels or advisory boards with scientists, clinicians, and leading experts and have an equal voice and vote in deliberations. Consumers also use their experiences to offer fresh, new perspectives and insights that other panel members may not have, and they bring a sense of urgency to the discussions.

In both the peer review and programmatic review processes, consumers bring passion and

a true appreciation of how different research applications can affect the human dimension of science. For more information on consumer involvement, see the consumer involvement pages on the CDMRP website (http://cdmrp.army.mil).

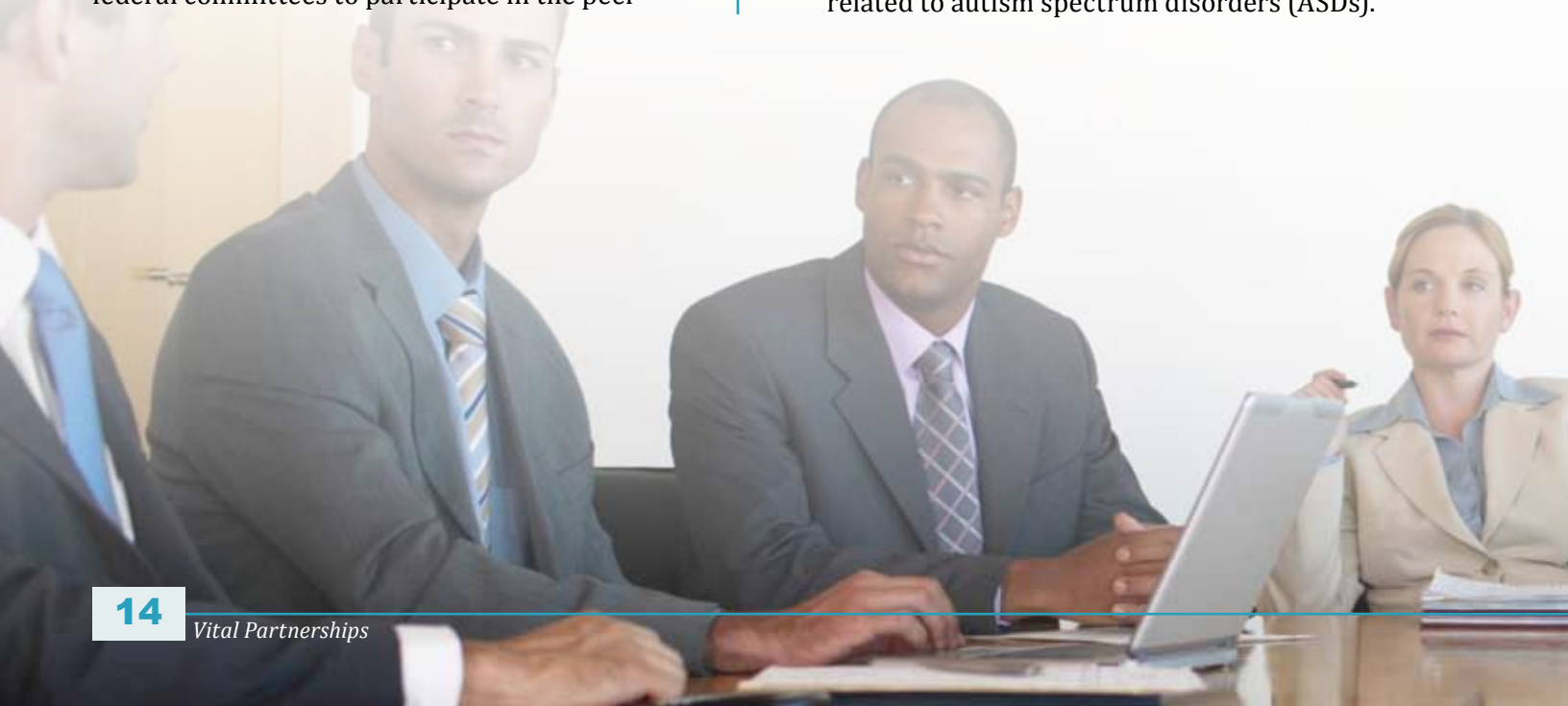
The Scientific Community

The fulfillment of program goals requires cooperation, communication, and integration across multiple scientific and clinical disciplines. To date, more than 8,600 scientists and clinicians have provided necessary subject matter expertise on peer review panels. In FY13, more than 375 scientists and clinicians served as advisory panel members, and nearly 200 ad hoc reviewers were recruited to these panels. Finally, approximately 8,790 researchers have been funded by the CDMRP in an effort to tackle the complex causes of diseases, conditions, and injuries, and they translate this knowledge into improved prevention, treatment interventions, patient survival, and quality of life.

Networking with Federal and Non-Federal Agencies

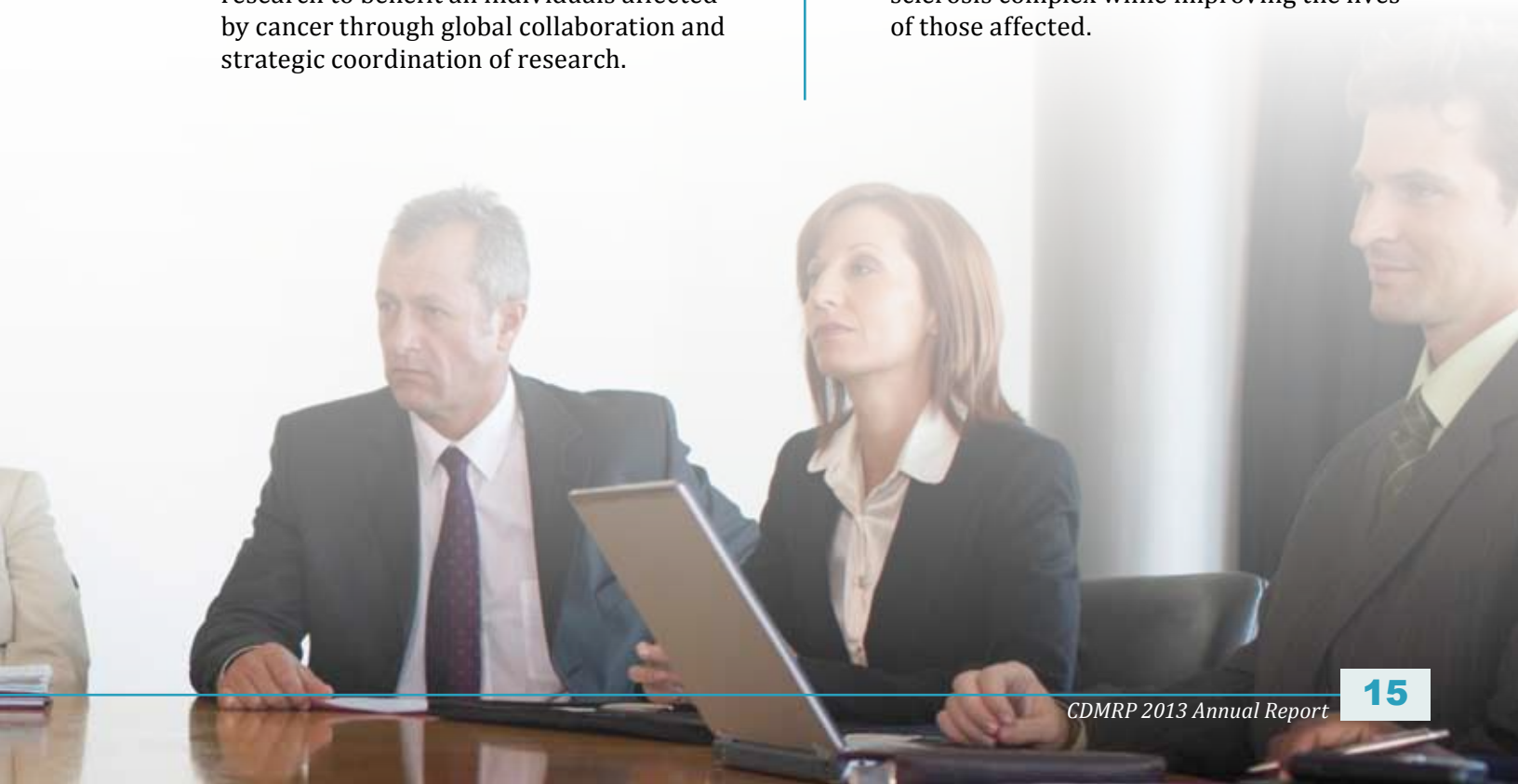
The CDMRP networks with multiple federal and non-federal committees to compare research portfolios, identify gaps in research funding, and improve existing research efforts. In addition, the CDMRP encourages reciprocity by engaging individuals from federal and non-federal committees to participate in 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 and 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.
- ***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 (TBI) across agencies.
- ***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.

- ***Interagency Breast Cancer and Environmental Research Coordinating Committee***, a congressionally mandated group co-chaired by the National Institute of Environmental Health Sciences and the National Cancer Institute that has made recommendations to the Secretary of Health and Human Services on federal research efforts in the areas of environmental research and prevention of 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.
- ***Trans-Agency Early Life Exposures and Cancer Working Group***, a working group composed of representatives from NIH, CDC, and the CDMRP. The group's goals are (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.



Eliminating Health Disparity

Current strategies to address and eliminate the burden of disease disparities in minority and underserved populations developed out of a unique partnership first begun in 1997 between the CDMRP's Initiative for Biomedical and Behavioral Minority Health and a diverse cohort of investigators and consumers. These partners came together to form the Minority Initiative Committee (MIC), whose original purpose was to identify methodologies that would increase breast cancer research by minority scientists to reduce breast cancer incidence, morbidity, and mortality rates among the most heavily affected populations. The MIC proposed a number of goals to increase funding focused on the study of minority populations, support minority investigators, and invest in research being conducted at Historically Black Colleges and Universities and Minority Institutions (HBCU/MIs). To implement these goals, the CDMRP established the Minority and Underserved Populations Program (MIUP), which integrated the MIC's objectives across multiple CDMRP programs and facilitated the development of new funding opportunities focused on addressing health disparities and encouraging research by minority investigators and HBCU/MIs. In addition, the MIUP worked toward increased representation of scientist and consumer reviewers from minority and underserved populations in the CDMRP's application review process. The CDMRP continues its efforts through several avenues including:

- Solicitation of health disparity-focused research,
- Outreach with information about specific funding mechanisms for HBCU/MIs,
- Collaboration with other funding agencies to ensure complementary efforts, and
- Exchange of information with public and private advocacy and research organizations, including data on trends and standard of care relevant to disproportionately affected populations.

Military Partnerships

U.S. Army Medical Research and Materiel Command

MISSION: Responsively and responsibly create, develop, deliver, and sustain medical capabilities for the warfighter.

VISION: Lead the advancement of military medicine.

The CDMRP is located within USAMRMC, the largest medical research organization within the DoD. USAMRMC is responsible for managing medical research programs that address both military and civilian groups. The USAMRMC motto, "Protect, Project, Sustain," underscores its support of the warfighter through ensuring that service members are protected from disease and treated for injuries or conditions. USAMRMC's medical research programs are divided into core and non-core research programs based on their alignment with DoD and Army missions. Core programs are funded through the DoD's planning and budget process and align with the principle needs and military operations within the DoD. Non-core programs are funded through congressional line item additions to the DoD budget, which includes the CDMRP. The CDMRP works in synergy with USAMRMC partners to ensure that its budgetary funds and congressional appropriations are used to the benefit of service members, their families, and the American public, as shown in **Figure 4**. For example, the CDMRP works closely with Research Area Directorates (RADs) within USAMRMC. The RADs manage research activities related to military infectious diseases, combat casualty care, military operational medicine, and clinical and rehabilitative medicine. Additional information about USAMRMC can be found at http://mrmc.amedd.army.mil/.

USAMRMC designed and implemented a Decision Gate process to manage medical materiel development in a cost-effective and transparent process. Decision Gate is grounded in the DoD 5000 series and the U.S. Food and Drug Administration (FDA)/Environmental Protection Agency regulatory requirements

Figure 4. The USAMRMC Team

with the goal of getting the right products to the field faster, more efficiently, and at less cost. As such, projects funded by the CDMRP that have strong potential for development into a beneficial, military-relevant medical product are included in the Decision Gate process. To facilitate the Decision Gate process, the CDMRP evaluates products from its research portfolio and assigns a technology readiness level (TRL) code to them. The TRL system tracks product progress from basic research and technology development through manufacturing, production, and deployment. This information is used by USAMRMC to determine whether any CDMRP-funded projects meet Decision Gate criteria. If a CDMRP-funded project meets Decision Gate criteria, it will be entered into the Decision Gate process, a point called the materiel development decision. Various teams and oversight committees will then provide support and guidance over the development of the medical product. One of the oversight committees is called the product-level Integrated Product Team (IPT) and is responsible for the day-to-day execution of the product. SOs from the CDMRP are often asked to participate on the IPTs due to their scientific expertise and relationship to the product developer. A product will go through a series of decision points (called milestones) to determine whether it should continue as planned, continue with a revised plan, or have development terminated (see **Figure 5** for the life cycle of a medical product). There are three decision points called Milestones A, B, and C, which correspond with Phase 1 clinical trial, Phase 2 clinical trial, and

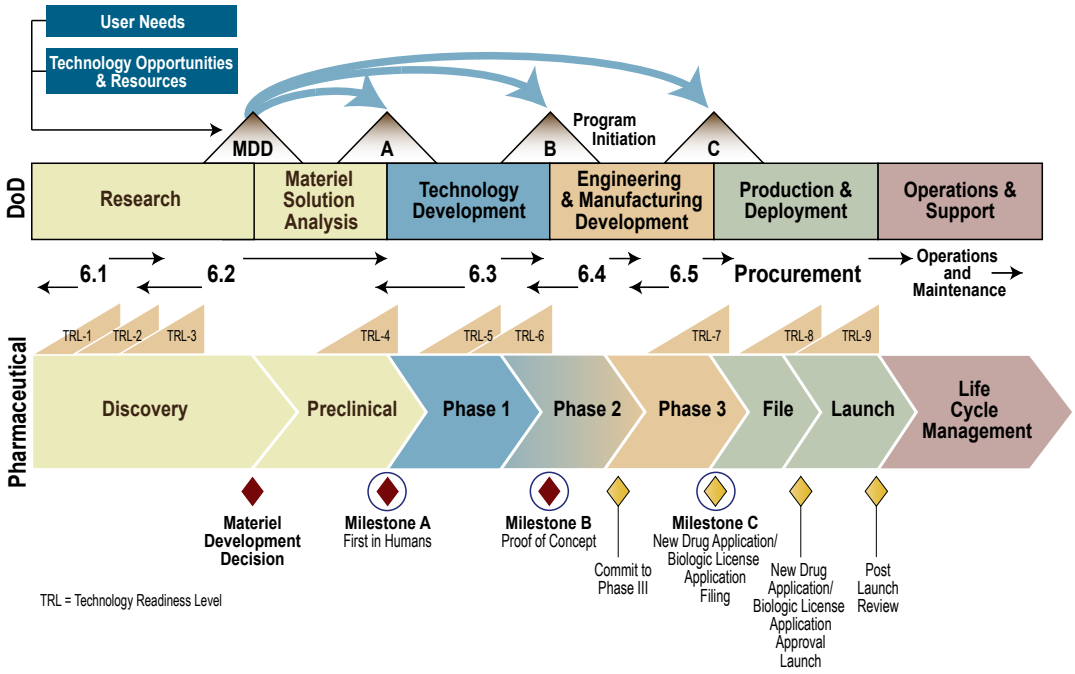


Figure 5. Decision Gate Life Cycle

FDA approval, respectively. The Decision Gate process reflects USAMRMC's commitment to remain a good steward of taxpayer dollars and world-class medical research and development organization.

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, see pages 48–49.) 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 FY13, the CDMRP assisted with program execution in a number of areas relevant to battlefield injury and military service, including: basic and applied psychological health, post-traumatic stress disorder (PTSD), TBI, neurotrauma, neuroplasticity, wound infections, infectious diseases, prosthetics, vision, hearing, balance, and other rehabilitative and regenerative medicine efforts.

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

U.S. Department of Veterans Affairs

In support of the August 31, 2012, Presidential Executive Order 13625, the DoD and the VA are combining more than $100M in a collaborative effort to fund two new consortia aimed at improving diagnosis and treatment of mild TBI (mTBI) and PTSD. Once in place, these consortia, the Consortium to Alleviate PTSD and the Chronic Effects of Neurotrauma Consortium will be jointly managed by the VA and the CDMRP on behalf of the DoD. Ongoing oversight of each consortium will be provided by a government steering committee that includes representation from the DoD, VA, NIH, and Department of Education. Through this collaborative effort, PTSD prevention strategies, interventions, improved treatments, and the after-effects of mTBI as well as comorbidity with other conditions will be studied.

In addition, the CDMRP 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) (see pages 52–53 for additional details on the GWIRP). VA scientists and clinicians serve on both peer and programmatic review panels for the GWIRP to inform and help make funding recommendations, as well as provide valuable resources and expertise as investigators on many GWIRP-funded awards.

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.

PCRP Advance

- Research from **Dr. Michael Milosevic** identifying hypoxia in prostate cancer culminates in the finding that prostate cancer hypoxia is an indicator for disease recurrence after therapy, providing key insight on intermediate-risk disease and better therapies.

PH/TBIRP Advance

- The DoD and the VA collaborate to establish two new consortia focused on developing more effective diagnoses and treatment of PTSD and mTBI. The Consortium to Alleviate PTSD (CAP), led by **Dr. Alan Peterson**, and the Chronic Effects of Neurotrauma Consortium (CENC), led by **Dr. David Cifu**, are dedicated to improving the health and welfare of our nation's service members, veterans, and their family members.

CDMRP Milestones

- *The CDMRP executes research projects under the Army's Rapid Innovation Fund.*
- *The Breast Cancer Research Program (BCRP) sponsors its sixth Era of Hope conference.*
- *The Prostate Cancer Research Program (PCRP) sponsors its second Innovative Minds in Prostate Cancer Today (IMPaCT) conference.*
- *The Duchenne Muscular Dystrophy Research Program 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 Amyotrophic Lateral Sclerosis (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 call transport in the brain, as a determinant of GWI symptoms.

NFRP Advance

- **Dr. Bruce Korf** expands the neurofibromatosis (NF) Clinical Trials Consortium to include clinical trials for NF2.

CDMRP Milestone

- *The CDMRP provides pre- and post-award execution support for the DMRDP Execution.*

ALSRP Advance

- **Dr. James Connor** results to date indicate that intracerebroventricular infusion of artificial cerebralspinal fluid (CSF) or H-ferritin delays onset of ALS symptomology and increases lifespan in SOD1G93A mice. In addition, motor neuron survival is increased in animals receiving a CSF infusion compared to untreated controls.

ARP Advances

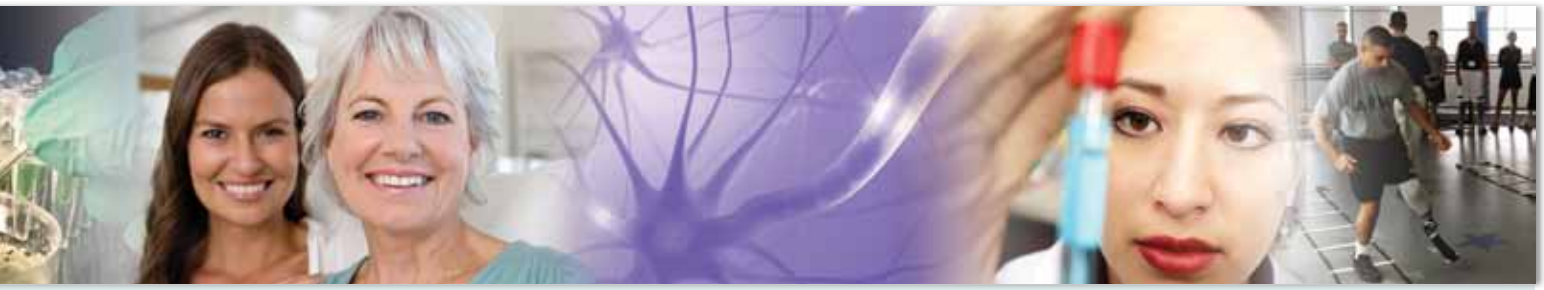
- **Dr. Daniel Cox** develops a virtual reality system to evaluate and enhance the driving skills of individuals with autism.
- **Dr. Paul Patterson** discovered that bone marrow transplant reversed autistic-like behaviors in a mouse model of ASD.
- **Dr. Eric Klann** showed that excessive protein synthesis in brains linked to autistic-like behaviors in the mouse model.

BMFRP Advance

- **Dr. Carla Hand** demonstrated that a novel erythropoietin (EPO) mimetic protects against acute radiation induced bone marrow failure.

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** continues to enroll subjects in an exploratory randomized clinical trial to evaluate how a sleep-focused mind-body program may enhance primary care for GWI and alleviate symptoms. Enrollment is on-going, trial continuing.
- **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.

NFRP Advance

- **Dr. Wei Mo** shows that CXCR4/CXCL12 mediates the cell-cycle progression in NF1-associated malignant peripheral nerve sheath tumor (MPNST).

OCRP Advances

- **Dr. Robert Kurman's** consortium develop and validate an inclusive scoring algorithm to assist pathologists in diagnosing Spatiotemporal Image Correlation Spectroscopy, the proposed precursor for most ovarian high-grade serous cancers.
- **Dr. Panogiotis Konstantinopoulos** develops the BRCAness gene expression profile, which can identify tumors with the "BRCAness" phenotype (characterized by increased sensitivity to platinum analogues and poly ADP ribose polymerase (PARP) inhibitors as well as improved survival).
- **Dr. Kathryn Terry** shows that women who take aspirin are at a reduced risk for non-dominant ovarian tumors, while women who take non-steroidal anti-inflammatory drugs (NSAIDs) other than aspirin are at a reduced risk for dominant and non-dominant ovarian tumors. Also finds that women who are smokers are at an increased risk for both tumor types, but women who quit are only at increased risk for non-dominant ovarian tumors.
- **Dr. Martina Bazzaro** demonstrates that combining bortezomib and vorinostat results in apoptotic morphology in ovarian cancer cells, but not in normal ovarian epithelial cells.
- **Dr. Rugang Zhang** determines that Wnt5a, a non-canonical Wnt ligand, induces cellular senescence by activating histone repressor A/ promyelocytic leukemia senescence pathway. Wnt5a suppresses the growth of epithelial ovarian cancer, and loss of Wnt5a predicts a poor outcome in epithelial ovarian cancer patients.

