CDMRP

Department of Defense

CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

2017 ANNUAL REPORT

US Army Medical Research and Materiel Command

Letter from the Director

For the past four years I have had the honor of serving as the Director of the Congressionally Directed Medical Research Programs (CDMRP). During this time, I have seen tremendous advances in medical research focused on our Service Members, Veterans and American public.

The CDMRP is focused on helping the men, women, and children living with illness, disease or medical affliction, by investing in groundbreaking medical research that will result in improved outcomes for the patients and their families. As a Department of Defense program, we partner with scientists, consumers, academia and private industry to develop the most innovative and impactful medical advancements.

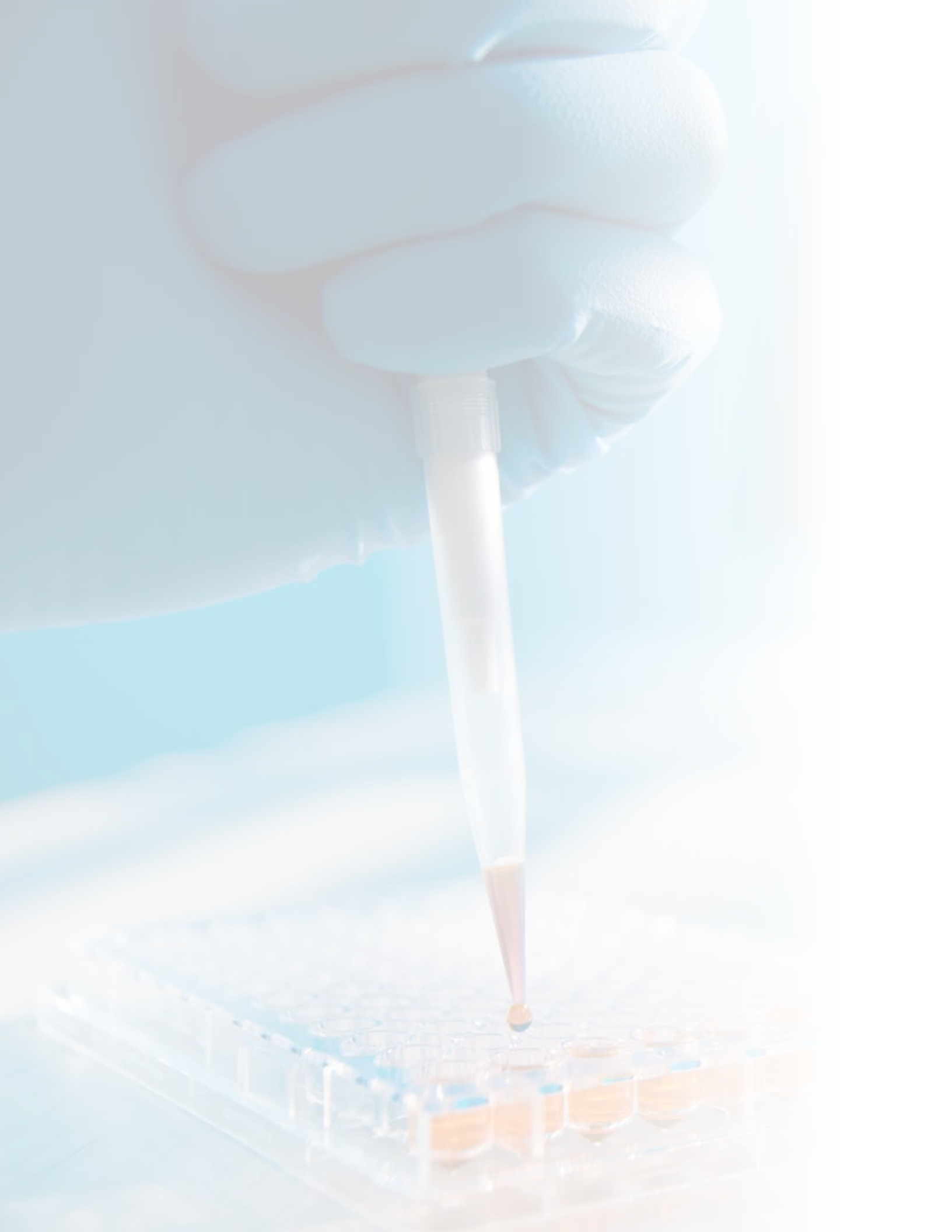
In all of our endeavors, and specifically through this report, we believe in transparency of all of our processes. The 2017 Annual Report reflects the composite work of our partnerships. This report shows program facts, funding profiles, the numbers and types of research projects awarded and specific highlights for each program.

The CDMRP will continue working towards transforming healthcare by maintaining focus on the patients and their families.

Colonel Wanda L. Salzer, M.D., M.H.Sc.,
US Air Force Medical Corps
Director, CDMRP

Department of Defense
US Army Medical Research and Materiel Command
Congressionally Directed Medical Research Programs
Annual Report
September 30, 2017

Congressionally Directed Medical Research Programs
ATTN: MCMR-CD
1077 Patchel Street
Fort Detrick, MD 21702-5024
Phone: 301-619-7071
Fax: 301-619-7796
http://cdmrp.army.mil



Introduction

Vision

Transform healthcare for Service Members and the American public through innovative and impactful research

Mission

Responsibly manage collaborative research that discovers, develops, and delivers healthcare solutions for Service Members, Veterans and the American public

History

Originated in 1992, the Congressionally Directed Medical Research Programs (CDMRP) is a global funding organization that represents a unique partnership among the US Congress, the military, and the public to manage individual programs for cancer research, military medical research, and other disease- and injury-specific research. All the programs managed by CDMRP share the common goal of advancing paradigm-shifting research, solutions that will lead to cures or improvements in patient care, or breakthrough technologies and resources for clinical benefit. CDMRP implements the investment of congressionally directed dollars provided to fund groundbreaking, high-impact, meritorious research that targets critical gaps that other agencies may not hazard to fund. CDMRP also provides support for the management of core dollars (presidential budget) directed at both intramural and extramural military medical research portfolio areas.

CDMRP is located within the Department of Defense (DoD) US Army Medical Research and Materiel Command (USAMRMC). USAMRMC's mission is to responsively and responsibly create, develop, deliver, and sustain medical capabilities for the Warfighter by leading the advancement of military medicine, which is achieved through innovative management and efficient execution of allocated funding (read more about USAMRMC under Military Partnerships on page 11). Since its first appropriation of congressional funding in fiscal year 1992 (FY92), CDMRP has been responsible for managing more than $11.7 billion (B) in appropriations.

Fiscal Year 2017

CDMRP continued in FY17 with increased congressional appropriations for certain programs and the addition of three new programs, the Hearing Restoration Research Program (HRRP; page 50), the Kidney Cancer Research Program (KCRP; page 54), and the Lupus Research Program (LRP; page 58). The research funding managed by CDMRP over the last 10 years is shown in **Figure 1**.

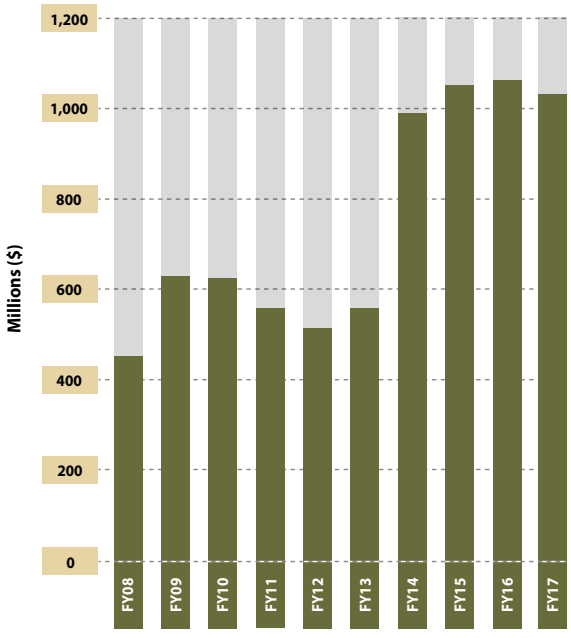


Figure 1. FY08–FY17 Research Funding

Currently Funded Research Programs:

- Alcohol and Substance Abuse Disorders
- Amyotrophic Lateral Sclerosis
- Autism
- Bone Marrow Failure
- Breast Cancer
- Breast Cancer Research Semipostal
- Duchenne Muscular Dystrophy
- Epilepsy
- Gulf War Illness
- Hearing Restoration
- Joint Warfighter Medical
- Kidney Cancer
- Lung Cancer
- Lupus
- Military Burn
- Multiple Sclerosis
- Neurofibromatosis
- Orthotics and Prosthetics Outcomes
- Ovarian Cancer
- Parkinson's
- Peer Reviewed Alzheimer's
- Peer Reviewed Cancer
- Peer Reviewed Medical
- Peer Reviewed Orthopaedic
- Prostate Cancer
- Reconstructive Transplant
- Spinal Cord Injury
- Tick-Borne Disease
- Trauma Clinical
- Tuberous Sclerosis Complex
- Vision

Major Undertakings in FY17 Are Summarized on the Following Pages

Institute of Medicine Review

Since its inception, CDMRP has followed guidance from the Institute of Medicine (IOM), now called the Health and Medicine Division (HMD) of the National Academy of Medicine. The highly regarded two-tiered review process utilized by CDMRP to review applications submitted in response to Program Announcements (PAs) is based on the first recommendations made by the IOM in 1993 (*Strategies for Managing the Breast Cancer Program: A Report to the U.S. Army Medical Research and Development Command*, 1993). In 1997 the IOM published A Review of the DoD's Program for Breast Cancer Research. In that report, the unique aspects of the Breast Cancer Research Program (BCRP) were called out, including emphasis on consumer participation and the focus on innovation in research. Recommendations in the 1997 report were taken into consideration by BCRP and other programs and were implemented where potential benefits and continued success could be identified.

Since CDMRP's review process had not been reviewed since the 1997 IOM report, in 2014 the Senate Committee on Appropriations, Senate Report Number 113-211, directed the DoD to contract with HMD to conduct a study of CDMRP's two-tiered review process and coordination of research priorities with the National Institutes of Health (NIH). The goal of this review was to identify how well the two-tier review processes and coordination efforts were working and whether there may be areas that could be improved. A review by HMD presented a great opportunity for assessment of CDMRP's processes by a distinguished panel of experts convened by HMD. Although HMD was contracted to prepare this assessment by the Defense Health Agency (DHA), CDMRP was actively engaged and responsive to HMD requests, providing presentations, written responses to questions, and participation in two open sessions with the HMD panel during the assessment period. In addition to the review of the two-tiered program cycle, the HMD panel assessed the coordination of CDMRP with NIH and the US Department of Veterans Affairs (VA). A full report from HMD on CDMRP's two-tiered review process and coordination efforts was published in November 2016. The HMD panel recommended areas for improvement, but found overall that the CDMRP review process was effective in allocating funding within each research program and also noted that, "the inclusion of consumers in both tiers of the review is a positive aspect of CDMRP review process that can benefit scientists and consumers alike." CDMRP appreciates and respects the assessment and viewpoints of the ad hoc HMD committee and is integrating their findings and recommendations as part of our ongoing efforts to improve the CDMRP review process and strengthen coordination with NIH and VA.

Electronic Biomedical Research Application Portal and the Electronic Grants System

Even though these systems are used by many others, they are managed and most heavily used by CDMRP. They provide critical support for CDMRP's management of programs and individual awards. The Electronic Biomedical Research Application Portal (eBRAP) and Electronic Grants System (EGS) are Defense Business Certified systems that provide mission-critical capabilities that are not supported through Grants.gov or any other federal system. eBRAP and EGS support multiple organizations for the processing and management of DoD medical research grants that have high visibility to Congress and the DHA.

eBRAP is an Extramural and Intramural research pre-application and full application receipt, processing, and management portal that supports the missions of the DHA, USAMRMC, the US Army Medical Research Acquisition Activity (USAMRAA), the Special Operations Command, and CDMRP. In response to 106 FY16 funding opportunities, eBRAP received and processed over 10,400 pre-applications and over 6,100 full applications. During FY17, eBRAP is managing about 120 funding opportunities, with pre-application and full application receipts extending from June 2017 through March 2018.

eBRAP highlights:

- Streamlines operational efficiency and effectiveness in retrieving and processing research applications through increased automation and greater data integrity.
- Is the front-end interface for bilateral communication with the research community in over 109 countries.
- Provides worldwide web-based accessibility for receipt and processing of pre-applications and full applications and documents required for award negotiations.
- Supports business process to fund biomedical research that meets congressional and DoD missions by providing nimble responsiveness to annual changes in appropriations, congressional language, and program focus.
- Provides functionality to the military medical community by directly accepting DoD intramural application submissions, which is not supported by Grants.gov.
- Has multi-user functionality allowing eBRAP to be easily customized for use by other organizations.
- Interfaces directly with Grants.gov for retrieval, processing, and administrative review of extramural applications.
- Provides "plug and play" pre-application component that provides modules to accommodate the varying needs of each PA.
- Performs computer-automated processing, modification, and compliance of pre-application and proposal applications according to each PA.
- Provides capability to allow researchers to review and modify application components (following submission to Grants.gov).
- Provides capability to communicate with the research community both on a one-to-one basis and in batches and uses milestone-triggered automated delivery of communications to the research community.
- Is responsive to Contracting, Human Use, and Animal Use regulations

The CDMRP Website

The CDMRP website is an important means to disseminate information to the public, the scientific community, and all CDMRP stakeholders, as well as the use of various social media techniques.

The website (http://cdmrp.army.mil) features videos, press releases, research highlights, consumer stories, program books, annual reports, abstracts for all awards, and significant research outcomes and accomplishments supported by CDMRP research programs. An overview of CDMRP's review processes along with the results of recent funding recommendations for each research program can also be found on the website. In FY16 and FY17, web pages for new research programs Tick-Borne Disease, Kidney Cancer, and Lupus were added to the website. Social media outlets used by the CDMRP to expand information dissemination strategies include YouTube (https://www.youtube.com/user/CDMRP) and Twitter (https://twitter.com/CDMRP).

- Provides real-time customer service to answer researchers' questions and manage the pre-application and application components required for award execution.
- Supports data transfer to EGS and other systems.

EGS is a business system that is designed to focus on activities related to management of funded awards from negotiations to closeout, allowing multiple organizations to collaborate in a virtual workspace.

EGS highlights:

- EGS enables real-time electronic workflows among USAMRMC offices, including Acquisitions (USAMRAA), the Office of Surety, Safety and Environment, and the Office of Research Protections (ORP).
- Multiple user groups are able to collaborate, allowing data inputs, generating of reports, and performing daily administrative tasks associated with research award management and monitoring progress in a central, secure location.
- Integrated processes include award, program, and financial management. Program evaluation is incorporated into EGS to create a seamless solution to enable efficiencies.
- System-to-system interfaces allow transfer of data between USAMRMC and DoD partner organizations.
- Research outcomes and findings are captured and categorized in customized modules for analysis in program evaluation efforts, interaction with funded investigators, and reporting to stakeholders.
- Award data in EGS are made publicly available nightly via a connection to the CDMRP website, in which users can view project abstracts and publications.
- Use of EGS has expanded to include management of DoD Intramural awards managed by several Joint Program Committees (JPCs)/Program Area Directorates (PADs) and other USAMRMC agencies.
- Recent enhancements allow the ORP to manage the complete life cycle of animal and human research protocols funded under CDMRP-managed awards and other DoD organizations.
- EGS supports data transfers to external systems, including the International Cancer Research Partnership and Federal RePORTER.

Federal RePORTER

In response to US Government Accountability Office recommendations, CDMRP continued its efforts to support government transparency and engage the public, research community, and federal agencies by participating in the STAR METRICS® Federal RePORTER initiative (http://federalreporter.nih.gov). This initiative was to create a searchable database of funded scientific awards across agencies, including the US Department of Health and Human Services (HHS), Department of Agriculture, DoD, National Science Foundation, VA, Environmental Protection Agency, and National Aeronautics and Space Administration. Federal RePORTER utilizes some of its basic functions on a core set of data required from all agencies, allowing analysis and comparison. Current functionality includes the ability to search for similar projects using fingerprinting technology, in addition to mapping and charting capabilities. These features can be explored to conduct analysis of research topics for program-specific needs and collaboration. Additional features are in the planning stages. CDMRP-funded awards from FY08 onwards are currently included in Federal RePORTER, and new awards will be posted by the end of each fiscal year.

> "The ALSRP has really given me a lot of hope because I've learned that we know a lot more about what's going on than we did even last year. Every year I go, I'm amazed at how much the body of knowledge has grown. It's exponential, so we're going to get there; I guarantee it."
> **Matt Belina, 2017**

Our Programs

Highlights of FY16–FY17 programs managed and/or supported by CDMRP can be found within the program pages in this Annual Report, beginning on page 31. As detailed in **Table 1**, CDMRP successfully completed obligation of FY16 appropriations across 28 programs encompassing 859 new research awards. In addition, in FY17, CDMRP initiated the management of $1,117.1 million (M) across 31 programs.

Table 1. CDMRP Programs, Appropriations and Applications Received and Awarded in FY16-FY17

Research Programs Managed by the CDMRP	FY16				FY17	
	Funds Received (in millions)	Applications Received	Applications Funded	Funding Modifications Completed	Funds Received (in millions)	Applications Received to Date
Alcohol and Substance Abuse Disorders	$4.0	n/a	-	2	$4.0	TBD
Amyotrophic Lateral Sclerosis	$7.5	39	9	-	$7.5	55
Autism	$7.5	72	10	-	$7.5	TBD
Bone Marrow Failure	$3.0	28	5	-	$3.0	TBD
Breast Cancer	$120.0	1,609	86	6	$120.0	863
Breast Cancer Semipostal [1]	$0.6	n/a	-	2	TBD	TBD
Duchenne Muscular Dystrophy	$3.2	27	4	-	$3.2	TBD
Epilepsy	$7.5	41	6	-	$7.5	TBD
Gulf War Illness	$20.0	61	29	6	$20.0	14
Hearing Restoration	n/a	n/a	n/a	n/a	$10.0	TBD
Joint Warfighter Medical [2]	$50.0	26	17	23	$50.0	TBD
Kidney Cancer	n/a	n/a	n/a	n/a	$10.0	TBD
Lung Cancer	$12.0	298	29	-	$12.0	173
Lupus	n/a	n/a	n/a	n/a	$5.0	TBD
Military Burn	$8.0	2	4	6	$8.0	1
Multiple Sclerosis	$6.0	53	10	-	$6.0	TBD
Neurofibromatosis	$15.0	51	12	-	$15.0	65
Orthotics and Prosthetics Outcomes	$10.0	48	14	-	$10.0	TBD
Ovarian Cancer	$20.0	204	29	2	$20.0	189
Parkinson's	$16.0	100	11	-	$16.0	136
Peer Reviewed Alzheimer's	$15.0	69	15	2	$15.0	TBD
Peer Reviewed Cancer	$50.0	463	89	-	$60.0	TBD
Peer Reviewed Medical	$278.7	1,145	143	16	$300.0	534
Peer Reviewed Orthopaedic	$30.0	95	19	1	$30.0	50
Prostate Cancer	$80.0	693	108	3	$90.0	142
Reconstructive Transplant	$12.0	142	22	1	$12.0	TBD
Spinal Cord Injury	$30.0	114	29	1	$30.0	TBD
Tick-Borne Disease	$5.0	56	7	-	$5.0	TBD
Trauma Clinical	$10.0	1	-	2	$10.0	TBD
Tuberous Sclerosis Complex	$6.0	54	11	-	$6.0	44
Vision	$10.0	-	4	2	$15.0	TBD
Additional Supported DoD Programs/Projects						
Centers of Excellence	$3.1	n/a	n/a	1	$2.9	TBD
Defense Medical Research and Development	$120.5	276	39	135	$96.0	233
Defense Medical Research and Development Congressional Special Interest Restoral	$31.6	n/a	23	30	$35.5	TBD
Psychological Health/Traumatic Brain Injury	$69.6	79	26	24	$75.0	6
Small Business Innovation Research/ Small Business Technology Transfer	$3.6	27	49	8	TBD	34
Vision Prosthesis	$0.2	n/a	-	3	n/a	TBD
Other Submission Processes						
MRMC - BAA [3]	n/a	156	n/a	n/a		119
Total	**$1,065.6**	**6,029**	**859**	**276**	**$1,117.1**	**2,658**

[1] Breast Cancer Research Semipostal funds applications received and reviewed by the Breast Cancer Research Program.

[2] Joint Warfighter Execution Management Breakdown: 11 awards and 19 mods managed by CDMRP; 2 awards and 3 mods managed by the US Army Medical Materiel Development Activity (USAMMDA); 4 awards and 1 mod managed by the US Army Medical Materiel Agency (USAMMA).

[3] CDMRP manages the application receipt and review process for the USAMRMC Broad Agency Announcement. Proposals that are funded are counted in the program that provided the funding. Of the 156 applications received, CDMRP funded 30.

Our Management Cycle

CDMRP has always employed a flexible management cycle that is responsive to the needs of both the individual programs and the requirements of the stakeholders for each program, including Congress, the DoD, researchers, consumer communities, and the public. Programs follow the management cycle described in detail on the following pages, but they do so with consideration of the requirements and needs of each program's stakeholders. Each step in the management cycle is depicted in ***Figure 2*** *and discussed in detail in this section.*

Funding Process

CDMRP is funded through the DoD via annual congressional legislation known as the Defense Appropriations Act. For most programs, the DoD sends a multi-year budget request to Congress in the form of the President's Budget. However, dollars for CDMRP are not considered part of the DoD's core mission and are therefore not included in the DoD's requested budget. Rather, the dollars to fund CDMRP are added every year during the budget approval cycle by members of the House or Senate, in response to requests by consumers and disease survivors.

1. Core Dollars, Congressional Appropriation, and Receipt of Funds

Funds for programs are a direct response to the needs of Service Members, beneficiaries, research communities, and the public at large. The congressionally appropriated programs are added annually to the DoD appropriation. The Defense Health Program (DHP) also includes funds for military medical research from the President's Budget (core dollars). Over the years, CDMRP has been one of the main organizations within USAMRMC to serve as a research execution manager for these funds.

2. Stakeholders Meeting

For new programs, a Stakeholders meeting is held to survey the research landscape and identify important areas of gaps to scientists and consumers. Stakeholders are world-renowned consumers, scientists, and clinicians who have an interest in any given field related to the program. Recommendations from the Stakeholders meeting are used to facilitate vision setting.

3. Vision Setting

A Vision Setting meeting is held to define an annual investment strategy for a given program. The development of an annual investment strategy is based on the recommendations of the National Academy of Medicine's HMD. The purpose of an annual Vision Setting meeting is to discuss the current landscape of the disease, condition, or injury; identify scientific and clinical research gaps; and develop a strategy to fill these gaps. The process of vision setting brings together experts in science, the clinic, and the military, as well as consumers, to determine the program's goals and the award mechanisms to be offered. Based on the discussions, the vision setting process concludes with development of an investment strategy for the program's available funds. Funding opportunities/PAs are developed to support the most critical scientific and consumer interest area gaps identified by the panel of experts and consumers for the program year.

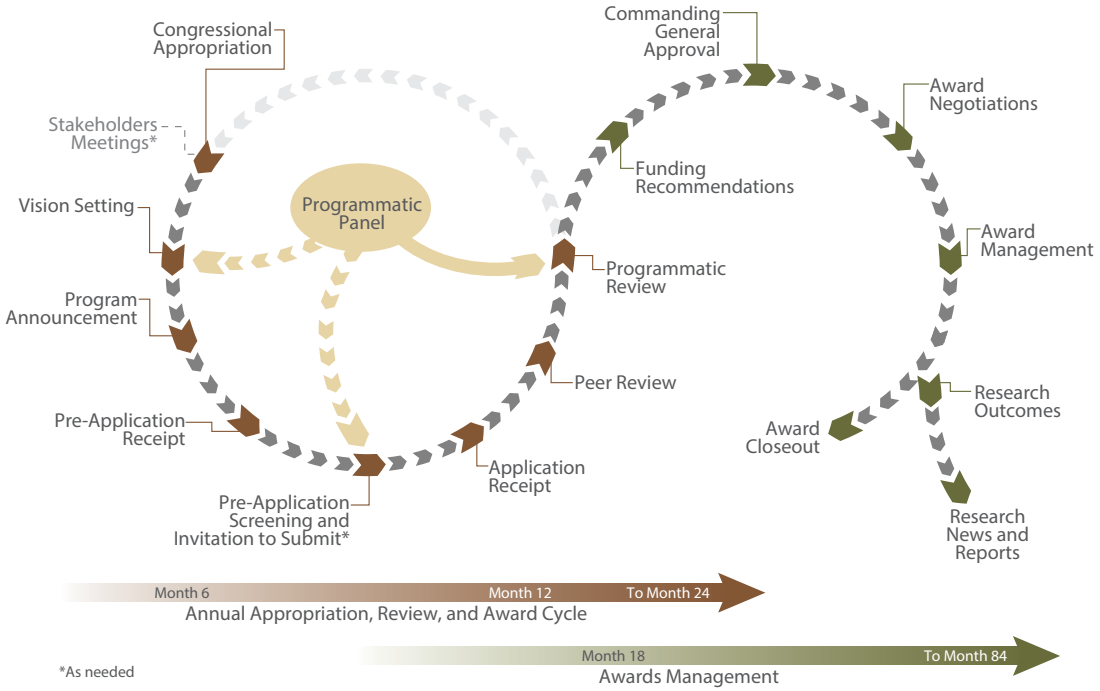


Figure 2. Program Management Cycle

4. Program Announcements and Broad Agency Announcements

The award mechanisms are released as PAs or Broad Agency Announcements (BAAs), depending on the goals of the program. Both of these solicitations provide applicants with details about a particular funding opportunity, including the programmatic intent, a description of the type of studies being requested, and eligibility and submission requirements, including the application review criteria and processes.

5. Applicant Submission and Receipt

For all of the award mechanisms, application submission requires a multistep process consisting of pre-application submission (which includes a letter of intent or a pre-proposal as specified in the PA or BAA), followed by full application submission. Pre-proposals are an abbreviated submission outlining the research aims, strategy, innovation, and/or impact of the project. Pre-proposals may be screened by either the programmatic reviewers or a scientific peer review panel, based on the requirements described in each PA or BAA. The final product of the pre-proposal screening is a recommended list of invited applicants. As summarized in **Table 2**, in FY16, CDMRP received 8,840 pre-proposals that, after screening and invitation, resulted in 2,748 full applications received. In addition, CDMRP received 2,737 full applications from mechanisms that required a letter of intent, for a total of 5,485 full applications received in this fiscal year.

On October 1, 2014, CDMRP began oversight of the receipt and review of submissions to the USAMRMC BAA for Extramural Medical Research, a funding opportunity that is open year-round and solicits projects aligned to research areas and topics of interest to USAMRMC. These areas of interests are determined annually by the USAMRMC PADs in response to evolving research priorities and knowledge gaps. For FY17, 461 pre-applications and 119 full applications were submitted to the BAA process and forwarded to the USAMRMC PADs for programmatic decisions.

Table 2. Number of Submissions Received October 1, 2016-September 30, 2017, across FY16-17 Programs

Mechanism Submissions	
Pre-proposals screened	8,840
Letters of intent received	3,592
Total pre-applications received	12,432
Full Application Submissions	
Full applications from invitations only	2,748
Full applications from letters of intent	2,737
Total full applications	5,485

6. Two-Tier Review Process

The two-tier review of applications is based on the recommendations set forth by the IOM committee in 1993 and affirmed in the most recent 2016 report. The two-tier review process includes both scientific peer review and programmatic review. The goal is to give every application a fair and balanced review, taking steps to ensure that conflicts of interest do not influence the process and the needs of the Warfighter and the general public are taken into account. Additional details regarding the two tiers of review can be accessed on the CDMRP website at http://cdmrp.army.mil/about/2tierrevprocess.shtml.

Scientific Peer Review: Scientific peer review is a criteria-based process where applications are evaluated based on their scientific and technical merit. The scientific peer review panel evaluates each application based on the review criteria outlined in the PA or BAA and rates the various criteria numerically or adjectivally. Each application is evaluated for its own merit, independent of other applications. The product of scientific peer review is a summary statement that describes the strengths and weaknesses of the application in accordance with the published review criteria and includes an overall scientific peer review score.

Programmatic Review: After applications have been peer reviewed, they go through a criteria-based review by experts including scientists, clinicians, military members, and/or consumers. This group of experts is termed the Programmatic Panel. At the programmatic review level, the Programmatic Panel uses the criteria published in the PA or BAA (i.e., programmatic relevance, portfolio balance, military impact, and scientific merit, etc.) in a comparison-based assessment of submitted applications. The product of Programmatic Review is a list of applications recommended for funding. To ensure impartiality and the integrity of the process, programmatic reviewers are prohibited from applying for funds for the fiscal year in which they participated in vision setting.

7. Approval of the Awards List

Following programmatic review, the recommended for funding list is reviewed and approved by the appropriate authority, the Commanding General, USAMRMC, and/or the DHA, Research and Development Directorate, within the Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]). Upon approval, electronic notification is sent to all program applicants to inform them of their funding status.

8. Award Negotiations and Management

Negotiation and management of awards are a major focus of USAMRMC offices and organizations, including CDMRP, USAMRAA, and ORP. During the period of performance for awards (which can be up to 4 years), CDMRP actively manages and monitors progress. The awards management process is depicted in **Figure 3**. Over the past 5 years, an average of 781 new awards were made each fiscal year. As of September 30, 2017, CDMRP has managed 15,797 awards throughout its funding history.

Once an application has been recommended and approved for funding, it is assigned a Science Officer, who serves as the technical representative for the lifetime of the award. The Science Officer also acts as a liaison, maintaining the proper flow of information between the awardee institution, the Principal Investigator (PI), CDMRP, and offices within USAMRMC. Technical analysis of the budget with

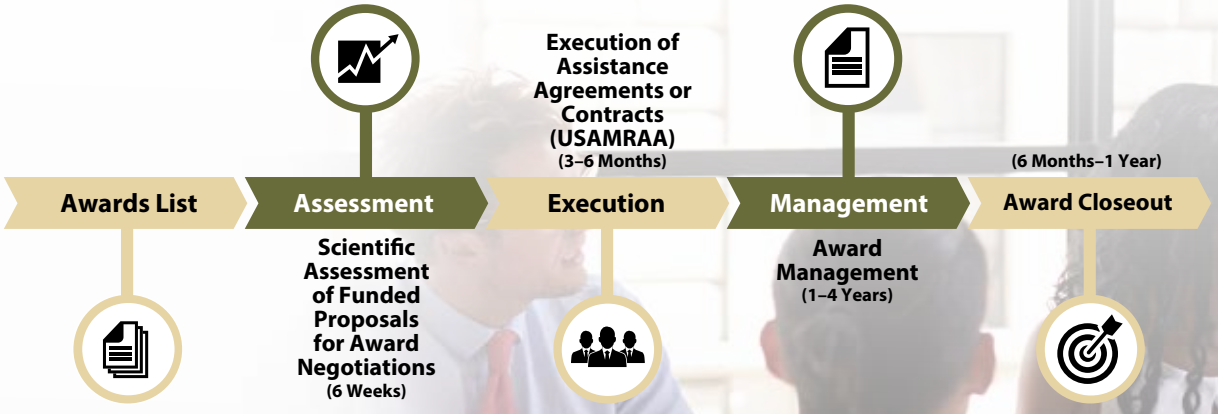


Figure 3. Awards Management Process

respect to the scope of work to be performed is completed prior to the award being made to maximize savings and avoid overlap in research funding with other funded projects within CDMRP, as well as other federal agencies. Once all aspects of negotiation are complete, an award is signed, and an assistance agreement (grant or cooperative agreement) or contract is issued. A CDMRP Grants Officer's Representative or Contracting Officer's Representative is assigned to each respective award and serves as the technical point of contact for the Contracting Officer. The life-cycle management of awards continues throughout the period of performance with monitoring of the technical progress through annual/quarterly reports, regulatory review, financial reporting, and funding duplication. At a minimum, all funded organizations are required to submit annual progress reports and quarterly financial reports. However, the progress, especially for larger complex awards and consortia, may also be monitored through other means, including quarterly progress reports, external advisory boards, Government Steering Committees, site visits, teleconferences, and other meetings throughout the entire period of performance.

9. Award Closeout

Award closeout takes place at both USAMRAA and CDMRP and is usually performed 6 months after the period of performance has expired. During this time, CDMRP carefully reviews 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, and the data is captured in CDMRP's EGS.

10. Research News and Reports/Public Relations

To maintain transparency, various communication processes and social media techniques are used to share information with stakeholders and the general public. The newly designed CDMRP website (http://cdmrp.army.mil) remains a central mode of communication to the public, featuring videos, press releases, research highlights, consumer stories, program books, annual reports, and abstracts and publications for all awards. Information on the progress of awards can be found on the Defense Technical Information Center website at http://www.dtic.mil/dtic/. Social media outlets used by CDMRP to expand information dissemination strategies include YouTube (http://www.youtube.com/user/CDMRP) and Twitter (https://twitter.com/CDMRP); in addition, CDMRP maintains an e-mail listserve of more than 85,000 unique recipients.

Multistep Process to Minimize Award Duplication and Overlap

Step 1

PIs are required to submit a list of past, current, and pending funding support at the time of application submission.

Step 2

Screen for duplicate submissions during compliance checks.

Step 3

Identification of project innovation, research duplication, and overlap during the two-tier review process by peers in the field (specifically program staff from other federal funding agencies).

Step 4

List of updated funding support at the time of award notification, which is certified by the award recipient's Sponsored Programs Office.

Step 5

Review of submitted documents and research program sites to assess pending and existing funding support during award negotiations.

Step 6

PIs are required to provide a list of updated funding support in annual technical progress reports.

Step 7

Technical review of progress and review of Federal RePORTER annually throughout the award period of performance, which includes a review for funding overlap and duplication.

Vital Partnerships

In FY17, nearly 335 consumers served on CDMRP peer review panels, and over 50 served as programmatic reviewers.

Today, over 2,100 consumers have represented their communities and lay organizations at least once since 1992, and their role continues to be vital.

In FY17, nearly 2,115 scientists and clinicians provided necessary subject matter expertise on peer review panels, and over 380 scientists and clinicians served as programmatic reviewers. As of September 30, 2017, over 140 scientists, clinicians, and consumers have served as ad hoc programmatic reviewers. Since its inception, approximately 11,350 researchers have been funded by CDMRP to improve the health and quality of life of all people.

Throughout the years, partnerships with the consumer and scientific communities, professional organizations, and military communities have been fostered to fund innovative and impactful research areas and gaps, as well as to reduce redundancy within each program's portfolio and across federal agencies. The following sections discuss these partnerships and collaborations with stakeholders and other federal and non-federal agencies.

Consumers

CDMRP has been a promoter for the inclusion of consumers (patients, survivors, family members, and/or caregivers) in the review of research applications as full voting members. Consumers 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. Consumers first served as reviewers for CDMRP at the programmatic review level in 1993, and their role was soon expanded to scientific peer review in 1995. CDMRP has developed a model of consumer inclusion that has been adopted by other funding agencies. Consumers are identified for scientific peer review panels through nominations submitted by the lay organizations. Consumers also serve at the programmatic review level of CDMRP. In each tier of review, consumers serve alongside scientists, clinicians, and leading experts, and all have an equal voice and vote in deliberations. Throughout the growth of CDMRP, consumers and stakeholders remain the foundation for many of the programs executed and managed by CDMRP. For more information on consumer involvement, see the consumer involvement pages on the CDMRP website (http://cdmrp.army.mil).

The Scientific Community

The scientific community has been an essential partner in assisting CDMRP to shape the future of healthcare. Scientists serve on both the peer and programmatic review panels during the review of applications; conduct the research that elucidates the complex causes of diseases, conditions, and injuries; and help to translate this knowledge into improved prevention, treatment interventions, patient survival, and quality of life. External experts in the program cycle bring the most current and up-to-date knowledge to the table when research strategies and field gaps are identified during vision setting and when applications are being peer and programmatically reviewed.

Military Partnerships

US Army Medical Research and Materiel Command

Vision
Lead the advancement of military medicine

Mission
Responsively and responsibly create, develop, deliver, and sustain medical capabilities for the Warfighter

CDMRP is located within USAMRMC, the largest medical materiel developer within the DoD, with the responsibility for medical research, development, and acquisition and medical logistics management. USAMRMC is responsible for managing medical research programs that address both military and civilian beneficiaries. The USAMRMC's motto, "Protect, Project, Sustain," underscores its support of the Warfighter through ensuring that solutions are provided for America's sons and daughters who serve the nation around the globe. 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 DoD's planning and budget process and align with the principal needs and military operations within the DoD. Non-core programs are funded through congressional line-item additions to the DoD budget. CDMRP provides management support for both types of funding and 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**.

Figure 4. The USAMRMC Team

Many of the research projects managed by CDMRP have the potential to become fielded products for our Warfighters. USAMRMC has designed and implemented a process called "Decision Gate" to effectively manage medical materiel development in a cost-effective, consistent, and transparent process. Decision Gate is grounded in the DoD Directive 5000 series, US Food and Drug Administration (FDA) regulations, and best industry practices, and it allows USAMRMC to remain responsive to the changing needs of the Warfighter. Projects funded through CDMRP that have strong potential for development into a beneficial, military-relevant medical product are included in the Decision Gate process. To facilitate this process, CDMRP evaluates products from its research portfolio and assigns to each a Technology Readiness Level (TRL) code. 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 the criteria to be entered into the Decision Gate process, a point called

the Materiel Development Decision (MDD). Once in Decision Gate, product development will be guided by an Integrated Product Team. Science Officers from CDMRP are sometimes asked to participate on the Integrated Product Teams due to their scientific expertise, history of managing relevant awards, and relationship to the product developer. As the product matures, it goes through a series of decision points (called milestones) to determine whether it should continue as planned, continue with a revised plan, or have its 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 roughly correspond with Phase I clinical trial, Phase II clinical trial, and FDA approval, respectively. The Decision Gate process reflects USAMRMC's commitment to remain a good steward of taxpayer dollars and a world-class medical research and development (R&D) organization.

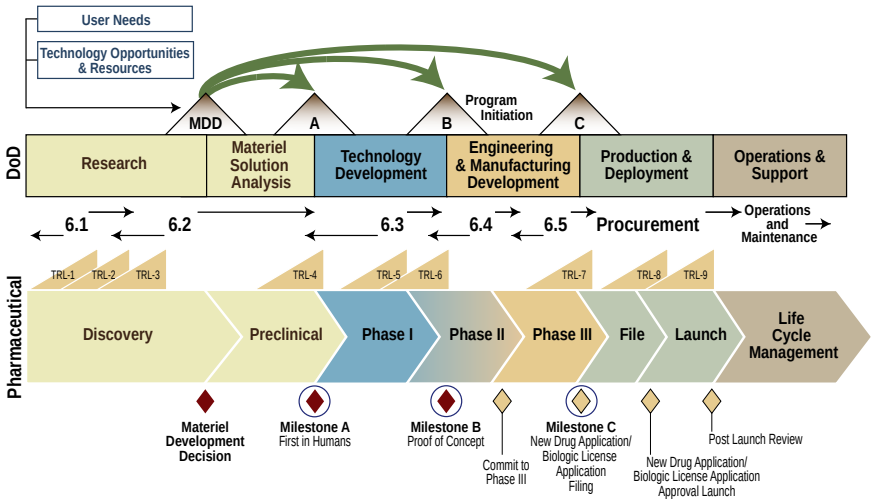


Figure 5. Decision Gate Life Cycle

Defense Health Agency, Research and Development Directorate

The DHA is a joint, integrated Combat Support Agency that reports to OASD(HA), as shown in **Figure 6**. The DHA enables the Army, Navy, and Air Force medical services to provide both a medically ready force and ready medical force to Combatant Commands in both peacetime and wartime.

Vision

Advance collaborative, innovative medical research and development to improve military community health and save lives on and off the battlefield

Mission

Implement best practices to responsibly design, prioritize and integrate medical research, development and acquisition programs across the continuum of care. By fostering strategic partnerships and transitioning medical discoveries to deployable products, R&D will enhance the readiness and resilience of the military community

The DHA, Research and Development Directorate, was established within DHA in 2014 as the core research program of the DoD to help coordinate and enhance the related medical research and development programs of the Army, Navy, Air Force, and Defense Advanced Research Projects Agency (DARPA). As directed by OASD(HA), the DHA, Research and Development Directorate, manages and executes the DHP Research, Development, Test, and Evaluation (RDT&E) appropriation. DHP congressional and core programs managed or supported by CDMRP are overseen by the DHA, Research and Development Directorate, which works closely with CDMRP to provide:

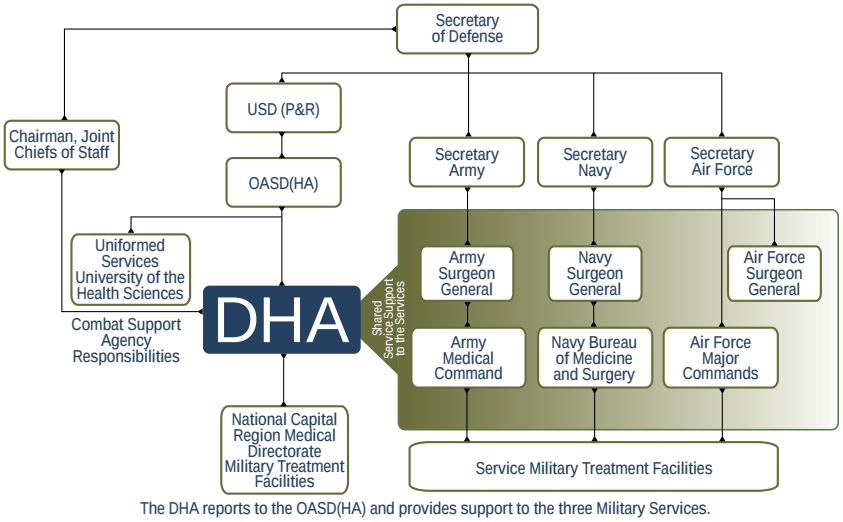


Figure 6. DHA Reporting and Support Structure

- Centralized oversight of R&D grants, projects, and initiatives across the Services and Military Health System to eliminate redundancy and reduce variance.
- Prioritization and direction of medical research to ensure maximal impact for Service Members and beneficiaries.

The DHA, Research and Development Directorate organizes annual focused Review and Analysis (R&A) meetings to facilitate short- and long-term planning of research within and across core medical R&D portfolios. These R&A meetings bring together senior leadership from across different military and government agencies (DoD, VA, NIH, and HHS) to give them visibility of the research, help identify program needs and issues, provide a forum for feedback and guidance, and identify possible sources of collaboration. While historically held only for core research and related portfolios, 16 additional CDMRP-assigned congressional programs were presented at R&A meetings for the first time in FY16, and these meetings continued into FY17. This opportunity allowed participants to highlight research gaps being addressed by current programs, identify gaps requiring additional support, highlight current areas of collaborative success, identify additional opportunities for further collaboration and coordination, leverage resources, and avoid overlap.

Joint Program Committees

The JPCs are DHA, Research and Development Directorate advisory bodies composed of DoD and non-DoD medical and military technical experts that provide guidance on funding recommendations and program management support for DHA, Research and Development Directorate-funded research. JPCs advise and work through the USAMRMC PADs, which provide strategic oversight of this research. There are currently 6 active PADs:

- Medical Simulation and Information Sciences Research Program (MSISRP).
- Military Infectious Diseases Research Program (MIDRP).
- Military Operational Medicine Research Program (MOMRP).
- Combat Casualty Care Research Program (CCCRP).
- Radiation Health Effects Research Program (RHERP).
- Clinical and Rehabilitative Medicine Research Program (CRMRP).

CDMRP provides award and program management support to the JPCs/PADs for DHP core research program areas. The combined effort leverages CDMRP's expertise in research program administration with the PADs' technical and strategic expertise to expedite the delivery of products and solutions for the advancement of the DHA mission. CDMRP administers these programs as the Defense Medical Research and Development Program (DMRDP). 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 beneficiaries. (For additional information about DMRDP and other programs/projects supported by CDMRP, see pages 97-105 in this report). In FY17, CDMRP assisted with program and award management in a number of areas

relevant to battlefield injury and military service, including psychological health and resilience, physiological health, neurotrauma, hemorrhage and resuscitation, en route and forward surgical care, medical simulation and training, wound infections, infectious diseases, prosthetics, vision, hearing, balance, pain, and other rehabilitative and regenerative medicine efforts. This partnership supports CDMRP's vision of transforming healthcare for Service Members and the American public through innovative and impactful research.

US Department of Veterans Affairs

Many CDMRP programs focus on topics that are relevant to the healthcare of Veterans, and several align closely with areas of VA research. CDMRP and VA program staffs communicate and actively coordinate on related areas of program research to identify gaps, leverage funding, and prevent duplication of effort. Both Veterans and VA investigators serve as reviewers on CDMRP peer and programmatic review panels, and CDMRP funds VA investigators for both individual and collaborative research efforts. To date, more than 210 investigators at VA institutions have been funded by CDMRP.

As one prime example, CDMRP's Gulf War Illness Research Program (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 48-49 for additional details on the GWIRP). VA scientists and clinicians serve on both peer and programmatic review panels for GWIRP to inform and help make funding recommendations, as well as to provide valuable resources and expertise as investigators on many GWIRP-funded awards. In another groundbreaking collaborative effort, the DoD and VA have combined more than $100M to fund two consortia aimed at improving diagnosis and treatment of mild traumatic brain injury (mTBI) and post-traumatic stress disorder (PTSD). These consortia include the Consortium to Alleviate PTSD (CAP; refer to page 18) and the Chronic Effects of Neurotrauma Consortium (CENC; refer to page 17), which are described in further detail on pages 17-19 of this Annual Report.

This year, CDMRP also worked with the VA to provide input and share information in support of the Veteran Engagement Initiative in VA Research, specifically as related to the integration of consumers into the review process and participation in research projects. In addition to individual staff meetings, CDMRP was invited to present a live, nationwide VA Health Services Research and Development Cyberseminar that described CDMRP's history and unique features, with a focus on highlighting how consumers are intricately involved in every aspect of CDMRP's program management cycle. Additionally, in 2016 and 2017, the VA was invited to have representation on the panel of senior leadership and present VA-funded research efforts during the R&As of CDMRP's programs.

