The Congressionally Directed Medical Research Programs

Sarah Fontaine, Ph.D.

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CDMRP

Department of Defense

10 March 2022

Outline

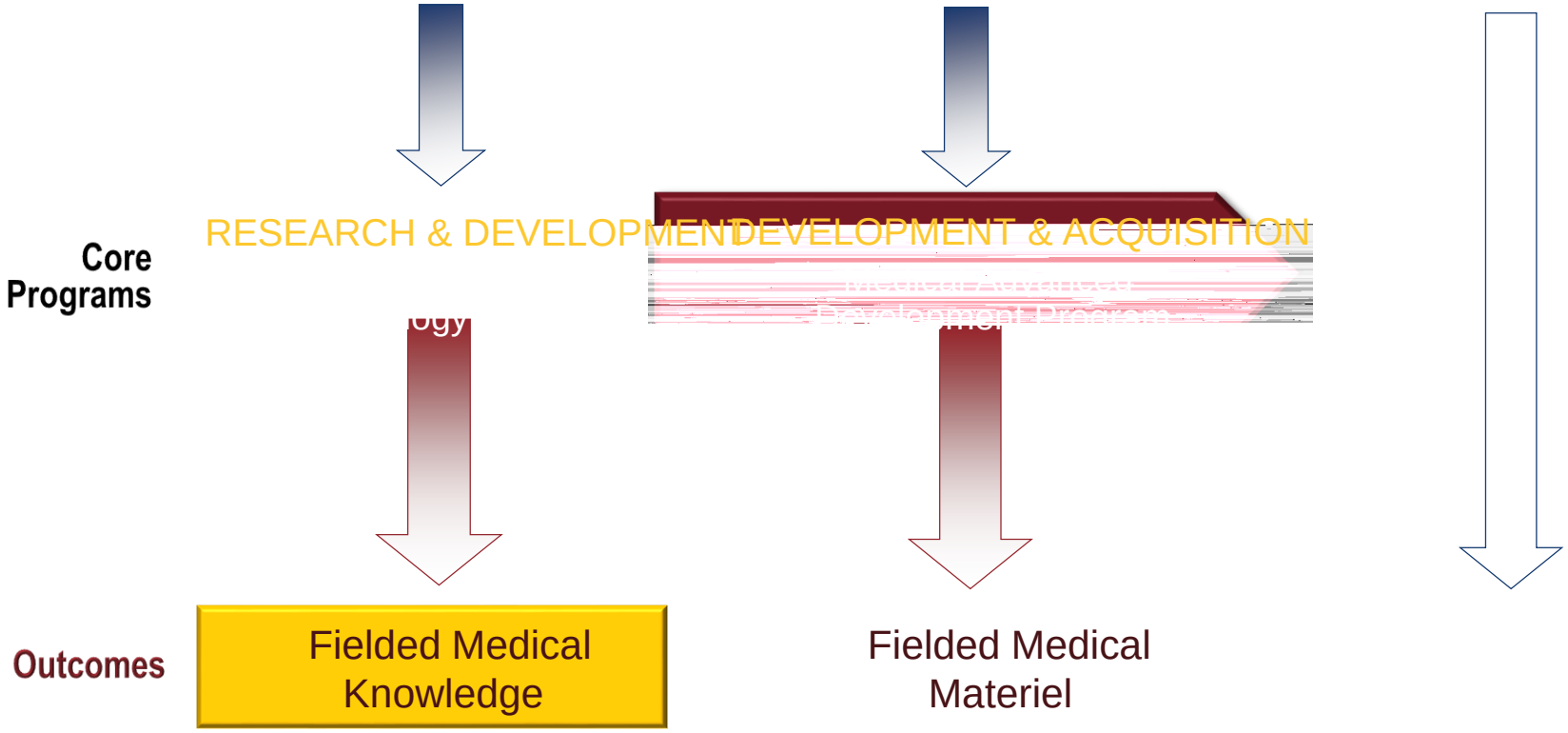
- Overview of the CDMRP
  - CDMRP Funding Process
  - CDMRP Funding Opportunities
  - Other DOD Funding Opportunities
- Peer Reviewed Alzheimer's Research Program
  - PRARP History, Vision, and Mission
  - PRARP Portfolio
- FY22 Opportunities*

**Pending FY22 Appropriation*

WHO is the CDMRP?

