Congressionally Directed Medical Research Programs

ANNUAL REPORT
SEPTEMBER 30, 2015

CDMRP
Department of Defense





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U.S. Army Medical Research and Materiel Command

Letter from the Director

I cherish the opportunity to serve as the Director of the Congressionally Directed Medical Research Programs (CDMRP), and over the past two years I have been impressed by the unrivaled dedication of our CDMRP team and the commitment of our colleagues and partners to use the resources provided to fund innovative and impactful research. Over the past 22 years, these research efforts have impacted and transformed healthcare for Service Members and the American public.

In all of our endeavors, and specifically through this report, we want to convey to you the transparency of our processes, our partnership throughout the Department of Defense with the Joint Program Committees who set the strategic focus for their scientific domains, our consumers who provide an invaluable perspective as we shape our programs, and the vast scientific community world-wide. The 2015 Annual Report reflects the composite work of our team in partnership with academia, industry, and our consumer representatives.

When reviewing this report, you will see interesting facts, funding profiles, the numbers and types of research projects awarded, specific highlights for each program, and the knowledge and material products which are the fruits of these efforts. What we hope to keep in the forefront every day, as we orchestrate and manage these programs, is the reason for these efforts, to make a difference in the lives of our Service Members, their families, our Veterans, and all who will be touched by the research programs our Congress has entrusted to us.

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

Department of Defense

U.S. Army Medical Research and Materiel Command

Congressionally Directed Medical Research Programs

Annual Report

September 30, 2015

Congressionally Directed Medical Research Programs
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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

Currently funded research programs include:

- Alcohol and Substance Abuse
- Amyotrophic Lateral Sclerosis
- Autism
- Bone Marrow Failure
- Breast Cancer
- Breast Cancer Semipostal
- Defense Medical Research and Development
- Duchenne Muscular Dystrophy
- Epilepsy Research Program
- Gulf War Illness
- Joint Warfighter Medical
- Lung Cancer
- Military Burn
- Multiple Sclerosis
- Neurofibromatosis
- Neurotoxin Exposure Treatment Parkinson's
- Orthotics and Prosthetics Outcomes
- Ovarian Cancer
- Peer Reviewed Alzheimer's
- Peer Reviewed Cancer
- Peer Reviewed Medical
- Peer Reviewed Orthopaedic
- Prostate Cancer
- Psychological Health and Traumatic Brain Injury
- Reconstructive Transplant
- Spinal Cord Injury
- Tuberous Sclerosis Complex
- Vision

History

The Congressionally Directed Medical Research Programs (CDMRP) is a global funding organization for cancer research, military medical research, and other disease- and injury-specific research. The CDMRP represents a unique partnership among the U.S. Congress, the military, and public. The CDMRP implements the investment of core dollars (presidential budget appropriation) and congressionally directed dollars provided to fund groundbreaking, high-impact research awards and contracts.

The CDMRP is located within the Department of Defense (DoD) U.S. Army Medical Research and Materiel Command (USAMRMC). The mission of the USAMRMC 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 the USAMRMC under Military Partnerships on page 11). Since its first appropriation of congressional funding in fiscal year 1992 (FY92), the CDMRP has been responsible for managing more than $9.7 billion (B) in appropriations.

Fiscal Year 2015

A major development for CDMRP in FY15 was the culmination of the merger of execution management activities previously performed by the Telemedicine and Advanced Technology Research Center (TATRC) into CDMRP's research execution and management operations. USAMRMC directed this merger to leverage CDMRP's excellence in review and management of awards with TATRC's exceptional ability to respond to the needs of the military. The result has been a streamlining of consistent processes and electronic tracking of research through the execution process. The new CDMRP greatly expanded with the FY14 programs that transitioned from TATRC and continued

to grow in FY15 with increased congressional appropriations for certain programs, and the addition of two new programs in Epilepsy and Reconstructive Transplant research. Growth over the last 10 years is shown in **Figure 1**.

To clearly define a path forward, CDMRP established new vision and mission statements (see page 1) to reflect its expansion and role as the primary execution management activity for extramural science and technology. Additionally, CDMRP realigned its organizational structure to more effectively execute the expanded mission and manage the significant workload increase in support of the Defense Health Agency (DHA) Joint Program Committees (JPCs) research initiatives.

The CDMRP and USAMRMC have made great strides to streamline processes and increase efficiencies as a result of this merger. All extramural and intramural applications submitted to USAMRMC are now submitted to one electronic portal, through the electronic Biomedical Research Application Portal (eBRAP). Most importantly, all extramural awards are moving toward one electronic management system, the Electronic Grants System (EGS), resulting in better visibility and a more efficient management paradigm for extramurally funded research.

Programs

Highlights of FY14–FY15 programs managed and/or executed by the CDMRP can be found within the program pages in this Annual Report, beginning on page 27. As detailed in **Table 1**, in FY15, the CDMRP completed the execution of FY14 appropriations by processing 838 new awards across 29 programs. In addition, in FY15, the CDMRP initiated the management of $1,024 million (M) across 29 programs.

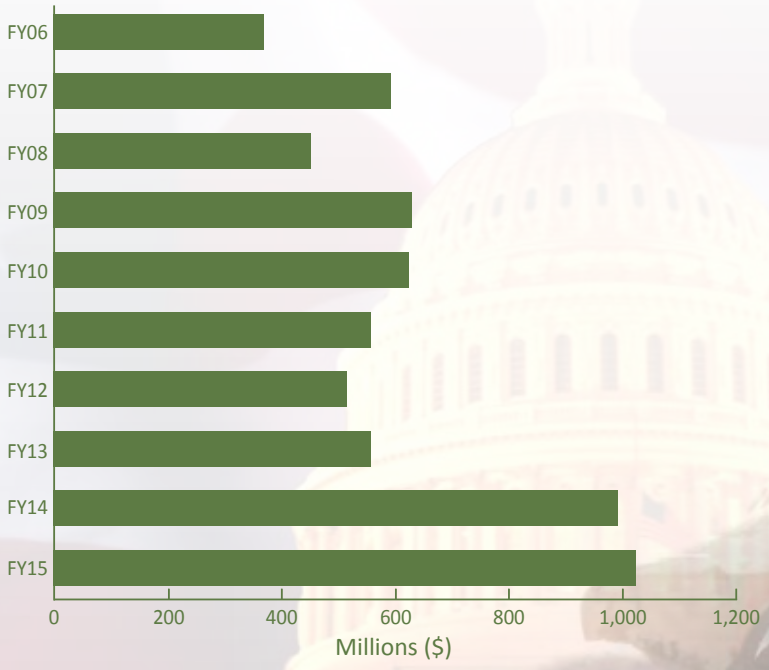


Figure 1. FY06–FY15 Research Funding

Table 1. CDMRP Programs, Appropriations, and Applications Received and Awarded in FY14–FY15

Programs Managed by the CDMRP	FY14				FY15	
	Funds Received (in millions)	Applications Received	Applications Funded	Funding Modifications Completed	Funds Received (in millions)	Applications Received to Date
Alcohol and Substance Abuse Disorders	$4.00	6	1	-	$4.00	TBD
Amyotrophic Lateral Sclerosis	$7.50	57	5	-	$7.50	41
Autism	$6.00	55	10	-	$6.00	TBD
Bone Marrow Failure	$3.20	37	5	-	$3.20	35
Breast Cancer/Breast Cancer Research Semipostal	$120.50	1,789	104	-	$120.54	892
Duchenne Muscular Dystrophy	$3.20	20	5	-	$3.20	TBD
Epilepsy	n/a	n/a	n/a	n/a	$7.50	TBD
Gulf War Illness	$20.00	62	26	-	$20.00	TBD
Joint Warfighter Medical Research [1]	$100.00	98	33	13	$50.00	14
Lung Cancer	$10.50	353	27	-	$10.50	329
Military Burn	$8.00	4	3	6	$8.00	2
Multiple Sclerosis	$5.00	39	9	-	$5.00	40
Neurofibromatosis	$15.00	66	19	-	$15.00	67
Neurotoxin Exposure Treatment Parkinson's	$16.00	2	2	9	$16.00	TBD
Orthotics and Prosthetics Outcomes	$10.00	54	11	-	$10.00	TBD
Ovarian Cancer	$20.00	186	33	-	$20.00	231
Peer Reviewed Alzheimer's	$12.00	65	13	-	$12.00	TBD
Peer Reviewed Cancer	$25.00	223	47	-	$50.00	367
Peer Reviewed Medical	$200.00	1,081	131	-	$247.50	471
Peer Reviewed Orthopaedic	$30.00	166	20	1	$30.00	TBD
Prostate Cancer	$80.00	912	167	11	$80.00	634
Reconstructive Transplant	n/a	n/a	n/a	n/a	$15.00	TBD
Spinal Cord Injury	$30.00	95	21	-	$30.00	TBD
Trauma Clinical Research Repository	$5.00	1	1	-	n/a	n/a
Tuberous Sclerosis	$6.00	44	10	-	$6.00	43
Vision [2]	$10.00	n/a	12	-	$10.00	TBD
Programs Executed on Behalf of Others						
Army Rapid Innovation Fund	$1.90	n/a	1	-	$5.00	TBD
Clinical Research Intramural Initiative	$2.30	33	4	-	TBD	16
Defense Medical Research and Development	$139.10	211	62	29	$89.50	123
Restore Core Research Funding Reduction	n/a	n/a	n/a	n/a	$41.40	TBD
Psychological Health/Traumatic Brain Injury	$86.00	198	49	5	$101.60	21
Small Business Innovation Research	$14.76	8	7	19	TBD	23
Other Submission Processes						
USAMRMC - Broad Agency Announcement						103
Total	$990.96	5,865	838	93	$1,024.44	3,452

[1] Joint Warfighter Execution Management Breakdown: 20 awards managed by CDMRP; 7 awards managed by U.S. Army Medical Materiel Development Activity and 6 awards managed by U.S. Army Medical Materiel Agency.

[2] Vision awards are the result of FY13/14 Program Announcements therefore all applications are counted in FY13.

Our Management Cycle

The 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, advocate 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 execution and management cycle is depicted in Figure 2 and discussed in detail in this section.

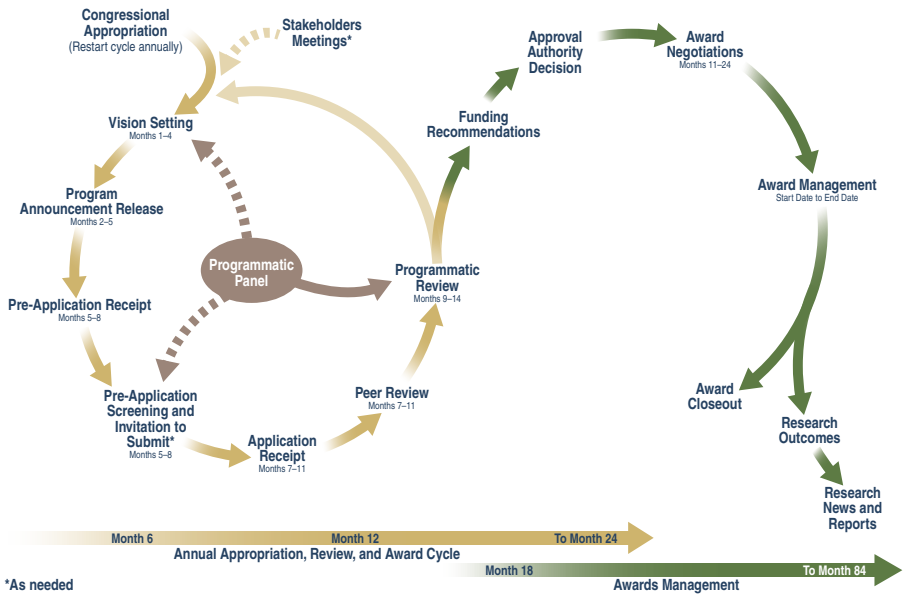


Figure 2. Execution and Management Cycle

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

Funds for programs are a direct response to the needs of Service Members and their families, research communities, and the public at large. The congressionally appropriated programs are added annually to the DoD appropriation. The Defense Health Program also includes funds for military medical research from the President's budget (core dollars). Over the years, the 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 gaps in both the scientific and consumer interest areas. Stakeholders are world-renowned consumers, scientists, and clinicians. Recommendations from the Stakeholders meeting are used to facilitate vision setting.

The CDMRP defines consumers as patients, survivors, family members, or caregivers of people living with a disease, injury, or condition, who serve as representatives of consumer advocacy, support, or military organizations (additional information about consumers can be found on page 9).

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 Sciences Institute of Medicine. 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 award mechanisms to be offered by the program. Based on the discussions, the vision setting process concludes with development of an investment strategy for the program's available funds. Program announcements/funding opportunities are developed and represent the most needed areas of scientific research for the program year.

4. Program Announcements and Broad Agency Announcements

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

5. Applicant Submission and Receipt

For many of the award mechanisms, application submission requires a multistep process consisting of a pre-application submission (which includes a letter of intent, pre-proposal, and/or nomination) followed by full application submission. The pre-application is an abbreviated submission outlining the research aims, strategy, innovation, and/or impact of the project. Pre-applications may be screened by either the programmatic reviewers or a scientific peer review panel, based on the requirements described in each Program Announcement or BAA. The final product of the screening is a recommended list of invited applicants. As summarized in **Table 2**, in FY15, the CDMRP received 7,330 pre-applications and nominations that, after screening and invitation, resulted in 2,888 full applications received. In addition, the CDMRP received 2,723 full applications from mechanisms that did not require pre-applications or nominations, for a total of 5,611 full applications received in this fiscal year.

Table 2. Number of Submissions Received October 1, 2014–September 30, 2015, across FY14–FY15 Programs

Mechanism Submissions	
Pre-proposals or nominations screened	7,330
Letters of intent received	3,627
Total pre-applications received	10,957
Full Application Submissions	
Full applications from invitations only	2,888
Full applications from letter of intent	2,723
Total full applications received	5,611

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 the USAMRMC. These areas of interests are determined annually by the USAMRMC Program Area Directorates (PADs) in response to evolving research priorities and knowledge gaps. For FY15, 424 pre-applications and 118 full applications were submitted to the BAA via the CDMRP's eBRAP site, and forwarded to the USAMRMC PADs for programmatic decisions.

6. Two-Tier Review Process

The two-tier review of applications is based on the recommendations set forth by the Institute of Medicine committee in 1993. The two tiers of review are scientific peer review and programmatic review. Every application is

given a fair and balanced review, taking steps to ensure that conflicts of interest do not influence the process, and that 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*.

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 Program Announcement or BAA, and rates the various criteria numerically or adjectively. 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, these go through a criteria-based programmatic review by experts including scientists, clinicians, military members, and/or laypersons. At the programmatic review level, the peer review summary statement, in addition to criteria published in the funding opportunity (Program Announcement or BAA), is compared and assessed for programmatic relevance, portfolio balance, and scientific merit. 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

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

8. Award Negotiations and Management

Negotiation and management of awards are a major focus of the USAMRMC offices and organizations, including the CDMRP, U.S. Army Medical Research Acquisition Activity (USAMRAA), and Office of Research Protections. During the period of performance for awards (which can be up to 5 years), the CDMRP actively manages and monitors progress. The awards management process is depicted in **Figure 3**. Over the past 5 years, an average of 675 new awards were made each fiscal year. As of September 30, 2015, CDMRP has managed 13,912 awards through its funding history, which includes 13,261 awards from applications submitted to CDMRP, and 651 awards that transitioned from TATRC to CDMRP for management.

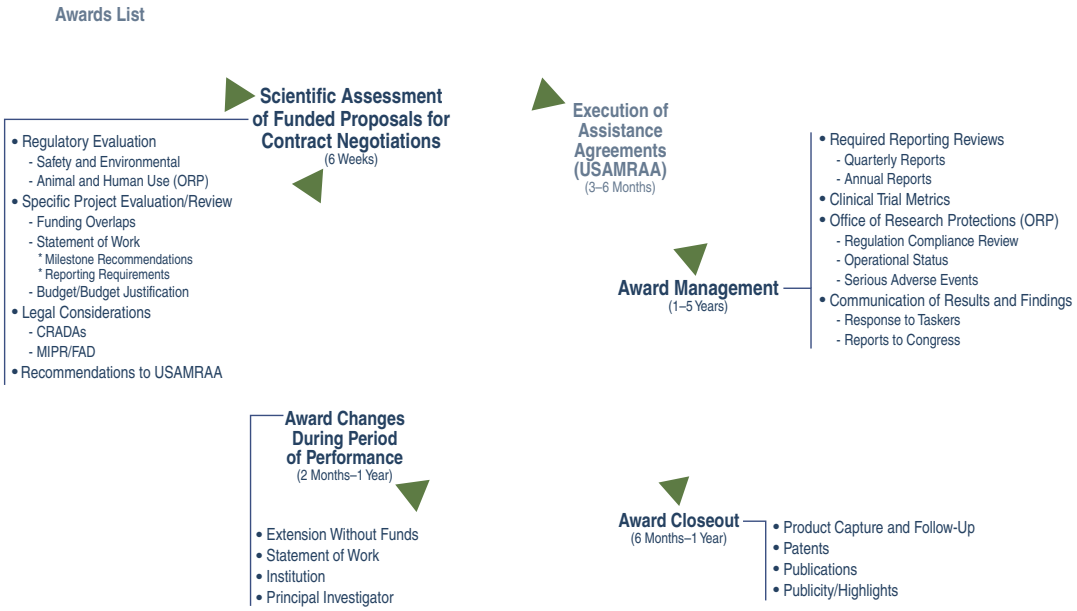


Figure 3. Execution and Management Cycle

Each award 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), the CDMRP, and offices within USAMRMC. Formal analysis of the budget with respect to the scope of work to be performed is completed to ensure cost sharing when possible, and avoidance of overlap in research funding with other funding agencies. Once all aspects of negotiation are complete, an award is signed and an assistance agreement (grant or cooperative agreement) or contract is issued. The life-cycle management of awards continues throughout the period of performance with monitoring of the technical progress, regulatory review, and financial reporting. At a minimum, all funded PIs are required to submit annual progress reports and quarterly financial reports. The progress of larger complex awards and consortia may also be monitored through external advisory boards, site visits, teleconferences, and other meetings throughout the entire period of performance.

9. Award Closeout

Award closeout takes place at both USAMRAA and the program office, and this is usually performed 6 months after the period of performance has expired. During this time, the CDMRP carefully monitors the final progress report and the patent report, while USAMRAA reviews the final financial accounting. Actions regarding any patents, invention disclosures, publications, and follow-up funding are captured during award closeout. When significant discoveries are identified, the awards are flagged for further follow-up.

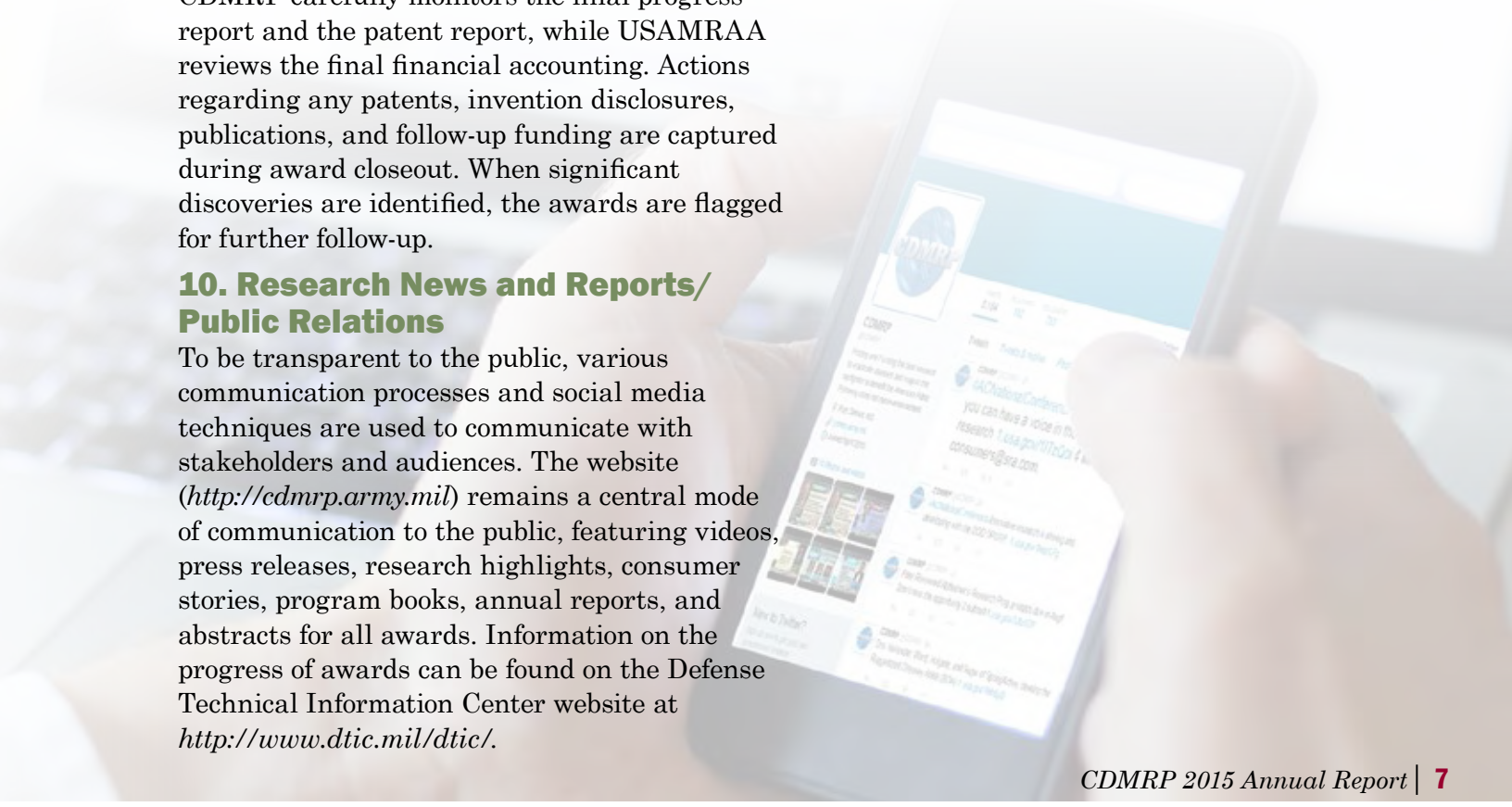
10. Research News and Reports/ Public Relations

To be transparent to the public, various communication processes and social media techniques are used to communicate with stakeholders and audiences. The 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 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 the CDMRP to expand information dissemination strategies include YouTube (*http://www.youtube.com/user/CDMRP*) and Twitter (*https://twitter.com/CDMRP*).

Multistep Process to Minimize Award Duplication and Overlap

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



Automated Business Processes

Two important electronic business systems are used in the receipt of applications, and negotiation and management of awards. These automated business processes enable multiple users to input data, download information, and manage the daily administrative tasks associated with application submission and grant processing in centralized, secure locations. As a result, users experience increased efficiency in data management throughout application submission and administration of awards.

Electronic Biomedical Research Application Portal

eBRAP is a research pre-application and full application processing and management tool.

- Worldwide web-based accessibility for receipt and processing of pre-applications and full applications, and documents required for award negotiations.
- Computer-automated processes associated with Program Announcement release, as well as batch retrieval, processing, modification, and compliance of full applications.
- Capability enabling researchers to review and modify application components (submitted to Grants.gov).
- Capability to communicate with research community on a one-to-one basis and in batches.

Electronic Grants System

EGS is a business system designed primarily to manage funded awards, allowing multiple organizations to view and access award data and files generated during the life of an award.

- Enables real-time electronic workflow and transfer of data among offices of USAMRMC.
- Multiple users are able to input data, download reports, and manage daily administrative tasks associated with grants processing in a central, secure location.
- During management of awards, research outcomes and findings are entered and categorized in EGS, and then subsequently analyzed by staff for program evaluation efforts, interacting with funded investigators, and reporting to stakeholders.
- The website automatically retrieves public information from EGS to provide up-to-date information on funded awards to end users and the public.

Vital Partnerships

In FY15, over 200 consumers served on CDMRP peer review panels, and approximately 50 served as programmatic reviewers.

Today, over 2,000 consumers have represented their communities and lay organizations at least once since 1992, and their role continues to be vital.

In FY15, more than 2,300 scientists and clinicians provided necessary subject matter expertise on peer review panels, and nearly 300 scientists and clinicians served as programmatic reviewers. As of September 30, 2015, over 150 scientists and clinicians have served as ad hoc programmatic reviewers. Since its inception, approximately 10,187 researchers have been funded by the 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 continue to fund innovative and impactful research areas and gaps, as well as to reduce redundancy within each program's portfolio. The following sections discuss these partnerships and collaborations with stakeholders and other federal and non-federal agencies.

Consumers

The CDMRP has been a catalyst for the inclusion of consumers (patients, survivors, family members, and/or caregivers) in the review of research applications as full voting members. Consumers first served as reviewers for the CDMRP at the programmatic review level in 1993, and their role was soon expanded to scientific peer review in 1995. The CDMRP has developed a model of consumer inclusion that has been adopted by other funding agencies. Consumers are nominated to scientific peer review panels by the lay organizations. Similar to scientific peer review panels, consumers also serve at the programmatic review level of the CDMRP. In each tier of review, consumers serve alongside scientists, clinicians, and leading experts, and all have an equal voice and vote in deliberations. 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. Throughout the growth of the CDMRP, consumers and stakeholders remain the foundation for many of the programs executed and managed by the 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 integral partner in assisting the CDMRP to shape the future of healthcare. They serve on the two-tier review of applications, research the complex causes of diseases, conditions, and injuries, and 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 reviewed.

Military Partnerships

Defense Health Agency Research, Development and Acquisition Directorate

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, RDA will enhance the readiness and resilience of the military community.*

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

Most of the programs managed by the CDMRP are overseen by the RDA within the DHA. The DHA is a joint, integrated Combat Support Agency that reports to the OASD(HA), as shown in **Figure 4**. 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. The RDA was established in 2014 as the core research program of the DoD to enhance the related medical research and development programs of the Army, Navy, Air Force, and Defense Advanced Research Projects Agency. The RDA works closely with the CDMRP by providing:

- Centralization of oversight of research and development grants, projects, and initiatives across the Services and Military Health System
- Prioritization and direct medical research to ensure maximal impact for Service Members and beneficiaries
- Elimination of redundancy and reduction of variance in the execution of research and development projects

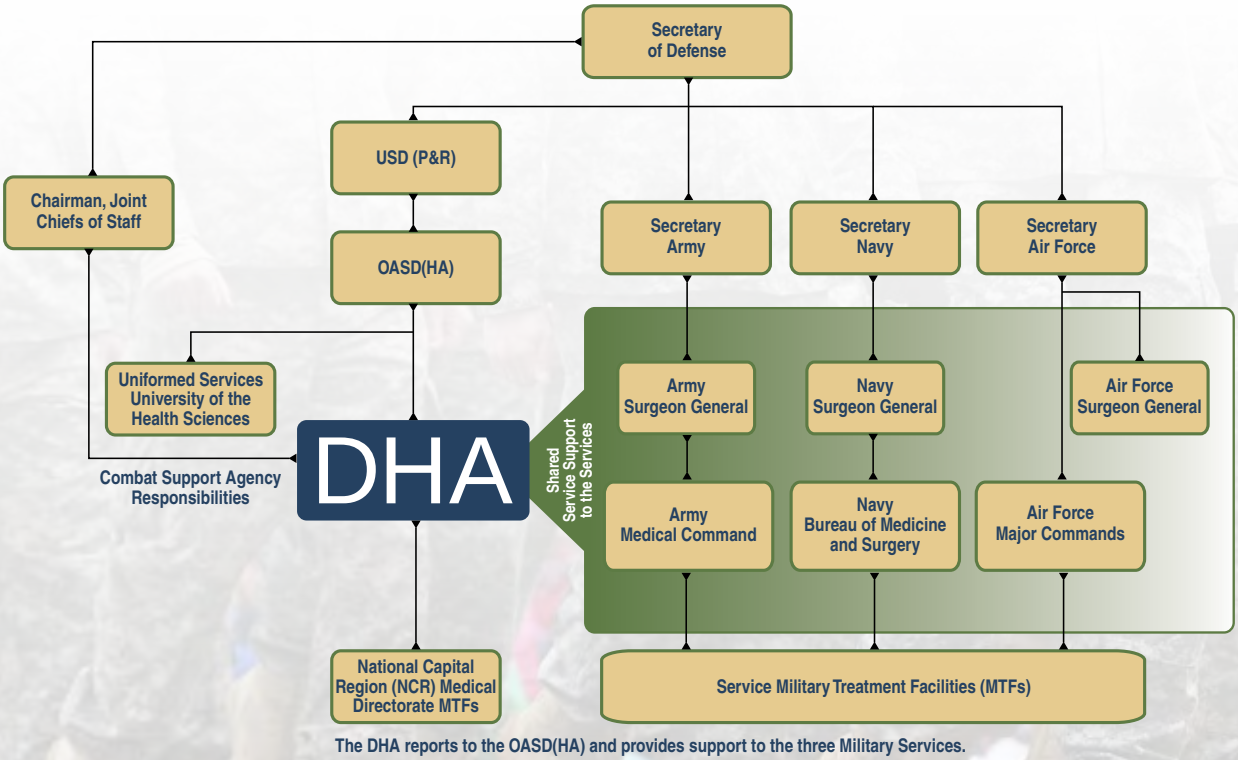


Figure 4. Organizational Structure of the DHA

U.S. Army Medical Research and Materiel Command

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

Vision: *Lead the advancement of military medicine.*

The CDMRP is located within USAMRMC, the largest medical research organization within DoD. USAMRMC is responsible for managing medical research programs that address both military and civilian groups. The USAMRMC motto, "Protect, Project, Sustain," underscores its support of the Warfighter through ensuring that Service Members are protected from disease and treated for injuries or conditions. USAMRMC's medical research programs are divided into core and non-core research programs based on their alignment with DoD and Army missions. Core programs are funded through the DoD's planning and budget process, and align with the principal needs and military operations within DoD. Non-core programs are funded through congressional line-item additions to the DoD budget. The CDMRP executes 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 5**.

Figure 5. The USAMRMC Team

Many of the research projects executed by the 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, U.S. 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 by the CDMRP that have strong potential for development into a beneficial, military-relevant medical product are included in the Decision Gate process. To facilitate this process, the 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 Decision Gate criteria. If a CDMRP-funded project meets Decision Gate criteria, it will be entered into the Decision Gate process, a point called the Materiel Development Decision. Once in Decision Gate, product development will be managed by an Integrated Product Team. Science Officers from the CDMRP are often asked to participate on the Integrated Product Teams due to their scientific expertise and relationship to the product developer. As the product matures, it will go through a series of decision points (called milestones) to determine whether it should continue as planned, continue with a revised plan, or have its development terminated (see **Figure 6** 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 organization.

Joint Program Committees

JPCs are DHA RDA advisory bodies composed of medical and military experts that provide funding recommendations and program management support for DHA RDA-funded

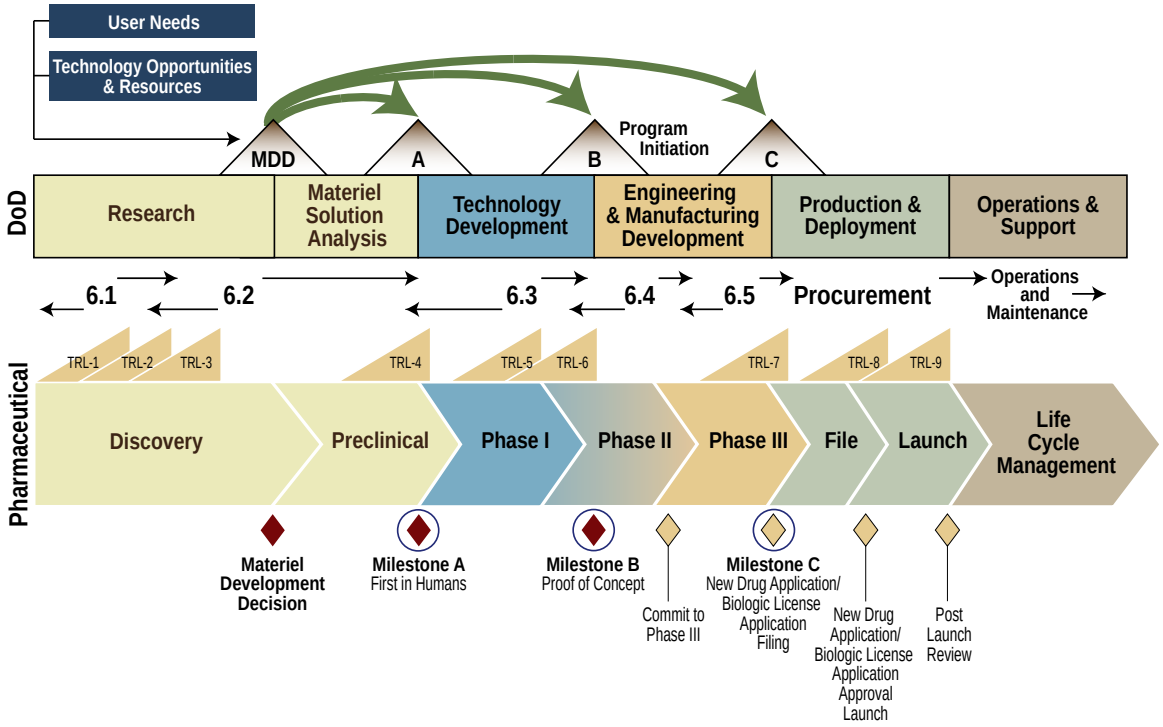


Figure 6. Decision Gate Life Cycle

research. The JPCs advise the USAMRMC PADs, which provide strategic oversite of this research. The CDMRP works with the PADs to execute a number of programs. The combined effort leverages the CDMRP's expertise in research program administration with the PADs' technical and strategic expertise for the advancement of the DHA RDA mission to expedite the delivery of products and solutions that address challenges related to Service Members and their families. The CDMRP administers these programs as the Defense Medical Research and Development Program (DMRDP). The DMRDP focuses on advancing the state of medical science as it relates to conditions directly relevant to battlefield injuries and other ailments that affect both Service Members and their families. (For additional information about the DMRDP, see pages 40–43 in this report). In FY15, the CDMRP assisted with program execution in a number of areas relevant to battlefield injury and military service, including basic and applied psychological health, Post-Traumatic Stress Disorder (PTSD), Traumatic Brain Injury (TBI), neurotrauma, neuroplasticity, wound infections, infectious diseases, prosthetics, vision, hearing, balance, and other rehabilitative and regenerative medicine efforts. This partnership supports the CDMRP's vision of finding and funding the best research to support the Warfighter and the American public.