PCRP Advance

- **Dr. Michael Pollack** pioneers work with silibinin, a protein from milk thistle plants, that inhibits prostate tumor growth and has now entered clinical testing.

PRCRP Advances

- **Dr. Srikanth Singamaneni** develops a sensitive urine based test to detect kidney cancer biomarker, AQP1.
- **Dr. Hui Zong** finds that glial ablation treatment resulted in complete remission of brain tumors even at late stage.

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.

TSCRP Advances

- **Dr. Mary Kay Koenig** leads a multi-center prospective, randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of a topically applied formulation of rapamycin to treat cutaneous angiofibromas in individuals with tuberous sclerosis complex (TSC).
- **Dr. Mark Zervas** generates TSC-like symptoms in mice and shows that the timing of Tsc1 deletion in neurons in developing thalamus impacted the extent of the disease in the brain, the degree of abnormality, and the severity of TSC-like symptoms.

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 Peer Reviewed Medical Research Program (PRMRP), GWIRP, and Psychological Health/Traumatic Brain Injury Research Program (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.

ARP Advance

- **Dr. Brooke Ingersoll** develops an internet-based training program for parents of children with ASD.

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 GWI.
- **Dr. Anne-Louis 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 Advances

- **Dr. John Chen** develops a myeloperoxidase-targeted magnetic resonance imaging (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.
- **Dr. Sicotte** develops a metric modeling morphometry of the corpus callosum with diffusion tensor imaging to study changes in relapsing remitting MS.
- **Drs. Yanming Wang** and **Robert Miller** develop a near infrared fluorescence imaging technique capable of direct quantification of myelination in vivo.

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 non-dominant tumors (tubal origin) are more strongly associated with a family history of ovarian cancer and genetic variation in a telomere-associated protein, TERT.

PCRP 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 Advance

- **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 Advances

- **Dr. Ying-Hsui Su** develops a padlock probe mediated DNA microarray method to detect colorectal cancer in urine samples.
- **Dr. Kitlinska** demonstrates neuropeptide Y and other stress mediators have potent effects on tumor development and progression.
- **Dr. Wenwei Hu** reveals that attentuation of p53 function is an important underlying mechanism for stress induced tumorigenesis.
- **Dr. Suzy Torti** demonstrates that the combination of NIR and nanotubes successfully inhibit human and mouse kidney cancer cells.
- **Drs. Ruth Halaban**, **Douglas Brash**, and **Marcus Bosenberg** discover photochemistry in the dark phenomena showing UV damage to DNA long after sun exposure, and this delayed damage process could be prevented with the use of a specific agent.

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.

SCIRP Advances

- **Drs. Gregory Dekaban** and **Arthur Brown** develop and optimize anti-CD11d antibody therapy in a rat SCI model to reduce inflammation and improve neurological recovery.
- **Drs. Damien Pearse**, **Mary Bunge**, and **James Guest** obtain preliminary results of schwann cell implantation for spinal cord injury repair. The data allow for FDA approval to begin clinical safety trials in humans.
- **Drs. Gordon Mitchell**, **Gillian Muir**, and **Randy Trumbower**, through preliminary animal experiments, show that acute intermittent hypoxia combined with daily training elicits sustained improvement in limb motor function of treated animals with chronic cervical SCI.

TSCRP Advances

- **Dr. Angelique Bordey** generates a mouse model to study the embryonic development of cortical tuber lesions and shows that up-regulation of Hif1a transcriptional activity in newborn neurons promotes the growth and persistence of TSC lesions.
- **Dr. Brendan Manning** demonstrates that rapamycin treatment in combination with low-dose tunicamycin results in a cytotoxic response in TSC null cells.
- **Dr. Teresa Woods** determines that TSC is a critical upstream regulator of mTORC1 and mTORC2 in oligodendrocyte lineage cells.

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) is 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.*

ARP Advances

- **Dr. John Shoffner** discovers that a subgroup of children with a mitochondrial dysfunction are at risk of developing ASD after a high fever.
- **Dr. Nobuki Nakanishi** finds that memantine, a drug used in the treatment of Alzheimer's disease, can reverse autism-like characteristics in mice lacking one copy of the MEF2C gene.

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. Results demonstrate the potential for acupuncture treatment to provide symptom relief for ill Gulf War Veterans.
- **Dr. William Meggs** continues to enroll subjects in a crossover clinical trial of naltrexone and dextromethorphan to treat neuroinflammation and relieve GWI symptoms.

NFRP Advance

- **Dr. Nancy Ratner** provides evidence supporting clinical trials of MEK inhibitors for NF1 MPNSTs.

OCRP Advances

- **Dr. Christine Walsh** observes that a natural dietary phytochemical, indole-3-carbinol, sensitizes 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.
- **Dr. Brad Nelson** develops a new bioinformatics program for assembling high throughput sequence data and querying for the presence of single nucleotide variants (SNVs) in ovarian cancer.

PCRP Advances

- **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.
- **Dr. Paul Cho** develops an innovative system, incorporating fluoroscopy, ultrasound, and an advanced probe, that makes major improvements to the efficacy of prostate cancer brachytherapy.

PRMRP Advance

- **Dr. Gabrielle Gusella** discovers that knocking out Integrin beta 1 is an essential mediator of cyst formation in autosomal dominant polycystic kidney disease (ADPKD), identifying it as a potential target for the first therapeutic to treat ADPKD.

TSCRP Advances

- **Dr. Thomas Darling** shows that tranilast, an antiallergic and antifibrotic drug, has selective inhibitory effects on the viability of TSC skin tumor cells, indicating that it may be useful as an adjunctive agent for the treatment of TSC.
- **Dr. Kun-Liang Guan** identifies multiple regulators of the mTORC1 pathway and shows that cAMP elevation inhibits TORC1.

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 PH/TBIRP is established by a $301M appropriation.*
- *The PCRP sponsors its first IMPaCT conference.*

ALSRP Advance

- **Dr. Serge Przedborski** targets 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. Feng-Chun Yang** develops a mouse model of NF1 that displays similar skeletal manifestations as humans with NF1.
- **Dr. Karen Cichowski** establishes different mechanisms of NF1 inactivation occur in different tumors, which may result in changes in the tumor response to specific therapies.

OCRP Advances

- **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.
- **Drs. David Bowtell** and **Gillian Mitchell** find that 44% of the 141 women with nonmucinous ovarian tumors carrying BRCA1/2 mutations did not have a family history of ovarian cancer or breast cancer.

PCRP Advances

- **Dr. Karen Cichowski** discovers a key mechanism for the development of prostate cancer metastasis whereby the protein nuclear factor kB (NF-kB) is constitutively activated via loss of the protein disabled homolog 2 interacting protein (DAB2IP). DAB2IP expression and activity, which control cell signaling to NF-kB, 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 TMPRSSS2 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.

2007 cont.

PH/TBIRP Advances

- Two multidisciplinary research consortia, **Strong Star** and **Mission Connect**, are established to advance research in PTSD, and another multidisciplinary research consortium called INTRUST is established to conduct clinical trials in the areas of PTSD and TBI.
- **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 is 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 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.
- **Dr. Michael Vitek** measures the safety and toxicity of COG1410 in rats and dogs to form the basis of an Investigational New Drug 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.
- **Dr. Ismene Petrakis** demonstrates that prazosin, an alpha-1 adrenergic receptor antagonist, is an effective treatment for PTSD and co-morbid alcohol dependence.

CDMRP Milestones

- *The 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 Advances

- **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.
- **Drs. Lance Liotta** and **Kirsten Edmiston** discover a key role of autophagy in DCIS, leading to a Phase 1 neoadvjuvant clinical trial testing chloroquine to prevent progression to invasive breast cancer.
- **Dr. Leisha Emens** develops and conducts a clinical trial for a GM-CSF-secreting vaccine to treat breast cancer, showing efficacy and further potential for more clinical trials.

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.

NFRP Advance

- **Dr. Bruce Korf** and colleagues establish the NF Clinical Trials Consortium.

OCRP 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.

PCRP 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 docetaxel, 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.

2005

CDMRP Milestone

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

BCRP Advance

- Breast cancer advocates on a team led by **Dr. Pat Steeg** develop BrainMetsBC.org, an online resource that provides the latest information about brain metastases; available in English and Spanish.

NFRP Advances

- **Dr. Allan Belzberg** develops the tibial neuroma transposition animal model of neuroma pain and hyperalgesia associated with neuropathic pain.
- **Dr. Victor-Felix Mautner** demonstrates that imatinib mesylate (Gleevec®) inhibits Schwann cell viability and reduces the size of PNF in a xenograft model and reduces tumor volume of PNF fragments obtained from NF1 patients.
- **Dr. David Gutmann** developes a non-invasive technique to detect optic glioma in mouse model of NF1.
- **Dr. Marlan Hansen** demonstrates the ErbB2 signaling pathway is essential for vestibular schwannoma growth and an attractive therapeutic target.

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 approval, 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 and Phase 2 trials testing this antibody (MORAb-004) in a variety of cancers.

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 2013, accrues more than 3,500 prostate cancer patients to more than 80 Phase 1 and Phase 2 clinical trials studying more than 50 new drugs. The PCCTC rapidly advances nine therapeutic candidates to Phase 3 clinical testing, including abiraterone acetate (ZYTIGA), enzalutamide (XTANDI), and radium-223 chloride (Xofigo), each 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 on the surface of prostate cells. The radiotracers were later commercialized and are now in Phase 1 clinical trials to significantly improve imaging for patients with 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, offering reduced fluid volume while maintaining effective arterial pressure and neuroprotection compared to lactated Ringer's or hypertonic saline solutions.
- **Dr. Roy Bloebaum** develops an osseointegrated device that allows direct skeletal attachment of prostheses to amputated limbs and demonstrates load-bearing ability and lack of infection for up to 12 months in a animal model. An early feasibility study with human implants is now being implemented.

TSCRP Advance

- **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.

CDMRP Milestone

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

BCRP Advance

- **Dr. Dennis Slamon** discovers estrogen-receptor-positive breast cancer is sensitive to CDK inhibitor PD-0332991; now in Phase 3 clinical trials with Pfizer.

NFRP Advances

- **Dr. Karen Cichowski** identifies a negative feedback signaling pathway that protects benign lesions from becoming malignant in patients with NF.
- **Dr. Feng-Chun Yang** demonstrates that the growth factor TGF-beta secreted from mast cells plays a critical role in the initiation and progression of neurofibromas.

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 the blocks activation of androgen receptors. The synthetic version, EPI-001, shrinks prostate tumors without toxicity in animal models, and shows promise for greater efficacy than currently available therapies.

TSCRP Advance

- **Dr. Steven Sparagana** develops a clinical database that documents the natural history and variability of TSC which is currently managed by TS Alliance with 1,187 people enrolled as of March 2013.

BCRP Advances

- **Dr. Mary (Nora) Disis** develops a HER2 peptide-based vaccine that, when administered with trastuzumab, elicits robust immune response. The vaccine has been licensed for commercial development.
- **Dr. Edward Newman** conducts preclinical studies on fluorodeoxycytidine, a drug to reverse DNA methylation in breast cancer cells, which leads to Phase 2 clinical trials.

NFRP Advance

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

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** makes the key discovery that castration-recurrent prostate cancer results from an inflammatory response involving lymphotoxin and NF-kB, opening new opportunities for targeted therapies for advanced disease.

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.

TSCRP Advances

- **Dr. Bernardo Sabatini** conducts studies that show that the 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.

CDMRP Milestones

- *The National Prion Research Program is established by a $42.5M appropriation.*
- *The Chronic Myelogenous Leukemia Research Program is established by a $5M appropriation.*
- *The Tuberous Sclerosis Complex Research Program (TSCRP) 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), 119–36.*
- *The CDMRP publishes "Department of Defense Congressionally Directed Medical Research Programs: Innovations in the federal funding of biomedical research," Clinical Cancer Research, 8(4), 957–62.*
- *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), 379–88.*

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.
- **Dr. Ben Seon** develops and tests TRC105, an anti-endoglin monoclonal antibody that inhibits angiogenesis and is now in Phase 2 clinical trials.

NFRP Advances

- **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.
- **Dr. Karen Cichowski** demonstrates that neurofibromin regulates the mTOR pathway, through activated Ras.

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.

PCRP Advances

- **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 ultimately recruits over 2,500 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.
- **Dr. David Curiel** invents a method to enhance gene therapy for prostate cancer by genetically modifying the cell surface receptor CAR. The enhanced therapeutic approach has now entered Phase 1 clinical trials.

PRMRP Advances

- **Dr. Barbara Soller** develops CareGuide™, a portable sensor system that noninvasively measures 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 telediagnosis.
- **Dr. Mark Horwitz** develops a novel tularemia vaccine against aerosolized *F. tularensis* bacteria and shows in animal tests that it is less virulent and more efficacious than the available, relatively toxic vaccine.

TSCRP Advance

- **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.

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.
- **Dr. Bing Xia** with **Dr. David Livingston** discovers PALB2, a BRCA2 binding protein. PALB2 mutations increase risk of breast cancer. A commercialized test is now available.

NFRP Advances

- **Dr. Kevin Shannon** develops mouse models of MPNSTs, PNF, astrocytomas, and ependymomas for assessing the mutagenic potential of NF1 tumor therapies.
- **Dr. Alcino Silva** demonstrates that lovastatin treatment reverses learning deficits in a Nf1 mouse model.

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.

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 and completes first clinical testing of OGX-011, 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.

CDMRP Milestones

- *The CDMRP offers the first electronic application submission.*
- *The BCRP sponsors its second Era of Hope conference.*
- *The Ovarian Cancer Research Program (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 Advances

- **Dr. William Slattery III** characterizes growth rates and clinical course of tumors associated with NF2.
- **Dr. Margaret Wallace** demonstrates that steroid hormones can significantly affect the growth of NF1 tumor cells.

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 gene is significantly associated with protection against endometrioid ovarian cancer.

PCRP Advance

- **Dr. David Jaffray** and colleagues develop cone-beam computed tomography with a flat-panel imager that later revolutionizes image-guided radiotherapy as the Elekta Synergy system, FDA-cleared in 2003 and now used to treat prostate and other cancers in over 3,500 U.S. hospitals.

CDMRP Milestone

- *The 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 Advances

- **Dr. Kathryn North** establishes that MRI T2 hyperintensities measured in children with NF1 are a good predictor of cognitive dysfunction in adulthood.
- **Dr. Karen Stephens** uses MRI to detect schwannomas in a transgenic mouse model of NF2.

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 increases sensitivity to cisplatin treatment. Her research is among the first to indicate novel, extra-telomeric functions of telomerase.

PCRP 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, diethyltoluamide, and permethrin bromide, suggested as a cause of GWI, does not adversely impact physical or cognitive performance.

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.

NFRP Advance

- **Dr. Andrea McClatchey** provides insight into the function of the NF2 (merlin) protein, which acts as a tumor and metastasis suppressor by controlling cell-cell contact.

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.

CDMRP Milestones

- *The PCRP is established by a $45M appropriation.*
- *The 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 Advances

- **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.
- Research by **Dr. Laurie Fajardo** and **Dr. Daniel Kopans** advances digital mammography and leads to development of a digital breast tomosynthesis system now FDA approved and commercialized for clinical use.

NFRP Advances

- **Dr. Bruce Korf** studies the natural history of NF1 plexiform neurofibromas and establishes volumetric MRI as the standard approach for measuring these tumors in clinical trials.
- **Dr. William Slattery III** establishes a consortium of nine international sites to study natural history of NF2 and develops standard operating procedures for MRIs and a NF2-specific database.

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 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 an APC-100 derivative, APC-110, begin in 2011.

CDMRP Milestone

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

NFRP Advances

- **Dr. Margaret Wallace** identifies that the loss of neurofibromin is associated with tumorigenesis.
- **Dr. Mia MacCollin** establishes associations between types of NF2 mutations and clinical features; also developes novel methods for detecting NF2 mutations.
- **Dr. Tyler Jacks** developes the first mouse model of NF1-related MPNSTs.
- **Dr. Luis Parada** characterizes loss of Nf1 in various cell types and demonstrates that loss of Nf1 in the Schwann cell lineage was sufficient to generate tumors.

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.*

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.
- **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 in 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 Milestone

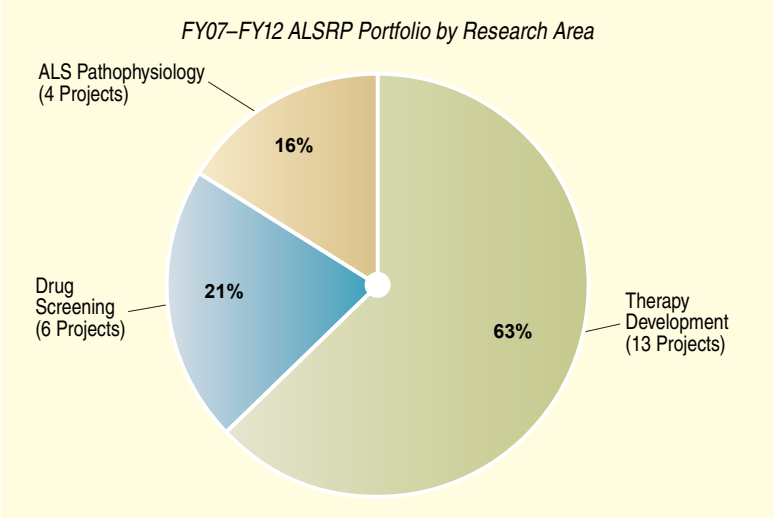
- *$25M appropriated to the BCRP for research on breast cancer screening and diagnosis for military women and their family members.*

Programs

In FY12–FY13, the CDMRP managed or executed 19 research programs. While the programs within the CDMRP share many common features, each program is unique and emphasizes the specific needs of its research and advocacy communities. Highlights of these programs are detailed on the following two-page spreads throughout the remainder of this section.

Amyotrophic Lateral Sclerosis Research Program

Background and Program History



Amyotrophic Lateral Sclerosis (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 years, and about 10% of patients with ALS live more than 10 years after diagnosis.[1] 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 well understood.[2]

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 $39M, including $7.5M in FY13.

[1,2] ALS Association

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

Nicholas Maragakis, M.D., Johns Hopkins University

ALS is a degenerative disease affecting the upper and lower motor neurons in the brainstem and spinal cord. A recent development in stem cell technology called induced pluripotent stem cells (iPSCs) is helping scientists understand the abnormalities in the cell biology behind ALS. iPSCs start as skin cells harvested from an ALS patient that are re-programmed in culture (through exposure to certain transcription factors), first into stem cells that have the capacity to become any type of cell, and then differentiated into glial-restricted precursor cells ([iPSC]-GRPs). Evidence suggests that glial cells, non-neuronal support cells of the nervous system, including astrocytes, could play a central role in inhibiting the neurodegeneration of ALS. These cells may ultimately be transplanted into patients to treat ALS.

continued on next page

Using funding from an FY09 ALS Research Program Therapeutic Development Award, Dr. Nicholas Maragakis of Johns Hopkins is initiating pre-clinical studies of iPSC-GRPs both in culture and transplanted into animals to test their therapeutic potential. Dr. Maragakis will examine whether human iPSC-GRPs derived from either sporadic ALS (sALS), familial SOD1-mediated ALS (fALS), or normal control subjects have the capacity for neuroprotection following transplantation. By comparing normal iPSC-GRPs with sALS iPSC-GRPs and fALS iPSC-GRPs, Dr. Maragakis hopes to reveal inherent differences in astrocyte biology related to ALS, providing potential insight into ALS disease mechanisms.

This assessment will be coupled with studies of iPSC-GRP cells transplanted in normal and ALS mutant (SOD1-G93A) rats. Survival, differentiation, and other properties of the cells will be examined across the different cell types.

Thus far in the study, fibroblast cultures have been developed from ALS patients and iPSC-GRP cell lines have been established. Initial transplantation efforts in normal rats have been successful, with transplantation into ALS mutant rats pending.

The results of this study could represent the initial development of a viable autologous cell therapy for ALS patients.

Rethinking Drug Treatment Approaches in ALS by Targeting ABC Efflux Transporters

Piera Pasinelli, Ph.D., Thomas Jefferson University

Despite numerous efforts at pharmacological approaches to treat ALS, only one drug, riluzole, is currently available and its impact on the disease is limited. Dr. Piera Pasinelli is using an FY10 ALSRP Therapeutic Development Award to investigate disease-driven pharmacoresistance mediated by ABC drug efflux transporters, a mechanism that may impede drug effectiveness. These transporters actively pump out "foreign" substances from the central nervous system, including drugs like riluzole.

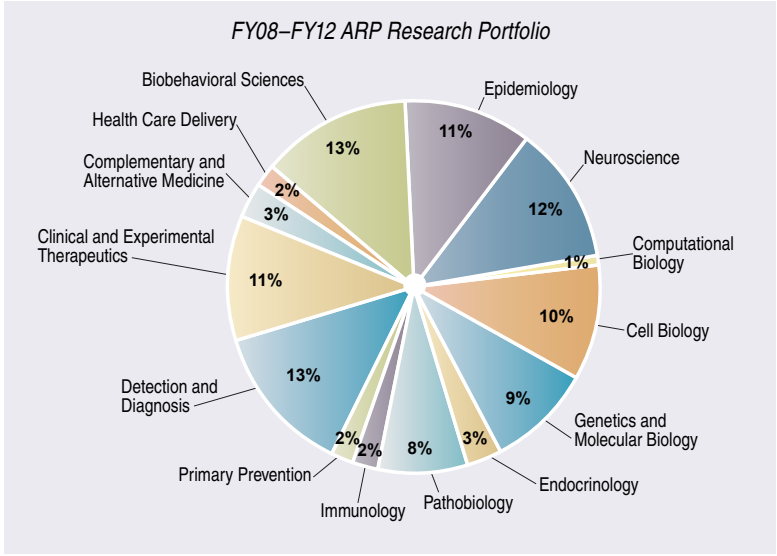
Dr. Pasinelli proposes to counter the ABC transporter's activity with an inhibitor, elacridar, that could be co-administered with riluzole to "open the door" for improved activity by the known drug. In the early stages of the award, Dr. Pasinelli is confirming an effective, non-toxic dose and delivery route for elacridar in an animal model of ALS (SOD1-G93A). In addition, a reliable method of riluzole administration must be developed. Riluzole administration will begin at symptom onset in an attempt to better translate the effects of this treatment (and combined elacridar treatment) to the human ALS patient population. Initial testing of riluzole administration confirmed its ability to improve survival in SOD1-G93A animals. Methods are now being optimized to measure riluzole bioavailability in the blood and central nervous system of the test animals using mass spectrometry.