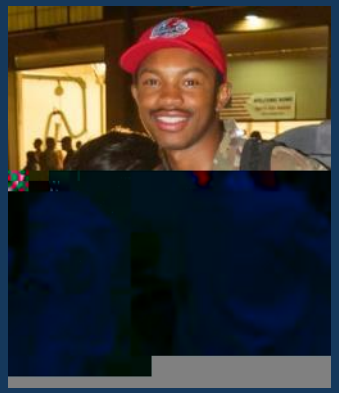
- Department of Defense
  - Department of the Army
    - Army Futures Command
      - U.S. Army Medical Research and Development Command (USAMRDC)
        - Congressionally Directed Medical Research Programs

Congressional Special Interest Programs



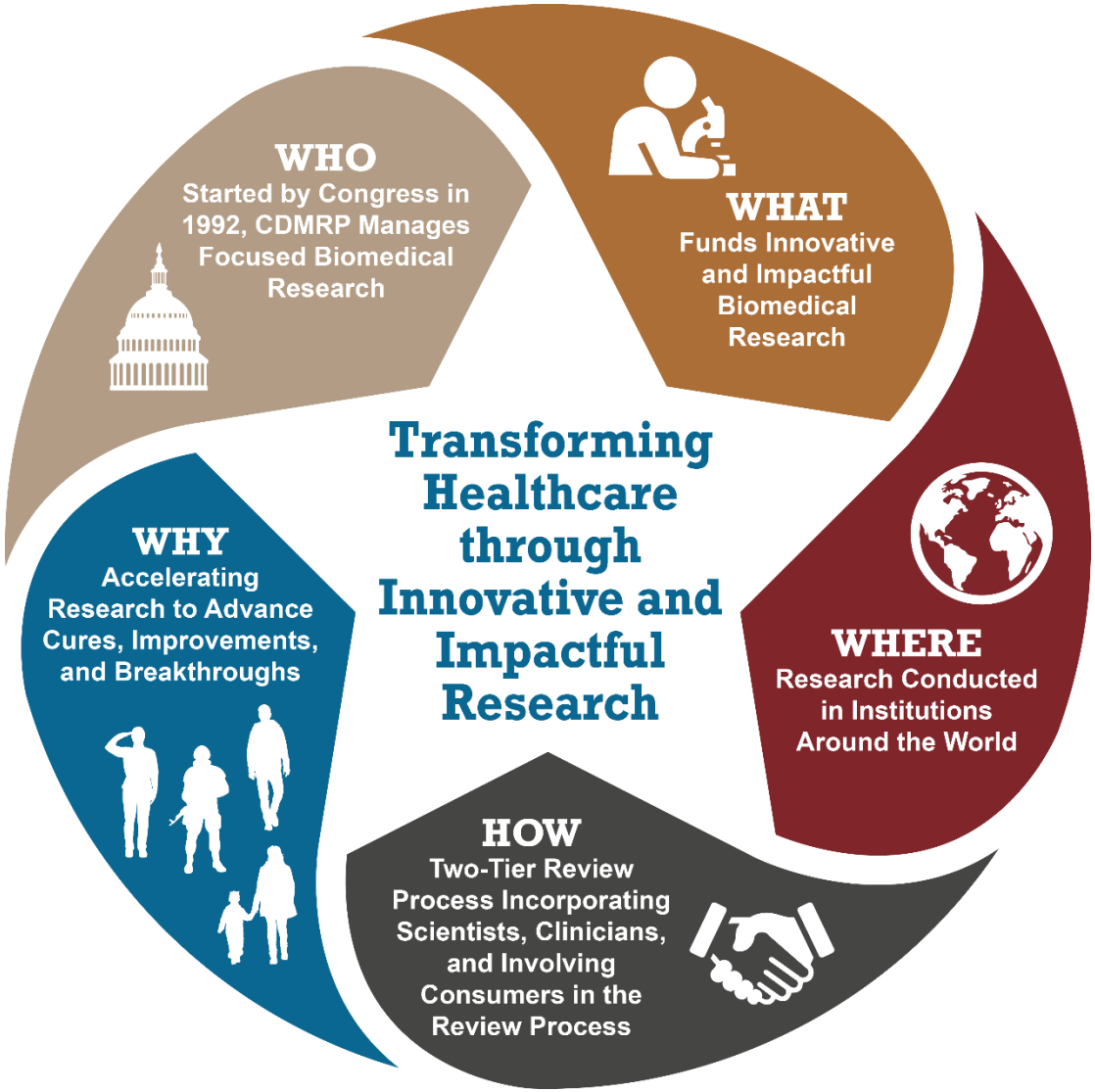
- Medical knowledge products, such as guidelines
- Pharmaceuticals, such as vaccines, drugs, and biologics, and medical devices