U.S. Department of Veterans Affairs

In support of the August 31, 2012, Presidential Executive Order 13625, the DoD and the U.S. Department of Veterans Affairs (VA) have combined more than $100M in a collaborative effort to fund two new consortia aimed at improving diagnosis and treatment of mild TBI (mTBI) and PTSD. These consortia include the Consortium to Alleviate PTSD (CAP) and the Chronic Effects of Neurotrauma Consortium (CENC). These collaborative efforts are described in further detail on pages 15–16 of this Annual Report. In addition, the CDMRP coordinates with the VA to enrich projects within the Gulf War Illness Research Program (GWIRP). The GWIRP is collaborating with the VA to make the best possible use of available resources in support of high-quality, Veteran-focused research on Gulf War Illness (GWI) (see pages 46–47 for additional details on 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.

Collaborative Research

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, as well as 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 DoD Alzheimer's Disease Neuroimaging Initiative (ADNI) is to examine the possible connections between TBI and PTSD, and the signs and symptoms of Alzheimer's Disease (AD) on Veterans as they age. TBI and PTSD are highly prevalent consequences of military service and combat. 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 the ADNI will help determine the extent to which TBI and PTSD are risk factors for the development of dementia due to AD or other factors:

- 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
- 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
- Effects of Traumatic Brain Injury and Post-Traumatic Stress Disorder and Alzheimer's Disease on Brain Tau in Vietnam Veterans using Alzheimer's Disease Neuroimaging Initiative

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. Military and VA records are used to identify Vietnam War Veterans with either: 1) evidence of ongoing PTSD; 2) a well-documented history of moderate or severe TBI (this group includes those who

have both PTSD and a TBI); or 3) comparable Veteran controls. The initial study enrolled subjects who met criteria for normal cognition. The study was later expanded to include these same three cohorts, but include subjects who also meet criteria for mild cognitive impairment. All subjects are contacted by mail/telephone and pre-screened for eligibility. Evidence of current and lifetime PTSD is determined by the Structured Diagnostic Interview for DSM-IV and the Clinician Administered PTSD Scale. Subjects meeting criteria for one of the three cohorts (with or without minimal cognitive impairment) are referred to one of 19 selected ADNI clinics for clinical examination, cognitive tests, amyloid positron emission tomography (PET) using F18 Florbetapir, MRI (structural, diffusion tensor, and resting state BOLD functional MRI), lumbar puncture for cerebrospinal fluid, markers of tau, P tau amyloid beta, and blood for genetics. After one year, the clinical/cognitive battery and MRI are repeated. The objective is to detect an increase in AD markers (measured with PET, MRI and cerebrospinal fluid biomarkers, as well as cognitive testing) associated with history of TBI or ongoing PTSD. Because considerable evidence suggests that while brain Aß might precipitate cognitive decline in aging, the actual severity of the decline is more closely linked to deposition of brain tau. Therefore, 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 PET scanning. Vietnam Veteran subjects already enrolled in either of the first two studies are invited to enroll in the third study and receive the additional PET scan. A separate cohort of civilian subjects, currently enrolled in the ADNI2, is also invited to participate. Read more about the ADNI at *http://www.adni-info.org/DOD.aspx*.

Advanced Developments for Exceptional Rehabilitation Consortium

The Bridging Advanced Developments for Exceptional Rehabilitation 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. Clinical trials addressing lower-extremity trauma are currently aimed at improving step-to-step control during walking, improving limb-loading on the prosthetic and the intact limb via gait training, analyzing the benefits of powered ankle prostheses for amputees with differing levels of mobility, and maximizing outpatient rehabilitation effectiveness. Consortium projects focused on prosthetic devices strive to determine the optimal height and stiffness of a running-specific leg prosthesis, as well as to characterize the response of prosthetic feet to applied loads and impacts representative of military tasks, and the effects of such loads upon gait. A clinical study to examine functional outcome measures for individuals with upper-extremity trauma is also included.

The Chronic Effects of Neurotrauma Consortium

The CENC is a joint DoD and VA effort dedicated to establishing a comprehensive understanding of the chronic sequelae associated with neurotrauma, primarily focused on mTBI/concussion. This includes establishing the association, causality, diagnosis, and treatment/rehabilitation of mTBI to neurodegeneration. In addition, the Consortium efforts will address the common co-morbidities associated with chronic mTBI, such as neurosensory system involvement (vision, balance, hearing, pain) and psychological dysfunction. CENC is led by PI Dr. David Cifu at Virginia Commonwealth University, and Co-Directors Dr. Ramon Diaz-Arrastia at the Uniformed Services University of the Health Sciences and Dr. Rick Williams at RTI International. Currently, CENC leverages collaborations among 28 participating institutions across academia, industry, DoD, and VA. Studies under way include efforts in the area of epidemiology, neurosensory co-morbidities, neuroimaging standardization, and follow-up from studies initiated in-theater. 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/*.

Concussion Assessment, Research, and Education

The Concussion Assessment, Research, and Education (CARE) Consortium is a joint National Collegiate Athletic Association (NCAA) and DoD research effort within the NCAA-DoD Grand Alliance. The consortium is dedicated to studying the development and recovery from sports-related concussion, and will enroll student athletes at 30 NCAA universities and cadets at four Service Academies. The CARE Consortium will allow scientists to develop evidence-based approaches to understanding the risks, management, and possible treatment strategies for concussion. The CARE team is composed of an Administrative Operations Core at Indiana University, a Clinical Study Core at the University of Michigan, and an Advanced Research Core at the Medical College of Wisconsin. Data collection is currently under way at 19 institutions, and results are expected to be available in 2016. Additional information can be found at *http://careconsortium.net/*.

The Consortium to Alleviate Post-Traumatic Stress Disorder

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. The CAP has two main objectives: one focusing on the advancement of treatment strategies for PTSD, including interventions for early, chronic, and latent onset cases, and one to identify and confirm clinically relevant biomarkers as diagnostic and prognostic indicators of PTSD and co-occurring disorders. Research within CAP focuses across a range of topics, including behavioral health disorders, mood and anxiety disorders, sexual dysfunction, neurologic disorders, pain, cognitive deficits, and neuroendocrine deficits. The CAP is led by the Consortium

Director Dr. Alan Peterson of the University of Texas Health Science Center San Antonio (UTHSCSA) and the South Texas Veterans Health Care System (STVHCS), and Co-Director Dr. Terry Keane of the VA Boston Healthcare System (VABHCS) and Director of Behavioral Science division of the National Center for PTSD. The consortium's coordinating center is responsible for the administration of the consortium, which is distributed among UTHSCSA, STVHCS, VABHCS, and Duke University. In addition, the consortium has funded the following core facilities to augment the studies: an Assessment Core, Biomarkers and Genomics Core, Neuroimaging Core, and a Data Management and Biostatistics Core. Nine 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 the 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 *http://delta.uthscsa.edu/consortiumtoalleviateptsd/*.

Detection of Early Lung Cancer Among Military Personnel Consortium

The Detection of Early Lung Cancer Among Military Personnel Consortium is designed to develop and 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 military treatment facilities, and two academic hospitals as clinical study sites, and several molecular biomarker laboratories, along with biostatics, bioinformatics, pathology, and biorepository cores. The Biostatistics and Data Management Center will handle the clinical trial infrastructure, protocol development, clinical trial data management, quality assurance, regulatory compliance, imaging analysis, and site management. Two projects have been initiated 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 scan, and the second is developing and testing new noninvasive molecular biomarkers in the airway and blood to identify those smokers at highest risk for developing lung cancer.

Gulf War Illness Consortium

The Gulf War Illness Consortium is led by Dr. Kimberly Sullivan of Boston University and brings together established GWI researchers across the Nation to investigate the pathobiological mechanisms responsible for GWI symptoms as they relate to brain-immune interactions. This consortium has initiated a series of clinical and preclinical studies to specifically identify brain-immune pathways that can be targeted for intervention by a variety of glial-modulating 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. Results from this integrated approach should lead to a rational and efficient basis for identifying diagnostic markers and beneficial treatments for GWI.

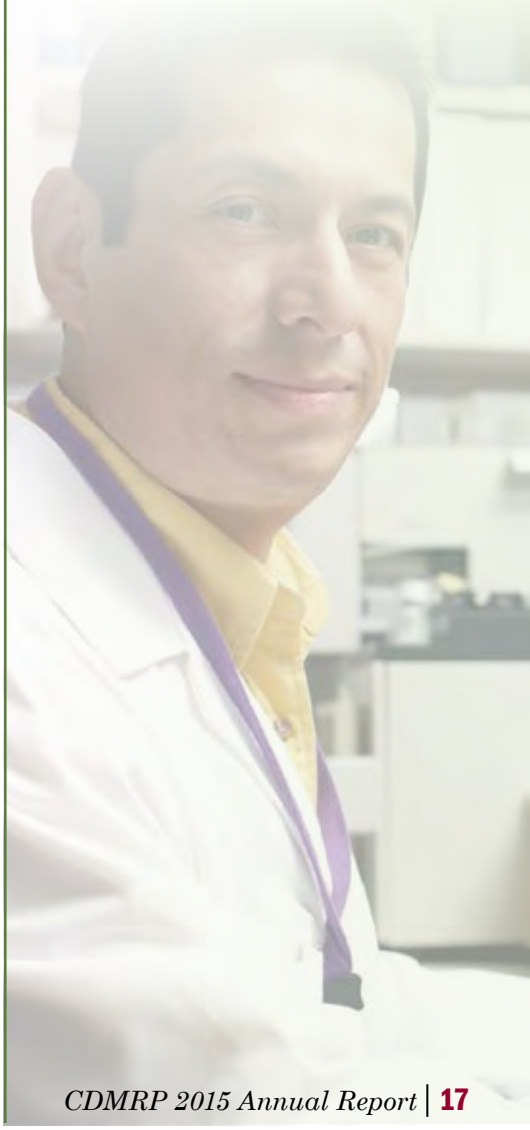
Institute for Translational Neuroscience

The Institute for Translational Neuroscience (ITN), a consortium comprised of 18 institutions, was established with congressionally directed funding in 2010 to address the growing concern regarding alcohol and substance use disorders (SUDs) within the military and civilian populations. Now in its fifth year of operation, the ITN has formed a unique and promising strategy to accelerate the development of novel therapeutics for SUDs. The scientific objectives of the ITN are to: 1) identify molecular mechanisms, targets, and candidate compounds; 2) determine the efficacy of the candidate compound(s) in vitro and in vivo (animal models); 3) conduct proof-of-principle pilot-scale clinical experiments or trials; and 4) rapidly translate findings into fullscale clinical experiments/trials. To facilitate the transition from bench to bedside, a Translational Coordinating Core (TCC) was established to attract collaborations with outside sources, such as the 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. Thus far, 18 unique clinical and pre-clinical studies have been successfully awarded and supported through the consortium. More information regarding three of these studies and their results can be found at *http://cdmrp.army.mil/asarp/*

Military Suicide Research Consortium

The DoD has funded a number of studies proposing to investigate methods to better identify who is at risk for, and to decrease the likelihood of, suicidal behavior. The Denver Research Institute and Florida State University received funding from the Military Operational Medicine Research Program in FY08 to create a consortium with the goal of integrating and synchronizing DoD and civilian efforts to implement a multidisciplinary approach to suicide prevention. These awards, which comprise the Military Suicide Research Consortium (MSRC), are led by Drs. Peter Gutierrez and Thomas Joiner.

The MSRC-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. Twenty-one studies have been funded by the MSRC in addition to several Postdoctoral Pilot Projects and Dissertation Completion Awards. These studies are being 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 family members of Service Members and Veterans.

The MSRC has developed a database to capture Common Data Elements collected in each of the funded studies. 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.

Three of the funded studies are now complete and have yielded important results. For more information related to these studies, please visit *http://cdmrp.army.mil/dmrdp/research_ highlights/15gutierrez_joiner_highlight*.

Neurofibromatosis Clinical Trials Consortium

The Neurofibromatosis Clinical Trials Consortium (NFCTC, *http://www.uab.edu/nfconsortium*) was established by the DoD Neurofibromatosis Research Program 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. Composed of 19 clinical sites, the consortium is led by the Operations Center based at the University of Alabama at Birmingham under the direction of Dr. Bruce Korf. The University 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, and an established patient population available for clinical trials.

To date, the NFCTC has successfully initiated 8 clinical trials and supported 3 additional trials.

For additional information please see pages 56–57.

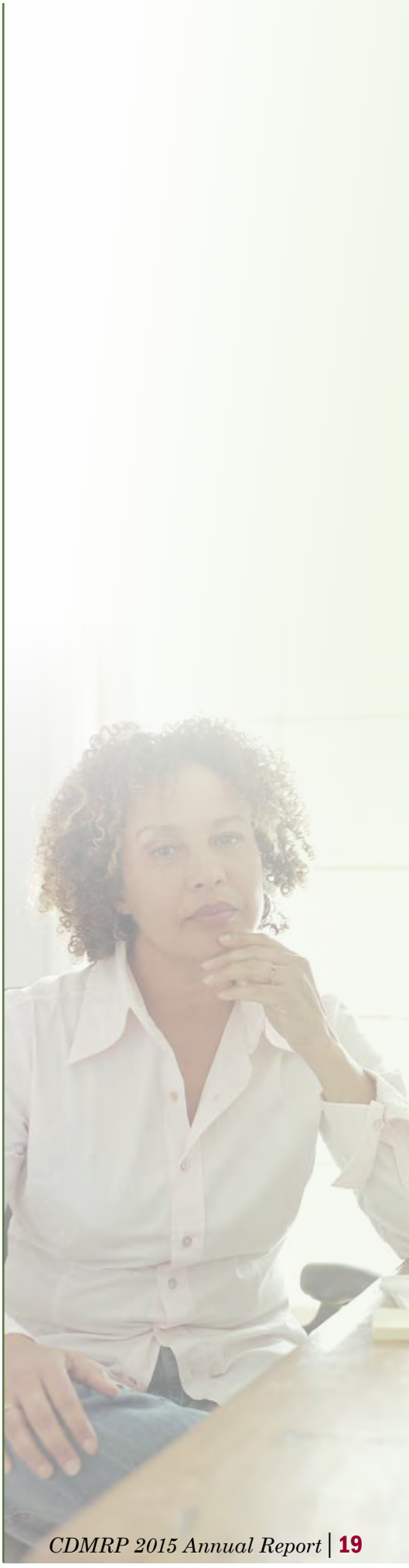
Ovarian Cancer Academy

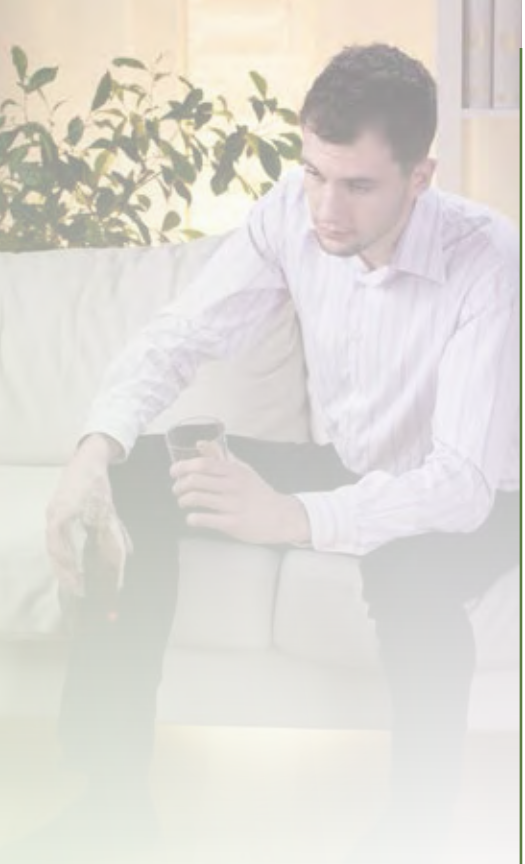
In FY09, a Dean and seven Early-Career Investigator (ECI) Awards marked the realization of the Ovarian Cancer Research Program's vision of a unique, virtual Ovarian Cancer Academy (OCA) that supports the development of career ovarian cancer researchers. This Academy brings together a group of talented and highly committed ECIs with their mentors and an Academy Dean. The Ovarian Cancer Research Program 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. The Academy has expanded with inclusion of ECIs in FY12, FY13,

and FY14 to 14 ECI–Mentor pairs. The ECIs have demonstrated remarkable progress, including over 160 publications and over 100 abstracts to date focused on ovarian cancer. Their growth as independent, committed ovarian cancer researchers is evident in the 49 funded grants obtained (including NIH R01s), as well as their service on the boards of well-established journals and women's cancer foundations. Additionally, in the span of 5 years, the ECIs have advanced well along the tenure track, mentored increasing numbers of personnel, and collaborated within the Academy on publications, grant applications, and technical ventures. The annual OCA in-person workshop in Chicago in March 2015 promoted further collaborations and fostered cross-mentoring within the group of ECIs. It preceded a special session at the annual Society of Gynecologic Oncology meeting where the original seven FY09 ECIs delivered oral presentations on their OCA award research, which was very well received. FY14 heralded a transition in OCA leadership from the first OCA Dean, Dr. Patricia Donohoe, to the new Dean, Dr. Nita Maihle, and Assistant Dean, Dr. Douglas Levine, whose combined vision for the OCA is certain to propel this Academy to new heights. FY14 also saw the introduction of the OCA Collaborative Award mechanism, which supported expansion and enrichment of the OCA by requiring applications from existing ECIs to include a partnering PI from outside the Academy on proposed research projects that were an offshoot or an idea that developed from research performed under the OCA ECI Award.

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 majority of cases (61%) are diagnosed at late stages, for which the 5-year survival rate is 27% (United States, 2014). A multi-institutional team headed by Dr. Robert Kurman's research group at Johns Hopkins University, along with collaborators at the gynecologic oncology powerhouses of Memorial Sloan Kettering Cancer Center, University of Toronto, and Yale University, successfully competed for the first Ovarian Cancer Consortium Award (OCCA) offered in 2010. 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, 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, 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, and a fifth epidemiological study designed to evaluate whether these STIC characteristics are modifiable by oral contraceptives or anti-inflammatory agents.





Several major accomplishments of the Consortium are as follows:

- Verified several new identifying markers in STICs.
- Identified a putative pre-malignant precursor to STICs, known as STILs, or serous tubal intraepithelial lesions, and examining the gain or loss of markers in STILs, STICs, and high-grade serous carcinomas.
- Made progress in evaluating whether the presence of a STIC is associated with different clinical manifestations and/or outcomes as compared to patients in whom STICs were not identified.
- Identified molecular changes preceding STICs in high-risk women using in vitro and in vivo models. The latest discoveries were presented at the 5th Annual Ovarian Cancer Symposium on the Prevention and Early Detection of Ovarian Cancer, held in September 2014 at the Princess Margaret Cancer Center in Toronto.

Pharmacotherapies for Alcohol and Substance Abuse

On September 30, 2015, Research Triangle Institute (RTI) was awarded a $10.8M 5-year award from the FY14 Alcohol and Substance Abuse Disorders Research Program (ASADRP) Consortia Award Program Announcement. The consortium is led by Dr. Rick Williams, from RTI in collaboration with Baylor College of Medicine and Uniform Services University of Health Sciences. The consortium is named "Pharmacotherapies for Alcohol and Substance Abuse." The consortium has three aims in developing pharmacotherapies for ASUDs, particularly in the context of the reciprocal relationship between ASUD 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.

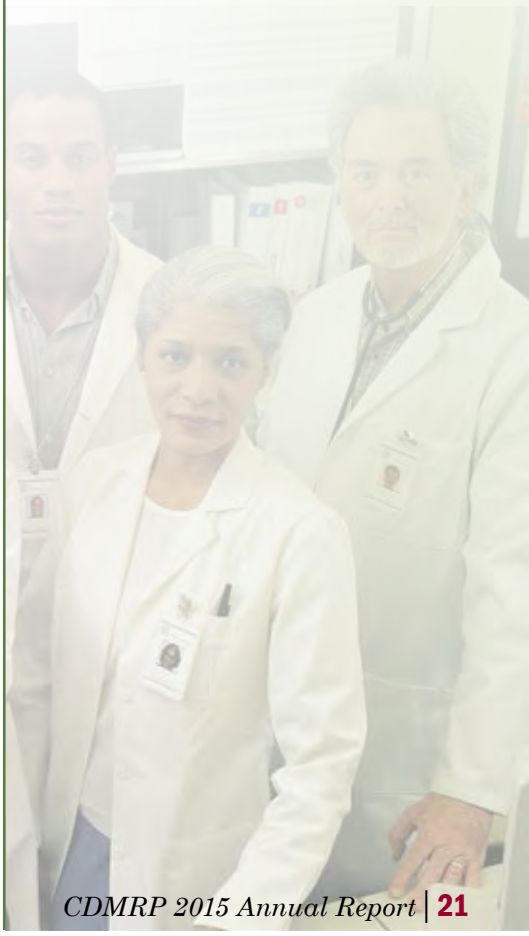
Prostate Cancer Clinical Trials Consortium

The Prostate Cancer Clinical Trials Consortium (PCCTC) has received support from the Prostate Cancer Research Program (PCRP) since 2005 and, in February 2014 became a limited liability company (Prostate Cancer Clinical Trials Consortium, LLC). Led by Memorial Sloan Kettering Cancer Center, the PCCTC currently has 15 sites funded with PCRP grants and four participating non-funded affiliate sites. The PCCTC also has contracts with four pharmaceutical companies and is in the negotiation process with three additional companies to develop contracts to collaboratively run clinical trials for new developing therapies for prostate cancer. The PCCTC has 170 clinical trials approved for activation, of which 118 have been completed (closed to accrual) with an additional 52 trials either active or pending

activation. Over 4,750 patients have been enrolled in these trials, 10% representing patients from disproportionately affected populations. Since biomarkers are increasingly being recognized as essential in the evaluation of treatment response, as well as for risk assessment, early detection, prediction of aggressiveness, and/or progression of prostate cancer, biomarker studies are being strongly pursued and validated across institutions. In 2008, PCCTC investigators led a collaborative initiative, the Prostate Cancer Working Group, to issue recommendations on the design and end points for prostate cancer clinical trials. These recommendations have had a profound impact on the clinical research community and how clinical trials are designed; Consortium investigators are currently working on releasing an update to this effort. 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, 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, preventing transcription of AR-regulated genes. 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 established itself as the nation's premier prostate cancer clinical trials group and remains poised to make a significant impact on the lives of patients by keeping the drug pipeline primed with promising novel agents.

PTSD and TBI Clinical Consortium Award – INTRuST

The INjury and TRaumatic STress Consortium (INTRuST) was established to combine the research efforts of the Nation's leading experts on PTSD and TBI to bring to market novel treatments or interventions for those who suffer from PTSD and/or TBI. The INTRuST Consortium is composed of the Coordinating Center, located at the University of California, San Diego; 10 competitively selected clinical sites; a biorepository core; a neuroimaging repository core; a biostatistics core; an informatics core; and 19 additional military treatment and Veterans' facilities—all conducting clinical trials or collecting samples for clinical trials in PTSD and/or TBI. Concluding its seventh year, the INTRuST Consortium has completed enrollment, and data analysis is under way or complete, for seven core trials and five pilot clinical trials. The portfolio of clinical trial advances spans psychotherapies to drug therapies to device therapy (e.g., transcranial magnetic stimulation of the prefrontal cortex). All trials are designed to decrease the impact of military-relevant PTSD and TBI for the benefit of Service Members, their families, and their caregivers, and the American public. In addition, the repositories will serve as a resource for future investigators, providing blood and DNA/



ribonucleic acid (RNA) samples, as well as neuroimages, of clinical trial subjects for future use. This consortium mechanism has provided clinicians with a new understanding of the PTSD–TBI interface, and has established valuable infrastructure and scientific collaborations that will continue into the future.

PTSD Multidisciplinary Research Consortium Award – STRONG STAR

The South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (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 approximately 100 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 15 collaborating investigators from across the country. The goal of the STRONG STAR Consortium is to reduce or eliminate combat-related PTSD in active duty military and recently discharged Veterans. The STRONG STAR Consortium is conducting 12 projects, including retrospective data analyses, epidemiological studies, a data repository, a biorepository, and 10 clinical studies. The results of one animal 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 expected to be available in 2016–2017.

TBI Multidisciplinary Research Consortium Award – Mission Connect

Mission Connect was established in 1997 by The Institute for Rehabilitation and Research Foundation to address difficult problems in neurotrauma research by capitalizing on the expertise and research at the Texas Medical Center in Houston, Texas. Under the FY07 Psychological Health and Traumatic Brain Injury Research Program (PH/TBIRP), Mission Connect was funded to improve the diagnosis and treatment of mTBI through collaborative basic and clinical research. Now in its final year, Mission Connect has made several contributions to the field. In a longitudinal study that follows mTBI patients from the first 48 hours to 6 months post injury, researchers have used advanced magnetic resonance imaging (MRI) protocols to uncover a correlation between loss of consciousness and neuronal tract disruption in patients within the first 48 hours of mTBI and 3 months post injury. Researchers have developed a functional MRI biofeedback protocol that improves the function of damaged neural networks of mTBI patients. Investigators also performed preclinical evaluations of several promising treatments in animal models characterized and standardized within the Consortium. One of the most promising agents, ARA290, is being further developed using funding from the National Institutes of Health (NIH) and an industry partner. Investigators are currently

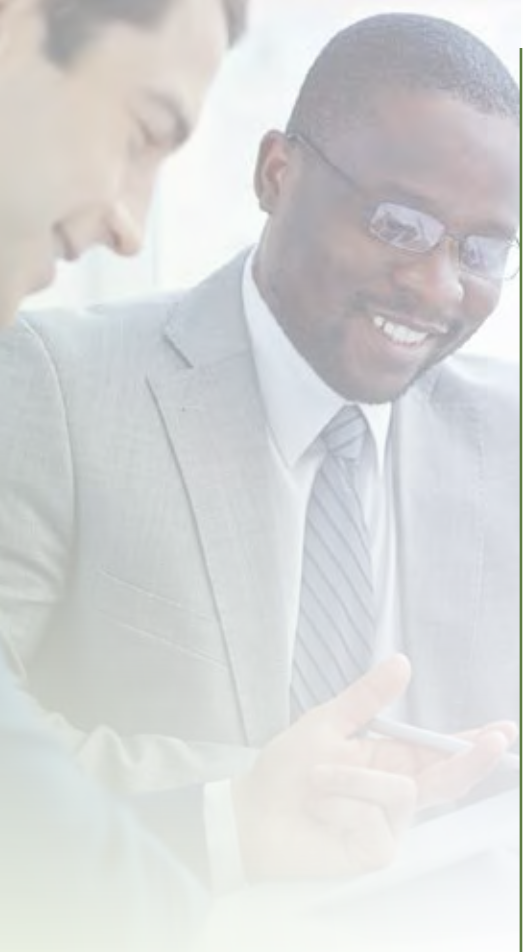
completing the final analysis of a Phase II Clinical Trial using the FDA-approved drug Atorvastatin (Lipitor®) as a potential treatment for mTBI.

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

TAPTE's goal is to establish a multi-center, multi-investigator research team focused on post-traumatic epilepsy (PTE) that will rapidly translate patient-relevant findings at the molecular, cellular and systems level into novel therapies. The ultimate goal will be to use this research to prevent the development of PTE from TBI. Based on previous successes within the epilepsy community, the Citizens United for Research in Epilepsy (CURE) Foundation will use their scientific model to rapidly advance the most promising research in PTE. The model will build 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 the CURE foundation, who will proactively monitor research progress and advise the consortium on which directions to take to ensure ultimate success. Key opinion leaders in both TBI and epilepsy research have been assembled to guide the development of a Request for Applications and their subsequent review. The opinion leaders will work closely with the consortium to ensure the TAPTE's goal will be reached, and the two groups will have continuous dialog mediated by the CURE foundation.

Traumatic Brain Injury Endpoints Development Award

With FY13 PH/TBI Research Program funding, the TBI Endpoints Development (TED) Award mechanism established a collaborative, multi-disciplinary research team to advance clinically validated endpoints which 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 no FDA-approved diagnostics or therapeutics currently. These endpoints include clinical outcome assessments, blood-based biomarkers, and neuroimaging biomarkers. The TED team is led by PI Dr. Geoff Manley at the University of California, San Francisco. 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. Stage I of the TED award is focused on integrating existing data and identifying the most promising endpoints to move forward, with contributions from expert working groups, consensus decisions, and close interactions with the FDA. Stage II allows for larger-scale validation studies of candidate clinical outcome assessments and biomarkers selected in Stage I, leveraging existing research infrastructure and clinical study networks of Transforming Research and Clinical Knowledge in Traumatic Brain Injury, the Concussion Research Consortium, and the CENC.



Understanding Gulf War Illness: An Integrative Modeling Approach

Under the leadership of Dr. Mariana Morris, Dr. Nancy Klimas, and Dr. Gordon Broderick, this GWIRP-funded consortium represents expertise in neurotoxicology, animal modeling, computational modeling, clinical research, and drug development. This multidisciplinary research team, based at the Institute for Neuroimmune Medicine at NOVA Southeastern University, aims to develop a translational model of GWI that will rapidly identify molecular targets and predict effective therapeutic interventions while also uncovering underlying mechanisms of disease. Through the use of computational modeling, genomic, immunological, autonomic, and endocrine pathway information from animal models of Gulf War-era chemical exposures and observed in symptomatic Gulf War Veterans are integrated to discern the pathways and mediators underlying GWI. The key mediators identified from the model will then be targeted with potential therapeutic interventions that will address the altered homeostasis of GWI. Finally, the two or three best performing pharmacological treatments will be tested in a well-defined Gulf War Veteran cohort.

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. 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 provides a check and balance for duplicative research efforts as well as an opportunity to encourage complementary investment strategies. These interagency collaborations strive toward synergy with other agencies and diversification of funded research portfolios, underscoring the importance of research coordination efforts. Examples of interagency collaborations include 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.

Federal Interagency Traumatic Brain Injury Research Working Group

An NIH-sponsored group whose mission is to enhance communication, coordination, and collaboration in the field of 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 U.S. Department of Health and Human Services (HHS) related to autism spectrum disorders (ASDs). Federal and non-federal members are included on the committee to ensure that a wide range of ideas and perspectives pertaining to ASDs is represented and discussed in a public forum.

Interagency Urology Coordinating Committee

A federal advisory committee, facilitated by the National Institute of Diabetes and Digestive and Kidney Disorders of the HHS, that coordinates the research activities of all national research institutes relating to urologic diseases to ensure their adequacy and technical soundness, and to provide for the exchange of information necessary to maintain adequate coordination.

International Cancer Research Partners

A group of 56 cancer-funding organizations that work together to enhance the impact of research to benefit all individuals affected by cancer through global collaboration and strategic coordination.

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.

On the Horizon: Federal RePORTER

In response to the U.S. Government Accountability Office recommendations, the CDMRP continued its efforts to support government transparency by participating in the STAR METRICS Federal RePORTER initiative (*http://federalreporter.nih.gov*), which consolidates award data from several agencies including HHS, Department of Agriculture, DoD, National Science Foundation, VA, Environmental Protection Agency, and National Aeronautics and Space Administration. This initiative allows for multiple agencies to house award data in a central database. Although separate from the NIH RePORTER, the Federal RePORTER utilizes some of its basic functions on a core set of data required from all agencies, allowing for analysis and comparison. The site is still in development but is live to the public. Additional features are in the planning stages. 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. Progress on this initiative has been successful, and currently, CDMRP-funded awards from FY08 through FY13 are included in the Federal RePORTER system, and new awards will be posted by the end of each fiscal year.

Trans-Agency Early-Life Exposures and Cancer Working Group

A working group composed of representatives from NIH, CDC, and the CDMRP. The group's goals are: 1) stimulating and facilitating research on early-life events/exposures and cancer within the context of the missions of the federal agencies; 2) planning and hosting lecture series to foster awareness, stimulate new scientific interest, and generate transdisciplinary collaborations among intramural and extramural research communities; and 3) conducting portfolio analysis to address current research funding portfolios on early-life events/exposures and cancer, and to determine gaps and future needs.

Trans-NIH Neurofibromatosis Working Group

An NIH-sponsored group that meets to enhance communication and collaboration about the state of the science and progress on funded awards.

Tuberous Sclerosis Alliance

A group dedicated to finding a cure for tuberous sclerosis complex while improving the lives of those affected.

Small Business Innovation Research & Small Business Technology Transfer Research Programs

USAMRMC Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Program Objectives:

- Stimulate technological innovation;
- Increase private-sector commercialization of federal research and development;
- Increase small business participation in federally funded research and development;
- Foster participation by minority and disadvantaged firms in technological innovation.

The SBIR and STTR programs are competitive funding opportunities designed to strengthen the role of innovative small businesses in federally funded research and development. Established by Congress, the goal of these programs is to provide small businesses with critical startup and development support that will allow them to compete successfully with larger businesses and commercialize products while fulfilling government needs. Eleven federal agencies participate in the SBIR program and five participate in the STTR program, including DoD. The CDMRP has worked with these programs since FY00 and FY04, respectively, to fill gaps and leverage research and product development not supported elsewhere in the CDMRP portfolio. In FY15, the CDMRP managed more than $14.8M in SBIR awards and more than $1M in STTR awards from the overall USAMRMC SBIR and STTR programs.

Our Programs

The 26 research programs highlighted throughout the remainder of this annual report 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.