Initial results of the project have been positive, and it is hoped that this new approach will enhance the effectiveness of riluzole as well as provide a mechanism to improve the action of other potential pharmacotherapies. Dr. Pasinelli is optimistic that, if proven effective, this treatment can move quickly into clinical application to help those suffering with ALS.

Autism Research Program

Background and Program History

With the alarming increase in the reported incidence of Autism Spectrum Disorder (ASD), Congress has answered the concerned call of parents and advocates to appropriate funds for the DoD Autism Research Program (ARP). Recent reports indicate that as many as 1 in 50 children may be identified as living with ASD, and boys are four times more likely than girls to be autistic. Since its inception in FY07 through FY13, appropriations totaling $47.4M have been directed to the ARP to promote innovative research that advances the understanding of ASD and to improve outcomes. 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 last five 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 the future. The ARP is committed to the Vision and Mission and collaborates with other agencies, both federal and non-federal, to ensure the best possible investment of limited funds to advance ASD research and assist in the lives of all affected by ASD.



Ann Gibbons, J.D., Autism Speaks, IP member

"It has been my privilege to serve both as a consumer reviewer and a member of the Integration Panel for the Autism Research Program. I am most deeply affected by the sincerity and commitment of the researchers I've met who want to unravel the mystery of autism. As a mom, my mission was chosen for me; it is an honor to have these brilliant, caring professionals adopt my cause as their own."

Stephen R. Dager, M.D., University of Washington School of Medicine, FY12–FY13 IP Chair

"The DoD's Congressionally Directed Medical Research Program on Autism provides a unique forum for parents of affected children and scientists working together to support and encourage innovative research. An emphasis of the panel has been to fund research that holds promise for timely advances that directly and positively impact the lives of affected individuals and their families. Having participated on the Vision and Integration Panel since its inception, I have been gratified by the very high quality of science supported by this 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

Achievements

Drs. Ascherio, Santangelo, and Weisskopf *determined gestational diabetes, maternal exposure to air pollutants during pregnancy to be risk factors for autism.*

Drs. Noble, James, and Hepel *developed analytical platforms for oxidative stress; determined that ASD children have a more oxidized microenvironment; and found ASD children to be more vulnerable to oxidative stress and inflammation.*

Drs. Wegiel, Wisniewski, and Chauhan *observed enhanced Aβ deposition in ASD brains.*

Dr. Mandell *determined ASD in adult psychiatric hospitals to be under-diagnosed.*

Dr. Shoffner *demonstrated that fever plus mitochondrial disease are risk factors for autistic regression.*

Dr. Ingersoll *developed an internet-based parent training program for caregivers of children with ASD.*

Dr. Roth *discovered a class of medications that could reverse the genetic defect associated with autistic-like disorder in neurons.*

Dr. Platt *determined the neurophysiological mechanisms that mediate social function and impact of intranasal Oxytocin on social function*

Dr. Patterson *demonstrated maternal immune activation during pregnancy lead to increased risk of offspring with ASD.*

Dr. Kimchi *developed a video and radio frequency identification system-based platform capable of automatically identifying and quantifying a wide range of animal behaviors. Such device is useful for conducting animal behavioral studies.*

Drs. Cox and Brown *develop a virtual reality system with eye tracking to enhance the driving skills of teenagers with ASD.*

Craig Powell, M.D., Ph.D., University of Texas Southwestern Medical Center, Incoming FY14-15 IP Chair

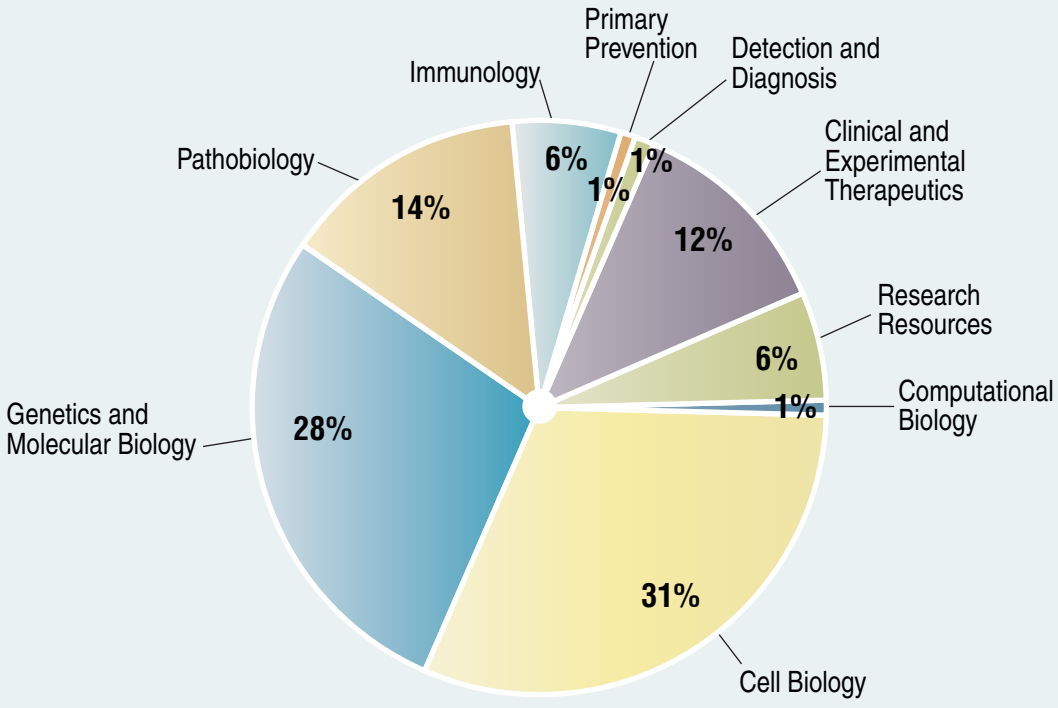
"In my years of involvement with the DoD Autism Research Program, I find it to be a unique venue where all points of view are respected and considered in the funding of autism research. This is a program in which affected individuals, families, and other advocates have made an impact and are involved at every level. I am proud to serve as chair of the DoD ARP IP and look forward to guiding the funding of research that fulfills the vision of making a difference across the spectrum . . . now."

Bone Marrow Failure Research Program

Background and Program History

Bone marrow failure research funding was initiated by Congress in FY08 with an appropriation of $1M. With continued appropriations, the Bone Marrow Failure Research Program (BMFRP) has been established, and is executed and managed by the CDMRP. From FY08 through FY12, $16.95M has been designated by Congress for bone marrow failure research with another $3.2M appropriated in FY13. The BMFRP encourages ingenuity and invention in research through funding innovative studies that are high risk but with the opportunity for high gain and impact. 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. The syndromes of bone marrow failure are considered rare conditions with high mortality and morbidity. Bone marrow failure can be inherited or acquired and lead to hematological diseases as well as effects on other biological systems, for example the dermatological, gastrointestinal, and/or cardiac systems. Some of the inherited forms of bone marrow failure include Fanconi anemia, dyskeratosis congenita, Shwachman-Diamond syndrome, and Diamond-Blackfan anemia. Acquired bone marrow failure diseases include aplastic anemia, myelodysplasia, paroxysmal nocturnal hemoglobinuria, and pure red cell aplasia. Exposures to viruses, medical treatments (e.g. radiation or chemotherapy), or chemical or environmental toxins (a risk for service members) may lead to acquired bone marrow failure. Additionally, bone marrow failure patients have a higher risk of developing blood cancers and solid tumors. The choice of treatment for bone marrow failure 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–FY12 BMFRP Research Portfolio



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 diseases, thereby improving the health of affected individuals, with the ultimate goals of prevention and cure

Lisa Minter, Ph.D., University of Massachusetts/Amherst

"I consider working alongside my colleagues on the CDMRP Bone Marrow Failure Research Program's Integration Panel to be a true privilege. Participating on this panel allows me to look into the very promising future of bone marrow failure research and provides me with the opportunity to play a small part in shaping that future. It gives me great hope for patients faced with the challenges of bone marrow failure, that here will be brighter days ahead."

Achievements and Outcomes

Dr. Bertuch *discovered three novel truncating TINF2 mutations causing severe dyskeratosis congenita in early childhood.*

Dr. Verma *demonstrated quantitative and qualitative alterations in myelodysplastic syndrome (MDS) stem cells and their persistence during clinical remissions.*

Dr. Lin *uncovered an immune tolerance mechanism that protects hematopoietic stem/progenitor cells (HSPC) in the bone marrow niche. For more information, see the highlight at our webpage: http://cdmrp.army.mil/bmfrp/highlights/13lin_highlight.*

Dr. Cancelas *demonstrated intracellular communications of hematopoietic stem cells (HSC) with bone marrow mesenchymal stem cells is crucial to protect HSC from ROS-dependent senescence and damage. He also demonstrated that the combination of Fanconi Anemia-A hematopoiesis and niche Cx43 deficiency synergistically impair hematopoiesis development.*

Dr. Starczynowski *showed 1) TNF receptor associated factor-interacting protein with a forkhead-associated domain B (TIFAB) is primarily expressed in hematopoietic progenitor cells; 2) knockdown of TIFAB results in increased survival and altered hematopoietic progenitor function; 3) TIFAB inhibits TRAF6 expression and lowers NF-kB activation; 4) TIFAB expression affects leukemic cell survival.*

Dr. Park *characterized the expression of more than 750 microRNAs in MDS HSC purified from MDS patient samples.*

Dr. Wang *identified a fraction of embryonic stem cell extracts containing immunomodulatory capacity; identified milk fat globule-EGF factor 8 to be an immunomodulatory protein.*

Dr. de Figueiredo *showed the FDA-approved histone deacetylase inhibitors can ameliorate the growth and proliferation defects of CD34+ cells.*

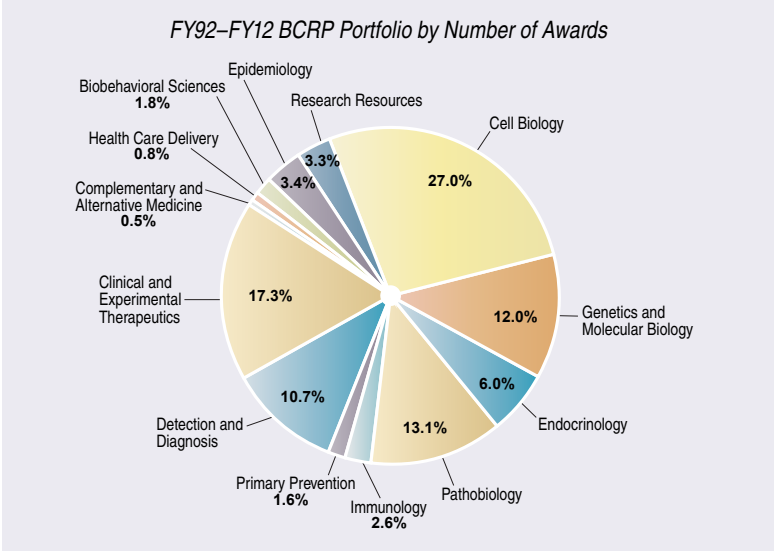
Dr. Hand *demonstrated that EPO-mimetic peptide decreased mortality associated with bone marrow failure.*

Dr. Zhang *determined a balanced TGFβ-activated kinase 1 (Tak1) activity is critical for maintaining the HSPCs. Down-regulation of Tak1 activity promotes the death of HSPCs through necroptosis, where up-regulation of Tak1 activity promotes apoptosis in HSPCs.*

Breast Cancer Research Program

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 dedicated efforts of breast cancer advocates. Their continued efforts, in concert with the program's successes, have resulted in more than $2.9B in congressional appropriations through FY13. The BCRP enables researchers 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 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.



BCRP-Funded Breakthroughs

Research supported by the BCRP has led to many discoveries that have transformed breast cancer research or resulted in clinical breakthroughs for breast cancer patients. A sampling is shown below.

Clinical Breakthroughs

Trastuzumab: Characterization of this monoclonal antibody led to 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. (PI: Kathryn Verbanac)

ATLAS Clinical Trial: Data analysis indicates that the rate of recurrence or death was reduced in women who took tamoxifen for 10 years vs. 5 years; follow-up phase is through 2015. (PI: Richard Peto)

Genetic Discoveries

PTEN Tumor Suppressor Gene: Discovery of this frequently mutated oncogene enabled development of a genetic test used for clinical diagnosis. (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, Susan Neuhausen)

PALB2 mutations: Discovery of PALB2, a BRCA2-binding protein, led to identification of mutations that account for some familial breast cancers. (PI: Bing Xia)

Technology Development

Digital Breast Tomosynthesis: Clinical validation of digital mammography for cancer detection in dense breast tissue led to development and clinical evaluation of digital breast tomosynthesis. (PIs: Laurie Fajardo, Daniel Kopans)

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

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

Vision

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

Laurel Macartney, BCRP Consumer Reviewer

"As I continue my own fight, I hold onto the hope that the DoD BCRP will eventually find cures and preventions. Intellectually, I understand the reality of my personal journey, but I know that the process of supporting innovative scientific inquiries, with a specific goal, will eventually keep the five beautiful women in my family from having to follow my climb."

Many discoveries initially supported by the BCRP have advanced innovations into the clinical pipeline, including the following examples.

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)

PD-0332991: Discovery that ER-positive breast cancer is sensitive to this CDK inhibitor and that combined treatment with letrozole improves progression-free survival led to FDA "Breakthrough Therapy" status and a current Phase 3 clinical trial supported by Pfizer. (PI: Dennis Slamon)

HER2 Bi-Armed Activated T-Cells: Discovery that these cells stimulate an immune response against HER2 led 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 a Phase 2 clinical trial. (PI: George Prendergast)

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

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

MM-111 Antibody: This bispecific antibody capable of simultaneously engaging HER2 and HER3 receptors is in early phase clinical trials for HER2+ advanced breast cancer. (PI: Gregory Adams)

GM-CSF-Secreting Vaccine: Advanced development of this therapeutic vaccine and clinical testing of its efficacy in breast cancer led to a current Phase 2 clinical trial. (PI: Leisha Emens)

Targeting Autophagy: Discovery that autophagy may play a role in emergence of DCIS progenitor cells led to a current Phase 2 clinical trial using chloroquine to prevent progression of DCIS to invasive breast cancer. (PIs: Lance Liotta and Kirsten Edmiston)

HER2 Peptide-Based Vaccine: Development of a therapeutic vaccine against HER2 led to a Phase 2 clinical trial that demonstrated efficacy in combination with trastuzumab; now licensed commercially for further investigation. (PI: Mary Disis)

Molecular Breast Imaging (MBI): Evaluation of this nuclear medicine technique and advances in its software technology led to two FDA-approved MBI units. (PI: Carrie Hruska)

TRC105 Antibody: Development and preclinical studies of this monoclonal antibody, which targets endoglin and inhibits angiogenesis, led to current early phase clinical trials. (PI: Ben Seon)

Fluorodeoxycytidine (FdCyd): Preclinical studies on FdCyd reversal of DNA methylation in breast cancer cells led to a current Phase 2 clinical trial. (PI: Edward Newman)

Breast Cancer Research Semipostal Program

Background and Program History

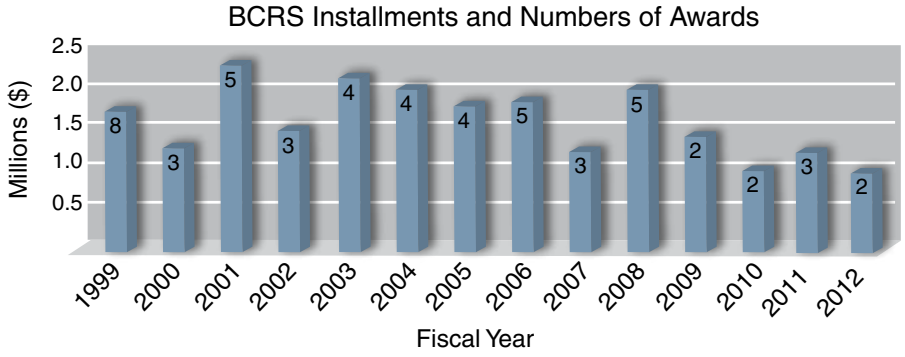
As a result of the efforts of breast cancer advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the U.S. Postal Service's issuance of a new first-class stamp, the Breast Cancer Research Semipostal (BCRS) in 1998. Net revenues from sales of the BCRS, which costs 55 cents, are provided to two designated funding agencies, the DoD BCRP and the 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 between FY99 and FY12 has been used to fully or partially fund 50 Idea Awards and 3 Synergistic Idea Awards. 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	$23,106,942.91
Research	$21,451,770.31
Management Costs	$1,053,605.60

Note: Funds yet to be allocated—$601,567



Andy Minn

Roger Greenberg

Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements

Andy Minn, M.D., and Roger Greenberg, Ph.D., University of Pennsylvania
FY11 Idea Award

Transposable elements (TEs) are small pieces of DNA that have the ability to move within the genome and are often referred to as "jumping genes." Although TEs are normally repressed and silenced, recent sequencing of cancer genomes has revealed aberrant expression of TEs, suggesting that failure to properly silence TEs may be an important property that drives cancer-associated pathways. Drs. Minn and Greenberg are studying how the inappropriate transcription of TEs might influence responsiveness to chemotherapy and radiation, and how this may lead to breast cancer progression. They are exploring how nontraditional genes may be the basis for predicting response to therapeutics.

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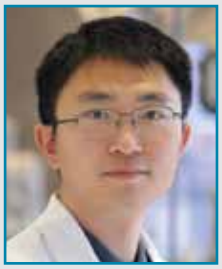
In the short term, this research may lead to the identification of novel pathways that regulate breast cancer metastasis and response to therapy. In the long term, such pathways may reveal new biomarkers and therapeutic targets that are based on the biology of largely underexplored parts of the human genome.

The partnership between Drs. Minn and Greenberg arose as a result of basic findings from each of their laboratories. The Minn group had been characterizing gene signatures for metastasis and treatment resistance with an emphasis on the signaling events in the cell cytoplasm that can regulate these genes. The Greenberg laboratory had identified novel events that involve silencing of repetitive DNA regions after the DNA damage response. These complementary interests naturally led to a synergistic collaboration exploring novel mechanisms of breast cancer metastasis and response to DNA damaging agents.

Of this research, Drs. Minn and Greenberg have noted, "An important strength of collaborative science is that it brings together seemingly unrelated research interests to explore novel connections. However, exploring these types of ideas is often deemed high-risk, and they prove difficult to get funded. BCRP funding has enabled us to take this higher risk approach with the hope of accelerating breakthroughs."



Xiaosong Wang

Rachel Schiff

Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer

Xiaosong Wang, M.D., and Rachel Schiff, Ph.D., Baylor College of Medicine
FY11 Idea Award

Gene fusions are genetic abnormalities resulting from chromosome translocations in which pieces of two unrelated genes are fused together. Gene fusions have an important role in tumor initiation in many types of cancer and provide specific targets for therapeutic design.

Drs. Wang and Schiff received an Idea Award to identify and investigate new therapeutic targets revealed by a novel bioinformatics analysis called "fusion copy number signature analysis." Using this integrative bioinformatics strategy, the investigators linked several publically available genomic, molecular, and pharmacologic datasets and nominated Nemo-like kinase (NLK) as a candidate target. They found that NLK promotes endocrine resistance in a subset of breast tumors and may be a new drug target in tumors with deregulation of this pathway by either overexpression or gene fusion. About half of breast cancer patients treated with targeted endocrine therapy will eventually relapse with therapy-resistant disease; therefore, new drugs to overcome endocrine resistance are urgently needed.

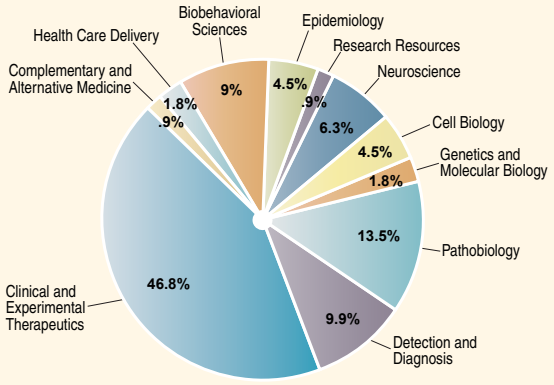
Targeted therapies are designed to attack tumors based on the molecular characteristics of the cancerous cells. The long-term goal of Drs. Wang and Schiff is to move their laboratory discoveries to the bedside and, ultimately, contribute to the goal of ending breast cancer. A potent inhibitor of NLK is currently in clinical trials for treating other diseases. If targeting NLK is validated in Dr. Schiff"s breast cancer therapeutic models, then this type of treatment could be tested for its ability to prevent or overcome endocrine resistance. Breast tumor types exhibiting hyperactive NLK signaling could benefit from NLK-targeted adjuvant therapy.

Defense Medical Research and Development Program

Background and Program History

CDMRP provides operational execution management support for the OASD(HA) Defense Medical Research and Development Program (DMRDP). The DMRDP was established in FY10 under the Defense Health Program and continues to date. The DMRDP is focused on advancing the state of medical science in those areas of most pressing need and relevance to today's battlefield experience. The objectives of the DMRDP are to discover and explore innovative approaches to protect, support, and advance the health and welfare of military personnel, families, and communities; to accelerate the transition of medical technologies into deployed products; and to accelerate the translation of advances in knowledge into new standards of care for injury prevention, treatment of casualties, rehabilitation, and training systems that can be applied in theater or in the clinical facilities of the Military Health System. Additional information on the DMRDP is available at http://dmrdp.fhpr.osd.mil.

DMRDP FY10–FY12 Portfolio by Research Area



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 are:

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

Terry Rauch, Ph.D., 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 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."

Each of these major research program areas is managed by a committee, called a Joint Program Committee, or JPC, which consists of DoD and non-DoD medical and military technical experts. Within the USAMRMC, operational support responsibility is managed by two primary execution agents, the CDMRP and the Telemedicine and Advanced Technology Research Center.

CDMRP Portfolio Execution Assignments

From FY10 through FY12, the CDMRP has executed $190.31M in support of the DMRDP, funding basic through translational 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 (including PTSD), polytrauma and blast injury, wound infection, blood products and safety, operational health and performance, and device development.

Mission

The CDMRP strives to provide full life-cycle operational management support to the Defense Medical Research and Development Program, a core Department of Defense research program within the Office of the Assistant Secretary of Defense for Health Affairs

Research to Advance and Accelerate

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 of CDMRP-managed DMRDP projects grouped by key program research areas.