> "Through my advocacy work, I have learned that like-minded individuals can work together to create a tidal wave of hope in the sea of change. As part of this tidal wave, the Muscular Sclerosis Research Program brings together the MS and scientific communities to create a viable, productive partnership to fund impactful research that will change the course of MS forever."
> **John Platt, 2016**

Over the years, several programs funded the development of research consortia to build strong partnerships and collaborations in the scientific community. These multi-institutional organizations serve the scientific community by addressing overarching issues in biomedical research, combining and sharing their resources, and fostering real-time communication and research results. Highlights of ongoing consortia are provided in the following sections.

Alzheimer's Disease Neuroimaging Initiative

The purpose of the DoD's Alzheimer's Disease Neuroimaging Initiative (ADNI) (http://www.adni-info.org/DOD.html) is to examine how both traumatic brain injury (TBI) and PTSD influence the signs and symptoms of Alzheimer's disease (AD) in Veterans as they age. TBI and PTSD are common combat-related problems consequent to military service and may be associated with a greater risk of developing AD. Medical attention has focused on the acute treatment of these conditions; however, long-term consequences may be greater than the immediate morbidity in terms of human suffering, economic cost, and pain to families. Three studies supported by DoD ADNI projects will help determine the extent to which TBI and PTSD are risk factors for the development of dementia due to AD. DoD ADNI is comprised of 3 grants that combine state-of-the-art Alzheimer's diagnostics and imaging with a multi-centered approach for recruiting and referring study participants. The 19 study centers participating in DoD ADNI all use standardized study protocols for all diagnostic, cognitive, and behavioral testing. All 3 studies were fully funded by the Peer Reviewed Alzheimer's Research Program (PRARP):

- Effects of Traumatic Brain Injury and Post-Traumatic Stress Disorder on Alzheimer's Disease in Veterans Using Imaging and Biomarkers in the Alzheimer's Disease Neuroimaging Initiative (FY11).
- Effects of Traumatic Brain Injury and Post-Traumatic Stress Disorder on Alzheimer's Disease in Veterans with Mild Cognitive Impairment Using the Alzheimer's Disease Neuroimaging Initiative (FY12).
- Effects of Traumatic Brain Injury and Post-Traumatic Stress Disorder and Alzheimer's Disease on Brain Tau in Vietnam Veterans Using the Alzheimer's Disease Neuroimaging Initiative (FY13).

ADNI
Results from these studies are expected to lead directly to greater efforts to detect AD in military Veterans, as well as to the development of appropriate treatment and prevention studies, leading to the prevention of cognitive decline, AD, and dementia in Veterans and in the general population.

The initial (FY11) study did not enroll subjects who met criteria for having mild cognitive impairment/dementia. In FY12, the study was expanded to include subjects who did meet the criteria for mild cognitive impairment in addition to the previous cohorts. In FY13, the study was again expanded to determine the effects of prior TBI and ongoing PTSD on brain tau and the longitudinal change of brain tau measured with the tau-specific ligand 18F-AV-1451([F-18] T807) and positron emission tomography (PET) scanning. Vietnam Veteran subjects already enrolled in either of the first two studies were invited to enroll in the third study and receive the additional PET scan.

AFIRM
The AFIRM is dedicated to repairing battlefield injuries through the use of regenerative medicine.

Armed Forces Institute of Regenerative Medicine

The Armed Forces Institute of Regenerative Medicine (AFIRM) was established in March 2008 by USAMRMC in partnership with the Office of Naval Research, US Air Force Office of the Surgeon General, NIH, Veterans Health Administration of the VA, and DHP. This interdisciplinary network is focused on regenerative medicine for the treatment of severely wounded servicemen and women. AFIRM was initially composed of 2 independent civilian research consortia: the Rutgers – Cleveland Clinic Consortium and the Wake Forest – Pittsburgh Consortium, both of whom worked closely with the US Army Institute of Surgical Research (USAISR) at Fort Sam Houston, Texas. AFIRM supported 9 clinical trials, resulting in the treatment of more than 200 patients with novel therapeutic strategies in wound repair and tissue replacement. In 2013, based on AFIRM's successes, funding for AFIRM II was made available by the same partnership of government agencies. AFIRM II was selected for this next phase of AFIRM. AFIRM II includes members from both of the initial AFIRM consortia, along with new investigators. AFIRM II's 60 research projects span 5 focus areas that represent critical clinical challenges needing advanced solutions for Wounded Warriors:

- Extremity Repair.
- Craniomaxillofacial Reconstruction.
- Skin Regeneration.
- Composite Tissue Allotransplantation and Immunomodulation.
- Genitourinary Repair and Lower Abdomen Reconstruction.

Each focus area addresses restoring and regenerating tissue at the component and complex integrated structure levels (i.e., multiple tissues such as muscle, bone, nerve, skin, and vasculature as a functional unit, such as the face or hand), with the goal of not only improving the form and cosmetic appearance of traumatically injured sites, but also providing full functional recovery to the tissues affected by trauma. AFIRM combines the efforts of the nation's leading experts in regenerative medicine into a team whose work spans from R&D to clinical translation, implementation, and commercialization.

BADER
The BADER Consortium will improve the quality of life for Warfighters who suffer significant limb injuries in combat through orthopaedic rehabilitation research conducted at several military and civilian research institutions across the country.

Bridging Advanced Developments for Exceptional Rehabilitation Consortium

The Bridging Advanced Developments for Exceptional Rehabilitation (BADER) Consortium, led by Dr. Steven Stanhope of the University of Delaware, supports the advancement of orthopaedic rehabilitation research capabilities at DoD Military Treatment Facilities (MTFs) and VA sites. Its overarching goal is to partner with MTFs and the Extremity Trauma and Amputation Center of Excellence (EACE) to strengthen and support evidence-based orthopaedic rehabilitation care that results in optimal functional outcomes for Service Members with limb loss and limb difference. The BADER Consortium helps strengthen a research-intensive culture at each MTF and works in concert with them to conduct high-impact research studies and help establish self-sustaining research enterprises at these sites, with

DoD and VA employees serving as PIs in research projects. BADER Consortium studies have helped change patient care in rehabilitation at many of the facilities, including the prescription of devices for optimal running gait. BADER has funded 8 clinical research projects totaling $7.7M and supported 32 projects for the DoD/VA. To date, the consortium has generated 56 published abstracts and 15 published manuscripts and has obtained grants to fund an additional 7 projects.

BADER Consortium-funded projects include:

- A virtual reality-based training intervention to reduce falls in patients with lower-limb amputations.
- Walk-to-run training using real-time kinetic feedback to improve amputee running.
- A qualitative study of patient-reported outcomes in people with major limb trauma to measure their level of recovery.
- Identifying the enhanced gait function benefits from using a powered BionX Medical Technologies (BiOM) ankle prosthesis for lower-limb amputees.
- A science-based method for prescribing running-specific leg prosthesis to optimize running performance.
- Assessing rehabilitation outcomes in the clinical environment to support evidence-based practice in MTFs.
- Studying community reintegration, functional outcomes, and quality of life after a major extremity trauma to enhance patient care and future health studies.
- Criteria to identify prosthetic foot characteristics that best support physically demanding tasks.

The Chronic Effects of Neurotrauma Consortium

The Chronic Effects of Neurotrauma Consortium (CENC) is a joint DoD and VA effort dedicated to establishing a comprehensive research network focused on understanding the chronic sequelae associated with neurotrauma, primarily focused on combat-related and military-relevant mTBI/concussion. This includes establishing the association, causality, diagnosis, and treatment/rehabilitation of mTBI to neurodegeneration. CENC is led by PI Dr. David Cifu at Virginia Commonwealth University, with the assistance of 2 Co-PIs: COL Sid Hinds at USAMRMC and Dr. Rick Williams at Research Triangle Institute (RTI) International. Currently, CENC leverages collaborations with over 30 participating institutions across academia, industry, DoD, and VA. Ten studies were initiated spanning efforts in the area of epidemiology, neurosensory co-morbidities, neuroimaging standardization, and follow-up from studies initiated in-theater. One of these studies was completed under CENC sponsorship and is continuing under NIH funding. CENC leverages current and past funding efforts across numerous government agencies to effectively target studies to meet current and evolving research priorities in the field. Additional information can be found at http://cenc.rti.org/.

CENC

The consortium's efforts will address the common co-morbidities associated with chronic mTBI, such as neurosensory system involvement (vision, balance, hearing, pain) and psychological dysfunction.

Concussion Assessment, Research, and Education Consortium

The National Collegiate Athletic Association (NCAA)–DoD Grand Alliance Concussion Assessment, Research, and Education (CARE) Consortium is a joint DoD and NCAA research effort dedicated to studying the natural history of sport-related concussion in order to better understand the development and trajectory of recovery from concussion. Since its inception in 2014, the 3-year consortium project has enrolled more than 30,000 student athletes and service academy cadets at 30 performance sites (26 NCAA universities and 4 service academies). The consortium is comprised of 3 arms. The Administrative and Operation Core, the first arm, is directed by Dr. Tom McAllister at Indiana University and provides oversight, management, and support to the Consortium. The second arm is the Longitudinal Clinical Study Core (CSC), directed by Dr. Steve Broglio at the University of Michigan. The CSC is focused on studying the natural history of concussion through a multi-site, longitudinal investigation of concussive and repetitive head impacts in NCAA student athletes and service academy cadets. As of April 2017, the study team has captured more than 2,100 concussions from the over 30,000 student athletes and service cadets enrolled, one-third of which were captured at the service academies. The third arm is the Advanced Research Core (ARC), directed by Dr. Mike McCrea at the Medical College of Wisconsin. The ARC builds upon the work being performed by the CSC, allowing for more advanced research projects, such as testing impact sensor technologies, studying potential biomarkers, and evaluating concussion with advanced neuroimaging. The ARC has 6 performance sites, including 4 NCAA universities and 2 service academies. As of April 2017, more than 1,700 athletes and service cadets have been enrolled, and almost 200 concussions have been captured; over half of the concussions studies were athletes and cadets at the service academies. The data the CARE Consortium has and will continue to collect will allow scientists to develop evidence-based approaches to understanding the risks, management, and possible treatment strategies for concussion. Data from the study are continually submitted to the Federal Interagency Traumatic Brain Injury Research (FITBIR) informatics system and will be released to the public at project completion. The NCAA recently released new guidelines regarding football practice, as well as guidance for diagnosis and management of concussion, based in part on the findings from the CARE Consortium. The studies performed by the consortium have been presented in several forums, and initial results from the study were published in March 2017 in the *American Journal of Sports Medicine*. The full research article and more information can be found at http://careconsortium.net/.

The Consortium to Alleviate Post-Traumatic Stress Disorder

The Consortium to Alleviate PTSD (CAP) is a cutting-edge, joint VA and DoD effort to understand and treat PTSD and related conditions in active duty military Service Members and Veterans. CAP has assembled an unprecedented collaboration of highly qualified researchers and clinicians with expertise in PTSD, neuroscience, genetics, TBI, research in military settings, and comorbid conditions such as depression, sleep disturbances, and substance abuse. CAP is led by Director Dr. Alan Peterson, a retired US Air Force lieutenant colonel and clinical psychologist who

has personally treated Service Members suffering from PTSD symptoms on the battlefields of Iraq. Dr. Peterson is located at the University of Texas Health Science Center San Antonio and the South Texas Veterans Health Care System. The Co-Director of CAP, Dr. Terry Keane of the VA Boston Healthcare System and Boston University, is the Director of the Behavioral Science Division of the National Center for PTSD. The CAP coordinating center is responsible for administration of the consortium, which is distributed among the University of Texas Health Science Center San Antonio, South Texas Veterans Health Care System, VA Boston Healthcare System, Boston University, Durham VA Medical Center, and Duke University. In addition, CAP has funded core facilities to augment the studies: an Assessment Core, a Biomarkers and Genomics Core, and a Data Management and Biostatistics Core. Ten studies have been approved for implementation by the CAP Government Steering Committee, including the following: a Randomized Clinical Trial for Cognitive-Behavioral Therapy for Post-Traumatic Headache and a Clinical Trial of Ketamine for Antidepressant Resistant PTSD. Numerous VA, academic, and military institutions across the United States participate in CAP. Additional information can be found at https://tango.uthscsa.edu/consortiumtoalleviateptsd/.

CAP

CAP has two main objectives: (1) focusing on the advancement of treatment strategies for PTSD, including interventions for early, chronic, and latent onset cases, and (2) identifying and confirming clinically relevant biomarkers as diagnostic and prognostic indicators of PTSD and co-occurring disorders.

Detection of Early Lung Cancer Among Military Personnel Consortium

The Detection of Early Lung Cancer Among Military Personnel (DECAMP) Consortium is led by Dr. Avrum Spira and is designed to develop and validate biomarkers that could be used to improve the early detection of lung cancer among military personnel, military family members, and Veterans believed to be at high risk. The consortium is a multidisciplinary and translational research program that includes seven VA hospitals, four MTFs, and two academic hospitals as clinical study sites, as well as several molecular biomarker laboratories, along with Biostatics, Bioinformatics, Pathology, and Biorepository Cores. The Biostatistics and Data Management Center handles the clinical trial infrastructure, protocol development, clinical trial data management, quality assurance, regulatory compliance, imaging analysis, and site management. Two projects are ongoing at all sites: one is focused on validating a number of airway and blood-based molecular biomarkers that can distinguish benign vs. malignant lung diseases among smokers with indeterminate pulmonary nodules found on chest-computed tomography (CT) scans; the second is focused on developing and testing new noninvasive molecular biomarkers in the airway and blood to identify those smokers at highest risk for developing lung cancer. Samples from the DECAMP patients were used to help validate a commercially available (Affymetrix) bronchial genomic classifier that was developed by the PI and collaborators to facilitate diagnosis of lung cancer in patients with indeterminate lung nodules. Further discovery efforts with the DECAMP patient samples have led to preliminary data on a number of other potential biomarkers and biomarker panels.

Gulf War Illness Consortium

The GWI Consortium is led by Dr. Kimberly Sullivan of Boston University and brings together established GWI researchers from across the nation to investigate the pathobiological mechanisms responsible

Gulf War Illness Consortium
Results from this integrated approach should lead to a rational and efficient basis for identifying diagnostic markers and beneficial treatments for GWI.

for GWI symptoms as they relate to brain-immune activation and chronic inflammation. This consortium has initiated a series of clinical and preclinical studies to identify pathways that can be targeted by glial-modulating interventions and other currently available treatments. Ongoing investigations include clinical case-control studies examining markers in the blood and brain fluid, brain imaging, and memory testing. Parallel preclinical studies are evaluating persistent effects of Gulf War neurotoxicants in vitro and in rodent models of GWI. Preliminary results from the preclinical studies provide strong evidence for a neuroinflammatory component to the illness, and studies of potential treatments are currently underway in animal models. On the clinical side, preliminary results comparing cytokine, chemokine, monocyte and lymphocytes between ill Gulf War Veteran cases and controls indicate significant differences. Brain-behavior relationships in GWI have been identified from correlations between cognitive assessment data, neuroimaging data, and cytokine profiles. The consortium has also established neuronal cell lines differentiated from Gulf War Veteran-derived induced pluripotent stem cells.

ITN
Thus far, 29 unique clinical and preclinical studies have been successfully awarded and supported through the consortium. Twelve awards are currently active. More information regarding these studies can be found at https://itn.ucsf.edu/.

Institute for Translational Neuroscience

The Institute for Translational Neuroscience (ITN), a consortium comprised of 22 institutions, was established with congressionally directed funding in 2010 to address the growing concern regarding PTSD and alcohol and substance abuse disorders (ASUDs) within the military and civilian populations. Now in its sixth year of operation, the ITN has formed a unique and promising strategy to accelerate the development of novel therapeutics for substance use disorders and PTSD. The scientific objectives of the ITN are: (1) to identify molecular mechanisms, targets, and candidate compounds; (2) to determine the efficacy of the candidate compound(s) in vitro and in vivo (animal models); (3) to conduct proof-of-principle, pilot-scale clinical experiments or trials; and (4) to rapidly translate findings into full-scale clinical experiments/trials. To facilitate the transition from bench to bedside, a Translational Coordinating Core was established to attract collaborations with outside sources, such as NIH and commercial pharmaceutical and biotechnology companies, to support follow-on clinical trials to promising ITN projects. The ITN also established an Advisory Council, consisting of members from the government, academia, and industry, to provide strategic advice, set research priorities, and serve as the primary external scientific and programmatic review for proposed research projects.

Major Extremity Trauma and Rehabilitation Consortium (formerly the Major Extremity Trauma Research Consortium)

The Major Extremity Trauma Research Consortium (METRC) was initially established in September 2009 with funding from the DoD and the Orthopaedic Extremity Trauma Research Program (OETRP). The consortium would later be expanded in both size and scope 1 year later through a cooperative agreement with the DoD's Peer Reviewed Orthopaedic Research Program (PRORP) under which METRC2 was funded. CDMRP assumed management of the METRC2 studies in 2015. METRC was selected for additional funding via the competitive FY15 PRORP Orthopaedic Care and Rehabilitation Consortium

Award (OCRCA) PA. The OCRCA allowed METRC to again expand in size and scope by adding additional studies that will be funded under METRC3. With this new award, the METRC's historically acute care focus has shifted to incorporate several rehabilitation focus areas, leading to the newly titled Major Extremity Trauma and Rehabilitation Consortium (METRC). The coordinating center for METRC 1, 2, and 3 studies is located at the Johns Hopkins Bloomberg School of Public Health. This center collaborates with four MTFs, 22 core civilian trauma centers (12 of those being Level 1 trauma centers), and over 40 satellite centers to conduct 14 total studies under the METRC core umbrella. A number of other studies associated with METRC core studies are also being conducted. Led by Dr. Ellen MacKenzie of Johns Hopkins University and Dr. Michael Bosse at Carolinas Medical Center, the core METRC2 studies include:

METRC
The mission of METRC is to provide the evidence needed to establish better treatment guidelines for optimal care of the Wounded Warrior and to improve the clinical, functional, and quality-of-life outcomes of Service Members and civilians who sustain high-energy trauma to the extremities.

- Comparing patient outcomes post limb salvage and amputation among patients with severe foot and ankle trauma.
- Comparing outcomes in patients undergoing transtibial amputation with or without tibia-fibula synostosis.
- Developing a novel tool to aid clinicians in timely and accurate diagnoses of acute compartment syndrome.
- Evaluating multimodal approaches for peri-operative pain management in treatment of lower limb fractures.
- Implementing a collaborative care intervention to address patients' psychosocial needs and improve health-related quality of life.

Core METRC3 studies include:

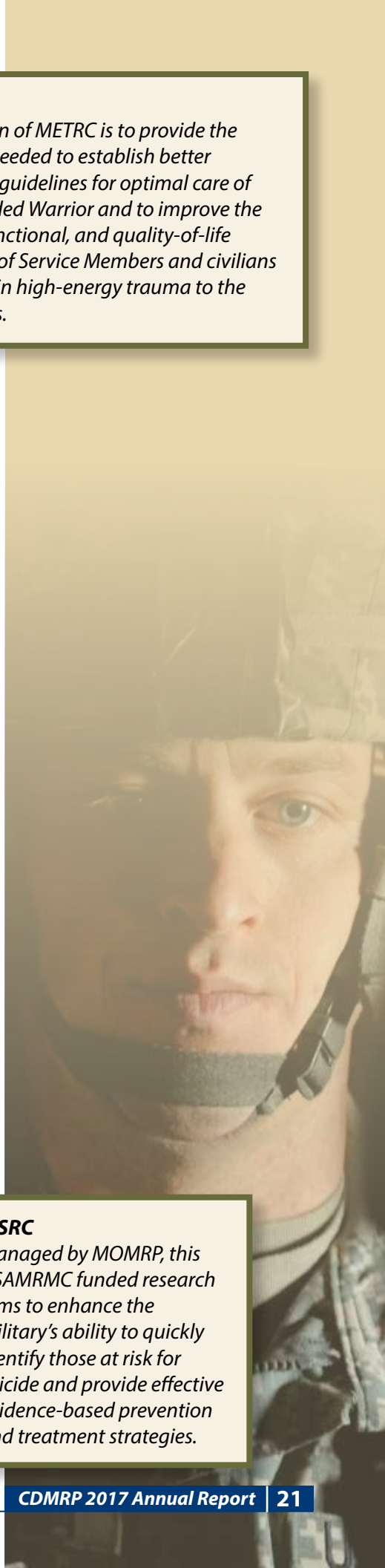
- Measuring Patient-Specific Injury and Progression of Immunologic Response to Optimize Orthopaedic Interventions in Multiply Injured Patients.
- Improving Pain and Function Following Orthopaedic Trauma: A Cognitive-Behavioral Based Physical Therapy Approach.
- Early Advanced Weight Bearing for Periarticular Knee and Pilon Injuries: An RCT Using the Antigravity Treadmill.
- Early Mechanical Stabilization of Bleeding in Disruption of the Pelvic Ring: A Multicenter, Prospective Observational Study.
- Long-Term Consequences of Major Extremity Trauma: A Pilot Study.

More information regarding these studies and their results can be found at http://metrc.org.

Military Suicide Research Consortium

In response to the high rate of suicide among military personnel, the Military Suicide Research Consortium (MSRC) was created in FY10 with funding from the DHP as a part of an ongoing strategy to synchronize and leverage the DoD and civilian efforts of implementing a multidisciplinary research approach to suicide prevention. Consortium oversight is provided by COL Dennis McGurk, MOMRP Director, with research awards being led by Drs. Thomas Joiner and Peter Gutierrez from Florida State University and the University of Colorado Denver School of Medicine, respectively.

MSRC
Managed by MOMRP, this USAMRMC funded research aims to enhance the military's ability to quickly identify those at risk for suicide and provide effective evidence-based prevention and treatment strategies.



To date, 26 studies have been funded by MSRC, in addition to several Postdoctoral Pilot Projects and Dissertation Completion Awards. These studies were conducted at numerous VA and military installations across the country and cover a broad spectrum of the research continuum, ranging from etiological to prevention/screening and treatment. Populations being studied include Service Members, Veterans, and beneficiaries. In FY16, 5 years of additional DoD funding was obtained by MSRC to continue research into expanding knowledge, understanding, and capacity to prevent, treat, and enhance the quality of life of persons in military communities who are affected by suicide-related problems; additional studies will be funded over the next few years.

MSRC has developed a database to capture Common Data Elements (CDEs) that are consistent across all projects. This database allows for secondary analysis of aggregate data across all funded studies. Additionally, the MSRC is specifically identified in *The National Research Action Plan for Improving Access to Mental Health Services for Veterans, Service Members, and Military Families*, a plan developed by multiple federal agencies in response to an Executive Order issued by the President, as playing a role in achieving the vision for suicide prevention research.

Sixteen of the funded studies are now complete and have yielded important results. For more information related to the funded studies, please visit https://msrc.fsu.edu/funded-research.

Neurofibromatosis Clinical Trials Consortium

The Neurofibromatosis Clinical Trials Consortium (NFCTC) (http://www.uab.edu/nfconsortium) was established by the DoD Neurofibromatosis Research Program (NFRP) in 2006 to develop and perform clinical trials for the treatment of neurofibromatosis (NF) complications in children and adults. The NFCTC was subsequently funded in 2011 to conduct additional trials. This includes the development of clinical trials for the treatment of NF complications, including plexiform neurofibromas, cognitive disorders, low-grade gliomas, vestibular schwannomas, and malignant peripheral nerve sheath tumors. The consortium is composed of 13 clinical sites, 5 collaborating sites and an Operations Center based at the University of Alabama at Birmingham under the direction of Dr. Bruce Korf. The Operations Center provides administrative, data management, and statistical support to the NFCTC. Each of the clinical and collaborating sites has expertise in the treatment and management of NF, as well as an established patient population available for clinical trials.

NFCTC
To date, the NFCTC has successfully initiated 7 clinical trials and supported 3 additional trials. The NFRP offered the Clinical Trial Consortium Award again in FY16.

Ovarian Cancer Academy

Since FY09, the Ovarian Cancer Academy (OCA) has brought together talented and highly committed Early Career Investigators (ECIs) with their mentors and Academy Leadership to fulfill the Ovarian Cancer Research Program's (OCRP) vision of a unique, virtual OCA that supports the development of career ovarian cancer researchers. In FY14, Dr. Nita Maihle of Georgia Regents University and Dr. Douglas Levine, now at New York University Langone Medical Center, embraced their responsibilities as the new Dean and Assistant Dean of an expanding OCA and infused it with broader interactions between the ovarian cancer survivor and research communities. Two new FY15 and FY16

ECI-mentor pairs were welcomed into the OCA, which currently brings the numbers of OCA ECIs (FY12- FY16) to 12. All 7 of the original FY09 ECIs successfully completed their awards, contributing 260 publications, 129 presentations, and 63 grants worth $17.10M. To date, the OCA ECIs have demonstrated remarkable progress, resulting in 329 publications and 192 abstracts focused on ovarian and other gynecologic cancers. Their growth as independent, committed ovarian cancer researchers is evident in their 81 funded (non-OCA) grants totaling $21.00M, as well as their service on the editorial boards of scientific journals and on review and panel groups for women's cancer foundations. The annual OCA in-person workshop held in Seattle in September 2016 included programming geared toward leadership development and a panel discussion with the Rivkin Foundation about support for biomedical research philanthropy. It promoted collaborations within the ECIs, which resulted in two main groups who continue to build on the Team Science projects initiated at the workshop. Following the workshop, the majority of the Academy ECIs participated in the organization, presentation, and written summation of the Rivkin Ovarian Cancer Symposium to be published. In 2016 the OCA launched the www.ovariancanceracademy.org website that informs the public about OCA accomplishments and has a private interactive platform that also allows the geographically dispersed ECIs and OCA leadership to collaborate effectively.

OCA
The OCRP envisions that the synergy produced from sharing information, ideas, and research findings, as well as the substantial research funding provided to the ECIs, will create opportunities to establish them as the next generation of successful and highly respected ovarian cancer researchers.

Ovarian Cancer Consortium

Early ovarian cancer usually has no obvious symptoms, and currently there is no sufficiently accurate screening test for the early detection of ovarian cancer in average-risk women. The National Cancer Institutes, (NCIs) Surveillance, Epidemiology, and End Results (SEER) Program estimates diagnosis of 22,440 new cases and 14,080 deaths due to ovarian cancer in 2017. The majority of cases are diagnosed at late stages, for which the 5-year survival rate is 28.9% (United States, SEER 2007-2013). A multi-institutional team headed by Dr. Robert Kurman's research group at Johns Hopkins University, with collaborators at the University of Toronto and Yale University, successfully competed for the first Ovarian Cancer Consortium Award (OCCA) offered in FY10. Their objective is to develop a prevention strategy to reduce the burden of ovarian cancer, and toward this end, they are focused on definitively identifying and characterizing early changes associated with the disease. To accomplish this, the OCCA is testing the hypothesis that an early lesion in the fallopian tube, called a serous tubal intraepithelial carcinoma (STIC), is the precursor of ovarian high-grade serous carcinomas (HGSC), which account for a majority of ovarian cancers and ovarian cancer-related mortalities. The consortium's research plan has four preclinical projects focused on the molecular and morphological characterization of the precursor lesions/STICs, as well as a fifth epidemiological study designed to evaluate whether these STIC characteristics are modifiable by oral contraceptives or anti-inflammatory agents.

Ovarian Cancer Consortium
Data from this consortium will ultimately help to shape prevention and early detection approaches for ovarian cancer.

Major accomplishments of the consortium include:

- Evaluating STICS as precursor lesions of HGSCs: They found STIC lesions present in ~41% of 228 HGSC cases, indicating that nearly all HGSCs develop from the distal fallopian tube through STICs. Via fluorescent in-situ hybridization studies, they demonstrated that gene amplification of CCNE1 (Cyclin E1 gene) is a mechanism in STIC

development. They also identified other ovarian cancer-associated protein markers on STICs via immunohistochemistry: LAMC1 (Laminin subunit gamma-1), topoisomerase II, RSF-1 (Remodeling and Spacing Factor 1), and the loss of ALDH1A1 (Aldehyde Dehydrogenase 1 Family, Member A1).

- Identifying the early molecular changes that precede the development of STICs: Microarray data comparison of malignant HGSCs and non-malignant ovarian tissue samples suggests that increased tumor risk in the fimbria is likely due to differences in hormonal expression between fimbria and ampulla.
- Introducing the role of epigenetic modulator Ten-Eleven Translocation protein 1 (TET1): The consortium showed that the TET1 is upregulated in STICs, in addition to HGSCs. Epigenetic reprogramming by TET1 increases malignant phenotypes and confers a poor prognosis in ovarian cancer. Targeting TET1 in patients with TET1-expressing ovarian tumors may provide a new avenue of personalized therapy.
- Exploring the chemopreventative efficacy of a combination statin and nonsteroidal anti-inflammatory drug (NSAID) regimen: They demonstrated that lovastatin significantly reduced the development of STICs in mogp-Tag mice and inhibited ovarian tumor growth in the mouse xenograft model.
- Identifying that differential gene expression exists between patients with ovarian cancer with a BRCA1 (breast cancer 1) mutation status and a non-mutated status: Their microarray results showed that loss of one such differentially expressed gene, LKB1 (liver kinase B1), is frequently observed in tubal cancer precursor lesions. Their data suggests this may be an early event in disease progression and highlights LKB1 as a potential therapeutic target for disease control.

Ovarian Cancer Outcomes Consortia
Two teams were funded to identify predictors of long-term survival to enable tailored therapies that maximize patient survival and quality of life.

Ovarian Cancer Outcomes Consortia

In FY12, OCRP offered the Outcomes Consortium Development Award to lay the groundwork needed to build a multi-institutional research effort that could specifically identify and understand predictors of disease outcomes in patients with ovarian cancer. The intention was to bring together teams of talented researchers to focus on discovering what distinguishes the small subset of patients with ovarian cancer who become long-term survivors (≥ 10-year survival from diagnosis) from other ovarian cancer survivors. In FY15, OCRP offered the Outcomes Consortium Award to move the consortiums from the development phase to the research phase, where each consortia would use its own set of resources and focus areas in an effort to identify predictors of long-term survival to enable tailored therapies that maximize patient survival and quality of life.

Two teams, one led by Dr. Malcom Pike and the other by Dr. Michael Birrer, were chosen for the FY15 Outcomes Consortium Award. The Multidisciplinary Ovarian Cancer Outcomes Group (MOCOG), led by Dr. Pike at Memorial Sloan Kettering Cancer Center, is studying the role of the immune response; genetics, especially those related to DNA repair; and epidemiological and lifestyle factors that contribute to long-term survival in women diagnosed with advanced-stage ovarian cancer. The MOCOG is a collaboration of 10 sites that will leverage samples, data,

and techniques to search out novel immune therapy approaches to ovarian cancer treatment and the patients who would benefit from these targeted immune therapies. The Ovarian Cancer Consortium for the Genomic, Epigenetic, and Quality of Life Characteristics of Long-Term Survival, led by Dr. Birrer at Massachusetts General Hospital, is focused on finding predictive biomarkers that will help in the design of individualized care for patients with ovarian cancer who were diagnosed with early-stage disease.

Dr. Birrer's group utilized data obtained from a longitudinal analysis of quality of life obtained from patients participating in Gynecologic Oncology Group trial-172 (GOG-172), a clinical trial testing intraperitoneal and intravenous chemotherapy, to develop a descriptive profile for short (STS), intermediate, and long-term survivors (LTS). Initial analysis indicates LTS were significantly younger at diagnosis, had lower-grade disease, and had significantly higher/better social well-being with fewer ovarian cancer-specific concerns compared to STS and intermediate-term survivors. They posit that this initial analysis supports the case for quality of life as an independent and significant predictor for long-term survival and may be useful as a stratification factor in clinical trials or in counseling patients as they examine treatment options.

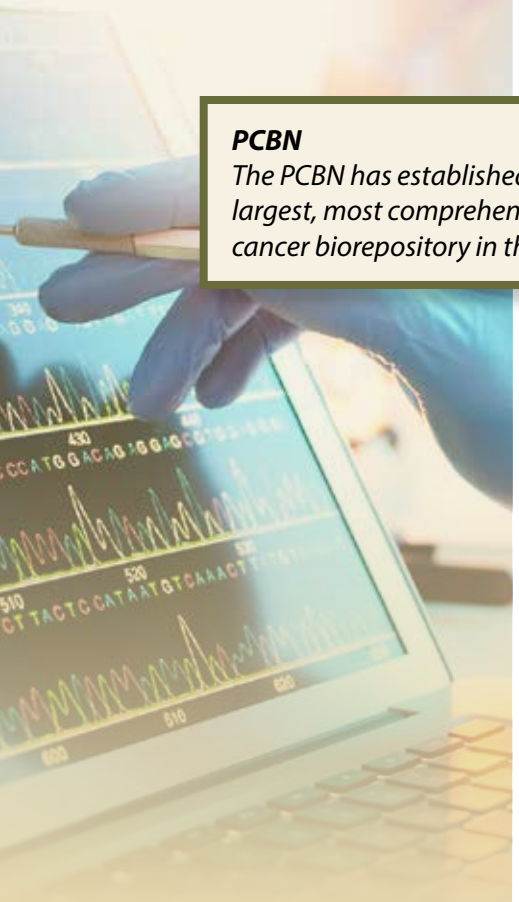
Dr. Pike's group completed the exhaustive task of confirming their 1,506 LTS, moderate (5-7 years) survivors, and STS samples as HGSC, as well as matching the LTS samples with an equal number of moderate survivors and STS based on study population, year of diagnosis, and age at diagnosis. They have tissue microarrays ready for most and blocks to be made into tissue microarrays for the rest.

Pharmacotherapies for Alcohol and Substance Abuse Consortium

On September 30, 2015, RTI was awarded a $10.8M, 5-year award from the Alcohol and Substance Abuse Disorders Research Program (ASADRP) to establish the Pharmacotherapies for Alcohol and Substance Abuse (PASA) Consortium.. The Consortium is led by Dr. Rick Williams from RTI, in collaboration with Baylor College of Medicine and the Uniformed Services University of the Health Sciences (USU). The PASA Consortium has three aims in developing pharmacotherapies for ASUDs, particularly in the context of the reciprocal relationship between ASUDs versus stress and anxiety, as manifested in PTSD/TBI. The three broad aims are: (1) discover novel medications and combination medications for ASUDs and PTSD/TBI; (2) develop these medications through a rational proof-of-concept pipeline model; and (3) conduct Phase II preliminary efficacy trials of potential medication combinations in optimal target populations and explore functional genetic polymorphisms for matching patients to these medications. Four studies were initially funded, covering topics that assessed the effectiveness of pharmacotherapies on alleviating PTSD and alcohol use disorder (AUD). A second Request for Applications was recently released, and proposals submitted will undergo peer and programmatic review.

Prostate Cancer Biorepository Network

The Prostate Cancer Biorepository Network (PCBN) is a bioresource that provides prostate cancer tissue and other patient samples to prostate cancer investigators worldwide. The Prostate Cancer Biorepository Resource Network Award was first offered in FY09, with the intention of providing infrastructure support for the development of the PCBN – envisioned



PCBN
The PCBN has established itself as the largest, most comprehensive prostate cancer biorepository in the world.

as a biorepository with high-quality, well-annotated specimens obtained in a systematic, reproducible fashion using optimized and standardized protocols. That award funded two sites, Johns Hopkins University and New York University, and they developed a shared infrastructure, including establishment of a website; optimized processes for specimen collection, processing, and annotation; informatics and data management; intellectual property, legal/ethical/regulatory issues; and policies for specimen distribution.

Today, the PCBN consists of 5 Prostate Cancer Research Program (PCRP)-funded sites – Johns Hopkins University, New York University, the University of Washington, Memorial Sloan Kettering Cancer Center, and Washington University in St. Louis – led by Johns Hopkins University's Dr. Bruce Trock.

The 5 sites specialize in different types of patient samples, providing complementary resources including metastatic tissue (rapid autopsy and lymph node); biospecimens with long-term follow-up for biochemical recurrence, metastasis and death, active surveillance, hormone and neoadjuvant therapy; tissues from African American men; and patient-derived xenograft (PDX) models. The PCBN derives its specimen resources from extensive, well-characterized patient populations with a long history of supporting clinical and biomarker research. All specimens in the PCBN contain standard pathology data, and the majority of specimens are linked to clinical and outcome data; some also have epidemiologic data, and all are supported by an informatics infrastructure.

The types of specimens that are available include tissue microarrays, fresh frozen and paraffin-embedded tissue, body fluids, and derived DNA, RNA, and protein. They have distributed more than 3,000 patient samples. As a resource for the prostate cancer research community, PCBN biospecimen usage has resulted in 25 publications, including articles in *Nature, The New England Journal of Medicine, The Proceedings of the National Academy of Sciences, Cancer Research,* and *The Journal of Clinical Investigation*. Today, the PCBN is the largest, most comprehensive prostate cancer biorepository in the world (for additional information, see http://prostatebiorepository.org/).

PCCTC Mission
The PCCTC has established itself as the nation's premier prostate cancer clinical trials group and remains poised to make a significant impact on patients' lives by keeping the drug pipeline primed with promising novel agents.

Prostate Cancer Clinical Trials Consortium

The Prostate Cancer Clinical Trials Consortium (PCCTC) was originally established in 2005 through the collective efforts of the PCRP and the Prostate Cancer Foundation. The goal was to combine the work of leading investigators with the unique institutional resources of outstanding clinical research sites across the United States to bring to market high-impact, novel therapeutic interventions that would ultimately and significantly decrease the impact of prostate cancer. Since then, the PCCTC's extensive clinical trial experience and collaborative efforts have helped bring numerous potential new therapeutics into Phase III clinical trials, with two agents having now received approval by the FDA: (1) abiraterone acetate, which blocks formation of testosterone by inhibiting CYP17A1 (Cytochrome P450 17A1), and (2) enzalutamide, which binds to the ligand-binding domain of the androgen receptor (AR), prevents nuclear translocation, and blocks AR interaction with coactivator proteins, thereby preventing transcription of AR-regulated genes. In 2014,

the PCCTC became a Limited Liability Company (Prostate Cancer Clinical Trials Consortium, LLC) and today boasts 9 clinical research sites and 21 participating affiliated sites supported with funding from other sources.

The consortium's successful acceleration and streamlining of the clinical trial process can be attributed to its unique infrastructure, which addresses the scientific, legal, regulatory, database, budgetary, and management concerns of its members. The PCCTC has 215 clinical trials approved for activation, 162 of which have been completed (closed to accrual), with an additional 43 trials either active or pending activation. More than 5,966 patients have been enrolled in these trials, 10% representing patients from disproportionately affected populations. The consortium is also at the forefront of the personalized medicine arena, incorporating liquid biopsies to identify distinct prostate cancer subtypes for which specific drugs are available and to monitor how an individual's cancer changes biologically in response to particular treatments. Through the collaborative nature and intellectual synergy of its leadership, the PCCTC remains poised to make a significant impact on patients' lives by keeping the pipeline primed with the most promising novel agents and validated biomarkers (for additional information, see http://pcctc.org/).

South Texas Research Organizational Network Guiding Studies on Trauma and Resilience

STRONG STAR
The goal of the STRONG STAR Consortium is to reduce or eliminate combat-related PTSD in active duty military and recently discharged Veterans.

The South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) is a multidisciplinary and multi-institutional research consortium funded by the DoD. STRONG STAR is dedicated to the development and evaluation of the most effective interventions for the detection, prevention, and treatment for combat-related PTSD. The STRONG STAR team of more than 150 military, civilian, and VA investigators and clinicians is centered at the University of Texas Health Science Center, San Antonio, and also embedded within nearby Fort Hood, where they coordinate recruitment of human subjects with other military and Veteran locations for collaborating investigators from across the country. The STRONG STAR Consortium has completed 14 projects, including retrospective data analyses, epidemiological studies, and 8 clinical studies. The results of one animal study, one neuroimaging study, and one clinical study have been published. Final results of the clinical trials conducted by STRONG STAR, several of which are highly anticipated as the first testing of evidenced-based treatments for PTSD in military populations, are available (https://tango.uthscsa.edu/strongstar/scipubs.asp). In addition to the STRONG STAR studies funded under the PTSD Multidisciplinary Research Consortium Award mechanism, the consortium has partnered with nationwide investigators and institutions of higher education to secure approximately $50M in additional peer-reviewed funding from the DoD, VA, NIH, and private foundations to support over 20 additional STRONG STAR-affiliated projects.

Team Approach to the Prevention and Treatment of Post-Traumatic Epilepsy

The ultimate goal of the Team Approach to the Prevention and Treatment of Post-Traumatic Epilepsy (TAPTE) is to establish a multi-center, multi-investigator research team focused on post-traumatic epilepsy (PTE) that will rapidly translate research findings into novel therapeutics

TAPTE
TAPTE's goal is to establish a multi- center, multi-investigator research team focused on PTE that will rapidly translate patient-relevant findings at the molecular, cellular, and systems level into novel therapies.

for treating PTE resulting from TBI. Based on previous successes within the epilepsy community, the Citizens United for Research in Epilepsy (CURE) will use their scientific model to rapidly advance the most promising research in PTE. The model is building a "critical mass" of investigators with similar research interests and diverse backgrounds to address and execute PTE research via a team science approach. The investigative team will work closely with CURE, CDMRP, and USAMRMC, who will proactively monitor research progress and advise the consortium on which directions to take to ensure ultimate success. The key opinion leaders from USU, DoD, and academia met in February 2016 to discuss the state of the science of PTE and to identify capability gaps that research could address over the award's 5-year period of performance. This information was obtained from the research community, which solicited research proposals. The investigative team should begin research in mid to late 2017.

TED
This initiative leverages collaborations among 23 academic institutions, as well as a number of government, private, and philanthropic organizations, along with data from a number of other current and past funding efforts spanning several government agencies.

Traumatic Brain Injury Endpoints Development Initiative

With support of a $17M, 5-year award from the DoD, and direct collaboration with the FDA, the TBI Endpoints Development (TED) Initiative established a collaborative, multi-disciplinary research team to advance clinically validated endpoints that can support regulatory approvals for trials involving the diagnosis and treatment of mild to moderate TBI, a complex and heterogeneous disease for which there are currently no FDA-approved diagnostics or therapeutics. These endpoints include clinical outcome assessments (COAs), blood-based biomarkers, and neuroimaging biomarkers. The TED team is led by PI Dr. Geoff Manley at the University of California, San Francisco. Stage I of the TED award has been focused on establishing a TED database consisting of integrated clinical outcomes, imaging, proteomic, and genomic data from ongoing and legacy TBI studies across civilian, military, and sports cohorts. Stage II allows for large-scale validation studies of candidate clinical outcome assessments and biomarkers selected in Stage I, leveraging the existing research infrastructure and clinical study networks of the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI), the Concussion Research Consortium (CRC), and CENC. Four Seed Projects were initiated under Stage I, and a fifth project was initiated under Stage II:

- Project 1: An Evidence-Based Clinical Outcome Assessment Platform (EB-COP) to Advance the Identification and Validation of COAs for use as FDA-qualified Drug Development Tools.
- Project 2: Development and Validation of a Cognition Endpoint for Traumatic Brain Injury Clinical Trials.
- Project 3: Enhancing the 'Regulatory Readiness' of Top TBI Biomarkers Toward FDA Drug Development "Biomarker Qualification Program" Submission.
- Project 4: CT and MRI Prognostic Biomarkers for Mild to Moderate Traumatic Brain Injury.
- Project 5: TED Control Population Study Leveraging the Infrastructure of the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) Network.

In addition, the TED initiative has received letters of support and recognition from the FDA in support of the initiative's efforts related to specific TBI-related outcomes. More information about the TED initiative can be found at https://tbiendpoints.ucsf.edu/.

Understanding Gulf War Illness: An Integrative Modeling Approach

Under the leadership of Drs. Mariana Morris, Nancy Klimas, and Gordon Broderick, this GWIRP-funded consortium represents expertise in neurotoxicology, animal modeling, computational modeling, and clinical research. This multidisciplinary research team, based at the Institute for Neuro Immune Medicine at Nova Southeastern University, aims to develop a translational model of GWI that will identify molecular targets and predict effective therapeutic interventions, while also uncovering underlying mechanisms of disease. Using computational modeling, genomic, immunological, autonomic, and endocrine pathway information from animal models of Gulf War–era chemical exposures are being integrated with observational studies of symptomatic Gulf War Veterans to discern the pathways and mediators underlying GWI. Key mediators identified from the model will then be targeted with potential therapeutic interventions. Preliminary comparative analysis of cytokine expression profiles between GWI Veterans and GWI animal models, paired with computer simulations, led to animal trials of candidate treatment protocols. Following preclinical validation, the team has moved forward with gaining approval to test a combination treatment strategy using a tumor necrosis factor (TNF) receptor antagonist, followed by a glucocorticoid receptor blockade in a Phase I study of Gulf War Veterans. The research team plans to repeat the dynamic modeling before treatment and during the trial to further inform the computation model and the impact of the intervention. Additional research outcomes from the consortium include examination of the physiological effects of Gulf War-era chemical exposure and exercise stress in GWI animal models, with a focus on cardiac, autonomic, and body compositions parameters. Results to date suggest there are cardiac changes associated with Gulf War-era exposure.

Networking with Federal and Non-Federal Agencies

Partnering with multiple federal and non-federal committees to compare research portfolios, identify gaps in research funding, and improve existing research efforts is a major effort of CDMRP. We invite members of other federal and non-federal agencies to participate in the peer and programmatic review processes, as well as to serve on review boards to monitor and oversee the progress of awards, which ensures no research effort is duplicated, as well as an opportunity to encourage complementary investment strategies. Examples of interagency collaborations include, but are not limited to, the following:

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 to promote the early detection of breast cancer and support of young women who develop the disease.

Networking with Federal and Non-Federal Agencies

These interagency collaborations strive toward synergy with other agencies and diversification of funded research portfolios, underscoring the importance of research coordination efforts.

FITBIR Working Group
An NIH-sponsored group whose mission is to enhance communication, coordination, and collaboration in the field of 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 HHS related to autism spectrum disorder (ASD). Federal and non-federal members are included on the committee to ensure that a wide range of ideas and perspectives pertaining to ASD is represented and discussed in a public forum.

Interagency Urology Coordinating Committee
A federal advisory committee, facilitated by HHS's National Institute of Diabetes and Digestive and Kidney Disorders, that coordinates the research activities of all national research institutes related to urologic diseases to ensure their adequacy and technical soundness and to provide 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.

Metastasis Cancer Research Task Force
As directed by Congress to the Assistant Secretary of Defense for Health Affairs (ASD[HA]), an interagency group led by the Murtha Cancer Center that is tasked to provide recommendations on research for metastasized cancer, with a focus on extending the lives of advanced-state and recurrent patients.