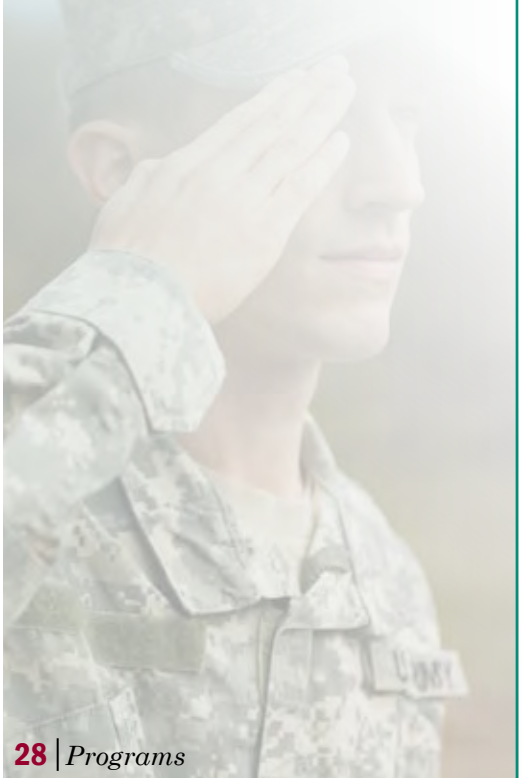
Alcohol and Substance Abuse Disorders Research Program

Vision

Decrease the clinical impact of alcohol and substance abuse

Mission

Explore new opportunities to address alcohol and substance abuse disorders, especially related to TBI and PTSD, through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical protocols

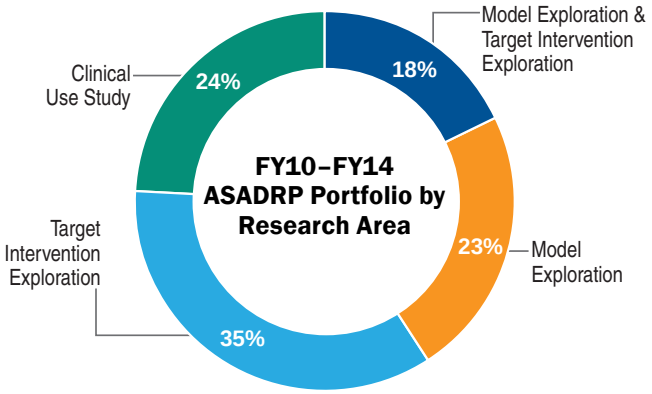


Program History

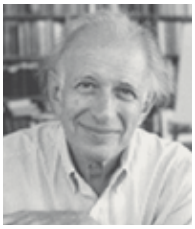
The problem of alcohol and substance abuse is a growing concern among the general public, as well as military personnel and Veterans alike. Impacts include reduced levels of readiness, increased crime, mental health problems, and suicides. PTSD and other psychological health problems are strongly linked to SUDs. 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 SUDs, and federal funding for its research has led to a total appropriation of $20.075M to the ASADRP.

The goal of the program is to identify and develop new medications to improve treatment outcomes for SUDs, 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 SUDs.

SUDs present a significant cost to the military and complicate the treatment of PTSD and related conditions. Successful identification of medications to treat SUDs, alone or together with psychological or neurological conditions, would decrease costs to the military and facilitate redeployment and increased readiness. Such medications also promise to improve public health and avoid significant social costs outside the military context. The ASADRP hopes these new medication-based therapeutic protocols will be helpful for treating those with SUDs.



Total number of awarded projects: 17
Total number of active projects: 7



*A Translational Epidemiological Approach to the Molecular Basis of PTSD and Substance Abuse Comorbidity**

Eric R. Kandel, M.D., Nobel Laureate, Columbia University

Dr. Eric Kandel's research has contributed to new insights into the epidemiology of PTSD and its comorbidity with substance abuse, such as the identification of TIA-1 as an RNA binding protein that regulates the cellular stress response and the establishment of TIA-1-deficient mice as a novel G x E model for stress vulnerability.

Most recently, Dr. Kandel's group demonstrated that increased conditioned odor avoidance behavior in TIA-1-deficient female mice requires associative learning which is likely to depend on the hippocampus, a key structure implicated in PTSD that has been shown to exhibit abnormal synaptic plasticity in female TIA-1 knockout mice. Dr. Kandel's team has also shown that TIA-1 deficiency has no impact on ventral hippocampal field recordings in response to corticosterone treatment in vitro, building upon the notion that TIA-1 deficiency reveals sex-specific differences in emotional regulation and synaptic plasticity. Their overarching findings raise the possibility that modulating the activity of TIA-1 or changing the expression ration of glucocorticoid receptor isoforms may have therapeutic benefit.

*Endogenous Modulators Suppress Substance Abuse Disorders Associated with Chronic Stress**

Jacqueline F. McGinty, Ph.D., Medical University of South Carolina

Dr. Jacqueline McGinty and her team are studying the suppressive effects of oxytocin on stress-induced exacerbation of drug abuse vulnerability in mice that have had previous exposure to traumatic, inescapable footshock.

Thus far, Dr. McGinty's group has found that Oxytocin suppresses drug-seeking with or without pre-exposure to predator odor-induced stress: When pretreated with oxytocin, self-administration of methamphetamine was significantly lower in rats pre-exposed to the predator odor TMT (experimental group) and rats pre-exposed to saline (control group). The potential value of Dr. McGinty's research is that results could strengthen the hypothesis that oxytocin may be a novel therapeutic treatment strategy for concurrent SUD with prior traumatic stress exposure in active Soldiers and Veterans.

*Development of an Animal Model and Novel Treatments for Comorbid PTSD and Cocaine Addiction**

Lori A. Knackstedt, Ph.D., University of Florida

Dr. Lori Knackstedt's team developed an animal model of comorbid PTSD and cocaine addiction to screen medications for their ability to reduce cocaine relapse. A single 10-minute exposure to a predator stressor (fox scent) induced anxiety symptoms one week later in approximately 20% of rats (termed "PTSD"), while the remaining rats were unaffected ("Resilient"). The researchers found that increased expression of metabotropic glutamate receptor 5 (mGluR5) in the prefrontal cortex and amygdala was associated with PTSD resilience. "PTSD" rodents displayed enhanced cue-primed reinstatement of cocaine-seeking and impaired extinction learning, relative to both Control and Resilient rats. Further studies indicated that the antibiotic ceftriaxone fully suppressed cue-primed reinstatement in Control and Resilient rats, while having only a modest effect in PTSD rats. These findings indicate that resilience to PTSD involves mGluR5 upregulation and that the PTSD phenotype alters the neurobiology underlying cocaine relapse.

Translational Coordinating Core

Howard L. Fields, M.D., Ph.D., University of California, San Francisco

The major goal of this core facility is to accelerate the development of new treatments for alcohol and substance abuse and comorbid conditions. The ITN TCC will guide, direct, and accelerate the exploitation of the discoveries of the ITN Consortium by identifying the most promising pharmacological targets, validating their usefulness for alcohol and substance abuse disorders treatment and, in certain cases, performing Phase II proof-of-principle human studies.

Over the past year, the TCC has actively contributed to a new multi-campus initiative of the ITN by establishing a research site at University of California, Berkeley in the Wheeler Brain Imaging Center. The TCC has also begun to coordinate ITN Consortium efforts with NIH programs and commercial pharmaceutical and biotechnology companies to help facilitate the movement of promising candidate medications to the next phase of development.

**Please note that these are only three of many sub-projects funded under the ITN Consortium.*

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

Program History

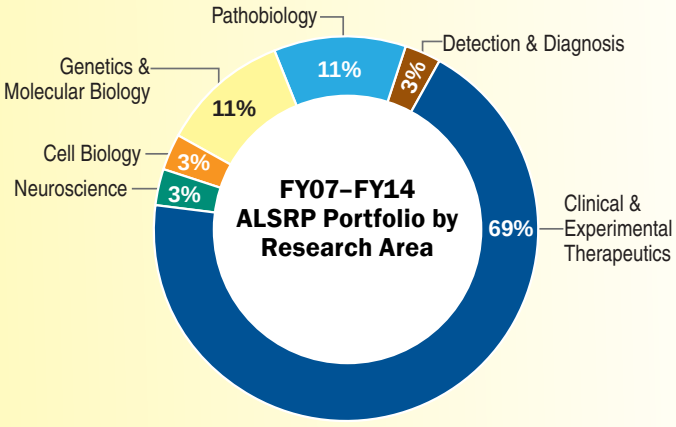
Amyotrophic Lateral Sclerosis (ALS), also known as "Lou Gehrig's disease," is an incurable, degenerative neurological disorder. The CDMRP Amyotrophic Lateral Sclerosis Research Program (ALSRP) is guided by a vision to improve treatment and find a cure for ALS. The ALSRP was created in FY07 with a $5M appropriation. Although the 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 $54M, including $7.5M in FY15. Through its award mechanisms and funding recommendations, the ALSRP supports innovative preclinical research to develop new treatments for ALS.

Program Portfolio

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

For FY15, the Programmatic Panel faces the challenge of continuing this effort of promoting innovative preclinical research toward novel ALS therapeutics.

The pie chart shows the distribution of awards the program has supported from FY07 through FY14.

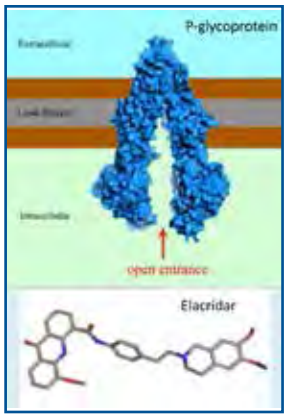


"With ALS, every day could be seen as a new defeat as muscles and function fall away. I have learned that every day is actually a blessing because of the things I can still do. I can't fly anymore or lead sailors, but if I dwell on the losses, then I think I will have lost. It is such a victory that I can wake up in the morning and see my kids' smiling faces. It is a victory that my wife gives me a kiss when I head out the door, and it is a staggering victory that today is one day closer to us finding a cure for ALS."

Matt Bellina, LCDR (Ret), United States Navy, Consumer Reviewer

Research Advances

Piera Pasinelli, Ph.D., Thomas Jefferson University, FY14 Therapeutic Idea Award



Currently, there are no known therapies to effectively halt the progression of ALS, although one FDA-approved drug, Riluzole, modestly slows progression of symptoms. Drs. Piera Pasinelli and Davide Trotti, and colleagues at Thomas Jefferson University believed that the modest effect of Riluzole might be due to membrane efflux proteins in the central nervous system that pump the drug out of cells, preventing accumulation to effective concentrations. With support from a Therapeutic Idea Award from the ALS Research Program, Dr. Pasinelli explored the possibility of enhancing the effectiveness of Riluzole by blocking P-glycoprotein (P-gp), the most common transport protein, along with another drug efflux transporter called the breast cancer resistance protein. As proof-of-principle, Dr. Pasinelli and colleagues first demonstrated that ALS patients have tissue-specific increases in P-gp and breast cancer resistance protein expression in endothelial cells at the blood-spinal cord barrier. Using a mouse model of ALS, Dr. Pasinelli then established that when P-gp protein was blocked by the use of a known P-gp/breast cancer resistance protein-inhibiting drug, Elacridar, the effectiveness of Riluzole therapy was improved. Inhibition of P-gp/breast cancer resistance protein by chronic treatment with Elacridar increased penetration of Riluzole in the central nervous system, improved behavioral measures including muscle function, and significantly extended survival of the mice.

Advancements in the Molecular Biomarker C9orf72

The hexanucleotide repeat expansion (HRE), (GGGGCC)n, present in a noncoding region of gene C9ORF72, was linked to ALS in 2011 (DeJesus-Hernandez et al., 2011; Renton et al., 2011). The ALSRP research portfolio features multiple awards to address this emerging target for ALS therapies, now recognized as the most common genetic cause of ALS.

Michael Benatar, M.D., Ph.D. ***University of Miami School of Medicine*** ***FY12 Therapeutic Idea Award***	C9ORF72 HRE may bring about its pathogenic effect through epigenetic mechanisms resulting in toxic RNAs that disrupt RNA metabolism. In this award, therapeutic agents to either reduce production of toxic RNAs (small molecule inhibitors) or degrade toxic RNAs (antisense oligonucleotides) are being screened. Screened "hits" are being validated in C9ALS patient fibroblasts and induced pluripotent stem cells. Early work has focused on bromodomain-containing proteins.
Samie Jaffrey, M.D., Ph.D. ***Weill Medical College*** ***Cornell University*** ***FY13 Therapeutic Idea Award***	Dr. Samie Jaffrey is developing a novel technology to overcome difficulties in imaging C9ORF72 mutant RNA. A small GFP-mimicking RNA tag, "spinach" or "spinach2," turns on the fluorescence of an imaging agent so that aggregates can be seen in live cells. A high-throughput screening assay for drug discovery will then be developed around this technology.
Leonard Petrucelli, Ph.D. ***Mayo Clinic, Jacksonville, FL*** ***FY13 Therapeutic Development Award***	Dr. Leonard Petrucelli and collaborators will initially screen small molecules that bind to the HRE and prevent c9RAN protein production and foci (aggregate) formation. Lead compounds will then be tested in human neuronal cultures derived from C9ALS patient induced stem cells as well as an animal model of C9ALS.
Justin Ichida, Ph.D. ***University of Southern California*** ***FY14 Therapeutic Development Award***	Dr. Justine Ichida will develop and screen a panel of ALS patient-derived and C9ORF72-affected neuronal cultures to identify small molecule therapeutic lead compounds to improve motor neuron survival. The screening assay will also employ automated image analysis of survival tracking and cytotoxic RNA/protein aggregates.
Jiou Wang, M.D. ***Johns Hopkins University*** ***FY14 Therapeutic Idea Award***	Dr. Jiou Wang proposes that C9ORF72 HREs form nucleic acid structures that are unusual yet stable and can incite pathogenic events including genome instability, transcriptional dysregulation, or sequestration. HRE structural modulating agents including macromolecules (e.g., proteins) and small-molecule drugs will be screened in invertebrate animal models and ALS patient neuronal cultures to identify potential therapeutic candidates.





Autism Research Program

Vision

Improve the lives of individuals with autism spectrum disorder now

Mission

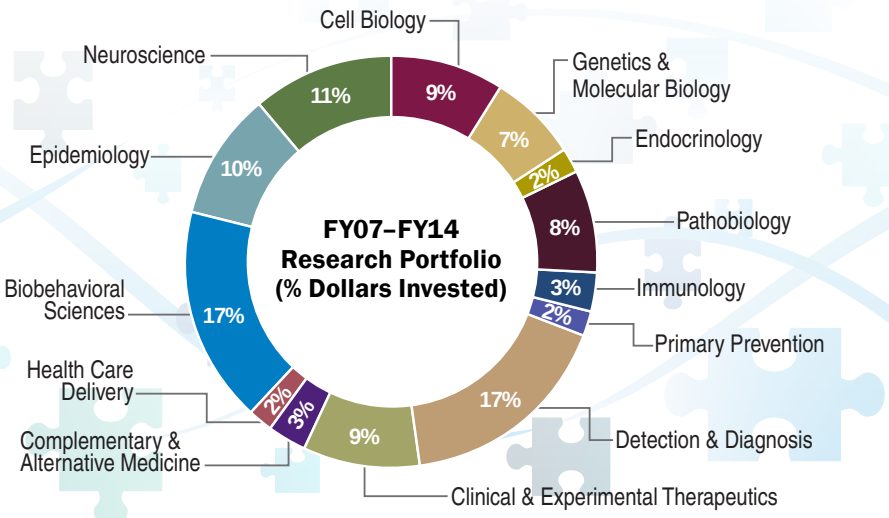
Promote innovative research that advances the understanding of autism spectrum disorders and leads to improved outcomes

"As an autism parent, I am honored to be a voice at the table with so many distinguished scientists who work every day to unravel the mysteries of autism. Every time we meet to renew our priorities and to review applications, I am delighted to be a part of the process to better the lives of individuals—living today and in the future—who are navigating an autism spectrum disorder."

Ann Gibbons
FY10–FY15 Programmatic Panel Member

Program History

Since its inception in FY07 through FY15, appropriations totaling $59.4M have been directed to the Autism Research Program (ARP) to promote innovative research that advances the understanding of ASD. The immediacy of the ARP vision, to improve the lives of individuals with autism now, has imparted a strong sense of action and continues to steer the investment strategy for the 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 such as anxiety, gastrointestinal (GI) issues, sleep disorders, and aggression, which 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. The ARP focuses on funding innovative and highly impactful research while trying to complement other funding agencies' initiatives. Recent progress by investigators funded by the ARP shows promise in the areas of 1) recognizing ASD early so that interventions may be initiated at an early 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) improved research tools to assist scientists on their quest to understand and improve the lives of individuals living with autism. Through the program's areas of interest, the ARP focuses on discovering ways to improve diagnosis, treatment, and treatment fidelity; understanding mechanisms underlying co-occurring conditions; identifying environmental influences; and finding ways to promote transitions to independence for individuals living with autism.



Research Advances

The GI Autism Link

Sarkis Mazmanian, Ph.D., California Institute of Technology, is continuing the work of the late Paul Patterson, who was a pioneer in autism research. Dr. Sarkis Mazmanian's team sought to examine whether treatment with a specific probiotic microbe may be able to improve behavioral symptoms and GI abnormalities in an ASD mouse model. Through support of an FY10 ARP Idea Development Award, they studied the maternal immune activation (MIA) mouse model of ASD. The group found that offspring of the MIA mothers exhibited increased intestinal permeability or "leaky gut," a phenomenon commonly seen in ASD individuals. These mice also displayed dysbiosis of the gut microbiota similar to what has been seen in humans. The Mazmanian laboratory showed that probiotic treatment of these mice with the human gut symbiont *Bacteroides fragilis* (*B. fragilis*) corrected the intestinal permeability in the mice and restored imbalances in their microbiota. Remarkably, *B. fragilis* treatment also ameliorated ASD-like behavioral symptoms in MIA mice. These findings suggest that microbiome-based therapies may be potential treatments for individuals with ASD.

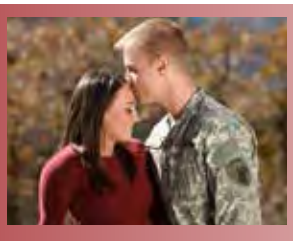
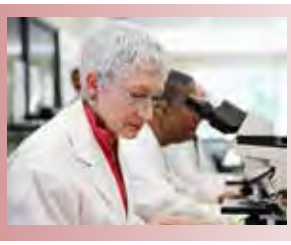
The Elusive Early ASD Biomarker

Janine LaSalle, Ph.D., University of California, investigated epigenetic alterations in human placenta to serve as molecular biomarkers specific for ASD. In most human tissue, a majority of the genome is highly methylated (>70%). Recent studies have revealed that there are large partially methylated domains (PMDs) in some human cell lines that cover up to 40% of the genome. PMDs are associated with gene repression and inactive chromatin marks. Thus far, PMDs have only been observed in cultured cells and cancers. Dr. Janine LaSalle and her colleagues performed MethylC-seq in full-term human placenta and demonstrated, for the first time, normal tissue showing clear evidence of PMDs. The results, published in a 2013 Proceedings of the National Academy of Sciences article, provided a comprehensive reference map of the human methylome in the human full-term placenta. Dr. LaSalle and her team demonstrated differential methylation between autism and typically developing individuals over one potential gene target. These results could be useful for future studies to determine whether epigenetic dysregulation of autism genes can be detected at birth.

The Optimal ASD Animal Model Tool

Tali Kimchi, Ph.D., Weizmann Institute of Science, developed a novel video-RFID (Radio Frequency Identification) tracking system that automatically tracks the locations of multiple animals, allowing for the evaluation of group characteristics on individual behavioral traits. The Kimchi laboratory demonstrated that their automated tracking and behavioral characterization system can be used to accurately classify the strain, sex, and social hierarchy of the animals. This system may allow standardization, rapid and systematic screening, as well as quantification of sets of sociobehavioral phenotypes in wild-type and genetically modified models for neuropsychiatric disorders (e.g., anxiety, autism). Currently, their new Video-RFID tracking and behavioral phenotyping technology has been registered with the U.S. patent office. This novel paradigm would allow scientists to attain a thorough understanding of the social behavioral phenotype in neurotypical colonies of mice, and eventually allow comprehensive screening for atypical phenotypes that properly reflect ASD.



Bone Marrow Failure Research Program

Vision

To understand and cure bone marrow failure disease

Mission

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

Some examples of inherited bone marrow failure diseases:

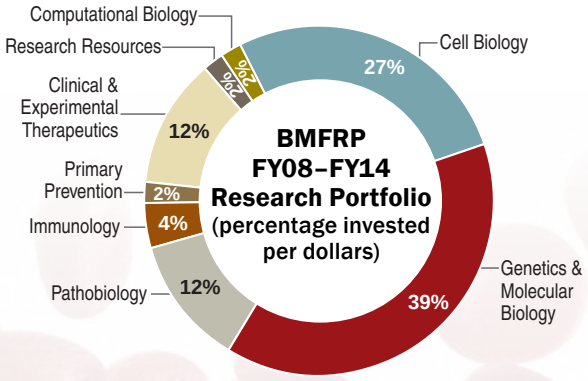
- Fanconi anemia
- Dyskeratosis congenital
- Shwachman-Diamond syndrome
- Diamond-Blackfan anemia
- Neutropenia

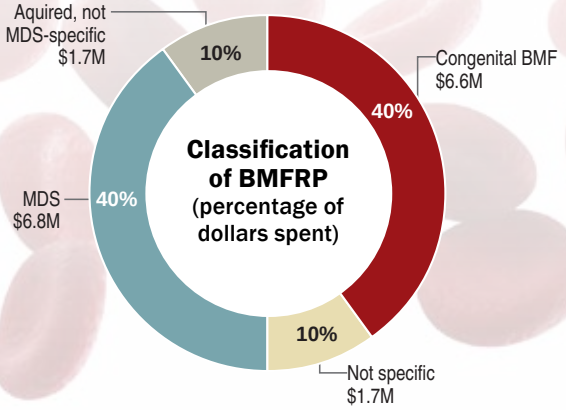
Some examples of acquired bone marrow failure diseases:

- Aplastic anemia
- Myelodysplasia
- Paroxysmal nocturnal hemoglobinuria
- Pure red cell aplasia

Program History

Inside bones, the marrow is the spongy-like tissue that contains blood-forming stem cells. These stem cells initiate the hematopoietic cascade for the development of the different cells within the blood including red blood cells, white blood cells, and platelets. Disorders affecting the stem cells or progenitor cells can lead to bone marrow failure – rare, potentially life-threatening diseases in which the bone marrow stops functioning or produces abnormal blood cells. These diseases are classified into two major categories: acquired bone marrow failure and inherited bone marrow failure. In FY08, Congress appropriated $1M for bone marrow failure research. With continued appropriations, the Bone Marrow Failure Research Program (BMFRP) was established. From FY08 through FY14, $23.4M has been appropriated by Congress to research the prevention, causes, and treatment of bone marrow failures diseases. The appropriation for FY15 is $3.2M. Thus far, the BMFRP has invested in 51 awards with the mission to support innovative research committed to advancing the understanding of inherited and acquired bone marrow failures diseases.





Timeline of Excellence in Bone Marrow Failure Research

ACHIEVEMENTS IN BONE MARROW FAILURE RESEARCH

2008

FY08 – Appropriation of $1M targeted toward Bone Marrow Failure Research

2009

FY09 – Charles Lin, Ph.D., Massachusetts General Hospital, showed the critical role of regulatory T cells in immune privilege mechanisms.

2010

FY10 – Jose Cancelas, M.D., Ph.D., Cincinnati Children's Hospital, examined the mechanism mediating hematopoietic stem cell recovery after exogenous stress (ionizing radiation, chemotherapy).

FY10 – Yi Zhang, M.D., Ph.D., Temple University, investigated graft versus host disease, and the role of Notch and Ezh2 in the progression to bone marrow failure.

FY10 – Daniel Starczynowski, Ph.D., Cincinnati's Children Hospital, explored novel research areas related to Myelodysplastic Syndrome (MDS) to identify and characterize a gene, TRAF-interacting protein with forkhead associated domain B (TIFAB). The gene is deleted in 10% of MDS patients, resulting in unrestricted immune pathway activation in MDS hematopoietic stem/progenitor cells. Dr. Starczynowski and his team of researchers at the Cincinnati Children's Hospital used a combination of mouse genetic and molecular biology approaches to understand the role of TIFAB in normal and MDS hematopoietic cells. With genetically engineered mice that carry a deletion of TIFAB, the researchers showed that hematopoietic defects the mice exhibit are consistent with human MDS and bone marrow failure. Further research will focus on finding alternative approaches to revert the phenotype associated with TIFAB deletion in MDS and other BMF diseases.

2011

FY11 – Omar Abdel-Wahab, M.D., Memorial Sloan Kettering Cancer Center, created a genetically relevant model showing the hallmark features of Myelodysplastic disorders by deletion of Asxl1.

FY11 – Kathleen Sakamoto, M.D., Ph.D., Stanford University, studied the rare inherited bone marrow failure syndrome known as Diamond Blackfan Anemia (DBA) that is associated with severe anemia, birth defects, and increased cancer risk. Approximately 25% of DBA patients have a mutation in the RPS19 gene, and Dr. Sakamoto's team at Stanford University investigated the molecular pathways contributing to the anemia phenotype due to RPS19 deficiency. Working in collaboration with Dr. Stan Nelson at UCLA, Dr. Sakamoto performed RNA-sequencing to identify genes and microRNAs that abnormally regulate RPS19-deficient hematopoietic stem cells. They found that the erythroid-specific transcription factor GATA-1 is abnormally regulated by the inflammatory cytokine TNF alpha p38 MAP kinase pathway, thus suggesting that anti-inflammatory agents could be useful in the treatment of patients with DBA.

2012

FY12 – Marshall Horwitz, M.D., Ph.D., University of Washington, and his research team examined neutropenia, a deficiency in the production of neutrophils, the major type of white blood cells, that offer a first line of defense against infection. Inherited forms of neutropenia often progress to MDS. Heritable mutations in several genes can cause congenital forms of neutropenia, although most often the gene ELANE, encoding neutrophil elastase, is responsible. Dr. Horwitz's team focused on a particular type of mutation disrupting the start site for protein synthesis, found in just a few patients. The researchers discovered that in these individuals, neutrophil elastase is still produced, but the protein initiates from internal start sites and bypasses appropriate signals responsible for directing its subcellular localization, preventing premature activity. These observations suggest that drugs inhibiting neutrophil elastase enzymatic activity could ultimately prove therapeutic.

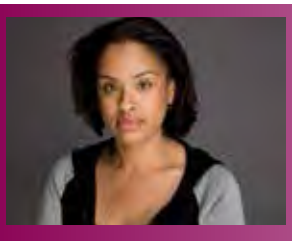
2013

FY13 – Appropriation of $3.2M and 5 research projects awarded

2014

FY14 – Appropriation of $3.2M and 5 research projects awarded





Breast Cancer Research Program

Vision

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

"Recently, my wonderful oncologist recommended adding a brand new drug, Ibrance, to the mix of things we are using to ward off any progression of my disease. I was thrilled to discover that some of the initial research on this drug had been supported by the DoD BCRP. What an amazing thing to know that, as a consumer reviewer, I am helping to advance research that could one day actually help me and thousands of other women stay alive."

Anne Abate, Consumer Reviewer

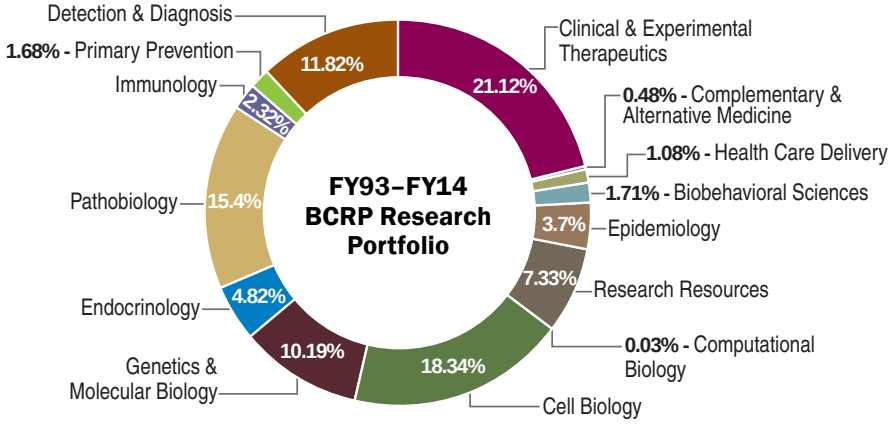
Program History

The Breast Cancer Research Program (BCRP) plays a leading role in the fight against breast cancer. The BCRP was established in 1993 as a result of the passionate efforts of breast cancer advocates. Their continued efforts, in concert with the program's successes, have resulted in more than $3.1B in congressional appropriations through FY15. The BCRP challenges the scientific community to design research that will address the urgency of ending breast cancer. The BCRP seeks to make breakthroughs in breast cancer, accelerate high-impact research with clinical relevance, and encourage innovation and creativity.

Overarching Challenges

Despite the significant progress that has been made in the breast cancer field since 1993, the BCRP recognizes that many overarching questions still remain unanswered in breast cancer, and that funding must be invested in critical areas of research to make breakthroughs that will save lives and lead to its eradication. To meet this urgent need, the FY15 BCRP required all applications to address at least one of the following overarching challenges within the breast cancer landscape:

- Prevent breast cancer (primary prevention)
- Identify what makes the breast susceptible to cancer development
- Determine why some, but not all, women get breast cancer
- Distinguish aggressive breast cancer from indolent 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 life-threatening metastases
- Determine why/how breast cancer cells lay dormant for years and then re-emerge (recurrence); determine how to prevent recurrence
- Revolutionize treatment regimens by replacing interventions that have life-threatening toxicities with ones that are safe and effective
- Eliminate the mortality associated with metastatic breast cancer



Portfolio analysis is by research dollars.

New Clinical Trials in 2015

Andy Minn, M.D., University of Pennsylvania

The focus of Dr. Andy Minn's research is the mechanism and treatment of oligometastases. These metastases are limited in their ability to spread and colonize to form large tumors, but also are resistant to standard treatments such as radiation therapy (RT) and chemotherapy. Dr. Minn received an FY08 Era of Hope Scholar Award to investigate how previously identified gene programs promote metastasis or treatment resistance, how these programs are regulated, and how oligometastases can be effectively treated. Recently, in a 2015 paper published in *Nature*, Dr. Minn and colleagues found in mouse models of breast cancer and melanoma that resistance to RT and anti-CTLA4 can be due to another checkpoint pathway called PD-L1. Results from a single institution Phase I clinical trial of RT + anti-CTLA4 for metastatic melanoma patients (funded from outside resources) revealed similar findings in patients as seen in mice. Next generation trials have begun and include metastatic breast cancer patients. With funding from Merck, one Phase I clinical trial examines RT to a metastatic lesion in combination with Pembrolizumab (PD-1 inhibitor) for patients with metastatic cancers for which anti-PD-1 therapy has failed, or patients who have progressed after at least one regimen of systemic therapy (*https://clinicaltrials.gov/ct2/show/NCT02303990*). A second Phase I trial will soon open to test RT in combination with tremelimuab (anti-CTLA-4) and MED14736 (anti-PDL1) for patients with breast, melanoma, or pancreatic cancer. For each clinical trial, funds from the FY08 Era of Hope Scholar Award will be used for biomarker analysis of mechanistic correlates and of clinical response in breast cancer patients.

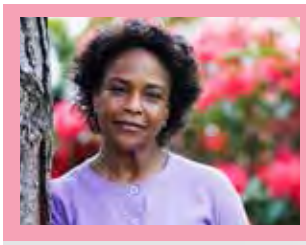
Mary L. (Nora) Disis, M.D., University of Washington

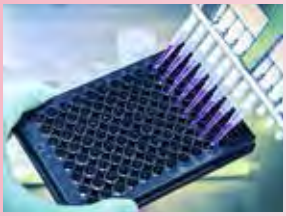
Breast cancer vaccines have been under scrutiny for several years – the etiology of most breast cancers is generally unknown and immunological targets remain elusive. Breast cancer stem cells are known to have the ability to drive tumorigenesis and are associated with self-renewal, drug resistance, and metastatic potential. Stem cell-like properties of cells, including their enhanced migratory ability, can be acquired through epithelial-mesenchymal transition (EMT); thus, proteins characteristic of stem cells or EMT may serve as ideal targets for a breast cancer vaccine. Dr. Nora Disis, recipient of an FY10 Transformative Vision Award, has found five breast cancer stem cell/EMT proteins that are immunogenic in breast cancer patients and healthy volunteers, and she has shown that these five proteins contain epitopes recognized by CD4+ T-helper 1 (Th1) cells, which secrete tumor eradicating interferon-gamma and establish immunologic memory. Dr. Disis has successfully created a multi-antigen vaccine, STEMVAC, comprised of Th1 epitopes derived from these five proteins. The vaccine has been shown to be safe and to inhibit tumor growth in mouse models of breast cancer, and Dr. Disis has recently started enrollment for a Phase I clinical trial in patients with HER2-negative, advanced stage breast cancer. The goals of this trial are to assess the vaccine's safety in patients and to determine the immunogenicity of specific doses of the vaccine. Furthermore, the trial will determine whether immunity can be enhanced or maintained by additional booster vaccinations as well as how the vaccine impacts development of immunologic memory. If the vaccine proves safe, further development will proceed to testing in the prevention setting.

Clinical Breakthrough in 2015

Dennis Slamon, M.D., University of California, Los Angeles

In FY10, Dr. Dennis Slamon received a BCRP Innovator Award to investigate the current limitations in treating certain breast cancer subtypes, including estrogen receptor-positive (ER+) breast cancer. Dr. Slamon found that ER+ breast cancer cells, which can develop resistance to traditional hormonal treatments, are sensitive to a cyclin-dependent kinase (CDK) inhibitor, PD-0332991. Preclinical work showed that PD-0332991 worked synergistically in combination with hormonal therapy. Using these preclinical data, Phase Ib and II clinical trials supported by Pfizer were launched to examine the safety and efficacy of combining PD-0332991 with letrozole, an aromatase inhibitor. The combination of palbociclib and letrozole significantly increased progression-free survival, with no clinically serious side effects. As a result of these promising results, PD-0332991 (under the manufactured name palbociclib), was given "Breakthrough Therapy" status by the FDA on April 10, 2013. Pfizer initiated a Phase III clinical trial of palbociclib combined with letrozole in February 2013. Though the Phase III trial is ongoing, preliminary data show that palbocliclib combined with letrozole improves progression-free survival. In February 2015, the FDA granted accelerated approval of palbociclib (IBRANCE®, Pfizer, Inc.) in combination with letrozole for the treatment of postmenopausal women with ER+, HER2- advanced breast cancer as an initial endocrine-based therapy for their metastatic disease. This is the first CDK4/6 inhibitor made available for any indication. If the ongoing Phase III trial confirms clinical benefit, palbociclib could become a new standard of care therapeutic for ER+ breast cancer.