Hallmarks



- Congress adds targeted research funds to the DOD budget
- Funds high-impact innovative research
- Avoids duplication with other funding agencies and targets unfunded/unmet gaps
- Follows the National Academy of Medicine-recommended model for application review
- Consumers participate throughout the process and are the “True North” and foundation of the programs
- Annually adapts each program’s vision and investment strategy allowing rapid response to changing needs
- Funding flexibility
  - Funds obligated up-front; limited out-year budget commitments
  - No continuation funding
  - No “pay line” – funding recommendations are based on portfolio composition, adherence to mechanism intent, relative impact, and technical merit
- Transparency and accountability to stakeholders
- Low management costs maximize research dollars

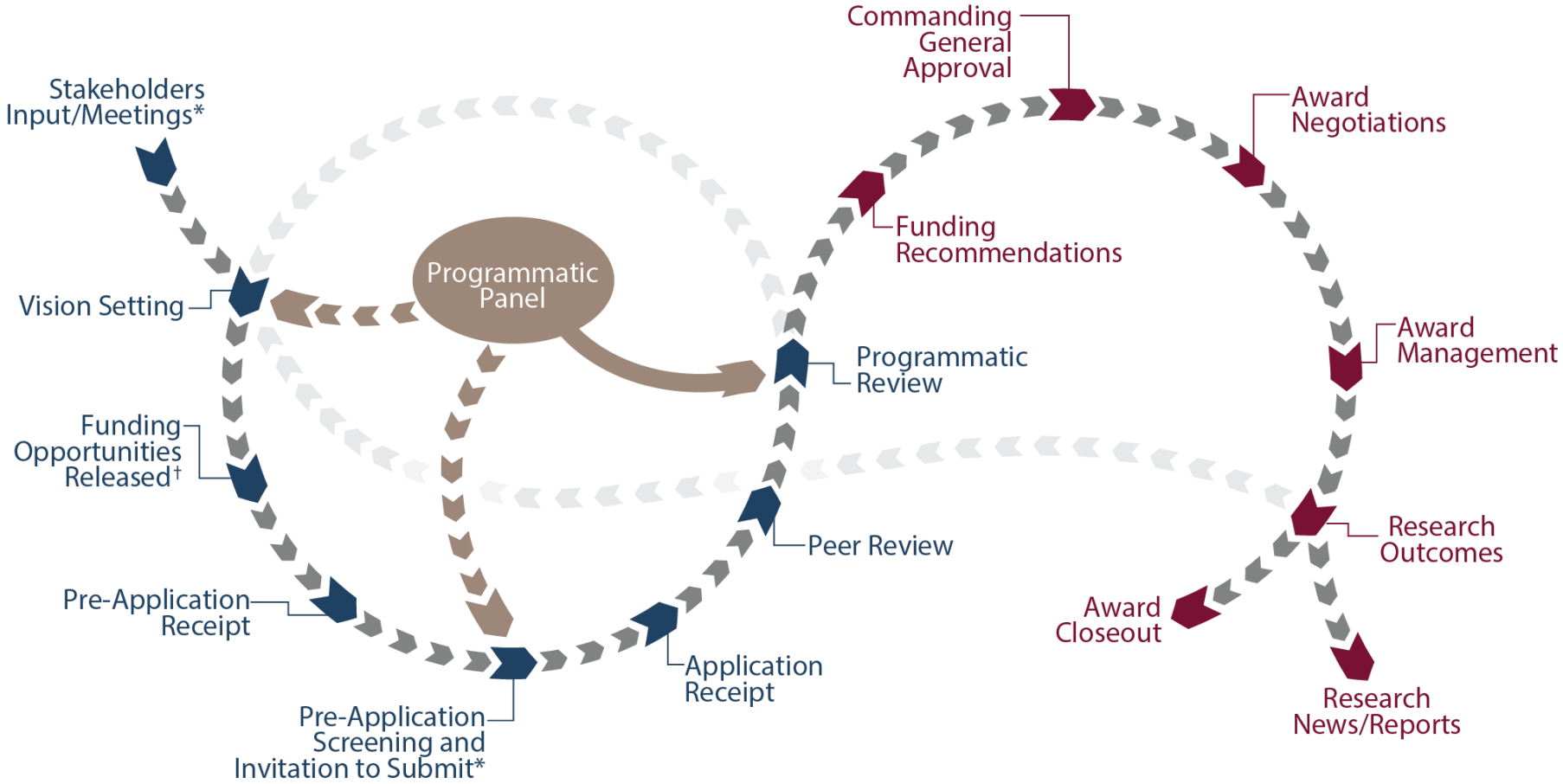
Unique Partnerships



Major Partners and Collaborations

- Strategic input and planning
  - 58 from DHHS (NIH, CDC, FDA, BARDA, etc.) and 29 from VA on programmatic and other panels across CDMRP
  - Coordinated funding
  - With federal and non-federal partners
- Research performers
  - Both extramural and intramural
  - Consumer inclusion
- Research and technology transitions
  - Next phase of research or development – commercial or federal
- Implementation and dissemination

Program Cycle

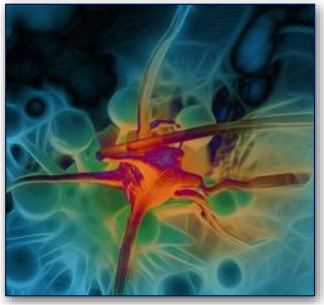


*As needed
†Pending Congressional appropriation

Vision Setting

Each year, the Programmatic Panel recommends an investment strategy, considering factors such as:

- Congressional language
- Input and guidance from senior leaders and stakeholders