Muscular Dystrophy Coordinating Committee
An NIH-established committee to foster collaboration among federal health programs and activities relevant to the various forms of muscular dystrophy.

National Alzheimer's Project Act
A group that combines federal efforts to coordinate Alzheimer's disease and related dementia (ADRD) research. The National Plan for ADRD is updated annually from this interagency collaboration in conjunction with the public-private Advisory Council on Alzheimer's Research, Care, and Services.

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.

Our Programs

The 31 research programs highlighted in this section share many common features, yet each program is unique and emphasizes the specific needs of the research and advocacy communities. These programs are detailed on the following pages.

Alcohol and Substance Abuse Disorders Research Program

Vision

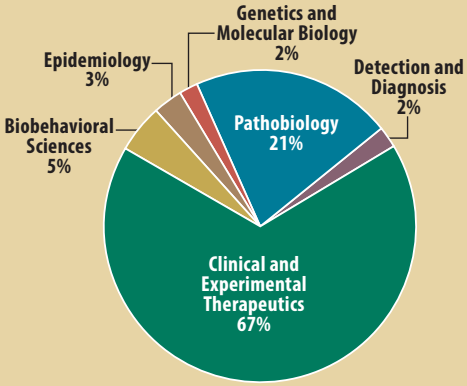
Decrease the clinical impact of alcohol and substance abuse

Mission

To explore integrated approaches to address alcohol and substance use disorders, especially related to TBI and PTSD, through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols for Service Members, Veterans, and the American public

Program History

The problem of alcohol and substance abuse is a growing concern among the general public, as well as military personnel and Veterans alike. In 2013, the IOM report, *Substance Use Disorders in the U.S. Armed Forces*, characterized the overall prevalence of heavy drinking at 20% and the overall prevalence of illicit drug use at 12%. Rates of acute and chronic incident alcohol diagnoses increased from 2001 through 2010, especially for the active duty component. The results indicate the increasing medical burden imposed on the Military Health System by excessive alcohol use. Substance abuse was involved in 30% of the Army's suicide deaths from 2005-2009 (National Institute of Drug Abuse, 2011). Furthermore ASUDs significantly worsen the hyper-arousal effects of PTSD, a disorder that affects 14% of all previously deployed US military personnel (RAND, 2012). Veterans have their PTSD complicated by chronic TBI effects, which are worsened by ASUDs. The 2013 IOM report recommended that the DoD assume leadership to ensure the consistency and quality of treatment services available to those with ASUDs, given the burden of ASUDs in the military. The Alcohol and Substance Abuse Disorders Research Program (ASADRP) was established in FY10 with a congressional appropriation of $6.375M. Since then, the program has established a network of multidisciplinary, translational research teams with the explicit goal of accelerating the delivery of new or improved treatments for ASUDs, and federal funding for research has led to a total appropriation of $34.075M to ASADRP. The goal of the program is to identify and develop new medications to improve treatment outcomes for ASUDs, especially related to TBI and PTSD. The program's approach is to organize multidisciplinary, team-based translational research efforts to identify promising compounds, conduct proof-of-principle basic research to determine which compounds are most appropriate for human research trials, and conduct human proof-of-principle trials with promising compounds. If successful, this approach could result in translation of contemporary basic science knowledge into enhanced clinical pharmacological treatment protocols for ASUDs.



FY10-FY16 ASADRP Portfolio (% of total investment)

Institute for Translational Neuroscience (ITN) Consortium

Elena Chartoff, Ph.D., Harvard McClean Hospital

Dr. Chartoff's studies will determine whether an orally available kappa opioid receptor antagonist administered during morphine withdrawal blocks withdrawal-induced negative affective states and the likelihood of engaging in oxycodone self-administration. The overall objective of Dr. Chartoff's project is to use an established rat model of opioid dependence that results in a robust opioid withdrawal syndrome to test potential treatments for preventing opioid abuse under conditions of opioid dependence, regardless of the initial cause of pain.

Michael Charness, M.D., Boston VA Research Institute

Dr. Charness' current work focuses on understanding the mechanism underlying N-acetlycystine protection against ethanol neurotoxicity. The overall objective of Dr. Charness' work is to determine the effects of the neuroprotective peptide, NAP, on the neurological effects of ethanol and TBI in cerebellar slice culture.

Josh Woolley, M.D., Ph.D., Northern California Institute for Research and Education

The objective of Dr. Woolley's study is to investigate the effects of oxytocin on alcohol-related behaviors, social abilities, and physiological startle responses in patients with PTSD and AUD using a randomized, placebo-controlled, dose-tiered, within-subject study design. Specifically, Dr. Woolley's group will determine whether intranasal administration of oxytocin decreases alcohol-related approach bias and cravings, enhances social abilities, and decreases physiological hyperactivity during a fear-potentiated startle paradigm. The proposed work has the potential to yield a novel pharmacological treatment for AUD and PTSD, both leading causes of disability in the US military, for which currently available treatments are inadequate.

The Pharmacotherapies for Alcohol and Substance Abuse (PASA) Consortium

Rick Williams, Ph.D., (pictured left), RTI International and Thomas Kosten, Ph.D., (pictured right), Baylor College of Medicine

PASA has five medications under development for combined AUD and PTSD: a kappa opiate antagonist (CERC-501, formerly LY2456302, from Lilly Pharma), an alpha adrenergic blocker (doxazosin), a cortisol blocker (PT150), a gamma amino butyric acid type B (GABAB) receptor allosteric modulator (ASP8062), and a complex anti-seizure medication (zonisamide). Four medications are undergoing preclinical investigation by Dr. Collin Haile at the University of Houston and Dr. Howard Becker at the Medical University of South Carolina. Two (PT150 and zonisamide) are undergoing clinical evaluations by Dr. Dewleen Baker at the University of California, San Diego, and Dr. Christopher Verrico at Baylor College of Medicine. Zonisamide is being clinically tested for its potential efficacy for PTSD, since two outpatient clinical trials have already shown efficacy for AUD. In order to broadly explore treatment of AUD and PTSD the team has selected compounds with a range of non-overlapping mechanisms of action that have been shown to be relevant in animal models of these diseases.

Amyotrophic Lateral Sclerosis Research Program

Vision

Improve treatment and find a cure for ALS

Mission

Fund innovative pre-clinical research to develop new treatments for ALS for the benefit of Service Members, Veterans, and the general public

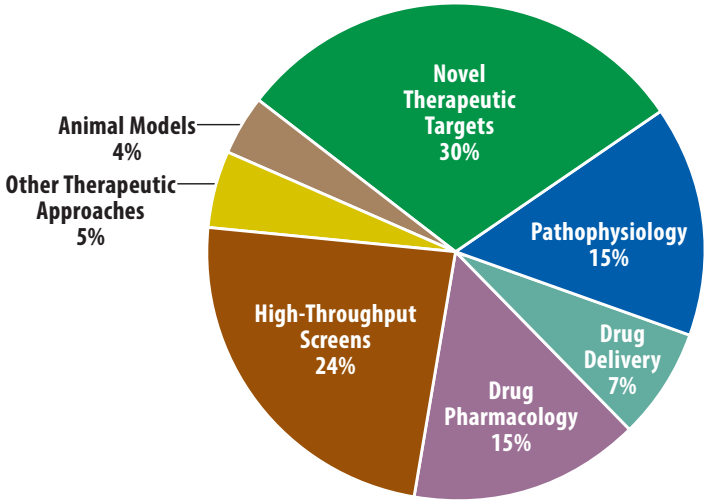
Program History

Amyotrophic lateral sclerosis (ALS), also known as "Lou Gehrig's disease," is an incurable, degenerative neurological disorder. CDMRP's Amyotrophic Lateral Sclerosis Research Program (ALSRP) is guided by a vision to improve treatment and find a cure for ALS. ALSRP was created in FY07 with a $5M appropriation. Although ALSRP was not funded in FY08, Congress subsequently appropriated funding in FY09 and has continuously provided funding since then, with a total appropriation of more than $69M, including $7.5M in FY17. Through its award mechanisms and funding recommendations, ALSRP supports innovative preclinical research to develop new treatments for ALS.

Program Portfolio

ALSRP has focused on awards that support preclinical development of therapeutics for ALS. Areas of emphasis include development and/or validation of high-throughput screens to define targets with therapeutic potential and development of pharmacologic agents through the adsorption, distribution, metabolism, excretion, and toxicity (ADMET) stage or Investigational New Drug (IND) application submission.

The pie chart shows the type of research the program has supported from its inception in FY07 through the FY16 program cycle.



ALSRP FY07-FY16 Funding by Topic Area

Targeting miR-155 in Peripheral Monocytes for the Treatment of ALS

Dr. Howard Weiner, Brigham and Women's Hospital, Inc.
AL120029, Therapeutic Development Award

Growing evidence supports a role for the immune system in the pathogenesis of ALS, but the mechanisms underlying the relationship between ALS and immunity are not well understood. Dr. Weiner, in an attempt to unravel the mechanisms underlying ALS and immunity, has observed in animal models of ALS that there is an infiltration of immune precursor cells, called monocytes, into the spinal cord. Interestingly, he has noted that this infiltration is parallel to and congruent with ALS symptom severity. Under an ALSRP Therapeutic Idea Award, Dr. Weiner discovered that modulation of the infiltration process appears to improve ALS symptoms in animal models. To gain a deeper understanding of this phenomenon, Dr. Weiner examined blood monocytes from patients with ALS and discovered that, not only do the monocytes express a pro-inflammatory phenotype, but they also have elevated expression of a small non-coding RNA, microRNA-155 (miR-155), which has been previously shown to play a role in inflammation. Therefore, Dr. Weiner hypothesized that activation of the downstream targets of miR-155 could potentially ameliorate the disease. Dr. Weiner is now collaborating with a company, miRagen Therapeutics, which specializes in developing microRNA (miRNA)-targeted therapies. Together, they are investigating the possibility of developing a therapeutic molecule designed to silence or inhibit the expression of miRNA, thus allowing expression of downstream target genes. The researchers are eager to investigate the effects of blocking miR-155 activity on ALS symptom abatement, as well as to discover whether it could extend survival in patients with ALS. These studies not only identify a new target to treating ALS; they also open up an important avenue focused on the immune system for the treatment of ALS.

Apo-Ferritin as a Therapeutic Treatment for Amyotrophic Lateral Sclerosis

Dr. James Connor, Pennsylvania State University, Milton S. Hershey Medical Center
AL100068, Therapeutic Idea Award

Free iron is harmful for cells because it acts as catalyst in the formation of free radicals that increase oxidative stress. Oxidative stress contributes to many neurodegenerative disease processes, and free or excess iron accumulation has been documented in patients with ALS. Dr. Connor hypothesizes that, in ALS, limiting or sequestering iron will decrease the oxidative stress burden and therefore attenuate ALS symptom progression and prolong survival. Under an ALSRP Therapeutic Idea Award, Dr. Connor set out to exploit the iron storage capacity of ferritin, a protein that stores and releases iron, to ameliorate ALS symptoms. Using infusions of cerebrospinal fluid containing apo-ferritin (i.e., ferritin without any iron bound), he found increased life span and delayed disease progression in ALS mice. Even greater delays in disease progression and increases in life span were achieved when the apo-ferritin was first encapsulated in liposomes before being added to the infusion. Dr. Connor and his colleague Dr. Amanda Snyder, have received follow-on funding from the ALS Association to further optimize their therapeutic formulation and are in discussions with a device company interested in partnering when it is ready for clinical trial. Their end goal is to develop a therapeutic infusion formulation that will improve clinical outcome in patients with ALS.

"It is a privilege to serve as a consumer reviewer in the ALSRP. It gives my family and I hope that these dedicated scientists and their novel research proposals will someday soon make the breakthrough we are all waiting for. It's very gratifying to know that the patient's experience, especially in a devastating disease such as ALS, is a part of the review and funding process."

Judy Keating, Peer Review Consumer

Autism Research Program

Vision

Improve the lives of individuals with autism spectrum disorder now

Mission

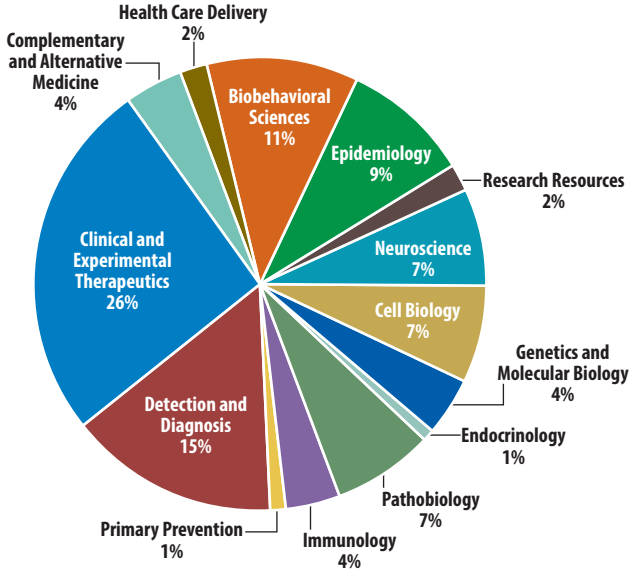
Promote innovative research that advances the understanding of autism spectrum disorders and leads to improved outcomes for Service Members, their families, and the American public

Program History

Since its inception in FY07 through FY17, appropriations totaling $74.4M have been directed to the Autism Research Program (ARP) to promote innovative research that advances the understanding of ASD. The immediacy of ARP's vision, to improve the lives of individuals with ASD now, has imparted a strong sense of action and continues to steer the investment strategy for ARP. ASD encompasses a wide range of complex developmental disorders, with characteristics from mild to severe in social, emotional, and communication abilities. Additionally, many individuals living with ASD are afflicted with co-occurring conditions (e.g., anxiety, gastrointestinal [GI] issues, sleep disorders, and aggression) that are not well understood and are only now being brought to the forefront of the research landscape. The causes of ASD are unknown; however, progress is being made on several fronts, and the answers will likely be multifaceted. ARP focuses on funding innovative and highly impactful research while trying to complement other funding agencies' initiatives. The population of ASD individuals entering adulthood is growing, and ARP recognizes the critical need for supporting and treating adults with ASD. Recently, ARP has placed emphasis on research that assists ASD individuals in their transition to adulthood, as well as research aimed at improving healthcare delivery to adults with ASD. Recent progress by investigators funded by ARP shows promise in the areas of (1) recognizing ASD early so that interventions may be initiated at an earlier life stage to make a difference; (2) understanding the gut-brain interactions and how to alleviate GI issues that may cause atypical developmental behaviors; and (3) understanding the needs of adult individuals with ASD.

"I was humbled and thrilled to be chosen as a Consumer Peer Reviewer. During orientation, we were reminded how important each consumer advocate is in the peer review process; oh, how I wish all grant funders and donors thought the same way. I was delighted with how professional and pleasant the whole experience was from start to finish. Through this experience, I gained a deeper appreciation for the scientists who devote themselves to improving the lives of youth and adults on the autism spectrum."

Karen Krejcha, Consumer Peer Reviewer, FY16
Karen Krejcha and her two sons, Justin and Ryan, have been diagnosed with ASD



FY07-FY16 ARP Research Investment

Treating Gastrointestinal and Autism Symptoms in Adults with Autism Using Microbiota Transfer Therapy

James Adams, Ph.D., Arizona State University, Tempe

Many individuals with ASD suffer from severe GI problems due to abnormal gut bacteria, and individuals with ASD who have GI problems exhibit significantly worse ASD symptoms. To establish healthy gut bacteria in patients with ASD, Dr. Adams and his collaborators, Dr. Rosa Krajmalnik-Brown and Dr. Dae-Wook Kang, utilize microbiota transfer therapy (MTT). This therapy involves administration of vancomycin (an antibiotic) to clean the gut and reduce pathogenic bacteria, followed by administration of a standardized human gut microbiota preparation to restore healthy gut microbiota. A pilot study in which MTT was administered to 18 children with ASD and GI problems revealed an 80% reduction in GI symptoms. Along with improved GI symptoms, there was a significant improvement in ASD symptoms. The improvement in GI and ASD symptoms remained 8 weeks after treatment stopped. After the MTT treatment, a significant increase in gut bacterial diversity was achieved, a signature of a healthy gut. With support from an FY15 ARP Clinical Trial Award, Drs. Adams, Krajmalnik-Brown, and Kang now hope to evaluate the efficacy of MTT in adults with ASD who have GI problems and to assess the potential role of gut bacteria on both GI and ASD symptoms. This clinical trial is a critical step toward gaining FDA approval for future clinical applications of MTT that could eliminate GI problems in individuals with ASD, improve their quality of life, and reduce their ASD symptoms.

Kang DW, et al. 2017. *Microbiome*. 5(1):10.

Maternal Brain-Reactive Antibodies and Autism Spectrum Disorder

Betty Diamond, M.D., Feinstein Institute for Medical Research

Maternal brain-reactive antibodies arise in adults due to immune responses and have the potential to alter development of the fetal brain and contribute to ASD. Dr. Diamond, with support from an FY13 ARP Idea Development Award, developed a novel strategy to test a series of monoclonal anti-brain antibodies to determine particular ASD characteristics that are associated with specific antibodies. Of the 40 antibodies isolated from mothers who were positive for brain-reactive antibodies and had a child with ASD, three antibodies targeted Contactin-Associated Protein-like 2 (Caspr2), a protein critical to normal brain development. One of these antibodies, C6, was extensively characterized. Mice were exposed in utero to isolated C6 antibodies through maternal mouse blood, and abnormalities were found in the developing brains of the mice that translated to ASD behavioral phenotypes. When the original human blood, from which C6 was isolated, was administered to pregnant mice, those fetuses also displayed developmental changes in the brain that were characteristic of ASD. In addition, Caspr2 antibodies were found more often in plasma from human mothers who were positive for brain-reactive antibodies and had a child with ASD (37%), compared to mothers who did not have a child with ASD (7.6%). This research identified a potential biomarker that could help identify pregnancies that are at an increased risk for an ASD child.

Brimberg L, et al. 2016. *Molecular Psychiatry*, 21(12):1663-1671.

Can Virtual Reality Pre-Exposure to Realistic Workplaces and Interactions Improve Job Placement, Anxiety, and Performance in Transitioning Adults with ASD?

ARP recently awarded an FY16 Idea Development Award to Brain Power, LLC. Dr. Joseph Salisbury (Project PI) and Dr. Ned T. Sahin (Founder and Chief Science Officer) will explore the use of virtual reality and smartglasses to aid in the successful transition of individuals with ASD into employment. The ASD population has specific needs that can affect their productivity and effectiveness in the workplace, specifically sensory sensitivity, anxiety, and training support. This project will explore the use of virtual reality-based workplace exposure to reduce anxiety prior to job placement. The research will also address the benefit of job coaching remotely via Brain Power's smartglasses-based system.

Eleanor, an employee at Brain Power, LLC, models the Brain Power System running on Glass Enterprise Edition. She joined the company as an intern through Aspire, a program for persons with high cognitive ASD. After her internship, Brain Power hired her full-time. Her roles include photo editing to prepare outreach materials, data analysis, and providing feedback on application design.

Bone Marrow Failure Research Program

Vision

To understand and cure bone marrow failure syndromes

Mission

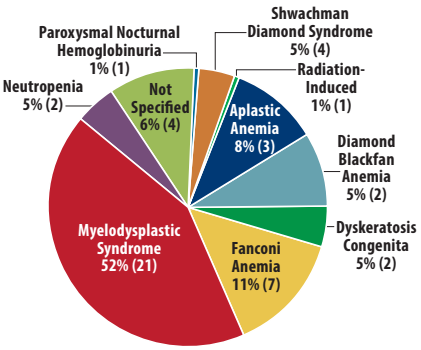
To encourage and support innovative research that is committed to advancing the understanding of inherited and acquired bone marrow failure syndromes, thereby improving the health of affected Service Members, Veterans, and the general public, with the ultimate goals of prevention and cure

"When your child is diagnosed with a life-threatening illness, it is easy to become overwhelmed with a sense of helplessness. Eight years ago, I had just joined the BMFRP Integration Panel, and my son with Fanconi Anemia was sliding into severe bone marrow failure. In fact, I flew directly from a BMFRP meeting to the medical center where my son was beginning his bone marrow transplant. The BMFRP gave me a sense of empowerment; I was helping to make an impact. In a small way, I was helping to direct research for a cure to bone marrow failure. Today, my son is a healthy 17-year-old Eagle Scout. I believe the BMFRP brings together incentive, ingenuity, imagination, and purpose. It has been an honor to be part of this dynamic process."

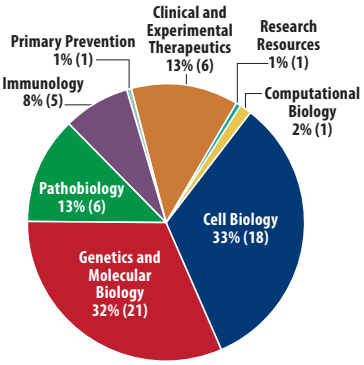
David Fiaschetti, D.D.S.
Programmatic Panel Member,
FY09-FY16

Program History

The cavities of bones are made up of a spongy tissue that contains stem cells capable of maturing to blood cells in a process known as hematopoiesis. The hematopoietic cascade is responsible for the development of all cellular blood components, including red blood cells, white blood cells, and platelets. Disorders affecting the stem cells or progenitor cells can lead to bone marrow failure (BMF)–rare, potentially life-threatening diseases in which the bone marrow stops functioning or produces abnormal blood cells. These diseases can be either inherited or acquired. Inherited BMF includes a group of diseases where somatic genetic mutations lead to a deficiency in hematopoiesis that presents itself in childhood or early adulthood. Acquired BMF includes a group of diseases that can occur following an environmental exposure such as ionizing radiation, chemical contamination, or the long-term effects of chemotherapeutics. Both types of BMF lead to life-long chronic illnesses with the potential to develop cancer. The Bone Marrow Failure Research Program (BMFRP) was initiated in FY08 to provide support for exceptional innovative research focused on BMF diseases. From FY08 through FY16, $29.55M has been appropriated by Congress to research the prevention, causes, and treatment of BMF diseases. The appropriation for FY17 for BMFRP is $3M. Thus far, BMFRP has invested in 61 awards in the pursuit of its mission to support innovative research committed to advancing the understanding of inherited and acquired BMF diseases.



FY08-FY16 Disease Classification*



FY08-FY16 Research Portfolio: Percent Dollars Invested*

*Percentages of total spent and (numbers of awards)

The Role of Necroptosis in the Pathophysiology of Bone Marrow Failure

Jiwang Zhang, M.D., Ph.D., Loyola University Chicago

Acquired aplastic anemia (AAA) is a serious BMF disorder where the immune system mistakenly targets the bone marrow, resulting in decreased blood cell numbers. Dr. Zhang established a mouse model that mimics AAA, in which a small population (1 to 3%) of bone marrow cells with genetic mutations is responsible for triggering an autoimmune reaction that results in BMF. With support from an FY12 BMFRP Idea Award, Dr. Zhang proposed to utilize his AAA mouse model to investigate whether persistent necroptosis in the small population of mutant bone marrow cells provokes BMF. Necroptosis is cell death due to disease or injury that stimulates immune responses. Receptor-interacting protein 3 (Rip3) is a key mediator of necroptosis. Depletion of Rip3 in the AAA mouse model completely prevented AAA development, suggesting that necroptosis is necessary for AAA initiation. Furthermore, depletion of T-cells or deletion of interferon gamma (INFγ), both of which are key players in the immune response, restored normal blood cell development and abated the immune response. These results confirm that necroptosis and the immune response involving the over-activation of T-cells and increased inflammatory responses (production of INFγ) contribute to AAA. Dr. Zhang's mouse model of AAA provides essential insight into the pathogenesis of the disease, as well as potential targets for therapeutic intervention.

Xin J, et al. 2017. *Haematologica*. 102(2):295-307.

The Role of U2AF1 Mutations in the Pathogenesis of Myelodysplastic Syndromes

Matthew Walter, M.D., Washington University

Myelodysplastic syndromes (MDS) are a family of disorders in which bone marrow cells display aberrant maturation, resulting in ineffective blood cell production. Over 50% of patients with MDS display mutations in spliceosomal genes. Spliceosome proteins are responsible for splicing RNA, which permits proper RNA processing and ultimately functional protein production. Specifically, mutations in the spliceosome gene U2AF1 (U2 Small Nuclear RNA Auxiliary Factor 1) occur in 11% of patients with MDS. The mechanisms by which these mutations contribute to MDS are unclear. Dr. Walter aimed to elucidate these mechanisms with support from an FY12 BMFRP Idea Award. Dr. Walter created a mouse model to study the most abundant U2AF1 mutation found in patients with MDS, coding for U2AF1(S34F). The mouse model revealed similar splicing patterns to human patients with MDS with U2AF1(S34F) mutations and also displayed characteristics of MDS, suggesting that it may be a valuable model to aid in understanding the disease pathogenesis induced by mutations of U2AF1. The treatment of U2AF1(S34F)-expressing cells with sudemycin, a splicing modulator drug, resulted in cumulative splicing events corresponding to changes in gene expression that may result in increased apoptosis in the mutant cells. Thus, diseases with spliceosome gene mutations, such as MDS, may have a therapeutic vulnerability to splicing modulating drugs.

Shirai CL, et al. 2015. *Cancer Cell*. 27(5):631-43.
Shirai CL, et al. 2017. *Nat Commun*. 8:14060.

Metformin Therapy for Franconi Anemia

Markus Grompe, M.D., Oregon Health and Science University

Pharmacological therapy for the devastating genetic BMF disease, Franconi anemia (FA), has changed little in the past 30 years. Dr. Grompe conducted a screen of small molecules that could present new therapeutic potential for FA. The lead molecule is the FDA-approved diabetes drug, metformin. Promising results have been seen in an FA mouse model. Metformin treatment caused increased blood cell numbers and reduced DNA damage, addressing two of the key pathological characteristics of patients with FA. Preliminary results are promising, and Dr. Grompe was awarded an FY15 BMFRP Idea Development Award to determine the efficacy of metformin therapy in multiple preclinical FA models, as well as in human FA cells. Guided by the results from this BMFRP award, a clinical trial of metformin is anticipated to start in 2018.

Breast Cancer Research Program

Vision

To end breast cancer for Service Members, Veterans, and the general public by funding innovative, high-impact research through a partnership of scientists and consumers

Program History

BCRP plays a leading role in the fight against breast cancer (BC). The BCRP was established in 1993 as a result of the passionate efforts of BC advocates. Their continued efforts, in concert with the program's successes, have resulted in more than $3.3B in congressional appropriations through FY17. BCRP challenges the scientific community to design research that will address the urgency of ending BC. BCRP seeks to make breakthroughs in BC, accelerate high-impact research with clinical relevance, facilitate collaborations and partnerships, support future BC leaders, and encourage innovation and creativity.

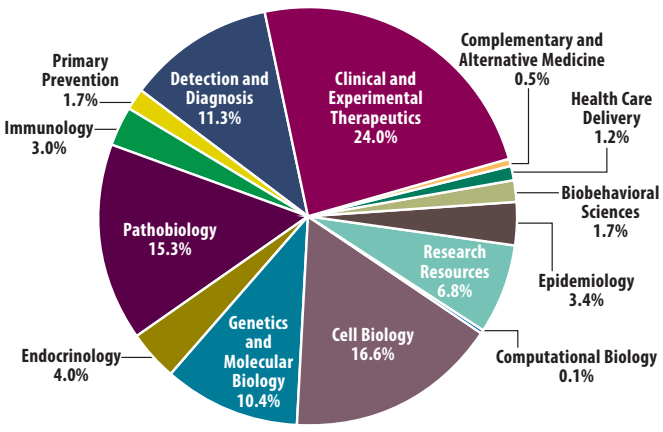
Overarching Challenges

Despite the significant progress that has been made in the BC field since 1993, BCRP recognizes that many overarching questions still remain unanswered in BC, and funding must be invested in critical areas of research in order to make breakthroughs that will save lives and lead to eradication of this disease. To meet this urgent need, the FY17 BCRP requires all applications to address at least one of the following overarching challenges within the *Breast Cancer Landscape*:

- Prevent breast cancer (primary prevention).
- Identify determinants of breast cancer initiation, risk, or susceptibility.
- Distinguish deadly from non-deadly breast cancers.
- Conquer the problems of overdiagnosis and overtreatment.
- Identify what drives breast cancer growth; determine how to stop it.
- Identify why some breast cancers become metastatic.
- Determine why/how breast cancer cells lie dormant for years and then re-emerge (recurrence); determine how to prevent recurrence.
- Revolutionize treatment regimens by replacing them with ones that are more effective, less toxic, and impact survival.
- Eliminate the mortality associated with metastatic breast cancer.

"Beyond my personal medical care provided by the military, it means so much to me that the DoD is also providing for military families by funding such important research on breast cancer and metastasis."

Alexis Rhoads

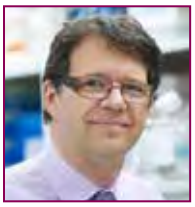


FY93-FY16 BCRP Research Portfolio (% Dollars Invested)

New Clinical Trials in 2016-2017


Folate Receptor Alpha Vaccines: *Keith Knutson (pictured left) and Edith Perez (pictured right), Mayo Clinic, Jacksonville*

Folate receptor alpha has been shown to be highly expressed in >80% of triple-negative breast cancers (TNBC). Dr. Keith Knutson and colleagues previously demonstrated the safety and immunogenicity of a folate receptor alpha vaccine in a Phase I trial. BCRP is supporting a Phase II trial to determine whether this vaccine can prevent or delay disease recurrence in patients with TNBC. The trial is anticipated to open in the summer of 2017.



Tumor Antigen-Targeted T-Cell Therapy for Metastatic Breast Cancer: *Michel Sadelain (pictured left), Prasad Adusumilli (pictured center), Shanu Modi (pictured right), Memorial Sloan Kettering Cancer Center*

BCRP is supporting a Phase I clinical trial of adoptive T-cell therapy in patients with metastatic TNBC. This trial (NCT027921), which opened in September 2016, is based on preclinical work that demonstrated mesothelin (MSLN) expression in patients with TNBC and found that those patients had an increased frequency and interval to develop distant metastases. The goal of the trial is to test the safety of MSLN-targeted chimeric antigen receptor (CAR) T-cells in patients with metastatic TNBC and to compare immune responses between patients who received MSLN CAR T-cells either intravenously or intrapleurally.


Aspirin as Adjuvant Therapy for Node-Positive Breast Cancer: *Eric Winer (pictured left), Dana-Farber Cancer Institute, and Michelle Holmes (pictured right), Brigham and Women's Hospital*

Epidemiological and preclinical data suggest aspirin may reduce BC recurrence and improve survival. A BCRP-supported Phase III trial (NCT02927249) of aspirin among patients with BC with node-positive disease opened in December 2016. Using invasive disease-free survival as the primary endpoint, the trial will assess treatment efficacy, outcomes, and adherence to and the toxicity of long-term aspirin use, and will create a biospecimen and epidemiologic data repository. If successful, the trial could establish aspirin as a cost-effective treatment to prevent recurrence in patients worldwide.

Clinical Research Breakthroughs

Targeted HER2 Radiotracer: *Gary Ulaner, Memorial Sloan Kettering Cancer Center*

Growing evidence suggests that human epidermal growth factor receptor 2 (HER2) expression at metastatic sites can differ from expression at the primary tumor. The BCRP supported a clinical trial that used a targeted HER2 radiotracer (89Zr-trastuzumab) to detect HER2+ metastases in patients with HER2-primary BC. Five out of nine patients showed evidence of HER2+ metastases, two of which were confirmed by image-guided biopsy. Those two patients were subsequently treated with trastuzumab, pertuzumab, and chemotherapy. One patient showed a complete response, while the other showed decreased size and avidity of metastases. A second radiotracer has been developed to improve accuracy and is currently being tested in a Phase I clinical trial (NCT03109977). This lays the groundwork for future HER2-targeted imaging techniques, as well as larger clinical studies.

Ribociclib (CDK4/6 Inhibitor): *Dennis Slamon, University of California, Los Angeles*

BCRP supported preclinical research on a series of cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. The data generated formed the basis for the recent clinical trials of ribociclib (Novartis) in estrogen receptor (ER)+/HER2-advanced BC in the MONALEESA trials and abemaciclib (Lilly) in the MONARCH trials. In 2017, the FDA granted approval for ribociclib as a first-line treatment of postmenopausal women with ER+/HER2- advanced or metastatic BC in combination with letrozole. This year, Lilly also announced that the MONARCH 2 study had met its study endpoint for efficacy and will form the basis of their submission for formal FDA and European Medicines Agency approval of abemaciclib to treat ER+/HER2- advanced or metastatic BC.

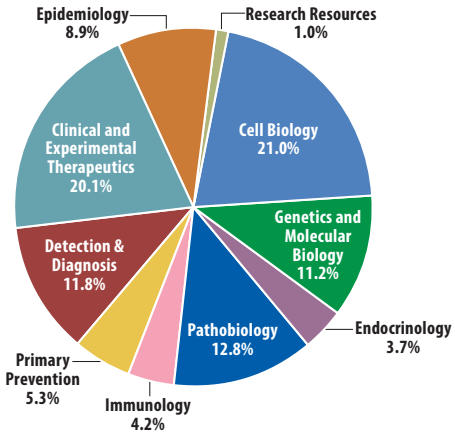
Breast Cancer Research Semipostal Program

Program History

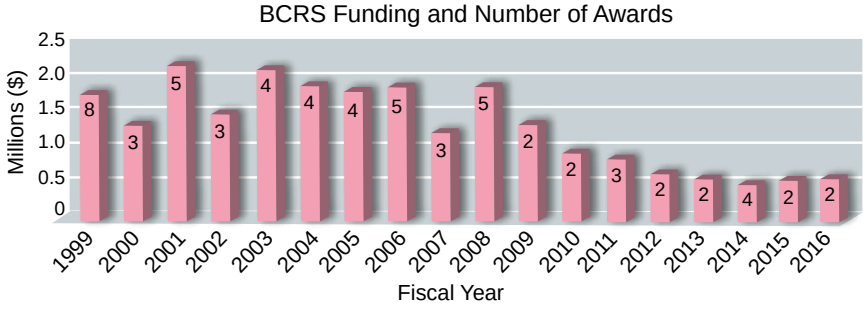
As a result of the efforts of BC advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the US Postal Service's issuance of a new first-class stamp, the Breast Cancer Research Semipostal (BCRS) in 1998. It was the first semipostal in US history. Net revenues from sales of the BCRS, which currently costs 60 cents, are provided to two designated funding agencies, the DoD BCRP and NIH, to support BC research. By law, 30 percent of the total amount raised is allocated to DoD's BCRP, and 70 percent is allocated to the NIH. The Breast Cancer Research Stamp Reauthorization Act of 2015 reauthorized the stamp through 2019.

Research and Management Costs

Breast cancer stamp funding received by the BCRP between FY99 and FY16 has been used to fully or partially fund 63 awards under three award mechanisms: the Idea Award, Synergistic Idea Award, and Breakthrough Award Funding Level 1. These award mechanisms support innovative, high-risk, high-reward research that could lead to major advancements in BC. Applications funded through the BCRS program were reviewed and recommended for funding according to the two-tier review system implemented by DoD's BCRP. An evaluation of the awards funded through the BCRS program shows that the projects encompass a diversity of research areas.



FY99-FY16 BCRS Research Portfolio (% dollars invested)

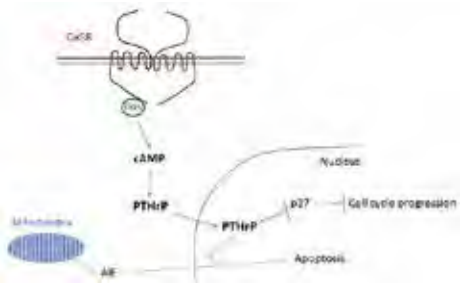


Total Proceeds from BCRS (through FY16)	$24,709,126.70
Research	$23,502,469.25
Management Costs	$1,206,657.45

A Potential Therapeutic Target to Limit Breast Cancer Tumor Growth in Bone Metastases

John Wysolmerski, M.D., (pictured left), Wonnam Kim, Ph.D., MBChB, (pictured right), Yale University School of Medicine

Breast cancer frequently metastasizes to bone, resulting in painful osteolytic lesions. Parathyroid hormone-related protein (PTHrP) secreted by tumor cells in the bone microenvironment stimulates osteoclast activity, promoting hypercalcemia and tumor growth. With support from an FY09 Idea Award funded by the BCRS and the BCRP, Dr. Wysolmerski began to elucidate the unknown mechanism of PTHrP signaling in breast tumors. The calcium-sensing receptor (CaSR) can be activated by extracellular calcium, and CaSR signaling inhibits PTHrP production in normal breast cells, but conversely stimulates PTHrP secretion in breast cancer cells. Findings reported in *Cancer Research* by Dr. Wysolmerski and his colleagues identified CaSR-PTHrP interactions as a potential therapeutic target to slow breast cancer tumor growth in bone metastases. They confirmed that CaSR activation stimulated production of PTHrP by breast cancer cells and promoted the proliferation of human breast cancer cell lines and tumor cells cultured from a mouse model of breast cancer. Furthermore, reduced expression of CaSR in mammary epithelial cells resulted in decreased tumor PTHrP expression, a slower rate of tumor growth, reduced tumor burden, and increased overall survival. Moreover, tumor cells were sensitized to the apoptotic effects of high extracellular calcium concentrations by a mechanism involving increased levels of nuclear PTHrP in tumor cells after CaSR activation. Taken together, these results indicate that CaSR-PTHrP interactions promote breast cancer cell growth. These promising findings by Dr. Wysolmerski and his colleagues led to additional funding from an FY15 BCRP Breakthrough Award to further investigate the mechanisms of CaSR inhibition on PTHrP production and bone metastases of breast cancer.



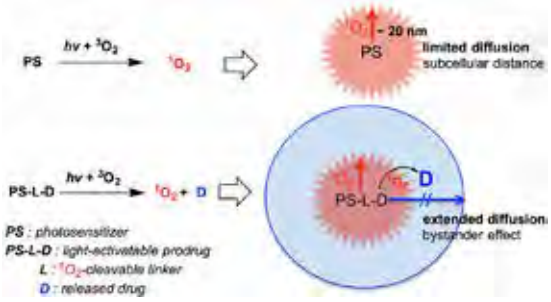
CaSR-induced PTHrP promotes breast cancer cell survival and proliferation via intracrine PTHrP signaling

Publications: Boras-Granic K, et al. 2014. *PLoS ONE.* 9(5):e90418 and Kim W, et al. 2016. *Cancer Res.* 76(18):5348-5360.

Near IR-Activated Prodrug Containing Novel Singlet Oxygen Cleavable Linker Decreases Cancer Cell Growth

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

Chemotherapy is a commonly used and effective treatment method for many types of cancer, but often has negative side effects. Dr. You sought to minimize the negative side effects of chemotherapy and enhance site-specific drug delivery to cancer cells using photodynamic therapy (PDT). PDT utilizes photosensitizers and near-infrared radiation (IR) to induce singlet oxygen (SO) production, resulting in cancer cell death; however, PDT is limited by the inability of SO to diffuse and by its short half-life. With support from an FY08 Idea Award funded from the BCRS, Dr. You and his colleagues coined the term "photo-unclick chemistry" by generating the novel SO cleavable linker, aminoacrylate, which is capable of delivering the vascular disrupting agent combretastatin A4 (CA4) to tumor cells after near-IR excitation of the photosensitizer, phthalocyanine (Pc). Results published in *Bioorganic and Medicinal Chemistry* show that CA4 conjugated to Pc by way of the aminoacrylate linker decreased cancer cell survivability and tumor volume. These encouraging results support the need for additional preclinical studies on the aminoacrylate prodrug molecule activated with photo-unclick chemistry. Dr. You received an FY13 Idea Expansion Award funded by the BCRP and is currently developing the aminoacrylate linker for use in an animal model of breast cancer to deliver site-specific chemotherapeutics via PDT.



Light-activatable prodrug (PS-L-D) overcomes both spatiotemporal barriers of PDT and systemic side effect of chemotherapy. Limited diffusion of $^1O_2$ can be overcome by unlimited diffusion of the site-specifically released drug (D) by illumination (hv).

Publication: Rajaputra P, et al. 2016. *Bioorg Med Chem.* 24(7):1540-1549.

Duchenne Muscular Dystrophy Research Program

Vision

To preserve and improve the function and quality of life, and to extend the life span of all individuals with Duchenne

Mission

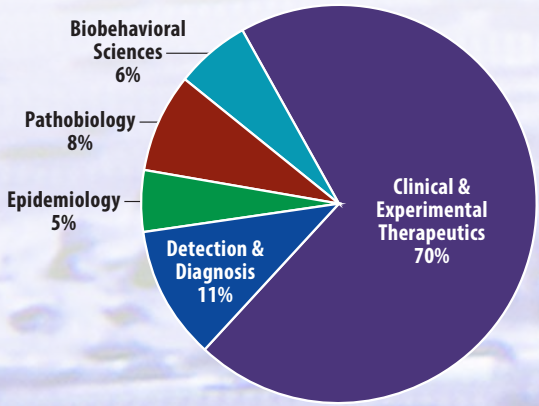
To better support discovery and development of therapeutics, devices, and other interventions, and to promote their rigorous clinical testing for the benefit of military beneficiaries and the general public

"My sons were diagnosed with Duchenne muscular dystrophy (DMD) in 1997 and 1999, both at age 5. I learned about the Congressionally Directed Medical Research Program's Duchenne Muscular Dystrophy Research Program at a conference and expressed an interest in becoming a consumer reviewer. It was my belief that my family experience and involvement in a number of DMD activities made me well prepared for this role. I spent much time reading and analyzing the proposals before writing my review. The scientist reviewers were genuinely interested in how consumer reviewers rated each proposal. I was pleased that many of my comments or concerns with an application were in agreement with the scientists' statements. In the process, I learned that my time was well spent and my work appreciated."

Brian Denger,
Consumer Peer Reviewer

Program History

Duchenne affects approximately 1 in 3,500 male births and is one of the most common and severe forms of muscular dystrophy. This form of muscular dystrophy results from mutations in the dystrophin gene that leads to an absence of dystrophin in muscle cells, allowing these cells to be easily damaged. Boys living with Duchenne experience devastating muscle weakness that affects the skeletal muscles, heart, and respiratory muscles. Symptoms of Duchenne typically develop prior to age 5, and by age 12 most patients are confined to a wheelchair. Currently, there is no cure for Duchenne, and young men with this disease rarely live beyond their early 30s. The Duchenne Muscular Dystrophy Research Program (DMDRP) was established in FY11, the result of passionate and tireless advocacy efforts. The initial congressional appropriation was $4M, and since that time, $23.2M has been appropriated to the program, including $3.2M in FY17. Currently, no treatment can stop or reverse the progression of Duchenne; however, during the past several years, research has identified many new potential therapeutic targets and significantly expanded the number of potential therapeutics in the pipeline for Duchenne. In order to assist in the development of treatments for Duchenne, DMDRP has focused on accelerating promising therapeutic ideas into clinical applications and supporting the training of new physician researchers as they pursue careers in Duchenne research.



FY11-FY16 DMDRP Research Portfolio (% Dollars Invested)

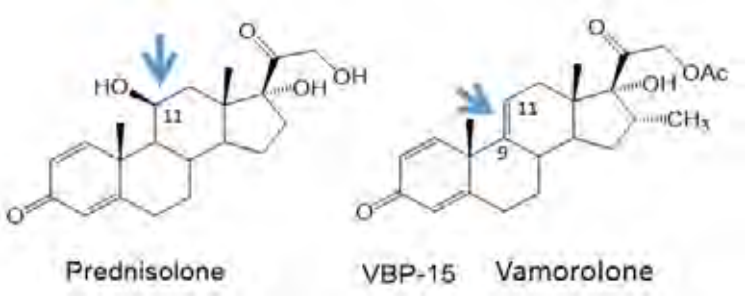
Advancement in Duchenne Therapeutics



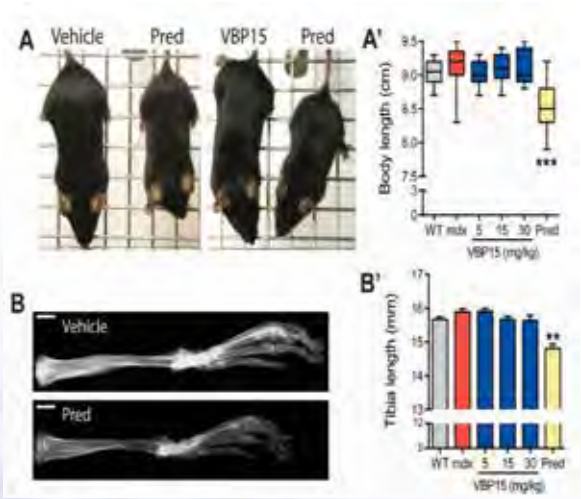
Eric Hoffman, Ph.D., (pictured left); Kanneboyina Nagaraju, D.V.M., Ph.D., (center); John McCall, Ph.D. (pictured right), Children's National Medical Center

DMD is a rare disease caused by a genetic mutation resulting in the lack of production of a structural protein called dystrophin. Patients with Duchenne suffer from progressive muscle damage, weakness, and disability. Glucocorticoids, such as prednisone and deflazacort, are the current standard of care for patients with Duchenne to reduce muscle damage and increase patient strength. While glucocorticoids provide a reduction in the inflammation caused by contraction-induced muscle damage in patients with Duchenne, they induce harsh side effects, particularly in children. These side effects include stunted growth, diabetes, mood swings, and weight gain, which reduce patient adherence and limit the therapeutic window.