Breast Cancer Research Semipostal Program

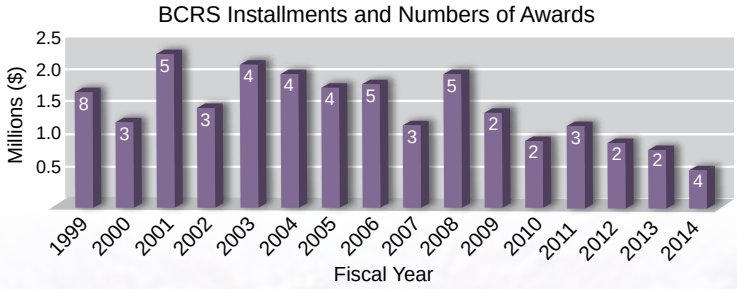
Program History

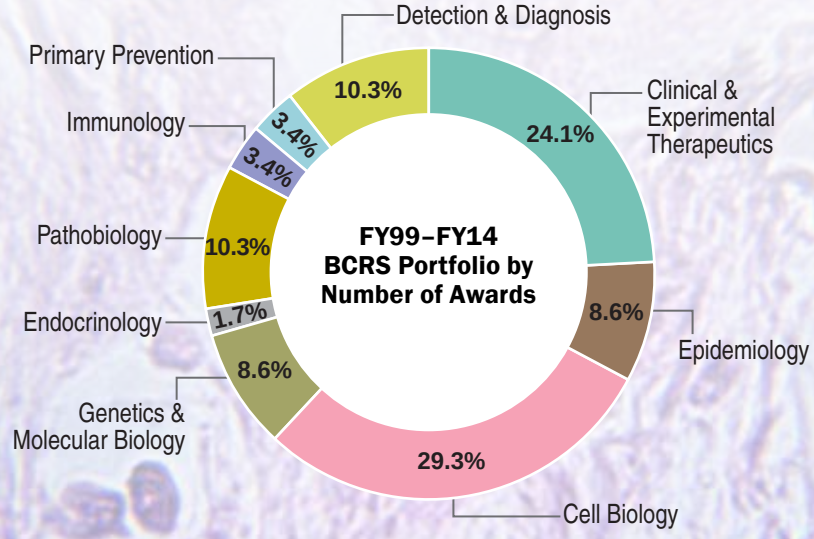
As a result of the efforts of breast cancer advocates, the Stamp Out Breast Cancer Act (Public Law 105-41) led to the U.S. Postal Service's issuance of a new first-class stamp, the Breast Cancer Research Semipostal (BCRS) in 1998. It was the first semipostal in U.S. history. Net revenues from sales of the BCRS, which currently costs 60 cents, are provided to two designated funding agencies: the DoD BCRP and the NIH, to support breast cancer research. Public Law 110-80 reauthorized the BCRS through December 31, 2015. By law, 30 percent is allocated to the DoD BCRP, and 70 percent of the total amount raised is allocated to the NIH.

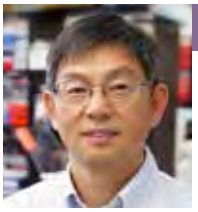
Research and Management Costs

Breast cancer stamp funding received by the BCRP between FY99 and FY14 has been used to fully or partially fund 59 awards under three award mechanisms: 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 breast cancer. Applications funded through the BCRS program were reviewed and recommended for funding according to the two-tier review system implemented by the DoD BCRP.

Total Proceeds from BCRS (through May 2015)	$23,795,004.40
Research	$22,648,319.30
Management Costs	$1,146,685.10







Genetic Polymorphisms, Mitochondrial DNA Damage, and Breast Cancer Risk

Qiuyin Cai, M.D., Ph.D., Vanderbilt University

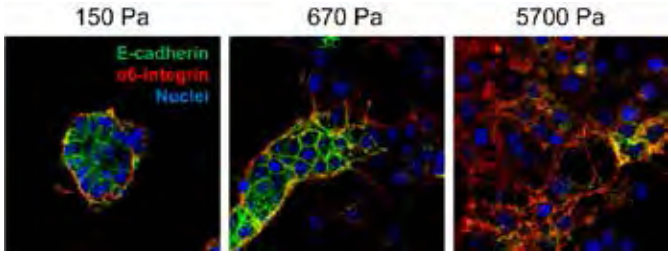
Established genetic risk factors, such as BRCA mutations, are effective predictors of breast cancer incidence; however, these factors do not account for the majority of breast cancers. Dr. Qiuyin Cai addresses this gap through his research on mitochondrial DNA (mtDNA) variations and genes that may the effect on mtDNA damage. Initially funded through the BCRS, Dr. Cai used samples and data from the Shanghai Breast Cancer Study to explore the role of the genetic polymorphisms of MnSOD and hOGG1, genes that code for important antioxidant enzymes in the cell's mitochondria, in breast cancer risk. Dr. Cai conducted this research in a population-based case-control study of Chinese women from the Shanghai Breast Cancer Study. His group found no link between known hOGG1 polymorphisms and breast cancer risk in Han Chinese women. While a slight elevation of risk was detected for MnSOD polymorphisms only, it was more pronounced in pre-menopausal women.

Dr. Cai's group was one of the first to publish findings on the association of germline mtDNA variations in the mtDNA Displacement loop (D-loop) region, with breast cancer risk and survival. They were able to rule out the mtDNA D-loop (CA)n repeat polymorphism in the mtDNA D-loop as a factor in breast cancer risk. He also detected mtDNA D-loop somatic mutations in breast tissues and found that these mutations may contribute to breast cancer development. He developed a sensitive method to measure large mtDNA deletion mutations. Furthermore, they examined the relationship of breast cancer risk and survival with polymorphisms in other genes that encode antioxidant enzymes and DNA damage in other mtDNA regions. The research showed that these mtDNA alterations may not be involved in breast carcinogenesis. These findings may inform future studies that seek to identify breast cancer susceptibility genes in other diverse populations of women.

Regulation of Breast Cancer Stem Cells by Tissue Rigidity

Jing Yang, Ph.D., (pictured top) and Adam Engler, Ph.D., University of California, San Diego

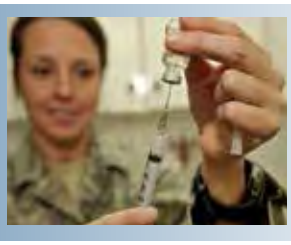
The presence of an area of increased stiffness within a breast tumor, or a fibrotic focus, is associated with cancer progression, distant metastases, and overall poor outcome. Also associated with metastases and poor outcome is an enhanced "stemness" of breast cancer cells. While the underlying mechanism for why tissue, or matrix, stiffness promotes cancer progression is not fully understood, Drs. Jing Yang and Adam Engler have hypothesized that tissue rigidity regulates breast cancer stem cell properties and function, thereby promoting tumor development and chemoresistance. With funding from an FY12 BCRP Idea Award and Breast Cancer Stamp funds, Drs. Yang and Engler have found that increasing matrix stiffness promotes EMT in human breast cancer cells, and that this regulation depends on the adhesion receptor ß1 integrin and the transcription factor TWIST1. Their findings, published in a 2015 *Nature Cell Biology* article, suggest a newly identified paradigm in which increasing matrix stiffness induces an integrin-dependent cell signaling cascade and subsequent release of TWIST1 from its cytoplasmic sequestration factor G3BP2. TWIST1 is then able to enter the nucleus and induce the transcription of EMT and invasion-promoting factors. Cells that have undergone EMT are shown to present many properties of cancer stem cells; thus, the ß1-G3BP2-TWIST1 mechanotransduction pathway may be a key to the regulation of breast cancer stem cell properties and chemoresistance. Further investigation into this pathway may lead to novel therapeutic strategies able to halt progression of a tumor before it has the chance to metastasize.



Mouse mammary epithelial were three-dimensional (3D)-cultured on polyacrylamide gel substrates with increasing rigidities from 150Pa (mimicking normal breast tissue) to 5700Pa (average rigidity of breast tumors), and stained for E-cadherin (green), integrin (red), and nuclei (blue).







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 Office of the Assistant Secretary of Defense for Health Affairs (OASD[HA]), the Defense Health Agency, Research, Development, and Acquisition (DHA RDA) Directorate manages and executes the Defense Health Program (DHP) Research, Development, Test, and Evaluation appropriation. The USAMRMC CDMRP provides Defense Medical Research and Development Program (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**

Joint Program Committees (JPCs), 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 the USAMRMC, operational support responsibilities for the JPCs are provided by multiple execution agents, including the CDMRP, individual laboratories, and advanced developers. In partnership with the JPCs, the CDMRP supports development of program announcements, solicitation and review of applications, full life-cycle management of awards, as well as program evaluation and planning.

Program and Portfolio Areas

From FY10–FY14, the CDMRP has managed 142 DMRDP awards totaling approximately $244M, funding basic, translational, and clinical research efforts. 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 RDA core research programs and recent research projects are listed on the following DMRDP pages.

JPC-1/Medical Simulation and Information Sciences

The JPC-1/Medical Simulation and Information Sciences (MSIS) research program 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.

JPC-1/MSIS works with the services and joint agencies to address gaps and requirements as 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 JPC-1/MSIS has enabled a more collaborative process to identify and validate the research initiatives pertaining to the military. The program assists in the identification, assessment, and transition of relevant emerging technologies that are of value to the MHS. This ultimately allows the USAMRMC and the DHA RDA to better align its research and development efforts with the needs of the MHS. Additional information about JPC-1/MSIS is available at: *https://mrmc.amedd.army.mil/index.cfm?pageid=medical_r_and_d.msis.overview*.

Recent JPC-1/MSIS DHP Research:

- Interactive Visualization Framework to Support Exploration and Analysis of TBI/PTSD Clinical Data; *Jesus Caban, National Intrepid Center of Excellence*
- Virtual Tissue Modeling for Realtime Surgical and Interventional Procedure Simulation; *Peyman Benharash, University of California, Los Angeles*
- Intelligent Focused Assessment of Ultrasound for Trauma (iFAST); *Ronald Grisell, U.S. Army Institute of Surgical Research*

Affiliated Research Programs:

- Joint Warfighter Medical Research Program

JPC-2/Military Infectious Diseases Research Program

JPC-2/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. JPC-2/MIDRP's DHA-aligned mission is focused on the following research portfolio area:

- Polytrauma and Blast Injury

JPC-2/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 focus on the development of host immune response and pathogen biomarkers associated with wound infection to inform clinical decisions, the development of tools for early detection of drug-resistant organisms, identification of nosocomial pathogens, and characterization of antimicrobial resistance patterns, as well as the development of novel and innovative delivery technologies to treat wound infections. This research also emphasizes treatment, with research involving the identification of druggable targets against wound infection pathogens and biofilm processes, the transition of new candidate therapeutics to preclinical testing, and the advancement of promising early leads to first-in-human clinical trials. Additional information about JPC-2/MIDRP is available at: *https://midrp.amedd.army.mil/*.

Recent JPC-2/MIDRP DHP Research:

- Broad-Spectrum Conjugate Vaccine to Prevent Klebsiella Pneumoniae (KP) and Pseudomonas Aeruginosa (PA) Wound Infections; *Raphael Simon, University of Maryland, Baltimore*
- Treatment of Orthopaedic Infections Using Activated Adult Mesenchymal Stem Cells; *Rocky Tuan, University of Pittsburgh*
- Recombinant Interleukin-12, a Broad-Spectrum Biologic for the Treatment of Battle and Traumatic Wound Infections; *Lena Basile, Neumedicines, Inc.*

Affiliated Research Programs:

- Joint Warfighter Medical Research Program
- Peer Reviewed Medical Research Program

JPC-5/Military Operational Medicine Research Program

JPC-5/Military Operational Medicine Research Program (MOMRP) seeks to develop effective countermeasures against stressors and to maximize health, performance, and well-being. JPC-5/MOMRP conducts biomedical research to deliver products and solutions to the Warrior that address health and fitness throughout the deployment cycle. JPC-5/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 JPC-5/MOMRP can be found at *https://momrp.amedd.army.mil/*.

Recent JPC-5/MOMRP DHP Research:

- Effectiveness and Patient Acceptability of Stellate Ganglion Block (SGB) for Treatment of Post-traumatic Stress Disorder (PTSD) Symptoms among Active Duty Military Members; *Bradford Walters, Research Triangle Institute*
- Permethrin Exposure Dosimetry: Biomarkers and Modifiable Factors; *Susan Proctor, U.S. Army Research Institute of Environmental Medicine*
- HomeFront Strong: Building Resiliency in Military Families; *Michelle Kees, University of Michigan*

Affiliated Research Programs:

- Alcohol and Substance Abuse Disorders Research Program
- Gulf War Illness Research Program
- Joint Warfighter Medical Research Program
- Peer Reviewed Medical Research Program
- Psychological Health and Traumatic Brain Injury Research Program

JPC-6/Combat Casualty Care Research Program

JPC-6/Combat Casualty Care Research Program (CCCRP) seeks to drive medical innovation through the 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. JPC-6/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 JPC-6/CCCRP is gap-driven and motivated with the urgency to generate solutions (clinical practice guidelines or FDA-approved products) to benefit the Warfighter and the American public. JPC-6/CCCRP supports the complete range of research activities needed to achieve its goals from foundational science to improvements in health care services and delivery. Additional information about JPC-6/CCCRP can be found at *https://ccc.amedd.army.mil*.

Recent JPC-6/CCCRP DHP Research:

- Bioengineered Blood Vessels for Vascular Trauma: A Pilot Clinical Study; *Alison Pilgrim, Humacyte, Inc.*
- Evaluation of Role 2 (R2) Medical Resources in the Afghanistan Combat Theater: Past, Present and Future; *Elizabeth Mann-Salinas, U.S. Army Institute of Surgical Research*
- Multiscale Technology for Rapid, Enhanced Bone Regeneration; *Alexandru Biris, University of Arkansas at Little Rock*

Affiliated Research Programs:

- Epilepsy Research Program
- Joint Warfighter Medical Research Program
- Military Burn Research Program
- Peer Reviewed Medical Research Program
- Peer Reviewed Orthopaedic Research Program
- Psychological Health and Traumatic Brain Injury Research Program
- Spinal Cord Injury Research Program

JPC-7/Radiation Health Effects Research Program

JPC-7/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 the JPC-7/RHERP is focused on the following key areas:

- Biomedical Technology for Radiation Countermeasures

Recent JPC-7/REHRP DHP Research:

- Advanced Development of Gamma-Tocotrienol as a Radiation Countermeasure, *Vijay Singh, Uniformed Services University of the Health Sciences*
- Advanced Development of Entolimod (CBLB502) to Mitigate and Treat the Acute Effects of Ionizing Radiation, *Andrei Gudkov, Cleveland BioLabs, Inc.*

Affiliated Research Programs:

- Joint Warfighter Medical Research Program
- Peer Reviewed Cancer Research Program
- Peer Reviewed Medical Research Program

JPC-8/Clinical and Rehabilitative Medicine Research Program

JPC-8/Clinical and Rehabilitative Medicine Research Program (CRMRP) seeks to ethically and responsibly develop long-term strategies to find, evaluate, and fund cutting-edge research in reconstruction, rehabilitation, and definitive care for injured Warfighters to improve the standard of care and outcomes, return Service Members to full form and function, and ultimately restore the Warfighter to duty and improve his/her quality of life.

Currently, research sponsored by JPC-8/CRMRP is focused on the following key areas:

- Neuromusculoskeletal Injury Rehabilitation
- Pain Management
- Regenerative Medicine
- Sensory Systems Traumatic Injury (including vision, hearing, and balance)

JPC-8/CRMRP's mission is to focus on definitive and rehabilitative care innovations required to reset our wounded warriors, both in terms of duty performance and quality of life. The program has multiple initiatives to achieve its goals, including improving prosthetic function, enhancing self-regenerative capacity, improving limb/organ transplant success, creating full functioning limbs/organs, repairing damaged eyes, treating visual dysfunction following injury, improving pain management, and enhancing rehabilitative care. Additional information about JPC-8/CRMRP can be found at: *https://crmrp.amedd.army.mil/.*

Recent JPC-8/CRMRP DHP Research:

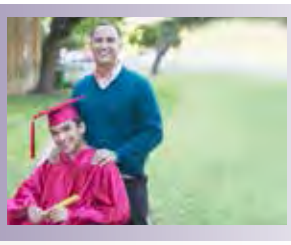
- Regenerative Approaches to Support Osseointegration Implants: Optimizing and Eliminating the Skin-Implant Interface; *Jonathan Forsberg, Naval Medical Research Center*
- Atypical Opioid Mechanisms of Control of Injury-Induced Cutaneous Pain by Delta Receptors; *Gregory Scherrer, Stanford University*
- Pre-clinical Testing of Sustained Release of Dasatinib to Prevent the Major Blinding Complications Following Eye Injury; *Shigeo Tamiya, University of Louisville*

Affiliated Research Programs:

- Joint Warfighter Medical Research Program
- Orthotics and Prosthetics Outcomes Research Program
- Peer Reviewed Medical Research Program
- Peer Reviewed Orthopaedic Research Program
- Psychological Health and Traumatic Brain Injury Research Program
- Restorative Transplant Research Program
- Spinal Cord Injury Research Program
- Vision Research Program







Duchenne Muscular Dystrophy Research Program

Vision

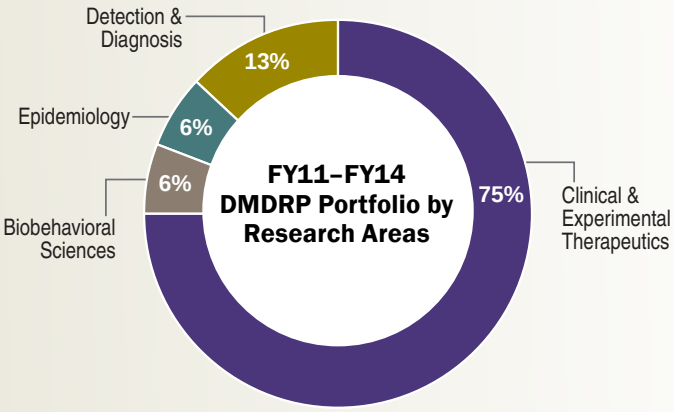
To extend and improve the function, quality of life, and life span for all individuals diagnosed with DMD

Mission

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

Program History

The Duchenne Muscular Dystrophy Research Program (DMDRP) was established in FY11, the result of passionate and tireless advocacy efforts. The initial congressional appropriation for DMDRP was $4M, and since that time, $16.8M has been appropriated to the program, including $3.2M in FY15. Over the past several years, research has identified many novel therapeutic targets and significantly expanded the number of potential therapeutics in the pipeline for Duchenne Muscular Dystrophy (DMD). To help support these current therapeutic development efforts, DMDRP solicits projects focused in several areas, including cardiopulmonary studies, discovery and qualifications of biomarkers, assessment of clinical trial outcomes, clinical studies and novel interventions to improve clinical care and quality of life, and advanced therapeutic preclinical studies. The DMDRP aims to accelerate the transformation of promising therapeutic ideas into clinical applications and support the training of new physician researchers to encourage careers in DMD research.



"The DMDRP brings together a knowledgeable team of stakeholders to evaluate the landscape, develop initiatives, and review proposals that address key gaps in the Duchenne research portfolio. From the perspective of a patient advocacy group engaged in Duchenne, the DMDRP is an important resource for our community."

John Porter, Ph.D., Programmatic Panel Member

Supporting the Research Objectives of the Muscular Dystrophy Action Plan

MECHANISMS

Gail Thomas, Ph.D., Pennsylvania State University, is evaluating a COX-inhibiting nitric oxide donor (Naproxcinod) as a way to increase nitric oxide to counteract functional muscle ischemia and thus improve muscle blood flow regulation and heart function in Duchenne/Becker Muscular Dystrophy.

PRECLINICAL THERAPY DEVELOPMENT

Justin Percival, Ph.D., University of Miami Health System, is assessing a drug that stimulates soluble guanylyl cyclase as a way to better harness the therapeutic potential of increased Nitric Oxide/Cyclic GMP Pathway activity as a palliative treatment for DMD.

Charles Gersbach, Ph.D., Duke University, is developing methods to restore dystrophin expression via targeted genome editing in vivo.

M. Carrie Micelli, Ph.D., University of California, Los Angeles, is exploring modulating calcium signaling through the ryanodine receptor to enhance antisense exon skipping and make it more therapeutically beneficial for DMD patients.

Kathleen Rodgers, Ph.D., University of California School of Pharmacy, is evaluating an angiotensin 1-7 peptidomimetic, MMX1902, as an oral treatment to induce recovery and regeneration in injured muscles and ameliorate DMD-related cardiac dysfunction.

Paul Martin, Ph.D., Nationwide Children's Hospital, is testing two different gene therapy vectors for GALGT2 gene therapy for prevention of cardiomyopathy in DMD patients.

Carmen Bertoni, Ph.D., University of California, Los Angeles, is conducting optimization, efficacy, tolerability, and safety testing of read-through drug 13 derivatives for DMD.

Elizabeth McNally, M.D., Ph.D., Northwestern University Feinberg School of Medicine, is evaluating the use of an LTBP4 antibody to prevent release of TGF-ß sequestered by LTBP4, and whether this will lead to muscle stabilization and reduced fibrosis in DMD.

Jill Rafael-Fortney, Ph.D., Ohio State University College of Medicine, is optimizing renin-angiotensin-aldosterone inhibitors as a treatment for DMD.

Barry Byrne, M.D., Ph.D., University of Florida College of Medicine, is developing advanced gene therapy using a mini-dystrophin gene for treatment of cardiomyopathy and respiratory insufficiency in DMD.

Dongsheng Duan, Ph.D., University of Missouri, will be conducting preclinical studies using the second-generation AAV micro-dystrophin vector to support an investigational new drug application and future clinical trial.

Elisabeth Barton, Ph.D., University of Florida College of Health and Human Performance, will be developing orally bioavailable therapeutics by the chloroplast expression system to counter muscle degeneration, weakness, and fibrosis in DMD.

DIAGNOSIS, SCREENING, AND BIOMARKERS

Yetrib Hathout, Ph.D., Children's National Medical Center, is validating a set of serum pharmacodynamic biomarkers for their ability to predict treatment efficacy and disease progression in DMD patients.

Glenn Walter, Ph.D., University of Florida College of Medicine, is evaluating near-infrared imaging as a way to monitor muscle cell response and therapeutic agent delivery in dystrophic and damaged muscle.

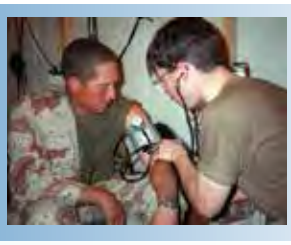
LIVING WITH MUSCULAR DYSTROPHY

Avital Cnaan, Ph.D., Children's National Medical Center, is establishing minimal clinically important differences for current clinical trial endpoints and composite outcome measures that are sensitive and responsive to changes produced by treatments in children and adults with muscular dystrophies.

Craig McDonald, M.D., University of California, Davis Health System, will be developing a lifespan-based novel composite person-reported outcome measurement tool using data from the Cooperative International Neuromuscular Research Group Duchenne Natural History Study to evaluate treatment effects in DMD.







Gulf War Illness Research Program

Vision

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

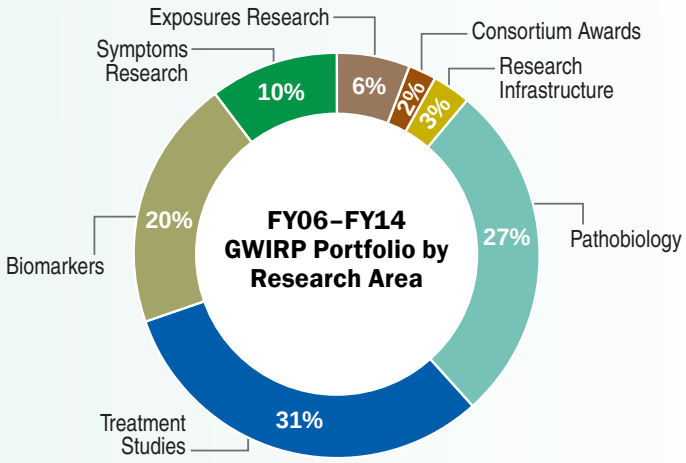
Mission

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

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

Program History

DoD-funded GWI research began in 1994 and was managed up to FY06 through a number of DoD programs. Although Gulf War-related research was not funded in FY07, a $10M appropriation renewed the program in FY08, renamed the GWIRP, to be managed fully by the CDMRP. From FY08 to FY14, the GWIRP has received a total of $84M in congressional appropriations. From these appropriations, the program has built a broad research portfolio of over 90 awards featuring clinical trials and basic research, as well as studies addressing chemical exposures and GWI symptomatology. Recent additions to the program have included incentives for new investigators, expansion of successful past investigations, and epidemiological studies to characterize patterns of health and disease in Gulf War Veterans. 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.



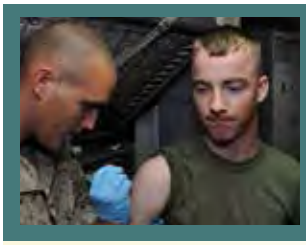
"On behalf of all Veterans, and especially Gulf War Veterans, I express the most sincere gratitude to all of those involved in trying to solve the mystery of Gulf War Illness through continuing research, effective treatments, and healthy coping mechanisms to treat Gulf War Veterans. It was J. Michael Bishop who said, "The modern research laboratory can be a large and complicated social organism," but through the collaboration of the Congressionally Directed Medical Research Programs, the Veterans, and the researchers, much can and will be accomplished."

Brent Casey, Consumer Reviewer

On the Horizon – GWI Treatment Investigations Currently Underway

Based on a conscious focus to fund research projects directly translatable to treating Veterans with GWI, half of the projects funded in FY13 (i.e., 8 of 16 awards) were directly related to advancing potential therapeutic treatments. This progression toward more clinically relevant projects reflects the overall maturing of GWI research as a whole and increases the hope for effective treatments for suffering Gulf War Veterans.

	Project Title and Principal Investigator	Treatment Proposed
Clinical Trials		
	*Gulf War Illness Inflammation Reduction Trial* Ronald Bach, Ph.D., Minnesota Veterans Administration Medical Center	Prednisone, to address chronic inflammation integral to the underlying pathophysiology of GWI; the treatment is hypothesized to alleviate symptoms of GWI and improve quality of life.
	*Development of Dietary Polyphenol Preparations for Treating Veterans with Gulf War Illness* Giulio Pasinetti, M.D., Ph.D., Mount Sinai School of Medicine	Dietary supplementation with a Flavonoid-Rich Preparation (FRP, to include Concord grape juice and resveratrol) focused on improving cognitive function and alleviating chronic fatigue in Veterans with GWI.
	*A Multimodal Evaluation of the Comparative Efficacy of Yoga versus a Patient-Centered Support Group for Treating Chronic Pain in Gulf War Illness* Peter Bayley, Ph.D., VA Palo Alto Health Care System	Demonstrating the efficacy and safety of a yoga treatment program to address symptom complexes associated with GWI; also to generate clinical symptom-based outcome measures of the treatment.
	*Use of a Portable Stimulator to Treat GWI* Jorge Serrador, Ph.D., Veterans Biomedical Research Institute, Inc.	Vestibular stabilization to treat balance issues and dizziness from GWI.
	*A Prospective Open-Label Clinical Trial of Methylphenidate plus a GWI-Specific Nutrient Formula in Patients with Gulf War Illness and Concentration Disturbances* Jon Kaiser, M.D., K-Pax Pharmaceuticals, Inc.	Low-dose methylphenidate hydrochloride plus a proprietary GWI nutrient formula to treat fatigue and concentration disturbance symptoms of GWI.
	*A Screening Trial of Botanical Microglia Modulators* Jarred Younger, Ph.D., Stanford University	Tests a panel of botanical microglia modulators (anti-inflammatory agents) intended to reduce pain, fatigue, and other symptoms associated with GWI.
Laboratory Studies Directly Investigating Treatments		
	*Novel Therapeutic Approaches for the Treatment of Depression and Cognitive Deficits in a Rodent Model of Gulf War Veterans' Illness* Laxmikant Deshpande, Ph.D., Virginia Commonwealth University	Tests dantrolene (Dantrium®) and experimental compounds to correct altered calcium signaling in the brain (in an animal model of GWI); this is hypothesized to address cognitive deficits and mood disorders commonly seen in GWI.
	*Monosodium Luminol for Improving Brain Function in Gulf War Illness* Ashok Shetty, Ph.D., Texas A&M University System Health Sciences System	Tests the anti-inflammatory and antioxidant drug monosodium luminol-GVT to improve cognitive dysfunction and depression in a rat model of GWI.





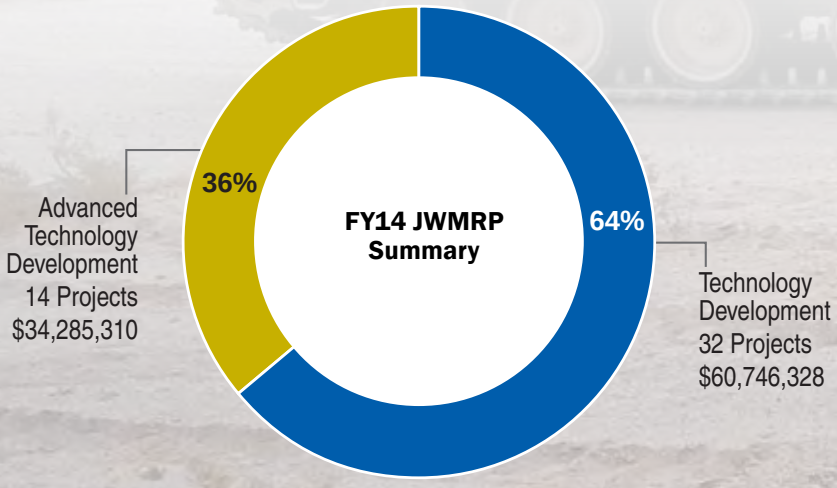
Joint Warfighter Medical Research Program

The 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, the JWMRP offers a pathway to transition products to military health care providers and the Warfighter.

Program History

The Joint Warfighter Medical Research Program (JWMRP) provides the DoD with a powerful tool for advancing previously funded Congressional Special Interest medical research and development projects that address military medical requirements of the Services while complementing and enhancing the DMRDP. The 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 development process.

Each year, a broad spectrum of research projects are considered for funding under the JWMRP. The projects align to the six JPC scientific domains represented in the DMRDP, including Medical Simulation and Health Information Sciences (JPC-1), Military Infectious Diseases (JPC-2), Military Operational Medicine (JPC-5), Combat Casualty Care (JPC-6), Radiation Health Effects (JPC-7), and Clinical and Rehabilitative Medicine (JPC-8). Congress first appropriated $50M for JWMRP in FY12 and again in FY13; it later doubled the appropriation to $100M in FY14, followed by $50M for FY15. Because the overall goal of the program is to deliver a product for the DoD, the ratio of funding allocation over the past three 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 are aligned to the FY13 JWMRP, and 46 projects are funded through the FY14 program. The graph on the next page depicts the demographics of the program for FY14.



Research and Product Development Efforts Funded by the JWMRP Include:

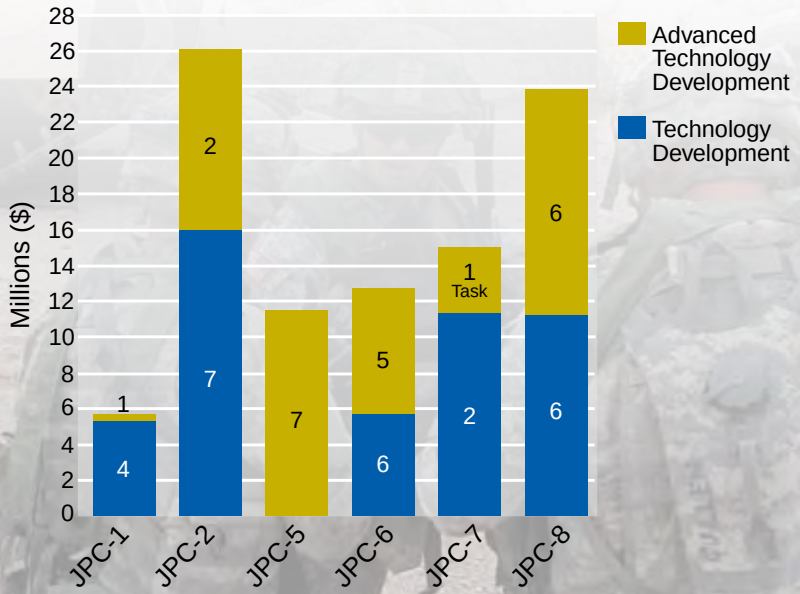
- Transportable pathogen reduction and blood safety system.
- Prototype development and testing of a miniaturized, remotely controlled, image-guided surgical robot for peritoneal cavity surgery.

- Development of a non-electric, disposable intravenous infusion pump.
- Intelligent tutoring system for emergency preparedness training.
- Phase III pivotal clinical trial for a Norovirus vaccine.

- Phase II Malaria clinical trial with the first live attenuated vaccine against protozoal disease in humans.
- Development of passive physiological monitoring system for use during medical evacuation.
- Development and clinical trial of a food supplement to prevent travelers' diarrhea.

- Development and evaluation of implantable nanosensors to monitor key physiological parameters of Warfighter health.
- Pivotal study on the regulatory approval pathway for a drug to treat acute radiation syndrome.
- Modifying and enhancing lower extremity prosthetics to restore balance and locomotion.
- Accelerating the development of the opioid Sufentanil for pain treatment.
- Development of bioengineered corneas for transplantation.