- Current research landscape
- Research, capability, and clinical gaps, and unmet needs
- Emerging technologies
- Impact
- Portfolio composition



Award Mechanisms Pipeline

Research Awards

Closing gaps through innovative and impactful research

Initial Concepts	Early Ideas	Clinical/ Translational	Clinical Trials	Team Science
• Concept • Discovery • Exploration-Hypothesis Development	• Idea • Synergistic Idea • Idea Development	• Translational Research • Therapeutic Development	• Clinical Trial • Pilot Clinical Trial	• Consortium • Multi-Team • Synergistic Idea • Translational Partnership

Predoctoral	Postdoctoral	Physician Scientist	New Investigator	Established Investigator

Funding for all career stages

Goal of the Two-Tier Review Process

To develop funding recommendations that balance the most meritorious science across many disciplines and offer the highest promise to fulfill the programmatic goals set forth in the funding opportunity

Peer Review

- Criterion-based evaluation of full proposal
- Determination of "absolute" scientific merit
- **Outcome: Summary Statements**
  - No standing panels; reviewers are recruited based on expertise needed
  - No contact between applicants, reviewers, and program staff

Partnership

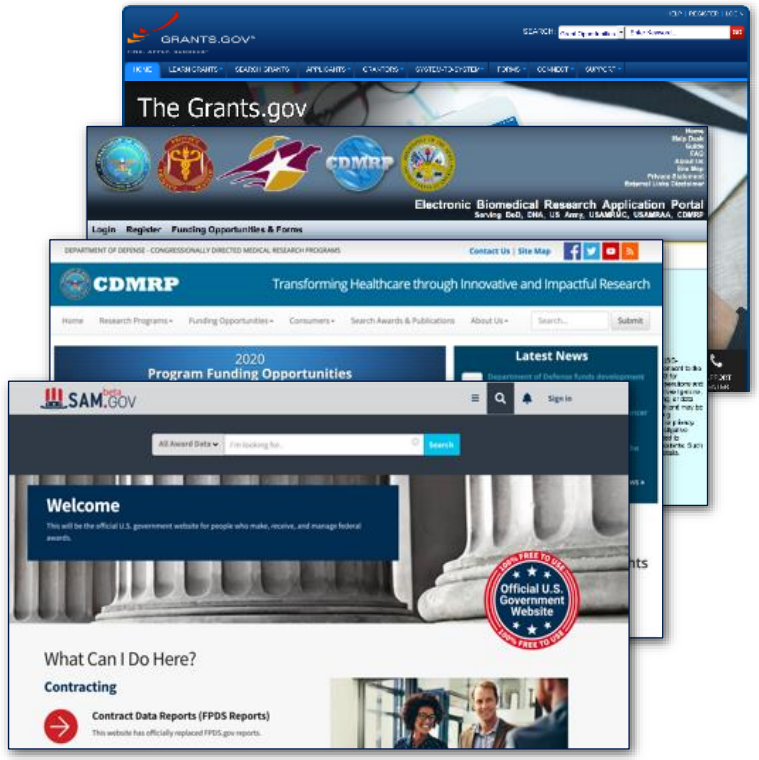
Programmatic Review

- Comparison among proposals of high scientific merit
- Determination of adherence to intent, program relevance, and potential for impact
- **Outcome: Funding Recommendations**
  - No "pay line" (portfolio balance)
  - Funds obligated up-front; limited out-year budget commitments (but milestones imposed)
  - No continuation funding