Military Infectious Diseases Research Program (MIDRP, JPC-2)

Wound Infection Prevention and Management

- *Rapid Screen for Bloodborne Pathogens; Eli Glezer, Ph.D., Meso Scale Diagnostics, LLC.*

Antimicrobial Countermeasures

- *Isolation of Microbial-Derived Compounds for Mitigating Drug-Resistant Bacteria Associated With Battlefield Wound Infections; Daniel Kadouri, Ph.D., University of Medicine and Dentistry of New Jersey, Newark*

Development of vaccines, drugs, diagnostics and vector control

- *Development of Novel Kinocidin-Based Anti-Infective Therapeutics; Michael Yeaman, Ph.D., Los Angeles Biomedical Research Institute*
- *Biologically Active Advanced Antimicrobial Human Skin Substitute for the Treatment of Combat Wounds; B. Lynn Allen-Hoffman, Ph.D., Stratatech Corporation*

Combat Casualty Care Research Program (CCCRP, JPC-6)

Traumatic Brain Injury

- *Tau Accumulation in TBI: Mechanisms and Treatment; Douglas Smith, M.D., University of Pennsylvania*

Forward Surgical/Intensive Care

- *Vibration and Shock Exposure Limits for Transport of the Acute Spinal Cord Injured; Peter Cripton, Ph.D., University of British Columbia*

Hemorrhage and Resuscitation

- *A Biophysical Plasma Volume Expander that Treats Traumatic Brain Injury; Bashir Zikria, M.D., Biophyzica, Inc.*

Treatments for Tissue Injury

- *Effects of Enhanced Oxygen Delivery by Perfluorocarbons in Spinal Cord Injury; Bruce Mathern, M.D., Virginia Commonwealth University*

Military Operational Medicine Research Program (MOMRP, JPC-5)

Psychological Health and Resilience, including Post-traumatic Stress Disorder

- *Novel Treatment of Emotional Dysfunction in PTSD; John Hart, M.D., University of Texas at Dallas*
- *Clinical Effectiveness Trial of in-Home Cognitive Processing Therapy for Combat-Related PTSD; Patricia Resick, Ph.D., VA Boston Healthcare System and Alan Peterson, Ph.D., University of Texas Health Science Center at San Antonio*

Injury Prevention and Reduction

- *Phase III Clinical Trials: D-Methionine to Reduce Noise-Induced Hearing Loss; Kathleen Campbell, Ph.D., Southern Illinois University*

Physiological Health

- *Psychophysiology of Delayed Extinction and Reconsolidation in Humans; Scott Orr, Ph.D., Massachusetts General Hospital*

Environmental Health and Protection

Clinical and Rehabilitative Medicine Research Program (CRMRP, JPC-8)

Neuromusculoskeletal Injury Rehabilitation

- *Improved Training Method for Rapid Rehabilitation of Amputees; Kenton Kaufman, Ph.D., Mayo Clinic and Foundation, Rochester*

Pain Management

- *Chronic Pain Management with Novel, Potent Analgesics; James Zadina, Ph.D., Tulane University*

Regeneration

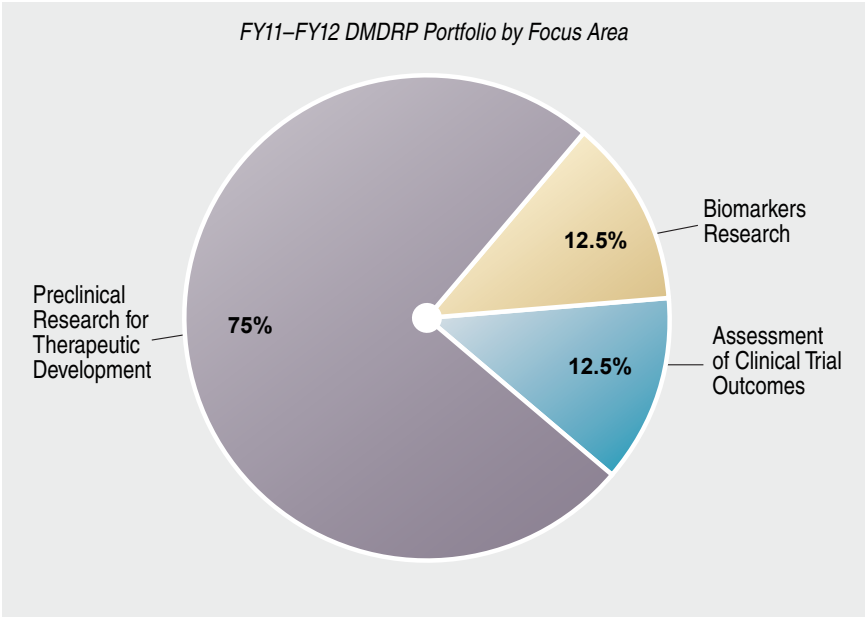
- *Nanofiber Nerve Guide for Peripheral Nerve Repair and Regeneration; Ahmet Hoke, M.D., Ph.D., Johns Hopkins University*

Sensory System Restoration

- *Diagnosis and Treatment of Blast-Induced Hearing Loss; John Oghalai, M.D., Stanford University*

Duchenne Muscular Dystrophy Research Program

Background and Program History



The Duchenne Muscular Dystrophy Research Program (DMDRP) was established in FY11 as a result of the passionate and tireless efforts of DMD advocates. The initial congressional appropriation for DMDRP was $4M, followed by appropriations of $3.2M for FY12 and FY13, for a total of $10.4M. Over the past several years research has identified many new potential therapeutic targets as well as significantly expanded the number of potential therapeutics in the pipeline for DMD. In order to assist in the development of treatments for DMD, the DMDRP has focused on accelerating promising therapeutic ideas into clinical applications and supporting training of new physician researchers to facilitate their pursuit of careers in DMD research. Duchenne muscular dystrophy affects approximately 1 out of every 3,500 male infants (about 20,000 new cases a year). This form of muscular dystrophy results from mutations in the dystrophin gene, which leads to an absence of dystrophin in muscle cells and thus allows these cells to be easily damaged. Boys living with DMD experience devastating muscle weakness that affects the skeletal muscles, heart, and respiratory muscles. Symptoms of DMD typically develop prior to age 5, and by age 12 most patients are confined to a wheelchair. Young men with DMD rarely live beyond their early 30s. A much milder version of DMD is Becker muscular dystrophy (BMD). The onset of BMD usually occurs in the teens or in early adulthood, and the course of the disease is slower and less predictable than for DMD.

Debra Miller, FY13 IP Member

"DMDRP brings valuable resources as we fight for the lives of our sons with Duchenne. The expertise and funding it provides will lead to better treatments and care for children and young adults that are afflicted with this progressive and fatal disease. One in 3,500 boys is born with Duchenne, and it can occur in any family, with no prior history of the disease. As a mother of a Duchenne boy and also as the founder of CureDuchenne, I am extremely appreciative for the hope that the DMDRP brings to our community."

Vision

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

Mission

To better inform the development of drugs, devices, and other interventions and promote their effective clinical testing

FY12 Award Highlights

A Read-Through Drug for Duchenne Muscular Dystrophy

Carmen Bertoni, Ph.D., University of California, Los Angeles

Objective: Determine the therapeutic potential of Read-Through compound-13 (RTC13) derivatives that target and rescue dystrophin. This project will focus on optimizing the viability, pharmacokinetics, and biodistribution of lead RTC13 derivatives that are administered orally followed by assessment of efficacy, tolerability, and safety studies.

Long-term goal: Establish parameters for predicting the clinical outcome of different therapeutic strategies and clinical applicability of RT technologies to the treatment of DMD patients.

Advanced Gene Therapy for Treatment of Cardiomyopathy and Respiratory Insufficiency in Duchenne Muscular Dystrophy

Barry Byrne, M.D., Ph.D., University of Florida

Objective: Develop and evaluate a novel gene therapy approach to restore dystrophin levels in DMD patients by using intrapleural administrations of a Herpes Simplex virus type I system (HSV) derivied rAAV serotype9 (HSV-rAAv9) vector encoding a codon-optimized mini dystrophin gene in the golden retriever muscular dystrophy (GRMD) model. Both cardiac and respiratory outcome measures in the GRMD model will be evaluated.

Long-term goal: To develop highly effective transmission and large-scale quantities of AAV vector necessary to move gene therapies from small clinical trials into clinical practice.

Optimization of Renin-Angiotensin-Aldosterone Inhibitors as a Treatment for Duchenne Muscular Dystrophy

Jill Rafael-Fortney, Ph.D., Ohio State University

Objective: Determine what combination of renin-angiotensin-aldosterone (RAA) pathway inhibitors including angiotensin converting enzyme inhibitors and non-specific mineralocorticoid receptor antagonists show the greatest improvement in dystrophic limb skeletal muscles, respiratory muscles, and heart. Molecular markers will be defined on the optimal treatment combinations that can then be translated into clinical biomarkers for DMD patients.

Long-term goal: Develop more refined therapeutics with combination RAA inhibitor therapies that will provide improved mobility and longevity for the entire DMD patient population.

Preclinical Testing of a Novel Method to Block TGFbeta Family Proteins in DMD

Elizabeth McNally, M.D., Ph.D., University of Chicago

Objective: LTBP4 stabilizes the plasma membrane and reduces muscle fibrosis by binding and sequestering TGFβ, a mediator of tissue injury and repair. This project will conduct in vivo studies to determine whether using anti-LTBP4 antibodies to block proteolysis of LTBP4 and release of TGFβ is effective in stabilizing muscle and reducing fibrosis in DMD.

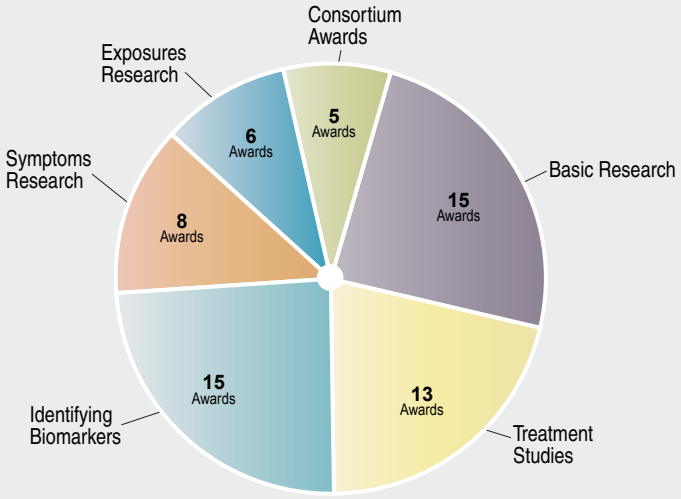
Long-term goal: Develop a humanized monoclonal antibody-based therapy that targets LTBP4 and inhibits TGFβ for clinical trials in DMD patients.

Gulf War Illness Research Program

Background and Program History

Gulf War Illness (GWI) is characterized by persistent symptoms such as chronic headache, widespread pain, cognitive difficulties, unexplained fatigue, gastrointestinal problems, respiratory symptoms, and other abnormalities that are not explained by traditional medical or psychiatric diagnoses. This complex set of chronic symptoms may affect as many as 250,000 veterans of the 1990–1991 Gulf War, of the nearly 700,000 deployed to that region. The Gulf War Illness Research Program (GWIRP) focuses its funding on innovative projects that have the potential to make a significant impact on GWI, improving the health and lives of affected service members and their families.

GWIRP Portfolio FY06–FY12, Funding by Research Area
(6 projects fit into 2 different Research Areas)



DoD-funded GWI 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 GWI 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. From FY08 to FY13, the GWIRP has received a total of $64M in appropriations. The program is directed to support peer-reviewed research of treatments for the complex of symptoms that comprise GWI, identification of objective markers (biomarkers) for the disease, and understanding the pathobiology underlying GWI.

Gudrun Lange, Ph.D., Rutgers University, FY13 IP Chair

"It is my most distinct honor to be involved with the CDMRP's Gulf War Illness Research Program. The program is evolving as a primary funding source to pursue cutting edge, Gulf War Veteran-relevant, peer-reviewed research in this important area of deployment-related research. CDMRP leadership can be especially congratulated for their persistent inclusion of scientific and veteran stakeholders to participate in peer and programmatic reviews of the research projects submitted. Through active engagement of veterans, clinicians, and researchers, the CDMRP's GWIRP has built a research portfolio that encourages integrative and collaborative proposals addressing tangible treatment options for Gulf War Illness."

IN THE NEWS

GWIRP Awards Program's First GWI-focused Research Consortia in FY12

Investigators at two institutions have been selected to create and manage the first-ever GWIRP-supported research consortia focused on GWI. The consortia represent the biggest awards ever offered by the GWIRP and an opportunity to significantly impact the field of GWI research. The investigators, Dr. Kimberly Sullivan, at the Boston University School of Public Health (BUSPH), and Dr. Mariana Morris, at Nova Southeastern University, will each receive approximately $5M in funding for the two consortia.

Dr. Kim Sullivan
Photo by Vernon Doucette

The two new consortia will conduct multidisciplinary preclinical and clinical trials research at leading universities, VA treatment facilities, and civilian hospitals. Because the consortia already share several key investigators, synergy will play an important role in the research, creating opportunities to capitalize on expected as well as unexpected results. Integrating complementary models and methods will lead to unique findings from the varied perspectives of the two consortia. Collaboration will enable scientists and clinicians at the participating organizations to more effectively analyze the research results and the benefits of potential treatments, to move the most important findings forward more rapidly.

Kim Sullivan, Ph.D., Assistant Professor in BUSPH Department of Environmental Science will serve as PI and Director for the Gulf War Illness Consortium, which will explore a brain-immune interaction hypothesis of GWI. The investigators aim to elucidate the pathobiological mechanisms responsible for the symptoms of GWI as they relate to neuroinflammation in the central nervous system. The findings will support a scientific basis for identifying both diagnostic biomarkers and rational therapies.

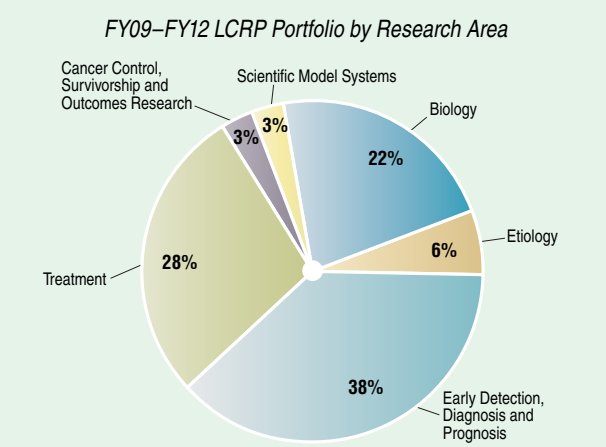
Mariana Morris, Ph.D., Professor and Director of Gulf War Illness Research in the Institute of Neuro-Immune Medicine at Nova Southeastern University, will serve as PI and Director for the second consortium, Understanding Gulf War Illness: An Integrative Modeling Approach, which will examine aberrant metabolic signaling affecting autonomic function, immune response, and endocrine function in GWI. Investigators will gain an understanding of abnormal signaling that can be used to drive translational models of GWI to facilitate more effective treatments.

A long-term goal of each consortium is to create and sustain a lasting infrastructure of relationships among the participating organizations. This will allow the consortia to operate beyond the funding period as independent entities committed to finding treatments for GWI.

Lung Cancer Research Program

Background and Program History

Lung cancer is the leading cause of cancer deaths in the United States. It is estimated there will be more than 228,000 new cases of lung cancer this year and almost 160,000 associated deaths. The Lung Cancer Research Program (LCRP) was established in FY09 with a congressional appropriation of $20M. Since then, the dedicated efforts by lung cancer advocates to increase public awareness of this disease and federal funding for its research have led to a total appropriation of $68.5M to the LCRP, including $10.5M for FY13. To address the critical needs of the lung cancer research and patient community, the LCRP adapts its investment strategy annually, focusing its support in underfunded and under-represented areas. Areas of specific focus include development of non- or minimally invasive detection and screening tools, understanding the mechanisms leading to various sub-types of lung cancer and the progression to clinically significant lung cancer, prevention and treatment, predictive and prognostic markers to identify responders and non-responders, and understanding susceptibility or resistance to treatment.



Innovative Projects in the Pipeline

Improving the Diagnostic Specificity of CT for Early Detection of Lung Cancer: 4D CT-Based Pulmonary Nodule Elastometry.
Peter Maxim, Ph.D., and Billy Loo, M.D., Ph.D., Stanford University

Electromagnetic-Optical Coherence Tomography Guidance of Transbronchial Solitary Pulmonary Nodule Biopsy.
Melissa J. Suter, Ph.D., Massachusetts General Hospital

Immunobiomarkers for Screening and Early Detection of Lung Cancer.
Qiuyin Cai, M.D., Ph.D., Vanderbilt University Medical Center

Salivary Proteomic and microRNA Biomarkers Development for Lung Cancer Detection.
David Wong, D.M.D., DMSc., University of California at Los Angeles

Up to 90% of lung cancers are non-small cell, and it is generally diagnosed at an advanced, incurable stage because patients often lack signs and symptoms in the early stages of the disease. Although several factors have been shown to contribute to the development of lung cancer, smoking and exposure to environmental carcinogens may be among the most prevalent. Importantly, military personnel are at a higher risk of developing lung cancer than the general population due to increased rates of smoking as well as an increased likelihood of being exposed to numerous environmental carcinogens during their service.

Regina Vidaver, Ph.D., FY13 IP Member

"As an advocate, my role is to ensure that the voice of the person with lung cancer is never lost to discussions of science, systems, and interventions. At the CDMRP LCRP, not only is my voice heard, it is genuinely appreciated. My colleagues and I have had the pleasure of developing and shepherding this incredible program, which is pushing the envelope of research into the early stages of lung cancer and how best to detect and treat it. The funding provided by the LCRP is making an enormous difference in the field, and helping find new ways to enable the best possible outcomes for the patients of today and the future."

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 risk assessment, early detection, diagnosis, prevention, and treatment for the control and cure of lung cancer

Fred Hirsch, M.D., Ph.D., University of Colorado, FY12 IP Member

"It is a great pleasure for me as a medical oncologist and a lung cancer researcher to be a part of the DoD lung research program. Over the few years which I have been involved in this program, I have seen significant grants supporting both young investigators and more senior investigators in innovative scientific projects searching for a better understanding of cancer biology and for improving early detection and treatment of cancer."

Recent Accomplishments Making an Impact

National Resource for Lung Cancer Biospecimens

Christopher Moskaluk, M.D., Ph.D., University of Virginia

Created the first national early lung cancer biospecimen repository that contains tissues and biological fluid samples linked to clinical and outcome data. This resource is available to all biomedical researchers and aims to assist clinical investigators in the study of lung cancer genetics, novel diagnostic and prognostic tests for cancer, and candidate biomarkers.

www.lcbrn.org

Inhalable Nanoparticles to Treat Lung Cancer

Oleh Taratula, Ph.D., Oregon State University

Developed new drug delivery system using nanoparticles that allows inhalation of chemotherapeutic drugs and small interfering RNA that shut down the ability of cancer cells to resist attack. Laboratory and animal tests indicate that this treatment reduces the systemic damage done to other organs while significantly improving the treatment of lung tumors.

DDR2 a Target for Squamous Cell Lung Cancer

Peter Hammerman, M.D., Ph.D., Dana-Farber Cancer Institute

Demonstrated that Discoidin Domain Receptor 2 (DDR2)-driven cellular transformation sensitizes cancer cells to treatment with tyrosine kinase inhibitors (e.g., dasatinib), which target DDR2. Based on the study results, initiated a Phase 2 clinical trial of dasatinib in squamous cell lung cancer. In addition, dual DDR2 and Src inhibition was identified as a potential better therapeutic approach for treating tumors with DDR2 mutations.

Novel Lung Cancer Model

Inder Verma, Ph.D., University of California at San Diego

Developed a mouse model of lung cancer using a novel lentiviral gene delivery system that demonstrated this technique is feasible for producing mouse models of interest without generating and crossing multiple mouse lines. Using this technique, the PI tested the crosstalk between multiple tumor-suppressor pathways during tumorigenesis, including Kras, p53, p16, LKB1, and PTEN. Preliminary data suggest that the crosstalk of tumor suppressor pathways lead to synergistic or antagonistic effect in regulating tumor progression.

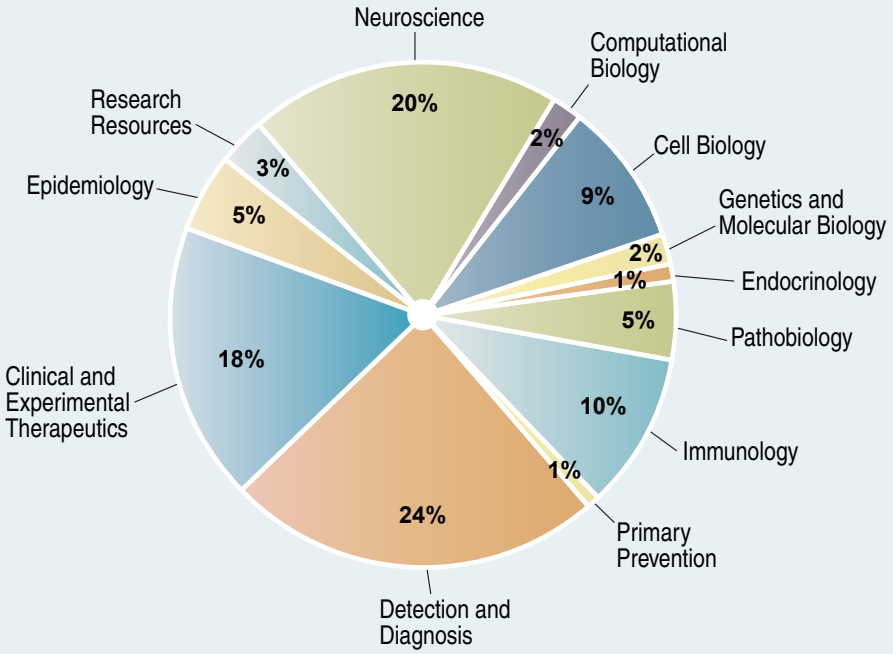
Multiple Sclerosis Research Program

Background and Program History

Multiple sclerosis (MS) is characterized by neural lesions due to an autoimmune attack on the myelin sheath covering axons. The demyelination leads to subsequent disruption of nervous system transmission and the degenerative, chronic inflammatory disease known as MS. Although MS affects more than 400,000 individuals in the United States and about 2.1 million individuals worldwide, its etiology and pathogenesis are largely unknown. 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. Signs and symptoms of the disease differ from person to person as does the severity and progression. The disease has four major subtypes: Relapsing-Remitting, Secondary Progressive, Primary Progressive, and Progressive Relapsing MS. In FY09, Congress first appropriated funds for the establishment of the Multiple Sclerosis Research Program (MSRP) at the CDMRP.