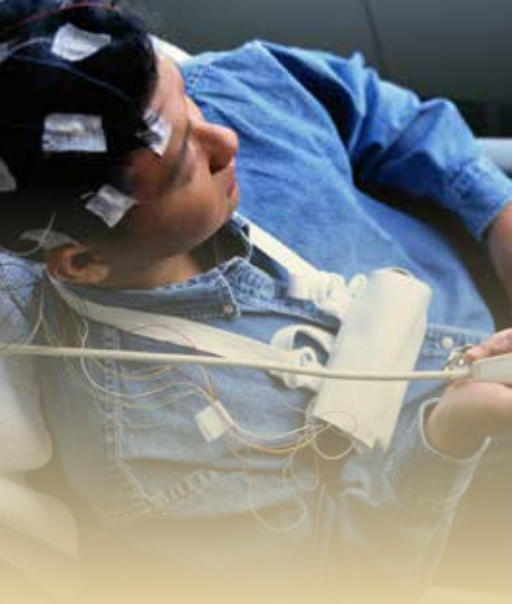
Research indicates the harmful side effects induced by glucocorticoids are a result of transcriptional gene activation, termed "transactivation," whereas the beneficial anti-inflammatory effects occur through inhibition of inflammatory transcription factors, such as Nuclear Factor kappa B (NFκB), termed "transrepression." Drs. Hoffman, Nagaraju, and McCall sought to develop a novel therapeutic that could dissociate the beneficial transrepressive and anti-inflammatory effects of glucocorticoids from the harmful transactivation-induced side effects. They hypothesized a compound with these properties would continue to provide improvements in muscle inflammation and increase strength for patients with Duchenne without the harmful side effects of traditional glucocorticoids. Beginning with several DoD awards managed by CDMRP, the research team screened compounds for inhibition of NFκB, a key signaling protein in inflammation, and binding to the glucocorticoid receptor of a signaling protein that is central to glucocorticoid functioning. They determined that the compound, vamorolone (previously VBP15), had the cellular signaling characteristics that were promising for therapeutic efficacy for inflammatory diseases with a reduced side effect profile. They used this compound for preclinical testing in murine models of DMD.



Vamorolone demonstrated efficacy equal to prednisone in the treatment of muscular dystrophy, both in vitro and in vivo in the mdx mouse model of Duchenne, but lacked the associated side effects. These studies led to successful IND studies supported by NIH followed by Phase I safety trials of vamorolone in healthy individuals that were supported by various non-profit foundations. The Phase I trials were successful, and Phase II trials have begun in steroid-naïve Duchenne boys 4-7 years of age. Vamorolone represents an exciting opportunity for improving the lives of patients with Duchenne, and it is being explored as a potential therapeutic in other inflammatory disorders where the side effects of glucocorticoids detract from patient quality of life and sometimes outweigh the benefit.



Mice exposed to increasing concentrations of VBP15 show dramatic decreases in prednisone-associated side effects, as indicated above by (A/A'), body length, and (B/B'), tibia length.



Epilepsy Research Program

Vision

The Epilepsy Research Program (ERP) envisions a time when the causative links between TBI and epilepsy are understood and post-traumatic epilepsy is preventable

Mission

The ERP's mission is to fund research to understand the magnitude, and the underlying mechanisms of PTE, especially in Service Members and Veterans

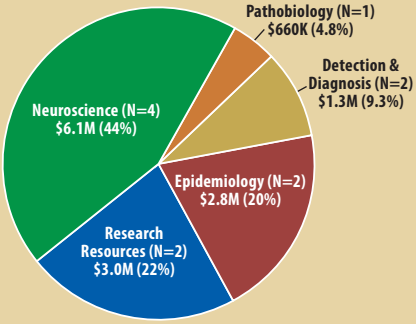
"The Epilepsy Research Program will play a critical role in elucidating and understanding post-traumatic epilepsy and the role of trauma in non-epileptic seizures. Post-traumatic epilepsy is a consequence of traumatic brain injury, and post-traumatic epilepsy is the most common cause of new-onset epilepsy in young adults. The panel's work will have a direct impact on Service men and women, as well as civilians who have sustained traumatic brain injury."

CPT Karen Parko, M.D.,
US Public Health Service, Ret.,
Inaugural National Director,
VA Epilepsy Centers of Excellence

Program History

The DoD's ERP was established in FY15 to address the critical need to understand the magnitude and underlying mechanisms of PTE, especially in Service Members and Veterans, while also benefiting the civilian community. With a total of $15M in congressional appropriations over the past 2 years, the ERP funds innovative research through the Idea Development Award mechanism using two funding levels. Level I is intended to support research that is high-risk and/or high-gain. Level II is intended to support advanced studies that may be multidisciplinary in nature. Through collaborative efforts of academic scientists, subject matter experts, and advocates, ERP's FY17 4 focus areas have been established and are listed below:

1. Epidemiology: Epidemiological characterization of PTE following traumatic brain injury (TBI), may include:
   - Risk factors such as demographics, genetic factors, organic head injury factors, or type of insult.
   - Differentiation of PTE and Psychogenic Non-Epileptic Seizures (PNES).
   - Outcomes including latency to epilepsy, morbidities and comorbidities, and mortality.
   - Pre-existing conditions including psychological and psychiatric risk factors.
2. Markers and Mechanisms: Identifying markers or mechanisms (via clinical prospective or preclinical models) that address PTE including: early detection, diagnosis, prognosis, morbidity and comorbidity, mortality and risk stratification.
3. Models of PTE: Development of new models or better characterization of existing etiologically relevant models for PTE, including repetitive TBI.
4. Psychogenic Non-Epileptic Seizures: Exploration of the epidemiology, mechanisms, risk factors, or markers of PNES subsequent to TBI.



FY15-FY16 ERP Research Portfolio Investment

About the ERP Programmatic Panel

The Programmatic Panel is responsible for directing ERP's overall mission and vision. In addition to reviewing the program's mission, vision, and focus areas, the Panel also makes recommendations to the CDMRP regarding investments for the ERP's research portfolio, based on the program goals and scientific peer review. While the Programmatic Panel does not re-review the technical nature of the proposals received in response to the ERP's PAs, the Panel members serve a critical need in that they are directly responsible for identifying the best research investments for ERP to meet the program's needs. The Programmatic Panel receives guidance from ERP's peer reviewers and considers this guidance as it reviews applications and recommends which projects should be funded. In addition to peer reviewer comments, the Panel weighs the relevance of each proposal to both ERP's goals and its portfolio composition in order to maintain a well-balanced portfolio of research.

Consumer Participation

Consumers represent the voice and vision of individuals affected by PTE. Consumers for ERP are military Service Members living with, or family members/caregivers of a person living with, PTE. (For more information, please go to cdmrp.army.mil.) ERP incorporates consumers as active participants in virtually all aspects of program execution. Consumers work collaboratively with leading scientists and clinicians in setting priorities, reviewing proposals, and contributing their unique perspectives and a sense of urgency to program processes. Consumers also serve as liaisons between their constituencies and the scientific community and increase awareness about ERP in the consumer community.

Research Highlight

The Epidemiology of Epilepsy and Traumatic Brain Injury: Severity, Mechanism, and Outcomes

Mary Jo Pugh, Ph.D., RN South Texas Veterans Health Care System

Roughly 360,000 Service Member-related cases of TBI were reported to the Defense and Veterans Brain Injury Center (DVBIC) between 2000 and 2016. While previous wars have long shown a strong correlation between combat-related TBI and epilepsy, the current conflicts in Iraq and Afghanistan have produced more survivable injuries than in previous wars. While these injuries are now treatable, the long-term consequences of these injuries with respect to PTE are unknown. This is especially true for individuals who have sustained mTBI. Dr. Mary Jo Pugh was awarded an FY15 Idea Development Award that proposed an innovative study to address the association of TBI with PTE in Veterans who served in Operations Iraqi Freedom (OIF) and Enduring Freedom (OEF). This study will conduct an exhaustive evaluation of PTE using data from the DoD and VA databases in addition to surveys and interviews that identify lifetime TBI exposures. The study is designed to identify the associations between mTBI and PTE and to describe the impact of mTBI and/or epilepsy on the social, emotional, and physical functioning of individuals. Selected participants in this study will also be eligible to participate in advanced clinical, cognitive, and magnetic resonance imaging (MRI) testing. The study design will identify populations at highest risk for developing PTE after mTBI, which may allow clinicians to develop protocols to target individuals at highest risk so that they can identify epilepsy and the most appropriate treatments early. Additional outcomes may include identifying individuals who may benefit from specific types of non-pharmacological therapy such as cognitive or lifestyle interventions. These types of interventions may benefit Service Members and Veterans with PTE or other epilepsy by improving their ability to manage their epilepsy and decrease some of their symptoms thereby leading to better quality of healthcare and improving health outcomes for these individuals and their families.

What is Gulf War Illness?

GWI is characterized by persistent symptoms such as widespread pain, cognitive difficulties, debilitating fatigue, gastrointestinal problems, respiratory symptoms, chronic headache, sleep problems, 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, out of the nearly 700,000 troops deployed to that region.

Gulf War Illness Research Program

Vision

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

Mission

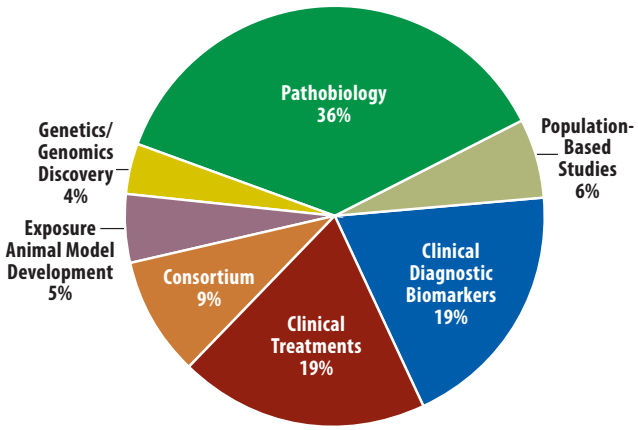
Fund innovative Gulf War Illness research to identify effective treatments, improve definition and diagnosis, and better understand pathobiology and symptoms

Program History

DoD-funded research into GWI began in 1994 with the establishment of a Gulf War Veterans' Illnesses Research Program (GWVIRP) to study the health effects of Service Members deployed in the 1990–1991 Persian Gulf War. From FY94 to FY05, GWVIRP was managed by USAMRMC's MOMRP. Research pertaining to GWI also was funded intermittently through CDMRP's Peer Reviewed Medical Research Program (PRMRP), which supports selected military health-related research topics each fiscal year. MOMRP shared management responsibility for GWVIRP with CDMRP in FY06, with separate $5M appropriations. Although Gulf War–related research was not funded in FY07, a $10M appropriation renewed the program in FY08, renamed the Gulf War Illness Research Program (GWIRP), to be managed fully by CDMRP. Since FY08, GWIRP has received a total of $149M in congressional appropriations, including $20M in FY17. From these appropriations, the program has built a broad research portfolio of over 140 projects featuring clinical trials and basic research, as well as studies addressing chemical exposures and GWI symptomatology. In 2012, two major multidisciplinary, multi-institutional research efforts by leading GWI investigators were initiated to address specific aspects of autonomic dysregulation and neuro-inflammation in investigations spanning the range from basic research to clinical trials.

Program Portfolio

GWIRP has placed emphasis on finding treatments for GWI. Pathobiological investigations are aimed at the identification of molecular targets for treatments and molecular abnormalities that might be used as markers.



GWIRP FY06-FY16 Funding by Topic Area

Examination of Plasma PON1 Paraoxonase Activity and Genotype in Gulf War Veterans

Linda Chao, Ph.D., Northern California Institute for Research and Education

Exposures to organophosphates (OPs), such as certain pesticides and chemical nerve agents, have been identified as risk factors for the development of GWI, but there is significant variability in the extent of illness developed by cohorts of Gulf War Veterans with identical OP exposures. Under a GWIRP Investigator-Initiated Research Award, Dr. Chao is conducting a large genetic study of Gulf War Veterans in order to test the hypothesis that individual differences, called polymorphisms, in the paraoxonase 1 (PON1) gene influence the risk for the development of GWI. The PON1 gene codes for a member of the paroxonase family of enzymes that is involved in the metabolism and detoxification of OPs. Different polymorphisms in the PON1 gene are known to confer different benefits. For example, one variant of the PON1 gene is better at detoxifying pesticides, while another variant is better at detoxifying nerve agents. Dr. Chao plans to exploit this knowledge in her analysis of Veterans in order to help tease apart which exposures were the major contributors to the development of GWI in specific cohorts. This study has the potential to provide essential insights about the etiology and pathobiology of GWI, yielding both long-needed answers for ill Gulf War Veterans and important information that may help to prevent similar problems in future deployments.

Monosodium Luminol for Improving Brain Function in Gulf War Illness

Dr. Ashok K. Shetty, Ph.D., Texas A&M University System Health Science Center

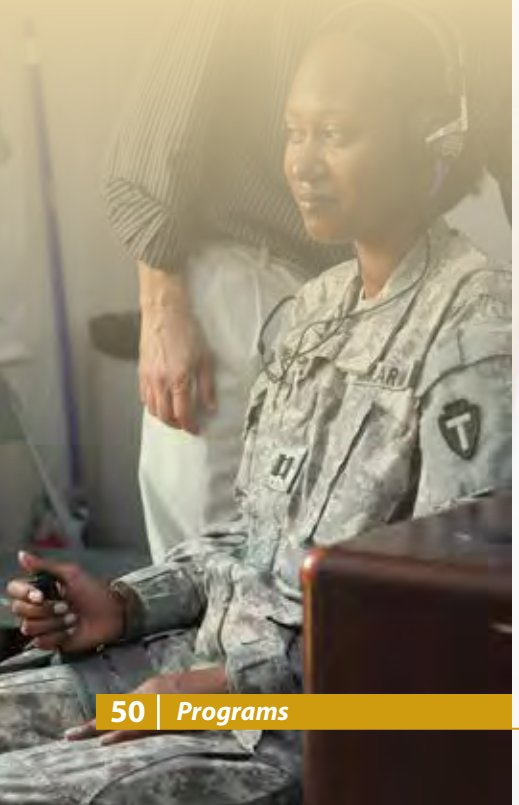
Dr. Shetty is studying the efficacy of a potent anti-inflammatory and antioxidant drug, monosodium luminol-GVT (MSL-GVT, Bach Pharma), for easing cognitive and memory dysfunction and depressive-like behavior in a well-characterized rat model of GWI. Under a GWIRP Investigator-Initiated Research Award, Dr. Shetty demonstrated that MSL-GVT administered to rats for 8 weeks is effective at alleviating cognitive impairments, improving memory, and reducing depressive activity following various behavioral tests. These improvements were associated with suppression of oxidative stress, reduced inflammation, and subsequent enhancement of hippocampal neuron production. These findings validated the pathophysiological targets of the drug, demonstrating the promise of MSL-GVT as a therapeutic for treating cognitive impairment associated with GWI. Future plans include determining whether MSL-GVT can improve cognitive impairment and reduce depressive-like behaviors in rats if given 6 months after exposure to suspected Gulf War agents. In terms of rat life span, this 6 months equates to ~17-year survival period after exposure in humans, a result which should suggest whether MSL-GVT holds promise for treating latent and chronic symptoms faced by Veterans suffering from GWI.

"I've been involved in CDMRP's Gulf War Illness Research Program for 7 years now. The reason CDMRP has Veterans involved is so that we're able to provide input and opinions to the physicians and scientists with whom we serve on the panel as to whether or not a particular study demonstrates the potential to provide effective treatments to sick Gulf War Veterans. We also want to make every effort to eventually determine the etiology of Gulf War Illness so that America's future Warriors are spared from having to experience the same thing."

David Winnett, FY10-FY17 GWIRP Programmatic Review Consumer

"What's really exciting to me about this program is that it involves not just scientists and medical doctors who are experts in their field, but also Gulf War Veterans who are actually dealing with this condition. We sit with equal footing on the panel, and we weigh in on research that is most likely to help us and to speed effective treatments through to the finish line. When we served, we had the expectation that our country would take care of us if we came home injured. This program is very clearly helping to fulfill that promise."

Anthony Hardie, FY10-FY17 GWIRP Programmatic Review Consumer and FY15-FY17 Programmatic Panel Chair



Hearing Restoration Research Program

Vision

Improve the operational effectiveness, medical readiness and quality of life of Service Members and Veterans with auditory system injuries

Mission

Advance the science of hearing restoration by delivering groundbreaking research and solutions that remove barriers to the successful treatment of auditory system injury

Program History

HRRP was initiated in 2017 to pursue promising, necessary research for treatment of burdensome and very prevalent auditory system injury. It is estimated that more than 30 million Americans over the age of 12 years have hearing loss in both ears and an estimated 48 million have hearing loss in at least one ear. In the military, the two most prevalent service-connected disabilities are related to hearing disorders. The most recent data from the VA's Veterans Benefits Administration indicates that there are 1.1 million Veterans with service-connected disability due to hearing loss. HRRP will fund innovative research that has the potential to maximize operational effectiveness, medical readiness, and quality of life for Service Members, Veterans, and others living with significant auditory system injuries.

"Nearly every fellow military member I've ever met, either active duty or Veteran, is facing some sort of hearing challenge. Whether it's hearing loss, tinnitus, or a combination; it's the battle after the battle that almost all of us still fight long after our service has ended. The importance of the Hearing Restoration Research Program and its potential to mitigate such a widespread health issue cannot be overstated, and it's a privilege to be a part of the effort to significantly improve the lives of our Service Members."

MSgt Sean Lehman (Ret), Heroes With Hearing Loss, Programmatic Panel Consumer Representative

FY17 Focus Areas

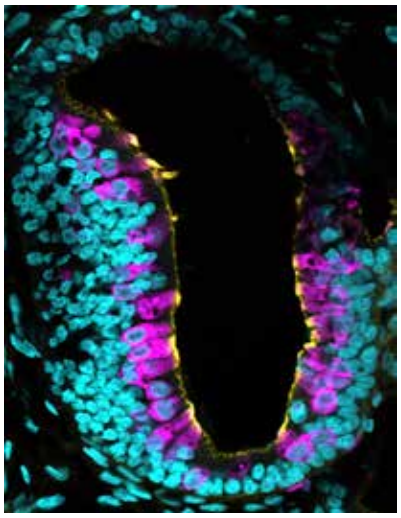
Develop reliable in vitro human models for evaluating hearing restoration therapies

Accelerate translation of biological regeneration into therapies that restore auditory function, including for example, treatments that enhance:

- Synaptic plasticity.
- Hair cell and neural regeneration.

Develop and validate assessment techniques and or treatment methods that address functional hearing restoration including for example:

- Personalized prognostic indicators of therapeutic success.
- Better differential diagnostic tests.
- Improved evaluation of treatment methods.



Human Stem Cell-Derived Auditory Hair Cell

Photo courtesy of Dr. Eri Hashino, Ph.D., Indiana University School of Medicine

FY17 Award Mechanisms

Translational Research Award (TRA)

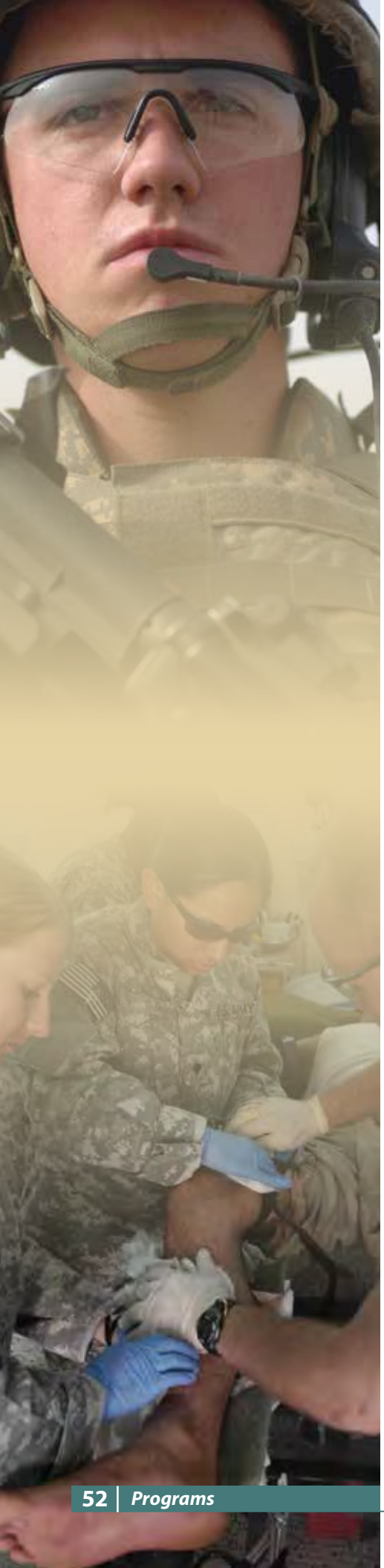
- The FY17 HRRP TRA is intended to support preclinical translational research that will accelerate the movement of promising initiatives that are relevant to hearing restoration into clinical applications. In this first year of the program, the proposals submitted must focus on the development of reliable in vitro human models to evaluate hearing restoration therapies or research that translates biological regeneration initiatives into therapies that restore auditory function.

Focused Research Award (FRA)

- The FY17 HRRP FRA is intended to support functional hearing restoration research that develops and validates assessment techniques and treatment methods using patient-centric outcomes to identify potential predictive indicators for successful treatment of functional auditory system deficits. The research in this area should result in refined diagnostic tools and improved evaluation of the effectiveness of therapeutic approaches for functional hearing restoration.

"The FY17 Hearing Restoration Research Program marks the first time that the Department of Defense will have a research effort specifically focused on hearing restoration. As stewards of this vital resource, we have the opportunity to propel the science forward, concentrate our efforts on the most promising technological solutions for the treatment of permanent hearing loss, and impact the operational effectiveness, medical readiness, and the quality of life for our Service Members, Veterans, and others living with impaired hearing."

Col LaKeisha Henry, M.D., US Air Force, Programmatic Panel Chair



Joint Warfighter Medical Research Program

Vision

Move military relevant medical solutions forward in the acquisition life-cycle to meet the needs of Service Members and other military health system beneficiaries

Mission

Accelerate research and development projects that have the potential to close high priority Department of Defense medical capability gaps

Program History

The Joint Warfighter Medical Research Program (JWMRP) provides the DoD with a powerful tool for advancing previously funded Congressional Special Interest (CSI) medical R&D projects that address military medical requirements of the Services while complementing and enhancing DMRDP. JWMRP leverages the efforts of industry and academia for projects that show promise in closing identified military medical capability gaps and provides the funding to move these products through the developmental process.

Each year, a broad spectrum of research projects are considered for funding under JWMRP. The projects align to the six JPC/PAD scientific domains represented in DMRDP, including Medical Simulation and Information Sciences, Military Infectious Diseases, Military Operational Medicine, Combat Casualty Care, Radiation Health Effects, and Clinical and Rehabilitative Medicine.

Congress first appropriated $50M for JWMRP in FY12 and again in FY13; later doubling the appropriation to $100M in FY14, followed by $50M In FY15, FY16, and FY17. Because the overall goal of the program is to deliver a product for the DoD, the ratio of funding allocation over the past 4 years has intentionally reduced the percentage of funds directed toward early technology development and increased the proportion of funding for advanced technology development initiatives. A total of 28 projects were funded through the FY12 JWMRP, 35 projects for the FY13 program, 46 projects for the FY14 program, 30 projects for the FY15 program and 35 projects for the FY16 program. The graph on the next page depicts the program investments for FY16.

JWMRP is a dynamic program that facilitates the maturation of previous congressionally funded research efforts that demonstrate the potential to close identified military medical capability gaps. By focusing on both early and advanced technology development, JWMRP provides a pathway to transition products to military healthcare providers and the warfighter.

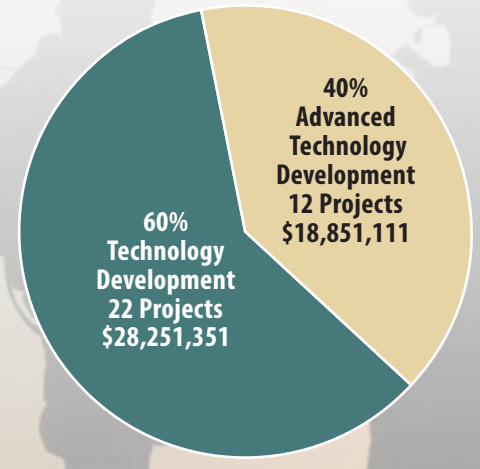
Research and Product Development Efforts Funded by the JWMRP Include:

- A focused effort on improving cognitive and functional deficits after TBI using virtual technology.
- Ultra wide-band wearable ultrasound probe for battlefield use.
- Phase II b clinical trial for a Norovirus vaccine.
- Phase II Malaria clinical trial with the first live attenuated vaccine against protozoal disease in humans.
- Development and clinical trial of a food supplement to prevent travelers' diarrhea.
- Development of a lyophilized injectable for point-of-care therapeutic for post-traumatic osteoarthritis.
- Development of Passive Physiological Monitoring System during Medical Evacuation.
- Device development of the Transportable Pathogen Reduction and Blood Safety System.
- Development of a non-electric, disposable IV infusion pump.
- Pivotal study on the regulatory approval pathway for a drug to treat acute radiation sickness.
- Accelerating the development of the opioid Sufentanil for pain treatment.
- Development of electronic capture and seamless communication of point-of-injury information using ultra-wide-band technology integrated with the Nett Warrior Platform.
- Development of bioengineered corneas for transplantation.
- Light-Activated Sealing to improve outcomes following penetrating bowel trauma.
- Non-Invasive Intracranial Pressure Assessment Using a Compact Portable Monitor.

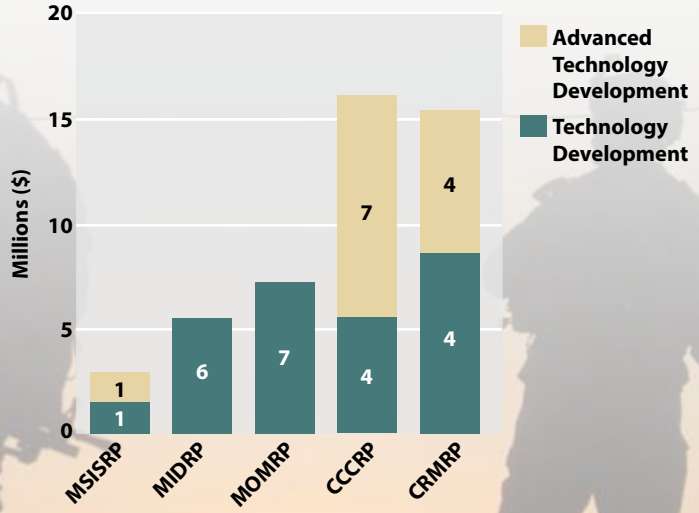
Prosthetic With Moisture Management Liner and Active Cooling System

Pathogen Reduction and Blood Safety System

Non-Invasive Intracranial Pressure Assessment



FY16 JWMRP Investment



FY16 JWMRP Final Funding Distribution (Number of awards granted indicated in each bar)

Kidney Cancer Research Program

Vision

To eliminate kidney cancer through collaboration and discovery

Mission

To promote rigorous, innovative, high impact research in kidney cancer for the benefit of Service Members, Veterans, and the American public

Program History

Kidney Cancer research has been funded by CDMRP for many years under various programs, including PRMRP, the Tuberous Sclerosis Complex Research Program (TSCRP), and, most recently, by the Peer Reviewed Cancer Research Program (PRCRP). From FY10 through FY16, PRCRP invested $9.8M in kidney cancer research. In FY17, Congress directed $10M to kidney cancer research in the DoD appropriation, thus establishing KCRP. The American Cancer Society estimates that, in 2017, approximately 63,990 new cases of kidney cancer will occur, and 14,400 people will die from some form of kidney cancer.[1] There are three main types of kidney cancer: renal cell cancer (RCC), Wilms tumors, and transition cell cancer (TCC, also known as urothelial carcinomas).[1] RCC is the most common type of kidney cancer, with the subtype Clear Cell RCC accounting for 66-75% of all RCC diagnoses.[2] Wilms tumor is a type of kidney cancer that is diagnosed almost exclusively in children under 15 years of age. TCC is relatively rare and accounts for 5-10% of kidney cancer cases.[1] The 5-year survival rate of patients diagnosed with stage I kidney cancer is 92.6%, while for patients diagnosed at stage II, it is 66.7%.[3] With a new program, KCRP will be able to focus on the issues regarding prevention, detection, and treatment, as well as the long-term effects of treatment for kidney cancer.

During KCRP's inaugural year, a Stakeholders meeting was held, where experts from different subject areas pinpointed the knowledge gaps, mapped the landscape of kidney cancer research, identified the outcome and product needs for patient care, and identified the way forward toward a successful research funding program. After the Stakeholders meeting, a Programmatic Panel was established, including clinicians, research scientists, consumers, and an active duty military oncologist. Following the Stakeholders meeting, a Vision Setting meeting was held. The Programmatic Panel met during vision setting to discuss the outcomes of the Stakeholders meeting, craft vision and mission statements for the program, and recommend an investment strategy for the coming year. This culminated in the recommendation of a programmatic investment strategy for the current fiscal year and the construction of long-term strategic plans.

[1] https://www.cancer.org/cancer/kidney-cancer/about.html
[2] https://www.cancer.gov/types/kidney
[3] https://seer.cancer.gov/statfacts/html/kidrp.html

FY17 KCRP Idea Development Award Areas of Emphasis

Ablation	Managing Toxicity	Radiation
Biomarker Development	Metabolism	Rare Cancers
Chromatin and Gene Regulation	Microenvironment	Resistance
Early Detection	Novel Imaging Technologies	Screening
Genetic Risk Factors	Novel Interventions	Surveillance
Immunotherapies	Novel Surgical Approaches	Survivorship and Patient Experience
Liquid Biopsy	Prognosis	Targeted Therapies

FY17 Award Mechanisms

Consortium Development Award

- Supports infrastructure development to establish the necessary multi-institutional collaborations among a coordinating center and at least 2 clinical sites.
- Supports clinical trials of novel interventions with the potential to have a significant impact on patient care in kidney cancer.

Idea Development Award

- Supports the development of ideas that represent innovative, high-risk/high-gain approaches to kidney cancer research and have the potential to make an important contribution to kidney cancer.

Concept Award

- Supports highly innovative, untested, potentially groundbreaking novel concepts in kidney cancer.

Translational Research Partnership Award

- Supports partnerships between clinicians and laboratory scientists that accelerate ideas in kidney cancer into clinical applications.

"It was an honor and a privilege to serve on both the stakeholders and vision setting Panels for the newly created Kidney Cancer Research Program (KCRP) of CDMRP. I am also very excited to be selected to serve as a programmatic member of the KCRP. We kidney cancer advocates look forward to the KCRP in providing the critical funding of innovative and significant projects that will eventually lead to the early detection and elimination of kidney cancer as a deadly disease."

Frederick L. Atkin, Action to Cure Kidney Cancer, FY17 KCRP Programmatic Panel Member

"With support from advocacy groups and a vision to eliminate kidney cancer by promoting discovery and collaboration, the KCRP sets off with a high-impact investment strategy that will influence kidney cancer research hereafter."

Dr. James Brugarolas, University of Texas, Southwestern Medical Center, FY17 KCRP Programmatic Panel Chair

Lung Cancer Research Program

Vision

Eradicate deaths from lung cancer to better the health and welfare of Service Members, Veterans, and the American public

Mission

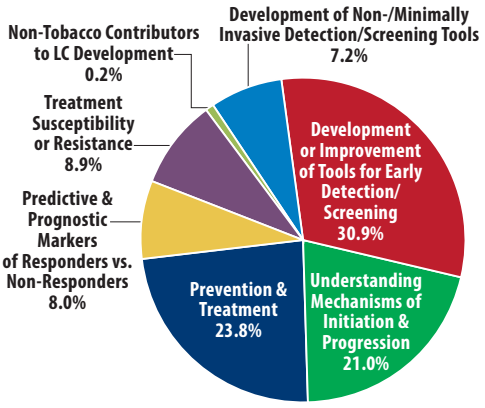
Support and integrate research from multiple disciplines for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer

Program History

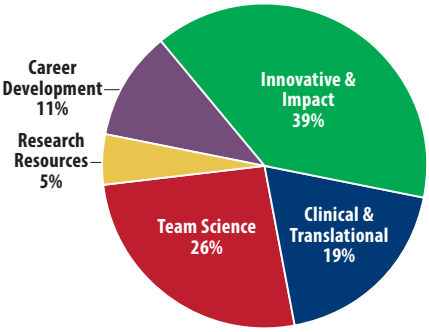
Lung cancer is the most common cancer worldwide and is the leading cause of cancer deaths in the United States. It is estimated that, in 2017, 155,870 people will die from lung cancer in the United States alone. The Lung Cancer Research Program (LCRP) was established in FY09, and over the past 8 years, the dedicated efforts by lung cancer advocates and scientists to increase public awareness of this disease, together with federal funding for research, have led to total congressional appropriations of $113.5M to LCRP, including $12M for FY17. To address the critical needs of the lung cancer research and patient community, LCRP adapts its investment strategy annually, focusing its support on underfunded and underrepresented areas. In addition, it is important to note that 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 exposure to environmental carcinogens during their Service. To address our military's higher risk, all applicants to LCRP's funding opportunities are required to describe how their research is relevant to the healthcare needs of military Service Members, Veterans, and their families.

Program Portfolio

To accomplish the vision of eradicating deaths from lung cancer, the LCRP has developed an investment strategy that emphasizes high-impact translational research, innovation, unique partnerships, resources, and career development. The charts below illustrate the breakdown of the LCRP portfolio by the current areas of emphasis, as well as by the developmental stages of the ideas funded.



FY09-FY16 Portfolio by Areas of Emphasis (% Dollars Invested)



FY09-FY16 Portfolio by Development of Ideas (% Dollars Invested)

"I have engaged in an ongoing, pleasant debate with my immunotherapy oncologist, who insists that my long-term immune system response is making history. From my perspective, I am merely a successful research data point in a clinical trial, along with 20 percent of other long-term non-small cell lung cancer (NSCLC) responders. The real hope is in the research ahead to perhaps see combinations of yet-to-be-discovered treatments that might yield 100 percent long-term remission responses."

John Ryan,
Consumer Peer Reviewer

LCRP Immunotherapy Portfolio

Recent studies have demonstrated the considerable potential of immunotherapy in the treatment of lung cancer. LCRP has invested in many aspects of immunotherapy research, including development, optimization, and/or evaluation of new immunotherapies beyond antibodies for immune checkpoint blockade; enhancers to current immunotherapies; acquired resistance to immune checkpoint inhibitors; novel delivery methods to improve response to immunotherapies; vaccine development; and various approaches to reactivate tumor immune surveillance and immune response.

Immunotherapy + Radiotherapy

Karen Kelly, M.D., University of California, Davis: The goal of this project is to combine immunotherapy with stereotactic ablative radiotherapy (SAR), with the aim of jump-starting a stronger immune response to the immunotherapy. SAR is expected to activate the creation of tumor antigens and up-regulate immune response in the treated area to attack micrometastatic disease, thereby improving the effects of the treatment.

Bo Lu, M.D., Ph.D., Thomas Jefferson University: Combination therapies involving immunotherapies and radiotherapy are being tested for therapeutic synergism, since PD-1 (programmed cell death protein 1) inhibitors are now widely used among patients with lung cancer. Based upon preclinical data showing a combination treatment of SMAC (second mitochondria-derived activator of caspases mimetic) and radiotherapy resulted in synergism that is mediated by CD8+ T-cells, this group aims to further improve the efficacy of immunotherapy+radiotherapy combination therapies by adding a novel immune-modulating agent. This DoD-funded project aims to identify the role of SMAC in lung carcinogenesis and response to therapies. The end goal is to identify therapies with an optimal therapeutic ratio for the treatment of lung cancer.

T-cell Targeting Therapy

Prasad Adusumilli, M.D., Memorial Sloan-Kettering Cancer Center: Identified and validated MSLN as a marker for aggressive, therapy-resistant adenocarcinoma tumors. Based on this knowledge, new MSLN-targeted CARs were developed, which, when transduced into T-cells, target and kill these therapy-resistant cells. This new CAR T-cell therapy was sufficiently developed that a clinical trial to determine their efficacy and safety in patients with lung cancer has been launched (NCT02414269).

PD-1/PD-L1 Associated Therapies

Sarah Goldberg, M.D., M.P.H., Yale University: Currently, little is known about the responsiveness of patients with NSCLC brain metastases to the PD-1 inhibitor, pembrolizumab. This project will define the characteristic immunological blueprints of both primary tumors and metastases and identify biomarkers that predict response to immunotherapy in conjunction with a Phase II trial.

Julio Camarero, Ph.D., University of Southern California: Monoclonal antibodies (mAbs) are the new industry standard for immunotherapy. PD-1/PD-L1 (programmed cell death-ligand 1)-specific mAbs have shown significant success as cancer treatments recently, but are cost-prohibitive. This project investigates cyclotides, which have similar inhibitory properties to mAbs, but cost a fraction of the price. In particular, this project will create and screen a library of cyclotides against PD-1/PD-L1 before conducting in vivo efficacy tests of the most promising agent.

Nejat Egilmez, Ph.D., University of Louisville: Current immune checkpoint inhibitor treatments for lung cancer, while popular, have a number of negative side effects associated with their systemic delivery method (typically IV delivery). In this effort, the PI proposes to deliver an anti-PD-1 antibody directly to the lungs via an inhaled, sustained-release, micro-encapsulated formulation. The project will compare this new, local delivery method to the existing sustained delivery methods and identify the mechanisms of response associated with local anti-PD-1 treatment.

Vaccine Development

Laura Riolobos, Ph.D., University of Washington: This project proposes to identify immunogenic proteins in pre-malignant lung lesions that can be targeted by a vaccine and prevent progression of the disease by inducing a Th1 CD4+ T-cell immune response. The end goal of this work will involve vaccine evaluation in mouse models of lung cancer.

Lupus Research Program

Vision

To cure lupus through partnership of scientists, clinicians, and consumers

Mission

Fund research to understand, prevent, and diagnose lupus and to improve treatments and quality of life of patients, including Service Members, Veterans, and beneficiaries

Program History

LRP was first funded in FY17 to support innovative and impactful research that addresses significant issues and gaps in lupus.

Lupus is a heterogenous autoimmune disease that is difficult to diagnose and treat. There is currently no test available to diagnose lupus, and it may take months or years for a person to be correctly diagnosed. Because lupus attacks healthy cells and tissues in many parts of the body, patients can experience a wide range of symptoms, such as fatigue, joint pain, skin lesions, and headaches. Lupus can also cause inflammation in the kidneys, brain, blood vessels, lungs, and heart, which can result in serious complications, including organ damage. Patients with lupus require a diverse team of healthcare specialists depending on their symptoms.

Treatment options for lupus are highly dependent on an individual patient's symptoms. Some of the most commonly used drugs to treat lupus include NSAIDs, corticosteriods, and immunosuppressants. Long-term use of these treatments can result in serious side-effects, including kidney problems, stomach bleeding, liver damage, increased risk of infection, decreased fertility, and increased risk of cancer. Better treatment options are a critical need for patients with lupus.

"Lupus is a disorder that is frequently misunderstood. Its symptoms vary from patient to patient; the available treatments are far from perfect; and its very difficult to predict in advance whether patients will have a mild course of the disease or a devastating course of the disease. That's why the Lupus Research Alliance is so excited to be part of the CDMRP. We believe that the research funded by CDMRP will help us understand the causes of lupus, which is a prerequisite to developing new and better treatments. We were honored to participate in the stakeholders meeting designed to help establish the parameters of the new program. The meeting was informative and stimulating and provided a wonderful opportunity for members of the lupus community to share ideas and suggestions. We are confident that the stakeholders meeting will result in an outstanding funding program for lupus research."

Kenneth Farber, Lupus Research Alliance, Stakeholder,

FY17 Focus Areas

The FY17 LRP is asking for research that addresses the following areas:

- Understand lupus disease heterogeneity including, but not limited to, progressive stages of lupus disease over time, strategies and technologies to subtype patients, lupus disease mechanisms, biopsychosocial studies, personalized medicine, variation in treatment and its effects on patient outcomes, socioeconomic studies, environmental studies, and epidemiological studies.
- Understand how the underlying genetic components of lupus disease relate to clinical disease characteristics using functional genomic studies.
- Determine the pathobiology of lupus in target human tissues including, but not limited to, imaging studies, genetics of lupus disease in particular tissues, metabolomics, and how understanding the underlying pathobiology will improve quality of life of patients.

FY17 Award Mechanisms

Concept Award

- The FY17 LRP Concept Award is intended to support highly innovative research with the potential to introduce a new paradigm, look at existing problems from new perspectives, or exhibit other highly creative qualities in lupus research. The Concept Award may be used to generate sufficient preliminary data to enable the PI to apply for future funding to move the research forward. Proposals submitted through this mechanism must address at least one of the FY17 LRP focus areas.

Idea Award

- The FY17 LRP Idea Award is intended to support research that will impact an area of paramount importance in lupus research. Inclusion of preliminary data that are relevant to the proposed research project is encouraged, but not required for this award mechanism. Proposals submitted through this mechanism must address at least one of the FY17 LRP focus areas.

"As a person living with lupus, many aspects of my life often feel beyond my control. It is wonderful to participate on the Lupus Research Programmatic Panel and feel that my opinions and suggestions are just as important as the doctors and scientists who are around the table. It is empowering to me to represent those of us who live with lupus and to feel that I too am an expert on my disease and should have a voice in the way that funding is spent."

Cindy Coney, Lupus Foundation of America, Programmatic Panel Member

Military Burn Research Program

Vision

Deliver the best burn trauma care to improve health and performance outcomes in support of the warfighter

Mission

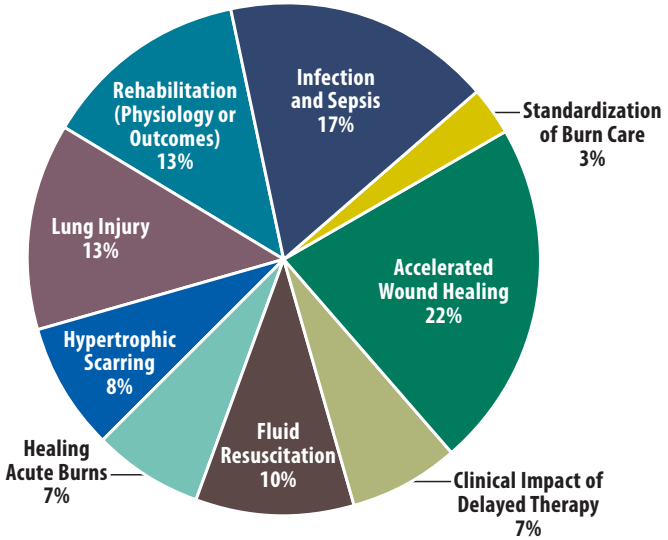
Identify and address gaps in burn trauma care through military focused translational research

Program History

The Military Burn Research Program (MBRP) was initiated in 2011 to address capability gaps for treating combat burn injuries. These gaps were identified by CCCRP, and they address injuries obtained from the point of injury to treatment at stateside Military Burn Centers. Combat burn injuries are devastating and are often more severe than burns obtained in the civilian setting.

The majority of combat burns result from explosive device detonation, leading to a greater Injury Severity Score, an increase in inhalation injuries, and a larger, full-thickness burn size.[1] In addition to burns, Service Members may also suffer from fractures, amputations, smoke inhalation, and head injuries at the same time. This traumatic assault adds additional burden to the body's innate immune response and, thus, increases the likelihood of infections and organ damage.

MBRP-funded projects explore innovative approaches to accelerate the translation of advances in knowledge into new standards of care for the treatment of injured Service Members, Veterans, and those within the civilian community who sustain burn injuries. The continued efforts, in concert with the program's successes, have resulted in more than $54M in congressional appropriations through FY17.



MBRP Portfolio FY11-FY16 (% based on total dollar amounts)

[1] Kauver DS, Cancia LC, Wolf SE, et al. 2006. Comparison of combat and non-combat burns from ongoing U.S. military operations. *J Surg Res.* 132:195-200.

Modulation of Burn Scars Through Laser-Assisted Delivery of Stem Cells

Evangelos V. Badiavas, M.D., Ph.D., University of Miami Miller School of Medicine

Advances in the acute management of burn injuries have led to the improved survival of Warfighters with large body surface area burns. Those Warfighters that survive traumatic and complex burn injuries are inevitability left with burn scars, which develop as a result of the healing process, as the skin surrounding the site of the burn contracts and tightens. Burn scars often cause substantial functional impairment that restricts the Warfighter's return to duty and has a tremendous impact on a Veteran's adjustment to civilian life. The current treatments for mitigating the effects of burn scars are very limited in their effectiveness, and there is great need to improve the functional outcomes associated with burn scars.

With support from an FY11 MBRP Award, Dr. Badiavas and his team are modulating burn scars through laser-assisted delivery of stem cells. He hopes that the combination of laser treatment and stem cell use will have a synergistic effect on skin regeneration that may lead to better functional and aesthetic outcomes for Warfighters with significant burn scars. Preliminary results suggest that laser treatments, as well as administration of stem cells, may have benefit in treating hypertrophic burn scars. Currently, Dr. Badiavas is examining multiple schemes to maximize the response to these potential treatments. Taken together, Dr. Badiavas' research holds promise for the use of laser-assisted stem cell delivery for the treatment of burn-related injuries.

Reassessing the Criterion of the US Army's Standards of Medical Fitness as Related to Burn Injury

Craig G. Crandall, Ph.D., University of Texas Southwestern Medical Center

The US Army's Standards of Medical Fitness currently prohibit the enlistment of individuals with a prior burn injury covering more than 40% of their body surface area. To challenge these standards, Dr. Crandall received FY15 MBRP funding to evaluate core temperature and cardiovascular responses during exercise in an extreme environment (39°C, 29% relative humidity) in individuals with severe burn injuries, as well as using a simulated burn injury model. The ultimate goal of this MBRP-funded research is to provide recommendations to the Army for a revised Standards of Medical Fitness that will improve the health, safety, and performance of Soldiers who have suffered burn injuries. Dr. Crandall's efforts could potentially save costs for the Army if it is determined that Soldiers who have suffered burn injuries resulting in discharge from military service are able to continue serving. Preliminary results suggest burned individuals who are smaller in body size may be at greater risk for hyperthermia, especially in physically demanding occupational settings. The preliminary results from this study show that the current Standard of Medical Fitness requirements in relation to burn injury should be re-evaluated. Dr. Crandall's work could possibly inform, not only on military readiness, but also on exercised-based rehabilitation programs for Service Members and civilians who have suffered burn injuries.

"Burn injuries are a particularly devastating battlefield injury that challenge the military medicine team, the injured Service Member, and battlefield leaders. The Military Burn Research Program endeavors to develop the most effective tools for stabilizing battlefield burn injuries, evacuating burn-injured Service Members, and maximizing their recovery. The consumer advocate provides the MBRP team with a unique patient perspective and lessons learned from the battlefield to help tailor burn-related research and products to the unique qualities of the battlefield environment."