Video and additional information available at: https://cdmrp.army.mil/about/2tierRevProcess

Funding Opportunities

- Each funding opportunity is made available through a program announcement (PA) or program-specific broad agency announcement (BAA)
  - Awarded primarily as grants and cooperative agreements
- Numerous types of award mechanisms
  - Tailored to the goals of each program
  - Programs, topics, and focus areas may vary from year to year
- Pre-announcement release
  - CDMRP website and email blast
- Funding opportunity postings
  - Grants.gov (CFDA 12.420)
  - electronic Biomedical Research Application Portal (eBRAP) system
  - CDMRP website
  - beta.SAM.gov (BAAs)



USAMRDC Funding Opportunities

- Broad Agency Announcement (BAA)
  - FY18-FY22 BAA, posted 1 October 2017
  - Continuously open through 30 September 2022
  - Announcement lists Topic Areas of current interest

- Postings
  - USAMRAA: http://www.usamraa.army.mil/
  - SAM.gov: https://beta.SAM.gov
    (keyword search: USAMRMC)
  - Grants.gov: http://www.grants.gov
    (F.O. Number W81XWH18SBAA1)

- Process
  - Pre-applications submitted to eBRAP.org
  - Full Applications are invited only;
    submitted through Grants.gov
  - Full Applications undergo external peer review

CDMRP Department of Defense

CDMRP FY21 Appropriations

Research Program	FY21 $M
Alcohol and Substance Abuse Disorders	$4.0
Amyotrophic Lateral Sclerosis	$40.0
Autism	$15.0
Bone Marrow Failure	$7.5
Breast Cancer	$150.0
Chronic Pain Management	$15.0
Combat Readiness Medical	$10.0
Duchenne Muscular Dystrophy	$10.0
Epilepsy	$12.0
Gulf War Illness	$22.0
Hearing Restoration	$10.0
Joint Warfighter Medical	$40.0
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Orthotics and Prosthetics Outcomes	$15.0
Ovarian Cancer	$35.0
Pancreatic Cancer	$15.0
Peer Reviewed Alzheimer's	$15.0
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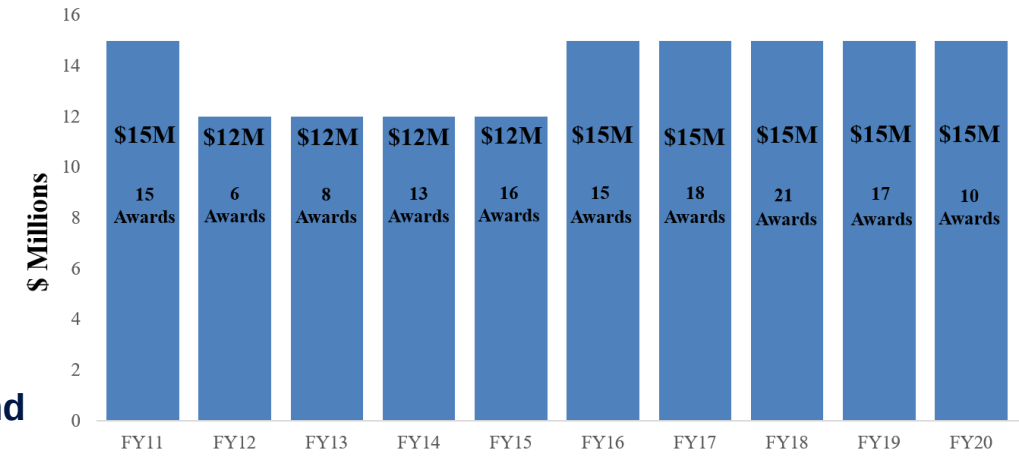
Peer Reviewed Orthopaedic	$30.0
Prostate Cancer	$110.0
Rare Cancers	$17.5
Reconstructive Transplant	$12.0
Scleroderma	$5.0
Spinal Cord Injury	$40.0
Tick-Borne Disease	$7.0
Traumatic Brain Injury and Psychological Health Research	$175.0
Tuberous Sclerosis Complex	$8.0
Vision	$20.0
TOTAL =	**$1.5B**

Peer Reviewed Alzheimer's Research Program (PRARP)

Vision and Mission

- The PRARP was initiated in FY11. Since inception, the PRARP has funded $138M supporting 138 awards from FY11-FY20
- The PRARP is guided by Congressional language which provides a framework for the research it supports.
- Mission: Support research to (1) understand the association between TBI and other military service-related risk factors and Alzheimer's disease/Alzheimer's disease-related dementias, and (2) improve quality of life and reduce the burden on affected individuals and caregivers for the military, Veterans, and the public.