From its inception through FY13, $23.1M has been received to support innovative and impactful research that addresses fundamental issues and gaps in MS. The program has funded 51 awards ranging from the research-driven Idea awards to high-risk/high-gain Concept awards to the technological advancement Metric Development and Validation awards. The program focuses on not only hunting down the cause of MS, but also developing new metrics to diagnose the disease as well as new therapies. The MSRP is dedicated to supporting cutting edge projects that will move the field forward and assist all people affected by MS.

FY09–FY12 MSRP Research Portfolio



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

Achievements and Outcomes

Dr. Elledge *developed proteomic technology to screen for specific and novel auto-antibodies important in understanding the pathogenesis of MS.*

Dr. Cross *used Gradient Echo Plural Contrast Imaging technique on cerebral white matter which showed potential as an improved quantitative measure of central nervous system injury in MS as compared to standard MRI and could discriminate among the four major clinical subtypes: Relapsing-Remitting MS, Secondary Progressive MS, Primary Progressive MS, and Progressive Relapsing MS.*

Dr. Schwartz *used patient-reported outcome measures to assess symptom burden to monitor disease progress and evaluate efficacy of disease therapies.*

Dr. Chen *found the imaging contrast agent, bis-5HT-DTPA-Gd (MPO-Gd) to be highly sensitive as an imaging biomarker for reporting early, preclinical, and subclinical disease activity in vivo before symptom onset in the mouse EAE model.*

Dr. Sicotte *developed a metric modeling corpus callosum morphometry and diffusion tensor imaging parameter to study changes in Relapsing-Remitting MS.*

Drs. Wang *and* ***Miller*** *developed and tested in mice, a near-infrared fluorescence imaging technique capable of direct quantification of myelination in vivo.*

Drs. Ramanathan, Weinstock-Guttman, *and* ***Zivadinov*** *investigated the impact of environmental factors including exposures to human herpes viruses, vitamin D, and smoking in disease progression in clinically isolated syndrome.*

Dr. Wishart *developed and validated an fMRI pain metric tailored for patients with MS. This metric may be used to test for alterations in the brain's processing of pain in MS.*

Nancita Rogers

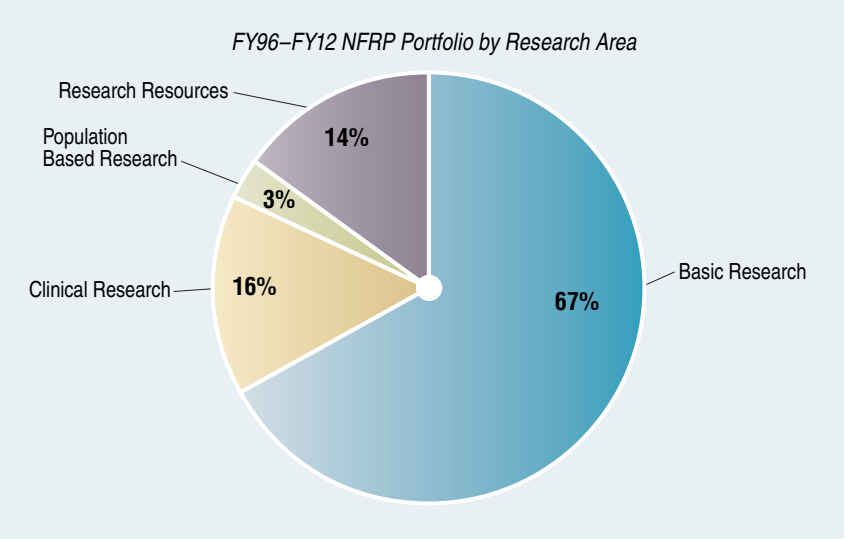
"It has been a great honor to represent the MS community as a consumer member of the MSRP IP. I've learned so much about MS and how important effective, informed research gets us closer to resolving some of the devastating impact of this disease. The esteemed members of the MSRP IP respectfully listen and genuinely welcome and appreciate my perspective and input as to how specific research efforts directly impact the lives of people living with MS. They have tremendous passion and an increased sense of urgency to fund the high-risk, high-impact research needed to prevent the occurrence, reverse, cure or slow the progression of MS.

Tremendous strides have been made in diagnoses, there's better understanding of MS symptoms, improved treatments to slow disease progression and lots more talk about restoring lost function. All this leads me to believe there really is hope for an eventual cure. Meanwhile, we are all better served with improved quality of life thanks to the dedication of MSRP IP."

Neurofibromatosis Research Program

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 that time, $257.85M has been appropriated to the program, including $15M in FY13. Over its 17-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 research portfolio includes 294 awards spanning basic, clinical, and population-based research.



Mr. Andrés Lessing, NFRP Consumer Reviewer

"It was amazing to be part of the peer review process in selecting the best research to pursue. It was very rewarding to be at the same table as researchers, clinicians, and others affected by NF. Everyone valued everyone's opinion and questions asked, and I left knowing that the limited funds would go to the best projects."

Yuan Zhu, Ph.D., University of Michigan

Clinical studies have shown that siblings with the same NF1 mutation may have dramatically different symptoms of the disease, suggesting that the severity of neurofibromatosis type 1 symptoms may be influenced by other factors. Dr. Zhu previously used sophisticated genetic manipulations in mice to inactivate the Nf1 gene in neural stem cells during embryonic development, and he discovered that mice with inactivation of both copies of the Nf1 gene had enlarged brains soon after birth, similar to abnormalities observed in some human NF1 patients. With funding from an FY10 Investigator-Initiated Focused Research Award, Dr. Zhu used this model to demonstrate that treatment with a MEK/ERK inhibitor beginning at one week of age completely prevented the enlarged brain phenotype of the Nf1 mutant mice. This study demonstrates that deregulated ERK signaling is critical for the development of some of the brain abnormalities associated with Nf1 gene inactivation, and identifies a potential therapeutic agent for treating children with NF1-associated brain abnormalities.

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

Wei Mo, Ph.D., University of Texas Southwestern Medical Center, Dallas

Malignant peripheral nerve sheath tumors (MPNSTs) occur sporadically in a subset of patients with NF1 and are highly aggressive and resistant to therapeutic treatments. With funds from an FY10 NFRP Postdoctoral Traineeship Award, Dr. Wei Mo has been working in Dr. Luis Parada's laboratory to identify genes involved in the development of MPNSTs. The cellular source of MPNSTs has been traced to skin-derived precursor cells, a population of neural crest-like stem cells. Dr. Mo observed that CXCR4, a G-protein-coupled receptor, was highly expressed in a mouse model of NF1-deficient MPNSTs. Blockade of CXCR4 activity by either shRNA or the antagonist AMD3100 decreased MPNST cell growth in culture and inhibited tumorigenesis in several mouse MPNST models. AMD3100 is currently FDA approved for use in patients with non-Hodgkin's lymphoma and multiple myeloma, making it an attractive candidate for MPNST treatment. Dr. Mo's postdoctoral work has resulted in pivotal findings moving the NF field forward and has provided him with the foundation to build his career as an independent NF researcher.

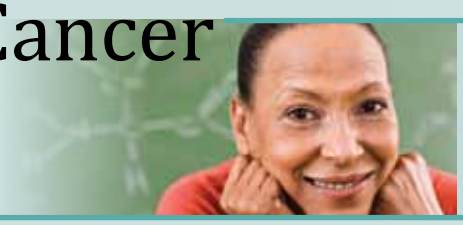
Jeremie Vitte, Ph.D., House Research Institute

Schwannomatosis patients develop extremely painful spinal, peripheral, and cranial nerve Schwann cell tumors (schwannomas) and frequently suffer from additional neurological symptoms including numbness and weakness in the extremities. Although the mechanism of Schwann cell tumor development is not fully understood, recent studies suggest that mutation of the tumor suppressor gene Snf5/Ini1/SMARCB1 may be involved in familial schwannomatosis. Recent data also suggests that inactivation of the NF2 gene may also play a role in SMARCB1-initiated schwannoma development. Dr. Vitte, with funding from an FY09 NFRP Postdoctoral Traineeship Award, successfully developed a preclinical animal model to better understand the role of Snf5 in Schwann cell tumor development and schwannomatosis-related neurological pain. Interestingly, preliminary data suggests that inactivation of both Nf2 and Snf5 in the novel preclinical model results in the development of nerve lesions. Dr. Vitte has also developed a collaboration with investigators at the University of California, Los Angeles, to evaluate the role of Snf5 in schwannomatosis neuropathic pain.

Peggy Burke, Ed.D., NFRP Consumer Reviewer

"Serving as a consumer reviewer has been a tremendously rewarding experience. It empowers me to think I am making a contribution that might lead to better treatment options and understanding of neurofibromatosis. My faith in science and in the scientists who pour so much passion into their work has been renewed as I see the tremendous amount of work that is underway. My input on the panels has been valued and while I can't take away my granddaughter's NF, by serving as a reviewer I can try to make her life better."

Ovarian Cancer Research Program

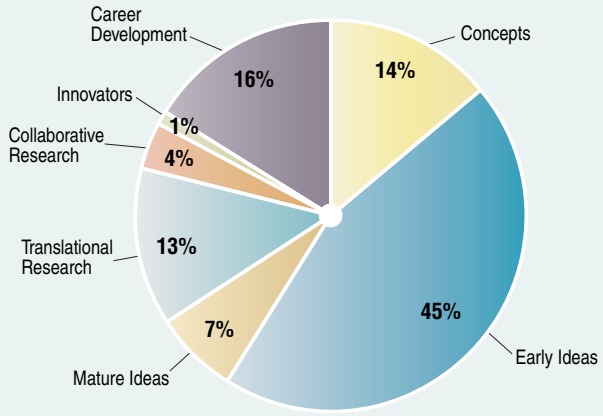


Background and Program History

The DoD Ovarian Cancer Research Program (OCRP) began in 1997 with a congressional appropriation of $7.5M. Since that time, the dedicated efforts of 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 $216M to the OCRP, including $20M in FY13.

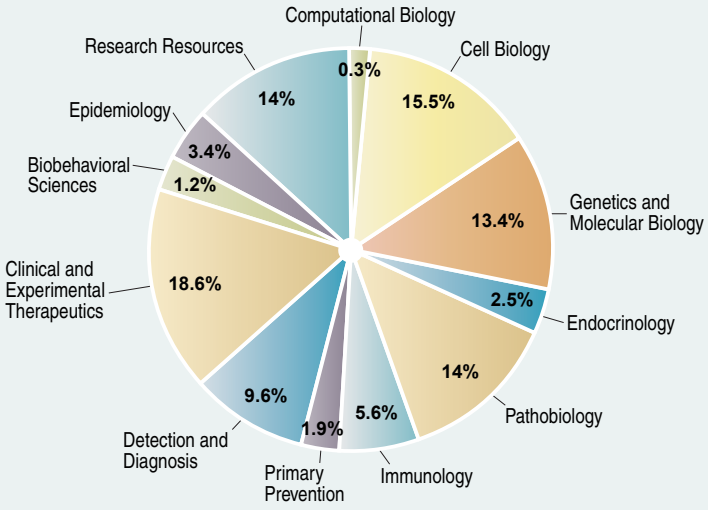
The OCRP vision is adapted yearly to target critical research areas and to be responsive to the needs of the ovarian cancer community. Every year, the OCRP evaluates the funding landscape by comparing research portfolios and award mechanisms of other federal and non-federal agencies, and then develops 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. The OCRP's award mechanisms support complementary approaches to answer questions that are vital to the advancement of science, exemplifying the innovative and focused nature of this program.

FY97–FY12 OCRP Portfolio by Development of Ideas



The OCRP's current portfolio includes 284 awards made through 25 award mechanisms available over the past 16 years.

FY97–FY12 OCRP Portfolio by Research Phases



Long-Term Initiatives of the DoD OCRP

- Understand precursor lesion/stem cell, microenvironment, and pathogenesis/progression of ovarian cancer
- Improve performance and reliability of disease markers and imaging toward screening and selecting the best therapeutic approaches
- Address issues in survivorship
- Enhance pool of ovarian cancer scientists
- Investigate tumor response to therapy including tumor survival, dormancy, cell death, clonal evolution, and tumor heterogeneity

Vision
Eliminate ovarian cancer

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

Making an Impact

Dr. Animesh Barua *– Improving Detection - Developing an early detection test for ovarian cancer using markers in the blood and noninvasive, tumor-targeted ultrasound imaging with enhanced resolution, using nuclear matrix proteins, interleukin-16 expressing tumor epithelium and death receptor 6 as enhancing agents.*

Dr. Sally Kornbluth *– Identifying New Avenues for Therapy - Identified that inhibition of fatty acid synthase by drugs such as orlistat induced ovarian cancer cell death through a series of signals in the cell that result in induction of caspase 2, leading to apoptosis (programmed cell death).*

Dr. Fergus Couch *– Identifying Genetic Modifiers of Ovarian Cancer Risk - Identified several novel modifiers of ovarian cancer risk for women with BRCA1 mutations, including the 4q32.3 locus which is specific to these women.*

Dr. Panagiotis Konstantinopoulos *– Gene Expression Profile - Developed the BRCAness gene expression profile, which can identify tumors with the "BRCAness" phenotype (characterized by increased sensitivity to platinum analogues and PARP inhibitors as well as improved survival).*

Drs. Elizabeth Swisher *and* ***Anton Krumm*** *– Elucidating Ovarian Carcinogenesis - Identified a premalignant expression signature which may reflect early steps in BRCA1-mediated ovarian carcinogenesis.*

Dr. Laurie Hudson *– Novel Therapeutic Strategy - Characterized the FDA-approved R-enantiomer of naproxen, an NSAID, as an inhibitor of small GTPase activation, epidermal growth factor receptor degradation, as well as ovarian cancer cell migration and invasion, making this NSAID a potential novel therapy for ovarian cancer metastasis.*

Dr. Tomas Walsh *– Genetic Risk - Confirmed loss-of-function mutations in RAD51D predispose women without BRCA1/2 mutations to ovarian cancer but not breast cancer.*

Dr. David Bowtell *– BRCA Mutations and Ovarian Cancer Subtypes - Identified that BRCA1 mutant tumors are associated with a specific molecular subtype of high grade serous carcinoma (HGSC) and have a distinct gene expression signature, which is heavily influenced by specific amplification events at 8q24 and on the X chromosome. By contrast, BRCA2 mutant tumors more closely resemble 'wild-type' HGSC.*

Drs. David Bowtell *and* ***Gillian Mitchell*** *– BRCA Mutations Without Family History - Found that 44% of 141 women with nonmucinous ovarian tumors carrying BRCA1/2 mutations did not have a family history of ovarian cancer or breast cancer.*

Dr. Rugang Zhang *– Prognostic Indicator and Therapeutic Target for Epithelial Ovarian Cancer - Determined that Wnt5a, a non-canonical Wnt ligand, induces cellular senescence by activating histone repressor A/ promyelocytic leukemia senescence pathway. Wnt5a suppresses the growth of epithelial ovarian cancer, and loss of Wnt5a predicts a poor outcome in epithelial ovarian cancer patients.*

Dr. Bryan Toole *– Novel Therapeutic Intervention to Reduce Chemoresistance - Showed that treatment with small oligomers of hyaluronan (a polysaccharide expressed at elevated levels in ovarian carcinoma's pericellular matrix) reversed resistance to doxorubicin and paclitaxel, and may be a novel, non-toxic method of improving chemoresistance.*

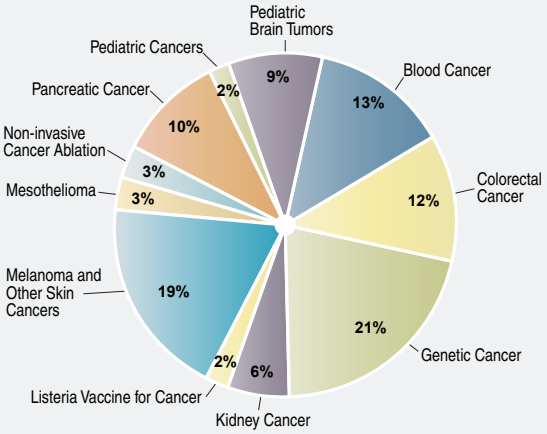
Dr. Zhen Zhang *– OVA1™ Helps Determine Whether an Ovarian Mass Is Malignant - Developed OVA1, the first IVDMIA (in vitro diagnostic multivariate index assay) of proteomic biomarkers cleared by the U.S. Food and Drug Administration to help physicians determine whether a pelvic mass is benign or malignant before it is removed. This information will help physicians identify patients who should be referred to a gynecologic oncologist.*

Peer Reviewed Cancer Research Program

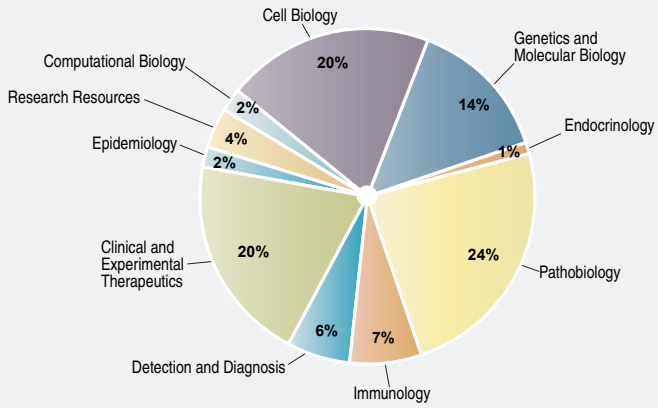
Background and Program History

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. 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%, including more than 60 different cancer types (Crawford et al., Military Medicine 172 (2007) 1084-1088). Both a healthy force and healthy family support unit, free of serious illnesses, allow the service member to focus on his or her role as a service member and facilitate the overarching military mission. Funding studies on the detection, diagnosis, treatment, and prevention of cancer benefits not only the service members and their families, but also the American public, ultimately leading to increased survival rates, improved quality of life, and decreased costs of medical care.

FY09–FY12 PRCRP Portfolio by Topic Area



FY09–FY12 PRCRP Research Portfolio



Jonathan Brody, Ph.D.
FY14 IP
Chair-Elect

"I am involved in a number of national and international scientific review committees, yet being involved with CDMRP is particularly an honor and rewarding experience. The integrity of the review process matches the importance of providing funding for young cancer researchers with innovative ideas that have a focus on military relevance (duty service members and their families)."

Nancy Roach,
Fight Colorectal Cancer,
FY13 IP Member

"When I look at research proposals, I ask myself questions like: Could this lead to a better way to screen people, maybe soldiers who are on active duty? Could it help us learn if there are military-specific situations that increase the risk of colorectal cancer?

My PRCRP work is very gratifying. Our reviews include vigorous debate between scientists and consumers about the merits of research proposals, and I walk away having learned a lot and feeling satisfied that we invested our funds wisely."

Vision

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

Mission

To foster the next generation of cancer research by providing new and early-career investigators opportunities to successfully pursue high-impact research for the prevention, detection, and treatment of cancer

Achievements and Outcomes

Blood Cancer	***Dr. Cantor*** *identified 5'UTR mutations in ANKRD26 gene as a novel cause of leukemia predisposition and thrombocytopenia in humans.* ***Drs. Lanza*** *and* ***Tomasson*** *demonstrated the cMyc Sn-2 prodrug had markedly improved bioactivity over the free drug in several myeloma cell types. The prodrug was highly retained in lipids.*
Human Colorectal Carcinoma (CRC)	***Dr. Su*** *developed a colorectal cancer (CRC) biomarker test that uses urine.* ***Dr. Jessup*** *demonstrated that NANOGP8 is involved in regulating cancer stem cells in CRC.* ***Dr. Ellis*** *observed endothelial cell secreted factors are involved in the promotion of cancer stem cells in CRC.*
Genetic Cancer	***Dr. Kitlinska*** *demonstrated neuropeptide Y and other stress mediators have potent effects on tumor development and progression.* ***Drs. Alvarez***, ***Couto***, *and* ***Huang*** *identified specific genetic variations and environmental exposures resulting in epigenetic profiles capable of modifying cancer risk.* ***Dr. Hu*** *established a direct link between chronic stress and tumorigenesis in mouse models.*
Kidney Cancer	***Dr. Torti*** *demonstrated the combination of near infrared and nanotubes could successfully inhibit both human and mouse kidney cancer cells.* ***Dr. Singamaneni*** *developed a sensitive urine-based test to detect the kidney cancer biomarker AQP1.* ***Drs. Tewari*** *and* ***Pantuck*** *optimized a detection method for miR-210 and demonstrated its elevation in renal carcinoma serum samples.*
Listeria	***Dr. Chung*** *demonstrated that Listeria induces dendritic cell (DC) activation and maturation, and stimulates T cell proliferation, indicating it could be used as a DC vaccine adjuvant.*
Melanoma	***Dr. Yennu-Nanda*** *determined that excessive melanin production leads to increases in melanocyte proliferation and oncogenic transformation that is dependent on skin type.* ***Dr. Brooks*** *demonstrated UV radiation of extracellular matrix proteins altered the adhesion, migration, and proliferation of fibroblasts, melanoma cells, and macrophages in vitro.* ***Drs. Halaban***, ***Brash***, *and* ***Bosenberg*** *discovered a "photochemistry in the dark" phenomena, showing that DNA damage by UV light continued after sun exposure. The delayed sunlight damage could be prevented by an identified agent. This finding could lead to a new formulation of sunscreen to protect the delayed skin damage by sun exposure.*
Pediatric Cancers (including Brain Tumor)	***Drs. Gilbertson***, ***Malkin***, ***Guy***, *and* ***Ellison*** *screened 1.26 million compounds for childhood choroid plexus carcinoma and identified 23 hits. Five compounds were selected for preclinical study.* ***Dr. Zong*** *found that glial-ablation treatment resulted in complete remission of tumors even at a late stage.* ***Dr. Paddison*** *isolated pediatric glioma stem cells and developed a protocol for Glioblastoma multiforme tumor classification from RNA-sequencing data.*
Cancer Ablation	***Dr. Pan*** *developed and tested folate-conjugated killer tRNA nanoparticles as a potential blood cancer treatment strategy.* ***Dr. Berdis*** *developed gold-containing nucleosides as target agents to increase the efficacy of ionizing radiation for maximal tumor ablation.*

Pancreatic cancer and mesothelioma topics were first included in FY11 with grants initiated in 2012. Progress is underway.

Peer Reviewed Medical Research Program

Background and Program 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 FY12, Congress has appropriated $594.5M, which has supported 493 research awards. From its inception, the PRMRP has funded research projects in 97 different 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 FY13 appropriation is $50M.

The PRMRP is committed to funding basic, translational, and clinical research that will strongly affect 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.