FY14 Final Funding Distribution







Lung Cancer Research Program

Vision

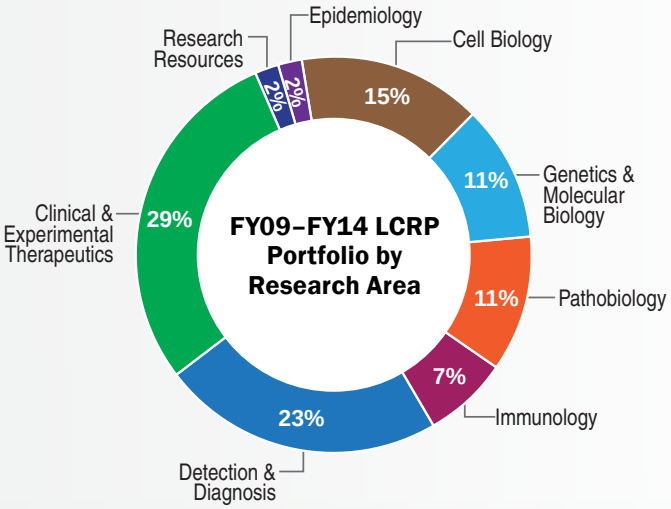
Eradicate deaths from lung cancer to better the health and welfare of the military and the American public

Mission

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

Program History

The Lung Cancer Research Program (LCRP) was established in FY09, and over the past 6 years it has played a critical role in supporting high-impact, innovative research within the military and general public for risk assessment, prevention, early detection, diagnosis, and treatment for the control and cure of lung cancer. The dedicated efforts by lung cancer advocates to increase public awareness of this disease, and federal funding for its research, have led to total congressional appropriations of $89.5M to the LCRP, including $10.5M for FY15. To address the critical needs of the lung cancer research and patient community, the LCRP adapts its investment strategy annually, focusing its support in underfunded and underrepresented areas. Importantly, military personnel are at a higher risk of developing lung cancer than the general population due to increased rates of smoking as well as an increased likelihood of exposure to environmental carcinogens during their service. To address our military's higher risk, all applicants to the 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. In addition to military relevance, specific focus areas for the LCRP include development of non- or minimally invasive detection and screening tools, understanding the mechanisms leading to various sub-types of lung cancer and the progression to clinically significant lung cancer, prevention and treatment, predictive and prognostic markers to identify responders and non-responders, and understanding susceptibility or resistance to treatment.



"Lung cancer has a way of changing not only your perspective, it changes the entirety of your life....As the son of a father who died from lung cancer, as someone who has survived lung cancer, and as the dad to three young daughters, my efforts with peer review are a means toward ensuring that my daughters will not have to share my experience with lung cancer. I don't know if we can ever eradicate the disease, but we are changing how we diagnose it, how we treat it, and we are changing our ability to survive it."

Jim Pantelas, Consumer Reviewer

Innovative LCRP Projects Spanning the Research Pipeline

Early Ideas	Advanced Ideas	Translational Research	Clinical Trials
• A New Molecular Target for Small Cell Lung Cancer, *Linda Malkas, Ph.D., City of Hope Beckman Research Institute*	• Impact of Inhibition of KRAS/STK11-Induced Immune Suppression in Enhancing Immunotherapy Response, *Amer Beg, Ph.D., University of Florida H. Lee Moffitt Cancer Center & Research Institute*	• Targeted Repolarization of Tumor-Associated Macrophages in Lung Cancer, *Sunil Singhal, M.D., University of Pennsylvania*	• A Phase I Trial of an Immune Checkpoint Inhibitor Plus Sterotactic Ablative Radiotherapy in Patients with Inoperable Stage I Non-Small Cell Lung Cancer, *Karen Kelly, M.D., University of California, Davis*
• Targeting Cholesterol Metabolism for Prevention of Small Cell Lung Cancer, *Kwon-Sik Park, Ph.D., University of Virginia*	• Drosophila as a Screening Platform for Novel Lung Cancer Therapeutics, *Ross Cagan, Ph.D., Icahn School of Medicine at Mount Sinai*	• Evaluation of Biomarkers Predictive of Benefit from the PD-1 Inhibitor MK-3475 in Patients with Non-Small Cell Lung Cancer and Brain Metastases, *Sarah Goldberg, M.D., M.P.H., Yale University*	
• Induced Tumor Cell Heterogeneity by the Sleeping Beauty Transposon System to Generate an Improved Model of Drug Resistance, *Robert Doebele, M.D., Ph.D., University of Colorado at Denver*	• Development of a Blood-Based Biomarker Panel for Indeterminate Lung Nodules, *Ayumu Taguchi, M.D., Ph.D., University of Texas MD Anderson Cancer Center*		

Research Highlight

Identification of a New Biomarker for Lung Cancer Tumor Aggression Points to Promising New Therapies

Prasad S. Adusumilli, M.D., Memorial Sloan Kettering Cancer Center

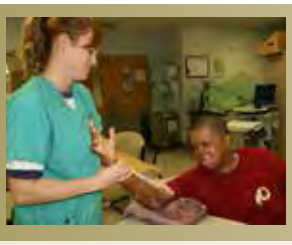
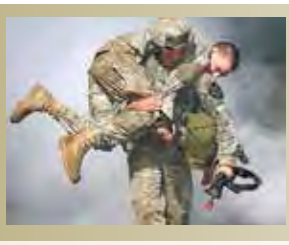
Currently, no biomarkers have been validated that can be used to inform decision making for chemotherapy-resistant lung cancers. Dr. Prasad Adusumilli at the Memorial Sloan Kettering Cancer Center has taken on this challenge. Through a project funded by an FY11 LCRP Promising Clinician Research Award, Dr. Adusumilli has identified a biomarker that corresponds with the presence of aggressive, therapy-resistant tumors, and he has begun work using immunotherapy for targeting this antigen to improve treatment outcomes.

Dr. Adusumilli discovered that mesothelin, a cancer-cell surface antigen, is overexpressed in 69% of lung adenocarcinoma tumors with minimal or no expression in normal tissues. In vitro studies confirmed that mesothelin overexpression correlates to increases in tumor cell proliferation, migration, and invasion, while mouse studies revealed that high mesothelin expression corresponds to a decrease in overall survival. These observations were further validated in 1200 lung adenocarcinoma patients. These data suggested mesothelin expression is a reasonable biomarker for tumor aggressiveness and may be an attractive target for immunotherapies.

As a next step, Dr. Adusumilli developed and investigated the anti-tumor efficacy of CAR (chimeric antigen receptor) T cells, patients' own immune cells genetically engineered to kill cancer cells expressing mesothelin. Based on this successful identification of mesothelin as a biomarker and development of T-cell therapy, Dr. Adusumilli has been able to successfully launch a series of clinical trials. Among these are studies investigating the effectiveness of T-cell therapies engineered to target mesothelin-expressing tumor cells, as well as work designed to evaluate mesothelin's capacity as a biomarker in other cancers.

Dr. Adusumilli's success at the identification of an evaluative biomarker indicative of aggressive behavior and resistance to currently available therapies, as well as his progress toward a targeted T-cell therapy for lung cancer patients is a step forward in a promising field for lung cancer treatment.




Military Burn Research Program

Vision

Deliver the best combat burn trauma care to improve health and performance outcomes for the Warfighter

Mission

Identify and address the traumas of burn, especially those combat-related injuries that affect the military population

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 the CCCRP, and are focused on injuries obtained from the point of injury to treatment at the stateside military burn centers. 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 and those within the general public at large who sustain burn injuries. The funded research is expected to benefit both the military and civilian communities.

MBRP Achievements

Hypertrophic Scar Prevention
Evangelos Badiavas, M.D., Ph.D., University of Miami Hospital, is using a large animal model to investigate novel methodologies for remodeling hypertrophic burn scars using stem cells combined with laser therapy.

Burn Care Standardization Checklist
LTC Jeremy Pamplin, M.D., Brooke Army Medical Center, San Antonio, and his team are developing a new checklist model to improve burn patient care. Preliminary reviews of medical practices show clear differences in how different types of clinicians review patient information and subsequently prioritize treatment. Thus, a new paradigm that relies heavily upon this checklist model, called the phases of illness paradigm, is slated to provide a benefit to targeted therapies.

Rehab Physiology
Oscar E. Suman, Ph.D., University of Texas Medical Branch at Galveston, is leading a multi-center study that is investigating the effects of a quantifiable exercise program in patients with acute burn injuries with the goals of decreasing both intensive care unit and hospitalization stays, and improving overall physical performance.

Accelerated Wound Healing
Booker King, M.D., FACS, U.S. Army Institute of Surgical Research, is leading the team that will conduct a randomized controlled pilot study of hyperbaric oxygen therapy as a possible treatment for deep partial thickness burns.

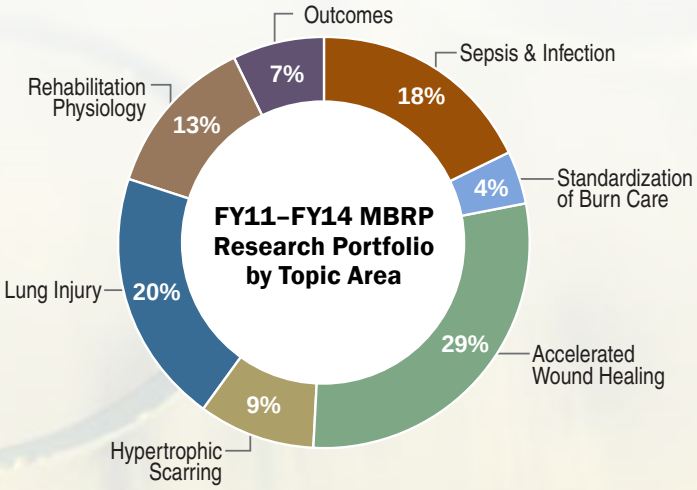
Recombinant Human CC10 for Treatment of Burn and Inhalation Lung Injury

Specific Problem: Smoke inhalation causes a severe inflammatory response in the lungs and increases mortality.

Approach: Intravenous administration of recombinant human CC10 protein (rhCC10) to reduce mortality and inflammatory responses, and improve lung function.

Investigation: Dr. Aprile Pilon, M.D., and her team at Therabron Therapeutics, Inc. (formerly Clarassance, Inc.) evaluated rhCC10 protein to suppress acute lung injury (ALI) and inflammatory responses resulting from smoke inhalation injury. Pre-clinical study using an ovine model was carried out to evaluate the efficacy of rhCC10 for decreasing mortality and morbidity from smoke inhalation lung injury with and without dermal burns. Pre-clinical data showed rhCC10 protein administration to improve survival in ovine models of smoke inhalation lung injury and dermal burn plus smoke inhalation by reducing mortality by nearly half. In parallel, methods were worked out to simulate the chemical modifications to rhCC10 protein by reactive oxygen species in vivo during acute lung inflammation, and a prototype ELISA was developed to assess pulmonary status. The modified rhCC10 protein preparations enable not only a new diagnostic/prognostic test, but also novel therapeutic compositions for treatment of inflammatory diseases and conditions.

Research Impact: Burns in combination with inhalation lung injury can be especially lethal, resulting in acute respiratory distress syndrome. The modified and unmodified rhCC10 proteins could improve the mortality rate, respiratory health, and long-term recovery in these injuries. The development of these drugs will enable clinical and trauma care centers to address the urgent need for therapies to treat burn injuries and ALI due to smoke inhalation and viral infections. Proof of concept for the efficacy of rhCC10 in ALI has already been obtained in numerous animal models of ALI, and in premature infants in respiratory distress and at high risk for developing neonatal chronic lung disease. It also has the potential to improve long-term outcomes in injured military personnel. Overall, rhCC10 therapy could be developed to improve survival of ALI from multiple causes, including burn casualties sustaining smoke inhalation injury, on the battlefield or from civilian burn traumas.



"Over the next few years, we will leverage expertise and innovative thinking to fill combat casualty care gaps such as projecting full advanced life-sustaining therapies in prolonged field care, as they are currently limited."

Kevin K. Chung, M.D., FCCM, FACP
LTC, MC, USA
Director of Research (Interim), U.S. Army Institute of Surgical Research





Multiple Sclerosis Research Program

Vision

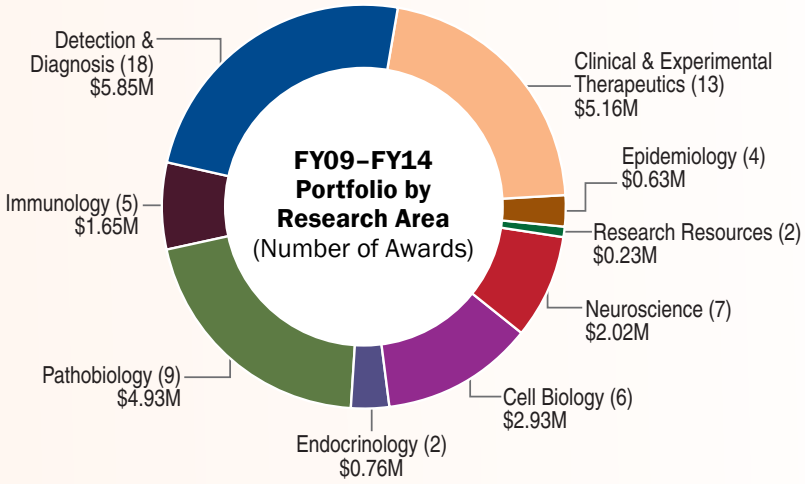
To prevent the occurrence, cure, reverse, or slow the progression, and lessen the personal and societal impact of multiple sclerosis

Mission

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

Program History

The Multiple Sclerosis Research Program (MSRP) was established in FY09 when the efforts of the multiple sclerosis (MS) advocates led to a congressional appropriation of $5M. Since then, a total of $33.1M has been appropriated to the program, including $5M in FY15. The MSRP has funded 66 awards through FY14, ranging from Idea Awards (22) supporting conceptually innovative, high-risk/potentially high-reward research; Synergistic Idea Awards (12) supporting multidisciplinary research collaborations; Concept Awards (14) supporting the exploration of highly innovative new concepts or untested theories; Metric Development and Validation Awards (9) supporting the development of readily accessible, cost-effective, validated analytical methods; and Investigator-Initiated Partnership Awards (9) supporting the 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.



"My experience of serving as a consumer reviewer with the MSRP is gratifying," and one in which "patient advocates were not just heard but respected. The opinions of the patient advocate reviewers were not just welcomed but were insisted upon and frequently figured prominently in the peer review process. Each application was assessed not just on scientific merit, but also on its potential benefit to patients. Indeed, the involvement of consumer advocates in the application review processes is invaluable in shaping the MSRP's investments toward the program's mission of lessening the personal and societal impact of MS."

Seth Morgan, M.D., Peer Reviewer Consumer (Retired)

Targeting the Chemerin: CMKLR1 Interaction to Treat Multiple Sclerosis

Brian Zabel, Ph.D., VA Palo Alto Health Care System

With funding from an FY10 Idea Award, Dr. Brian Zabel tested the hypothesis that blocking the interaction between chemerin and one of its receptors, CMKLR1, inhibits immune cell migration to the brain, which would prove useful for treating MS. From a library of 130,000 compounds, he identified a small molecule, 2-(α-naphthoyl) ethyltrimethyl ammonium iodide (α-NETA), that inhibited the ability of chemerin to activate CMKLR1. This inhibition prevented immune cell migration in an in vitro model. Next, Dr. Zabel used a widely studied experimental autoimmune encephalomyelitis (EAE) mouse model of MS, to determine if α-NETA might be effective in treating MS. He found that prolonged administration of the inhibitor significantly delayed the clinical onset (e.g., limb weakness and paralysis) of EAE, and limited immune cell infiltrates in the brain. Although the mice treated long-term with α-NETA eventually developed EAE symptoms, this study provided proof-of-concept that the chemerin:CMKLR1 interaction may be a useful target to prevent or treat MS.

Graham KL, Zhang JV, Lewén S, Burke TM, Dang T, Zoudilova M, Sobel RA, Butcher EC, Zabel BA. A novel CMKLR1 small molecule antagonist suppresses CNS autoimmune inflammatory disease. PLoS One. 2014 Dec 1;9(12):e112925.

"This year's CDMRP MSRP award is providing vital funding to build and develop translational research partnerships. These partnerships will join basic science and clinical researchers together, and also bring together researchers who have not previously been involved in MS research. This will provide an important opportunity to develop projects that directly connect basic research on MS with the clinical target – MS patients who need therapies. Consumer advocates are an important component of the CDMRP MSRP review process, as they ensure a clinical relevance and grounding to the proposed projects."

Robert Fox, M.D., Cleveland Clinic, Mellen Center, Peer Reviewer

Noninvasive Detection and Differentiation of Axonal Injury/Loss, Demyelination, and Inflammation

Sheng-Kwei Song, Ph.D., Washington University in St. Louis

Dr. Sheng-Kwei Song is using funding from an FY11 Idea Award to develop an advanced MRI technology called diffusion basis spectrum imaging (DBSI), which models tissue water diffusion characteristics in and around nerve axons. This technology could potentially identify the different types of nerve lesions commonly observed in MS patients. After testing this new MRI technology on two different mouse models of MS, Dr. Song demonstrated that DBSI can detect increases in the space surrounding nerve axons, which is an indication of demyelinated nerve fibers. Additionally, Dr. Song demonstrated that DBSI can quantify the extent of cellular inflammation and increased accumulation of fluid (edema) in the optic nerve. This is important as edema and inflamed cells hamper the ability of current imaging techniques to detect damage. Thus, the new technique delivers a clearer picture of nerve health for diagnosis, and enhances the ability to measure the effectiveness of potential therapies. Although Dr. Song is currently using DBSI in animal models of MS, he hopes to translate the technology into a method for noninvasively evaluating the complexities of nerve damage in MS patients, and accelerating the development of effective therapeutics for this disease.

Wang X, Cusick MF, Wang Y, et al. 2014. Diffusion basis spectrum imaging detects and distinguishes coexisting subclinical inflammation, demyelination and axonal injury in experimental autoimmune encephalomyelitis mice. NMR Biomed 27(7):843-852.

"The MSRP funds innovative research projects which address critical gaps in our understanding of the mechanisms that control the development and pathology associated with MS. It is satisfying to be a part of the MSRP, which in collaboration with other government and private funding agencies, is improving the lives of individuals with MS and providing hope that one day we will have a world free of MS."

Paul D. Drew, Ph.D., Department of Neurobiology and Developmental Sciences, College of Medicine, University of Arkansas for Medical Sciences





Neurofibromatosis Research Program

Vision

Decrease the clinical impact of neurofibromatosis

Mission

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

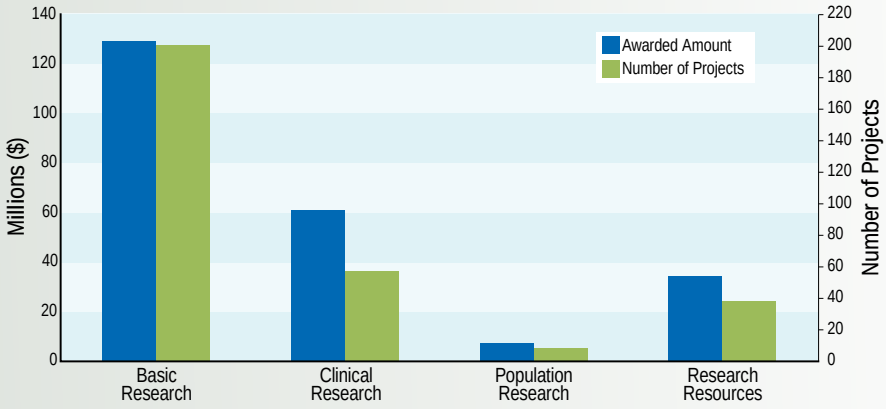
Program History

The Neurofibromatosis Research Program (NFRP) was established in FY96 when the efforts of NF advocates led to a congressional appropriation of $8M. Since that time, $272.85M has been appropriated to the program, including $15M in FY14. Over its 19-year history, the NFRP has funded 313 basic, clinical, population-based, and resources research projects 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.

Program Goals

- Accelerating discoveries that support high-impact, innovative research
- Encouraging new investigators
- Delivering research resources and tools
- Fostering collaborations between basic and clinical researchers
- Accelerating promising therapeutics
- Promoting translational and clinical studies

FY96–FY14 NFRP-Funded Research Classifications

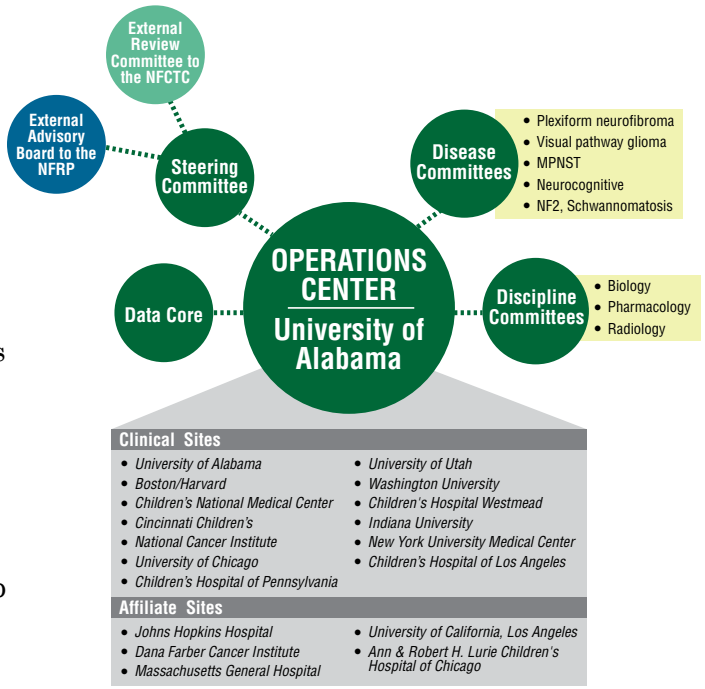


"The NFRP can seem daunting, but like any task (or when dealing with NF), you break it down into manageable segments. The program was incredibly supportive and answered any questions I had, and kept me well informed. The scientists and physicians were also very supportive during the peer review meetings, and truly listened to my input. Once the meetings were completed, I felt as if I had been part of something special, and was making a difference."

Linda Manth, Consumer Peer Reviewer

NF Clinical Trials Consortium

The Neurofibromatosis Clinical Trials Consortium (NFCTC, *http://www.uab.edu/nfconsortium*) was established by the DoD NFRP in 2006 to develop and perform clinical trials for the treatment of NF complications in children and adults. The NFCTC was subsequently funded in 2011 to conduct additional trials. Composed of 19 clinical sites, it is led by the Operations Center based at the University of Alabama at Birmingham under the direction of Dr. Bruce Korf. The University 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, and an established patient population available for clinical trials.



The NFCTC has allowed its investigators to develop mature protocols through collaborative discussions with various disease and discipline committees, allowing for quicker turnaround of scientific reviews and regulatory approvals. Inclusion of sites around the country has also allowed more NF patients a more feasible means of participating in nearby clinical trials with promising investigational therapeutics. In addition, the consortium has leveraged its collaboration to work with pharmaceutical companies to acquire therapeutic agents and other organizations to facilitate exchange of information and assist in conducting other trials.

To date, the NFCTC has successfully initiated 8 clinical trials and supported 3 additional trials.

"NFRP-funded research has contributed to important advances in the understanding of the molecular bases of various aspects of NF, and to important therapeutic efforts now in progress to improve the survival and quality of life of NF patients. I am pleased that in my long association with the NFRP as a scientific peer reviewer, then as a member of the Programmatic Panel, and now as Chair of the Programmatic Panel, I have been able to contribute in small ways in assisting the NFRP in choosing and supporting the most scientifically meritorious studies for funding by the NFRP, and I am confident that the Programmatic Panel will help keep the NFRP on a trajectory to further improve knowledge and treatment for patients with neurofibromatosis."

Douglas Miller, M.D., Ph.D., University of Missouri School of Medicine, Programmatic Panel Chair





Neurotoxin Exposure Treatment Parkinson's Research

Vision

Slow the progression of, prevent, and cure Parkinson's disease in order to lessen personal and societal impact of the disorder

Mission

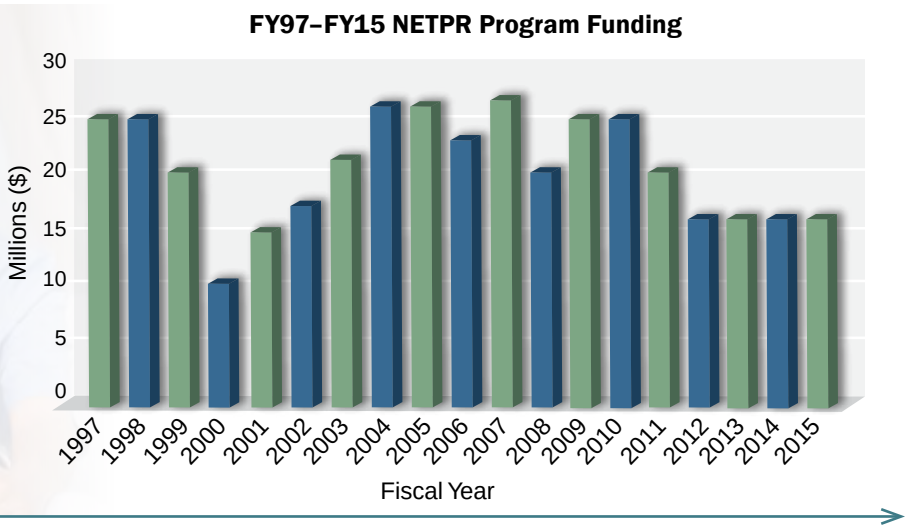
- *Identify surrogate markers of the disease,*
- *Correlate distinctive clinical features with specific clusters of these markers, and*
- *Develop interventions in bimolecular pathways that link markers and expressed clinical features*

Program History

The Neurotoxin Exposure Treatment Parkinson's Research (NETPR) program began in 1997. Projects examine neurodegenerative mechanisms and compensatory effects that compromise motor, autonomic, and cognitive systems that are characteristic alterations in Parkinson's disease (PD) patients, and which also present performance and health risks for military personnel. The overall goals of the program are: 1) develop means to correlate risk factors and dysfunction associated with PD, 2) develop means to identify risk factors for subsets of the affected population, 3) correlate clinical phenotype and molecular underpinning, and 4) develop candidate therapeutics, based on identified molecular pathway intervention points, to halt progression and extend quality of life for the at-risk population.

Research Highlights

- Research outcomes included means to identify susceptibility to development of PD prior to development of motor signs. See articles on outcomes from the NETPR-funded PARS longitudinal study and PROBE studies at: *https://www.ncbi.nlm.nih.gov/pubmed/25298306* and *https://www.ncbi.nlm.nih.gov/pubmed/26220939*.
- Significant advances in methodological development occurred in studies continuing at Georgetown University. The initial publication, on early diagnosis of Minimal Cognitive Impairment (MCI) (prior to clinical signs of disease) may be found at: *https://www.ncbi.nlm.nih.gov/pubmed/24608097*. MCI is considered an harbinger of PD, and successful application of the methodology is expected for identification of susceptibility to PD prior to development of the motor signs as well as providing new therapeutic targets for individuals in whom the motor signs are manifest.
- Important work identifying splice variants for both diagnosis and early identification of susceptibility for PD also permits the potential development of a blood-based diagnostic kit. An article on this work is available at: *https://www.ncbi.nlm.nih.gov/pubmed/24108702*.
- Independent work at Massachusetts General Hospital and Northwestern University provided candidate therapy for disease modification of PD. The work is now in advanced clinical trials. Read the background publications at: *https://www.ncbi.nlm.nih.gov/pubmed/24816140* and *https://www.ncbi.nlm.nih.gov/pubmed/24880154*.



Karl Friedl, Ph.D., University of California, San Francisco
NETPR Programmatic Panel Chair

The Army Parkinson's [NETPR] program is a true dual-use program that serves the needs of the Military at the same time that every project serves the needs of the Parkinson's community. In the program today, it's possible to bring together a collection of experts from around the country and actually discuss what the next step should be. This is a good time to re-examine what the priorities are, what the key gaps are, and the areas that also overlap with concerns that are specific to Soldiers, and the risk factors that affect their long-term health.

Garry Cooper, Ph.D., Northwestern University
NETPR-Funded Investigator

In early 2010, we received DoD funding that helped us to test a CaV1.3 L-type calcium channel selective inhibitor as a way to slow and prevent Parkinson's disease [PD] progression. We showed that a selective inhibitor of the channel reduces mitochondrial stress and prevents dopaminergic cell death. We've identified a more specific inhibitor to this type of calcium channel with funding from a second NETPR award. I believe that our research will be impactful for every PD patient. Some of the work over the past decade has resulted in Phase III clinical trials at Northwestern and represents one of the few trials for a disease-modifying drug for PD patients that might be able to slow progression of the disease.

Lisa Bain, Parkinson's Action Network, Idaho
Advocate/Caregiver

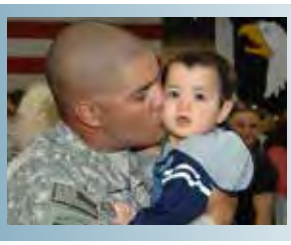
My dad was diagnosed with Parkinson's disease. He's a Vietnam Veteran, and I am wearing his dog tags in his honor. His exposure to Agent Orange is what we believe initiated his Parkinson's disease. The DoD program is very warrior-specific, but the entire Parkinson's community benefits. The DoD Parkinson's Research Program has done extensive research on neurotoxins and how people develop Parkinson's, and the links to those. It is one of the smallest budget items out there, and yet they have so much impact on the entire Parkinson's community.

Israel Robledo, Parkinson's Action Network
Programmatic Panel Member

As I've advocated through the years for the NETPR program, I've always been upfront with our legislators that this program helps our Warfighters as it looks at risk factors that are common to development of Parkinson's, as well as risks to which people in the military are exposed. Any research that's being done applies to people with Parkinson's, particularly where TBI is a risk factor for development of Parkinson's. I think that is the most important part of the program, the TBI research, it captures the attention of the general population since sports concussions can have long-term health consequences. I know that the research has a dual purpose: it helps the Parkinson's community and the military; we don't leave anybody out.







Orthotics and Prosthetics Outcomes Research Program

Vision

Helping our Warfighters achieve the highest possible quality of life through the advancement of revolutionary amputee and human performance-related research

Mission

Advance research towards more effective prosthetic and orthotic devices, treatment, rehabilitation, and the prevention of negative secondary health effects for military personnel, Veterans, and persons with injured limb function

Program History

Loss of limb or limb functionality is one of the most debilitating traumatic injuries suffered by U.S. 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 and associated rehabilitation treatments that provide demonstrable improvement in user functionality and 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 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 policymakers.

Award Description

The OPORP Award supports research that evaluates the comparative effectiveness of and functional outcomes associated with prosthetic and orthotic clinical interventions and/or other rehabilitation interventions for Service Members and Veterans who have undergone limb salvage or limb amputation.

Key Features

- Collaboration with military researchers and clinicians is encouraged, as are joint DoD-VA studies, including longitudinal outcome studies.
- Studies are sought that:
  - Compare different patient care approaches.
  - Include patient-centric outcome assessments.
  - Have the potential to generate new knowledge that can be developed into new clinical practice guidelines, and/or new prescription algorithms for prosthetic and orthotic devices.
  - Have the potential to develop new technology for improved prosthetic and orthotic devices, thereby improving patient outcomes.
  - Provide information on quality of life, reintegration, and/or return to duty/return to work as it pertains to those patients who use a prosthetic or orthotic device due to limb trauma.





Ovarian Cancer Research Program

Vision

Eliminate ovarian cancer

Mission

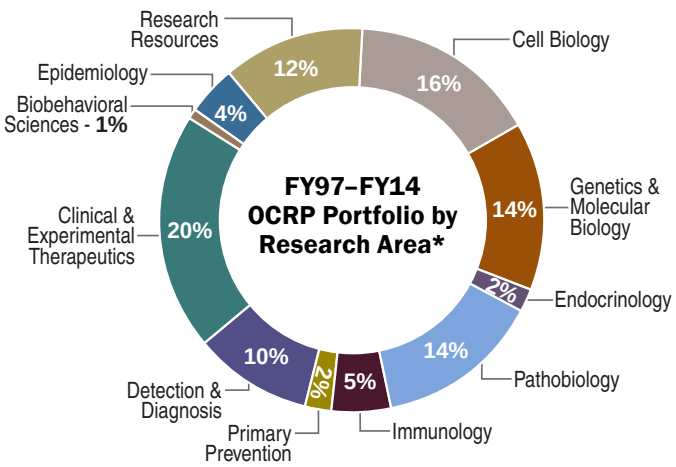
To support patient-centered research to prevent, detect, treat, and cure ovarian cancer

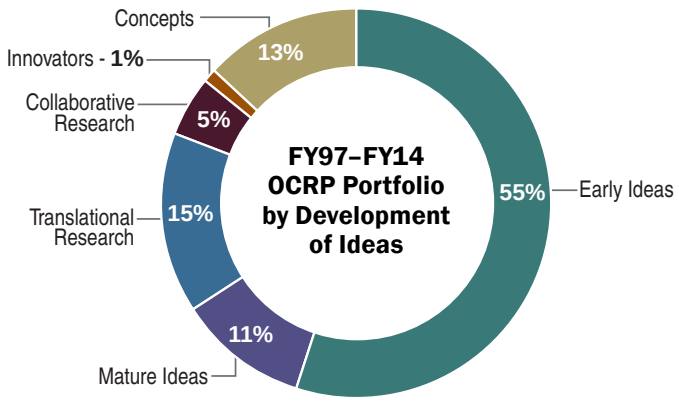
Program History

The DoD Ovarian Cancer Research Program (OCRP) plays a major role in supporting biomedical research to understand, prevent, detect and treat ovarian cancer. In concert with the OCRP's accomplishments, the dedicated efforts of ovarian cancer advocates to increase public awareness of and research funding for ovarian cancer have resulted in congressional appropriations totaling over $256M from FY97 through FY15. As a leader in funding ovarian cancer research, the OCRP invests in high-impact, cutting-edge research that fills unmet needs and accelerates research toward clinical practice.

To be responsive to the needs of the ovarian cancer community, the OCRP vision is adapted yearly. The OCRP Programmatic Panel meets annually to deliberate the issues and concerns unique to ovarian cancer and to establish a program strategy by considering research gaps, critical research areas, and the needs of the ovarian cancer community. After evaluating the funding landscape by comparing research portfolios from over 70 federal and non-federal agencies throughout the world, the OCRP determines its program priorities, develops award mechanisms, and establishes an investment strategy to target the most critical needs along the pipeline from basic to translational to clinical research. The OCRP's annual investment strategy and associated award mechanisms provide the framework and direction necessary to most effectively invest the congressional appropriation in ovarian cancer research.

The significant impact of the OCRP can be attributed to the collective wisdom and synergistic efforts of many talented and dedicated partners: ovarian cancer survivors (consumers), clinicians, scientists, and the military. As partners in vision setting, peer review, and programmatic review, they have shaped the OCRP by focusing on research that reflects the needs of survivors and their families as well as the clinicians who treat them.