Lt Col Byran Forney, MBRP Consumer Reviewer

"Burn injury as a specialty is a relatively small niche due to the fact that it does not occur very often. However, when burn injury does occur, it puts a tremendous strain on the healthcare system, while resulting in significant long-term physical and emotional disabilities for the injured individual. It is vital for the Military Burn Research Program to leverage the vast amount of knowledge that exists in this small niche community of subject matter experts who deal with this on a daily basis."

LTC Kevin Chung, MBRP Programmatic Panel Chair

Multiple Sclerosis Research Program

Vision

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

Mission

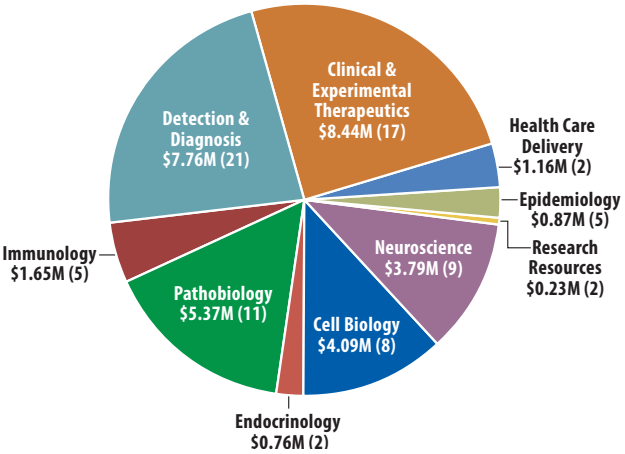
To support pioneering concepts and high impact research relevant to the prevention, etiology, pathogenesis, assessment, and treatment of multiple sclerosis for the benefit of Service Members, Veterans, and the American public

Program History

Multiple sclerosis (MS) is a degenerative, chronic inflammatory disease of the central nervous system that leads to cumulative neurologic disability over several years. It is a heterogeneous and unpredictable disease that can manifest in many ways across the patient population with MS. Common manifestations include pain, fatigue, cognitive dysfunction, visual impairment, motor impairment, impaired mobility, loss of bladder control, sexual dysfunction, depression, and anxiety. Although MS affects over 400,000 individuals in the United States and about 2.1M 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. Currently, there is no cure for MS. In FY09, Congress appropriated $5M for MS research, and the Multiple Sclerosis Research Program (MSRP) was established. Since then, a total of $45.1M has been appropriated to the program, including $6M in FY17.

Program Portfolio

Through FY16, MSRP funded 82 awards to support the exploration of highly innovative new concepts or untested theories; development of readily accessible, cost-effective, validated analytical methods; conceptually innovative, high-risk/potentially high-reward research; multidisciplinary research collaborations; development of translational research collaborations among clinicians and research scientists from within and outside the MS research field to accelerate the movement of promising ideas in MS research into clinical applications; and pilot clinical trials to investigate innovative interventions that could potentially have a profound impact on the management of MS symptoms.



FY09-FY16 Portfolio by Research Area (numbers of awards)

Reducing MS Activity in Animal Models by Activation of the Protective Arm of RAS

Brett T. Lund, Ph.D., University of Southern California, Keck School of Medicine

Dr. Lund received an FY13 Idea Development Award to explore how components of the renin-angiotensin-system (RAS), a system associated with regulating blood pressure, are relevant to the pathology of MS. RAS has both pro- and anti-inflammatory arms that work in conjunction to achieve and maintain blood pressure and inflammation homeostasis. The anti-inflammatory arm of RAS, also referred to as the regulatory or protective arm, includes the angiotensin-converting enzyme 2 (ACE2), angiotensin-(1-7) (Ang-[1-7]), angiotensin type 2 (AT2) receptor, and Mas receptor. Dr. Lund hypothesized that dysregulation of the regulatory arm may lead to demyelinating injuries during the progressive phases of MS. To test this hypothesis, he treated a mouse model of MS (EAE mice) with Ang-(1-7), expecting that initiating treatment at the first signs of disease would diminish the effects of the pro-inflammatory arm and attenuate disease severity by preventing significant tissue damage. After administering an optimal dose of Ang-(1-7) at the onset of clinical disease, there was a significant abatement in MS symptoms. These promising data suggest the therapeutic potential of Ang-(1-7) for attenuating disease severity in MS and other demyelinating neurodegenerative diseases, as well as highlight the contribution of the regulatory arm of the RAS pathway to MS pathology.

Detection of Brain Reorganization in Pediatric MS Using fMRI

Ralph Suarez, Ph.D., Boston Children's Hospital

Predicting disease progression and severity in patients with pediatric-onset MS (POMS) is difficult due to compensatory functional reorganization in response to disease-induced brain injury, which masks symptoms despite the accumulation of disease burden. With an FY12 Idea Award, Dr. Suarez used functional MRI (fMRI), a non-invasive diagnostic tool, to detect brain dysfunction prior to symptom onset when therapeutic interventions could be effective. He compared language, verbal memory, and visual-motor brain activation patterns in patients with POMS to normal volunteers and demonstrated that, although patients with POMS maintained an adequate level of performance on the cognitive tasks, they had a significant level of abnormal brain activation of non-dominant cerebral structures in the opposing hemisphere and/or adjacent cortex. Dr. Suarez has been able to extend the use of this fMRI technique to additional pediatric neurological conditions (i.e., epilepsy and brain tumors). He has acquired and analyzed pre-surgical fMRIs for the purposes of motor-specific and language-specific functional mapping, which provide surgical teams with a view of brain activity relative to planned surgical sites. The fMRI information was found to significantly improve post-surgical outcomes, as surgeons were able to preserve essential brain regions.

"Multiple sclerosis is the most common non-traumatic cause of neurological disability in young adults. The CDMRP MS Research program is addressing several unmet needs in MS, including strategies to promote repair of central nervous system tissue damage, symptomatic therapies, and approaches to restore function."

Jeffery Cohen, M.D., Cleveland Clinic, FY15-FY17 Programmatic Panel Member

"Being in a room full of PhDs was quite intimidating, but when I presented my critiques, they nodded in approval and agreement. This response was very humbling and affirming! This experience gave me confidence in the process, knowing how much they truly value the perspective of the patient! …. I am so honored to have my voice be heard in how certain research concepts could really impact the lives of those living with MS. I am so thankful for the brilliant minds who dedicate their time to finding ways to improve the lives of those with MS and ultimately find a cure! It was a privilege to serve on this panel and be a part of cutting edge research ideas!"

Emily Reilly, FY16 Consumer Peer Reviewer

Neurofibromatosis Research Program

Vision

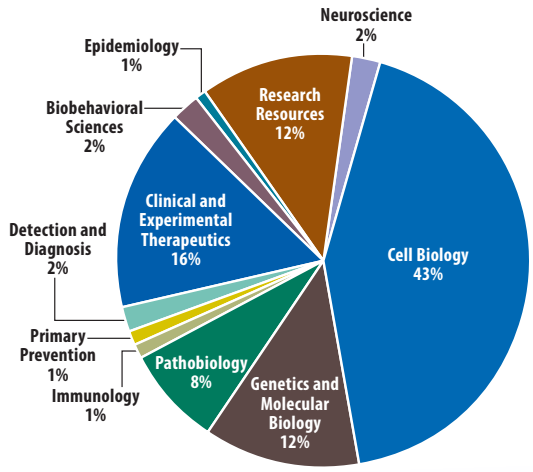
Decrease the clinical impact of neurofibromatosis

Mission

Promote research directed toward the understanding, diagnosis, and treatment of NF1, NF2, and schwannomatosis to enhance the quality of life for persons with these disorders that impact Service Members, Veterans, and the general public

Program History

NFRP was established in FY96, when the efforts of NF advocates led to a congressional appropriation of $8M. Since that time, $317.85M has been appropriated to the program, including $15M in FY17. Over its 20-year history, 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 353 awards spanning basic, clinical, and population-based research.



NFRP FY96-FY16 Portfolio Investment

"We learned about the NFRP and what the program has accomplished as part of our advocacy work on Capitol Hill. When given the opportunity to review the scientific proposals that are submitted to the NFRP and help determine how the annual research budget of the NFRP would be spent, I was thrilled at the opportunity to participate. The review process ensures that everyone's opinion counts, and the scientists are all very helpful and appreciative of the consumer reviewers. Considering most of the scientists, including those writing the grant proposals, have no direct connection to NF, it is truly phenomenal the dedication the scientists have toward finding a way to positively impact patients with NF. They all showed remarkable empathy whenever I shared how NF has impacted my child."

Herb Sarnoff, Consumer Advocate Peer Reviewer

"The NF Clinical Trials Consortium remains a beacon of hope for people with all forms of neurofibromatosis. We have assembled a group of world-class clinicians and scientists who have been collaborating on developing and testing therapies for NF for over a decade. As we enter our third cycle of funding from the DoD, we are looking at clinical trials for NF1, NF2, and schwannomatosis, informed by years of experience in conducting such trials and in working together. As more is learned about the underlying mechanisms of the complications of NF, we are seeing new potential therapeutic approaches, and the consortium stands ready to put the most promising of these to test in the clinic."

Bruce Korf, M.D., Ph.D. Clinical Trials Consortium PI

Vijaya Ramesh, Ph.D., Massachusetts General Hospital

Neurofibromatosis type 2, or NF2, causes growth of different types of tumors in the nervous system, including meningiomas, and the current treatments for NF2-related meningiomas are limited. The majority of non-NF2-associated meningiomas involve loss of the NF2 tumor suppressor gene (which encodes the protein merlin). Previous data from Dr. Ramesh's laboratory indicated that merlin functioned to shut off signaling through a group of other proteins, the mammalian target of rapamycin complex 1 (mTORC1) in meningiomas. Without merlin, mTORC1 was always turned on, and its signaling could drive tumor growth; however, treatment with rapamycin, a drug that targets mTORC1, inhibited meningioma growth. With an award from NFRP, Dr. Ramesh and her colleagues performed a high-throughput kinome screen in an effort to understand the mechanism behind the activation of mTORC1 due to loss of merlin. They found that serum/glucocorticoid-regulated kinase 1 (SGK1), a target of mTORC2 (a protein complex related to mTORC1), and p21-activated kinase 1 (PAK1) were mediating the activation of mTORC1 in these cells. The Ramesh laboratory had previously reported that suppression of NF2 expression in human arachnoidal cells (cell of origin for meningiomas) led to increased activation of SGK1. In this study, they demonstrated that signaling through mTORC2/SGK1 and PAK1 independently led to activation of mTORC1. They performed experiments with inhibitors of these kinases on meningioma cells. Treatment with AZD2014, a compound that inhibits both mTORC1 and mTORC2, was quite effective, suggesting that dual inhibitors, such as AZD2014, may be useful therapeutic options. This work has helped to inform future clinical trials.

Karen Cichowski, Ph.D., Brigham and Women's Hospital, Boston, Massachusetts

Neurofibromatosis type 1 (NF1) is an autosomal dominant genetic disorder that is primarily characterized by tumorigenic manifestations in the nervous system. NF1 is caused by a mutation in the NF1 gene that normally codes for neurofibromin, a tumor suppressor protein, resulting in unregulated cell proliferation and differentiation. While most of the tumors associated with NF1 are benign, some develop into malignant tumors known as malignant peripheral nerve sheath tumors (MPNSTs). MPNSTs are clinically aggressive tumors and the leading cause of mortality for patients with NF1. With support from an NFRP award, Dr. Cichowski and her research team proposed to utilize a mouse model of MPNSTs to dissect signaling pathways in an effort to identify the most promising therapeutic targets, as well as to explore the efficacy of combination-targeted therapies and potential real-time biomarkers of that efficacy. In previous studies, they demonstrated that the phosphoinositide 3-kinase (PI3K)-mammalian target of mTORC1 signaling pathway is abnormal in NF1-deficient MPNSTs. In current studies, Dr. Cichowski and her team identified that mTORC1 plays a key role in NF1-deficient MPNST. Only sustained treatment of combined mTORC1 and mitogen-activated protein kinase (MEK) protein inhibition promoted tumor regression; all mice treated with MEK inhibitor PD-0325901 and mTORC1 inhibitor Rapamycin responded to treatment, with more than half of the tumors exhibiting a 50% regression and several shrinking by 75% or more. Additionally, Dr. Cichowski discovered the potential use of glucose transporter 1 (GLUT1), a membrane-bound glucose carrier that is involved in 18F-fluorodeoxyglucose (F18-FDG) uptake, as a potential imaging biomarker. During combined mTORC1-MEK inhibition, but not in response to single agents, GLUT1 levels dramatically decreased. F18-FDG uptake quantified by PET represents a potential method of quantifying combined mTORC1-MEK inhibition, thereby providing a means to determine effective doses of both drugs and minimize toxicity during treatment. The information obtained from these studies can be translated into clinical trials for patients with MPNST.

"Having a child with NF has changed my and my family's entire lives; we live with a lot of uncertainty. However, we decided to be part of the solution by creating the Littlest Tumor Foundation, which advocates for research in NF, but also by serving on the peer review panel for the NFRP. Being a part of such a well-run program that is a crucial part of moving us toward a treatment for NF has made me even more passionate about the NFRP and is a highlight in my life."

Tracy Wirtanen, Consumer Advocate Peer Reviewer

Orthotics and Prosthetics Outcomes Research Program

Vision

The highest possible quality of life for our injured warfighters through the advancement of knowledge in orthotics and prosthetics related research

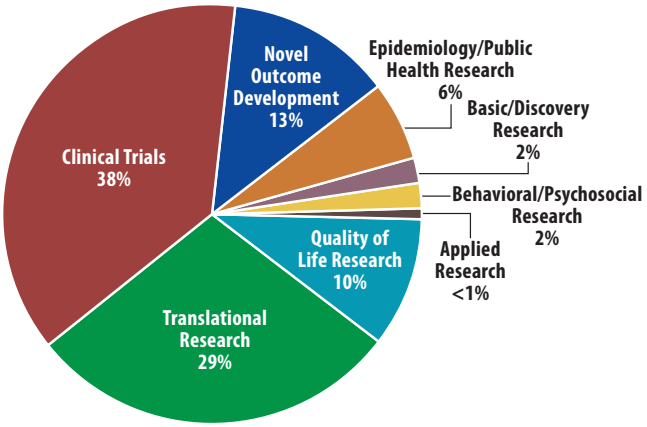
Mission

Advance evidence based research in prosthetic and orthotic devices, treatment, rehabilitation, and the prevention of negative secondary health effects of military-related neuromusculoskeletal injury

Program History

Limb deficit is one of the most debilitating traumatic injuries suffered by US military personnel. Recent advancements in commercially available orthotics and prosthetics have dramatically improved device capability; however, there remains an urgent need for continued development of devices, associated rehabilitation treatments, and an evidentiary basis for their prescription and use to provide improved quality of life for our Service Members.

The Orthotics and Prosthetics Outcomes Research Program (OPORP), was established by Congress in FY14 to support military-relevant personal assistive technology outcomes research. The program seeks to improve rehabilitation and reintegration strategies for wounded Service Members, replace the function of injured limbs, prevent and mitigate the secondary health effects of neuromusculoskeletal injuries, and support validated metrics for rehabilitation and reintegration after injury. The goal of the OPORP is to improve our understanding and ultimately advance the implementation of the most effective prescriptions for prosthetic and orthotic devices, treatment, rehabilitation, and secondary health effect prevention options for patients, clinicians, other caregivers, and policy makers.



OPORP Program Investment FY14–FY16
$28,268,849 in 32 Awards

"Each year, I am thrilled to receive an invitation to serve on the OPORP Peer Review Panel. The roster of panel members typically includes new members, each with a diverse background and expertise, including a consumer reviewer. Serving on the panel is a wonderful experience. The review process fully engages each participant in such a way that brings out their insightful and important perspective; in short, it shows why they were chosen. This richness and breadth of project deliberations are among the unique and highly innovative aspects of the CDMRP review process. Participation gives me a valuable perspective on the importance of each proposed project, a greater appreciation for diversity and teamwork in science, and a deepened reassurance that the proposed research was well served by the peer review panel."

Steven J. Stanhope, Ph.D., Professor and Director of the BADER Consortium, University of Delaware, FY16 Peer Review Panel Member

Brian Hafner, Ph.D.

Dr. Brian Hafner is the recipient of an FY14 Orthotics and Prosthetics Outcomes Research Award titled, "A Novel Prosthetic Foot Designed to Maximize Functional Abilities, Health Outcomes, and Quality of Life in People with Transtibial Amputation." Dr. Hafner's team at the University of Washington is conducting a randomized crossover study to compare outcomes associated with the use of a modified running-specific foot (mRSF) to a traditional energy-storing foot (ESF). Dr. Hafner's research team compared the performance of these two prosthetic feet across a number of different health domains, including metabolic energy cost, endurance, perceived exertion, gait quality, and step activity. Dr. Hafner found that physical exertion between the two prosthetic feet was variable among users, but generally similar between the two feet for an individual. Likewise, many functional outcomes (endurance, walking speed, step activity) were, on average, comparable between the feet. However, participants in the study reported about 20% less exertion when walking long distances and generally walked with a more even step pattern in the mRSF. Participants also reported feeling significantly less fatigued and more satisfied when using the mRSF. Results of the study collectively indicate that mRSF and ESF prostheses are generally equivalent in function during level ground walking, but the mRSF may offer benefits to users in real-life conditions. Dr. Hafner suggests that future comparisons between these types of devices include activities or situations where prosthesis users experience challenges, such as walking over uneven terrain, jogging, or playing sports.

David Morgenroth, M.D.

Dr. Morgenroth is a physician-scientist who is seeking to improve the process for prescribing prosthetic feet to individuals with lower limb amputation. As the recipient of an FY15 Level 2 Prosthetics Outcomes Research Award, Dr. Morgenroth and his team of co-investigators are studying a patient centered test-drive strategy for prescribing prosthetic feet. They will use a novel, customizable, robotic prosthetic foot that mimics the mechanical properties of commercial prosthetic feet through software control without physically changing feet. This "prosthetic foot emulator" can provide people with leg amputations the opportunity to quickly "test-drive" many prosthetic foot designs within a single test session. In order to give study participants a chance to test-drive feet under a variety of environmental terrains, laboratory testing will include walking on flat ground at different speeds, walking on slopes, and walking up stairs. After laboratory testing, participants will wear each of the actual prosthetics for normal activity for 2 weeks and return for re-evaluation in the laboratory. The study will compare users' preference for emulated feet to their preference for use of the actual prosthetic to ensure that the emulation is accurately capturing the feeling of wearing and using the foot. By allowing patients a chance to offer valuable experiential feedback during the prescription process, this study has the potential to provide meaningful benefit to clinicians, as well as to Service Members and Veterans with leg amputations. Patients who are engaged in medical decision making are known to have better outcomes; allowing patients to participate and offer experiential feedback during the prosthetic foot prescription process, using either the emulator or a brief trial of commercial prosthetic feet, has great potential to enable increased patient satisfaction, walking ability, and achievement of functional goals.

"As the Director of Research and Grants at the Amputee Coalition, the nation's leading nonprofit patient advocacy organization serving the limb loss community, I've talked with tens of thousands of individuals with limb loss, their family members, and the clinicians who provide care to them about the challenges individuals with limb loss endure. The Orthotics and Prosthetics Outcomes Research Program represents one of only a few sources of federal funding to support research aimed at addressing these issues and improving the quality of life for US military personnel who lose a limb. The results of this research play a critical role in shaping the care and rehabilitation of individuals who lose limbs within the VA/DoD and in civilian healthcare systems. I am honored to serve on the OPORP Programmatic Panel and consider my service as a highlight of my year."

Mr. George Gondo, Director of Research and Grants at the Amputee Coalition

"Serving as a consumer reviewer for the Ovarian Cancer Research Program was an incredibly humbling and inspiring experience for me. The thoughtfulness and exquisite attention to all facets of the proposals by the team members, as well as the breadth of research proposals, gives me tremendous hope that breakthroughs in areas of early detection and developing novel treatments will be made. I am so grateful to have had this opportunity to see first-hand the amazing work the DoD/OCRP does."

Margaret Mastrangelo

Ovarian Cancer Research Program

Vision

To eliminate ovarian cancer

Mission

Supporting patient-centered research to prevent, detect, treat, and cure ovarian cancer to enhance the well-being of Service Members, Veterans, and all women impacted by this disease

Program History

The DoD's OCRP was established in 1997 to define and address the critical research gaps facing the ovarian cancer community. With $296.45M in congressional appropriations through FY17, OCRP is the second-leading funder of ovarian cancer research in the United States. OCRP has transformed the landscape of ovarian cancer to the benefit of patients everywhere by funding high-impact research in the prevention, screening, diagnosis, and treatment of ovarian cancer, as well as quality of life issues.

Outcomes Consortium

Providing Hope: Increasing Long-Term Survivorship of Ovarian Cancer Patients

With a 5-year survival rate of just 45%,[1] ovarian cancer is the deadliest gynecologic cancer. However, a subset of patients with this disease become long-term survivors (greater than 10 years survival from their date of diagnosis), providing hope to those recently diagnosed. To improve the prognosis for patients with ovarian cancer, OCRP granted the Outcomes Consortium Award in 2016 to 2, multi-institutional research teams, with the goal of identifying and understanding specific predictors of ovarian cancer outcomes.

- ***The Ovarian Cancer Consortium for Long-Term Survival, led by Dr. Michael Birrer*** at Massachusetts General Hospital, is an international consortium comprised of nine sites focused on finding predictive biomarkers that will aid in the early detection of ovarian cancer.
- ***The Multidisciplinary Ovarian Cancer Outcomes Group (MOCOG), led by Dr. Malcom Pike*** at Memorial Sloan Kettering Cancer Center, is a collaboration of 10 international sites working with patients who have advanced stage, high-grade serous cancer.

The combined efforts of the world's leading investigators in these consortia studies will have a major impact on understanding the genetic and lifestyle predictors of ovarian cancer outcomes, developing individualized therapies for patients, and accelerating progress toward long-term survivorship.

[1] American Cancer Society, February 4, 2016.

High-Impact Advances of the OCRP in the Prevention, Detection, Diagnosis, and Treatment of Ovarian Cancer

New Research Tools

- Animal Model of Spontaneous Epithelial Ovarian Cancer.
- Animal Models of Endometriosis Ovarian Cancer.
- 3D Spheroid Model of Patient-Specific Tumors.
- Model to Study the Effect of BRCA1 on Ovarian Cancer.
- Effect of Two Oncogenes on the Development of Ovarian Leiomyosarcoma.
- Using Animal Proteins to Predict Ovarian Cancer Risk in Humans.
- The Ovarian Cancer Research Academy.
- Australian Ovarian Cancer Study – Shared Biorepository of Clinical Data and Biospecimens.

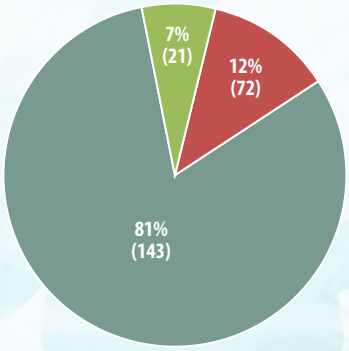
Prevention, Detection, and Diagnosis

- RAD51D Genetic Testing Kit.
- mAGIC App to Encourage Genetic Counseling.
- OVA1™ Diagnostic Index Test.
- Genetic Testing Guidelines in the United States and Australia.
- Computational Approach to Diagnosing Precursor Lesions.
- Ovarian Cancer Risk-Reducing Surgery: A Decision Making Resource.
- Salpingectomy to Reduce Mortality.
- AZA Immune (AIM) Gene Biomarkers to Predict and Monitor Epigenetic Therapy.
- Adapting Pap Smears to Detect Ovarian Cancer.
- Linking PTSD to Ovarian Cancer Risk.
- Adapting a Novel PET Tracer to Predict Drug Response.

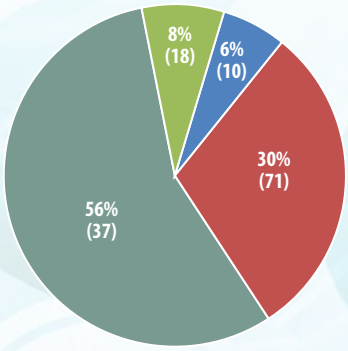
Treatment

- NSAIDs to Reduce Cancer Cell Adhesion.
- Statins and Anti-Tumor Effects.
- Targeting Tumor Vasculature to Eliminate Ovarian Cancer Cells.
- MSC1 Immunotherapy to Create an Anti-tumor Response.
- Virus-based Toxin Delivery to Solid Tumors.
- Accelerated FDA Approval for Rucaparib.
- Junctional Opener 1 to Improve Penetrance of Chemotherapy.
- Sitagliptin/Antidiabetic Drug to Improve Anti-Tumor Immune Activation.
- Delivery of Drugs Using Tumor-Targeted Nanotechnology.
- FLASH Radiotherapy to Treat Metastases.

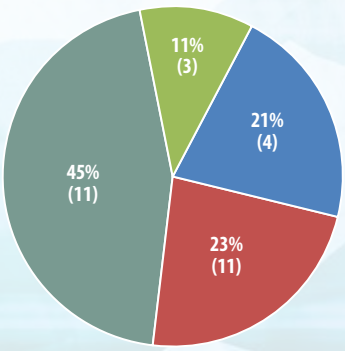
Funding Research from Bench to Bedside



FY97-FY10 by $ (# awards)



FY11-FY15 by $ (# awards)



FY16 by $ (# awards)

Patents Created by OCRP Investigators

- Vaccines (MORAb-004/ Ontuxizumab) against tumor vascular markers, to George Coukos.
- Chemical compounds for targeting cancer stem cells, to Ronald Buckanovich.
- Cell lines that produce alphavirus vectors for gene therapy, to Daniel Meruelo.
- Enzyme-mediated tumor imaging and therapy, to Amin Kassis.
- Detection of cancer by elevated levels of BCL-2, to Patricia Kruk.
- Use of Elafin to detect ovarian cancer, to Michael Seiden and Ronny Drapkin.
- Use of modified Herpes Simplex Virus-2 as a cancer therapy, to Xiaoliu Zhang.

Parkinson's Research Program

Vision

To stop Parkinson's disease by funding research through a partnership of scientists and consumers

Mission

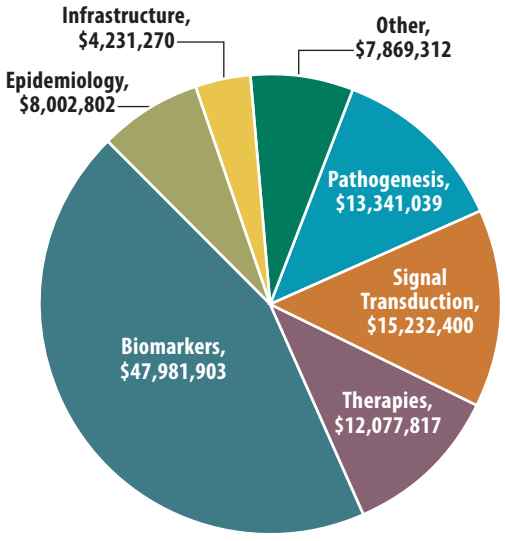
Support research to understand, prevent, diagnose, and treat Parkinson's disease in patients, including Service Members and Veterans

Program History

Parkinson's disease (PD) is a degenerative movement disorder of the central nervous system resulting from a loss of neurons in a region of the brain called the substantia nigra. These neurons produce dopamine, a neurotransmitter important for motor control; however, as PD progresses, the death of dopaminergic neurons results in reduced dopamine levels and impairment of motor control. The Parkinson's Research Program (PRP) funded under the Neurotoxin Exposure Treatment Parkinson's Research (NETPR) appropriation was initiated in FY97 to provide support for research of exceptional scientific merit leading to an understanding of the cause, prevention, and treatment of the loss of dopaminergic neurons in the substantia nigra that result in PD. Projects examine neurodegenerative mechanisms and compensatory effects that compromise motor, autonomic, and cognitive systems that are characteristic alterations in patients with PD and also present performance and health risks for military personnel. From FY97 through FY16, $404.75M has been appropriated by Congress for PD research. The FY17 appropriation is $16M. PRP challenges the scientific community to develop the most impactful research that will advance the understanding of PD, with the ultimate goal of ending this disease.

Program Portfolio

The PRP funded 254 awards through FY16 to support innovative research with the potential to yield new avenues of investigation and make a major impact in the understanding, prevention, diagnosis, and treatment of PD.



PRP Portfolio FY10-FY16

Alpha-synuclein: Promising Molecular Test for Parkinson's Disease

Clemens Scherzer, M.D., Harvard Medical School, Brigham and Women's Hospital

Alpha-synuclein, a protein encoded by the SNCA gene, accumulates in the brains of patients with PD, but it was thought the protein was only found in neurons and was not useful as a clinical biomarker of developing disease. However, work by Dr. Clemens Scherzer and others revealed that alpha-synuclein is also expressed peripherally, and more accessibly, in blood cells and could therefore potentially serve as a biomarker for PD. With funding from the PRP, Dr. Scherzer investigated whether levels of SNCA transcripts are associated with the presence of early-stage PD. He observed that SNCA blood transcript levels are reduced in patients with PD, suggesting that the accumulation of alpha-synuclein protein in the brain leads to a feedback repression of SNCA transcription. He also found that SNCA transcript levels were reduced in patients, even before they met clinical diagnostic criteria, indicating that SNCA transcript levels might be used to predict the risk of developing PD. Further, Dr. Scherzer found that low SNCA transcript levels in the blood of patients with PD predicted cognitive decline during a 5-year follow-up period, an important finding, as many patients with PD may suffer declining cognitive function that is correlated with the presence of alpha-synuclein-containing Lewy bodies in the brain. In summary, Dr. Scherzer's studies suggest that SNCA transcript levels could be used both to identify individuals at risk for developing PD and to predict disease progression. Dr. Scherzer received a PRP follow-up award to investigate the role of non-coding RNAs in PD risk, which may result in the identification of additional biomarkers, as well as potential therapeutic intervention points for treatment of PD.

Methods for Analyzing Protein Expression in Dopaminergic Neurons

Angus Nairn, Ph.D., Yale University School of Medicine

A number of genes have been implicated in both familial and sporadic cases of PD. Some of these genes, known as PARK genes, may have mutations that result in the death of dopaminergic neurons in the substantia nigra, and, through negative effects on the brain's striatal region, result in the primary motor symptoms of PD. With PRP funding, Dr. Angus Nairn developed unique methods to study discrete nerve cells in the brain. By isolating individual cellular structures, he was able to investigate the function of proteins and the nerve cells sub-cellular organelles, which may be important in the development of PD. In addition, using molecular findings from his studies in mouse models of PD, Dr. Nairn identified functional alterations that lead to aberrant protein expression in striatal neurons and demonstrated that specific PARK2 mutations interfere with the regulation of important molecular functions and may contribute to the altered cellular signaling associated with PD.

"The opportunity to represent patients in the application review process of the DoD's Congressionally Directed Medical Research Programs is first and foremost an honor. Serving on the Programmatic Panel for the Parkinson's Research Program and seeing the inclusion of consumer reviewers alongside scientists throughout the two-tier review process is rewarding in its detail, specification, application, and new and exciting thinking. The opportunity to recommend research projects for funding that benefit our past and current military personnel and the total Parkinson's patient community is truly a win/win. This year's PRP awards will hopefully provide early biomarkers and analysis of PD-associated conditions, leading to a better understanding of the disease and ultimately helping the PD scientific community better battle this crippling ailment."

Kelly Sweeney, FY16-FY17 Programmatic Panel Member

Peer Reviewed Alzheimer's Research Program

Vision

To address the long-term consequences of traumatic brain injury (TBI) as they pertain to Alzheimer's disease (AD) and Alzheimer's disease-related dementias (ADRD)

Mission

The PRARP's mission is devoted to (1) understanding the association between TBI and AD/ADRD and, (2) reducing the burden on affected individuals and caregivers, especially in the military and Veteran communities. Support for the PRARP's mission is anticipated to be delivered by the research community through a combination of mechanistic and preclinical studies

"The PRARP is the only program focused on the relationship of military risk factors to the development of dementia and improvements in quality of life for those affected as well as their caregivers. These resources promote collaborations between researchers from dementia and traumatic brain injury across a variety of disciplines. The program has an impressive track record of scientific discovery that has opened windows for all dementia research and is fortunate to have the collaboration of key federal agencies and the Alzheimer's Association."

Michael Jaffee, M.D.,
FY17 Programmatic Panel Chair

Program History

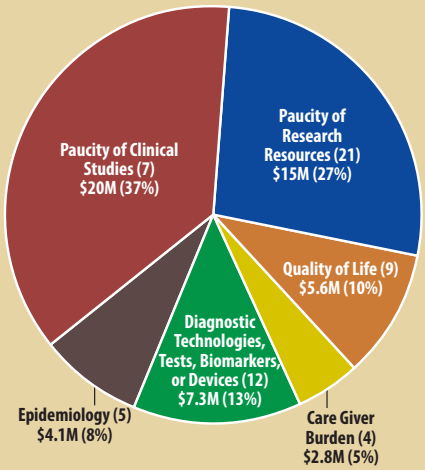
PRARP (formerly the Militarily Relevant Peer Reviewed Alzheimer's Disease Research Program) was initiated in 2011 to address the long-term consequences of TBI as they pertain to AD. Military personnel and other individuals who suffer from TBI face an increased risk for developing several long-term health problems. These conditions include Alzheimer's-like dementia, aggression, memory loss, depression, and symptoms similar to those of other neurological diseases. Consistent with PRARP's mission, the program faces 6 overarching challenges.

- Paucity of Research Resources.
- Paucity of Clinical Studies.
- Diagnostic Technologies, Tests, Biomarkers, or Devices.
- Quality of Life.
- Caregiver Burden.
- Epidemiology.

In order to answer these overarching challenges, the PRARP has identified 7 scientific focus areas that support innovative and systematic research:

- Genomics/Proteomics.
- Mechanisms of Pathogenesis.
- Quality of Life.
- Caregiver support.
- Biomarkers.
- Novel Target Identification.
- Epidemiological Research.

Between FY11 and FY16, the program administered $78M in funding across 73 awards that are intended to address at least one of the PRARP's overarching challenges. Currently, the PRARP research portfolio is balanced between pathological studies, epidemiology, new diagnostics, and quality of life research.



FY11-15 PRARP Research Investment by Overarching Challenge

Tau and Beta-Amyloid Deposition, Microhaemorrhage, and Brain Function After Traumatic Brain Injury in War Veterans

Christopher Rowe, M.D., University of Melbourne

International partners make up a small, but important component of the PRARP research portfolio. This study, in conjunction with the larger DoD ADNI studies, has increased understanding of some of the subtle changes that occur in military populations as they age. The aging of military populations is different from their civilian counterparts because comorbidities such as TBI and PTSD can be sustained on the battlefield. Dr. Christopher Rowe was awarded an FY13 Convergence Science Research Award to study the relationship between TBI and PTSD in Australian Veterans who served in Vietnam. More than 116 Australian Veterans have participated in this study. Australian Veterans with PTSD and/or TBI, as well as those who did not sustain either injury, took part. The study used state-of-the-art imaging (magnetic resonance imaging and nuclear imaging) to characterize each arm of the cohort. Early results hint at subtle differences between the groups, but a more robust data analysis is still required to fully appreciate the long-term effects of TBI and PTSD in terms of AD. Both the Australian and American ADNI studies use methods that are interchangeable, so this permits comparisons between the groups that may reveal even more subtle differences among the three cohort arms. It is anticipated that data from both the Australian and DoD ADNI studies will be made available to the scientific research community so that these datasets can be used as the basis for further research.

Sleep, Traumatic Brain Injury, and Chronic Traumatic Encephalopathy

Dr. Maiken Nedergaard, M.D., DMSc, University of Rochester

The brain's physiological response to stressors, such as lack of sleep, has recently been discovered to be mediated by an intricate network of channels called the glymphatic system. The glymphatic system is key to restoring the brain's proper function as you sleep by removing toxins or waste products, such as proteins associated with AD. Tau, a pathological hallmark of many neurological diseases and disorders, is associated not only with AD, but also with chronic traumatic encephalopathy (CTE). CTE is becoming more closely associated with TBIs, in particular in sports such as football. One hallmark of CTE is the deposit of Tau in the brain. Dr. Nedergaard was awarded an FY15 Convergence Science Research Award to study how TBI affects sleep and how some aspects of the pathology of TBI, namely reactive gliosis, compromise the removal of toxins that are normally removed by the glymphatic system during sleep. Dr. Nedergaard's findings thus far suggest that sleep disorders associated with TBI can significantly decrease the removal of proteins such as Tau by negatively altering the glymphatic system. In addition to the careful mechanistic studies necessary to characterize the physiology of the glymphatic system, Dr. Nedergaard's team will evaluate how the alterations impact cognition. While this work is in its early stages, it is conceivable that this research will result in a novel diagnostic platform for neuroscience in the coming years. It is also hoped that this study may lead to new ways of improving how the glymphatic system works in order to overcome the effects of aging, injury, or disease.

"It is only through research that we will find ways of preventing and effectively eliminating the devastating effects of Alzheimer's and dementia. The Alzheimer's Association is proud of our collaboration with the PRARP funding program. The scientific investigations made possible through this program are critical to advancing our understanding of dementia risk in those who served in the military. These efforts are not only essential to supporting individuals in our military and Veteran communities as they age, but may help lead to improvements in diagnosis and treatment for all who are affected by dementia."

Heather M. Snyder, Ph.D., Senior Director of Medical and Scientific Operations at the Alzheimer's Association

"It was a privilege to participate in the robust and comprehensive discussion surrounding each application. I was particularly impressed with the integrity of the reviewing investigators and their demand for excellence. Although not a scientist, my suggestions were valued and respected as a spokesperson for people who have been affected by brain tumors. I am grateful to have been nominated by the National Brain Tumor Society for this vital program."

Lisa Peabody,
National Brain Tumor Society

Peer Reviewed Cancer Research Program

Vision

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

Mission

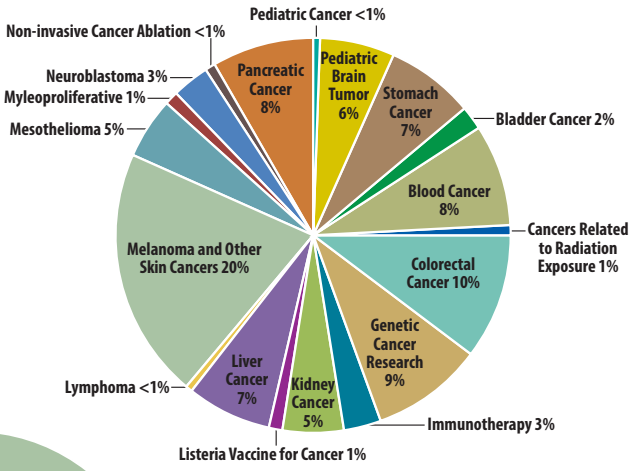
To successfully promote high-impact research for cancer prevention, detection, treatment, and survivorship

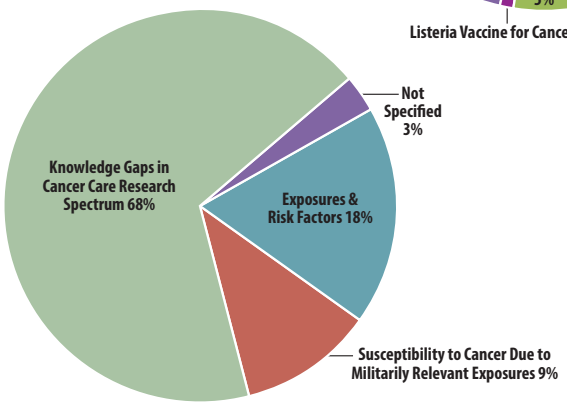
Program History

The PRCRP's overarching vision remains the same as it has been since its inaugural year. This singular theme emphasizes PRCRP's strategy of funding research into cancers that may develop due to exposures relevant to unique military situations/settings, as well as knowledge gaps in cancer care that may have a profound effect on mission readiness and the health and well-being of all military beneficiaries. Through innovative mechanisms, militarily relevant focus areas, and targeted investment strategies to develop the next generation of cancer researchers, PRCRP has answered the need to successfully promote high-impact research for cancer prevention, detection, treatment, and survivorship for Service Members, their families, and the American public.

PRCRP FY09-16 Research Portfolio Percent Dollars Invested

Not all PRCRP topic areas are included in congressional language every fiscal year. For more information on FY specific Congressional language please go to http://cdmrp.army.mil/prcrp/topicareas/topicareas17.





PRCRP FY13-16 Research Portfolio Percent Dollars Invested by Military Relevance Focus Areas

Cancer Care Research Spectrum covered by the PRCRP

Biology/Etiology

A Primary Neural Crest Assay for Neuroblastoma Oncogenesis

Kevin Freeman, Ph.D., St. Jude Children's Research Hospital

Topic Area: Neuroblastoma

Dr. Freeman, with support from an FY13 Career Development Award, is investigating the oncogenic drivers of neuroblastoma. Using the novel approach of inducing neuroblastoma from primary neural crest cells, Dr. Freeman has confirmed the requirement of N-Myc for neuroblastoma oncogenesis and is assessing other putative oncogenic factors.

Prevention

Identifying Targets and Biomarkers for Liver Cancer Chemoprevention

Yujin Hoshida, M.D., Ph.D., Icahn School of Medicine at Mount Sinai

Topic Area: Liver Cancer

With support from an FY15 Idea Award with Special Focus, Dr. Hoshida is developing a cell culture model that uses oncogenic variants of the hepatitis C virus for fast-track identification of cancer preventive targets and biomarkers, thus identifying molecular changes that persist after viral clearance that could lead to liver cancer.

Diagnosis/Detection

Nanoparticles for Detection and Treatment of Colorectal Cancer

Nicole Levi-Polyachenko, Ph.D., (right) Wake Forest University Health Sciences

Topic Area: Colorectal Cancer

Dr. Levi-Polyachenko, with funds from an FY14 Career Development Award, is working to develop a new nanotechnology using inherent nanoparticle fluorescence targeting colorectal cancer cells. This will help visualize the cells and, when exposed to infrared light, also generate heat at the surface of any micrometastases in order to kill the tumor.

Diagnosis/Detection

Evaluation of Altered Metabolism and Pancreatic Cancer Risk

Brian Wolpin, M.D., M.P.H., Dana-Farber Cancer Institute

Topic Area: Pancreatic Cancer

The research supported by Dr. Wolpin's FY13 Career Development Award aimed to understand how pancreatic cancers use nutrients to promote their growth. Unique metabolic changes may signal early pancreatic cancer. Over 2,000 plasma metabolites in pancreatic cancer cases and controls have been analyzed using a LC-MS platform approach.

Prognosis

Hyperpolarized 13^C MR Markers of Renal Tumor Aggressiveness

Renuka Sriram, Ph.D., University of California, San Francisco

Topic Area: Kidney Cancer

With an FY11 Visionary Postdoctoral Fellowship Award, Dr. Sriram addressed the clinical need to reliably distinguish renal cell carcinoma from benign renal tumors. Using hyperpolarized 13^C magnetic resonance in patient-derived tissues, Dr. Sriram found that increased lactate efflux can be used to differentiate benign from malignant renal tumors.

Treatment

Development of Novel p16INK4a Mimetics as Anticancer Therapy

Mark Klein, M.D., VA Medical Center, Minneapolis, MN

Topic Area: Mesothelioma

With funds from an FY12 Career Development Award, Dr. Klein determined that targeting the cell cycle in mesothelioma by either modified peptides or the CDK4 inhibitor palbociclib is effective against mesothelioma. A clinical trial utilizing CDK4 inhibitors for mesothelioma is being planned, and the modified peptides are under further development.

Treatment

Treating Melanoma Metastases with a Novel Photodynamic Approach

Jin Xie, Ph.D., University of Georgia

Topic Area: Melanoma and Other Skin Cancers

The goal of the work supported by an FY14 Idea Award with Special Focus led by Dr. Xie is to develop a novel methodology, called X-ray-induced photodynamic therapy, to treat melanoma lung metastases. This technology uses nanosensitizers coupled to a tumor-targeting ligand that homes to tumors in the lung. Study results have shown these nanosensitizers to be effective in killing cancer cells while maintaining low systemic toxicity.

Treatment

Anti-CDR3 Therapy for B-Cell Malignancies

David FitzGerald, Ph.D., National Cancer Institute

Topic Area: Blood Cancer

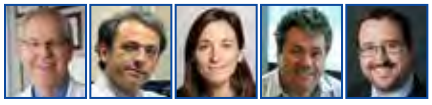
With funds from an FY12 Discovery Award, Dr. FitzGerald used a proof-of-concept approach to develop a strategy that produced CDR3 specific antibodies that discriminate between target and non-target B cells in blood cancers. The data generated from this study support the viability of this approach to go forward into the clinic.

Survivorship

Mechanisms of Acquired Resistance to Sorafenib in Hepatocellular Carcinoma

Scott Friedman, M.D., Icahn School of Medicine at Mount Sinai

Topic Area: Liver Cancer



With an FY15 Translational Team Science Award, Drs. Friedman, Llovet, Lujambio, Lowe and Villanueva (shown left to right) are investigating the mechanism of sorafenib treatment evasion by primary hepatocellular carcinoma (HCC). Determining mechanisms of resistance will improve outcomes, aid in drug development, and impact survivorship.

Peer Reviewed Medical Research Program

Vision

Improve the health and well-being of all military Service Members, Veterans, and beneficiaries

Mission

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

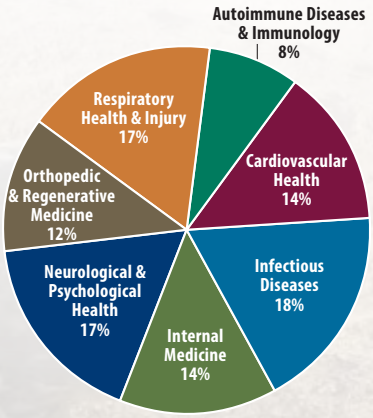
Program History

Since 1999, the PRMRP has supported research with the underlying goal of enhancing the health and well-being of military Service Members, Veterans, retirees, and their families. Through FY16, Congress has appropriated $1.37B to the program, which has supported nearly 1,000 research awards in 128 different congressionally-directed topic areas. The FY17 congressional appropriation is $300M to solicit research applications in 48 topic areas.