Merle Zuel, Consumer Reviewer

"I have always tried to make it easier for the next person with this illness. What better way to do so than to act as a voice of the consumer on cutting edge medical research? I often find myself thinking, I wish they had this technology when I was being treated. I get a great sense of satisfaction knowing that in some small way, I helped shape the policies and proposals of the future."

FY12 and FY13 PRMRP Topic Areas

FY12	FY13	Topic Area
✔		Arthritis
	✔	Chronic Kidney Disease
	✔	Chronic Migraine and Posttraumatic Headache
✔	✔	Composite Tissue Transplantation
	✔	Dengue Fever
	✔	DNA Vaccine Technology for Postexposure Prophylaxis
✔		Drug Abuse
✔	✔	Dystonia
✔	✔	Epilepsy
✔	✔	Food Allergies
✔	✔	Fragile X Syndrome
	✔	Hantavirus
✔	✔	Hereditary Angioedema
✔	✔	Inflammatory Bowel Disease
✔	✔	Interstitial Cystitis
	✔	Leishmaniasis

FY12	FY13	Topic Area
✔		Listeria Vaccine for Infectious Diseases
✔	✔	Lupus
✔	✔	Malaria
✔	✔	Nanomedicine for Drug Delivery Science
✔		Neuroblastoma
✔		Osteoporosis and Related Bone Disease
✔		Paget's Disease of the Bone
	✔	Pancreatitis
✔	✔	Polycystic Kidney Disease
✔	✔	Post-traumatic Osteoarthritis
	✔	Pulmonary Hypertension
	✔	Rheumatoid Arthritis
✔	✔	Scleroderma
✔	✔	Tinnitus
✔		Tuberculosis

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

Recent Research Accomplishments

Dean Li, M.D., of the University of Utah identified small molecule inhibitors of the ARF6 receptor and showed that these inhibitors are effective in reducing fluid leakage and damage in the eye of animal models of age-related macular degeneration and diabetic retinopathy.

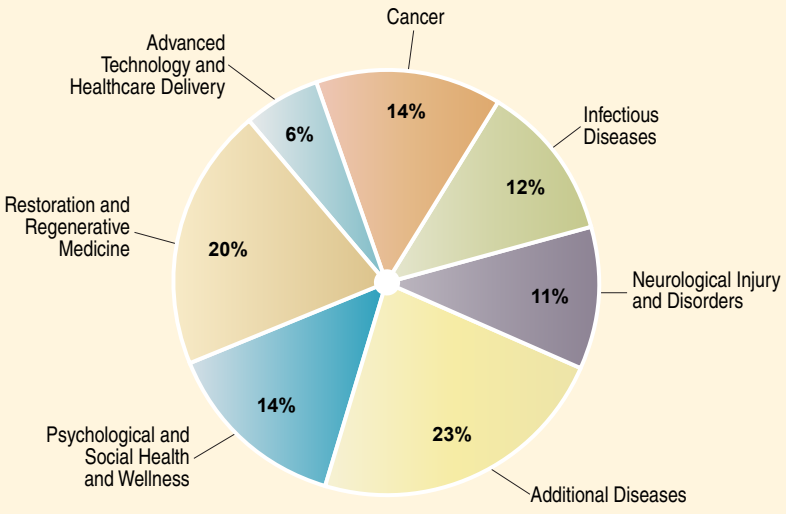
Mary De Souza, Ph.D., of the Pennsylvania State University found that increasing caloric intake without lowering physical activity can reverse the chronic energy deficiency and amenorrhea of women who restrict food intake for weight loss, and can also lead to an increase in bone mineral density.

Yogen Saunthararajah, M.D., of the Cleveland Clinic Foundation demonstrated that decitabine was able to deplete DNMT1 without inducing cytotoxicity/apoptosis in normal cells in leukemia patients, and the lower but more frequent doses administered targeted more cancer cells for cell death and reduced nausea and hair loss.

Teng Ma, Ph.D., of Florida State University developed a bioreactor-based approach to infusing human mesenchymal stem cells (hMSC) into chitosan-based scaffolds incorporated with bone morphogenetic protein 2 to enhance hMSC bone regeneration capabilities.

Ricardo Saban, D.V.M., Ph.D., of the University of Oklahoma Health Sciences Center found that anti-vascular endothelial growth factor antibodies were able to reduce inflammation and nerve density in an animal model of chronic bladder inflammation, providing a potential first therapeutic for treating interstitial cystitis and bladder pain syndrome.

FY99–FY12 PRMRP Award Portfolio by Category and Percentage of Total Funding



Peer Reviewed Orthopaedic Research Program

Background and Program History

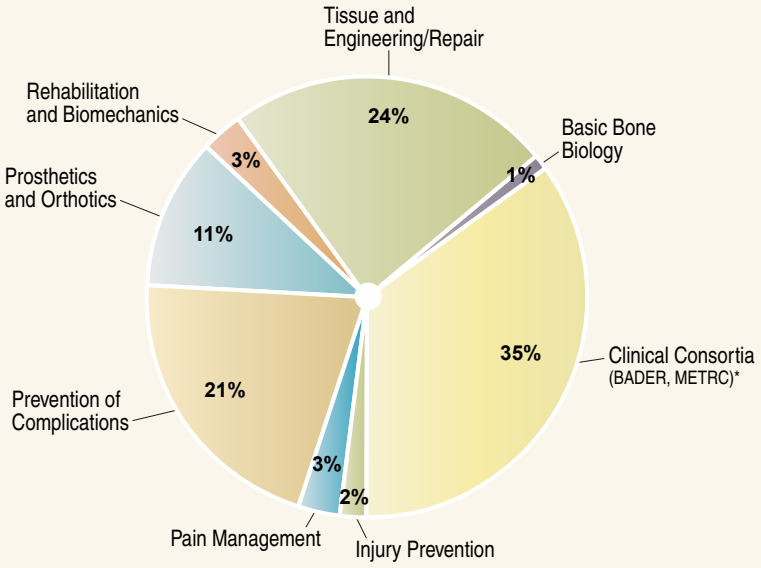
A large majority of the injuries sustained by military personnel in U.S. war efforts involve soft tissue wounds and skeletal fractures, pointing to an urgent need for orthopaedic research that will provide superior medical care and treatment options for injured service members. Since its inception in FY09, the Peer Reviewed Orthopaedic Research Program (PRORP) has dedicated its congressional appropriations, totaling $218.5M, toward supporting military-relevant orthopaedic research.

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.

Brent Jurgersen, U.S. Army (Ret.), PRORP Consumer Reviewer

"...the rewards [of the PRORP review process] are evident as you walk the halls of our Military Treatment Facilities and Veteran Centers and see our wounded warriors and veterans thriving, whether that is returning to active duty, or transitioning out of the service to a successful life as a veteran."

FY09–FY12 PRORP Awards by Research Area and Dollar Amount



*Bridging Advanced Developments for Exceptional Rehabilitation Consortium (BADER), Major Extremity Trauma Research Consortium (METRC)

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

With an FY09 Hypothesis Development Award, **Jessica Jennings, Ph.D.,** at the University of Memphis demonstrated that low-dose administration of the fatty acid C2DA prevents biofilm formation in vitro. These effects were more pronounced when C2DA is combined with antibiotics. She plans to pursue refinement of a delivery system to test the antibiofilm activity of C2DA in vivo. (Jennings JA, Courtney HS, and Haggard WO. Cis-2-decenoic acid inhibits *S. aureus* growth and biofilm in vitro: A pilot study. Clin Orthop Relat Res 470(10) 2012: 2663–2670).

W. P. Andrew Lee, M.D., of Johns Hopkins University used funding from an FY09 Hypothesis Development Award to investigate how to overcome immunosuppression and immunorejection issues associated with composite tissue allotransplantation such as hand and face transplants through mesenchymal stem cell (MSC) therapy in an animal model. He demonstrated that local or systemic injections of the subject's own bone marrow-derived MSCs provided a significant enhancement of functional recovery and nerve regeneration following hind limb transplants. He also showed the MSCs possess potent immunomodulatory properties with minimal immunogenicity in vitro.

Michael Buys, M.D., formerly of Wilford Hall Medical Center and currently at the University of Utah, used support from an FY09 Career Development Award to develop and characterize a novel animal limb fracture/open repair pain model that parallels battlefield injuries sustained by wounded warriors. The reproducible behaviors and healing rates of the animals will facilitate the development and testing of novel analgesics, with the ultimate goal of providing better pain relief options for military service members and civilians who suffer traumatic injuries.

With support from an FY09 Technology Development Award, Northwestern University's **Stefania Fatone, Ph.D.,** has developed a prototype prosthetic socket and vacuum pump system that is shorter than current prosthetic sockets, allowing greater range of motion for transfemoral amputees. Volunteers that tested the device found it more comfortable for walking than their original sockets. Once socket fabrication and performance has been maximized, Dr. Fatone and her team plan to produce educational materials so other prosthetists can cast, fit, and fabricate this custom socket for their transfemoral amputee patients.

Prostate Cancer Research Program

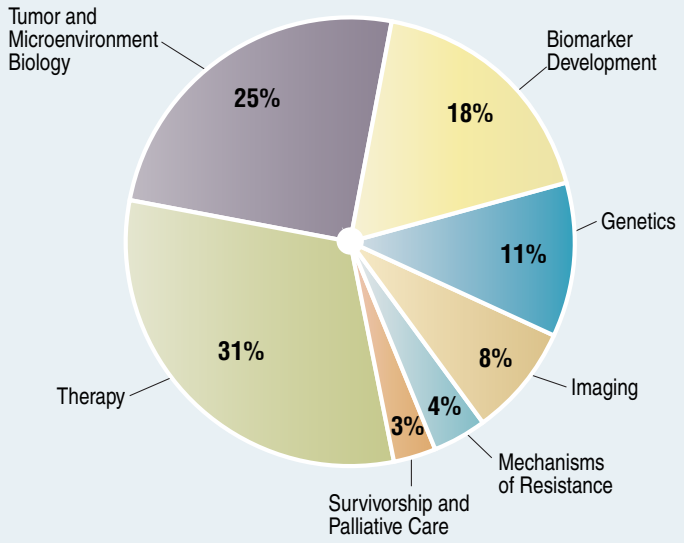
Background and Program History

Since its inception in 1997, and over its 17-year history of congressional support totaling nearly $1.3B, 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 decidedly collaborative, innovative, and impactful on prostate cancer. The PCRP has made unprecedented inroads in supporting the development of new treatments for advanced prostate cancer and has been the leading supporter of research toward understanding and resolving ethnic disparities in prostate cancer incidence and mortality. The program has also fostered the development of more than a thousand trainees and new investigators, many of whom have become leaders in cutting-edge research that is making a difference for millions of prostate cancer patients and will ultimately conquer the disease.

Program Portfolio

From 1997–2012, the PCRP funded 2,604 research and training awards. The projects supported range from exploratory studies leading to new research avenues to developing multi-institutional consortia designed to provide resources that will transform prostate cancer clinical care. By achieving 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 the relative numbers of awards the program has supported in these areas from FY09 through FY12.

FY09–FY12 Portfolio by PCRP Focus Area



Overarching Challenges

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

- *Developing better tools to detect clinically relevant disease in asymptomatic men*
- *Distinguishing aggressive from indolent disease in men newly diagnosed with prostate cancer*
- *Developing effective treatments and address mechanisms of resistance for men with high risk or metastatic prostate cancer*

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*

Vision
Conquer prostate cancer

Mission
Fund research that will lead to the elimination of death from prostate cancer and enhance the well-being of men experiencing the impact of the disease

PCRP Research Achievements at a Glance

The PCRP funds innovative, high-impact research that addresses the critical needs identified in the program's overarching challenges and focus areas. Projects funded by the PCRP have led to the below examples of advancements for prostate cancer patients, with many more in development and pushing toward the clinic.

Biomarker Development

*Dr. Michael Milosevic demonstrated that low oxygen (hypoxia) in prostate tumors predicts radiotherapy treatment failure, **suggesting combination of radiotherapy with hypoxia-targeted therapeutics**.*

*Dr. Neal Fedarko demonstrated that a set of related proteins called SIBLINGs can be used as blood **biomarkers of prostate cancer disease progression**.*

*Dr. Lorelei Mucci **enhanced prostate cancer risk assessment** with her discovery that several biomarkers (BRCA1, p63, cIAP1, and MTA1) are associated with increased risk of death.*

Genetics

*Dr. Arul Chinnaiyan discovered that the gene SPINK1 is overexpressed in 10% of prostate cancers and that these tumors are very aggressive, **identifying an important prostate cancer subtype** that may respond to specific treatments.*

*Dr. Lloyd Trotman discovered a new tumor suppressor gene, PHLPP1 ("flip one") that cooperates with the gene PTEN to **prevent progression to aggressive prostate cancer**, providing new insight for therapeutic targeting.*

*Dr. Michael Rosenfeld discovered that the TMPRSS2-ETS gene fusions are orchestrated by the androgen receptor, providing a **breakthrough in prostate cancer genetics** and strategies for therapy.*

Therapy

Dr. Shankar Vallabhajosula developed a radiolabeled antibody, called Lu177-J591, that targets prostate specific membrane antigen on prostate cancer cells and **decreases tumor size and pain symptoms** in patients with metastatic disease.*

Dr. Kim Chi developed a cytotoxic small molecule targeting the protein clusterin that **increases prostate cancer cell killing** (now in Phase 3).*

*The Prostate Cancer Clinical Trials Consortium played a critical role in accelerating FDA approval of two new drugs **ZYTIGA®**** and **XTANDI®**** for the treatment of metastatic, castration-resistant prostate cancer; demonstrating how collaboration can **bring life-prolonging drugs to patients faster**.*

*Dr. Evan Keller discovered that blocking the protein RANKL slows progression of prostate cancer skeletal metastases, leading to development of XGEVA®**, now available for **prevention of bone loss during therapy**.*

Imaging

Dr. Ethan Halpern demonstrated that contrast-enhanced transrectal ultrasound **can improve prostate cancer detection during biopsy** and identify more aggressive, clinically significant disease.*

Dr. Martin Pomper developed PET radiotracers that target prostate cancer through prostate specific membrane antigen and **enhance detection of metastatic disease**.*

*Dr. Gregory Fischer developed an integrated MRI-guided robotic needle placement system to **improve tumor imaging** during biopsy and seed placement for brachytherapy.*

Mechanisms of Resistance

Dr. Charles Graham demonstrated that low oxygen in prostate cancer cells causes resistance to chemotherapeutic agents and that drugs that increase oxygen levels (glycerin trinitrate), **sensitize cancer cells to chemotherapy**.*

*Dr. Marianne Sadar discovered a marine sponge-derived compound, called EPI-001, that shrinks prostate tumors and may **overcome resistance to current androgen receptor therapies**.*

Survivorship and Palliative Care

*Dr. Nathaniel Fried developed a laparoscopic laser nerve imaging probe to identify cavernous nerves during prostate cancer surgery and **preserve both urinary and sexual function**.*

*Dr. Susan Greenspan developed a virtual bone biopsy using high-resolution MRI that showed **improved assessment of bone fracture risk** in men undergoing prostate cancer therapy.*

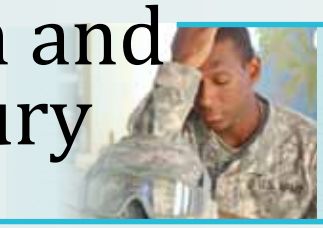
Tumor and Microenvironment Biology

*Dr. Michael Karin discovered that castration-recurrent prostate cancer results from an inflammatory response involving lymphotoxin and NK-kB, **opening new opportunities for therapeutic targeting**.*

Dr. Douglas McNeel developed an immuno-therapy-based DNA vaccine to **inhibit prostate cancer recurrence** in patients after treatment for primary disease.*

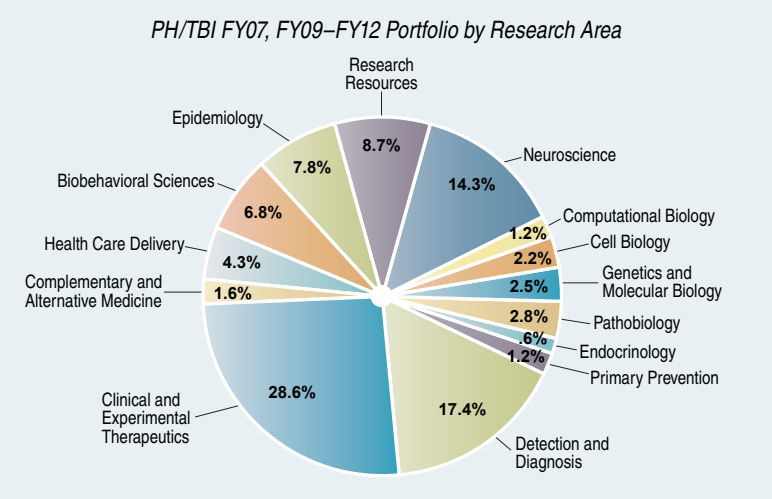
**now in clinical trials*
***now in clinical use*

Psychological Health and Traumatic Brain Injury Research Program



Background and Program 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 PH and TBI) were assigned to the CDMRP for the purpose of soliciting and managing critical PH- and TBI-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 FY12, and a modified execution model, including assignment of program strategic oversight to USAMRMC-based JPCs aligned with the OASD(HA), was established. These JPCs provide recommendations to the OASD(HA) on research gaps, focus areas, and funding options for the PH/TBIRP. Operational execution management, including development of PAs, solicitation and review of applications, as well as full life-cycle management of awards, is supported by multiple organizations, including the CDMRP. The CDMRP-managed application review for the PH/TBIRP follows a two-tiered model, where consumer involvement continues to be a hallmark. Our nation's wounded warriors serve in that capacity for the PH/TBIRP, representing fellow service members and veterans to help identify the most relevant and impactful research. The modified execution process allows greater flexibility for leveraging PH/TBIRP

The Way Forward: Collaboration between DoD and VA

Among the challenges in treating PTSD and mTBI are comprehensive understandings of the complex mechanisms which influence the acute and chronic progression of the injuries. In response to this need and the Presidential Executive Order 13625, the DoD and VA are collaborating to fund and execute two new multi-institutional consortia aimed at the diagnosis and treatment of PTSD and mTBI. These collaborative five-year efforts are the Consortium to Alleviate PTSD, or CAP, and the Chronic Effects of Neurotrauma Consortium, or CENC. Approximately $20.336M of DoD funding and up to $25M of VA funds are available for a single consortium award under CAP, while $37.175M of DoD funds and up to $25M of VA funds are available for a single consortium award under CENC. The DoD funds for these consortia are provided from FY12 PH/TBIRP funds. The VA will provide up to $5M per year for five years for both CAP and CENC.

Dr. Alan Peterson, University of Texas Health Science Center, San Antonio, will serve as the PI and director of the CAP award. This effort will be focused on developing the most effective diagnostic, prognostic, novel treatment, and rehabilitative strategies to treat acute PTSD and prevent chronic PTSD. A significant

Vision	Mission
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	**Establish, fund, and integrate both individual and multiagency research efforts that will lead to improved prevention, detection, and treatment of PH/TBI**

congressional special interest funds to complement core DoD research and development efforts. For more information on this execution model, see page 48 (DMRDP Execution).

With over $570M in appropriations, the CDMRP has supported and managed the execution of more than 320 PH/TBIRP projects since FY07, 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.

PH/TBIRP Recent Research Focus

Research supported by the DoD PH/TBIRP extends and complements ongoing DoD efforts towards promoting a better standard of care for PH (including PTSD) and TBI in the areas of prevention, detection, diagnosis, treatment, and rehabilitation.

- Development and Evaluation of Veteran Supportive Supervisor Training: Improving Reintegration of the Oregon National Guard and Reserves into the Workplace; *Leslie Hammer, Ph.D., Portland State University*
- Basic Cognitive Neuroscience of Memory and Self-Appraisals in PTSD; *Adam Brown, Ph.D., New York University School of Medicine*
- When Parents Go to War: Psychosocial Adjustment among the Families of Deployed OEF/OIF Service Members; *Deborah Beidel, Ph.D., University of Central Florida*
- PET Ligands for Measuring Tau in the Brains of Combatants after Traumatic Brain Injury; *Stanley Prusiner, M.D., University of California San Francisco*
- In Vivo Neuroimaging Biomarker Panel for Chronic Traumatic Encephalopathy; *David Okonkwo, M.D., Ph.D., University of Pittsburgh*
- Demyelination as a Target for Cell-Based Therapy of Chronic Blast-Induced Traumatic Brain Injury; *Piotr Walczak, M.D., Ph.D., and Miroslaw Janowski, M.D., Ph.D., Johns Hopkins University*

focus of the CAP will be a research effort to identify and confirm clinically relevant biomarkers for PTSD and co-occurring disorders.

Dr. David Cifu, Virginia Commonwealth University, will serve as the PI and director of the CENC award. This effort focuses on examining the factors which influence the chronic effects of mTBI and common comorbidities in order to develop improved diagnostic and treatment options. One area of critical understanding is to establish the relationship between mTBI and neurodegenerative disease.

The CAP and CENC are composed of multiple organizations to include academia, VA, and military research and treatment facilities. It is expected that additional studies will be incorporated to address evolving research needs in the areas of PTSD and mTBI, providing opportunities for expansion of the consortia and additional collaborations throughout the life of the CAP and CENC awards. Both consortia are part of the National Research Action Plan for Improving Access to Mental Health Services for Veterans, Service Members, and Families and will leverage existing resources and knowledge gained through DoD and VA infrastructure and research investments, as well as public and private academia and industry to advance highly translational PTSD and TBI research.