*Analysis by number of awards.

Exceptionally Promising Results in Ovarian Cancer Research in FY14–FY15

In striving to achieve the vision of eliminating ovarian cancer, the DoD OCRP designed an investment strategy that continues to emphasize high-impact translational research, innovation, unique partnerships, collaborative research, and training for talented, young investigators.

Anil Sood, M.D., MD Anderson Cancer Center – Has made the game changing discovery that circulating tumor cells seem to be responsible for metastases to more distant organs such as the liver and spleen, which seems to indicate arrival through the bloodstream. The finding that the ErbB3(HER3)- neuregulin 1(NRG1) axis is a dominant pathway in tumor metastases could lead to better predictors of survival and development of targeted cancer treatments.

Tomas Walsh, M.D., M.S., University of Washington – Identified a gene called checkpoint kinase 1 (CHEK1), which coordinates the cellular DNA damage response and helps control cell division. These results suggest that CHEK1 may be a new ovarian cancer susceptibility gene and could lead to advanced screenings for CHEK1 mutations to prevent a subset of ovarian cancer.

Susan Bellis, Ph.D., University of Alabama at Birmingham – Identified ST6Gal-I as a regulator of the ovarian cancer phenotype. Further studies are under way to pursue ST6Gal-I as a biomarker for ovarian cancer and as a potential therapeutic target.

Carrie Rinker-Schaffer, Ph.D, University of Chicago – Showed that milky spots of the omentum that contain immune cells play distinct and complementary roles in omental metastatic tumor colonization.

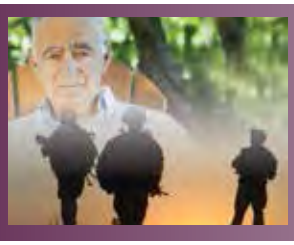
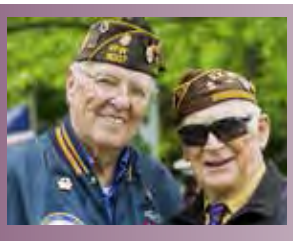
Andrew Wilson, M.D., Boston University School of Medicine – Identified that nuclear factor-kappa B gene (NFKB) activation in macrophages plays an important role in ovarian tumor progression.

FY14–FY15 heralded a transition in the OCRP Ovarian Cancer Academy leadership from the first Ovarian Cancer Academy Dean, Dr. Patricia Donahoe, to the incoming Dean, Dr. Nita Maihle, and Assistant Dean, Dr. Douglas Levine, whose combined vision for the next five years will propel this Academy to new heights. FY14–FY15 also saw the Academy expand from 11 to 14 Early Career Investigators from 12 different institutions across the United States. The vision of this unique, virtual Academy, to develop productive and passionate researchers who will be the leaders in ovarian cancer, will continue to be accomplished by providing enriching research and collaborative opportunities, networking within and outside of the Academy, and a peer group for these junior faculty members.

Did you know?

- **Ovarian cancer is the deadliest female reproductive cancer in the United States.**
- **Over the past 19 years, the OCRP has had a critical role in supporting high-impact, innovative research to address the issues and concerns unique to ovarian cancer.**
- **The DoD OCRP is the second-leading federal funding agency for ovarian cancer research in the United States.**
- **Approximately 21,290 women will receive a new diagnosis of ovarian cancer in 2015, and 14,180 women will die from the disease this year (per the American Cancer Society).**




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)

Mission

The PRARP is devoted to (1) understanding the association between TBI and AD; and (2) reducing the burden on affected individuals and caregivers, especially in the military and Veteran communities

Program History

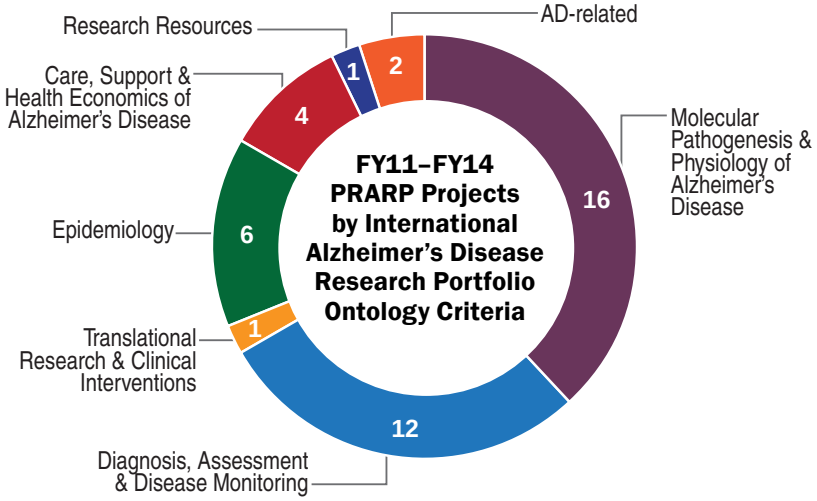
The Peer Reviewed Alzheimer's Research Program (PRARP) (formerly the Militarily Relevant Peer Reviewed Alzheimer's Disease Research Program) was initiated in 2011 to address the long-term consequences of TBI as they pertain to AD. Military personnel and other individuals who suffer from TBI face an increased 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 the PRARP's mission, the PRARP faces 5 Overarching Challenges:

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

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

- Genomics/Proteomics/Bioinformatics
- Pathology of Tau
- Roles of Non-Neuronal Cells in TBI/AD Pathogenesis
- Novel Target Identification
- Imaging
- Care Interventions and Quality of Life
- Caregiver support

Between FY11 and FY13, the program has administered $40M in funding across 29 grants that are intended to address at least one overarching challenge. Currently, the PRARP research portfolio is balanced between pathological studies, epidemiology, new diagnostics, and quality of life research.

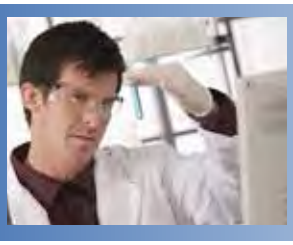
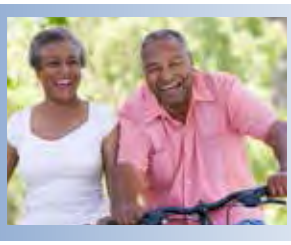


Principal Investigator and Contracting Organization	Proposal Title	Fiscal Year
Convergence Science Research Awards		
Sameer Shah, Ph.D. University of California, San Diego	Mouse and Human Models for Investigating Influences of Tau on Progression of Alzheimer's Disease Following Traumatic Neuronal Injury	2014
Allen Brown, M.D. Mayo Clinic and Foundation, Rochester	Understanding the Connection Between Traumatic Brain Injury and Alzheimer's Disease: A Population-Based Medical Record Review Analysis	2014
Ottavio Arancio, M.D., Ph.D. Columbia University Medical Center	TBI-Induced Formation of Toxic Tau and Its Biochemical Similarities to Tau in AD Brains	2014
Jose Abisambra, Ph.D. University of Kentucky	The Impact of PERK on Post-traumatic Tauopathy in Alzheimer's Disease	2014
Utkan Demirci, Ph.D. Stanford University	Biofidelic Three-Dimensional Brain Surrogate Models of mTBI-Induced Alzheimer's Disease Pathology	2014
Joseph Quinn, M.D. Oregon Health & Science University	microRNA in Cerebral Spinal Fluid as Biomarkers of Alzheimer's Disease Risk After Brain Injury	2014
Alexander Lin, Ph.D. Brigham and Women's Hospital	Measuring Glial Metabolism in Repetitive Brain Trauma and Alzheimer's Disease	2014
Sally Frautschy, Ph.D. University of California, Los Angeles	Role of Nonneuronal Cells in Tauopathies After Brain Injury	2014
Bruce Lamb, Ph.D. Cleveland Clinic Foundation	The Role of Inflammation in Development of AD Following Repetitive Head Trauma	2014
Neal Zondlo University of Delaware	Mechanisms of Tau Structural Changes and Aggregation Upon Tau Hyperphosphorylation	2014
Military Risk Factors Research Award		
Lon White, M.D., M.P.H. Pacific Health Research and Education Institute (PHREI)	Brain Injury and Military Service as Risk Factors for Alzheimer's Disease and Other Conditions	2014
Quality of Life Research Awards		
Patrick Richard Henry M. Jackson Foundation	Symptoms of Traumatic Brain Injury and Alzheimer's Disease and Their Impact on Military Service Members' Quality of Life (QOL) and Caregivers' Burden	2014
Jennifer Fairchild, Ph.D. Palo Alto Veterans Institute for Research	Combined Online Assistance for Caregiver Health (COACH): The Efficacy of a Combined Physical Activity and Coping Skills Training Intervention for Caregivers	2014

"The PRARP has provided an important foundation for the scientific investigation of the relationship between military factors and dementia. As the only Alzheimer's Disease program focused on the military and Veteran population, it has an important role in the National Plan to Address Alzheimer's Disease. The Programmatic Panel combines experts in a variety of related disciplines from NIH, DoD, VA, the Institute of Medicine, and academia as well as having an important collaboration with the Alzheimer's Association, all of whom work together to foster initiatives to strategically expand scientific discovery and translate these findings to clinical application that will benefit our Service Members, Veterans, and all individuals with Traumatic Brain Injury or Alzheimer's Dementia, as well as those who care for them."

Michael Jaffee, M.D., FY14 Programmatic Panel Chair



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 the prevention, detection, and treatment of cancer

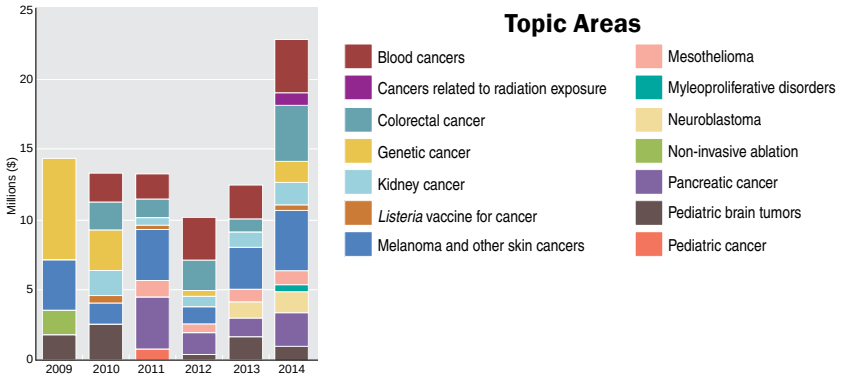
"As President and Founder of Debbie's Dream Foundation: Curing Stomach Cancer, and as a stage IV stomach cancer patient myself, I am honored to participate in the CDMRP Peer Reviewed Cancer Research Program. The $50 million in funding will support cutting-edge research for stomach cancer as well as draw new researchers to the field. Debbie's Dream Foundation has supported many stomach cancer patients who were or currently are in the military, and we see the impact that this disease has on their lives. This funding is therefore an opportunity to advance the best research to eradicate diseases and support cancer patients, Service Members, and their families."

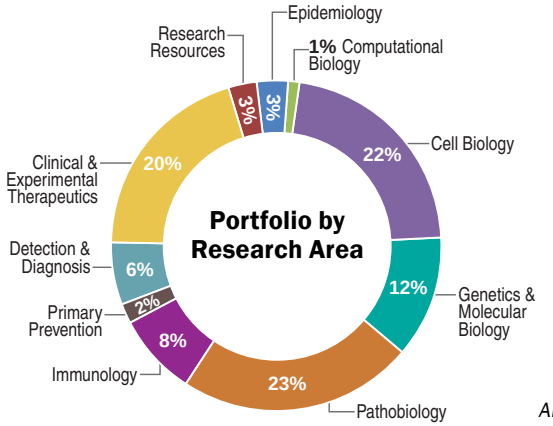
Debbie Zelman,
FY15 Programmatic Panel Member

Program History

Since FY09, the Peer Reviewed Cancer Research Program (PRCRP) has been charged by Congress to fund innovative basic, applied, and translational cancer research to support Service Members, their families, and the American public. Members of the military are exposed to hazardous environments due to the nature of their service and deployments and, thus, are at risk for the development of many types of cancers. The mission of the PRCRP is to successfully promote high-impact research. To accomplish this task, the PRCRP seeks to fund different areas of the research landscape. Seeking innovative and translational research, the PRCRP offers funding opportunities directed toward the special focus of Service Members and potential cancer risks; focusing on the gaps in cancer research with respect to unique situations and military environments. Additionally, the PRCRP addresses growing and developing future research with targeted funding opportunities for early career investigators. With a funding program focused on military health and welfare in cancer research, the PRCRP strives to improve quality of life by decreasing the impact of cancer on Service Members, their families, and the American public by funding highly relevant and innovative research.

FY09–FY14 Program Portfolio





Analysis by research dollars.

Outstanding Achievements in Cancer Research

Blood Cancer

Yue Wei, Ph.D., MD Anderson Cancer Center, University of Texas

Dr. Yue Wei identified a mutation in Toll-like receptor 2 (TLR2) that deregulates innate immune signaling in bone marrow stem cells; the mutation is found in 10% of Myelodysplastic Syndrome (MDS) patients. Working with Opsona Therapeutics, Dr. Wei manufactured an antibody targeting TLR2 that is being tested in a Phase I/II trial in MDS patients.

Colorectal Cancer

Daniel LaBarbera, Ph.D., University of Colorado Denver

Utilizing a high-throughput 3D cell culture model of colorectal cancer, Dr. Daniel LaBarbera identified a new class of drugs derived from the giant barrel sponge (e.g., neoamphimedine [neo]) that inhibits a key transcriptional pathway. Dr. LaBarbera filed a patent on neo derivatives, and will identify the best derivatives for further development.

Genetic Cancer

Wenwei Hu, M.D., Ph.D., State University of New Jersey

Dr. Wenwei Hu established a direct link between chronic stress and enhanced tumorigenesis. Furthermore, Dr. Hu determined that glucocorticoids activated by the stress response negatively regulate p53, thereby promoting tumorigenesis. This work resulted in publications in *PNAS* and *Nature* journals.

Kidney Cancer

Zhen Jane Wang, M.D., University of California, San Francisco

Dr. Zhen Wang applied novel hyperpolarized 13C pyruvate magnetic resonance to differentiate renal cancer cells with low metastatic potential from those with high metastatic potential in an ex vivo system. High metastatic potential was linked to increased rate of lactate production and export, potentially making this a new class of renal cancer biomarkers.

Listeria Vaccines

Keith Bahjat, Ph.D., Providence Cancer Center, Oregon

During this two-year award, Dr. Keith Bahjat created a novel strain of *L. monocytogenes* that secretes a protein engineered to inhibit the function SOCS1, a suppressor of cytokine signaling. Inhibiting SOCS1 improved the immune response in a mouse model. In the future, this *L. monocytogenes* vector could be engineered to target specific tumor antigens.

Melanoma

Paul Andrew Antony, M.D., University of Maryland, Baltimore

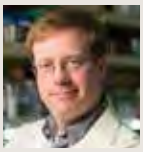
The mechanisms driving tumor relapse after successful immunotherapy are not well understood. Using a mouse model of melanoma relapse, Dr. Paul Antony found that regulatory T cells (Tregs) can exhaust the effector T cell population, leading to relapse. Current work is exploring the use of antibody therapies that prevent effector T cell exhaustion.

Mesothelioma

Haining Yang, M.D., Ph.D., University of Hawaii Cancer Center

In 2014, Dr. Haining Yang filed two U.S. patents and published a paper in *Carcinogenesis* describing how patients with a germline mutation in BRCA1 associated protein-1 (BAP1) exhibit seven-fold improved long-term survival compared to patients with stochastic mutations.

Neuroblastoma



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

Dr. Kevin Freeman received a Career Development Award in FY13 to search for the specific genes that cause high-risk neuroblastoma, which are currently unknown. Identification of candidate genes would facilitate the development of targeted therapeutic options and models for preclinical studies.

Pancreatic Cancer

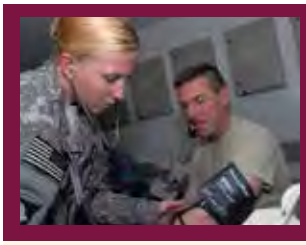
David Tuveson, M.D., Ph.D., Cold Spring Harbor Laboratory

A recent *Cell* publication highlights Dr. David Tuveson's achievements in creating a 3D cell culture system to study the progression of normal pancreatic cells to cancerous cells from patient biopsy samples. Pancreatic cells, normal or cancerous, are notoriously difficult to culture in a laboratory setting, and mouse models can take a year to develop; this new model system overcomes both of these hurdles.

Pediatric Brain Tumors

Amy K. Keating, M.D., University of Colorado School of Medicine

Dr. Amy Keating published three articles detailing the development of a xenograft model of human glioma, and how a commercially available small molecule inhibitor of Mer and Axl (two receptor tyrosine kinases overexpressed in glioma) leads to enhanced tumor cell death.





Peer Reviewed Medical Research Program

Vision

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

Mission

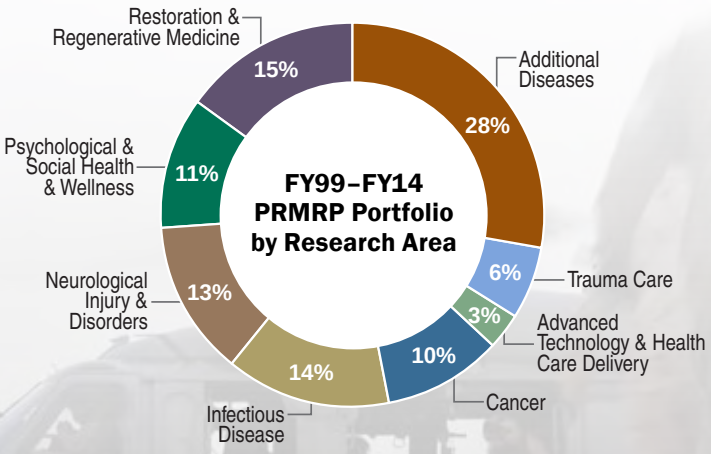
Identify and select military health-related research of exceptional scientific merit

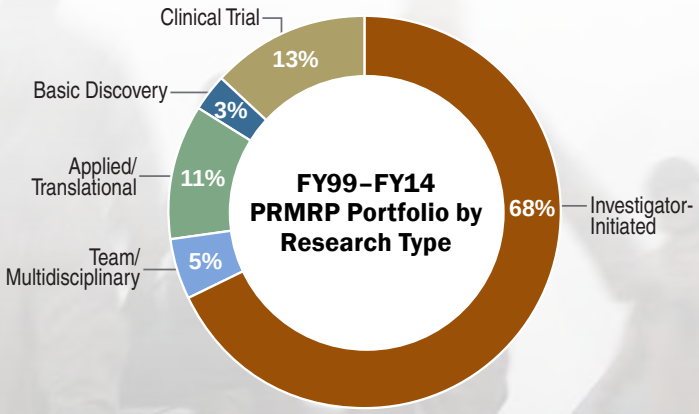
Program History

Since 1999, the Peer Reviewed Medical Research Program (PRMRP) has supported research under topic areas directed by Congress, with an underlying goal of enhancing the health and well-being of military Service personnel, the Veteran population, and their families. Through FY14, Congress has appropriated $844.5M, which has supported 675 research awards. The PRMRP has funded research projects in more than 100 different congressionally directed topic areas that address a wide range of fields of study including infectious diseases, cancer, neurological injury and disorders, psychological disorders, health and wellness, restoration and regenerative medicine, advanced technology, healthcare delivery, and a variety of disease conditions. The FY15 appropriation is $247.5M.

The PRMRP is committed to funding basic, translational, and clinical research that will strongly impact the understanding of disease and injury etiology, and the development and implementation of devices, therapies, and clinical guidance that will change the face of prevention, diagnosis, and treatment for a broad range of clinical applications.

Program Portfolio





Recent Accomplishments Supported by the PRMRP

Tinnitus

Thanos Tzounopoulos, Ph.D., University of Pittsburgh, discovered that two types of ion channels are crucial for resilience to noise-induced tinnitus, crucial preliminary work that paves the way for therapeutics that modulate the channels and prevent or treat the development of tinnitus.

Mesothelioma

Michael Sadelain, M.D., Ph.D., Memorial Sloan Kettering Cancer Center, demonstrated a novel approach to treating malignant pleural mesothelioma by regional delivery of mesothelin-targeted chimeric antigen receptor-transduced T cells, an approach that may be translated to other types of aggressive, unresponsive solid tumors such as triple negative breast cancer that have proven difficult to treat.

Inflammatory Bowel Disease

Xiaonan Han, Ph.D., Cincinnati Children's Hospital Medical Center, showed that activation of the signaling molecule STAT5 confers resistance to intestinal injury by increasing intestinal stem cell proliferation and regeneration, identifying it as a potential therapeutic target for fighting diseases such as inflammatory bowel disease that are characterized by persistent enteric infection or inflammation.

Neuroblastoma

Michael Hogarty, M.D., The Children's Hospital of Philadelphia, demonstrated that combining multiple polyamine-targeting drugs with conventional chemotherapy is more effective in eliminating neuroblastoma in cell lines and animal models, which has led to a Phase I clinical trial of combination therapy in children with relapsed neuroblastoma.

Drug Abuse

Chuanbin Mao, Ph.D., University of Oklahoma, created iron oxide-based conjugated nanoparticles and demonstrated in vitro that the particles are capable of crossing the blood brain barrier and binding to cocaine, important steps toward an anti-cocaine drug whose delivery can be imaged via MRI.

Post-Traumatic Osteoarthritis

X. Lucas Lu, Ph.D., and **Christopher Price, Ph.D.,** showed that zoledronic acid (ZA), a bisphosphonate used to treat osteoporosis-related bone loss, can exert direct chondroprotective action on chondrocytes after traumatic damage, which supports the work they are doing to determine whether a single intra-articular injection of ZA can prevent the development or progression of post-traumatic osteoarthritis.

Epilepsy

Detlev Boison, Ph.D., showed that DNA hypermethylation modulated by adenosine is important for the initiation and progression of epilepsy, and transient, focal delivery of adenosine via silk-based brain implants can reduce DNA hypermethylation and prevent epileptogenesis in an animal model of epilepsy.

2014–2015 Topic Areas

Acupuncture
Acute Lung Injury†
Advanced Prosthetics†
Arthritis
Burn Pit Exposure†
Cardiovascular Health†
Chronic Migraine and Post-traumatic Headache
Congenital Heart Disease
Dengue†
Diabetes†
DNA Vaccine Technology for Post-exposure Prophylaxis
Dystonia
Epilepsy*
Focal Segmental Glomerulosclerosis†
Food Allergies
Fragile X Syndrome
Healthcare-acquired Infection Reduction†
Hepatitis B†
Hereditary Angioedema
Hydrocephalus†
Illnesses Related to Radiation Exposure*
Inflammatory Bowel Disease
Integrative Medicine†
Interstitial Cystitis
Lupus
Malaria
Metabolic Disease*
Metals Toxicology†
Mitochondrial Disease†
Nanomaterials for Bone Regeneration†
Neuroprosthetics*
Osteoarthritis†
Pancreatitis
Pathogen-inactivated Dried Plasma†
Polycystic Kidney Disease
Post-traumatic Osteoarthritis
Psychotropic Medications
Pulmonary Fibrosis†
Respiratory Health
Rheumatoid Arthritis
Scleroderma†
Segmental Bone Defects*
Sleep Disorders†
Tinnitus
Vascular Malformations†
Women's Heart Disease†

*2014 only
†2015 only

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

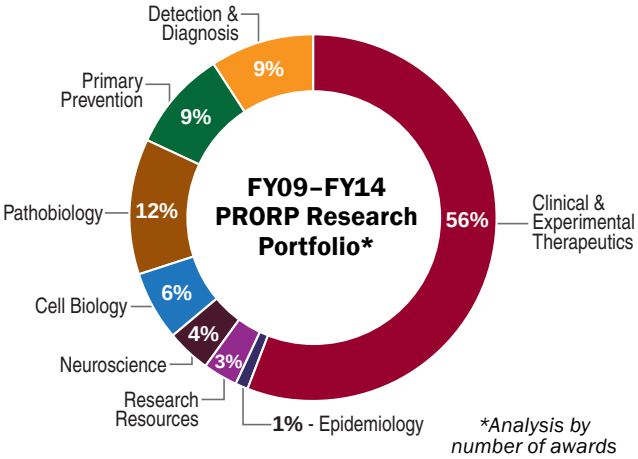
Mission

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

Program History

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. Since its inception in FY09, the Peer Reviewed Orthopaedic Research Program (PRORP) has dedicated its congressional appropriations, totaling $278.5M, toward supporting military-relevant orthopaedic research with the expectation that any research findings would also provide benefit to the general population.

Orthopaedic injuries sustained during combat-related activities tend to be both heterogeneous and complex in nature. 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. The PRORP crafts investment strategies to address these challenges, with the goal of helping injured Service Members achieve optimal recovery from combat-related orthopaedic injuries.



"[In collaboration with the other Programmatic Panel members,] I work hard to prioritize the existing needs of our wounded which, in turn, encourages the development of innovative products, techniques, and procedures that combat the issues at hand. Through their personal sacrifice, both Soldiers and civilians will benefit from the research being conducted and funded by the PRORP. Our Soldiers deserve the best care, and I am honored to represent them and speak up for their needs."

CPT Matthew Anderson (Ret), Consumer Reviewer

Expanding Upon Previously Funded, High-Impact Orthopaedic Research

Enhancing the Prevention and Treatment of Orthopaedic Infections Associated with Traumatic Injury

Mark Smeltzer, Ph.D., University of Arkansas

A common consequence of traumatic battlefield injury is the onset of infection following injury. Dr. Mark Smeltzer received an FY14 PRORP Expansion Award to continue previous work from his FY09 PRORP Idea Development Award where sarA was explored as a target for the prevention and treatment of staphylococcal-associated biofilm infections. Dr. Smeltzer will continue to investigate sarA-based therapeutics in combination with bone-targeting and antibiotic therapy in an effort to enhance the treatment of bone infection post-injury.

Manufacture Articular Cartilage from Human Adipose-Derived Stromal/ Stem Cells for Cartilage Repair

Zongbing You, M.D., Ph.D., Tulane University

The incidence of osteoarthritis among U.S. military populations is more than twice that of the general population largely due to articular cartilage injury. Dr. Zongbing You received an FY09 PRORP Hypothesis Development Award to develop a novel tissue engineering protocol for producing articular cartilage using adipose-derived stem cells. As a recipient of an FY14 PRORP Expansion Award, Dr. You will continue efforts to validate this technology and lay the groundwork for a Phase 0/I clinical trial where the engineered cartilage will be tested for its ability to repair damaged human joints.

Adult Stem Cell-Based Enhancement of Nerve Conduit for Peripheral Nerve Repair

Rocky Tuan, Ph.D., McGowan Institute for Regenerative Medicine

Currently available treatments for peripheral nerve injuries resulting from battlefield wounds are limited by graft availability and the risk of adverse immune responses. With funding from an FY09 PRORP Translational Research Partnership Award, Dr. Rocky Tuan and his team determined that mesenchymal progenitor cells can be used to grow 3D bioactive nerve conduits. Dr. Tuan will optimize this technology using funds from an FY14 PRORP Expansion Award to provide proof of concept in small animal models of nerve repair.

Joint Distraction Treatments of Intra-Articular Fracture-Induced Post-traumatic Osteoarthritis in a Large Animal Model

Jessica Goetz, Ph.D., The University of Iowa

Post-traumatic osteoarthritis (PTOA) is a common complication following intra-articular fracture, and is one of the leading factors preventing Service Members from returning to duty following injury. Using funding from an FY09 PRORP Technology Development Award, Dr. Jessica Goetz developed a large animal model of PTOA. With her FY14 PRORP Expansion Award, she will determine if mechanically unloading joints during early injury treatment prevents the development of PTOA in animals, as well as prepare to conduct a clinical trial with human subjects in the near future.

Enhancing Notch Activation for Improved Bone Regeneration

Kurt Hankenson, D.V.M., M.S., Ph.D., University of Pennsylvania

The Notch signaling pathway is a highly conserved cell-signaling pathway involved in the regulation of embryological bone development. Using funding from an FY09 PRORP Translational Research Partnership Award, Dr. Kurt Hankenson and his team determined that this pathway is highly regulated during bone regeneration in animals, and that activation of Notch signaling at the site of bone regeneration enhances healing. As a recipient of an FY14 PRORP Expansion Award, Dr. Hankenson will continue to validate the utility of Notch-based therapeutics for bone regeneration and healing in rodent bone injury models.





Prostate Cancer Research Program

Vision

Conquer prostate cancer

Mission

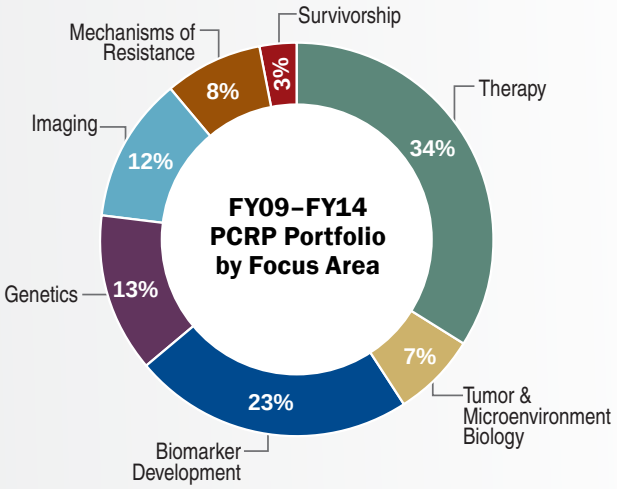
Fund research that will lead to the elimination of death from prostate cancer and enhance the well-being of men experiencing the impact of the disease

Program History

Since its inception in 1997, and over its 19-year history of congressional support totaling nearly $2.2B, the Prostate Cancer Research Program (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. The 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 more than one thousand trainees and new investigators, many of whom have become leaders in cutting-edge research that is making a significant difference for millions of PCa patients.

Program Portfolio

From 1997–2014, the PCRP funded 2,902 research and training awards. 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 PCa patients, PCRP-supported researchers can realize the goal of making a direct, positive impact on patients and their families. Since 2009, the PCRP has required that all research funded by the program address the most critical needs of PCa patients, as identified by the PCRP Programmatic Panel. The chart on the right shows the relative numbers of awards the program has supported in these focus areas from FY09 through FY14.



"[The PCRP] is truly where the rubber meets the road in terms of identifying new research that could lead to a cure for prostate cancer, and identifying treatment options to improve the quality of life for men living with the disease."

Robert Ginyard, FY12–FY14 Peer Reviewer, ZERO-The End of Prostate Cancer

"I look forward to an ever brighter future for all the men and families who are dealing with or will deal with prostate cancer. I am certain a significant part of that brighter future rests with the PCRP."

Thomas Blank, FY04–FY08, FY12, FY14 Peer Reviewer, Hartford Hospital Support Group

From Detection to Survivorship: Impacting Patients at Every Stage

Impact: Transforming Clinical Care through High-Impact Research

Jun Luo, Ph.D., Johns Hopkins University
Utilizing samples from the PCRP-supported Prostate Cancer Biorepository Network (PCBN), Dr. Luo analyzed AR-V7 expression in metastatic tissue and found that detection of AR-V7 in circulating tumor cells of patients with castration-resistant PCa (CRPC) indicated resistance to enzalutamide and abiraterone. The PCRP is now funding him and his colleagues through a Biomarker Development Award to perform a multi-institutional validation of a blood-based assay to predict resistance to androgen deprivation therapy CADT.

Dirk Brockstedt, Ph.D., Aduro BioTech
Using Aduro Biotech's novel LADD immunotherapy platform, Dr. Brockstedt and his team have developed a new PCa vaccine, LM-PCaVx, that uses a unique combination of PCa antigens overexpressed in prostate tumors and stem cells. This vaccine successfully elicits antitumor responses in animal models and is moving rapidly to clinical trials. LM-PCaVx was licensed to Janssen for further development.

Bettina Drake, Ph.D., M.P.H., University of Washington
Dr. Drake is exploring the association between obesity, type II diabetes, and PCa recurrence in African American men. She was recently awarded a Prostate Cancer Biospecimen Resource Site Award and will join the PCBN, providing specimens, particularly African American samples, from PCa patients on active surveillance and those with high-risk disease.

Isla Garraway, M.D., Ph.D., University of California, LA
Dr. Garraway is being funded through separate awards to (1) validate the role of a novel biomarker of aggressive disease, discovered in benign PCa stem cells, that appears in bone metastases; and (2) validate, for the first time, known PCa biomarkers for progression and poor prognosis in African American men with aggressive disease.

Russell Szmulewitz, M.D., University of Chicago
Dr. Szmulewitz is being funded through a Clinical Exploration Award to conduct a Phase I/II clinical trial of a combinational drug therapy to target both glucocorticoid and AR in an effort to overcome resistance to AR therapies in patients with metastatic CRPC.

Innovation: Groundbreaking Ideas to Push the Field Forward

David Karow, M.D., Ph.D., University of California, San Diego
Dr. Karow is developing a low-cost, noninvasive, rapid imaging procedure for PCa, called Restriction Spectrum Imaging, that has shown potential for discriminating between aggressive tumors and benign tissue or indolent disease.

Mohamed El-Sayed, Ph.D., University of Michigan
Dr. El-Sayed is developing new nano-bubbles that can "recognize" and bind to PCa cells to allow imaging of microscopic cancer lesions. He has also demonstrated the ability of these targeted nano-bubbles to achieve selective destruction of PCa cells when combined with low-frequency ultrasound.

Elahe Mostaghel, M.D., Ph.D., Fred Hutchinson Cancer Research Center
Dr. Mostaghel found that a combination of abiraterone treatment with several cycles of low-dose docetaxel (which, by itself, did not exhibit significant antitumor activity) actually improved treatment efficacy over abiraterone therapy alone.

Scott Dehm, Ph.D., University of Minnesota, Twin Cities
Dr. Dehm's preclinical studies on a new class of drugs that target the AR-DNA binding domain – thereby circumventing the resistance that develops to current hormone therapies – may help to extend the lives of patients suffering from advanced stage disease.

Training: Investing in the Future Generation of Prostate Cancer Researchers

Adam Murphy, M.D., Northwestern University
Dr. Murphy found that severe vitamin D deficiency increased the odds of being diagnosed with higher stage and higher grade of PCa in both African American and European American men, and that this association was stronger for African American men.