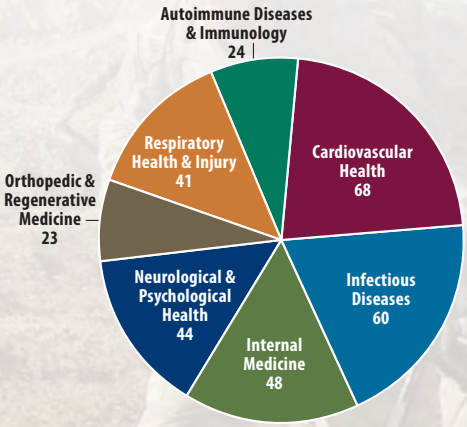
PRMRP is committed to funding the full spectrum of laboratory, translational, and clinical trial research to have a strong impact on the understanding of disease and injury etiology, as well as the development and implementation of devices, therapies, and clinical guidance that will change the face of prevention, diagnosis, treatment, and quality of life.

The PRMRP supports research in congressionally specified topic areas that address a wide range of fields, including:

- Autoimmune diseases and immunology.
- Cardiovascular health.
- Infectious diseases.
- Internal medicine.
- Neurological and psychological health.
- Orthopedic and regenerative medicine.
- Respiratory health and injury.



FY99-FY16 PRMRP Funding by Research Area (% based on total dollar amount of funding)



FY15-FY16 PRMRP Awards by Research Area (% based on total number of awards)

Autoimmune Diseases and Immunology

Development of CD109 as a Novel TGF-Beta Antagonist and Anti-Fibrotic Agent for the Treatment of Scleroderma

Anie Philip, Ph.D., McGill University Health Centre Research Institute

Scleroderma, or systemic sclerosis (SSc), is an autoimmune disease that is characterized by blood vessel damage and scarring (fibrosis) of the skin and internal organs, which can lead to organ failure. The cause is unknown, but has been speculated to be linked to chemical and environmental exposures, which is in line with an increase in SSc development reports in military Service Members. Currently, there are no curative treatments for SSc.

- Dr. Philip's team has developed candidate recombinant proteins to block a signaling pathway involved in fibrosis development.
- Initial studies showed one recombinant protein candidate to have promising anti-fibrotic effects in an SSc mouse model. The Philip team plans to perform more in-depth studies with SSc mice to better understand the disease and their candidate protein treatment.
- A provisional patent has been submitted. If this candidate continues to show promise in preliminary studies and is successful in clinical trials, a new treatment option would be available to prevent further development of fibrosis in patients with SSc.

Topic Areas

Arthritis	FY17
Guillain-Barre Syndrome	FY17
Hereditary Angioedema	FY16 & FY17
Immunomonitoring of Intestinal Transplants	FY17
Inflammatory Bowel Disease	FY16 & FY17
Lupus	FY16
Rheumatoid Arthritis	FY16 & FY17
Scleroderma	FY16 & FY17

Cardiovascular Health

Preclinical Development of EpiReady, a Novel Therapeutic to Treat Nonhealing Diabetic Foot Ulcers

Cathy Rasmussen, Ph.D., Stratatech – A Mallinckrodt Company

Chronic, non-healing diabetic foot ulcers (DFUs) are major health complications that are associated with high infection and hospitalization rates, amputation, and an increased risk of death. Unfortunately, as the aging population increases, diabetes and DFU incidences are rising in both US Veteran and civilian populations.

- Dr. Rasmussen's team proposed to further develop a therapeutic called EpiReady. EpiReady is a dehydrated, full-thickness, tissue-engineered human skin substitute that contains enhanced levels of pro-wound healing and anti-microbial factors to reduce the threat of infection and boost regeneration.
- With PRMRP support, Dr. Rasmussen's team hopes to optimize manufacturing, performance, and safety testing to enable FDA submission. These tests include barrier properties characterization, protein expression profiling, and efficacy and safety animal studies of the EpiReady tissues.
- EpiReady has the potential to be the first treatment approach to DFUs and other complex skin wounds to address both infection and wound healing.

Congenital Heart Disease	FY16 & FY17
Diabetes	FY16 & FY17
Vascular Malformations	FY16 & FY17
Women's Heart Disease	FY16 & FY17

Orthopedic and Regenerative Medicine

Broadly Applicable Nanowafer Drug Delivery System for Treating Eye Injuries

Stephen Pflugfelder, M.D., Baylor College of Medicine

Eye injuries require immediate and effective treatment to avoid vision loss. Current treatments require multiple doses by eye drop per day, a treatment strategy that is not always feasible for critically injured and deployed patients.

- The research team created biodegradable nanowafers with arrays of nanoreservoirs loaded with drugs to deliver medicine to the eye in a sustained, controlled-release manner.
- Drugs delivered by the nanowafer are retained for significantly longer time periods than normal eye drops.
- The system has the potential for use in treating ocular surface injuries, as well as dry eye, corneal ulcers, glaucoma, and eye infections.

Musculoskeletal Disorders	FY17
Nanomaterials for Bone Regeneration	FY16 & FY17
Non-Opioid Pain Management	FY16 & FY17
Post-Traumatic Osteoarthritis	FY16 & FY17

Infectious Diseases

A Novel Vector Control Measure to Combat the Spread of Artemisinin Resistance in the Greater Mekong Subregion

Dr. Jetsumon Prachumsri, Ph.D., Mahidol University

Malaria is the number one infectious disease threat to US military personnel. There is a strong sense of urgency to develop effective mosquito control measures due to the development of antimalarial drug resistance in Southeast Asia.

- This multi-site Clinical Trial Award is a collaborative study with Mahidol University, Walter Reed Army Institute of Research, and the Armed Forces Research Institute of Medical Sciences.
- The study uses ivermectin (an anti-parasitic) in mass drug administration to assist with malaria elimination efforts in six remote Thai villages.
- This novel treatment will make human blood meals lethal to mosquitoes, regardless of vector feeding location or time, thus reducing the malaria parasite transmission by directly targeting outdoor malaria transmission.

Internal Medicine

A Novel Antifibrotic for Chronic Kidney Disease

Prakash Narayan, Ph.D., Angion Biomedica Corporation

Untreated chronic kidney disease leads to renal failure, requiring dialysis and/or kidney transplantation. Approximately 1.1 million patients are on renal replacement therapy, and the prevalence is increasing each year. Chronic kidney disease is significantly more prevalent in the Veteran population than in the general population.

- This project consists of IND-enabling studies of a novel fibrokinase inhibitor in preclinical models of chronic kidney disease with common comorbidities.
- The lead compound has been shown to reduce markers of renal damage and fibrosis in preclinical models of chronic kidney disease.
- The goal is to develop a novel therapeutic that will slow or even reverse kidney disease, delaying or avoiding the need for renal replacement therapy.

Topic Areas

Antimicrobial Resistance	FY16 & FY17
Diarrheal Diseases	FY17
Emerging Infectious Diseases	FY16 & FY17
Hepatitis B	FY16
Hepatitis B and C	FY17
Influenza	FY16 & FY17
Malaria	FY16 & FY17
Pathogen-Inactivated Dried Plasma	FY16
Pathogen-Inactivated Dried Cryoprecipitate	FY17
Tuberculosis	FY16 & FY17
Vaccine Development for Infectious Disease	FY16 & FY17
Early Trauma Thermal Regulation	FY17
Eating Disorders	FY17
Epidermolysis Bullosa	FY17
Focal Segmental Glomerulosclerosis	FY16 & FY17
Integrative Medicine	FY16 & FY17
Interstitial Cystitis	FY16 & FY17
Mitochondrial Disease	FY16 & FY17
Pancreatitis	FY16 & FY17
Polycystic Kidney Disease	FY16 & FY17
Sustained Release Drug Delivery	FY17

Bench → **Bedside**

FY16-FY17 PRMRP Award Mechanisms

- **Discovery Award:** Support innovative, non-incremental, high-risk/potentially high-reward research that will provide new insights, paradigms, technologies, or applications (direct cost limit - $200,000).
- **Investigator-Initiated Research Award:** Support research with the potential to yield highly impactful data that could lead to critical discoveries or major advancements (direct cost limit - $1.2M single PI/ $1.5M Partnering PI).
- **Technology/Therapeutic Development Award:** Product-driven award mechanism intended to provide support for the translation of promising preclinical findings into products for clinical applications (direct cost limit - $3M).
- **Focused Program Award:** Support a unifying, overarching challenge that is addressed by a set of research projects to optimize research and accelerate the solution for a critical question (total cost limit - $10M).
- **Clinical Trial Award:** Support the rapid implementation of clinical trials (small proof-of-concept trials to demonstrate feasibility through large-scale trials to determine efficacy) with the potential to have a significant impact on a disease or condition (no budget limit).

Neurological and Psychological Health

Targeted Alteration of Dietary Omega-3 and Omega-6 Fatty Acids for the Treatment of Post-Traumatic Headaches

Kimbra Kenney, M.D., USU

Post-traumatic headache (PTH) is found in up to 35% of Service Members returning from Iraq and Afghanistan. PTH is frequently disabling, and current therapies have limited efficacy and are often associated with significant side effects.

- This clinical trial is a collaborative study between USU, Walter Reed National Military Medical Center, Fort Belvoir, the University of North Carolina, and the National Institute on Alcohol Abuse and Alcoholism.
- A previous study showed that lipid derivatives from omega-6 polyunsaturated fatty acids intensified chronic daily headache pain, while derivatives from omega-3 fatty acids relieved it.
- This study is testing whether altering diet by elevating the intake of omega-3 fatty acids and concurrently decreasing the intake of omega-6 fatty acids is effective in relieving PTH in Service Members.

Topic Areas

Chronic Migraine and Post-Traumatic Headache	FY16 & FY17
Dystonia	FY16 & FY17
Fragile X Syndrome	FY16 & FY17
Hydrocephalus	FY16 & FY17
Psychotropic Medications	FY16
Rett Syndrome	FY16 & FY17
Sleep Disorders	FY16 & FY17
Spinal Muscular Atrophy	FY17
Tinnitus	FY16 & FY17

Respiratory Health and Injury

STAT6-Dependent Bridging of Innate and Th2 Adaptive Immunity in the Lung

Elizabeth Fixman, Ph.D., (pictured left) and Brian Ward, M.D., C.M., (pictured right) McGill University Health Centre Research Institute

Asthma and allergy incidences and their severity in both civilian and military populations have been steadily rising within the last three decades. Recent epidemiology studies have found evidence that early-life respiratory syncytial virus (RSV) infection may be an important risk factor for subsequent development and persistence of asthma. However, the relationship is unknown.

- With PRMRP support, Dr. Fixman's and Dr. Ward's laboratories are collaborating together to characterize the ability of a new compound they developed, STAT6-IP, to inhibit asthma and respiratory infections.
- Current initial results show that STAT6-IP delivery to the lung effectively inhibits both development and persistence of asthma markers in mice, suggesting that STAT6-IP works in a way that is different from current therapies.
- Future work includes optimization of a STAT6-IP delivery vehicle, in-depth efficacy experiments in mice, and evaluation of immune, molecular, and physiological responses to STAT6-IP.
- STAT6-IP has the potential to offer a novel approach to addressing both asthma symptoms and development. Studying the mechanism by which STAT6-IP is potentially effective could provide an understanding of the immune system's response to RSV infection and asthma, as well as elucidate the relationship between early-life RSV infection and asthma development.

Acute Lung Injury	FY16 & FY17
Burn Pit Exposure	FY17
Constrictive Bronchiolitis	FY16 & FY17
Metals Toxicology	FY16 & FY17
Pulmonary Fibrosis	FY16 & FY17
Respiratory Health	FY16 & FY17

Peer Reviewed Orthopaedic Research Program

Vision

Provide all Warriors affected by orthopaedic injuries sustained in the defense of our Constitution the opportunity for optimal recovery and restoration of function

Mission

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

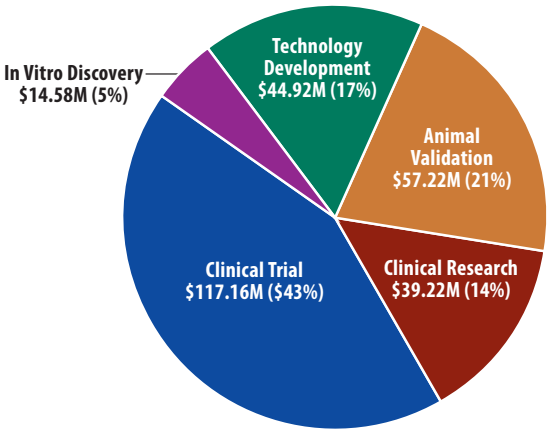
"The PRORP has become one of the most impactful and influential organizations in the development of new research, with the goal of helping injured Service Members and Veterans achieve optimal recovery from combat and combat-related orthopaedic injuries. The integrated partnerships with consumer, scientific, professional, and military experts are invaluable to the process of finding and funding the best research to support the Warfighter and shape the future of orthopaedic medicine. It is an honor to serve with this group of individuals who are dedicated to transforming healthcare for Service Members and the American public through innovative and impactful research."

CAPT Lanny Boswell
Commanding Officer
USNS Comfort
FY16 PRORP Programmatic Panel Member

Program History

Orthopaedic injuries represent more than half of all injuries seen in combat and are the largest source of long-term disability in returning Service Members. The impact of these injuries points to an urgent need for orthopaedic research that will provide superior medical care and treatment options for injured Service Members. 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, heterotopic ossification, and functional muscle loss, among others. PRORP crafts investment strategies to address and consider all aspects of orthopaedic injury, as well as other related medical challenges, with the goal of helping injured Service Members and Veterans achieve optimal recovery from combat and combat-related orthopaedic injuries. Since its inception in FY09, PRORP has dedicated its congressional appropriations, totaling $300.5M, toward supporting military-relevant orthopaedic research with the expectation that any research findings will also benefit the general population.

PRORP has funded more than 230 awards through FY16 to support high-impact, innovative research; foster the development of research resources and tools; promote the translation of new research findings to patient care; and advance orthopaedic care.



FY09-FY16 PRORP Program Investment

Gordon Hirschman

Commonly used prosthetic liners limit air circulation and evaporation at the prosthetic socket interface. Inadequate heat and moisture management within the prosthetic socket often result in residual limb skin irritation, bacterial growth, and patient discomfort.

With an FY12 PRORP Idea Development Award, Gordon Hirschman, Todd Farrell, and their teams at Vivonics, Inc., and Liberating Technologies, Inc., aimed to develop an active cooling system that could be incorporated into lower-limb prosthetic sockets. The developed cooling system, the Intra-socket Cooling Element (ICE), was designed to contain a heat pumping mechanism for active heat removal that would fit into the prosthetic limb socket. Results from initial human use studies showed that the custom-fabricated cooling sockets were able to decrease the temperature of the residual limb after exercise by an average 3 to 5 degrees Celsius, a clinically significant value when compared with subjects who did not have the ICE. Users noted that the ICE was as comfortable as their normal prosthesis and added that they would use the ICE if it were available to them. The team is working on finalizing the design under FDA Quality Systems Regulations with ISO 13485 (Quality Management Systems) compliance, performing further validation testing of the device, and preparing for commercialization. The ICE active cooling system has the potential to markedly reduce the incidence of the skin irritation, breakdown, sores, and infection experienced by individuals who wear prosthetic devices, thus improving the quality of life for Service Members, Veterans and civilians.

Wesley Thayer (pictured top) and Curt Deister (pictured bottom)

Peripheral nerve injuries represent one of the major sources of long-term disability in Service Members returning from deployment. Currently, there are limited options for peripheral nerve repair. Nerve regeneration is a very slow process, and even with the most advanced nerve repair techniques, the period between treatment and functional recovery is often months to years. Drs. Wesley Thayer and Curt Deister were awarded an FY12 PRORP Translational Research Partnership Award to develop a device that delivers an axonal sealant to the severed nerve to promote nerve repair and to prepare this technology for human application.

Drs. Thayer and Deister developed the polyethylene glycol (PEG) Fusion Wrap Assist Device, which secures a short needle at the site of nerve injury to reliably deliver the PEG sealant. Additionally, the needle can be removed without disturbing the surgical repair. The investigators have determined that securing the needle with their device will eliminate some of the variability caused by manual application of PEG. Animals treated using the removable device had better functional recovery than those that underwent the current standard for PEG application. Drs. Thayer and Deister are hopeful that their research will help to standardize PEG application and contribute to improvements in nerve injury repair.

"As a former Army officer, a combat-wounded amputee, and a taxpayer, it has been an incredible privilege to serve with the PRORP panel. Those of us who have borne the brunt of a battle are well aware of the costs of combat. We are less aware, however, of the incredible effort that our nation undertakes to reduce those costs. CDMRP and its associated research programs are at the core of that effort. I hope that my participation as a consumer programmatic reviewer adds value to this incredibly important and robust program. So many people serve in so many ways for the purpose of keeping our fighting forces healthy, and for that I am eternally grateful."

CPT Dan Berschinski, USA Ret.
Chairman of the Board for the Amputee Coalition and FY16 PRORP Programmatic Panel Member

"The PRORP review panel combines the talent of prominent research scientists with knowledgeable consumer reviewers. Together, we perform an impartial and full scientific peer review to identify the best science, which will be readily translated into orthopaedic solutions for our wounded Service Members and Veterans. As Chair of the Review Panel, it is a great privilege to serve with these dedicated individuals."

Dr. Kenton Kaufman
Research Professor, Mayo Clinic, FY16 PRORP Peer Review Chair

Prostate Cancer Research Program

Vision

Conquer prostate cancer

Mission

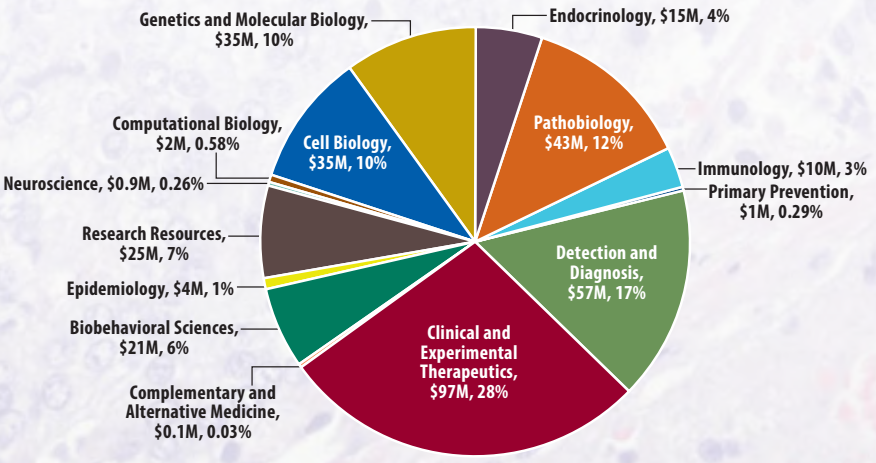
Fund research that will lead to the elimination of death from prostate cancer and enhance the well-being of Service Members, Veterans, and all men experiencing the impact of the disease

Program History

Since its inception in 1997 and over its 20-year history of congressional support totaling nearly $1.62B, PCRP has changed the landscape of biomedical research and energized the prostate cancer (PCa) research community to conduct high-risk research that is decidedly collaborative, innovative, and impactful, ultimately aiming to conquer the disease. PCRP has made unprecedented inroads in supporting the development of new treatments for advanced PCa; has been the leading supporter of research aimed at understanding and resolving ethnic disparities in PCa incidence and mortality; and has fostered the development of over a thousand young investigators, many of whom have become leaders in cutting-edge research that is making a significant difference for millions of patients with PCa.

Program Portfolio

From 1997–2016, PCRP funded 3,158 research awards. PCRP strives to diversify its research portfolio to address the critical needs of patients with PCa from different scientific approaches. The supported projects range from exploratory studies that generate cutting-edge ideas to multi-institutional consortia designed to create resources that will transform PCa clinical care. By achieving innovative solutions to critical challenges faced by patients with PCa, PCRP-supported researchers can realize the goal of making a direct, positive impact on patients and their families.



FY12–FY16 PCRP Research Portfolio

"Clinical cancer research and therapeutic healthcare are in the midst of an evolutionary process driven by expansion of the concepts of big data, artificial intelligence, and technological integration. Many research organizations are unclear as to direction or constrained by traditional research foci. The PCRP has no such boundaries because, each year, it will reinvent itself to meet the needs of the patient and professional communities in funding research. While broad in scope, the PCRP is precise in patient-centered delivery. Vision is the driving force for the PCRP."

Virgil Simons, M.P.A.
The Prostate Net,
FY17 Programmatic Panel Member

Dr. David Karow, M.D., Ph.D., University of California, San Diego (UCSD)

Dr. David Karow and his team developed a new, noninvasive, imaging technique termed Restriction Spectrum Imaging-Magnetic Resonance Imaging (RSI-MRI), that is capable of more accurately detecting and localizing prostate tumors than conventional imaging techniques and highly correlates to pathological analysis of Gleason grade. In addition, they have shown that this 5-minute technique is equally capable of detecting high-grade PCa as a full 60-minute, contrast-enhanced, multiparametric MRI. This imaging technique is currently utilized on all patients imaged at UCSD medical center and provided improved detection, grading, and directed biopsy of PCa. UCSD recently received an FY16 PCRP award for further development of RSI-MRI in PCa.

James Korkola, Ph.D., (pictured left) and Joshi Alumkal, M.D., (pictured right) Oregon Health & Science University

Castration-resistant prostate cancer (CRPC) cells develop genetic mutations that make them resistant to androgen-deprivation drugs such as enzalutamide. One common resistance feature in CRPC cells is activation of the androgen receptor (AR). Drs. James Korkola and Joshi Alumkal and their team from Oregon Health & Science University found that PCa cells expressing a specific mutation (F877L) are resistant to enzalutamide, but interestingly are not able to activate the AR when androgens are present, indicating that androgens may interfere with enzalutamide activation of AR in CRPC cells. Their studies showed that BET bromodomain inhibition suppressed both androgen and enzalutamide activation of mutant F877L AR and blocked enzalutamide-induced growth of mutant F877L AR CRPC tumors implanted in castrated mice, making this a promising target for treatment of tumors with this mutation. The team at Oregon Health & Science University is currently testing a new BET bromodomain inhibitor, ZEN-003694, in men with enzalutamide-resistant PCa to suppress CRPC tumor growth.

Douglas McNeel, M.D., Ph.D., University of Wisconsin, Madison

Dr. Douglas McNeel is developing DNA vaccines and combination immunotherapies for the treatment of PCa. He developed a DNA vaccine (pTVG-HP) encoding prostatic acid phosphatase, a protein commonly expressed in PCa. In a PCRP-funded Phase I clinical trial in patients with PCa, he demonstrated that vaccination with pTVG-HP elicits a measurable immune response and slows cancer growth in some patients. A PCRP-funded Phase II clinical trial is currently underway to test whether this vaccine can delay the development of metastases. While this trial remains ongoing, the pTVG-HP DNA vaccine, combined with pembrolizumab, an antibody that targets the PD-1 receptor, is being studied in another Phase II clinical trial. While PD-1 inhibitors have shown little success in PCa clinical trials, they have shown great promise in other cancers. Preliminary findings suggest that combination of the pTVG-HP DNA vaccine with PD-1 inhibitors leads to a much more dramatic antitumor response to PCa compared to PD-1 inhibitors given alone.

Alicia Morgans, M.D., Vanderbilt University

Men living with metastatic castration-resistant prostate cancer (mCRPC) have many treatment options available to them, each with different side effects, treatment schedules, and costs. However, each therapy will extend their life by approximately the same amount. There are no tools or tests to match the right treatment with a particular man, and often the treatment chosen is based on the physician's personal experience or assumed patient preference. Dr. Alicia Morgans is conducting a study in which she will survey mCRPC survivors to determine their preferred role in the treatment decision-making process and examine how their role in that process relates to overall patient satisfaction and quality of life. She hopes that this research will lead to greater understanding of the decision-making process among men with advanced PCa. If shared decision-making appears beneficial, results from this study will enable Dr. Morgans to develop decision-support aids to optimize methods of decision-making that will improve the physical and emotional well-being for men living with mCRPC.

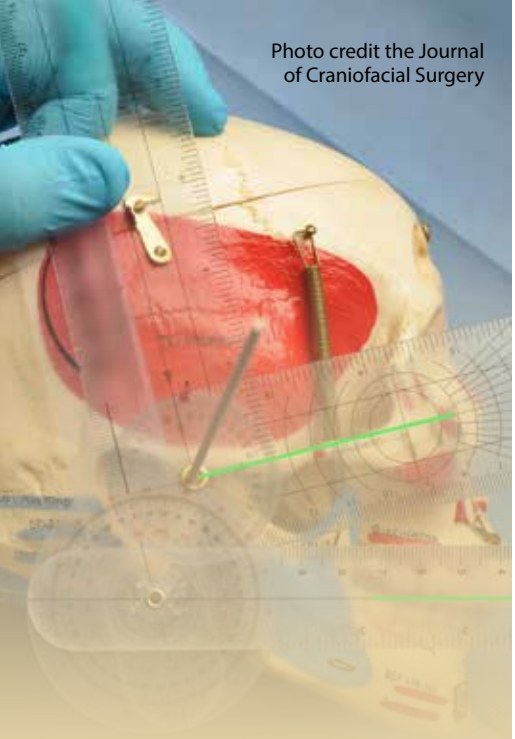


Photo credit the Journal of Craniofacial Surgery

Reconstructive Transplant Research Program

Vision

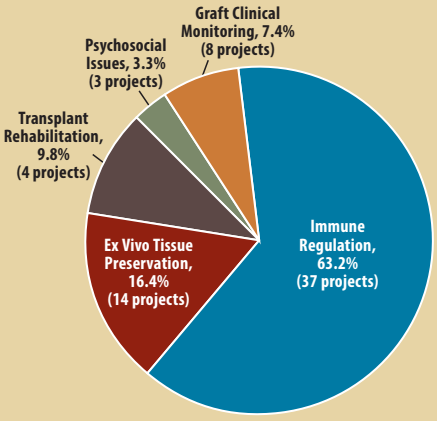
Removing the barriers to vascularized composite allotransplantation (VCA)

Mission

Developing innovative solutions for the field of vascularized composite allotransplantation to expand public awareness, enhance patient selection, and optimize the restoration of form, function, appearance, and psychosocial health for catastrophically injured military Service Members and beneficiaries, Veterans, and American civilians

"The RTRP is really one of few initiatives that offer hope to our most severely injured Service Members who lost one or more extremities or suffered catastrophic injuries to their face. The scientific diversity within our programmatic review panel balances the many facets a potential VCA patient may come across when considering this life-giving intervention."

Dr. Rodney Chan, FY17 RTRP Programmatic Panel Member



FY12-FY16 Research Portfolio
(% Dollars Invested)

Program History

Since its inception in FY12, the Reconstructive Transplant Research Program (RTRP) has received appropriations totaling $69M to advance the science and execution of vascularized composite allotransplantation (VCA) procedures. Factors related to weaponry, personal protection, and trauma care during OEF and OIF resulted in greater survival of those sustaining increasingly severe combat injuries, particularly injuries to the face and extremities. Repairing such injuries via a donor transplant requires composite tissues, including skin, muscle, bone, fat, nerves, vasculature, and lymph nodes. VCA procedures, including approximately 40 face transplants, 20 abdominal wall transplants, and over 100 upper-extremity transplants have been performed.[1,2,3] Success rates are improving, while morbidity and mortality are decreasing, but VCA is still a young science. The RTRP strives to advance the field of VCA to make the procedure possible for a broader population of patients and to restore Wounded Warriors to duty or to meaningful lives. Beneficiaries of the practices developed with this funding include injured Service Members, Veterans, their caregivers, and family members, as well as civilians who have suffered catastrophic tissue loss.

RTRP Research Focus

The FY16 RTRP focus areas and their current representation in the RTRP portfolio are shown below:

- Immune system regulation as specifically applied to VCA.
- Improve ex vivo VCA tissue preservation techniques or technologies to extend the time between procurement and transplantation, with a goal of 24 hours.
- Reconstructive transplant rehabilitation.
- Graft clinical monitoring – acute and chronic, as applied to VCA.
- Psychosocial issues associated with VCA.

[1] Kueckelhaus M, Fischer S, Seyda M, et al. 2016. *Transpl Int*. 29(6):655-662.
[2] Broyles JM, Berli J, Tuffaha SH, et al. 2015. *J Reconstr Microsurg*. 31(1):39-44.
[3] Dalal A. 2016. *World J Transplant*. 6(4):646-649.

Trying New Things: Life After a Double Hand Transplant

Chris Pollock lost his hands in a farming accident in 2008. He was later fitted with prosthetic hands, but longed to feel the touch of his children again. Chris explored alternatives and decided to pursue a hand transplant. A donor with hands of the same size and skin color was found, and 21 doctors worked for over 11 hours to complete Chris's hand transplants. After 5 years of intense occupational therapy, Chris regained 90 percent function in both arms. He is the second person in the United States to undergo a double hand transplant and the first to receive an entire forearm. Before the accident Chris was a mechanic in the Army National Guard. Now he focuses on learning new things and a career in teaching. He enjoys encouraging children who are working through adversity and sharing his experience with patients, therapists, and doctors. He reminds us, "Most things in life are temporary, and somehow always work out… be concerned about today and don't worry about tomorrow." Chris serves as a consumer on RTRP peer review panels to provide a patient's perspective. He praises the efforts of RTRP and the scientific community to advance the field of VCA. Chris notes that transplant options are important for people needing to regain the sensation of human touch, and ways to improve public perception of hand transplantation are needed.

Research Highlights

Utilizing Vascularized Bone to Improve Outcomes of Face Transplantation

Daniel J. Ceradini, M.D., (pictured left) and Dr. Eduardo D. Rodriguez, M.D., (pictured right) New York University

Severe face injuries are difficult to repair with reconstructive surgery, but face transplants have become an option to help restore normal function and appearance. Drs. Ceradini and Rodriguez and their colleagues are conducting a clinical trial to develop "personalized" transplant techniques that will improve functional, aesthetic, and immunological outcomes of patients who receive a facial VCA. The clinical team led by Dr. Rodriguez will design a personalized surgery plan for each patient, and the recipients will each receive a face transplant containing pieces of bone from a donor. They hypothesize that the fragments of bone will keep the structure of the face intact, allowing more functional and aesthetic improvements over time. The marrow contained within the bone will also help the recipient's immune system develop tolerance and accept the donor's facial tissue. This approach was used to successfully perform the most comprehensive face transplant reported to date.

Long-Term Banking of Vascularized Composite Grafts Using Ice-Free Cryopreservation by Vitrification and Nanowarming Technologies

Kelvin Brockbank, Ph.D., Tissue Testing Technologies, LLC

Freezing tissues prior to transplant is not suitable due to damage caused by ice. Dr. Brockbank will establish an ice-free vitrification method to prevent ice from forming during rapid tissue cooling, as well as a novel radiofrequency warming strategy using iron nanoparticles for thawing. Dr. Brockbank will then test the viability of cryopreserved limbs in rodent a model of VCA. The results of this study have the potential to radically change current tissue preservation capabilities.

Developing a Tool for Predicting Nonadherence in VCA Recipients

Dorry Segev, M.D., Ph.D., Johns Hopkins University

Non-adherence to medication is a major reason for allograft loss in VCA recipients. Dr. Segev seeks to identify the psychosocial attributes of transplant candidates that play an important role in success after surgery. Using this information, Dr. Segev will develop a risk prediction tool to help clinicians determine whether a candidate is likely to adhere to medication after surgery. This study will guide future interventions that improve the psychological well-being and outcomes for potential VCA recipients.

Spinal Cord Injury Research Program

Vision

Advance the treatment and management of spinal cord injury and ameliorate its consequences relevant to injured Service Members

Mission

To fund research and encourage multidisciplinary collaborations for the development and translation of more effective strategies to improve the health and well-being of Service Members, Veterans, and other individuals with spinal cord injury

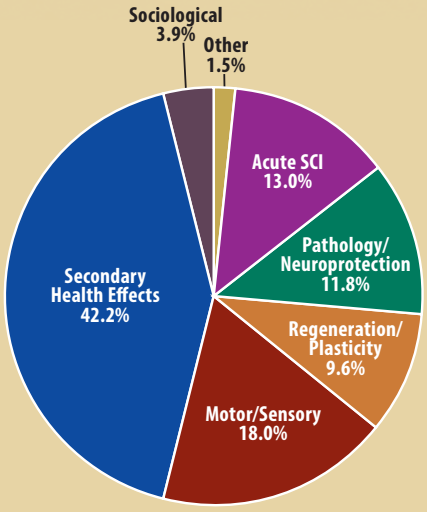
Program History

The Spinal Cord Injury Research Program (SCIRP) was established by Congress in FY09 to support research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies. With $187.85 in congressional appropriations between FY09 and FY16, the SCIRP has funded 170 projects (corresponding to 192 individual awards).

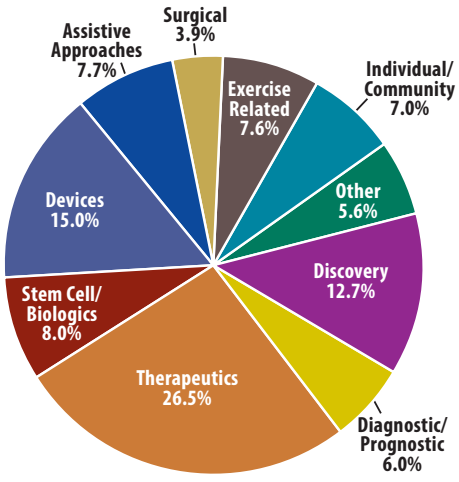
Program Portfolio

Spinal cord injuries (SCIs) are serious and complex neurotraumatic wounds affecting the individual with SCI, as well as their families and caregivers. As shown in the figures below, SCIRP funds research addressing problems from management of acute SCI through spinal cord regeneration and repair and on to treatment of secondary health effects (including loss of muscle and bone, development of pressure ulcers, neuropathic pain, and respiratory and autonomic dysfunction). This research includes discovery of mechanisms in SCI, as well as development of interventions using drug, neuroprosthetic, stem cell and surgical approaches, and covers basic, translational, and clinical studies.

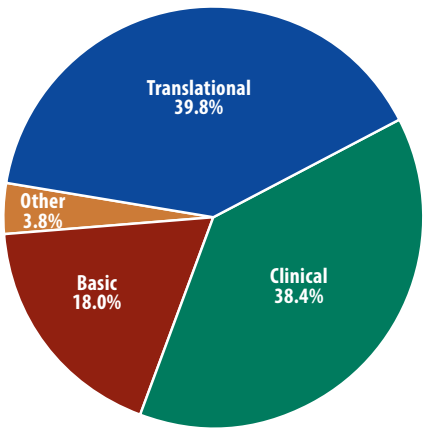
FY09-FY16 Research Portfolio (% Dollars Invested)



SCIRP System/Problem



SCIRP Approach/Intervention



SCIRP Research Stage

Bridging the Gap—Translational Research Awards Funded During FY16

Translational research has been a key part of the SCIRP program strategy from the beginning, with the goal of supporting research that will accelerate the movement of promising ideas in SCI research into clinical applications.

Christopher West, Ph.D., University of British Columbia— This innovative study in a porcine model aims to harness both peripheral tone and cardiac function to optimize the hemodynamic management of acute SCI. Improved hemodynamic management offers the potential for an immediately relevant neuroprotective strategy for patients with SCI.

Martin Mangino, Ph.D., Virginia Commonwealth University— Progressive spinal cord tissue swelling after SCI can aggravate neuronal damage. This research will develop, for acute SCI, a treatment to reduce swelling and stabilize spinal tissue after injury, with the goal of improving outcomes.

Mark Noble, Ph.D., University of Rochester—Based on preliminary animal studies where treatment of acute SCI with 4-aminopyridine (4AP) led to significantly better functional outcomes, this project will gather the necessary research to advance 4AP to a clinical trial in patients with SCI.

Nir Barak, M.D., RDD Pharma—Fecal incontinence is a significant complication affecting the health and quality of life of individuals with SCI. In this project, RDD Pharma will develop a novel formulation and method of use for a therapy targeting restoration of resting anal sphincter pressure to normal levels.

Katherine Bogie, D. Phil., Case Western Reserve University— Pressure ulcers (PrU) are one of the most common secondary health effects of SCI, with a substantial impact on patient health, quality of life, and healthcare costs. Development of a flexible, implantable, gluteal stimulator in this research could lead to prevention of PrU in individuals with SCI.

Stephen Sprigle, Ph.D., Georgia Tech Research Corporation— This project will employ a user-centered iterative approach to develop a prototype wheelchair in-seat activity tracker that monitors weight-shifting and pressure relief behaviors and provides this information to the user so the individual can better prevent PrU formation.

Nicholas Opie, Ph.D., University of Melbourne—Working towards development of a novel neural interface for implantation in humans, this project will place recording electrodes within a cerebral vein adjacent to the motor cortex using a stent. This approach avoids the need for invasive brain surgery and offers the potential for direct brain-machine control of vehicles, exoskeletons, and prosthetic limbs by individuals with SCI.

"Serving as a consumer reviewer was a rewarding experience, especially knowing that I provided input for funding research proposals that were most likely to improve patients' chances of obtaining useful test results and better outcomes. Participating in the evaluation of research proposals alongside a team of brilliant people was great. Providing these experts with the patient's perspective helped them to better understand the human side of their work. I have been involved in tick-borne diseases for over 20 years as a patient, caregiver, advocate, and educator. Educating the public has always been my top priority because I want to help people avoid the suffering I have seen. It was very gratifying to have the opportunity to take part in guiding research funding to help people affected by these diseases."

Doug Fearn, Lyme Disease Association of Southeastern PA

Tick-Borne Disease Research Program

Vision

To prevent the occurrence, better diagnose and resolve or minimize the impact of Lyme disease and other tick-borne illnesses, with emphasis on burden of disease

Mission

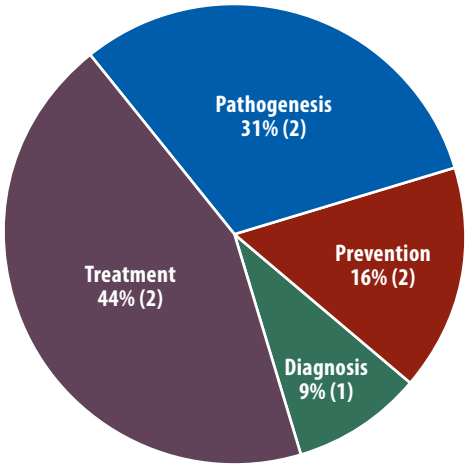
To understand the pathogenesis of Lyme disease and other tick-borne illnesses and to deliver innovative solutions to prevent, diagnose, and treat their manifestations for the benefit of US Service Members and the American public

Program History

The Tick-Borne Disease Research Program (TBDRP) was established in FY16 when the efforts of Lyme disease advocates led to a congressional appropriation of $5M. TBDRP's intent is to support innovative and impactful research that addresses fundamental issues and gaps in tick-borne diseases.

There are currently at least 16 known tick-borne illnesses, with emerging diseases being discovered all of the time. In the United States, the yearly cases of Lyme disease and other tick-borne diseases, including spotted fever rickettsiosis, anaplasmosis, and ehrlichiosis, have been increasing steadily for years, currently totaling tens of thousands of people diagnosed annually, with more likely undiagnosed. Globally, the US military prioritizes tick-borne Crimean-Congo hemorrhagic fever as an operational threat abroad.

Much remains to be determined regarding tick-borne disease pathogenesis, including host–pathogen interactions and the human immune response to these pathogens. There is a need for better disease prevention in terms of controlling the natural cycle of disease and protecting people from tick bites by various means. For people who are bitten, having methods of direct detection of tick-borne pathogens is critical in guiding treatment, and more must be learned about the cause of persistent symptoms in Lyme disease and other tick-borne illnesses in order to establish the best treatments.



FY16 TBDRP Portfolio by Research Area
Percentages of Total Spent and (Number of Awards)

Program Goals and Strategy

The FY17 TBDRP is seeking research focused in the following areas in Lyme disease and other tick-borne diseases, with emphasis on reducing public health burden. Applications addressing persistence and direct detection of Lyme borreliae are highly encouraged.

Diagnosis:

- Direct detection of agents of Lyme disease and other tick-borne diseases or their products in humans.
- Biomarkers for diagnosis, prognosis, and cure.

Pathogenesis:

- Mechanisms of persistence of Lyme disease.
- Host-pathogen interactions.
- New research tools to support studies of pathogenesis.

Treatment:

- Innovative approaches to treatment.
- Studies aimed at safe and effective treatments for the cause(s) of persistent symptoms in Lyme disease.

Prevention:

- Vaccines.
- Interrupting the cycle of the disease agents in nature.

The FY17 TBDRP Idea Award funds conceptually innovative, high-risk/potentially high-reward research in the early stages of development that could lead to critical discoveries or major advancements that will accelerate progress in improving outcomes for individuals affected by Lyme disease and/or other tick-borne illnesses. This award mechanism promotes new ideas that represent innovative approaches to Lyme disease and other tick-borne diseases research and have the potential to make an important contribution toward the TBDRP mission. A New Investigator Option encourages applications from investigators in the early stages of their careers, and their applications undergo peer and programmatic review in separate groups from the Established Investigator submissions.

The FY17 TBDRP Investigator-Initiated Research Award funds highly rigorous, high-impact studies that have the potential to make important contributions to Lyme disease and other tick-borne diseases research, patient care, and/or quality of life. This award mechanism promotes a wide range of research from basic through translational, including preclinical studies in animal models or human subjects, as well as correlative studies associated with an existing clinical trial to establish proof-of-principle for further development in future studies.

Trauma Clinical Research Program

Vision

Improve treatment and outcomes in both military and civilian trauma

Mission

To address the military relevant priorities and gaps in trauma care and facilitate the transition of lessons learned into best practice guidance and products

Program History

In FY15, CDMRP partnered with USAMRMC CCCRP to begin development of the Linking Investigations in Trauma and Emergency Services (LITES) Request for Proposals (RFP). In FY16, a congressional appropriation established the Trauma Clinical Research Program (TCRP) to support the LITES initiative. The RFP was released June 2016 and the award was made to Dr. Jason Sperry of the University of Pittsburgh in September 2016.

The award supports the creation of a research network of US trauma systems and centers with the capability to conduct prospective, multicenter, injury care and outcomes research of relevance to the DoD. The network will be a platform in which comparative effectiveness studies can be performed on materiel products to assess the feasibility and effectiveness of such products in limited and controlled populations prior to their wider study or operational use. The LITES Network may also conduct observational and epidemiological studies to gather preliminary findings for future study and analysis.

In FY17, Congress provided additional funds to TCRP to support LITES. These funds will be used to support the execution of new LITES research projects that will facilitate the transition of lessons learned from combat into improvements in trauma care practice.

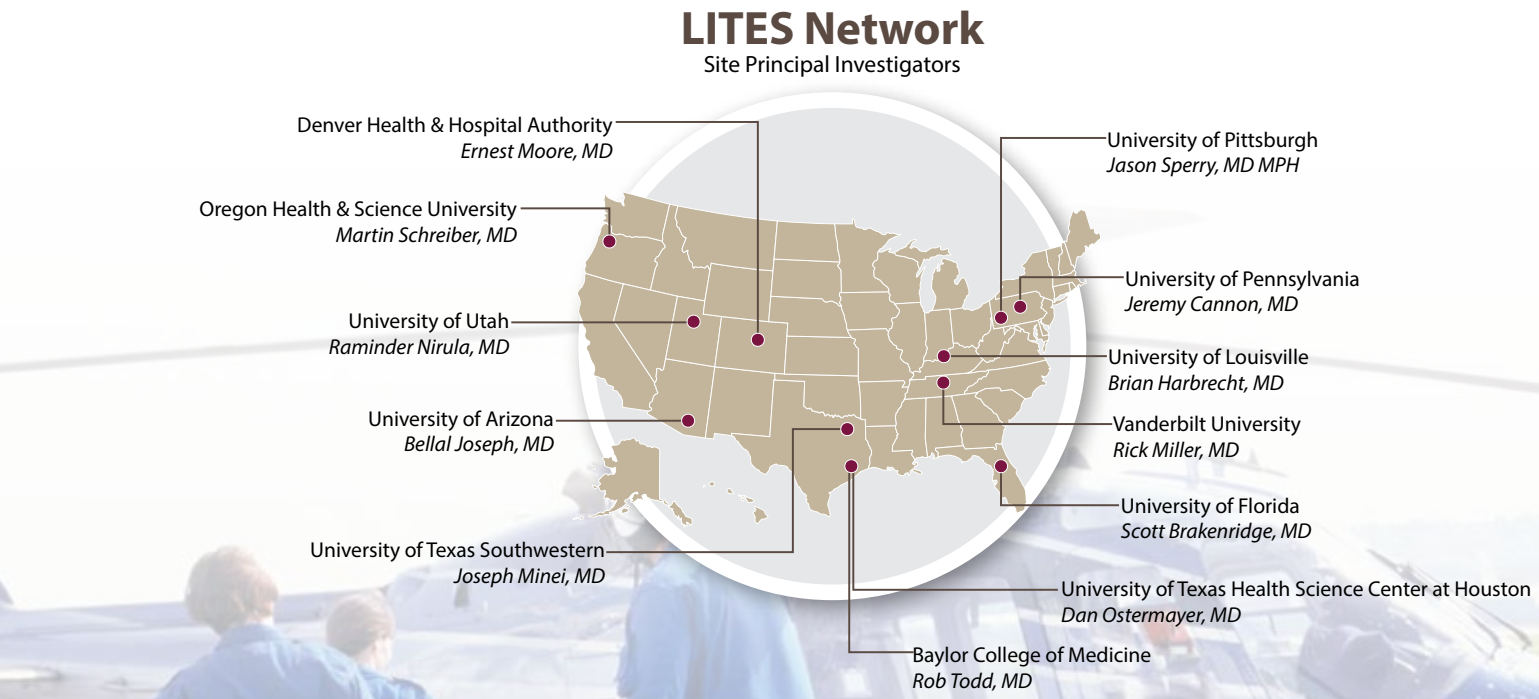
> "[Tactical Combat Casualty Care] TCCC has become the gold standard in combat care and has achieved the best casualty outcomes in the history of modern warfare. It is imperative that we sustain these advances and ensure that lessons learned are being incorporated into best practice trauma care guidelines throughout the military. The Committee encourages the Department to ensure that military advances in combat casualty care are rapidly, uniformly, and permanently implemented throughout the U.S. military."
>
> *United States Senate Report 114-263, May 26, 2016*
> *https://www.congress.gov/114/crpt/srpt263/CRPT-114srpt263.pdf*

The LITES Network: A Platform to Study Trauma Care and Improve Outcomes for Trauma Patients

Jason L. Sperry, M.D., MPH, University of Pittsburgh

The first funded study of the LITES Network is a 5-year, prospective, multicenter observational cohort study to characterize the burden of moderate and severe physical injury in the United States using a dataset obtained from trauma registries and electronic health records. The study aims to characterize the epidemiology of moderate and severe physical injury across the LITES Network, investigate regional variations, and characterize those factors associated with preventable mortality. This initial foundational study will yield important guidance and create opportunities to improve efficiency for subsequent clinical research to be conducted within the network. Currently, the research teams are securing regulatory approvals for the network sites. Findings from the LITES Network may inform new or update existing clinical practice guidelines and clinical recommendations and ultimately improve outcomes for trauma patients. Studies performed through this network are vital to learning lessons from recent conflicts and readying for future, more-complex operational environments.