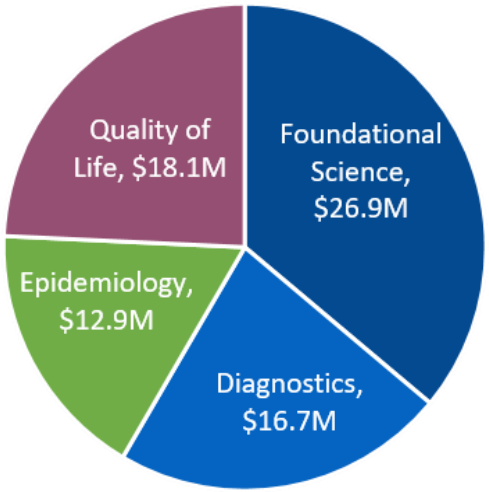
Vision: To address and mitigate long-term implications of traumatic brain injury and military service as they pertain to Alzheimer's disease and Alzheimer's disease-related dementias

PRARP Portfolio at a glance

FY21 Overarching Challenges

Foundational Studies | Diagnostics and Prognostics | Epidemiology | Paucity of Clinical Studies | Quality of Life | Family and Care Support

PRARP Portfolio Areas



Investment($M) by portfolio area, PRARP active portfolio (FY15-20)

Foundational Science
- Pathophysiology
- Mechanism
- Non-pharmacological treatments

Diagnostics/ Prognostics
- Biomarkers
- Diagnostics development

Quality of Life
- Includes family care and support and cognitive function interventions

Epidemiology
- Population studies
- Imaging and postmortem incidence studies

Tips and Tricks: Applying to the PRARP

FY22 Mechanisms – *Anticipated**

Award Mechanism	Eligibility	Key Mechanism Elements	Funding
NEW: Investigator-Initiated Research Award	The Principal Investigator (PI) must be an independent investigator as named by their institution. Early-Career-Investigator Partnering PI Option: Must be a junior investigator within 10 years of a terminal degree or new to the field.	• Supports research with high innovation/impact in one of the PRARP Focus Areas. • Early-Career Investigator Partnering PI Option available. • Clinical trials will not be supported, but studies with prospective human subjects' enrollment may be allowed. • Submission of a Letter of Intent is required prior to full application submission.	• Maximum funding of $750,000 for total costs. • Maximum period of performance is 3 years.
NEW: Translational Research Award	The PI must be an independent investigator as named by their institution.	• Supports the translation of promising research into clinical application (i.e., preclinical to clinical translation) and clinical care (i.e., implementation science). • Submission of a Letter of Intent is required prior to full application submission. • Community Collaboration element is required	• Maximum funding of $1.2 million (M) for total costs. • Maximum period of performance is 3 years.
Accelerating Diagnostics Research Award	The PI must be an independent investigator at or above the level of Assistant Professor (or equivalent).	• Supports validation and implementation of innovative diagnostic modalities to better determine the trajectory, long-term outcomes, and impact of AD/ADRD following military service and/or TBI. • Submission of a Letter of Intent is required prior to full application submission. • Community Collaboration element is required	• Maximum funding of $2.5M for total costs. • Maximum period of performance is 4 years.

Anticipated FY22 Focus Areas

The process: applying to the PRARP

Read the FOAs

Determine which mechanism is most appropriate for your project and research team

Review the Award Information, containing the intent of the mechanism and focus area(s) to determine if your project is in alignment

Carefully read the attachments. Ensure you write to the appropriate audience described in each attachment.

Check the eligibility and funding restrictions

Peer review criteria are provided for each mechanism.

The process: applying to the PRARP

Read the FOAs – PI Eligibility

All investigators should be considered independent by their institution

IIRA and TRA mechanisms have no restriction of the seniority of investigator who can be PI

Early Career/New to the Field Investigators: Within 10 years of a terminal degree or no/nominal publications or support in the field

The process: applying to the PRARP

Read the FOAs – Community Collaboration

New for FY22!