Small Business Innovation Research & Small Business Technology Transfer Research Programs

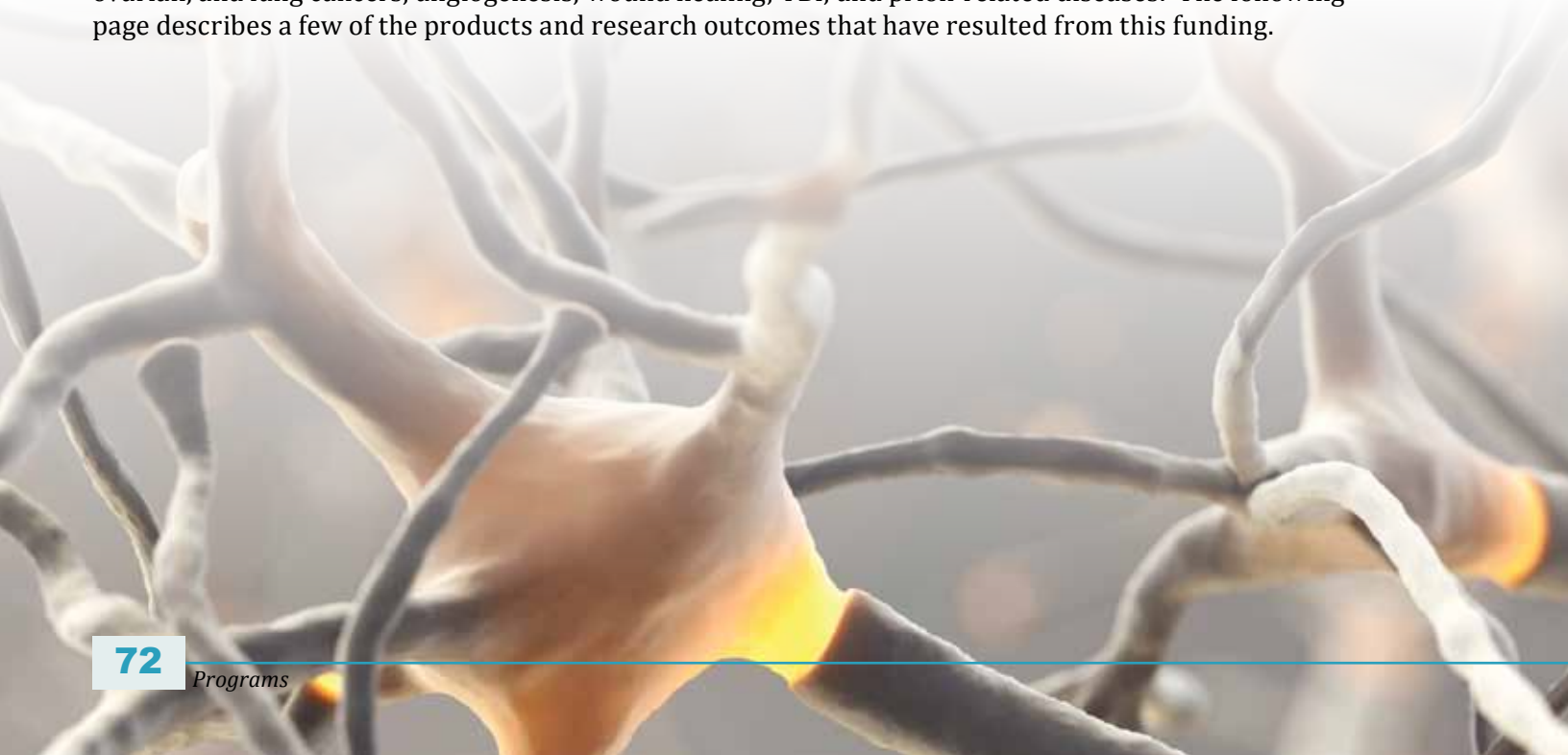
Background and Program History

The Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) Programs are competitive funding opportunities designed to strengthen the role of innovative small businesses in federally funded R&D. Initiated by the establishment of the SBIR program in 1982 by Congress, the goal of the programs is to provide small businesses with critical startup and development support that will allow them to compete successfully with larger businesses and commercialize products while fulfilling government needs. Congress established the STTR program, which requires that the small business work with a nonprofit research institution, in 1992 with a primary objective of bridging the gap between basic science and commercialization of its innovative discoveries.

DoD SBIR/STTR Program Objectives

- Stimulate technological innovation
- Increase private sector commercialization of federal research and development (R&D)
- Increase small business participation in federally funded R&D
- Foster participation by minority and disadvantaged firms in technological innovation

The programs are organized in three phases of development: Phase 1 establishes proof of principle, Phase 2 involves prototype development and testing, and Phase 3 centers on commercialization. SBIR/STTR funding is available for Phase 1 and Phase 2 projects, while Phase 3 support must come from private and non-SBIR government sources. Eleven federal agencies participate in the SBIR program and five participate in the STTR program, including the DoD. The CDMRP has worked with these programs since FY00 and FY04, respectively, to fill gaps and leverage research and product development not supported elsewhere in the CDMRP portfolio. Since that time, the CDMRP has managed more than 50 Phase 1 contracts and 25 follow-on Phase 2 contracts, for more than $26M, in areas such as breast, prostate, ovarian, and lung cancers; angiogenesis; wound healing; TBI; and prion-related diseases. The following page describes a few of the products and research outcomes that have resulted from this funding.



Research Outcomes

Oceanit Laboratories, Inc. received SBIR funding to address the off-target effects and limited bioavailability in solid tumors of current cancer therapeutics by creating a virus-like system that can target to surface molecules on cancer cells and deliver drugs in a focused manner to increase efficacy and reduce side effects. Thomas Hasling, Ph.D., and his colleagues combined self-assembling nanotubes (NanoVector) with anti-ErbB2 and demonstrated preferential targeting to breast cancer cells in vitro and release of a drug analog by photoactivation. Excitingly, in a mouse xenograft model, a NanoVector-antibody-Taxol conjugate was able to enhance tumor reduction over Taxol alone. Oceanit has filed a utility patent for the NanoVector technology, and is currently seeking funding for its further development. The company is also exploring the use of the NanoVector system in other applications such as gene delivery in genetic engineering and medical imaging.

Martin Baruch, Ph.D., of **Empirical Technologies, Inc.** partnered with the University of Virginia in an STTR award to design and build a prototype Computerized Brain Injury Assessment System, or CBIAS. The CBIAS uses eye movement and stance tests to assess the function of cranial nerves that are affected in mTBI. The system is portable and ruggedized for field deployment, and designed for operation by field medics and other early responders. The CBIAS was able to detect mTBI with high specificity and sensitivity in a clinical study of control and concussed patients conducted at Virginia Neurocare, Hunter-McGuire VA Hospital, and Fort Lee. Dr. Baruch and his colleagues hope to continue development of the CBIAS for deployment in and up to echelon/role II areas of care, as well as civilian care settings.

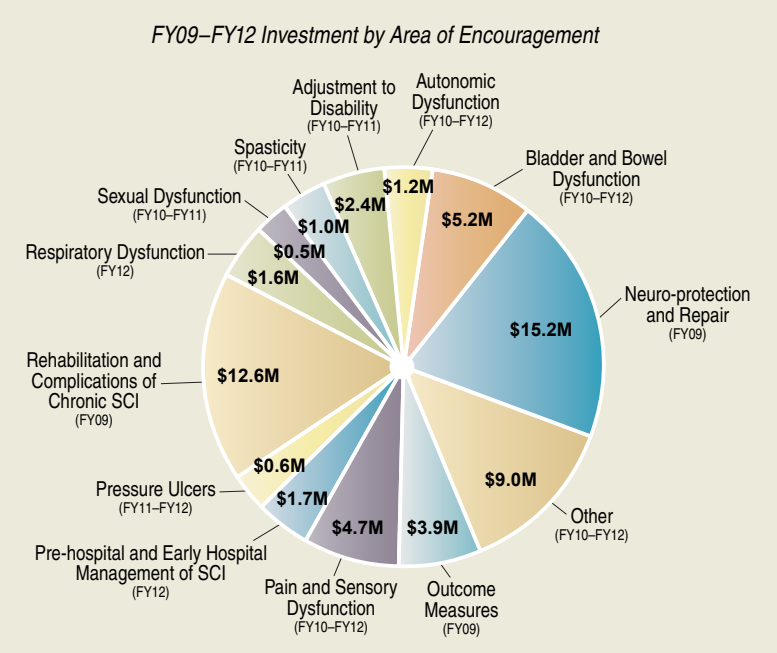
Ramila Philip, Ph.D., of **Immunotope, Inc.** was supported by SBIR funds to identify prostate cancer-specific autoantibody biomarkers that are potential early diagnostic targets. The company was awarded subsequent non-SBIR funds by the DoD to develop ImmuChip, an early diagnostic test for ovarian and prostate cancers.

Vladimir Gilman, and his colleagues at **Vivonics, Inc.** (formerly Infoscitex Corp.) were awarded STTR funding in partnership with Colorado State University to develop an antemortem test for animal prion infections such as transmissible spongiform encephalopathy and scrapie. The company used a proprietary high-throughput technique for isolating DNA aptamers specific for the disease isoform of the prion protein, developed assays to screen for the protein in animal biofluids, and demonstrated that the resulting system is capable of a detection limit more than 1,000 times more sensitive than traditional immunochemistry methods.

Spinal Cord Injury Research Program

Background and Program History

The Spinal Cord Injury Research Program (SCIRP) was established by Congress in FY09 with a $35M appropriation. Since then, a total of $97.85M has been appropriated to the program, including $30M in FY13. 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 spinal cord injury (SCI). The program's portfolio includes 98 awards spanning basic, translational, clinical, and qualitative research.



Mr. Paul Tobin, SCIRP IP member

"The work of the Spinal Cord Injury Research Program is critical because with a multi-disciplinary team of physicians, scientists and experts, the SCIRP IP members and peer reviewers can help identify gaps in our knowledge base about the injured spinal cord and create targeted opportunities for further investigation. Emphasis is placed on advancing medical discoveries and treatments that will ultimately impact the care received by our men and women in uniform, but this knowledge normally translates well to the civilian population as well. I thoroughly appreciate my participation in the SCIRP because I believe that the research that is funded through this program has made, and will continue to make, a significant difference in the lives of paralyzed Americans."

Linda Noble, Ph.D., University of California, San Francisco

Following acute SCI, matrix metalloproteinases (MMPs) are upregulated and promote early inflammation and disrupt the extracellular matrix and the blood-spinal cord barrier. Dr. Noble received an FY10 Investigator-Initiated Research Award to study the efficacy of an MMP inhibitor in a mouse model of SCI as well as a larger animal model with naturally occurring SCIs as the result of spontaneous rupture of an intervertebral disk. Studies in mice subjected to severe SCI show that the MMP inhibitor therapy given 8 hours post injury results in improved neurological outcome as well as bladder function by 6 weeks. In a larger animal model, baseline urodynamic data have been collected in both uninjured animals and animals with acute SCI. The unique two species design of this study will enable the rapid preclinical optimization of a promising MMP inhibitor for the treatment of SCI, laying the ground work for the rapid transition of this compound into human clinical trials.

Vision

Advance the treatment and management of spinal cord injury and ameliorate its consequences relevant to injured service members

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 service members, veterans, and other individuals living with spinal cord injury

Gordon Mitchell

Gillian Muir

Randy Trumbower

Gordon Mitchell, Ph.D., University of Wisconsin, Madison
Gillian Muir, D.V.M., Ph.D., University of Saskatchewan
Randy Trumbower, Ph.D., Emory University

While spinal plasticity can contribute to spontaneous recovery of limb and respiratory function following SCI, this recovery is slow, variable, and of limited extent. Drs. Mitchell, Muir, and Trumbower received an FY10 Translational Research Partnership Award to study the potential value of repeated acute intermittent hypoxia (AIH), alone or in combination with locomotor training, for improving limb function in animals with chronic SCI. Preliminary animal experiments have shown that AIH combined with daily training elicits sustained improvement in limb motor function and a sustained increased in walking speed and distance in treated animals with chronic cervical SCI. AIH represents a novel method for stimulating spinal plasticity in individuals with SCI, providing an avenue for controlled restoration of motor neuron excitability, and eventual restoration of volitional movement after incomplete SCI.

Adina Michael-Titus, D. Sc., Queen Mary College, University of London

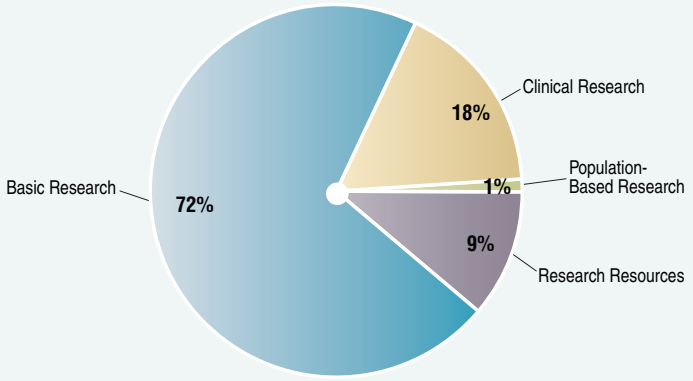
Presently, there is no treatment that can be administered immediately following SCI to mitigate the progression of damage. Building on previous work showing that omega-3 polyunsaturated fatty acids are potently neuroprotective when administered acutely following experimental SCI, Dr. Michael-Titus received an FY09 Investigator-Initiated Research Award to determine the optimum formulation, dosage, and treatment regimen of docosahexaenoic acid (DHA) to improve functional outcomes following experimental SCI. Mice treated with DHA free fatty acid 30 minutes following contusion injury showed significant locomotor improvement beginning 11 days following injury. Improved locomotion was associated with an increase in immune cells, suggesting an increase in inflammation in the DHA-treated injured spinal cord, contradicting the hypothesis that improved functional outcome following SCI is associated with reduced inflammation. Dr. Michael-Titus will continue to characterize the protective effect of DHA treatment on experimental SCI and will begin pharmacological experiments to study the tissue distribution and pharmacokinetics of DHA administration, in preparation for human clinical trials.

Tuberous Sclerosis Complex Research Program

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 then, a total of $47M has been appropriated to the program, including $6M in FY13. Today, the TSCRP is one of the leading sources of extramural TSC research funding in the United States. The TSCRP fills important gaps in TSC research not addressed by other funding agencies. The program's investment strategy is adapted yearly to facilitate rapid change and to better target funding to the most critical TSC research areas, thus ensuring that the program remains responsive to current needs and future opportunities. A total of 97 awards have been made through FY12, bridging basic, clinical, and population-based research.

FY02–FY12 TSCRP Portfolio by Research Area



Mark Zervas, Ph.D., Brown University

TSC results from the loss of both alleles of the TSC1 or TSC2 gene, where one bad allele is often inherited from a parent and the other allele develops a mutation during embryonic development. Dr. Mark Zervas received FY10 and FY11 TSCRP awards to investigate the effect of Tsc1 loss in the mouse brain at different points during embryonic development. He used a novel mouse model to delete both Tsc1 alleles specifically in thalamic neurons at different time points in embryonic development. This work has demonstrated that deletion of Tsc1 in the developing thalamus leads to both behavioral symptoms (in neurons in these mice) and anatomical changes in the brain; and that the severity of this phenotype depends on the timing and distribution of cells with Tsc1 loss during development. Further, the growth-regulating mTOR pathway, which is overactive in patients with TSC, was disrupted in neurons these mice, suggesting a previously unknown temporal role of the mTOR pathway in brain development.

Ms. Nikki Seefeldt, TSCRP Consumer Reviewer

"I was very impressed with the whole process; it is well thought-out, organized and planned. I think it's the smartest way to conduct research, actually, because you are getting the entire perspective of how the research has the potential to impact the community. Valuable input from clinicians, researchers, but also patients and caregivers all balance quite nicely."

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

Kevin Ess, M.D., Ph.D., Vanderbilt University Medical Center

Novel tools to facilitate the understanding of TSC gene function and disease pathogenesis are needed because traditional mouse models of TSC are limited due to a very mild disease phenotype. Dr. Ess received an FY09 Idea Development Award to characterize brain abnormalities and hamartoma formation in tsc2-deficient zebrafish. He found that alterations in brain development in tsc2-deficient zebrafish lead to extensive disorganization of gray and white matter and ectopically positioned cells. Tsc2-deficient fish also have increased mTOR Complex 1 (TORC1) activity, which was reversed by treatment with rapamycin or expression of TSC2 mRNA. Further, transplantation of fluorescently labeled tsc2-deficient cells into wild-type zebrafish embryos caused wild-type neurons in the host brain to become mispositioned, with tsc2-deficient cells with increased TORC1 signaling found in multiple organs by eight months, and apparent hamartomas of tsc2-deficient cells in the brain after one year. Dr. Ess concluded that the tsc2 mutant cells have cell autonomous and possibly non-cell autonomous mechanisms that lead to aberrant brain development.

Aristotelis Astrinidis, Ph.D., Drexel University[1]

TSC results from loss of function of the TSC1 or TSC2 proteins, which leads to uncontrolled cell growth through the hyperactivation of the mTOR signaling pathway. While the protein mTOR is sensitive to treatment with the antibiotic rapamycin, this drug has not been effective at killing TSC tumor cells. Dr. Astrinidis believes that targeting multiple proteins in the TSC/mTOR pathway including polo-like kinase 1 (PLK1) may yield novel treatment avenues for this disease. He received an FY08 Idea Development Award to investigate the role of PLK1 in cell survival and determine the effect of PLK1 inhibition on TSC1/TSC2- null cells. Dr. Astrinidis demonstrated that the observed increased levels of PLK1 in TSC1/TSC2-null cells were due to increased protein stability and were reduced following treatment with rapamycin. Treatment of TSC1/TSC2-null cells with the PLK1 inhibitor BI-2536 decreased cell viability and clonogenic survival through induction of apoptosis and disruption of autophagy, the process of the breakdown and recycling of damaged or unnecessary cellular components. These results suggest that BI-2536, which has already been found to be safe and effective in a subset of leukemia patients, may be an effective treatment against TSC tumors.

[1]Currently at the University of Ioannina School of Medicine in Ioannina, Greece

Ms. Reico Donato, TSCRP Consumer Reviewer

"It has been a wonderful experience to be able to participate in this program after advocating for funding of it for many years. I particularly like the fact that the consumer reviewers have the equal weight votes as scientific reviewers to make sure that grants are awarded to proposals which show potential for improving the quality of lives of those who are affected by TSC."

Appendix A: FY92–FY12

Table A-1. Overview of Appropriations, Applications Received, and Awards Made for FY92–FY12

Programs Managed by CDMRP (a)	Fiscal Year	Appropriations Received (in millions)	Applications Received	Applications Funded
Amyotrophic Lateral Sclerosis	2007, 2009-2012	$31.90	241	23
Autism	2007-2012	$41.40	988	97
Bone Marrow Failure	2008-2012	$16.95	307	41
Breast Cancer	1992-2012	$2,803.90	47,659	6,314
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	51
DOD/VA	1999-2000	$6.79	88	9
Duchenne Muscular Dystrophy	2011-2012	$7.20	42	8
Genetic Studies of Food Allergies	2009-2010	$4.38	60	9
Gulf War Illness	2006, 2008-2012	$49.00	212	57
Institutionally Based Programs	1995-2010	$486.31	306	267
Lung Cancer	2009-2012	$58.00	1,192	81
Multiple Sclerosis	2009-2012	$18.10	489	51
Myeloproliferative Disorders	2004	$4.25	18	9
National Prion	2002	$42.50	136	38
Neurofibromatosis	1996-2012	$242.85	1,217	294
Osteoporosis	1995	$5.00	105	5
Ovarian Cancer	1997-2012	$196.45	2,753	284
Peer-Reviewed Cancer	2009-2012	$59.80	1,905	139
Peer-Reviewed Medical	1999-2006, 2008-2012	$594.50	6,036	493
Peer-Reviewed Orthopaedic	2009-2012	$188.50	620	159
Prostate Cancer	1997-2012	$1,210.00	14,314	2,604
Spinal Cord Injury	2009-2012	$67.85	510	98
Tuberous Sclerosis	2002-2006, 2008-2012	$41.00	445	97
Programs Executed on Behalf of Others (b)				
Army Rapid Innovation Fund	2011-2012	$19.46	-	8
Chiropractic Clinical Trials	2010	$8.10	5	1
Defense Medical (DHPe)	2010-2012	$190.31	575	113
Psychological Health/Traumatic Brain Injury	2007, 2009-2012	$574.00	3,012	322
Total		**$7,132.45**	**85,140**	**11,802**