> "The LITES Network is evolving into an efficient U.S. clinical trial network, which is poised to make significant advances in narrowing high-priority knowledge gaps in the care of the critically injured of relevance to the DoD."
>
> "The LITES Network is looking forward to executing those trials which correspond to its own area of expertise, including prehospital, exception from informed consent (EFIC) clinical trials."
>
> *Dr. Jason Sperry*



> "This unique collaboration has the potential to make historic changes in how trauma patients are managed in both military and civilian settings."
>
> *Dr. Martin A. Schreiber*
> *Oregon Health & Science University*

Ron Heffron,
FY13-FY17 Programmatic
Panel Member

Tuberous Sclerosis Complex Research Program

Vision

Accelerate high-impact research to improve treatment and find a cure for TSC

Mission

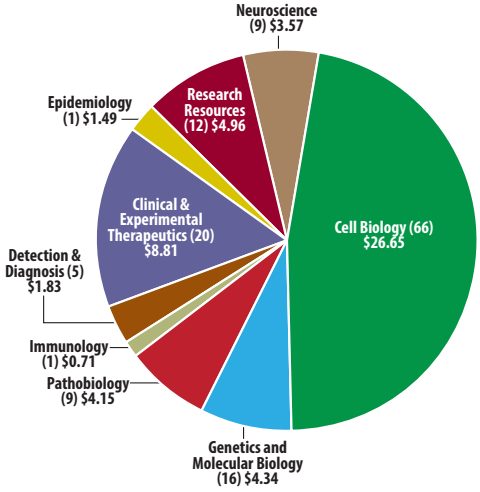
Fund pioneering and transformative science that promotes new discoveries in TSC, from mechanistic insights to clinical application, for the benefit of Service Members, their beneficiaries, and the American public

Program History

Tuberous sclerosis complex (TSC) is a genetic disorder that causes non-malignant tumors in many different organs, primarily in the brain, eyes, heart, kidney, skin, and lungs. It has several clinical manifestations; however, seizures, developmental delay, intellectual disability, and autism have the greatest impact on quality of life. The incidence and severity of the various aspects of TSC vary widely between individuals—even between identical twins. TSC can be inherited as an autosomal dominant trait or can be the result of a spontaneous genetic change on the TSC1 (hamartin) or TSC2 (tuberin) gene. The TSC1 and TSC2 genes are located on chromosome 9 and chromosome 16, respectively. It is estimated that TSC affects approximately 50,000 individuals in the United States and 1 to 2 million individuals worldwide. Many cases may remain undiagnosed for years or decades due to the relative obscurity. The Tuberous Sclerosis Complex Research Program (TSCRP) was first funded in FY02, when the efforts of TSC advocates led to a congressional appropriation of $1M. Since then, a total of $71M has been appropriated to the program, including $6M in FY17. Today, TSCRP is one of the leading sources of extramural TSC research funding in the United States.

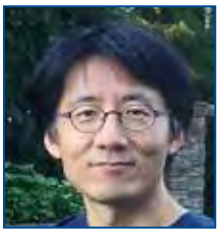
Program Portfolio

TSCRP funded 139 awards through FY16 to support high-impact, innovative research; foster the development of research resources and tools; promote the translation of new research findings to patient care; and advance the knowledge of TSC and its clinical manifestations.



TSCRP FY02–FY15 Research Portfolio

Targeting Amino Acid-mTORC1 Signaling for Treatment of TSC



Do-Hyung Kim, Ph.D., University of Minnesota, Twin Cities

The mechanistic target of mTORC1 plays a key role in the cell growth response to amino acid availability. Dr. Do-Hyung Kim was awarded an FY12 Idea Development Award to study amino acid-mTORC1 signaling in TSC, focusing on the protein SH3BP4, a negative regulator of amino acid-mTORC1 signaling that may be involved in endosomal trafficking. His laboratory found that mTORC1 binds to and phosphorylates the endosomal protein UVRAG, attenuating endosome maturation and lysosomal degradation of growth factor receptors. Furthermore, his group observed that TSC null mouse cells expressed high levels of several growth factor receptors that are often found overexpressed in tumor cells, indicating that amino acid/SH3BP4/mTORC1 signaling, through UVRAG, can increase levels of cell surface growth factor receptors in TSC cells. In looking for mediators of amino acid-mTORC1 signaling, Dr. Kim and colleagues found that mTORC1 promotes immunoproteasome formation in a manner dependent upon amino acids and mTORC1 activity, and that immunoproteasome activity is increased in TSC mutant mouse cells. This suggests that TSC cells might degrade unnecessary proteins at a greater rate than normal cells by up-regulating the immunoproteasome, as a result of a response to an inflammatory reaction. These studies have uncovered new pathways mediated by mTORC1 signaling that have resulted in novel potential targets for therapy in TSC.

Identifying the Roots of Myelin Dysfunction in the TSC Brain

Mustafa Sahin, M.D., Ph.D., Boston Children's Hospital

Hypomyelination, which occurs when glial cells in the brain are unable to generate the myelin sheath that surrounds nerve fibers and facilitates efficient transmission of nerve impulses, is a key feature of TSC and contributes to the neurological symptoms of TSC, including autism, developmental delays, and epilepsy. Dr. Mustafa Sahin has recently shown that neurons in TSC brains express increased levels of connective tissue growth factor (CTGF), a protein that is secreted by neurons and prevents proper myelination of oligodendrocytes. With funding from an FY12 Idea Development Award, Dr. Sahin investigated the role of CTGF in hypomyelination in the TSC brain. He found that deleting CTGF in neuronal cells that also lack TSC1 improves the ability of oligodendrocytes to produce myelin and develop normally. He also observed that the protein serum response factor, SRF, a repressor of CTGF gene transcription, is expressed at decreased levels in neurons lacking TSC2 and in TSC1 mouse model brains indicating that CTGF up-regulation, and the resultant hypomyelination may be due to the down-regulation of SRF. Dr. Sahin hopes that, by understanding the basis of the neurological symptoms in TSC, it will be possible to develop therapies to block the impact of CTGF expression and restore myelination to normal levels. In addition to patients with TSC, such a therapy would also impact patients suffering from similar myelination deficit disorders, including multiple sclerosis and cerebral palsy.

"The Tuberous Sclerosis Complex Research Program serves to fill gaps in the field of tuberous sclerosis research. This program brings experts in the field together to help fund exciting new ideas. This program has allowed me to work with others researching tuberous sclerosis to both share and expand my knowledge."

Mary Kay Koenig, M.D., University of Texas Health Science Center at Houston, FY13-FY17 Programmatic Panel Member (FY17 Chair)

"My experience with the TSCRP has been rewarding, enlightening, and empowering. My voice and experience representing the community was appreciated and respected, and it has been an honor to be afforded this opportunity. I wish to express my deepest gratitude for the passion and dedication from the CDMRP's staff, who devote their time to this cause. The TSC community is fortunate that there is a dedicated commitment from the scientific community to understanding the pathogenesis and manifestations of TSC with the goal of improving the lives of individuals with TSC."

Shelly Meitzler, FY16 Consumer Peer Reviewer

Vision Research Program

Vision

Be the model of transformational vision research for our armed forces and the nation

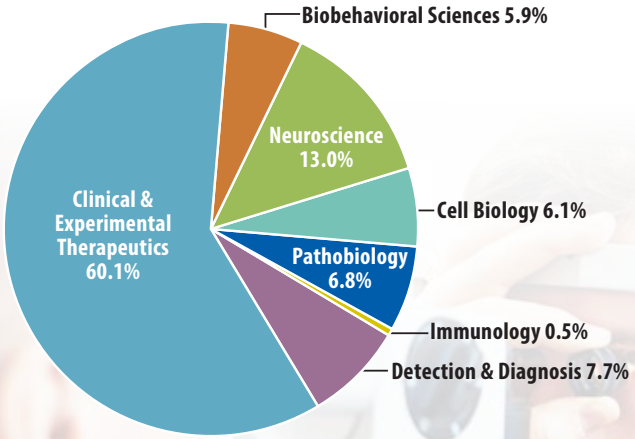
Mission

Improve the care of Service Members, Veterans, and the American public affected by eye injuries and diseases by identifying clinical needs and addressing them through directed medical research efforts

Program History

From 2002-2007, 13% of military personnel evacuated from Iraq and Afghanistan suffered a combat-related ocular injury.[1] Combat injuries such as blast injury and TBI may affect visual nerve pathways, even though there are no outward cuts or contusions to the eye. The causes, effects and treatment of eye injury and diseases that, despite their different pathogenesis, all have a common end result: degeneration of the critical components of the eye and impairment or loss of vision. The Vision Research Program (VRP) was created and funded by Congress in FY09, with the goal of fostering innovative research that has the potential to make a significant impact on improving the health and well-being of military Service Members, Veterans, their caregivers, family members, and the American public who are living with visual dysfunction. Since its inception, VRP has awarded 79 grants totaling $68.3M to researchers addressing penetrating eye injuries, corneal healing, retinal/corneal protection, visual dysfunction associated with TBI, the eye blast phenomenon, and vision rehabilitation.

In FY17, Congress appropriated $15.0M for VRP to fund meritorious applications.



FY09-FY16 VRP Portfolio Investment
(% of total investment)

[1] Weichel, E.D., Colyer, M.H., Ludlow, S.E., Bower, K.S., Eiseman, A.S. 2008. Combat ocular trauma visual outcomes during Operations Iraqi and Enduring Freedom. *Ophthalmology*. 115(12):2235-45.

Featured Vision Research Program Projects

Temporal Progression of Visual Injury from Blast Exposure

Dr. Brittany Coats, Ph.D., University of Utah

Closed-globe eye injuries often go undiagnosed initially, as there is no visible trauma to the eye. However, visual dysfunction can develop months or even years after blast exposure. With an FY11 VRP award, Dr. Brittany Coats has investigated the progression of eye injury from blast exposure and worked to identify early predictors of visual dysfunction, two uncharacterized phenomena. Using rat models, Dr. Coats found that there was a significant initial drop in visual acuity that was unable to resolve over the 8-week monitoring period. The drop in visual acuity was attributed to retinal and corneal damage. Dr. Coats aims to corroborate the animal findings in a cohort of Veterans that were not diagnosed with visual dysfunction at the time of blast exposure.

OCT Technology Development to Assess Ocular Integrity and Characterize Intraocular Scatterers

Dr. Joseph A. Izatt, Ph.D., Duke University

Optical coherence tomography (OCT) is a diagnostic imaging modality used worldwide in eye clinics to image the anterior and posterior portions of the eye; however, current systems are large, thus limiting their use to clinic settings. Dr. Izatt obtained an FY15 VRP award to improve upon a first-generation hand held OCT ocular imaging system platform that could be used by medics in theater to triage Service Members. With the award, a second-generation system that has 3D scanning abilities and is capable of scanning four times faster than the first-generation system will be produced. In addition to increased scan range and speed, the new system will also incorporate new technology to differentiate intraocular cellular response to injury.

Active Confocal Imaging System for Visual Prostheses

Dr. Eliezer Peli, O.D., Schepens Eye Research Institute

There have been significant advancements made in the field of vision prosthetics; however, current technologies are highly limited, as they are low-resolution and offer a low dynamic range and limited visual field. With an FY14 VRP award, Dr. Peli aims to use a new confocal technology to enable blind Service Members using any visual prosthetic or sensory substitution device to efficiently scan, focus, and "see" objects of interest in different depth planes while simultaneously eliminating background clutter. Two prosthetic devices, the BrainPort V100 and the BrainPort V200 Vision Pro, have been acquired by the research team and successfully tested in various tasks including recognition of simple stimuli such as line orientations, shapes, and letters for comparing the performance with and without background de-cluttering. Image mode testing for high-contrast and edge enhancement (3-grey scale level) is ongoing.

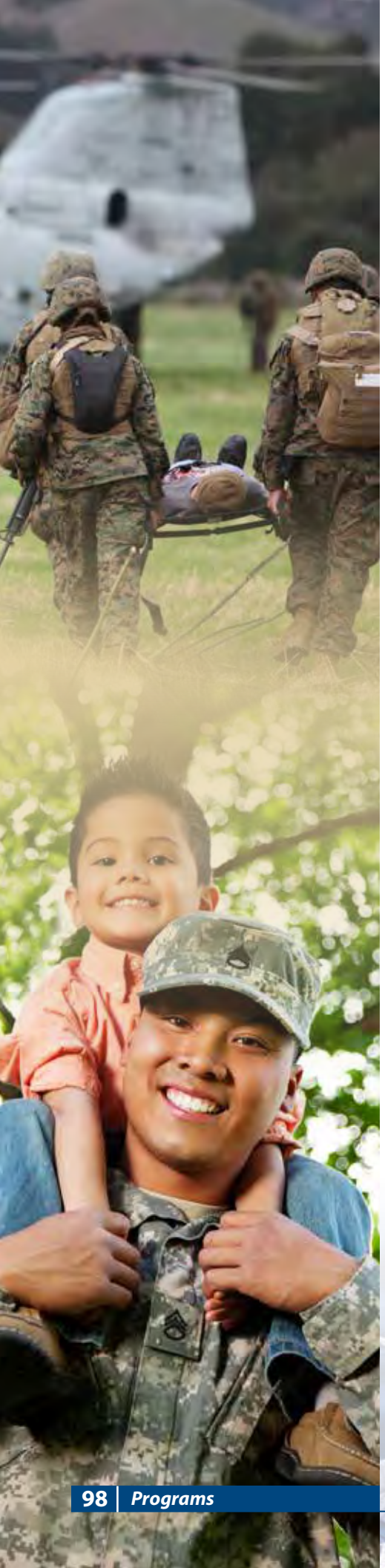
Maturation and Implantation of Engineered Retinal Tissue Grafts

Dr. Lawrence Rizzolo, Ph.D., Yale University

In both combat-related retinal injury and age-related macular degeneration (AMD), a retinal degeneration condition affecting many Veterans, retinal damage manifests in the retinal pigment epithelium (RPE) and photoreceptors. Advances in stem cell biology have led to Phase I/II clinical trials that use RPE grafts to restore vision; however, these grafts are only effective in patients with mild AMD or injury. With an FY13 VRP award, Dr. Rizzolo has engineered a scaffold that enhances the ability of stem cells to form a multilayered retinal tissue. Preliminary studies demonstrated that the scaffold promotes differentiation of stem cells into matured multilayered retinal cells which was enhanced by co-culture with human RPE. Pilot studies of transplantation in mice showed that the scaffolds were well tolerated and able to integrate in the host retina. Dr. Rizzolo plans to test the novel retinal scaffolds in a severe, acute retinal-injury pig model.

Additional Supported DoD Programs/Projects

CDMRP assists with management of certain aspects of programs managed by other offices. Some of the research managed by CDMRP for a few of these programs is highlighted here.



Defense Medical Research and Development Program

Mission

To provide full life-cycle operational execution management support for Defense Health Program core research program areas

Program History

As directed by the OASD(HA), the DHA, Research and Development Directorate manages and executes the DHP RDT&E appropriation. The USAMRMC CDMRP provides DMRDP execution management support for six DHP core research program areas, including:

- **Medical Simulation and Information Sciences.**
- **Military Infectious Diseases.**
- **Military Operational Medicine.**
- **Combat Casualty Care.**
- **Radiation Health Effects.**
- **Clinical and Rehabilitative Medicine.**

JPCs/PADs, which consist of DoD and non-DoD medical and military technical experts and representatives from the VA and HHS, provide strategic guidance for each of these major research program areas. Within USAMRMC, operational support responsibilities for the JPCs/PADs are provided by multiple execution agents, including CDMRP, individual laboratories, and advanced developers. In partnership with the JPCs/PADs, CDMRP supports development of PAs, solicitation and review of applications, full life-cycle management of awards, and program evaluation and planning.

Program and Portfolio Areas

From FY10–FY16, CDMRP has managed 202 DMRDP awards, totaling approximately $307M, to fund basic, translational, and clinical research efforts (including the Clinical Research Intramural Initiative). These projects 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. Information on the DHA R&D core research programs and recent research projects is listed on the following DMRDP pages 99-101.

Medical Simulation and Information Sciences Research Program

MSISRP plans, coordinates, and oversees a science and technology program focused on improving military medical training and education through medical modeling and simulation systems addressing combat casualty training, medical readiness, health-focused initiatives, and developer tools for medical educators, as well as improving health information sciences through increased interoperability, strategic planning, process development, and medical applications.

MSISRP works with the Services and joint agencies to address gaps and requirements identified by the Military Health System (MHS) and is responsible for programming research in the following areas:

- Medical Modeling, Simulation, and Training.
- Health Information Sciences.

The establishment of MSISRP has enabled a more collaborative process to identify and validate research initiatives pertaining to the military. The program assists in identification, assessment, and transition of relevant emerging technologies that are of value to the MHS. This ultimately allows USAMRMC and the DHA, Research and Development Directorate, to better align research and development efforts with the needs of the MHS. Additional information about MSISRP is available at: *https://mrmc.amedd.army.mil/index.cfm?pageid=medical_r_and_d.msis.overview.*

Recent MSISRP DHP Research

- Developing Assessment Tools to Better Understand the Mechanism of Clinical Reasoning in Military Simulation, *Steven Durning, USU.*
- The Burn Medical Assistant: Developing Machine-Learning Algorithms to Aid in the Estimation of Burn Wound Size, *Jeremy Pamplin, USAISR.*
- Virtual Intelligent Tutor for the Andragogy of Military Medicine INtegrated Skills (VITAMMINS), *James Niehaus, Charles River Analytics, Inc.*

Affiliated Research Programs

- JWMRP

Military Infectious Diseases Research Program

MIDRP supports research and development leading to the fielding of effective, improved means of bacterial, parasitic, and viral infection prevention, screening, diagnosis, and treatment to maintain maximal global operational capability with minimal morbidity and mortality. MIDRP's DHA-aligned mission is focused on the following research portfolio area:

- Polytrauma and Blast Injury.

MIDRP's DHP core research program-aligned projects are primarily within the portfolio task areas of Wound Infection Prevention and Management and Antimicrobial Countermeasures. Supported research efforts are focused on development of host immune response and pathogen biomarkers associated with wound infection to inform clinical decisions; development of tools for early detection of drug-resistant organisms; identification of nosocomial pathogens; characterization of antimicrobial resistance patterns; and development of novel and innovative delivery technologies to treat wound infections. This research also emphasizes treatment, with research involving identification of druggable targets against wound infection pathogens and biofilm processes; transition of new candidate therapeutics to preclinical testing; and advancement of promising early leads to first-in-human clinical trials. Additional information about MIDRP is available at: *https://midrp.amedd.army.mil/.*

Recent MIDRP DHP Research

- Preclinical Studies to Enable an IND Application for a First-in-Class LpxC Inhibitor to Treat Multidrug-Resistant (MDR) Trauma-Induced Wound Infections, *Adrian Jubb, Achaogen, Inc.*
- Evaluation of Multiple Potential Pharmacogenomic Risk Factors for Chronic Mefloquine Neurotoxicity Through the Establishment of a Drug Safety Registry, *Louis Cantilena, USU.*

Affiliated Research Programs

- JWMRP
- PRMRP
- TBDRP

Military Operational Medicine Research Program

MOMRP seeks to develop effective countermeasures against stressors and to maximize health, performance, and well-being. MOMRP conducts biomedical research to deliver products and solutions to the Warrior that address health and fitness throughout the deployment cycle. MOMRP is centered on cutting-edge scientific research and bringing science to the Soldier on the battlefield in a relevant, timely manner by focusing on the following research areas:

- Injury Prevention and Reduction.
- Psychological Health and Resilience.
- Physiological Health.
- Environmental Health and Protection.

Each area represents efforts to develop guidelines and criteria to predict, prevent, and mitigate physical and psychological injury and contribute to the shared responsibility of enabling our Armed Forces and providing them with the best care possible. Additional information about MOMRP can be found at *https://momrp.amedd.army.mil/*.

Recent MOMRP DHP Research

- Primary Blast Injury Criteria for Animal/Human TBI Models Using Field Validated Shock Tubes, *Namas Chandra, New Jersey Institute of Technology*.
- Evaluation of the Physiological Challenges in Extreme Environments: Implications for Enhanced Training, Operational Performance and Sex-Specific Responses, *Brent Ruby, University of Montana.*
- Baseline Psychological Testing of Recruits, *Howard Garb, Wilford Hall Medical Center.*

Affiliated Research Programs

- ASADRP
- GWIRP
- JWMRP
- PRMRP
- Psychological Health and Traumatic Brain Injury Research Program (PH/TBIRP)

Combat Casualty Care Research Program

CCCRP seeks to drive medical innovation through development of knowledge and materiel solutions for the acute and early management of combat-related trauma, including point-of-injury, en route, and facility-based care. CCCRP strives to optimize survival and recovery from combat-related injury by targeting the following research areas:

- Hemorrhage Control and Resuscitation.
- En Route Care.
- Forward Surgical and Intensive Critical Care.
- Neurotrauma and Traumatic Brain Injury.
- Traumatic Tissue Injury.

Research planned, programmed, and managed by CCCRP is gap-driven and motivated by the urgency to generate solutions (clinical practice guidelines or FDA-approved products) to benefit the Warfighter and the American public. CCCRP supports the complete range of research activities needed to achieve its goals, from foundational science to improvements in healthcare services and delivery. Additional information about CCCRP can be found at *https://ccc.amedd.army.mil.*

Recent CCCRP DHP Research

- Assessment of the Immediate, Short- and Long-Term Deleterious Consequences of Polytraumatic Injury in a Critical Care Non-Human Primate Model, *Matthew Bradley, USU.*
- A Multimodal Integrative Platform for Continuous Monitoring and Decision Support During Postoperative Care in Cardiac Patients, *Kayvan Najarian, University of Michigan.*
- Minimally Invasive Preperitoneal Balloon: An Alternative to Open Preperitoneal Packing for Massive Pelvic Hemorrhage in the Forward Surgical Environment, *Matthew Martin, Madigan Army Medical Center.*

Affiliated Research Programs

- ERP
- JWMRP
- MBRP
- PRMRP
- PRORP
- PH/TBIRP
- SCIRP
- TCRP

Radiation Health Effects Research Program

RHERP seeks to develop medical countermeasures for acute ionizing radiation injury. Research areas include post-exposure mitigation of radiation injury, protection and prevention of injury from ionizing radiation, understanding the mechanism of radiation injury, and development of novel biodosimetry tools.

Currently, DHP research sponsored by RHERP is focused on the following key area:

- Biomedical Technology for Radiation Countermeasures.

Recent RHERP DHP Research

- A Systems Biology Approach to Radiation Biodosimetry and the Host-Environment Interaction: Applications to Mass Casualty Triage in the Polytrauma Patient, *Robert Christy, USAISR.*

Affiliated Research Programs

- JWMRP
- PRCRP
- PRMRP

Clinical and Rehabilitative Medicine Research Program

CRMRP prioritizes research efforts based on the types of injuries and degree of trauma suffered by Warfighters, while tracking current state-of-the-art technologies. CRMRP innovations are expected to improve restorative treatments and rehabilitative care to maximize function for return to duty or civilian life. The priorities for funding research efforts are closely coordinated with other Services, partner agencies, and industry to help ensure a diverse portfolio with targeted focus areas to meet current needs.

Currently, research sponsored by CRMRP is focused on the following key areas:

- Neuromusculoskeletal Injury Rehabilitation.
- Pain Management.
- Regenerative Medicine.
- Sensory System Traumatic Injury (visual, auditory, and vestibular dysfunction).

CRMRP's mission is to implement long-term strategies to develop knowledge and materiel products to reconstruct, rehabilitate, and provide definitive care for injured Service Members. The ultimate goal is to return the Service Member to duty and restore their quality of life. Additional information about CRMRP can be found at *https://crmrp.amedd.army.mil/.*

Recent CRMRP DHP Research

- A Novel Approach for Personalized Acute Pain Management Following Injuries and Surgeries, *Saeed Jortani, University of Louisville.*
- Assessing the Effects of Concomitant Traumatic Brain Injury and Vision Loss on Wounded Warriors In Patients from Walter Reed National Military Medical Center, *Marcus Colyer, Henry M. Jackson Foundation/Walter Reed National Military Medical Center.*
- Transfemoral Amputee Osseointegration Study (TFAOS), *Jonathan Forsberg, USU.*

Affiliated Research Programs

- JWMRP
- OPORP
- PRMRP
- PRORP
- PH/TBIRP
- RTRP
- SCIRP
- VRP

Psychological Health and Traumatic Brain Injury Research Program

Vision

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

Mission

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

Program History

PH/TBIRP was established by Congress in FY07 in response to the devastating impact of TBI and psychological health (PH) issues, including PTSD, on our deployed Service Members in Iraq and Afghanistan. Appropriations totaling $300M, $150M each for TBI and PH (including PTSD), were assigned to CDMRP for the purpose of soliciting and managing critical TBI- and PH-related R&D efforts to benefit Service Members, Veterans, and other beneficiaries of the MHS.

Additional congressional appropriations for PH/TBIRP were assigned to USAMRMC between FY09 and FY16, and a modified execution model was established in which strategic oversight is provided by USAMRMC-based research program areas aligned with the OASD(HA). As directed by the OASD(HA), the DHA, Research and Development Directorate, manages and executes the DHP RDT&E appropriation, which includes the PH/TBIRP. The DHA, Research and Development Directorate, leverages PH/TBIRP funding to support ongoing research and development in three core DHP research program areas assigned to study PH and TBI, including:

- MOMRP
- CCCRP
- CRMRP

These JPCs/PADs provide recommendations to the DHA, Research and Development Directorate, on research gaps, focus areas, and funding options for the PH/TBIRP. CDMRP works in partnership with the JPCs/PADs to provide operational execution management support as needed for PH/TBIRP, including development of PAs, solicitation and review of applications, full life-cycle management of awards, and program evaluation and planning. The CDMRP-managed application review for PH/TBIRP follows a two-tiered model, where consumer involvement continues to be a hallmark. Our nation's Wounded Warriors serve in this capacity for 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 aligning PH/TBIRP CSI funds to complement core DoD research and development efforts.

Through FY16, CDMRP has managed 516 PH/TBIRP awards, totaling over $930M for projects 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.

More Information About the PH/TBI Supported Initiatives can be found at:

- Consortia (http://cdmrp.army.mil/phtbi/consortium/phtbictc)
- Research Resources - includes databases, methods, and repositories (http://cdmrp.army.mil/phtbi/resources/phtbiresources)

PH/TBIRP Recent Research Focus

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

MOMRP

- A POC Clinical Trial for PTSD with a First in Class Vasopressin 1a Receptor Antagonist, ***Neal Simon, Azevan Pharmaceuticals, Inc.***
- Human Head Impact Dose Concussion Risk Functions and Sensor-Based Military-Specific Environmental Monitoring System, ***Adam Bartsch, Cleveland Clinic Foundation.***
- Interventions for Parent Caregivers of Injured Military/Veterans Personnel, ***Linda Nichols, Memphis VA Medical Center.***

CCCRP

- Severe TBI Triage and Monitoring with Advanced Cerebral Hemodynamics, ***Seth Wilk, Neural Analytics.***
- Increasing Survival Rate Following Hemorrhagic Shock and Traumatic Brain Injury in Austere Environments, ***Andrew Mayer, The Mind Research Network.***
- Sustained V1A Receptor Activation for Prolonged Hemodynamic Support and Neurological Protection After Noncompressible Hemorrhage and Traumatic Brain Injury, ***Raul Gazmuri, Rosalind Franklin University.***

CRMRP

- Sensory Integration Balance Deficits in Complex mTBI: Can Early Initiation of Rehabilitation with Wearable Sensor Technology Improve Outcomes, ***Laurie King, Oregon Health and Science University.***
- Neuromodulatory Treatments for Pain Management in Complex TBI Using Mobile Technology, ***Eric Elbogen, Duke University.***
- Comorbidity and Health Care Utilization Patterns of Service Members with Refractory Complex Mild TBI Versus Those with Mild TBI Who Return to Duty After Treatment, ***Natalya Weber, Walter Reed Army Institute of Research.***

Small Business Innovation Research and Small Business Technology Transfer Programs

Vision

To advance health and medical solutions toward commercialization to benefit Warfighters and their families

Mission

To develop topics that address military medicine needs and provide management oversight of R&D projects, in support of broader SBIR/STTR goals

Program History

Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) are highly competitive programs that encourage US small businesses to engage in R&D with the incentive to profit from the product's commercialization. The programs are organized in three phases: Phase I establishes project feasibility; Phase II develops a prototype; and Phase III supports commercialization. SBIR/STTR funding is available for Phase I and Phase II; Phase III support requires non-SBIR/STTR funding sources.

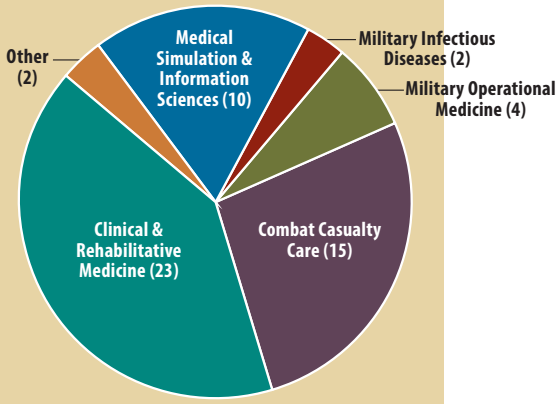
CDMRP has leveraged the SBIR and STTR programs since FY00 and FY04, respectively, to advance health and medical solutions for Warfighters and their families. CDMRP does this in coordination with JPCs/PADs and PADs by developing topics that address unmet military medicine needs. After a rigorous review process, approved CDMRP topics are announced on the DoD SBIR/STTR website, (http://www.acq.osd.mil/osbp/sbir/solicitations/index.shtml), under the Army or DHA components. CDMRP reviews proposals from small businesses, provides management oversight for the resulting awards, and coordinates with key stakeholders through all phases of development.

Projects Advancing Through the Phases

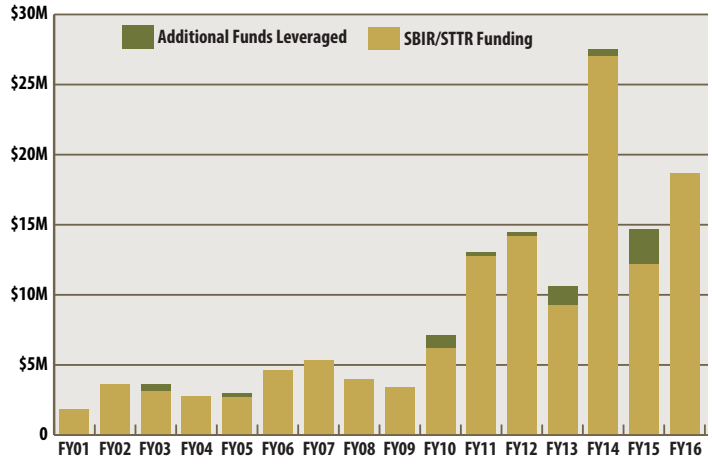
Topic Solicitation Year	Topics Managed by CDMRP	Phase I Awards	Phase II Awards	Phase III Awards*
2011	14	50	16	2
2012	9	30	12	1
2013	10	17	16	0
2014	2	6	3	1
2015	9	22	11	0
2016	5	19	3+	0
Totals	**56**	**167**	**61+**	**4**

+ Additional Phase II selections are pending.

* The number of Phase III awards will increase as Phase II projects mature.



Topics by Program Area (FY11-FY16)



Total SBIR/STTR Funds Managed by CDMRP

ADAPT-MP: Auto-Diagnostic Adaptive Precision Trainer for Myoelectric Prosthetic Users

More than 330 American servicemen have lost an upper limb due to traumatic injury in combat since 2001, which significantly affects individual independence and employment opportunities. Myoelectric prostheses provide upper limb movement control using electromyography (EMG) leads on the residual muscles to control prosthetic hand movements, but require intensive training to effectively operate, and many users abandon their prosthesis before mastery is achieved. Under DHA-funded SBIR Phase I and II efforts, Design Interactive developed the Auto-Diagnostic Adaptive Precision Trainer for Myoelectric Prosthesis Users (ADAPT-MP) system, which consists of: (1) a wearable, wireless EMG band, worn above the amputation site on the residual limb that reads user muscle signals to control training games; (2) a series of engaging mobile games that train various aspects of myoelectric prosthesis control and (3) a web-based Health Insurance Portability and Accountability Act (HIPAA) compliant provider portal to supply meaningful data to clinicians and therapists. ADAPT-MP is currently being tested in an ongoing national randomized clinical trial with 20 recent upper limb amputees under the Phase II effort.

Tourniquet Master Training System for Junctional and Inguinal Hemorrhage Control Devices

Battlefield medical treatment has advanced tremendously in recent years, particularly with the development of new types of tourniquets to address abdominal and junctional injuries. Charles River Analytics received an FY13 Phase II SBIR award to develop the Tourniquet Master Training (TMT) system to teach, assess, and provide refresher training on this new tourniquet technology. TMT is a hands-on, scenario-based training system that includes a sensor system linked to a software-based virtual mentor that provides automatic, objective assessment and feedback during training. A mobile application provides refresher training during deployment or when a manikin is not available for practice. TMT works with multiple types of manikins and adapts to future tourniquet technology advances.

A study of training effectiveness found that the TMT system improved providers' speed at applying the tourniquet while maintaining a very low error rate. Providers were also less likely to overinflate the tourniquet and showed a greater increase in confidence after training.

Hearing Fitness for Duty

Hearing loss remains the most common permanent disability among Veterans. However, existing standards do not suitably assess hearing fitness for duty. To address this military need, Creare, LLC, received Phase I, Phase II, Phase II Enhancement, and Phase III SBIRs to develop technologies and conduct studies necessary to implement new hearing fitness for duty standards. Current hearing tests assess the ability to hear very soft sounds, as well as speech in background "cocktail party" noise, but this does not indicate how they perform in more military-relevant settings with relatively loud, complex, background noise. Creare, in collaboration with DoD partners, developed hearing tests that use military phrases and sounds to ensure the tests are relevant. Human studies with active duty members to normalize and validate these tests are still ongoing. The hearing fitness for duty tests developed under this program are now integrated with a new wireless, noise-attenuating, audiometric headset (developed and refined by Creare under separate funding) that allows individuals to test their hearing without the need to travel to a clinic with a quiet booth.

Appendix A: FY92–FY16

Table A-1. Overview of Appropriations, Applications Received, and Awards Made for FY92-16

Research Programs Managed by CDMRP	Fiscal Year	Appropriations Received (in millions)	Applications Received	Applications Funded[1]
Alcohol and Substance Abuse Disorders [1]	2014-2016	$12.0	6	5
Amyotrophic Lateral Sclerosis	2007, 2009-2016	$61.9	439	54
Autism	2007-2016	$66.9	1,266	141
Bone Marrow Failure	2008-2016	$29.6	437	61
Breast Cancer	1992-2016	$3,261.3	54,205	6,678
Breast Cancer Research Semipostal [4]	1999-2016	$24.8	-	49
Chronic Myelogenous Leukemia	2002-2006	$22.1	252	61
Defense Women's Health	1995	$40.0	559	69
Deployment Related Medical [1]	2008-2013	$101.9	1,094	58
DOD/VA	1999-2000	$6.8	88	9
Duchenne Muscular Dystrophy	2011-2016	$20.0	127	25
Epilepsy	2015-2016	$15.0	66	11
Genetic Studies of Food Allergies	2009-2010	$4.4	60	9
Gulf War Illness	2006, 2008-2016	$129.0	461	154
Institutionally Based Programs [1]	1995-2010	$486.3	306	501
Joint Warfighter Medical [1]	2012-2016	$204.0	137	71
Lung Cancer	2009-2016	$101.5	2,579	195
Military Burn [1]	2014-2016	$24.0	42	31
Multiple Sclerosis	2009-2016	$39.1	657	82
Myeloproliferative Disorders	2004	$4.3	18	9
National Prion	2002	$42.5	136	38
Neurofibromatosis	1996-2016	$302.9	1,490	365
Orthotics and Prosthetics Outcomes	2014-2016	$30.0	164	32
Osteoporosis	1995	$5.0	105	5
Ovarian Cancer	1997-2016	$276.5	3,534	401
Parkinson's [1]	2014-2016	$48.0	125	65
Peer Reviewed Alzheimer's [1]	2014-2016	$39.0	209	73
Peer Reviewed Cancer	2009-2016	$199.8	3,332	412
Peer Reviewed Medical	1999-2006, 2008-2016	$1,370.7	10,079	983
Peer Reviewed Orthopaedic	2009-2016	$308.5	1,052	236
Prostate Cancer	1997-2016	$1,530.0	17,743	3,158
Reconstructive Transplant	2015-2016	$27.0	236	47
Spinal Cord Injury	2009-2016	$189.7	892	192
Tick-Borne Disease	2016	$5.0	56	7
Trauma Clinical	2014, 2016	$15.0	2	1
Tuberous Sclerosis	2002-2006, 2008-2016	$65.0	641	139
Vision	2013-2016	$38.9	220	52
Miscellaneous				23
Additional Supported DoD Programs/Projects				
Centers of Excellence	2015-2016	$13.8	-	1
Defense Medical Research and Development [2]	2010-2016	$599.6	1,421	451
Defense Medical Research and Development CSI Restoral [3]	2015-2016	$85.8	-	58
Psychological Health/Traumatic Brain Injury	2007, 2009-2016	$889.7	3,424	512
Rapid Innovation Fund	2011-2015	$35.7	-	15
Small Business Innovation Research/Small Business Technology Transfer	2014-2016	$29.6	71	147
Vision Prosthesis	2015-2016	$1.2	-	3
Other Submission Processes				
MRMC - BAA[5]			300	
Total		**$10,803.8**	**108,031**	**15,689**

[1] Includes awards transitioned to CDMRP with the merger.

[2] Includes 2013-2015 Clinical Research Intramural Initiative (CRII) and 2010 Chiropractic Clinical Trials.

[3] Includes 2016 Clinical Research Intramural Initiative (CRII).

[4] Breast Cancer Research Semipostal funds applications received and reviewed by the Breast Cancer Research Program. BCRS contributed to 63 awards; 45 fully funded and 18 partially funded.

[5] CDMRP manages the application receipt and review process for the USAMRMC Broad Agency Announcement. Proposals that are funded are counted in the program that provided the funding. Of the 156 applications received, CDMRP funded 30.

Appendix B: FY16–FY17

Table B-1. FY2016-2017 Alcohol and Substance Abuse Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$4.0M** for Alcohol and Substance Abuse Research	**Withholds** USAMRMC: $59,743 **Management Costs** $212,657 5.40%	**Research** Consortium Award: $3,727,600
	Total: $4.0M	**Total: $272,400**	**Total: $3,727,600**
2017	**$4.0M** for Alcohol and Substance Abuse Research	**Withholds** USAMRMC: $57,975 SBIR/STTR: $135,000 **Budgeted Management Costs** $265,025 7%	**Research** Budgeted Peer-Reviewed Research: $3,542,000
	Total: $4.0M	**Total: $458,000**	**Total: $3,542,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-2. FY2016-2017 Amyotrophic Lateral Sclerosis Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$7.5M** for Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $112,417 **Management Costs** $507,284 6.87%	**Research** Therapeutic Idea Award: $4,911,104 Therapeutic Development Award: $1,969,195
	Total: $7.5M	**Total: $619,701**	**Total: $6,880,299**
2017	**$7.5M** for Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $108,720 SBIR/STTR: $252,000 **Budgeted Management Costs** $499,280 7%	**Research** Budgeted Peer-Reviewed Research: $6,640,000
	Total: $7.5M	**Total: $860,000**	**Total: $6,640,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-3. FY2016-2017 Autism Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$7.5M** for Autism Research	**Withholds** USAMRMC: $164,601 **Management Costs** $446,857 6.09%	**Research** Idea Development: $3,131,841.00 Clinical Trial Award: $3,756,701.00
	Total: $7.5M	**Total: $611,458**	**Total: $6,888,542**
2017	**$7.5 M** for Autism Research	**Withholds** USAMRMC: $108,720 SBIR/STTR: $252,000 **Budgeted Management Costs** $499,280 7%	**Research** Budgeted Peer-Reviewed Research: $6,640,000
	Total: $7.5M	**Total: $860,000**	**Total: $6,640,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-4. FY2016-2017 Bone Marrow Failure Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$3.0M** for Bone Marrow Failure Research	**Withholds** USAMRMC: $44,643 **Management Costs** $384,719 13.02%	**Research** Idea Development Award - Early Career Investigator: $978,075 Idea Development Award - Established Investigator: 1,592,563
	Total: $3.0M	**Total: $429,362**	**Total: $2,570,638**
2017	**$3.0M** for Bone Marrow Failure Research	**Withholds** USAMRMC: $43,500 SBIR/STTR: $100,000 **Budgeted Management Costs** $198,500 7%	**Research** Budgeted Peer-Reviewed Research: $2,658,000
	Total: $3.0M	**Total: $342,000**	**Total: $2,658,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-5. FY2016-2017 Breast Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$120M** for Breast Cancer Research **$568,671** proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $1,798,250 **Management Costs** $11,409,568 9.62%	**Research** Breakthrough Award Funding Level 1: $7,816,133 Breakthrough Award Funding Level 2: $16,334,445 Breakthrough Award Funding Level 3: $18,335,351 Breakthrough Award Funding Level 1 Partnering PI Option: $8,347,388 Breakthrough Award Funding Level 2 Partnering PI Option: $18,189,587 Breakthrough Award Funding Level 3 Partnering PI Option: $2,500,000 Breakthrough Award Funding Level 4: $15,740,058 Breakthrough Award Funding Level 4 Clinical Trial: $1,500,000.00 Breakthrough Fellowship Award: $2,768,687.00 Broad Agency Announcement for Extramural Research: $460,464.00 Clinical Translational Research Award: $6,480,776.00 Era of Hope Scholar Award: $3,751,197 Transformative Vision Award: $5,136,767
	Total: $120,568,671	**Total: $13,207,818**	**Total: $107,360,853**
2017	**$120M** for Breast Cancer Research **$205,848** proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $1,739,625 SBIR/STTR: $4,025,000 **Budgeted Management Costs** $7,998,875 7%	**Research** Budgeted Peer-Reviewed Research: $106,442,348
	Total: $120,205,848	**Total: $13,763,500**	**Total: $106,442,348**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-6. FY2016-2017 Duchenne Muscular Dystrophy Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$3.2M** for Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $41,757 **Management Costs** $181,208 5.74%	**Research** Investigator Initiated Research: $2,495,785 Career Development Award: $481,250
	Total: $3.2M	**Total: $222,965**	**Total: $2,977,035**
2017	**$3.2M** for Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $46,395 SBIR/STTR: $107,000 **Budgeted Management Costs** $211,605 7%	**Budgeted Research** Budgeted Peer-Reviewed Research: $2,835,000
	Total: $3.2M	**Total: $365,000**	**Total: $2,835,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-7. FY2016-2017 Epilepsy Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$7.5M** for Epilepsy Research	**Withholds** USAMRMC: $112,500 **Management Costs** $524,636 7.10%	**Research** Idea Development Award - Funding Level 1: $3,175,114.46 Idea Development Award - Funding Level 2: $3,687,750.00
	Total: $7.5M	**Total: $637,136**	**Total: $6,862,864**
2017	**$7.5M** for Epilepsy Research	**Withholds** USAMRMC: $108,720 SBIR/STTR: $252,000 **Budgeted Management Costs** $499,280 7%	**Research** Budgeted Peer-Reviewed Research: $6,640,000.00
	Total: $7.5M	**Total: $860,000**	**Total: $6,640,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-8. FY2016-2017 Gulf War Illness Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$20M** for Gulf War Illness Research	**Withholds** USAMRMC: $299,911 **Management Costs** $749,521 3.58%	**Research** Clinical Partnership Award: $854,011 Consortium Award: $260,446 Gulf War Illness Epidemiology Research Award: $962,408 Investigator-Initiated Focused Research Award: $4,925,420 Investigator Initiated Research Award: $510,388 Investigator-Initiated Research Expansion Award - Collaborative Option: $54,500 New Investigator Award: $7,677,838 New Investigator Award - Transitioning Postdoctoral Fellow: $205,000 Treatment Evaluation Award: $3,500,557
	Total: $20M	**Total: $1,049,432**	**Total: $18,950,568**
2017	**$20M** for Gulf War Illness Research	**Withholds** USAMRMC: $290,760.00 SBIR/STTR: $616,000 **Budgeted Management Costs** $1,333,240 7%	**Research** Budgeted Peer-Reviewed Research: $17,760,000.00
	Total: $20M	**Total: $2,240,000**	**Total: $17,760,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-9. FY2017 Hearing Restoration Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2017	**$10M** for Hearing Restoration Research	**Withholds** USAMRMC: $335,000 SBIR/STTR: $144,975 **Budgeted Management Costs** $670,025 7%	**Research** Budgeted Peer-Reviewed Research: $8,850,000
	Total: $10M	**Total: $1,150,000**	**Total: $8,850,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-10. FY2016-2017 Joint Warfighter Medical Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$50M** for Joint Warfighter Medical Research	**Withholds** USAMRMC: $748,307 **Budgeted Management Costs** $2,149,232 4.36%	**Budgeted Research** Peer-Reviewed Research: $47,102,462
	Total: $50M	**Total: $2,897,538**	**Total: $47,102,462**
2017	**$50M** for Joint Warfighter Medical Research	**Withholds** USAMRMC: $725,385 SBIR/STTR: $1,641,000 **Budgeted Management Costs** $3,332,615 7%	**Budgeted Research** Budgeted Peer-Reviewed Research: $44,301,000.00
	Total: $50M	**Total: $5,699,000**	**Total: $44,301,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-11. FY2017 Kidney Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2017	**$10M** for Kidney Cancer Research	**Withholds** USAMRMC: $335,000 SBIR/STTR: $144,975 **Budgeted Management Costs** $952,003 10%	**Research** Budgeted Peer-Reviewed Research: $8,568,023
	Total: $10M	**Total: $1,431,978**	**Total: $8,568,023**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-12. FY2016-2017 Lung Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$12M** for Lung Cancer Research	**Withholds** USAMRMC: $170,884 **Management Costs** $845,863 7.15%	**Research** Career Development Award: $775,012 Concept Award: $1,992,578 Idea Development Award-Established Investigator: $2,842,069 Idea Development Award New Investigator: $2,189,921 Investigator-Initiated Translational Research Award: $3,183,673
	Total: $12M	**Total: $1,016,747**	**Total: $10,983,253**
2017	**$12M** for Lung Cancer Research	**Withholds** USAMRMC: $173,955 SBIR/STTR: $403,000 **Budgeted Management Costs** $793,045 7%	**Research** Budgeted Peer-Reviewed Research: $10,630,000
	Total: $12M	**Total: $1,370,000**	**Total: $10,630,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-13. FY2017 Lupus Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2017	**$5M** for Lupus Research	**Withholds** USAMRMC: $72,480 SBIR/STTR: $168,000 **Budgeted Management Costs** $334,520 7%	**Research** Budgeted Peer-Reviewed Research: $4,425,000
	Total: $5M	**Total: $575,000**	**Total: $4,425,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-14. FY2016-2017 Military Burn Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$8M** for Military Burn Research	**Withholds** USAMRMC: $280,000 **Budgeted Management Costs** $243,960 3.16%	**Research** Peer-Reviewed Research: $2,030,312 Burn Injuries Research Award - Funding Level 1: $175,424 Burn Injuries Research Award - Funding Level 2: $3,563,907 Clinical Study Award: $1,706,397
	Total: $8M	**Total: $523,960**	**Total: $7,476,040**
2017	**$8M** for Military Burn Research	**Withholds** USAMRMC: $280,000 **Budgeted Management Costs** $540,000 7%	**Research** Budgeted Peer-Reviewed Research: $7,180,000
	Total: $8M	**Total: $820,000**	**Total: $7,180,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-15. FY2016-2017 Multiple Sclerosis Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$6.0M** for Multiple Sclerosis Research	**Withholds** USAMRMC: $90,000 **Management Costs** $447,267 7.57%	**Research** Exploration - Hypothesis Development Award: $1,393,020 Investigator-Initiated Partnership Award: $3,115,141.00 Pilot Clinical Trial Award: $954,572.00
	Total: $6M	**Total: $537,267**	**Total: $5,462,733**
2017	**$6.0M** for Multiple Sclerosis Research	**Withholds** USAMRMC: $86,985 SBIR/STTR: $201,000 **Budgeted Management Costs** $398,000 7%	**Research** Budgeted Peer-Reviewed Research: $5,314,015
	Total: $6M	**Total: $685,985**	**Total: $5,314,015**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-16. FY2016-2017 Neurofibromatosis Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$15M** for Neurofibromatosis Research	**Withholds** USAMRMC: $525,000 **Management Costs** $522,001 3.61%	**Research** Clinical Consortium Award: $5,591,187 Clinical Trial Award: $3,228,969 Exploration - Hypothesis Development Award: $323,422 Investigator-Initiated Research Award: $3,474,583 New Investigator Award: $1,334,838
	Total: $15M	**Total: $1,047,001**	**Total: $13,952,999**
2017	**$15M** for Neurofibromatosis Research	**Withholds** USAMRMC: $525,000 **Budgeted Management Costs** $996,000 7%	**Research** Budgeted Peer-Reviewed Research: $13,479,000
	Total: $15M	**Total: $1,521,000**	**Total: $13,479,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-17. FY2016-2017 Orthotics and Prosthetics Outcomes Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$10M** for Orthotics and Prosthetics Outcomes Research	**Withholds** USAMRMC: $145,310 **Management Costs** $430,409 4.37%	**Research** Orthotics Outcomes Research Award - Funding Level 3: $1,998,325 Prosthetics Outcomes Research Award - Funding Level 1: $743,366 Prosthetics Outcomes Research Award - Funding Level 2: $3,629,970 Prosthetics Outcomes Research Award - Funding Level 3: $3,052,620
	Total: $10M	**Total: $575,719**	**Total: $9,424,281**
2017	**$10M** for Orthotics and Prosthetics Outcomes Research	**Withholds** USAMRMC: $144,975 SBIR/STTR: $335,000 **Budgeted Management Costs** $665,025 7%	**Research** Budgeted Peer-Reviewed Research: $8,855,000
	Total: $10M	**Total: $1,145,000**	**Total: $8,855,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-18. FY2016-2017 Ovarian Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$20M** for Ovarian Cancer Research	**Withholds** USAMRMC: $299,434 **Management Costs** $1,212,119 6.15%	**Research** Clinical Development Award: $3,863,560 Investigator-Initiated Research Award: $6,114,913 Outcomes Consortium Award: $5,321 Ovarian Cancer Academy - Early-Career Investigator Award: $2,339,417 Pilot Award: $4,267,442 Teal Expansion Award: $1,897,794
	Total: $20M	**Total: $1,511,553**	**Total: $18,488,447**
2017	**$20M** for Ovarian Cancer Research	**Withholds** USAMRMC: $289,935 SBIR/STTR: $671,000 **Budgeted Management Costs** $1,329,065 7%	**Research** Budgeted Peer-Reviewed Research: $17,710,000
	Total: $20M	**Total: $2,290,000**	**Total: $17,710,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-19. FY2016-2017 Parkinson's Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$16M** for Parkinson's Research	**Withholds** USAMRMC: $513,343 **Management Costs** $1,003,554 6.48%	**Research** Focused Idea Award: $2,114,638 Impact Award: $12,368,466
	Total: $16M	**Total: $1,516,896**	**Total: $14,483,104**
2017	**$16M** for Parkinson's Research	**Withholds** USAMRMC: $560,000 **Budgeted Management Costs** $1,080,000 7%	**Research** Budgeted Peer-Reviewed Research: $14,360,000
	Total: $16M	**Total: $1,640,000**	**Total: $14,360,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
Percent of management costs=management costs/(appropriation-withholds)