Community Collaboration elements are <u>required</u> in TRA and ADRA and *strongly preferred* in IIRA applications

The type, method, and execution of the community collaboration is for each investigator to decide for each project – there is no one size fits all approach

The process: applying to the PRARP

Submit your LOI

LOIs are submitted via CDMRP's eBRAP.org site

The LOI is used to ensure the appropriate expertise for peer review is recruited.

The LOI itself will not be peer or programmatically reviewed.

An LOI is required to be submitted by the deadline in order to be eligible to submit a full application.

Note - You will not receive an invitation or notification to submit a full proposal following the LOI.

The process: applying to the PRARP

Prepare and submit your full application

Ensure all required documents and elements are present.

Pay attention to withdrawal criteria listed in the FOA.

Remain compliant to page and budget limits. Applications will be withdrawn if they are not compliant.

Plan to submit early!

The full application should be submitted to grants.gov

The process: applying to the PRARP

Applications undergo two-tiered review

Individuals with lived experience are crucial members of both peer and programmatic review panels

Applications first undergo peer review - criteria are listed in each FOA to judge the merit of each application independently

Applications are then reviewed at the programmatic level for relevance and fit to the PRARP mission, vision, and portfolio

Following this process, all applicants are notified once the recommendations have been made for funding

The process: applying to the PRARP

Read the FOAs

- Determine which mechanism is most appropriate for your project and research team

Submit your LOI

- LOIs are used to ensure the most appropriate peer reviewers are recruited to assess your research
- LOIs will not be reviewed!

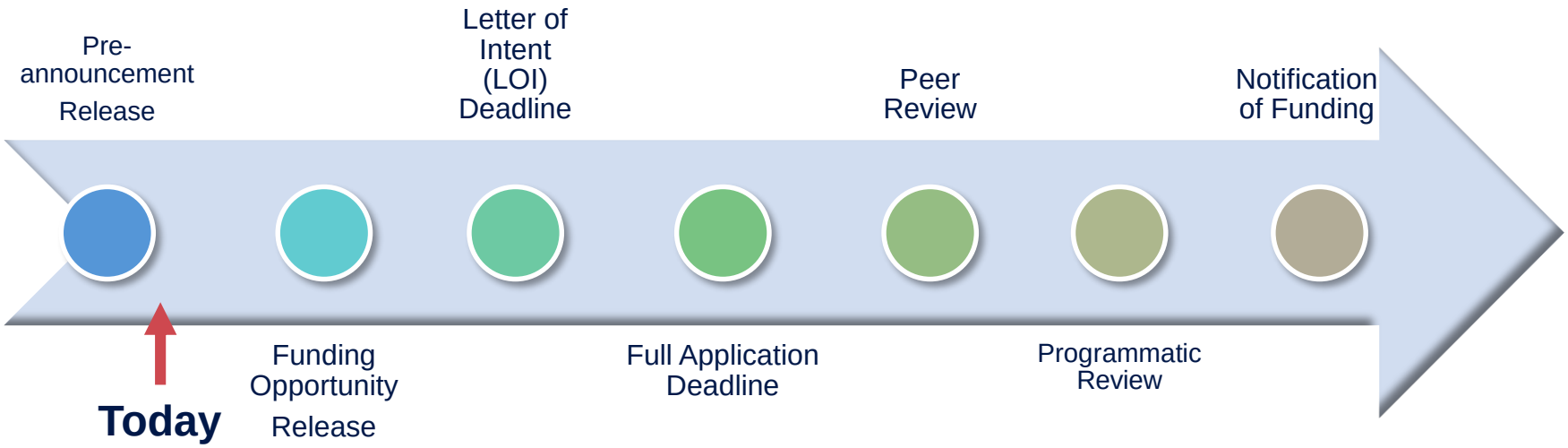
Prepare and submit your full application

- Cross reference the FOA to ensure all required elements are present and limits are maintained

Applications undergo two-tiered review

- → Notification of funding status

Timeline for applying to the PRARP



FAQs

- **What if I'm not in the US?**
  - CDMRP funds research across the globe and often makes awards to non-US institutions/investigators!
- **Can a company, non-academic institution or for profit organization apply?**
  - Yes! Commercial entities as primary applicants or partners are welcome to apply.
- **I applied last year but did not get an award. Can I resubmit?**
  - Yes - the PRARP does not have a specific mechanism for resubmissions as we up-front fund all our projects. All submission each year are considered new proposals.
- **Am I an eligible PI?**
  - IIRA and TRA – all independent investigators welcome
  - ADRA – Assistant Professor (or equivalent) and above
  - Early Career – within 10 years of terminal degree OR nominal publications/funding in the field
- **Do I need to use military population or partner?**
  - This is encouraged, but not required in order to apply to the PRARP
  - However, all applications must demonstrate relevance to military health
- **Can I submit more than one proposal per mechanism?**
  - You may submit more than one proposal per mechanism, provided they are distinct ideas and projects.