Renee DeLeeuw, Ph.D., Jefferson Medical College
Dr. DeLeeuw found that cabazitaxel was more effective than docetaxel at killing PCa cells that are resistant to androgen deprivation therapy, and that the retinoblastoma tumor suppressor protein can serve as a biomarker to identify patients who are more likely to benefit from chemotherapy.

Adam Sowalsky, Ph.D., Beth Israel Deaconess Medical Center, Boston
Dr. Sowalsky performed molecular comparisons of adjacent PCa tissue from the same patient and identified two mechanisms of progression from Gleason 3 (non-lethal) to Gleason 4 (potentially lethal), one involving the activation of the myc oncogene and the other involving increased oxidative phosphorylation.

Joshua Lang, M.D., University of Wisconsin, Madison
While developing skills in cancer immunology, microfluidics, and clinical research, Dr. Lang has made great strides in understanding how prostate tumor cells evade the immune system, thus contributing to the development of improved immune-based therapies and biomarkers for this disease.

Focus Areas Color Key

- Biomarker Development
- Mechanisms of Resistance and Response
- Tumor and Microenvironment Biology
- Imaging
- Genetics
- Survivorship and Palliative Care
- Health Disparity
- Therapy





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

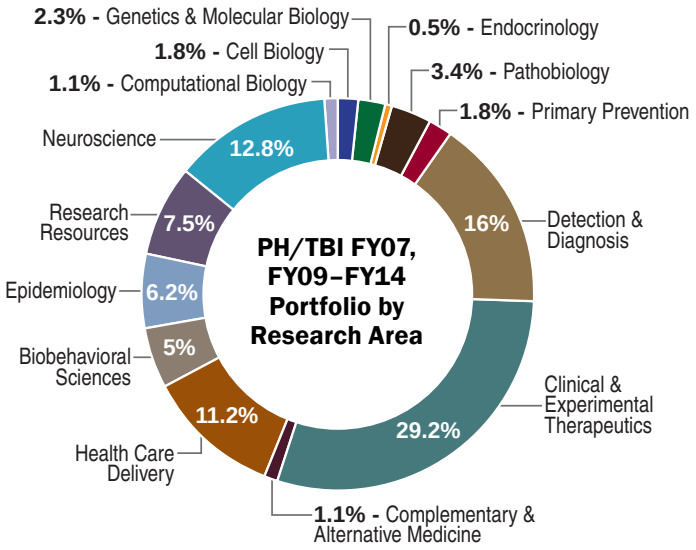
The Psychological Health and Traumatic Brain Injury Research Program (PH/TBIRP) was established by Congress in FY07 in response to the devastating impact of TBI and PH issues, including PTSD, on our deployed Service Members in Iraq and Afghanistan. Appropriations totaling $300M—$150M each for TBI and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

Additional congressional appropriations for the PH/TBIRP were assigned to the USAMRMC between FY09 and FY14, and a modified execution model, including assignment of program strategic oversight to USAMRMC-based research program areas aligned with the OASD(HA), was established. As directed by the OASD(HA), the DHA RDA Directorate manages and executes the DHP Research, Development, Test, and Evaluation appropriation, which includes the PH/TBIRP. The DHA RDA 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:

- JPC 5/Military Operational Medicine Research Program (JPC-5/MOMRP)
- JPC 6/Combat Casualty Care Research Program (JPC-6/CCCRP)
- JPC 8/Clinical and Rehabilitative Medicine Research Program (JPC-8/CRMRP)

These JPCs provide recommendations to the DHA RDA Directorate on research gaps, focus areas, and funding options for the PH/TBIRP. The CDMRP works in partnership with the JPCs to provide operational execution management support as needed for the PH/TBIRP, including development of program announcements, solicitation and review of applications, full life-cycle management of awards, as well as program evaluation and planning. The CDMRP-managed application review for the PH/TBIRP follows a two-tiered model, where consumer involvement continues to be a hallmark. Our nation's wounded warriors serve in this capacity for the PH/TBIRP, representing fellow Service Members and Veterans to help identify the most relevant and impactful research. The modified execution process allows greater flexibility for aligning PH/TBIRP congressional special interest funds to complement core DoD research and development efforts. For more information on this execution model, see page 40 (DMRDP Execution).

Through FY14, the CDMRP has managed 413 PH/TBIRP awards totaling over $651M 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.



PH/TBIRP Recent Research Focus

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

JPC-5/MOMRP

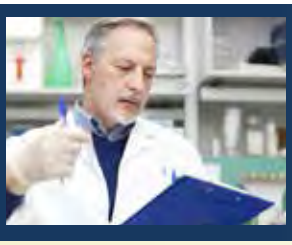
- **Investigating Resilience Training in Military Spouses**; Amishi Jha, Ph.D., University of Miami, Coral Gables
- **A Point of Care Clinical Trial for PTSD with a First-in-Class Vasopressin 1a Receptor Antagonist**; Neal Simon, Ph.D., Azevan Pharmaceuticals, Inc.
- **Primary Blast Injury Criteria for Animal/Human TBI Models Using Field Validated Shock Tubes**; Namas Chandra, Ph.D., New Jersey Institute of Technology

JPC-6/CCCRP

- **THE NCAA-DoD GRAND ALLIANCE: Concussion Assessment, Research, and Education Consortium (CARE)**; Thomas McAllister, M.D., Indiana University, Indianapolis
- **Team Approach to the Prevention and Treatment of Post-Traumatic Epilepsy (TAPTE)**; Susan Axelrod, MBA, CURE (Citizens United for Research in Epilepsy)
- **Comprehensive Study of Acute Effects and Recovery After Concussion**; Michael McCrea, Ph.D., Medical College of Wisconsin

JPC-8/CRMRP

- **TBI Assessment of Readiness Using a Gait Evaluation Test (TARGET): Development of a Portable mTBI Screening Device**; Christopher Rhea, Ph.D., University of North Carolina, Greensboro
- **Microglia Contribute to Ongoing Pain Caused by TBI**; Catherine Cahill, Ph.D., University of California, Irvine
- **Assessment and Rehabilitation of Central Sensory Impairments for Balance in mTBI**; Laurie King, Ph.D., Oregon Health & Science University


Spinal Cord Injury Research Program

Vision

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

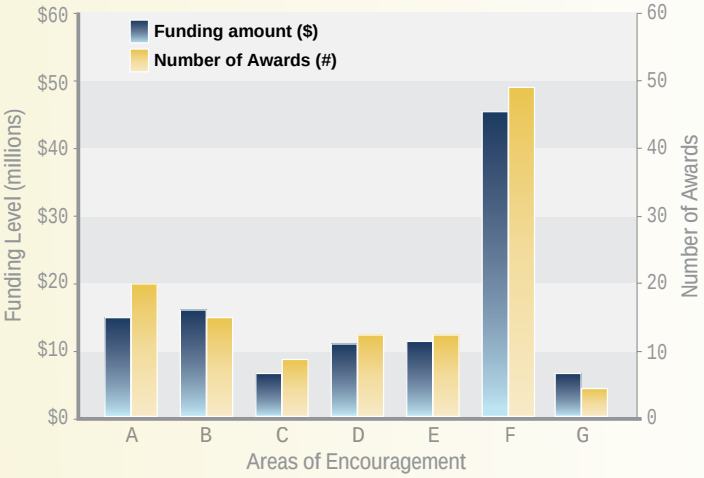
Mission

To fund research and encourage interdisciplinary collaborations environments 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

Spinal cord injuries are serious and complex neurotraumatic wounds affecting military Service Members serving in Iraq and Afghanistan. The Spinal Cord Injury Research Program (SCIRP) was established by Congress in FY09 with a $35M appropriation to support research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies. From FY10–FY14, Congress appropriated an additional $92.85M to continue this research. The SCIRP focuses its funding on projects that have the potential to make a significant impact on improving the function, wellness, and overall quality of life for military Service Members as well as their caregivers, families, and the American public. SCIRP funding between FY09 and FY14 by areas of encouragement is shown at right.

FY09–FY14 SCIRP Funding by Areas of Encouragement



A = Pre-hospital, en route care, and early hospital management of SCI

B = Development, validation, and timing of promising interventions to address issues during the first year after SCI

C = Identification and validation of best practices during the first year after SCI

D = Bladder, bowel, and sexual dysfunction

E = Neuropathic pain and sensory dysfunction

F = Functional deficits

G = Exoskeletal systems

"The SCIRP is comprised of leaders from the spinal cord injury community from academic, military, and commercial entities. From the beginning, our goal has been to identify and fill scientific and clinical gaps, leading to improved care for the spinal cord injured with a bias toward short- and intermediate-term solutions, and those that may benefit Veteran and military members. I am humbled and inspired by the devotion of the panel members and the CDMRP staff that support this effort."

Col Randal McCafferty, M.D., FY15 Programmatic Panel Chair

"Participating on the Programmatic Panel as a consumer reviewer has been a challenging and rewarding experience which has given me the opportunity, in some small way, to help determine the direction of SCI research and funding."

CW5 (Ret) Gary Linfoot, FY15 Consumer Programmatic Panel Member

Living with Pain After a Spinal Cord Injury

Eva G. Widerstrom-Noga, D.D.S., Ph.D., University of Miami

A major cause of disability in individuals with spinal cord injury is chronic neuropathic pain. Many individuals with spinal cord injury and chronic pain respond poorly to standard pain treatments, but not enough is known about chronic pain's underlying mechanisms or about barriers and facilitators of successful pain management in people with spinal cord injury. Dr. Widerstrom-Noga studies the experiences of living with pain after a spinal cord injury. With the support of a FY11 Qualitative Research Award she conducted interviews with Veteran and non-Veteran individuals with spinal cord injury she has identified key barrier and facilitators for optimal pain management. Dr. Widerstrom-Noga received a FY14 Qualitative Research Award to extend her work to include the experiences of family members and healthcare providers. As data collection and subsequent analyses continue, the information and knowledge gained has the potential to change how chronic pain in individuals with spinal cord injury is managed.

Glibenclamide Treatment for Limiting Progressive Hemorrhagic Necrosis Following Traumatic Spinal Cord Injury

Phillip Popovich, Ph.D. (pictured left), Ohio State University and J. Marc Simard, M.D., Ph.D., University of Maryland, Baltimore

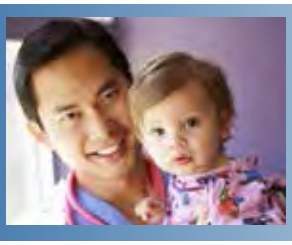
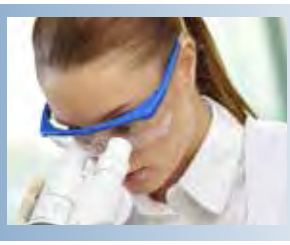
When the spinal cord is injured by trauma, bleeding within the spinal cord, in the area of the injury can contribute to injury and later disability after trauma. Recent studies suggest that glibenclamide (Glib), which has been approved by the FDA and has been safely used in patients with diabetes, can limit the bleeding in some spinal cord injuries in rodents. Dr. Phillip Popovich from The Ohio State University and Dr. J. Marc Simard from the University of Maryland, Baltimore, received an FY09 Translational Research Partnership Award to study Glib treatment for spinal cord injury. Using a rat model of spinal cord injury, the team showed that Glib treatment was associated with significantly better function 24 hours after injury with sustained significant improvement in functional outcome and lesion size after 6 weeks in rats that had been injured and then treated with Glib. The work done under this award also provided evidence that MRI is an accurate, non-invasive imaging biomarker of lesion expansion and can be used to measure the ability of Glib to reduce the expansion of bleeding in patients with spinal cord injuries. This work will contribute to pilot clinical trials of Glib in human spinal cord injury.

An Implantable Neuroprosthetic Device to Normalize Bladder Function After SCI

Changfeng Tai, Ph.D., University of Pittsburgh

One of the major challenges facing individuals with SCI is loss of bladder function. Individuals with SCI often have difficulty with urine leakage (incontinence) and with voiding (emptying) their bladder (micturition), yet there are currently no treatments that target both of these bladder functions. The pudendal nerve normally controls bladder function, but SCI can cause this nerve to lose its connection to the brain. A wireless stimulator is capable of bridging the gap created by the injury and restoring nerve function. Supported by an FY10 Investigator-Initiated Research Award from the SCIRP, Dr. Changfeng Tai of the University of Pittsburgh developed a novel neuroprosthetic device to restore urinary bladder function after SCI without damaging residual nerve function. The device consists of several components, including a stimulator and battery pack to be implanted under the skin on the left side of the lower back, two electrode cuffs to extend from the stimulator to the pudendal nerve, and a USB controller for programming the stimulator. Testing in both anesthetized and awake animals with chronic SCI demonstrated that low-frequency (5 Hz) stimulation inhibits urine flow (even with the bladder at 90% of capacity), while high-frequency (20-50 Hz) stimulation induces a strong sustained contraction for effective voiding of the bladder. Testing continued for up to four weeks after implantation of the device, demonstrating consistent effectiveness throughout the animals' typical daily routine. Dr. Tai is continuing this project through the Joint Warfighter Medical Research Program to modify and optimize the device for human use. The successful development of this device could greatly improve the quality of life for individuals with SCI who currently experience bladder dysfunction and enable them to live with a higher degree of independence.



Tuberous Sclerosis Complex Research Program

Vision

To lessen the impact of TSC

Mission

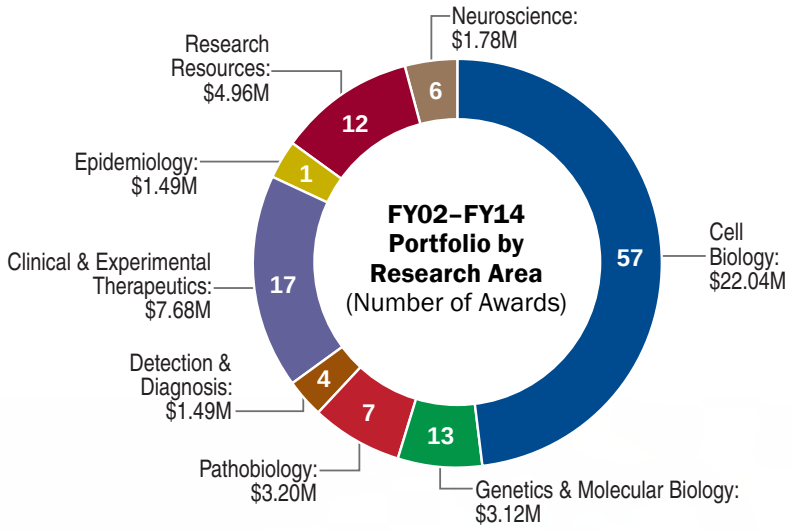
To encourage innovative research aimed at understanding the pathogenesis and preventing and treating the manifestations of TSC

Program Goals

- Support high-impact, innovative research
- Foster the development of research resources and tools
- Promote the translation of new research findings to patient care
- Advance the knowledge of TSC and its clinical manifestations

Program History

The Tuberous Sclerosis Complex Research Program (TSCRP) was established in FY02 when the efforts of TSC advocates led to a congressional appropriation of $1M. Since then, a total of $59M has been appropriated to the program, including $6M in FY15. Today, the TSCRP is one of the leading sources of extramural TSC research funding in the United States. The TSCRP fills important gaps in TSC research not addressed by other funding agencies. The program's investment strategy is adapted yearly to facilitate rapid change and to better target funding to the most critical TSC research areas, thus ensuring that the program remains responsive to current needs and future opportunities. A total of 116 awards have been made through FY14, bridging basic, clinical, and population-based research.



"Every year since the TS Alliance initiated its "March on the Hill," I have gone to Congress to advocate for research dollars for the TSCRP. I was honored to represent the community of people affected by TSC for the TSCRP. With more than twenty years of active involvement with the TS Alliance, I felt I could represent the broad TSC community with a personal commitment to improve the lives of those affected by TSC. I was very impressed by the members of my panel. Their presentations and discussions of the research proposals were illuminating. I am in awe of the commitment of the scientific community to understanding the pathogenesis and manifestations of TSC. I also appreciate how that knowledge can help in understanding other disorders and diseases."

Cathy Krinsky, FY14 Consumer Peer Reviewer

Elizabeth Henske, M.D., Brigham and Women's Hospital

Dr. Elizabeth Henske hopes to identify novel therapeutic options for the treatment of TSC by targeting cellular metabolism pathways. She recently discovered that TSC2-deficient cells have low autophagy (a process through which cells undergo "self-eating" to maintain metabolic homeostasis) levels and are highly dependent on autophagy for survival in vitro and in vivo. In recently published work, she elucidated that inhibition of autophagy in TSC2-deficient cells leads to altered metabolites in the pentose phosphate pathway and in glutamate biosynthesis pathways. Through additional experimentation, she found that these pathways can be targeted without the use of mammalian target of rapamycin complex 1 (mTORC1) inhibitors, although details of how these pathways alter metabolic reprogramming and contribute to the growth and survival of TSC2-deficient cells are still largely unknown. Dr. Henske has received FY11, FY12, and FY14 TSCRP awards to support independent clinical and non-clinical research as she further defines the mechanism of metabolic reprogramming in TSC. The results from these research efforts may provide the edge needed to successfully develop highly effective, metabolically targeted therapeutic strategies for children and adults with TSC.

Brendan Manning, Ph.D., Harvard University

With support from an FY09 TSCRP Idea Development Award, Dr. Brendan Manning found that loss of the TSC2 gene triggered a signaling cascade that activated mTORC1 and stimulated expression of every component of the proteasome, a large cellular complex that is responsible for the degradation of unneeded or damaged proteins. His laboratory determined that a gene called NRF1 is induced by mTORC1 activation and is required for the increased expression of proteasome genes in TSC2-deficient cells or upon stimulation of normal cells with growth factors. Their study further confirmed that this mTORC1-mediated activation of NRF1 and the proteasome occurs in the enlarged neurons of a TSC mouse model involving a neuron-specific mutation of TSC2. Importantly, he found that TSC2-deficient cells were especially sensitive to NRF1 inhibition, demonstrating that this response accompanying mTORC1's established role in promoting protein synthesis is required for survival of TSC2 mutant cells. This novel vulnerability makes NRF1 a potential new therapeutic target for TSC.

"I applaud the DoD-led effort to include consumers in the review process, and I have gotten positive feedback from the basic scientific reviewers who, after serving on the panel, can put a story to the disorder. I personally have expanded my appreciation of family issues as conveyed by consumers on our panels. Consumer representatives weigh in heavily on the potential impact of the research during the review, and this sometimes sways panel members to consider this aspect of the applications in a very different light. My impression is that the TSCRP grant review process will enable the field to move forward in a more timely manner. I feel honored to work with colleagues to advance the knowledge of TSC-related issues to the field of medical genetics and pediatrics."

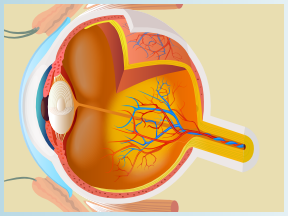
David Viskochil, M.D., Ph.D., University of Utah Health Sciences Center, FY14 Scientific Peer Reviewer

"The pace of discovery in tuberous sclerosis research over the past two decades rivals any in science. The molecular pathway that is deranged in TSC and LAM has been dissected in worms, fruit flies, and rodents, multiple molecular targets have emerged, and three FDA-approved therapies are now available for the most life-threatening TSC manifestations. The DoD TSCRP has filled a critical need by funding high-risk, high-reward innovation and pilot clinical trials that are difficult to support by any other available means. I have greatly enjoyed interacting with incredible scientists on the Programmatic Panel. The DoD staff are highly dedicated, efficient, knowledgeable and mission driven. I hope that the DoD will continue to support this vital program for a long time to come."

Francis McCormack, M.D., University of Cincinnati, FY13–FY14 Programmatic Panel Member







Vision Research Program

Vision

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

Mission

Improve the care of military personnel affected by eye injuries and diseases by identifying clinical needs and addressing them through directed medical research efforts

Program History

The Vision Research Program (VRP) was created and funded by Congress in FY09, and has awarded 67 grants totaling $49.7M to researchers addressing penetrating eye injuries, corneal healing, retinal/corneal protection, visual dysfunction associated with TBI, the eye blast phenomenon, and vision rehabilitation.

- FY09–FY10: 120 pre-applications were received, 50 were invited to submit full proposals, and 12 projects were funded for a total of $11M.
- FY11–FY12: 151 pre-applications were received, 50 were invited to submit full proposals, and 21 projects were funded for a total of $13.8M.
- FY13–FY14: 275 pre-applications were received, 151 were invited to submit full proposals, and 34 projects were funded for a total of $24.9M.

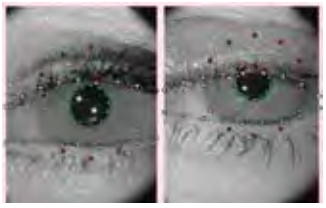
Challenges

Research to effectively treat acute eye damage can have long-term implications for an individual's vision health, productivity, and quality of life for the remainder of military service and into civilian life. The VRP focuses on the causes, effects, and treatment of eye injury and diseases that, despite their different mechanisms and pathogenesis, all have a common end result: degeneration of the critical components of the eye and impairment or loss of vision.

- A 2012 study using published data from 2000–2010 estimated that deployment-related eye injuries and blindness have cost the U.S. $2.3B a year, yielding a total of $25.1B, driven primarily by the present value of long-term benefits, lost wages, and family care.
- Traumatic eye injury from penetrating wounds and TBI-related visual disorders ranks second only to hearing loss as the most common injury among "active" military:
  - Traumatic eye injuries have accounted for upwards of 16 percent of all injuries in Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF).
  - Eye-injured Soldiers have only a 20 percent return-to-duty rate as compared to an 80 percent rate for other battle trauma injuries.
  - The Vision Center of Excellence reports 197,000 OEF/OIF Veterans with eye injuries since 2000, and that approximately 75 percent of all TBI patients experience short- or long-term visual disorders (double vision, light sensitivity, inability to read print, and other cognitive impairments).

Research Highlights

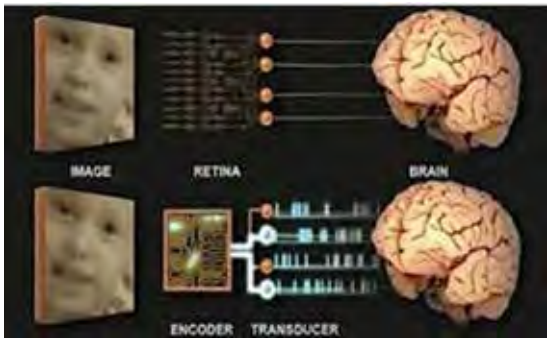
The VRP has supported the development of:



Randy Kardon, M.D., Ph.D, and Pieter Poolman, Ph.D., University of Iowa

A portable, hand-held device to analyze the pupil's reaction to light, enabling rapid diagnosis of TBI-related visual dysfunction.

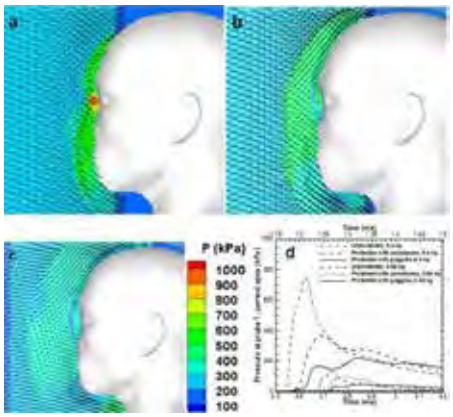
Examples of Neuroptics video frames with different eye features marked using the Componica EyeClipMarker™ system. Eye features include the pupil (green dots), limbus (yellow dots), upper eyelid (white dots), and lower eyelid (cyan dots). Occluded feature points are marked in red, and are excluded when training the tracking algorithms.



Sheila Nirenberg, Ph.D., Cornell University

A new kind of prosthesis that has the potential to be much more effective than standard vision restoration approaches by developing an algorithm which converts visual input (i.e., images) into a neural code that can be understood by the brain. Using this conversion as an "encoder" during the signal processing step, in combination with optogenetics (inserting the light-sensitive protein, channel rhodopsin into retinal cells) the prosthetic device may produce image representation much closer to normal vision.

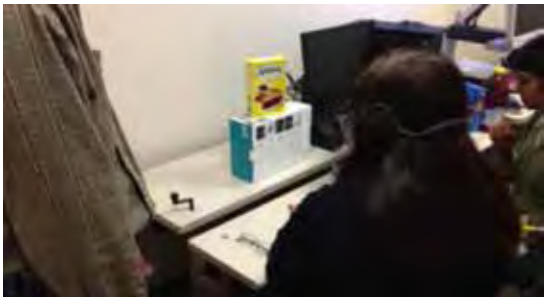
Top: In retinal degenerative diseases, suffered by civilians and Veterans alike, the photoreceptors and neighboring cells degenerate, but the retina's output cells remain largely intact. This opens the door to a prosthetic treatment. A device can jump over the damaged tissue and provide direct stimulation to the output cells, allowing them to send signals to the brain. Bottom: The device mimics the operations performed by the retina; that is, it transforms images into the code used by the output cells, and then it stimulates the output cells so they can send the code onto the brain. As shown, the device has two parts: a) a camera/encoder component, which takes images in and converts them into the code, and b) a transducer, which drives the output cells to send the code onward.



Thao (Vicky) Nguyen, Ph.D., Johns Hopkins University

A validated computational model of the human eye globe to investigate injury mechanisms of a primary blast wave from an Improvised Explosive Device, which has accounted for 70 percent of the blast injuries in Iraq and Afghanistan. The model determines the stresses on and deformations to the eye globe and surrounding supporting structures to enable the DoD to develop more effective eye protection strategies.

Simulation of the impact of the blast wave on the (a) unprotected eye, (b) eye protected by spectacles, and (c) the eye protected by goggles. The color contours indicate the blast pressure, and the black arrows indicate the velocity vectors of the blast wave. The highest pressure loading developed at the eye in the unprotected cases because the brow and nasal protrusion act as reflectors focusing the blast wave on the eye. The spectacles and goggles deflected most of the blast wave from the eye, but allowed a small fraction of underwash through the small gaps with the face. (d) The pressure history at a point on the eye comparing the unprotected eye, eye protected by spectacles, and eye protected by goggles for blasts from two different charge masses.



James Weiland, Ph.D., University of Southern California

A vision enhancement system that uses modern mobile computing and wireless technology, coupled with novel computer vision (i.e., object recognition programs) and human-computer interfacing strategies, to assist visually impaired Veterans undergoing vision rehabilitation to navigate, find objects of interest, and interact with people.

Veteran with TBI-related vision loss uses a prototype wearable visual aid to locate an object.

Appendix A: FY92–FY14

Table A-1. Overview of Appropriations, Applications Received, and Awards Made for FY92–FY14

Programs Managed by CDMRP	Fiscal Year	Appropriations Received (in millions)	Applications Received	Applications Funded	Transitioned with Merger	Total Funded
Alcohol and Substance Abuse Disorders	2014	$4.00	6	1	4	5
Amyotrophic Lateral Sclerosis	2007, 2009-2014	$46.90	359	35	-	35
Autism	2007-2014	$53.40	1,136	124	-	124
Bone Marrow Failure	2008-2014	$23.35	374	51	-	51
Breast Cancer	1992-2014	$3,045.00	50,969	6,525	-	6,525
Chronic Myelogenous Leukemia	2002-2006	$22.05	252	61	-	61
Defense Women's Health	1995	$40.00	559	69	-	69
Deployment Related Medical	2008	$101.90	1,094	51	7	58
DOD/VA	1999-2000	$6.79	88	9	-	9
Duchenne Muscular Dystrophy	2011-2014	$13.60	73	16	-	16
Genetic Studies of Food Allergies	2009-2010	$4.38	60	9	-	9
Gulf War Illness	2006, 2008-2014	$89.00	326	99	-	99
Institutionally Based Programs	1995-2010	$486.31	306	267	234	501
Joint Warfighter Medical Research	2012-2014	$103.95	100	35	7	42
Lung Cancer	2009-2014	$79.00	1,952	137	-	137
Military Burn	2014	$8.00	4	3	17	20
Multiple Sclerosis	2009-2014	$28.10	564	66		66
Myeloproliferative Disorders	2004	$4.25	18	9		9
National Prion	2002	$42.50	136	38		38
Neurofibromatosis	1996-2014	$272.85	1,372	332		332
Neurotoxin Exposure Treatment Parkinson's	2014	$16.00	2	2	45	47
Orthotics and Prosthetics	2014	$10.00	54	11		11
Osteoporosis	1995	$5.00	105	5		5
Ovarian Cancer	1997-2014	$236.45	3,096	346		346
Peer-Reviewed Alzheimer's	2014	$12.00	65	13	29	42
Peer-Reviewed Cancer	2009-2014	$99.80	2,309	213		213
Peer-Reviewed Medical	1999-2006, 2008-2014	$844.50	7,640	674		674
Peer-Reviewed Orthopaedic	2009-2014	$248.50	900	207		207
Prostate Cancer	1997-2014	$1,370.00	16,353	2,932		2,932
Spinal Cord Injury	2009-2014	$127.85	688	145		145
Trauma Clinical Research Repository	2014	$5.00	1	1		1
Tuberous Sclerosis	2002-2006, 2008-2014	$53.00	544	117		117
Vision	2013-2014	$18.92	142	24	17	41
Miscellaneous					23	23
Programs Executed on Behalf of Others						
Army Rapid Innovation Fund	2011-2014	$30.74	n/a	13		13
Chiropractic Clinical Trials	2010	$8.10	5	1		1
Clinical Research Intramural Initiative	2013-2014	$4.53	37	7		7
Defense Medical Research and Development (DHPe)	2010-2014	$363.09	929	190	169	359
Psychological Health/Traumatic Brain Injury	2007, 2009-2014	$737.51	3,320	416	39	455
SBIR/STTR	2014	$14.76	8	7	60	67
Total		**$8,681.08**	**95,946**	**13,261**	**651**	**13,912**

Appendix B: FY14–FY15

Table B-1. FY14-FY15 Alcohol and Substance Abuse Disorders 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
2014	**$4.0M** for Alcohol and Substance Abuse Disorders	**Withholds** USAMRMC: $36,666 **Management Costs** $250,736 (6.33%)	**Research** Consortium Award: $3,712,598
	Total: $4.0M	**Total: $287,402**	**Total: $3,712,598**
2015	**$4.0M** for Alcohol and Substance Abuse Disorders	**Withholds** USAMRMC: $80,000 **Budgeted Management Costs** $270,000 (6.89%)	**Research** Budgeted Peer-Reviewed Research: $3,650,000
	Total: $4.0M	**Total: $350,000**	**Total: $3,650,000**

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

Table B-2. FY14-FY15 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
2014	**$7.5M** for Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $73,999 **Management Costs** $475,634 (6.4%)	**Research** Therapeutic Development Award: $5,770,048 Therapeutic Idea Award: $1,180,319
	Total: $7.5M	**Total: $549,633**	**Total: $6,950,367**
2015	**$7.5M** for Amyotrophic Lateral Sclerosis Research	**Withholds** USAMRMC: $150,000 **Budgeted Management Costs** $515,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $6,835,000
	Total: $7.5M	**Total: $665,000**	**Total: $6,835,000**

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

Table B-3. FY14-FY15 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
2014	**$6M** for Autism Research	**Withholds** USAMRMC: $55,300 **Management Costs** $410,835 (6.91%)	**Research** Idea Development Award: $499,621 Idea Development Multi PI Award: $1,322,916 Clinical Trial Award: $3,711,328
	Total: $6.0M	**Total: $466,135**	**Total: $5,533,865**
2015	**$6M** for Autism Research	**Withholds** USAMRMC: $120,000 **Budgeted Management Costs** $411,600 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $5,468,400
	Total: $6.0M	**Total: $531,600**	**Total: $5,468,400**

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

Table B-4. FY14-FY15 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
2014	**$3.2M** for Bone Marrow Failure Disease Research	**Withholds** USAMRMC: $23,480 **Management Costs** $226,967 (7.15%)	**Research** Idea Development Award: $2,949,553
	Total: $3.2M	**Total: $250,447**	**Total: $2,949,553**
2015	**$3.2M** for Bone Marrow Failure Disease Research	**Withholds** USAMRMC: $64,000 **Budgeted Management Costs** $221,000 (7.05%)	**Research** Budgeted Peer-Reviewed Research: $2,915,000
	Total: $3.2M	**Total: $285,000**	**Total: $2,915,000**

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

Table B-5. FY14-FY15 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
2014	**$120M** for Breast Cancer Research **$497,166** in proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $1,190,547 **Management Costs** $7,341,410 (6.15%)	**Research** Breakthrough Award Funding Level 1: $14,040,948 Breakthrough Award Funding Level 2: $28,752,062 Breakthrough Award Funding Level 3 Clinical Trial: $2,575,108 Breakthrough Award Funding Level 4: $2,209,580 Breakthrough Award Funding Level 1 Partnering PI Option: $3,717,253 Breakthrough Award Funding Level 2 Partnering PI Option: $13,825,883 Breakthrough Award Funding Level 4 Partnering PI Option: $28,181,722 Era of Hope Scholar Award: $17,090,045 Idea Expansion Award: $681,677 Innovator Award: $348,245 Postdoctoral Fellowship Award: $542,686
	Total: $120,497,166	**Total: $8,531,957**	**Total: $111,965,209**
2015	**$120M** for Breast Cancer Research **$536,347** in proceeds from the Stamp Out Breast Cancer Act	**Withholds** USAMRMC: $2,400,000 **Budgeted Management Costs** $8,258,817 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $109,877,530
	Total: $120,536,347	**Total: $10,658,817**	**Total: $109,877,530**

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

Table B-6. FY14-FY15 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
2014	**$3.2M** for Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $23,480 **Management Costs** $155,520 (4.9%)	**Research** Investigator Initiated Research: $808,500 Investigator Initiated Research – Optional Qualified Collaborator(s): $1,282,428 Therapeutic Idea Award: $930,072
	Total: $3.2M	**Total: $179,000**	**Total: $3,021,000**
2015	**$3.2M** for Duchenne Muscular Dystrophy Research	**Withholds** USAMRMC: $64,000 **Budgeted Management Costs** $219,520 (7.0%)	**Budgeted Research** Budgeted Peer-Reviewed Research: $2,916,480
	Total: $3.2M	**Total: $283,520**	**Total: $2,916,480**