Table B-20. FY2016-2017 Peer Reviewed Alzheimer's Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$15M** for Peer Reviewed Alzheimer's Research	**Withholds** USAMRMC: $225,000 **Management Costs** $831,364 5.63%	**Research** Convergence Science Research Award: $5,627,758 Epidemiology of Military Risk Factors Award: $2,480,268 Quality of Life Research Award - Clinical Trial: $158,811 Quality of Life Research Award - Funding Level 1: $2,489,042.00 Quality of Life Research Award - Funding Level 2: $1,887,757 Translational Research Partnership Award: $1,300,000
	Total: $15M	**Total: $1,056,364**	**Total: $13,943,636**
2017	**$15M** for Peer Reviewed Alzheimer's Research	**Withholds** USAMRMC: $217,455 SBIR/STTR: $503,000 **Budgeted Management Costs** $999,545 7%	**Research** Budgeted Peer-Reviewed Research: $13,280,000
	Total: $15M	**Total: $1,720,000**	**Total: $13,280,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-21. FY2016-2017 Peer Reviewed Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$50M** for Peer-Reviewed Cancer Research	**Withholds** USAMRMC: $718,341 **Management Costs** $2,649,547 5.38%	**Research** Bladder Cancer: $5,410,134 Colorectal Cancers: $2,284,430 Immunotherapy: $8,159,874 Kidney Cancer: $2,729,013 Listeria Vaccine for Cancer: $567,969 Liver Cancer: $4,280,883 Lymphoma: $1,206,386 Melanoma and Other Skin Cancers: $5,657,337 Mesothelioma: $2,104,934 Neuroblastoma: $556,500 Pancreatic Cancer: $3,570,581 Pediatric Brain Tumors: $3,982,962 Stomach Cancer: $6,121,109
	Total: $50M	**Total: $3,367,888**	**Total: 46,632,112**
2017	**$60M** for Peer-Reviewed Cancer Research	**Withholds** USAMRMC: $869,805 SBIR/STTR: $2,013,000 **Budgeted Management Costs** $3,984,195 7%	**Research** Budgeted Peer-Reviewed Research: $53,133,000
	Total: $60M	**Total: $6,867,000**	**Total: $53,133,000**

The following abbreviations are used for withholds:

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SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer

Percent of management costs=management costs/(appropriation-withholds)

FY2016 Peer Reviewed Cancer Research Program: The agreement provides $50,000,000 for a peer-reviewed cancer research program to research cancers not addressed in the breast, prostate, ovarian, and lung cancer research programs currently executed by the Department of Defense. The funds provided in the peer-reviewed cancer research program are directed to be used to conduct research in the following areas: bladder cancer, colorectal cancer, immunotherapy, kidney cancer, listeria vaccine for cancer, liver cancer, lymphoma, melanoma and other skin cancers, mesothelioma, neuroblastoma, pancreatic cancer, pediatric brain tumors, and stomach cancer.

Table B-22. FY2016-2017 Peer Reviewed Medical Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$278.7M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $4,180,500 **Management Costs** $14,650,054 5.34%	**Research** Acute Lung Injury: $15,532,533 Antimicrobial Resistance: $10,859,386 Congenital Heart Disease: $19,156,631 Constrictive Bronchiolitis: $1,836,817 Diabetes: $12,765,104 Dystonia: $2,596,956 Emerging Infectious Diseases: $4,424,743 Focal Segmental Glomerulosclerosis: $2,844,942 Fragile X Syndrome: $7,215,740 Hepatitis B: $1,664,746 Hydrocephalus: $4,156,715 Inflammatory Bowel Disease: $5,581,168 Influenza: $16,038,326 Interstitial Cystitis: $350,000 Lupus: $2,126,098 Malaria: $8,101,272 Mitochondrial Disease: $9,380,478 Nanomaterials for Bone Regeneration: $604,846 Non-Opioid Pain Management: $23,798,082 Pancreatitis: $4,083,405 Pathogen-Inactivated Dried Plasma: $4,672,637 Polycystic Kidney Disease: $5,625,249 Post-Traumatic Osteoarthritis: $4,064,345 Psychotropic Medications: $6,579,356 Pulmonary Fibrosis: $22,530,064 Respiratory Health: $4,279,047 Rett Syndrome: $1,861,186 Sleep Disorders: $2,513,555 Tinnitus: $2,263,597 Tuberculosis: $16,628,103 Vaccine Development for Infectious Disease: $8,256,001 Vascular Malformations: $11,718,490 Women's Heart Disease: $15,759,828
	Total: $278.7M	**Total: $18,830,554**	**Total: $259,869,446**
2017	**$300M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $4,350,690 SBIR/STTR: $9,954,000 **Budgeted Management Costs** $19,945,310 7%	**Research** Budgeted Peer-Reviewed Research: $265,750,000
	Total: $300M	**Total: $34,250,000**	**Total: $265,750,000**

The following abbreviations are used for withholds:

USAMRMC: US Army Medical Research and Materiel Command

Percent of management costs=management costs/(appropriation-withholds)

SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer

FY2016 Peer Reviewed Medical Research Program: The agreement provides $278,700,000 for a peer-reviewed medical research program. The Secretary of Defense, in conjunction with the Service Surgeons General, is directed to select medical research projects of clear scientific merit and direct relevance to military health. Research areas considered under this funding are restricted to the following areas: acute lung injury, antimicrobial resistance, chronic migraine and post-traumatic headache, congenital heart disease, constrictive bronchioltis, diabetes, dystonia, emerging infectious diseases, focal segmental glomerulosclerosis, Fragile X syndrome, hepatitis B, hereditary angiodema, hydrocephalus, inflammatory bowel disease, influenza, integrative medicine, interstitial cystitis, lupus, malaria, metals toxicology, mitochondrial disease, nanomaterials for bone regeneration, non-opioid pain management, pancreatitis, pathogen-inactivated dried plasma, polycystic kidney

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disease, post-traumatic osteoarthritis, psychotropic medications, pulmonary fibrosis, respiratory health, Rett syndrome, rheumatoid arthritis, scleroderma, sleep disorders, tinnitus, tuberculosis, vaccine development for infectious disease, vascular malformations, and women's heart disease.

FY2017 Peer Reviewed Medical Research Program: The agreement provides $300,000,000 for a peer-reviewed medical research program. The Secretary of Defense, in conjunction with the Service Surgeons General, is directed to select medical research projects of clear scientific merit and direct relevance to military health. Research areas considered under this funding are restricted to the following areas: acute lung injury, antimicrobial resistance, arthritis, burn pit exposure, chronic migraine and post-traumatic headache, congenital heart disease, constrictive bronchiolitis, diabetes, diarrheal diseases, dystonia, early trauma thermal regulation, eating disorders, emerging infectious diseases, epidermolysis bullosa, focal segmental glomerulosclerosis, Fragile X syndrome, Guillain-Barré syndrome, hepatitis B and C, hereditary angioedema, hydrocephalus, immunomonitoring of intestinal transplants, inflammatory bowel diseases, influenza, integrative medicine, interstitial cystitis, malaria, metals toxicology, mitochondrial disease, musculoskeletal disorders, nanomaterials for bone regeneration, non-opioid pain management, pancreatitis, pathogen-inactivated dried cyroprecipitate, polycystic kidney disease, post-traumatic osteoarthritis, pulmonary fibrosis, respiratory health, Rett syndrome, rheumatoid arthritis, scleroderma, sleep disorders, spinal muscular atrophy, sustained-release drug delivery, tinnitus, tuberculosis, vaccine development for infectious disease, vascular malformations, and women's heart disease.

Table B-23. FY2016-2017 Peer Reviewed Orthopaedic Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $448,141 **Management Costs** $1,562,141 5.29%	**Research** Applied Research Award: $3,910,639.00 Applied Research Award - Funding Level 1: $500,000.00 Clinical Translational Research Award: $5,875,870.00 Clinical Trial Award: $10,001,508.16 Expansion Award: $2,101,671.00 Integrated Clinical Trial Award: $4,476,920.00 Orthopaedic Care and Rehabilitation Consortium Award: $1,123,110
	Total: $30M	**Total: $2,010,282**	**Total: $27,989,718**
2017	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $434,910 SBIR/STTR: $1,006,000 **Budgeted Management Costs** $2,000,000 7%	**Research** Budgeted Peer-Reviewed Research: $26,559,090
	Total: $30M	**Total: $3,440,910**	**Total: $26,559,090**

The following abbreviations are used for withholds:

USAMRMC: US Army Medical Research and Materiel Command

SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer

Percent of management costs=management costs/(appropriation-withholds)

Table B-24. FY2016-2017 Prostate Cancer Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$80M** for Prostate Cancer Research	**Withholds** USAMRMC: $1,207,750 **Management Costs** $4,674,250 5.93%	**Research** Clinical Consortium Award: $2,996,953 Clinical Consortium Research Site Award: $2,068,764 Early Investigator Research Award - Postdoctoral: $2,950,844 Early Investigator Research Award - Predoctoral: $466,074 Health Disparity Research Award - Established Investigator: $5,002,581 Health Disparity Research Award - Established Investigator with Qualified Collaborator Option: $878,593 Health Disparity Research Award - New Investigator: $1,242,951 Idea Development Award - Established Investigator: $17,846,135 Idea Development Award - Established Investigator - Partnering PI Option: $15,540,723 Idea Development Award - New Investigator: $4,015,062 Idea Development Award- Established Investigator: $948,867 Impact Award: $2,046,017 Impact Award - Partnering PI Option: $12,931,259 Physician Research Award: $5,183,177
	Total: $80M	**Total: 5,882,000**	**Total: $74,118,000**
2017	**$90M** for Prostate Cancer Research	**Withholds** USAMRMC: $1,304,715 SBIR/STTR: $3,019,000 **Budgeted Management Costs** $5,900,000 7%	**Research** Budgeted Peer-Reviewed Research: $79,776,285
	Total: $90M	**Total: 10,223,715.00**	**Total: $79,776,285**

The following abbreviations are used for withholds:

USAMRMC: US Army Medical Research and Materiel Command

SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer

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Table B-25. FY2016-2017 Reconstructive Transplant Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$12M** for Reconstructive Transplant Research	**Withholds** USAMRMC: $176,745 **Management Costs** $561,900 4.75%	**Research** Concept Award: $1,354,650 Investigator-Initiated Research Award: $5,053,369 Preclinical Studies Option: $270,212 Qualitative Research Award: $1,583,942 Technology Development Award: $2,999,182
	Total: $12M	**Total: $738,645**	**Total: $11,261,355**
2017	**$12M** for Reconstructive Transplant Research	**Withholds** USAMRMC: $173,955 SBIR/STTR: $403,000 **Budgeted Management Costs** $798,045 7%	**Research** Budgeted Peer-Reviewed Research: $10,625,000
	Total: $12M	**Total: $1,375,000**	**Total: $10,625,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds).

Table B-26. FY2016-2017 Spinal Cord Injury Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$30M** for Spinal Cord Injury Research	**Withholds** USAMRMC: $449,623 **Management Costs** $1,014,008 3.43%	**Research** Clinical Research Development Award: $256,373 Clinical Trial Award: $5,038,259 Investigator-Initiated Research Award: $9,289,215 Qualitative Research Award: $3,214,799 Translational Research Award: $10,737,723
	Total: $30M	**Total: $1,463,631**	**Total: $28,536,369**
2017	**$30M** for Spinal Cord Injury Research	**Withholds** USAMRMC: $434,910 SBIR/STTR: $1,006,000 **Budgeted Management Costs** $1,999,136 7%	**Research** Budgeted Peer-Reviewed Research: $26,559,954
	Total: $30M	**Total: $3,440,046**	**Total: $26,559,954**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-27. FY2016-2017 Tick-Borne Disease Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	$5M **for Tick-Borne Disease Research**	**Withholds** USAMRMC: $75,000 **Management Costs** $321,577 6.53%	**Research** Idea Award - Established Investigator: $771,745 Idea Award - New Investigator: $386,325 Investigator-Initiated Research Award: $3,445,353
	Total: $5M	**Total: $396,577**	**Total: $4,603,423**
2017	**$5M** for Tick-Borne Disease Research	**Withholds** USAMRMC: $72,480 SBIR/STTR: $168,000 **Budgeted Management Costs** $329,520 7%	**Research** Budgeted Peer-Reviewed Research: $4,430,000
	Total: $5M	**Total: $570,000**	**Total: $4,430,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-28. FY2016-2017 Trauma Clinical Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$10M** for Trauma Clinical Research	**Withholds** USAMRMC: $148,389 **Management Costs** $654,883 6.65%	**Research** Linking Investigations in Trauma & Emergency Services: $9,196,728
	Total: $10M	**Total: $803,272**	**Total: $9,196,728**
2017	**$10M** for Trauma Clinical Research	**Withholds** USAMRMC: $144,975 SBIR/STTR: $335,000 **Budgeted Management Costs** $665,025 7%	**Research** Budgeted Peer-Reviewed Research: $8,855,000
	Total: $10M	**Total: $1,145,000**	**Total: $8,855,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-29. FY2016-2017 Tuberous Sclerosis Complex Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$6M** for Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $88,949 **Management Costs** $416,627 7.05%	**Research** Exploration - Hypothesis Development Award: $872,649 Idea Development Award - Established Investigator: $2,643,641 Idea Development Award - New Investigator: $1,458,034 Postdoctoral Development Award: $520,100
	Total: $6M	**Total: $505,576**	**Total: $5,494,424**
2017	**$6M** for Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $86,985 SBIR/STTR: $201,000 **Budgeted Management Costs** $398,000 7%	**Research** Budgeted Peer-Reviewed Research: $5,314,015
	Total: $6M	**Total: $685,985**	**Total: $5,314,015**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-30. FY2016-2017 Vision Research Program Congressional Language and Appropriations, Withholds and Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2016	**$10M** for Vision Research	**Withholds** USAMRMC: $149,952 **Management Costs** $1,436,053 14.58%	**Research** Technology/Therapeutic Development Award: $5,878,091 Clinical Trial Award: $2,535,904
	Total: $10M	**Total: $1,586,005**	**Total: $8,413,995**
2017	**$15M** for Vision Research	**Withholds** USAMRMC: $217,455 SBIR/STTR: $503,000 **Budgeted Management Costs** $999,545 7%	**Research** Budgeted Peer-Reviewed Research: $13,280,000
	Total: $15M	**Total: $1,720,000**	**Total: $13,280,000**

The following abbreviations are used for withholds:
USAMRMC: US Army Medical Research and Materiel Command
SBIR/STTR: Small Business Innovation Research/Small Business Technology Transfer
Percent of management costs=management costs/(appropriation-withholds)

Table B-31. FY2016 Defense Medical Research and Development Restoral Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Management Costs	Investment Strategy
2016	**$42.4M** for Defense Medical Research and Development from the Guidance for the Development of the Force Funding	**Management Costs** $2,960,892.81 6.99%	**Research** Clinical Research Intramural Initiative: $3,808,408 Medical Simulation and Information Sciences Awards: $6,506,489 Military Operational Medicine Awards: $4,468,566 Combat Casualty Care Awards: $8,852,000 Clinical and Rehabilitative Medicine Awards: 15,789,707
	Total: $42.4M	**Total: $2,960,892.81**	**Total: $39,425,171**

Percent of management costs=management costs/CDMRP executed funds

Table B-32. FY2016 Defense Medical Research and Development Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Management Costs	Investment Strategy
2016	**$109.6M** for Defense Medical Research and Development from the Guidance for the Development of the Force Funding	**Management Costs** $8,110,396 7.40%	**Research** Medical Simulation and Information Sciences Awards: $27,495,549 Military Infectious Diseases Awards: $3,419,180 Military Operational Medicine Awards: $15,490,627 Combat Casualty Care Awards: $34,293,172 Clinical and Rehabilitative Medicine Awards: $20,778,022
	Total: $109.6M	**Total: $8,110,396**	**Total: $101,476,550**

Percent of management costs=management costs/CDMRP executed funds

Table B-33. FY2016 Psychological Health/Traumatic Brain Injury Research Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Management Costs	Investment Strategy
2016	**$81.5M** for Psychological Health and Traumatic Brain Injury Research	**Management Costs** $6,124,168 8%	**Research** Broad Agency Announcement: $16,716,422 Broad Agency Announcement for Extramural Medical Research: $13,087,538 Clinical Trial Award: $793,983 Neurosensory and Rehabilitation Research Award- Applied Research Option: $4,000 Psychological Health Research Award- Partner PI Option: $280,000 Traumatic Brain Injury Endpoints Development Award: $4,109,805 Implementation Science: $8,265,060 Prolonged Field Care Research Award - Funding Level 2 - Preclinical Research: $4,386,506 Prolonged Field Care Research Award - Funding Level 1 - Preclinical Research: $3,137,858 Prolonged Field Care Research Award - Funding Level 1 - Clinical Research: $1,482,841 Cognitive Resilience and Readiness Research Award - Applied Research: $2,240,574 Traumatic Brain Injury/Post-Traumatic Stress Disorder - Clinical Trial Award: $184,903 Psychological Health and Traumatic Brain Injury: $185,104 Applied Psychological Health Award with Clinical Trial - Partnering Option: $814,367 Complex Traumatic Brain Injury Rehabilitation Research Award - Funding Level 2 - Clinical Trial: $13,149,366 Complex Traumatic Brain Injury Rehabilitation Research Award - Funding Level 1:$1,832,899 Complex Traumatic Brain Injury Rehabilitation Research Award - Funding Level 2:$3,168,655 Complex Traumatic Brain Injury Rehabilitation: $1,499,715 Applied Research and Advanced Technology Development Award: $15,097
	Total: $81.5M	**Total: $6,124,168**	**Total: $75,354,693**

Percent of management costs=management costs/CDMRP executed funds

Table B-34. FY2016 Vision Prosthesis Pilot Study Award
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Management Costs	Investment Strategy
2016	**$222.2K** for Vision Prosthesis Research	**Management Costs**	**Research** Vision Prosthesis Pilot Study Award: $222,248
	Total: $222.2K	**Total:**	**Total: $222,248**

Table B-35. FY2016 Small Business Innovation Research/Small Business Technology Transfer
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	CDMRP Executed Funds	Management Costs	Investment Strategy
2016	**$23.3M** for Small Business Innovation Research/ Small Business Technology Transfer Research	**Management Costs**	**Research** Small Business Innovation Research: $19,379,222 Small Business Technology Transfer: $3,874,104
	Total: $23.3M	**Total:**	**Total: 23,253,325**

Appendix C: Breast Cancer Research Semipostal Awards FY99–FY16

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY99	Roger Daly	$283,649	Garvan Institute	Identification of Novel Prognostic Indicators for Breast Cancer through Analysis of the EMS1/Cortactin Signaling Pathway
	Thomas Deuel	$5,000[1]	Scripps Institute	Novel Angiogenic Domains: Use in Identifying Unique Transforming and Tumor-Promoting Pathways in Human Breast Cancer
	Wolf Heyer	$111,444	University of California, Davis	In Vitro Recombination Activities of the Breast Cancer Predisposition Protein BRCA2
	Elizabeth Musgrove	$222,652	Garvan Institute	Role of Cyclin D1 and p27 in Steroidal Control of Cell Cycle Progression in the Mammary Gland in Vivo
	Sudhir Shah	$279,000	University of Arkansas	Role of a Novel Matrix-Degrading Metalloproteinase in Breast Cancer Invasion
	Lihong Wang	$317,510	Texas A&M University	Scanning Microwave-Induced Acoustic Tomography
	Michael 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
	Daniel Wreschner	$225,000	Tel Aviv University	Analysis of the Secreted Novel Breast Cancer-Associated MUC1/Zs Cytokine
FY00	Eileen Adamson	$578,183	Burnham Institute	Cripto: A Target for Breast Cancer Treatment
	Emmanuel Akporiaye	$454,500	University of Arizona	Tumor-Mediated Suppression of Dendritic Cell Vaccines
	Linda Penn	$296,142	University of Toronto	Exploiting the Novel Repressed Transactivator Assay to Identify Protein Interactors and Peptide Inhibitors of the Myc Oncoprotein
FY01	Qiuyin Cai	$560,144	Vanderbilt University	Genetic Polymorphisms, Mitochondrial DNA Damage, and Breast Cancer Risk
	Kermit Carraway	$427,225	University of California, Davis	Identification of a Functional Human Homolog of Drosophila Kek1, an Inhibitor of Breast Tumor Cell Growth
	Preet Chaudhary	$312,000	University of Texas Southwest Medical Center	The Role of Ectodysplasin A (EDA) and Its Receptors in the Pathogenesis of Breast Cancer
	Robert Geahlen	$425,425	Purdue University	Characterization of Syk in Breast Carcinoma Cells
	William Rosner	$454,181	St. Luke's-Roosevelt Hospital Center	Autocrine and Paracrine Control of Breast Cancer Growth by Sex Hormone-Binding Globulin
FY02	Q. Ping 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
	Andrew Godwin	$504,000	Fox Chase Cancer Center	The Nuclear Death Domain Protein p84N5, a Candidate Breast Cancer Susceptibility Gene
	Archibald Perkins	$490,500	Yale University	Rapid Genomic Approach to Cancer Gene Discovery in Breast Cancer

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY03	Gina 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
	Rudolf 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)
	Paul Yaswen	$508,680	Lawrence Berkeley National Laboratory	Functional Analysis of BORIS, a Novel DNA-Binding Protein
	Elad Ziv	$767,171	University of California, San Francisco	Admixture and Breast Cancer Risk among Latinas
FY04	Mina Bissell	$386,569	Lawrence Berkeley National Laboratory	Use of HA-Metal Nanoparticles to Identify and Characterize Tumorigenic Progenitor Cell Subsets in Breast Tumors
	Christina 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
	Todd Giorgio	$453,000	Vanderbilt University	Surface Functionalized Nanoparticles and Nanocrystals for Proximity-Modulated, Early Neoplasia Detection, Imaging, and Treatment of Breast Cancer
	Mark Lemmon	$475,500	University of Pennsylvania	Harnessing Novel Secreted Inhibitors of EGF Receptor Signaling for Breast Cancer Treatment
FY05	Kurt Zinn[2]	$436,500	University of Alabama at Birmingham	Novel Screening and Precise Localization of Early Stage Breast Cancer in Animal Model
	Xin-Yun Huang	$483,600	Cornell University, Weill Medical College	Migrastatin Analogues as Potent Inhibitors of Breast Cancer Metastasis
	Yang Liu	$448,500	Ohio State University	Hunting for Novel X-Linked Breast Cancer Suppressor Genes in Mouse and Human
	Jianghong Rao	$468,000	Stanford University	Ribozyme-Mediated Imaging of Oncogene Expression in Breast Tumor Cells
FY06	Gayathri Devi	$155,085[3]	Duke University Medical Center	Modulation of Regulatory T Cells as a Novel Adjuvant for Breast Cancer Immunotherapy
	Amy Lee	$489,000	University of Southern California	A New Mechanism for Estrogen-Starvation Resistance in Breast Cancer
	Yi Li	$438,455	Baylor College of Medicine	The ER/PR Status of the Originating Cell of ER-Negative Breast Cancer
	Shaker Mousa	$377,620	Albany College of Pharmacy	Enhancing the Efficacy of Chemotherapeutic Breast Cancer Treatment with Non-anticoagulant Heparins
	Fraydoon Rastinejad	$454,500	University of Virginia	Structural Characterization of the Interdomain Features of the Estrogen Receptor
FY07	Charlotte Kuperwasser	$817,500	Tufts University	Mechanisms of Breast Cancer Associated with Obesity
	Kimberly Kelly	$244,450[4]	University of Virginia	Genetically Encoded Targeted, Amplifiable, Imaging Agents for Early Detection of Breast Cancer
	Susan Gerbi	$155,550[5]	Brown University	Hormonal Involvement in Breast Cancer Gene Amplification
FY08	Chung Park	$111,663	North Dakota State University	In Utero Exposure to Dietary Methyl Nutrients and Breast Cancer Risk in Offspring
	Maciej Radosz	$528,939	University of Wyoming	Breast Cancer-Targeting Nuclear Drug Delivery Overcoming Drug Resistance for Breast Cancer Therapy
	Ann Hill	$577,500	Oregon Health and Science University	Vaccine Vector for Sustained High-Level Antitumor CTL Response
	Youngjae You	$503,666	University of Oklahoma Health Science Center	Targeted Delivery and Remote-Controlled Release of Chemotherapeutic Agents
	Tiffany 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?

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

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

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

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

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY09	Peggy Reynolds	$730,000[7]	Cancer Prevention Institute of California	Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk
	John Wysolmerski	$620,626	Yale University	Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer
FY10	Pepper Schedin	$368,125[8]	University of Colorado, Denver	The Immune Modulatory Program of Post-Partum Involution Promotes Pregnancy-Associated Breast Cancer
	Anthony 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	Jing Yang	$465,000	University of California, San Diego	Regulation of Breast Cancer Stem Cell by Tissue Rigidity
	Filippo Giancotti	$174,837[11]	Memorial Sloan-Kettering Cancer Center	Autophagy and TGF-Beta Antagonist Signaling in Breast Cancer Dormancy at Premetastatic Sites
FY13	Seth Rubin	$457,075	University of California, Santa Cruz	Inhibition of Retinoblastoma Protein Inhibition
	Geoffrey Luke	$96,992[12]	University of Texas at Austin	Noninvasive Label-Free Detection of Micrometastases in the Lymphatics with Ultrasound-Guided Photoacoustic Imaging
FY14	Dan Shu	$364,343	University of Kentucky	Ultrastable Nontoxic RNA Nanoparticles for Targeting Triple-Negative Breast Cancer Stem Cells
	Leif Ellisen	$93,050[13]	Massachusetts General Hospital	Defining High-Risk Precursor Signaling to Advance Breast Cancer Risk Assessment and Prevention
	Edward Brown	$7,457[14]	University of Rochester	Prediction of Metastasis Using Second Harmonic Generation
	David DeNardo	$7,061[15]	Washington University	Reprogramming the Metastatic Microenvironment to Combat Disease Recurrence
FY15	Ricardo Bonfil	$254,765[16]	Wayne State University	Discoidin Domain Receptors: Novel Targets in Breast Cancer Bone Metastasis
	Carl Maki	$254,765[17]	Rush University Medical Center	Targeting Prolyl Peptidases in Triple-Negative Breast Cancer
FY16	Sridhar Mani	$174,992[18]	Albert Einstein College of Medicine	Inhibition of Microbial Beta-Glucuronidase as a Strategy Toward Breast Cancer Chemoprevention
	Sophie Lelievre	$353,879[19]	Purdue University	Risk-on-a-Chip for Tailored Primary Prevention of Breast Cancers

[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 $331,449; remaining funds were from the FY12 BCRP.
[12]Total award amount was $497,288; remaining funds were from the FY13 BCRP.
[13]Total award amount was $605,208; remaining funds were from the FY14 BCRP.
[14]Total award amount was $216,085; remaining funds were from the FY14 BCRP.
[15]Total award amount was $527,797; remaining funds were from the FY14 BCRP.
[16]Total award amount was $522,715; remaining funds were from the FY15 BCRP.
[17]Total award amount was $581,250; remaining funds were from the FY15 BCRP.
[18]Total award amount was $626,252; remaining funds were from the FY16 BCRP.
[19]Total award amount was $564,673; remaining funds were from the FY16 BCRP.

Appendix D: Acronyms

4AP.....4-Aminopyridine
AAA.....Acquired Aplastic Anemia
ACE2.....Angiotensin-Converting Enzyme 2
AD.....Alzheimer's Disease
ADAPT-MP.....Auto-Diagnostic Adaptive Precison Trainer for Myoelectric Prosthesis Users
ADMET.....Adsorption, Distribution, Metabolism, Excretion, and Toxicity
ADNI.....Alzheimer's Disease Neuroimaging Initiative
ADRD.....Alzheimer's Disease and Related Dementia
AFIRM.....Armed Forces Institute of Regenerative Medicine
AIM.....AZA Immune
ALDH1A1.....Aldehyde Dehydrogenase 1 Family, Member A1
ALS.....Amyotrophic Lateral Sclerosis
ALSRP.....Amyotrophic Lateral Sclerosis Research Program
AMD.....Age-Related Macular Degeneration
Ang-(1-7).....Angiotensin-(1-7)
AR.....Androgen Receptor
ARC.....Advanced Research Core
ARP.....Autism Research Program
ASADRP.....Alcohol and Substance Abuse Disorders Research Program
ASD.....Autism Spectrum Disorder
ASD(HA).....Assistant Secretary of Defense for Health Affairs
ASUD.....Alcohol and Substance Abuse Disorders
AT2.....Angiotensin Type 2 (Receptor)
AUD.....Alcohol Use Disorder
AZA.....5-Azacitidine
B.....Billions
BAA.....Broad Agency Announcement
BADER.....Bridging Advanced Development for Exception Rehabilitation (Consortium)
BC.....Breast Cancer
BCRP.....Breast Cancer Research Program
BCRS.....Breast Cancer Research Semipostal (Program)
BiOM.....BionX Medical Technologies
BMF.....Bone Marrow Failure
BMFRP.....Bone Marrow Failure Research Program
BRCA1.....Breast Cancer 1
CA4.....Combretastatin A4
CAP.....Consortium to Alleviate Post-Traumatic Stress Disorder
CAR.....Chimeric Antigen Receptor
CARE.....Concussion Assessment, Research, and Education (Consortium)
Caspr2.....Contactin-Associated Protein-Like 2
CaSR.....Calcium-Sensing Receptor
CCCRP.....Combat Casualty Care Research Program
CCNE1.....Cyclin E1
CDC.....Centers for Disease Control and Prevention
CDE.....Common Data Element
CDK4/6.....Cyclin-Dependent Kinase 4/6
CDMRP.....Congressionally Directed Medical Research Programs
CENC.....Chronic Effects of Neurotrauma Consortium
COA.....Clinical Outcome Assessment
CRC.....Concussion Research Consortium
CRMRP.....Clinical and Rehabilitative Medicine Research Program
CRPC.....Castration-Resistant Prostate Cancer
CSC.....Clinical Study Core
CSI.....Congressional Special Interest
CT.....Computed Tomography
CTE.....Chronic Traumatic Encephalopathy
CTGF.....Connective Tissue Growth Factor
CURE.....Citizens United for Research in Epilepsy
CYP17A1.....Cytochrome P450 17A1
D.....Drug
DARPA.....Defense Advanced Research Projects Agency
DECAMP.....Detection of Early Lung Cancer Among Military Personnel (Consortium)
DFU.....Diabetic Foot Ulcer
DHA.....Defense Health Agency
DHP.....Defense Health Program
DMD.....Duchenne Muscular Dystrophy
DMDRP.....Duchenne Muscular Dystrophy Research Program
DMRDP.....Defense Medical Research and Development Program
DoD.....Department of Defense
DVBIC.....Defense and Veterans Brain Injury Center
EACE.....Extremity Trauma and Amputation Center of Excellence
EB-COP.....Evidence-Based Clinical Outcome Assessment
eBRAP.....Electronic Biomedical Research Application Portal
ECI.....Early Career Investigator
EFIC.....Exception from Informed Consent
EGS.....Electronic Grants System
EMG.....Electromyography
ER.....Estrogen Receptor
ERP.....Epilepsy Research Program
ESF.....Energy-Storing Foot
F18-FDG.....18F-Fluorodeoxyglucose
FA.....Franconi Anemia
FDA.....US Food and Drug Administration
FITBIR.....Federal Interagency Traumatic Brain Injury Research
fMRI.....Functional Magnetic Resonance Imaging
FRA.....Focused Research Award
FY.....Fiscal Year
GABAB.....Gamma Amino Butyric Acid Type B

GI ..... Gastrointestinal
GLUT1 ..... Glucose Transporter 1
GOG ..... Gynecology Oncology Group
GWI ..... Gulf War Illness
GWIRP ..... Gulf War Illness Research Program
GWVIRP ..... Gulf War Veterans' Illnesses Research Program
HCC ..... Hepatocellular Carcinoma
HER2 ..... Human Epidermal Growth Factor Receptor 2
HGSC ..... High-Grade Serous Carcinoma
HHS ..... US Department of Health and Human Services
HIPAA ..... Health Insurance Portability and Accountability Act
HMD ..... Health and Medicine Division
HRRP ..... Hearing Restoration Research Program
ICE ..... Intra-socket Cooling Element
IFNγ ..... Interferon Gamma
IND ..... Investigational New Drug
IOM ..... Institute of Medicine
IR ..... Infrared Radiation
ITN ..... Institute for Translational Neuroscience
JPC ..... Joint Program Committee
JWMRP ..... Joint Warfighter Medical Research Program
KCRP ..... Kidney Cancer Research Program
LAMC1 ..... Laminin Subunit Gamma-1
LCRP ..... Lung Cancer Research Program
LITES .... Linking Investigations in Trauma and Emergency Services
LKB1 ..... Liver Kinase B1
LLC ..... Limited Liability Company
LRP ..... Lupus Research Program
LTS ..... Long-Term Survivors
M ..... Million
mAb ..... Monoclonal Antibody
MBRP ..... Military Burn Research Program
mCRPC ..... Metastatic Castrate Resistant Prostate Cancer
MDD ..... Materiel Development Decision
MDR ..... Multidrug-Resistant
MDS ..... Myelodysplastic Syndrome
MEK ..... Mitogen-Activated Protein Kinase
METRC .... Major Extremity Trauma and Rehabilitation Consortium (Formerly the Major Extremity Trauma Research Consortium)
MHS ..... Military Health System
MIDRP ..... Military Infectious Diseases Research Program
miR-155 ..... MicroRNA-155
miRNA ..... MicroRNA
MOCOG ..... Multidisciplinary Ovarian Cancer Outcomes Group
MOMRP ..... Military Operational Medicine Research Program
MPNST ..... Malignant Peripheral Nerve Sheath Tumor
MRI ..... Magnetic Resonance Imaging
mRSF ..... Modified Running-Specific Foot
MS ..... Multiple Sclerosis
MSISRP ..... Medical Simulation and Information Sciences Research Program
MSL-GVT ..... Monosodium Luminol-GVT
MSLN ..... Mesothelin
MSRC ..... Military Suicide Research Consortium
MSRP ..... Multiple Sclerosis Research Program
mTBI ..... Mild Traumatic Brain Injury
MTF ..... Military Treatment Facility
mTORC1 ..... Mammalian Target of Rapamycin Complex 1
MTT ..... Microbiota Transfer Therapy
NAP ..... Neuroprotective Peptide
NCAA ..... National Collegiate Athletic Association
NCI ..... National Cancer Institute
NETPR ..... Neurotoxin Exposure Treatment Parkinson's Research
NF ..... Neurofibromatosis
NF1 ..... Neurofibromatosis Type 1
NF2 ..... Neurofibromatosis Type 2
NFCTC ..... Neurofibromatosis Clinical Trials Consortium
NFRP ..... Neurofibromatosis Research Program
NFκB ..... Nuclear Factor Kappa B
NIH ..... National Institutes of Health
NSAID ..... Nonsteroidal Anti-Inflammatory Drug
OASD(HA) ..... Office of the Assistant Secretary of Defense for Health Affairs
OCA ..... Ovarian Cancer Academy
OCCA ..... Ovarian Cancer Consortium Award
OCRCA ... Orthopaedic Care and Rehabilitation Consortium Award
OCRP ..... Ovarian Cancer Research Program
OCT ..... Optical Coherence Tomography
OEF ..... Operation Enduring Freedom
OETRP ..... Orthopaedic Extremity Trauma Research Program
OIF ..... Operation Iraqi Freedom
OP ..... Organophosphate
OPORP ..... Orthotics and Prosthetics Outcome Research Program
ORP ..... Office of Research Protections
PA ..... Program Announcement
PAD ..... Program Area Directorate
PAK1 ..... p21-Activated Kinase 1
PASA ..... Pharmacotherapies for Alcohol and Substance Abuse (Consortium)
Pc ..... Phthalocyanine
PCa ..... Prostate Cancer
PCBN ..... Prostate Cancer Biorepository Network
PCCTC ..... Prostate Cancer Clinical Trials Consortium
PCRP ..... Prostate Cancer Research Program
PD ..... Parkinson's Disease
PD-1 ..... Programmed Cell Death Protein 1
PD-L1 ..... Programmed Cell Death-Ligand 1
PDT ..... Photodynamic Therapy
PDX ..... Patient-Derived Xenograft
PEG ..... Polyethylene Glycol
PET ..... Positron Emission Tomography
PH ..... Psychological Health

PH/TBIRP ..... Psychological Health and Traumatic Brain Injury Research Program
PI ..... Principal Investigator
PI3K ..... Phosphoinositide 3-Kinase
PNES ..... Psychogenic Non-Epileptic Seizures
POMS ..... Pediatric-Onset Multiple Sclerosis
PON1 ..... Paraoxonase 1
PRARP ..... Peer Reviewed Alzheimer's Research Program
PRCRP ..... Peer Reviewed Cancer Research Program
PRMRP ..... Peer Reviewed Medical Research Program
PRORP ..... Peer Reviewed Orthopaedic Research Program
PRP ..... Parkinson's Research Program
PrU ..... Pressure Ulcers
PS ..... Photosensitizer
PS-L-D ..... Photosensitizer Light-Activatable Prodrug
PTE ..... Post-Traumatic Epilepsy
PTH ..... Post-Traumatic Headache
PTHrP ..... Parathyroid Hormone-Related Protein
PTSD ..... Post-Traumatic Stress Disorder
R&A ..... Review and Analysis
R&D ..... Research and Development
RAS ..... Renin-Angiotensin-System
RCC ..... Renal Cell Cancer
RDT&E ..... Research, Development, Test, and Evaluation
RFP ..... Request for Proposals
RHERP ..... Radiation Health Effects Research Program
Rip3 ..... Receptor-Interacting Protein 3
RPE ..... Retinal Pigment Epithelium
RSF-1 ..... Remodeling and Spacing Factor 1
RSI-MRI ..... Restriction Spectrum Imaging-Magnetic Resonance Imaging
RSV ..... Respiratory Syncytial Virus
RTI ..... Research Triangle Institute
RTRP ..... Reconstructive Transplant Research Program
SAR ..... Stereotactic Ablative Radiotherapy
SBIR ..... Small Business Innovative Research
SCI ..... Spinal Cord Injury
SCIRP ..... Spinal Cord Injury Research Program
SEER ..... Surveillance, Epidemiology, and End Results
SGK1 ..... Serum/Glucocorticoid-Regulated Kinase 1
SMAC ..... Second Mitochondria-Derived Activator of Caspases Mimetic
SNCA ..... Alpha-Synuclein
SO ..... Singlet Oxygen
SRF ..... Serum Response Factor
SSc ..... Systemic Sclerosis
STIC ..... Serous Tubal Intraepithelial Carcinoma
STRONG STAR ..... South Texas Research Organizational Network Guiding Studies on Trauma and Resilience
STS ..... Short-Term Survivors
STTR ..... Small Business Technology Transfer
TAPTE ..... Team Approach to the Prevention and Treatment of Post-Traumatic Epilepsy
TBDRP ..... Tick-Borne Disease Research Program
TBI ..... Traumatic Brain Injury
TCC ..... Transition Cell Cancer
TCCC ..... Tactical Combat Casualty Care
TCRP ..... Trauma Clinical Research Program
TED ..... Traumatic Brain Injury Endpoints Development (Initiative)
TET1 ..... Ten-Eleven Translocation Protein 1
TFAOS ..... Transfemoral Amputee Osseointegration Study
TMT ..... Tourniquet Master Training
TNBC ..... Triple-Negative Breast Cancer
TNF ..... Tumor Necrosis Factor
TRA ..... Translational Research Award
TRACK-TBI ..... Transforming Research and Clinical Knowledge in Traumatic Brain Injury
TRL ..... Technology Readiness Level
TSC ..... Tuberous Sclerosis Complex
TSCRP ..... Tuberous Sclerosis Complex Research Program
U2AF1 ..... U2 Small Nuclear RNA Auxiliary Factor 1
UCSD ..... University of California, San Diego
USAISR ..... US Army Institute of Surgical Research
USAMRAA ..... US Army Medical Research Acquisition Activity
USAMRMC ..... US Army Medical Research and Materiel Command
USU ..... Uniformed Services University of the Health Sciences (Formerly USUHS)
VA ..... US Department of Veterans Affairs
VCA ..... Vascularized Composite Allotransplantation
VITAMMINS ..... Virtual Intelligent Tutor for the Andragogy of Military Medicine Integrated Skills
VRP ..... Vision Research Program

For more information, visit: http://cdmrp.army.mil

or contact us at:

usarmy.detrick.medcom-cdmrp.mbx.cdmrp-public-affairs@mail.mil

301-619-7071

September 30, 2017