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

Appendix B: FY12–FY13

Table B-1. FY12–FY13 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
2012	**$6.4M** for Peer-Reviewed Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $288,000 Sequestration: $465,000 **Management Costs** $490,000 (8.7%)	**Research** Therapeutic Development: $4,545,000 Therapeutic Idea: $612,000
	Total: $6.4M	**Total: $1,243,000**	**Total: $5,157,000**
2013	**$7.5M** for Peer-Reviewed Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $206,850 Sequestration: $595,000 Section 3001: $8,000 Section 3004: $2,000 **Budgeted Management Costs** $669,000 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $6,019,150
	Total: $7.5M	**Total: $1,480,850**	**Total: $6,019,150**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-2. FY12–FY13 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
2012	**$5.1M** for Autism Research	**Withholds** USAMRMC: $229,000 Sequestration: $362,000 **Management Costs** $382,060 (8.5%)	**Research** Idea Development: $3,022,823 Idea Development Multi PI: $359,899 Pilot Award: $744,218
	Total: $5.1M	**Total: $973,060**	**Total: $4,126,940**
2013	**$6M** for Peer-Reviewed Autism Research	**Withholds** USAMRMC: $165,480 Sequestration: $476,000 Section 3001: $6,000 Section 3004: $2,000 **Budgeted Management Costs** $532,052 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $4,815,468
	Total: $6.0M	**Total: $1,181,532**	**Total: $4,815,468**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-3. FY12–FY13 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
2012	**$3.2M** for Bone Marrow Failure Disease Research Program	**Withholds** USAMRMC: $144,000 Sequestration: $172,000 **Management Costs** $207,434 (7.2%)	**Research** Idea: $2,064,894 Postdoctoral Fellowship: $611,672
	Total: $3.2M	**Total: $523,434**	**Total: $2,676,566**
2013	**$3.2M** for Peer-Reviewed Bone Marrow Failure Disease Research Program	**Withholds** USAMRMC: $88,260 Sequestration: $254,000 Section 3001: $3,000 Section 3004: $1,000 **Budgeted Management Costs** $285,374 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $2,568,366
	Total: $3.2M	**Total: $631,634**	**Total: $2,568,366**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-4. FY12–FY13 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
2012	**$120M** for the Peer-Reviewed Breast Cancer Research Program **$695,475** in proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $5,400,000 Sequestration: $7,923,000 **Management Costs** $9,902,579 (9.3%)	**Research** Clinical Translational Research Award – Partnering PI Option: $5,861,445 Collaborative Scholars and Innovators Award: $13,081,477 Era of Hope Scholar Award: $11,395,180 Era of Hope Scholar Expansion Award: $6,200,574 Idea Award: $16,581,406 Idea Award – Partnering PI Option: $6,412,176 Idea Expansion Award: $5,901,523 Idea Expansion Award – Collaborative Option: $3,404,101 Innovator and Scholar Concept Award: $589,217 Innovator Award: $7,800,941 Innovator Expansion Award: $6,816,577 Postdoctoral Fellowship Award: $13,425,278
	Total: $120,695,475	**Total: $23,225,579**	**Total: $97,469,895**
2013	**$120M** for the Peer-Reviewed Breast Cancer Research **$601,567** in proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $3,309,900 Sequestration: $9,512,000 Section 3001: $119,000 Section 3004: $39,000 **Budgeted Management Costs** $10,119,953 (9.4%)	**Research** Budgeted Peer-Reviewed Research: $97,501,714
	Total: $120,601,567	**Total: $23,114,853**	**Total: $97,501,714**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-5. FY12–FY13 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
2012	**$3.2M** for Peer-Reviewed Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $144,000 Sequestration: $229,000 **Management Costs** $244,500 (8.7%)	**Research** Investigator-Initiated Research: $499,632 Investigator-Initiated Research – Optional Qualified Collaborator(s): $1,620,004 Therapeutic Idea: $462,864
	Total: $3.2M	**Total: $617,500**	**Total: $2,582,500**
2013	**$3.2M** for Peer-Reviewed Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $88,260 Sequestration: $254,000 Section 3001: $3,000 Section 3004: $1,000 **Budgeted Management Costs** $285,374 (10.0%)	**Budgeted Research** Budgeted Peer-Reviewed Research: $2,568,366
	Total: $3.2M	**Total: $631,634**	**Total: $2,568,366**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-6. FY12–FY13 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
2012	**$10M** for Peer-Reviewed Gulf War Illness Research	**Withholds** USAMRMC: $450,000 Sequestration: $742,000 **Management Costs** $769,699 (8.7%)	**Research** Consortium: $5,003,388 Investigator-Initiated Research: $3,034,913
	Total: $10M	**Total: $1,961,699**	**Total: $8,038,301**
2013	**$20M** for Peer-Reviewed Gulf War Illness Research	**Withholds** USAMRMC: $551,580 Sequestration: $1,588,000 Section 3001: $20,000 Section 3004: $6,000 **Budgeted Management Costs** $1,783,442 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $16,050,978
	Total: $20M	**Total: $3,949,022**	**Total: $16,050,978**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-7. FY12–FY13 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
2012	**$10.2M** for Peer-Reviewed Lung Cancer Research Program	**Withholds** USAMRMC: $459,000 Sequestration: $724,000 **Management Costs** $820,000 (9.1%)	**Research** Concept Award: $1,494,563 Idea Development: $2,140,457 Translational Research Partnership: $1,560,450 Translational Research Partnership – Optional Nested Clincal Fellow or Resident Traineeship: $3,001,530
	Total: $10.2M	**Total: $2,003,000**	**Total: $8,197,000**
2013	**$10.5M** for Peer-Reviewed Lung Cancer Research	**Withholds** USAMRMC: $289,560 Sequestration: $834,000 Section 3001: $11,000 Section 3004: $3,000 **Budgeted Management Costs** $936,244 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $8,426,196
	Total: $10.5M	**Total: $2,073,804**	**Total: $8,426,196**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-8. FY12–FY13 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
2012	**$3.8M** for Peer-Reviewed Multiple Sclerosis Research	**Withholds** USAMRMC: $171,000 Sequestration: $269,000 **Management Costs** $290,300 (8.6%)	**Research** Idea Award: $3,069,700
	Total: $3.8M	**Total: $730,300**	**Total: $3,069,700**
2013	**$5M** for Peer-Reviewed Multiple Sclerosis Research	**Withholds** USAMRMC: $137,880 Sequestration: $397,000 Section 3001: $5,000 Section 3004: $2,000 **Budgeted Management Costs** $445,812 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $4,012,308
	Total: $5M	**Total: $987,692**	**Total: $4,012,308**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-9. FY12–FY13 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
2012	**$12.8M** for Peer-Reviewed Neurofibromatosis Research Program	**Withholds** USAMRMC: $575,000 Sequestration: $1,100,000 FFRDC Reduction: $20,000 **Management Costs** $990,934 (8.9%)	**Research** Clinical Trial: $1,124,998 Clinical Consortium: $3,285,827 Exploration – Hypothesis Development: $758,196 Investigator-Initiated Research: $1,738,493 Investigator-Initiated Research Award – Nested Postdoctoral Traineeship: $1,058,541 Investigator-Initiated Research – Optional Qualified Collaborator: $916,011 New Investigator: $1,232,000
	Total: $12.8M	**Total: $2,685,934**	**Total: $10,114,066**
2013	**$15M** for Peer-Reviewed Neurofibromatosis Research Program	**Withholds** USAMRMC: $417,000 Sequestration: $858,000 SBIR/STTR: $207,000 Congressional: $20,000 **Budgeted Management Costs** $1,349,800 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $12,148,200
	Total: $15M	**Total: $2,851,800**	**Total: $12,148,200**

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. FY12–FY13 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
2012	**$16M** for Peer-Reviewed Ovarian Cancer Research Program	**Withholds** USAMRMC: $720,000 Sequestration: $1,137,000 **Management Costs** $1,227,908 (8.7%)	**Research** Outcomes Consortium Development Award: $1,933,151 Ovarian Cancer Academy Award – Early-Career Investigators: $2,262,079 Pilot Award: $2,270,285 Pilot Award – Optional Nested Teal Predoctoral Scholar: $1,367,037 Synergistic Translational Leverage Award: $1,073,924 Teal Innovator Award: $3,732,693 Translational Leverage Award: $275,923
	Total: $16M	**Total: $3,084,908**	**Total: $12,915,092**
2013	**$20M** for Peer-Reviewed Ovarian Cancer Research	**Withholds** USAMRMC: $551,580 Sequestration: $1,588,000 Section 3001: $20,000 Section 3004: $6,000 **Budgeted Management Costs** $1,783,442 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $16,050,978
	Total: $20M	**Total: $3,949,022**	**Total: $16,050,978**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-11. FY12–FY13 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
2012	**$12.8M** for Peer-Reviewed Cancer Research Program	**Withholds** USAMRMC: $576,000 Sequestration: $940,000 **Management Costs** $1,158,682 (10.3%)	**Research** Blood Cancer: $3,041,168 Colorectal Cancer: $2,146,329 Genetic Cancer: $417,501 Kidney Cancer: $746,160 Melanoma and Other Skin Cancers: $1,218,000 Mesothelioma: $636,613 Pancreatic Cancer: $1,539,122 Pediatric Brain Tumor: $440,425
	Total: $12.8M	**Total: $2,674,682**	**Total: $10,125,318**
2013	**$15M** for Peer-Reviewed Cancer Research	**Withholds** USAMRMC: $413,670 Sequestration: $1,191,000 Section 3001: $15,000 Section 3004: $5,000 **Budgeted Management Costs** $1,337,533 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $12,037,797
	Total: $15M	**Total: $2,962,203**	**Total: $12,037,797**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

FY12 Peer-Reviewed Cancer Research Program: The conference agreement provides $12.8M 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 no 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 service members and their families.

Note: The CDMRP requested congressional guidance regarding topic area changes between the PRCRP and the PRMRP again in FY12, 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.

FY13 Peer-Reviewed Cancer Research Program: The conference agreement provides $15M 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, neuroblastoma, and listeria vaccine for cancer. The funds provided under the Peer-Reviewed Cancer Research Program shall only be used for the purposes listed above. The conferees direct the Assistant Secretary of Defense (Health Affairs) to provide a report no 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 service members and their families.

Table B-12. FY12–FY13 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
2012	**$50M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $2,250,000 Sequestration: $3,602,000 **Management Costs** $3,449,611 (7.8%)	**Research** Arthritis: $3,289,681 Composite Tissue Transplantation: $1,042,576 Drug Abuse: $2,241,999 Dystonia: $176,800 Epilepsy: $3,865,335 Food Allergies: $748,549 Fragile X Syndrome: $1,121,277 Inflammatory bowel disease: $1,552,500 Interstitial cystitis: $945,142 Lupus: $1,461,048 Malaria: $1,949,680 Nanomedicine for Drug Delivery Science: $6,302,018 Neuroblastoma: $2,691,879 Osteoporosis and related bone disease: $2,773,160 Paget's Disease: $1,263,225 Post-traumatic osteoarthritis: $2,526,765 Scleroderma: $2,131,607 Tinnitus: $3,277,474 Tuberculosis: $1,337,674
	Total: $50M	**Total: $9,301,611**	**Total: $40,698,389**
2013	**$50M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $1,378,920 Sequestration: $3,970,000 Section 3001: $50,000 Section 3004: $16,000 **Budgeted Management Costs** $4,458,508 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $40,126,572
	Total: $50M	**Total: $9,873,428**	**Total: $40,126,572**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

FY12 Peer Reviewed Medical Research Program: The conference agreement provides $50M 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 FY12, 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.

FY13 Peer Reviewed Medical Research Program: The conference agreement provides $50M 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 the following areas: chronic kidney disease, chronic migraine and post-traumatic headaches, composite tissue transplantation, dengue, DNA vaccine technology for postexposure prophylaxis, dystonia, epilepsy, food allergies, Fragile X syndrome, hantavirus, hereditary angioedema, inflammatory bowel disease, interstitial cystitis, leishmaniasis, lupus, malaria, nanomedicine for drug delivery science, pancreatitis, polycystic kidney disease, post-traumatic osteoarthritis, pulmonary hypertension, rheumatoid arthritis, scleroderma, and tinnitus. The conferees emphasize that the additional funding provided under the Peer-Reviewed Medical Research Program shall be devoted only to the purposes listed above.

Table B-13. FY12–FY13 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
2012	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $1,350,000 Sequestration: $2,168,000 **Management Costs** $2,391,632 (9.0%)	**Research** Clinical Trial: $3,295,174 Idea Development Award: $8,537,693 Idea Development Award – Nested Career Development Option: $962,059 Translational Research Partnership Award: $9,811,150 Translational Research Partnership Award – Nested Career Development Option: $1,484,293
	Total: $30M	**Total: $5,909,632**	**Total: $24,090,368**
2013	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $827,340 Sequestration: $2,382,000 Section 3001: $30,000 Section 3004: $10,000 **Budgeted Management Costs** $2,675,066 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $24,075,594
	Total: $30M	**Total: $5,924,406**	**Total: $24,075,594**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-14. FY12–FY13 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
2012	**$80M** for Peer-Reviewed Prostate Cancer Research	**Withholds** USAMRMC: $3,600,000 Sequestration: $5,828,000 **Management Costs** $6,152,114 (8.7%)	**Research** Clinical Trial: $173,129 Clinical Consortium: $970,863 Postdoctoral Training Award: $3,530,756 Idea Development: $11,984,066 Idea Development Award – New Investigator Option: $2,849,832 Collaborative Undergraduate HBCU Student Summer Training Program: $992,855 Synergistic Idea Development: $7,302,202 Physician Research Training: $3,936,398 Laboratory-Clinical Transition: $3,448,343 Exploration – Hypothesis Development: $791,532 Health Disparity Research Award – New Investigator and Qualified Collaborator Options: $948,979 Health Disparity Research Award – Qualified Collaborator Option/ Nested HD Traineeship Option: $1,020,322 Health Disparity Research: $1,390,812 Health Disparity Research Award – Qualified Collaborator Option: $1,456,145 Transformative Impact: $22,952,099 Pathology Resource Network Site: $92,994 Clinical Consortium Award – Clinical Research Site: $578,559
	Total: $80M	**Total: $15,580,114**	**Total: $64,419,886**
2013	**$80M** for Peer-Reviewed Prostate Cancer Research	**Withholds** USAMRMC: $2,206,260 Sequestration: $6,352,000 Section 3001: $80,000 Section 3004: $26,000 **Budgeted Management Costs** $7,133,574 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $64,202,166
	Total: $80M	**Total: $15,797,834**	**Total: $64,202,166**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-15. FY12–FY13 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
2012	**$9.6M** for Peer-Reviewed Spinal Cord Research Program	**Withholds** USAMRMC: $432,000 Sequestration: $704,000 **Management Costs** $763,263 (9.0%)	**Research** Clinical Trial Award: $1,607,794 Investigator-Initiated Research: $3,036,455 Translational Research Award: Single PI Only: $3,056,488
	Total: $9.6M	**Total: $1,899,263**	**Total: $7,700,737**
2013	**$30M** for Peer-Reviewed Spinal Cord Research	**Withholds** USAMRMC: $827,340 Sequestration: $2,382,000 Section 3001: $30,000 Section 3004: $10,000 **Budgeted Management Costs** $2,675,066 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $24,075,594
	Total: $30M	**Total: $5,924,406**	**Total: $24,075,594**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-16. FY12–FY13 Tuberous 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
2012	**$5.1M** for Peer-Reviewed Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $229,000 Sequestration: $186,000 **Management Costs** $389,500 (8.3%)	**Research** Exploration – Hypothesis Development: $678,201 Idea Development: $2,860,253 Idea Development – Optional Qualified Collaborator: $757,046
	Total: $5.1M	**Total: $804,500**	**Total: $4,295,500**
2013	**$6M** for Peer-Reviewed Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $165,480 Sequestration: $476,000 Section 3001: $6,000 Section 3004: $2,000 **Budgeted Management Costs** $535,052 (10.0%)	**Research** Budgeted Peer-Reviewed Research: $4,815,468
	Total: $6M	**Total: $1,184,532**	**Total: $4,815,468**

The following abbreviation is used for withholds: USAMRMC, U.S. Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-17. FY12 Army Rapid Innovation Fund CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Withholds and Management Costs	Investment Strategy
2012	$5,887,000	**Management Costs** $236,491	**Research** Broad Agency Announcement: $5,650,508
	Total: $5,887,000	**Total: $236,491**	**Total: $5,650,508**

Table B-18. FY12 Defense Medical Research and Development Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Withholds and Management Costs	Investment Strategy
2012	$37,054,853	**Management Costs** $1,426,277	**Research** Advanced Technology/Therapeutic Development Award: $494,337 Applied Neurotrauma Research Award: $1,932,931 Applied Neurotrauma Research Award – Partnering Option: $2,543,280 Applied Neurotrauma Research Award with Clinical Trial: $619,239 Applied Psychological Health Award with Clinical Trial – Partnering Option: $822,447 Applied Research and Advanced Technology Development Award: $7,285,386 Basic Psychological Health Award: $572,026 Broad Agency Announcement: $10,237,229 Clinical Trial Award: $2,243,288 Clinical Trial Award – Regenerative Medicine, Pain, Sensory System: $8,310,012 DMRDP-IIRA-Broad Agency Announcement: $271,612 Military Infectious Diseases Applied Research Award: $134,000 PH/TBI-IIRA-Broad Agency Announcement: $87,258 PTSD New Investigator Award: $75,531
	Total: $37,054,853	**Total: $1,426,277**	**Total: $35,628,576**

The following abbreviations are used: DMRDP-IIRA, Defense Medical Research and Development Program Investigator-Initiated Research Award; PH/TBI-IIRA, Psychological Health and Traumatic Brain Injury Investigator-Initiated Research Award; PTSD, post-traumatic stress disorder

Table B-19. FY12 Psychological Health/Traumatic Brain Injury Research Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Withholds and Management Costs	Investment Strategy
2012	$91,660,309	**Management Costs** $9,316,657	**Research** Applied Neurotrauma Research Award: $6,474,313 Applied Neurotrauma Research Award – Partnering Option: $779,501 Applied Research and Advanced Technology Development Award: $299,728 Broad Agency Announcement: $11,767,133 Chronic Effects of Neurotrauma Consortium Award: $36,141,000 Consortium to Alleviate PTSD Award: $19,352,048 DMRDP-IIRA-Broad Agency Announcement: $330,018 Intramural PTSD Investigator-Initiated Research Award: $65,105 Investigator-Initiated Research Award: $261,856 PH/TBI-IIRA-Broad Agency Announcement: $2,637,767 TBI Multidisciplinary Research Consortium Award: $900,000 Traumatic Brain Injury Research Award: $1,377,801 Traumatic Brain Injury Research Award – Partnering PI Option: $1,957,382
	Total: $91,660,309	**Total: $9,316,657**	**Total: $82,343,652**

The following abbreviations are used: PTSD, post-traumatic stress disorder; DMRDP-IIRA, Defense Medical Research and Development Program Investigator-Initiated Research Award; PH/TBI-IIRA, Psychological Health and Traumatic Brain Injury Investigator-Initiated Research Award; TBI, traumatic brain injury

Appendix C: Breast Cancer Research Semipostal Awards FY99–FY12

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

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
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
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

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

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

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

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
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
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
FY12	Yang	$465,000	University of California, San Diego	Regulation of Breast Cancer Stem Cell by Tissue Rigidity
	Giancotti	$174,837[11]	Memorial Sloan-Kettering Cancer Center	Autophagy and TGF-Beta Antagonist Signaling in Breast Cancer Dormancy at Premetastatic Sites

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

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

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

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

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

[11]Total award amount was $331,499; remaining funds were from the FY12 BCRP.

Appendix D: Acronyms

ADPKD ..... autosomal dominant polycystic kidney disease

AIH ..... acute intermittent hypoxia

ALS.....Amyotrophic Lateral Sclerosis

ALSRP..... Amyotrophic Lateral Sclerosis Research Program

ARP .....Autism Research Program

ASD ..... Autism Spectrum Disorder

B .....billion

BADER .....Bridging Advanced Developments for Exceptional Rehabilitation Consortium

BCRP .....Breast Cancer Research Program

BCRS .....Breast Cancer Research Semipostal

BMD .....Becker muscular dystrophy

BMFRP .....Bone Marrow Failure Research Program

BUSPH .....Boston University School of Public Health

CAP .....Consortium to Alleviate PTSD

CCCRP .....Combat Casualty Care Research Program

CDC.....Centers for Disease Control and Prevention

CDMRP .Congressionally Directed Medical Research Programs

CENC ..... Chronic Effects of Neurotrauma Consortium

CRC .....colorectal cancer

CRMRP .....Clinical and Rehabilitative Medicine Research Program

CSF ..... cerebralspinal fluid

DAB2IP..... disabled homolog 2 interacting protein

DC ..... dendritic cell

DDR2.....Discoidin Domain Receptor 2

DHA .....docosahexaenoic acid

DIM..... diindolylmethane

DMDRP .....Duchenne Muscular Dystrophy Research Program

DMRDP .....Defense Medical Research and Development Program

DoD .....Department of Defense

DRMRP ..... Deployment Related Medical Research Program

DTIC .....Defense Technical Information Center

EDA .....Ectodysplasin A

EGS .....Electronic Grants System

EPIC .....European Prospective Investigation into Cancer and Nutrition

EPO ..... erythropoietin

eRA..... Electronic Research Administration

fALS .....familial SOD1-mediated ALS

FDA.....U.S. Food and Drug Administration

FdCyd ..... Fluorodeoxycytidine

FY .....fiscal year

GRMD ..... golden retriever muscular dystrophy

GRPs ..... glial-restricted precursor cells

GSFARP ..... Genetic Studies of Food Allergies Research Program

GWI .....Gulf War Illness

GWIRP .....Gulf War Illness Research Program

GWVIRP ..... Gulf War Veterans' Illnesses Research Program

HBCU/MIs..... Historically Black Colleges and Universities and Minority Institutions

HGSC .....high grade serous carcinoma

hMSC .....human mesenchymal stem cells

HSC .....hematopoietic stem cells

HSPC.....hematopoietic stem/progenitor cells

HSV .....Herpes Simplex virus type I system

HSV-rAAv9 .....derivied rAAV serotype9

IMPaCT .....Innovative Minds in Prostate Cancer Today

IOM..... Institute of Medicine

IP .....Integration Panel

iPSCs .....induced pluripotent stem cells

IPT.....Integrated Product Team

JPC.....Joint Programmatic Committee

LCRP ..... Lung Cancer Research Program

M.....million

MBI ..... Molecular Breast Imaging

MDS .....myelodysplastic syndrome

METRC ..... Major Extremity Trauma Research Consortium

MIC ..... Minority Initiative Committee
MIDRP ..... Military Infectious Diseases Research Program
MIUP ..... Minority and Underserved Populations Program
MMPs ..... matrix metalloproteinases
MOMRP ..... Military Operational Medicine Research Program
MPNST ..... malignant peripheral nerve sheath tumor
MPO-Gd bis-5HT-DTPA-Gd
MRI ..... magnetic resonance imaging
MS ..... Multiple sclerosis
MSC ..... mesenchymal stem cell
MSRP ..... Multiple Sclerosis Research Program
mTBI ..... mild TBI
NF ..... neurofibromatosis
NF-kB ..... nuclear factor kB
NFRP ..... Neurofibromatosis Research Program
NIH ..... National Institutes of Health
NLK ..... Nemo-like kinase
NSAIDs ..... non-steroidal anti-inflammatory drugs
OASD[HA] ..... Office of the Assistant Secretary of Defense for Health Affairs
OCRP ..... Ovarian Cancer Research Program
ORP ..... Office of Research Protections
PA ..... Program Announcement
PARP ..... poly ADP ribose polymerase
PCaP ..... Prostate Cancer Project
PCBN ..... Prostate Cancer Biorepository Network
PCCTC ..... Prostate Cancer Clinical Trials Consortium
PCRP ..... Prostate Cancer Research Program
PET ..... positron emission tomography
PH ..... psychological health
PH/TBIRP ..... Psychological Health and Traumatic Brain Injury Research Program
PI ..... Principal Investigator
PLK1 ..... polo-like kinase 1
PRCRP ..... Peer Reviewed Cancer Research Program
PRMRP ..... Peer Reviewed Medical Research Program
PRORP ..... Peer Reviewed Orthopaedic Research Program
PTEN ..... phosphatase and tensin homolog
PTSD ..... post-traumatic stress disorder
R&D ..... research and development
RAA ..... renin-angiotensin-aldosterone
RAD ..... Research Area Directorate
ROS ..... reactive oxygen species
RTC13 ..... Read-Through compound-13
sALS ..... sporadic ALS
SBIR ..... Small Business Innovation Research
SCC ..... squamous cell carcinomas
SCI ..... spinal cord injury
SCIRP ..... Spinal Cord Injury Research Program
SJA ..... Staff Judge Advocate
SNVs ..... single nucleotide variants
SO ..... Science Officer
SSE ..... Office of Surety, Safety, and Environment
STTR ..... Small Business Technology Transfer Research
Tak1 ..... TGFβ-activated kinase 1
TBI ..... traumatic brain injury
TEM1 ..... tumor endothelial marker 1
TEs ..... Transposable elements
TIFAB ..... forkhead-associated domain B
TORC1 ..... mTOR Complex 1
TRL ..... technology readiness level
TSC ..... tuberous sclerosis complex
TSCRP ..... Tuberous Sclerosis Complex Research Program
USAMRAA ..... U.S. Army Medical Research Acquisition Activity
USAMRMC ..... U.S. Army Medical Research and Materiel Command
VA ..... U.S. Department of Veterans Affairs

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