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

Table B-7. FY15 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
2015	**$7.5M** for Epilepsy Research	**Withholds** USAMRMC: $150,000 **Budgeted Management Costs** $514,500 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $6,835,500
	Total: $7.5M	**Total: $664,500**	**Total: $6,835,500**

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

Table B-8. FY14-FY15 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
2014	**$20M** for Gulf War Illness Research	**Withholds** USAMRMC: $190,627 **Management Costs** $1,119,102 (5.65%)	**Research** Investigator-Initiated Research Expansion Award – Clinical Trial: $1,085,000 Consortium Award: $253,256 Innovative Treatment Evaluation Award: $2,966,458 Investigator-Initiated Research Award: $5,731,560 New Investigator Award – New GWI Researcher: $2,083,560 New Investigator Award – Transitioning Postdoctoral Fellow: $542,092 Investigator-Initiated Research Expansion Award – Collaborative Option: $4,955,097 Investigator-Initiated Research Expansion Award – Clinical Trial – Collaborative Option: $1,073,248
	Total: $20M	**Total: $1,309,729**	**Total: $18,690,271**
2015	**$20M** for Gulf War Illness Research	**Withholds** USAMRMC: $400,000 **Budgeted Management Costs** $1,372,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $18,228,000
	Total: $20M	**Total: $1,772,000**	**Total: $18,228,000**

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

Table B-9. FY14-FY15 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
2014	**$100M** for Joint Warfighter Medical Research	**Withholds** USAMRMC: $995,466 **Management Costs** $3,972,894 (4.01%)	**Research** Peer-Reviewed Research: $95,031,640
	Total: $100M	**Total: $4,968,360**	**Total: $95,031,640**
2015	**$50M** for Joint Warfighter Medical Research	**Withholds** USAMRMC: $1,000,000 **Budgeted Management Costs** $3,430,000 (7.0%)	**Budgeted Research** Budgeted Peer-Reviewed Research: $45,570,000
	Total: $50M	**Total: $4,430,000**	**Total: $45,570,000**

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

Table B-10. FY14-FY15 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
2014	**$10.5M** for Lung Cancer Research	**Withholds** USAMRMC: $100,284 **Management Costs** $880,799 (8.47%)	**Research** Concept Award: $1,888,397 Idea Development Award: $2,762,994 Career Development Award: $1,935,849 Idea Development Award New Investigator: $959,434 Clinical Exploration Award: $1,389,492 Lung Cancer Biospecimen Resource Network Award: $300,000 Clinical Exploration Award – Correlative Studies: $282,751
	Total: $10.5M	**Total: $981,083**	**Total: $9,518,917**
2015	**$10.5M** for Lung Cancer Research	**Withholds** USAMRMC: $210,000 Budgeted Management Costs $720,300 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $9,569,700
	Total: $10.5M	**Total: $930,300**	**Total: $9,569,700**

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

Table B-11. FY14-FY15 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
2014	**$8M** for Military Burn Research	**Withholds** USAMRMC: $239,974 **Management Costs** $402,361 (5.19%)	**Research** Broad Agency Announcement: $5,465,936 Military Infectious Diseases Applied Research Award: $1,891,729
	Total: $8M	**Total: $642,335**	**Total: $7,357,665**
2015	**$8M** for Military Burn Research	**Withholds** USAMRMC: $160,000 **Budgeted Management Costs** $548,800 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $7,291,200
	Total: $8M	**Total: $708,800**	**Total: $7,291,200**

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

Table B-12. FY14-FY15 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
2014	**$5.0M** for Multiple Sclerosis Research	**Withholds** USAMRMC: $47,671 **Management Costs** $225,091 (4.55%)	**Research** Investigator-Initiated Partnership Award: $ 4,727,238
	Total: $5.0M	**Total: $272,762**	**Total: $4,727,238**
2015	**$5M** for Multiple Sclerosis Research	**Withholds** USAMRMC: $100,000 **Budgeted Management Costs** $340,000 (6.94%)	**Research** Budgeted Peer-Reviewed Research: $4,560,000
	Total: $5M	**Total: $440,000**	**Total: $4,560,000**

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

Table B-13. FY14-FY15 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
2014	**$15M** for Neurofibromatosis Research	**Withholds** USAMRMC: $450,000 **Management Costs** $1,092,578 (7.51%)	**Research** Clinical Trial Award: $2,625,444 Exploration – Hypothesis Development Award: $420,991 Investigator-Initiated Research Award: $3,635,504 Investigator-Initiated Research Award – Optional Qualified Collaborator: $4,178,692 New Investigator Award: $2,596,791
	Total: $15M	**Total: $1,542,578**	**Total: $13,457,422**
2015	**$15M** for Neurofibromatosis Research	**Withholds** USAMRMC: $300,000 **Budgeted Management Costs** $1,029,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $13,671,000
	Total: $15M	**Total: $1,329,000**	**Total: $13,671,000**

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

Table B-14. FY14-FY15 Neurotoxin Exposure Treatment 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
2014	**$16M** for Neurotoxin Exposure Treatment Parkinson's Research	**Withholds** USAMRMC: $480,000 **Management Costs** $1,009,516 (6.5%)	**Research** Budgeted Peer-Reviewed Research: $14,510,484
	Total: $16M	**Total: $1,489,516**	**Total: $14,510,484**
2015	**$16M** for Neurotoxin Exposure Treatment Parkinson's Research	**Withholds** USAMRMC: $320,000 **Budgeted Management Costs** $1,097,600 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $14,582,400
	Total: $16M	**Total: $1,417,600**	**Total: $14,582,400**

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

Table B-15. FY14-FY15 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
2014	**$10M** for Orthotics and Prosthetics Outcomes Research	**Withholds** USAMRMC: $50,545 **Management Costs** $732,259 (7.36%)	**Research** Research Award Level 1: $2,896,653 Research Award Level 2 – Clinical Trial: $5,335,579 Research Award Level 1 – Clinical Trial: $984,964
	Total: $10M	**Total: $782,804**	**Total: $9,217,196**
2015	**$10M** for Orthotics and Prosthetics Outcomes Research	**Withholds** USAMRMC: $200,000 **Budgeted Management Costs** $686,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $9,114,000
	Total: $10M	**Total: $886,000**	**Total: $9,114,000**

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

Table B-16. FY14-FY15 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
2014	**$20M** for Ovarian Cancer Research	**Withholds** USAMRMC: $191,710 **Management Costs** $1,212,702 (6.12%)	**Research** Clinical Translational Leverage Award: $371,043 Dean Leadership Award: $1,966,271 Ovarian Cancer Academy Award – Early Career Investigators: $4,604,043 Pilot Award: $3,287,268 Investigator-Initiated Research Award: $5,448,562 Ovarian Cancer Academy Collaborative Award: $1,062,000 Pilot with Optional Nested Teal Post Doctoral Scholar Award: $1,856,401
	Total: $20M	**Total: $1,404,412**	**Total: $18,595,588**
2015	**$20M** for Ovarian Cancer Research	**Withholds** USAMRMC: $400,000 **Budgeted Management Costs** $1,372,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $18,228,000
	Total: $20M	**Total: $1,772,000**	**Total: $18,228,000**

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

Table B-17. FY14-FY15 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
2014	**$12M** for Peer Reviewed Alzheimer's Research	**Withholds** USAMRMC: $117,211 **Budgeted Management Costs** $1,297,859 (10.92%)	**Research** Budgeted Peer-Reviewed Research: $713,018 Convergence Science Research Award: $7,023,534 Quality of Life Research Award: $1,356,668 Military Risk Factors Research Award: $1,491,710
	Total: $12M	**Total: $1,415,070**	**Total: $10,584,930**
2015	**$12M** for Peer Reviewed Alzheimer's Research	**Withholds** USAMRMC: $240,000 **Budgeted Management Costs** $823,200 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $10,936,800
	Total: $12M	**Total: $1,063,200**	**Total: $10,936,800**

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

Table B-18. FY14-FY15 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
2014	**$25M** for Peer-Reviewed Cancer Research	**Withholds** USAMRMC: $245,210 **Management Costs** $1,456,935 (5.89%)	**Research** Blood: $3,987,098 Colorectal: $3,309,425 Genetic: $1,544,383 Kidney: $1,608,921 Listeria Vaccine: $448,500 Melanoma & Other Skin Cancer: $5,131,154 Mesothelioma: $1,033,669 Myeloproliferative Disorders: $453,875 Neuroblastoma: $1,468,031 Pancreatic: $2,399,675 Pediatric Brain Tumors: $988,663 Related to Radiation Exposure: $924,461
	Total: $25M	**Total: $1,702,145**	**Total: $23,297,855**
2015	**$50M** for Peer-Reviewed Cancer Research	**Withholds** USAMRMC: $1,000,000 **Budgeted Management Costs** $3,430,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $45,570,000
	Total: $50M	**Total: $4,430,000**	**Total: $45,570,000**

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

FY14 Peer-Reviewed Cancer Research Program: The agreement provides $25,000,000 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 DoD. The funds provided in the peer-reviewed cancer research program are directed to be used to conduct research in the following areas: blood cancer, colorectal cancer, genetic cancer research, kidney cancer, listeria vaccine for cancer, melanoma and other skin cancers, mesothelioma, myeloproliferative disorders, neuroblastoma, pancreatic cancer, pediatric brain tumors, and cancers related to radiation exposure.

FY15 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 DoD. The funds provided in the peer-reviewed cancer research program are directed to be used to conduct research in the following areas: colorectal cancer, genetic cancer research, kidney cancer, listeria vaccine for cancer, liver cancer, melanoma and other skin cancers, mesothelioma, myeloproliferative disorders, neuroblastoma, pancreatic cancer, and stomach cancer.

Table B-19. FY14-FY15 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
2014	**$200M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $1,999,646 **Management Costs** $13,225,603 (6.68%)	**Research** Acupuncture: $3,950,202 Arthritis: $451,141 Chronic Migraine and Post-Traumatic Headache: $9,030,614 Congenital Heart Disease: $6,809,968 DNA Vaccine Technology for Postexposure Prophylaxis: $12,117,292 Dystonia: $3,038,539 Epilepsy: $4,126,294 Food Allergies: $3,592,652 Fragile X Syndrome: $4,028,779 Illnesses Related to Radiation Exposure: $27,961,729 Inflammatory Bowel Disease: $3,475,406 Interstitial Cystitis: $2,036,850 Leishmaniasis: $43,000 Malaria: $9,224,282 Metabolic Disease: $6,313,260 Neuroprosthetics: $3,894,168 Pancreatitis: $4,845,816 Polycystic Kidney Disease: $11,345,602 Post-Traumatic Osteoarthritis: $4,991,032 Psychotropic Medications: $11,466,732 Respiratory Health: $42,745,670 Rheumatoid Arthritis: $4,441,376 Scleroderma: $175,000 Segmental Bone Defects: $1,173,888 Tinnitus: $3,495,459
	Total: $200M	**Total: $15,225,249**	**Total: $184,774,751**
2015	**$247.5M** for Peer-Reviewed Medical Research	**Withholds** USAMRMC: $4,950,000 **Budgeted Management Costs** $16,978,500 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $225,571,500
	Total: $247.5M	**Total: $21,928,500**	**Total: $225,571,500**

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

FY14 Peer Reviewed Medical Research Program: The agreement provides $200,000,000 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: acupuncture, arthritis, chronic migraine and post-traumatic headache, congenital heart disease, DNA vaccine technology for postexposure prophylaxis, dystonia, epilepsy, food allergies, Fragile X syndrome, hereditary angioedema, illnesses related to radiation exposure, inflammatory bowel disease, interstitial cystitis, lupus, malaria, metabolic disease, neuroprosthetics, pancreatitis, polycystic kidney disease, post-traumatic osteoarthritis, psychotropic medications, respiratory health, rheumatoid arthritis, segmental bone defects, and tinnitus. The additional funding provided under the peer-reviewed medical research program shall be devoted only to the purposes listed above.

FY15 Peer Reviewed Medical Research Program: The agreement provides $247,500,000 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: acupuncture, acute lung injury, advanced prosthetics, arthritis, burn pit exposure, cardiovascular health, chronic migraine and post-traumatic headache, congenital heart disease, Dengue, diabetes, DNA vaccine technology for postexposure prophylaxis, dystonia, focal segmental glomerulosclerosis, food allergies, Fragile X syndrome, healthcare-acquired infection reduction, hepatitis B, hereditary angioedema, hydrocephalus, inflammatory bowel disease, integrative medicine, interstitial cystitis, lupus, malaria, metals toxicology, mitochondrial disease, nanomaterials for bone regeneration, osteoarthritis, pancreatitis, pathogen-inactivated dried plasma, polycystic kidney disease, post-traumatic osteoarthritis, psychotropic medications, pulmonary fibrosis, respiratory health, rheumatoid arthritis, scleroderma, sleep disorders, tinnitus, vascular malformations, and women's heart disease.

Table B-20. FY14-FY15 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
2014	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $293,481 **Management Costs** $1,972,589 (6.64%)	**Research** Clinical Trial Award: $5,101,668 Clinical Consortium Award: $418,521 Clinical Trial Development Award: $531,607 Expansion Award: $8,010,035 Expansion Award – Clinical Trial Option: $1,326,755 Idea Development Award: $2,983,464 Outcomes Research Award: $4,983,188 Translational Research Award – Single PI Only: $4,375,062 Translational Research Partnership Award: $3,630
	Total: $30M	**Total: $2,266,070**	**Total: $27,733,930**
2015	**$30M** for Peer-Reviewed Orthopedic Research	**Withholds** USAMRMC: $600,000 **Budgeted Management Costs** $2,058,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $27,342,000
	Total: $30M	**Total: $2,658,000**	**Total: $27,342,000**

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

Table B-21. FY14-FY15 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
2014	**$80M** for Prostate Cancer Research	**Withholds** USAMRMC: $799,188 **Management Costs** $4,248,517 (5.36%)	**Research** Biomarker Development Award: $6,267,265 Clinical Consortium Award – Coordinating Center with Clinical Research Site Option: $2,440,472 Clinical Consortium Award Clinical Research Site: $3,484,842 Collaborative Undergraduate HBCU Student Summer Training Program: $794,898 Exploration–Hypothesis Development Award: $3,368,071 Health Disparity Research Award – Established Investigator: $679,875 Health Disparity Research Award – Established Investigator with Qualified Collaborator Option: $3,226,633 Health Disparity Research Award New Investigator Option: $1,558,474 Idea Development Award New Investigator Option: $5,816,845 Idea Development Award Established Investigator: $18,723,029 Laboratory – Clinical Transition Award: $2,240,152 Physician Research Training Award: $3,307,975 Population Science Impact Award: $1,089,679 Postdoctoral Training Award: $3,278,815 Prostate Cancer Biospecimen Resource Site Award: $610,000 Prostate Cancer Pathology Resource Network Award – Partnering PI Option: $1,632,945 Synergistic Idea Development Award: $16,432,325
	Total: $80M	**Total: $5,047,705**	**Total: $74,952,295**
2015	**$80M** for Prostate Cancer Research	**Withholds** USAMRMC: $1,600,000 **Budgeted Management Costs** $5,488,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $72,912,000
	Total: $80M	**Total: $7,088,000**	**Total: $72,912,000**

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

Table B-22. FY14-FY15 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
2014	**$30M** for Spinal Cord Injury Research	**Withholds** USAMRMC: $290,975 **Management Costs** $1,700,285 (5.72%)	**Research** Clinical Trial Award: $11,890,689 Investigator-Initiated Research Award – Optional Qualified Collaborator: $3,868,826 Translational Research Award – Single PI Only: $1,855,650 Investigator-Initiated Research Award: $2,774,422 Investigator-Initiated Research Award – Optional Qualified Collaborator: $6,168,310 Qualitative Research Award: $1,211,987 Clinical Trial Award Rehabilitation Nested New Investigator Option: $238,856
	Total: $30M	**Total: $1,991,260**	**Total: $28,008,740**
2015	**$30M** for Spinal Cord Injury Research	**Withholds** USAMRMC: $600,000 **Budgeted Management Costs** $2,058,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $27,342,000
	Total: $30M	**Total: $2,658,000**	**Total: $27,342,000**

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

Table B-23. FY14 Trauma Clinical Research Repository 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
2014	**$5M** for Trauma Clinical Research Repository Program	**Withholds** USAMRMC: $37,139 **Management Costs** $320,001 (6.45%)	**Research** Applied Neurotrauma Research Award: $4,642,860
	Total: $5M	**Total: $357,140**	**Total: $4,642,860**

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

Table B-24. FY14-FY15 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
2014	**$6M** for Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $51,610 **Management Costs** $317,367 (5.34%)	**Research** Idea Development Award: $1,321,745 Pilot Clinical Trial Award: $612,090 Exploration–Hypothesis Development Award: $329,429 Idea Development Award Optional Qualified Collaborator: $3,367,759
	Total: $6M	**Total: $368,977**	**Total: $5,631,023**
2015	**$6M** for Tuberous Sclerosis Complex Research	**Withholds** USAMRMC: $120,000 **Budgeted Management Costs** $411,600 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $5,468,400
	Total: $6M	**Total: $531,600**	**Total: $5,468,400**

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

Table B-25. FY14-FY15 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
2014	**$10M** for Vision Research	**Withholds** USAMRMC: $99,771 **Management Costs** $643,729 (6.5%)	**Research** Translational Research Award: $8,506,679 Hypothesis Development Award: $749,821
	Total: $10M	**Total: $743,500**	**Total: $9,256,500**
2015	**$10M** for Vision Research	**Withholds** USAMRMC: $200,000 **Budgeted Management Costs** $686,000 (7.0%)	**Research** Budgeted Peer-Reviewed Research: $9,114,000
	Total: $10M	**Total: $886,000**	**Total: $9,114,000**

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

Table B-26. FY14 Army Rapid Innovation Fund
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2014	**$1.9M** for Army Rapid Innovation Fund	**Management Costs** $1	**Research** Army Rapid Innovation Fund: $1,894,944
	Total: $1.9M	**Total: $1**	**Total: $1,894,944**

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

Table B-27. FY14 Clinical Research Intramural Initiative 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
2014	**$2.3M** for Clinical Research Intramural Initiative Research	**Withholds** USAMRMC: **Management Costs**	**Research** Clinical Research Intramural Initiative: $2,316,000
	Total: $2.3M		**Total: $2,316,000**

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

Table B-28. FY14 Defense Medical Research and Development Program CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2014	**$139.1M** for Defense Medical Research and Development from the Guidance for the Development of the Force Funding	**Management Costs** $7,250,679 (5.2%)	**Research** Broad Agency Announcement: $99,649,273 Military Infectious Diseases Applied Research Award: 4,795,845 Applied Neurotrauma Research Award: $1,092,449 Applied Neurotrauma Research Award with Clinical Trial: $735,244 Applied Psychological Health Award with Clinical Trial – Partnering Option: $1,160,605 Applied Research and Advanced Technology Development Award: $195,678 Applied Research and Advanced Technology Development Psychological Health Award: $1,780,391 Basic Psychological Health Award: $530,565 Applied Neurotrauma Research Award – Partnering Option: $679,552 PH/TBI-IIRA-Broad Agency Announcement: $3,885,798 Neuromusculoskeletal Injuries Research Award: $10,451,044 Neurosensory and Rehabilitation Research Award – Applied Research Option: $509,194 Neurosensory Research Award: $5,369,820 Psychological Health Award – Applied/Combined Research: $530,899 Vision Research Program – Translational Research Award: $468,907
	Total: $139.1M	**Total: $7,250,679**	**Total: $131,835,264**

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

Table B-29. FY14 Psychological Health/Traumatic Brain Injury Research Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2014	**$86.0M** for Psychological Health and Traumatic Brain Injury Research	**Management Costs** $4,316,934 (5%)	**Research** Applied Research and Advanced Technology Development Award: $959,372 Psychological Health Award Applied/Combined Research: $21,916,119 Psychological Health Research Award: $3,294,211 Psychological Health Research Award – Partner PI Option: $9,943,667 PTSD Multidisciplinary Research Consortium Award: $511,645 Clinical Consortium Award: $474,008 TBI Multidisciplinary Research Consortium Award: $155,724 Traumatic Brain Injury Research Award: $1,477,944 Community Partners in Mental Health – Research Award: $4,617,322 Traumatic Brain Injury/ Post-Traumatic Stress Disorder – Clinical Trial Award: $4,761,697 Broad Agency Announcement: $33,578,340
	Total: $86.0M	**Total: $4,316,934**	**Total: $81,690,049**

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

Table B-30. FY14 Small Business Innovation Reports/Small Business Technology Transfer Program
CDMRP Executed Funds, Management Costs, and Execution of Investment Strategy

Fiscal Year	Congressional Language and Appropriations	Withholds and Management Costs	Investment Strategy
2014	**$14.76M** for Defense Medical Research and Development		**Research** Small Business Innovative Research: $13,770,088 Small Business Technology Transfer: $989,991
	Total: $14.76M		**Total: $14,760,079**

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

Appendix C: Breast Cancer Research Semipostal Awards FY99–FY14

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

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY03	Chung	$490,447	Yale University	Quantitative in Situ Assessment of the Somatostatin Receptor in Breast Cancer to Assess Response to Targeted Therapy with 111-in-Pentetreotide
	Kaaks	$367,639	International Agency for Cancer Research	Fatty Acid Synthesis Gene Variants and Breast Cancer Risk: A Study within the European Prospective Investigation into Cancer and Nutrition (EPIC)
	Yaswen	$508,790	Lawrence Berkeley National Laboratory	Functional Analysis of BORIS, a Novel DNA-Binding Protein
	Ziv	$767,171	University of California, San Francisco	Admixture and Breast Cancer Risk among Latinas
FY04	Bissell	$386,569	Lawrence Berkeley National Laboratory	Use of HA-Metal Nanoparticles to Identify and Characterize Tumorigenic Progenitor Cell Subsets in Breast Tumors
	Clarke	$588,738	Northern California Cancer Center	The Hygiene Hypothesis and Breast Cancer: A Novel Application of an Etiologic Theory for Allergies, Asthma, and Other Immune Disorders
	Giorgio	$453,000	Vanderbilt University	Surface Functionalized Nanoparticles and Nanocrystals for Proximity-Modulated, Early Neoplasia Detection, Imaging, and Treatment of Breast Cancer
	Lemmon	$475,500	University of Pennsylvania	Harnessing Novel Secreted Inhibitors of EGF Receptor Signaling for Breast Cancer Treatment
FY05	Zinn[2]	$436,500	University of Alabama at Birmingham	Novel Screening and Precise Localization of Early Stage Breast Cancer in Animal Model
	Huang	$483,600	Cornell University, Weill Medical College	Migrastatin Analogues as Potent Inhibitors of Breast Cancer Metastasis
	Liu	$448,500	Ohio State University	Hunting for Novel X-Linked Breast Cancer Suppressor Genes in Mouse and Human
	Rao	$468,000	Stanford University	Ribozyme-Mediated Imaging of Oncogene Expression in Breast Tumor Cells
FY06	Devi	$155,085[3]	Duke University Medical Center	Modulation of Regulatory T Cells as a Novel Adjuvant for Breast Cancer Immunotherapy
	Lee	$489,000	University of Southern California	A New Mechanism for Estrogen-Starvation Resistance in Breast Cancer
	Li	$438,455	Baylor College of Medicine	The ER/PR Status of the Originating Cell of ER-Negative Breast Cancer
	Mousa	$377,620	Albany College of Pharmacy	Enhancing the Efficacy of Chemotherapeutic Breast Cancer Treatment with Non-anticoagulant Heparins
	Rastinejad	$454,500	University of Virginia	Structural Characterization of the Interdomain Features of the Estrogen Receptor
FY07	Kuperwasser	$817,500	Tufts University	Mechanisms of Breast Cancer Associated with Obesity
	Kelly	$244,450[4]	University of Virginia	Genetically Encoded Targeted, Amplifiable, Imaging Agents for Early Detection of Breast Cancer
	Gerbi	$155,550[5]	Brown University	Hormonal Involvement in Breast Cancer Gene Amplification

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

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

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

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

Fiscal Year	Principal Investigator	Amount	Institution	Proposal Title
FY08	Park	$111,663	North Dakota State University	In Utero Exposure to Dietary Methyl Nutrients and Breast Cancer Risk in Offspring
	Radosz	$528,939	University of Wyoming	Breast Cancer-Targeting Nuclear Drug Delivery Overcoming Drug Resistance for Breast Cancer Therapy
	Hill	$577,500	Oregon Health and Science University	Vaccine Vector for Sustained High-Level Antitumor CTL Response
	You	$503,666	University of Oklahoma Health Science Center	Targeted Delivery and Remote-Controlled Release of Chemotherapeutic Agents
	Seagroves	$166,667[6]	University of Tennessee Health Science Center	The Role of HIF-1 Alpha in Breast Cancer: A Positive Factor in Cancer Stem Cell Expansion via Notch?
FY09	Reynolds	$730,000[7]	Cancer Prevention Institute of California	Hazardous Air Pollutants and Breast Cancer: An Unexplored Area of Risk
	Wysolmerski	$620,626	Yale University	Effects of Nuclear Parathyroid Hormone-Related Protein Signaling in Breast Cancer
FY10	Schedin	$368,125[8]	University of Colorado, Denver	The Immune Modulatory Program of Post-Partum Involution Promotes Pregnancy-Associated Breast Cancer
	Leung	$556,875[9]	Johns Hopkins University	The Role of Poly(ADP-Ribose) in microRNA Activity in Breast Cancers
FY11	Minn	$399,942	University of Pennsylvania	Regulation of Metastasis and DNA Damage Resistance Pathways by Transposable Elements
	Wang	$409,693	Baylor College of Medicine	Copy Number Signature of Recurrent Gene Fusions Reveals Potential Drug Targets in Invasive Breast Cancer
	Gonzalo Hervas	$58,975[10]	St. Louis University	Stabilization of 53BP1 in Triple-Negative and BRCA-Deficient Breast Tumors: A Novel Therapeutic Strategy
FY12	Yang	$465,000	University of California, San Diego	Regulation of Breast Cancer Stem Cell by Tissue Rigidity
	Giancotti	$174,837[11]	Memorial Sloan Kettering Cancer Center	Autophagy and TGF-Beta Antagonist Signaling in Breast Cancer Dormancy at Premetastatic Sites
FY13	Rubin	$457,075	University of California, Santa Cruz	Inhibition of Retinoblastoma Protein Inhibition
	Luke	$96,992[12]	University of Texas at Austin	Noninvasive Label-Free Detection of Micrometastases in the Lymphatics with Ultrasound-Guided Photoacoustic Imaging
FY14	Shu	$364,343	University of Kentucky	Ultrastable Nontoxic RNA Nanoparticles for Targeting Triple-Negative Breast Cancer Stem Cells
	Ellisen	$93,050[13]	Massachusetts General Hospital	Defining High-Risk Precursor Signaling to Advance Breast Cancer Risk Assessment and Prevention
	Brown	$7,457[14]	University of Rochester	Prediction of Metastasis Using Second Harmonic Generation
	DeNardo	$7,061[15]	Washington University	Reprogramming the Metastatic Microenvironment to Combat Disease Recurrence

[6]Total award amount was $554,987; remaining funds were from the FY08 BCRP.
[7]Total award amount was $860,883; remaining funds were from the FY09 BCRP.
[8]Total award amount was $556,028; remaining funds were from the FY10 BCRP.
[9]Total award amount was $585,652; remaining funds were from the FY10 BCRP.
[10]Total award amount was $744,661; remaining funds were from the FY11 BCRP.
[11]Total award amount was $331,449; 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.

Appendix D: Acronyms

3D ..... three-dimensional
AD ..... Alzheimer's Disease
ADNI ..... Alzheimer's Disease Neuroimaging Initiative
ALI ..... acute lung injury
ALS ..... Amyotrophic Lateral Sclerosis
ALSRP ..... Amyotrophic Lateral Sclerosis Research Program
AR ..... androgen receptor
ARP ..... Autism Research Program
ASADRP ..... Alcohol and Substance Abuse Disorders Research Program
ASD ..... autism spectrum disorders
B ..... billion
BAA ..... Broad Agency Announcements
BAP1 ..... BRCA1 associated protein-1
BCRP ..... Breast Cancer Research Program
BCRS ..... Breast Cancer Research Semipostal
BMFRP ..... Bone Marrow Failure Research Program
CAP ..... Consortium to Alleviate PTSD
CAR ..... chimeric antigen receptor
CARE ..... Concussion Assessment, Research, and Education Consortium
CCCRP ..... Combat Casualty Care Research Program
CDC ..... Centers for Disease Control and Prevention
CDK ..... cyclin-dependent kinase
CDMRP ..... Congressionally Directed Medical Research Programs
CENC ..... Chronic Effects of Neurotrauma Consortium
CHEK1 ..... checkpoint kinase 1
COACH ..... Combined Online Assistance for Caregiver Health
CRMRP ..... Clinical and Rehabilitative Medicine Research Program
CRPC ..... castration-resistant PCa
CURE ..... Citizens United for Research in Epilepsy
DBA ..... Diamond Blackfan Anemia
DBSI ..... diffusion basis spectrum imaging
DHA ..... Defense Health Agency
DHP ..... Defense Health Program
D-loop ..... Displacement loop
DMD ..... Duchenne Muscular Dystrophy
DMDRP ..... Duchenne Muscular Dystrophy Research Program
DMRDP ..... Defense Medical Research and Development Program
DoD ..... Department of Defense
EAE ..... experimental autoimmune encephalomyelitis
eBRAP ..... Electronic Biomedical Research Application Portal
ECI ..... Early-Career Investigator
EGS ..... Electronic Grants System
EMT ..... epithelial-mesenchymal transition
ER ..... estrogen receptor
FDA ..... U.S. Food and Drug Administration
FRP ..... Flavonoid-Rich Preparation
FY ..... fiscal year
GI ..... gastrointestinal
Glib ..... glibenclamide
GWI ..... Gulf War Illness
GWIRP ..... Gulf War Illness Research Program
HHS ..... U.S. Department of Health and Human Services
HRE ..... hexanucleotide repeat expansion
iFAST ..... Intelligent Focused Assessment of Ultrasound for Trauma
INTRuST ..... INjury and TRaumatic STress Consortium
ITN ..... Institute for Translational Neuroscience
JPC ..... Joint Program Committee
JWMRP ..... Joint Warfighter Medical Research Program
KP ..... Klebsiella Pneumoniae
LCRP ..... Lung Cancer Research Program
M ..... million
MBRP ..... Military Burn Research Program
MCI ..... Minimal Cognitive Impairment
MDS ..... Myelodysplastic Syndrome
mGluR5 ..... metabotropic glutamate receptor 5
MHS ..... Military Health System
MIA ..... maternal immune activation
MIDRP ..... Military Infectious Diseases Research Program
MOMRP ..... Military Operational Medicine Research Program

MRI ..... magnetic resonance imaging
MS ..... multiple sclerosis
MSIS ..... Medical Simulation and Information Sciences
MSRC ..... Military Suicide Research Consortium
MSRP ..... Multiple Sclerosis Research Program
mTBI ..... mild TBI
mtDNA ..... mitochondrial DNA
mTORC1 ..... mammalian target of rapamycin complex 1
NCAA ..... National Collegiate Athletic Association
NCDR ..... Neurotrauma Consortium Data Repository
NETPR ..... Neurotoxin Exposure Treatment Parkinson's Research
NF ..... Neurofibromatosis
NFCTC ..... Neurofibromatosis Clinical Trials Consortium
NFKB ..... nuclear factor-kappa B gene
NFRP ..... Neurofibromatosis Research Program
NIH ..... National Institutes of Health
OASD(HA) ..... Office of the Assistant Secretary of Defense for Health Affairs
OCA ..... Ovarian Cancer Academy
OCCA ..... Ovarian Cancer Consortium Award
OCRP ..... Ovarian Cancer Research Program
OEF ..... Operation Enduring Freedom
OIF ..... Operation Iraqi Freedom
OPORP ..... Orthotics and Prosthetics Outcomes Research Program
PA ..... Pseudomonas Aeruginosa
PAD ..... Program Area Directorate
PCa ..... prostate cancer
PCBN ..... Prostate Cancer Biorepository Network
PCCTC ..... Prostate Cancer Clinical Trials Consortium
PCRP ..... Prostate Cancer Research Program
PD ..... Parkinson's disease
PET ..... positron emission tomography
P-gp ..... P-glycoprotein
PHREI ..... Pacific Health Research and Education Institute
PH/TBIRP ..... Psychological Health and Traumatic Brain Injury Research Program
PI ..... Principal Investigator
PMD ..... partially methylated domain
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
PTE ..... post-traumatic epilepsy
PTOA ..... Post-traumatic osteoarthritis
PTSD ..... Post-Traumatic Stress Disorder
QOL ..... Quality of Life
RDA ..... Research, Development and Acquisition
RFID ..... Radio Frequency Identification
rhCC10 ..... recombinant human CC10 protein
RHERP ..... Radiation Health Effects Research Program
RNA ..... ribonucleic acid
RT ..... radiation therapy
RTI ..... Research Triangle Institute
SBIR ..... Small Business Innovation Research
SCIRP ..... Spinal Cord Injury Research Program
SGB ..... Stellate Ganglion Block
STIC ..... serous tubal intraepithelial carcinoma
STIL ..... serous tubal intraepithelial lesion
STRONG STAR ..... South Texas Research Organizational Network Guiding Studies on Trauma and Resilience
STTR ..... Small Business Technology Transfer
STVHCS ..... South Texas Veterans Health Care System
SUD ..... substance use disorder
TAPTE ..... Team Approach to the Prevention and Treatment of Post-Traumatic Epilepsy
TARGET ..... TBI Assessment of Readiness Using a Gait Evaluation Test
TATRC ..... Telemedicine and Advanced Technology Research Center
TBI ..... Traumatic Brain Injury
TCC ..... Translational Coordinating Core
TED ..... TBI Endpoints Development
Th1 ..... T-helper 1
TIFAB ..... TRAF-interacting protein with forkhead associated domain B
TLR2 ..... Toll-like receptor 2
Tregs ..... regulatory T cells
TRL ..... technology-readiness level
TSCRP ..... Tuberous Sclerosis Complex Research Program
USAMRAA ..... U.S. Army Medical Research Acquisition Activity
USAMRMC ..... U.S. Army Medical Research and Materiel Command
UTHSCSA ..... University of Texas Health Science Center San Antonio
VA ..... U.S. Department of Veterans Affairs
VABHCS ..... VA Boston Healthcare System
VRP ..... Vision Research Program
ZA ..... zoledronic acid

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