Questions?

Visit www.cdmrp.army.mil

- All FOAs are publically available on the CDMRP website
- Previous awardee abstracts and publications are also available
- Register to be the first to know of pre-announcement and funding opportunities

Neuroscience-related Research Programs and Topics

Research Program	FY21 $M
Alcohol and Substance Abuse Disorders	$4.0
Amyotrophic Lateral Sclerosis	$40.0
Autism	$15.0
Bone Marrow Failure	$7.5
Breast Cancer	$150.0
Chronic Pain Management	$15.0
Combat Readiness Medical	$10.0
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Tuberous Sclerosis Complex	$8.0
Vision	$20.0

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Overview of the CDMRP Neuroscience Programs

Presented by Dr. Sarah Fontaine

HIGH-IMPACT RESEARCH

Neuroscience Research Programs: Facts and Figures

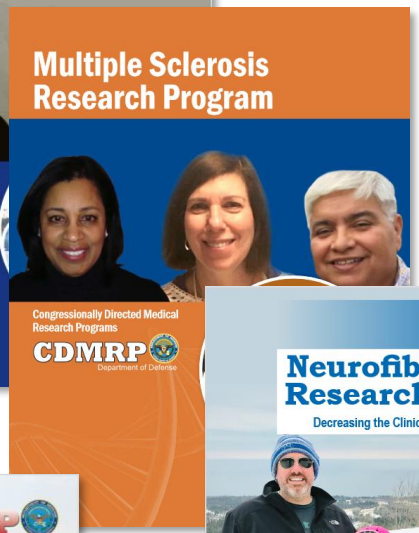
CDMRP Department of Defense

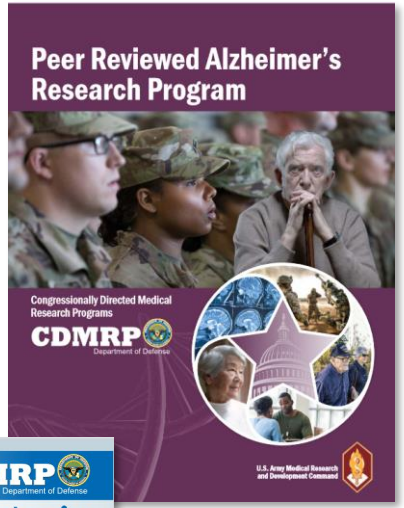
Research Program	Fiscal Year (FY) Established	Total Appropriations (through FY20)	Total Awards (through FY20)	FY21 Appropriation*
Alcohol and Substance Abuse Disorders	FY10	$28M (Millions)	2 (consortia)	$4M
Amyotrophic Lateral Sclerosis	FY07	$149.4M	108	$40M
Autism	FY07	$104.4M	180	$15M
Duchenne Muscular Dystrophy	FY11	$39.6M	51	$10M
Epilepsy	FY15	$49.5M	48	$12M
Gulf War Illness	FY06	$241M	224	$22M
Multiple Sclerosis	FY09	$64.6M	131	$20M
Neurofibromatosis	FY96	$362.9<	451	$20M
Neurotoxin Exposure Parkinson's	FY97	$484.8M	271	$16M
Peer Reviewed Alzheimer's	FY11	$138M	138	$15M

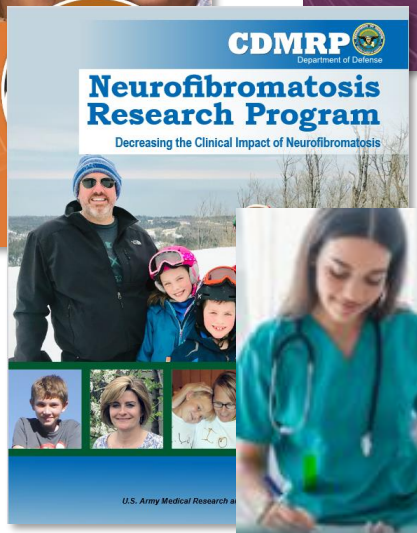
*Applications recommended for funding during programmatic review per program and finalized during negotiations to be completed by 30 September 2022.

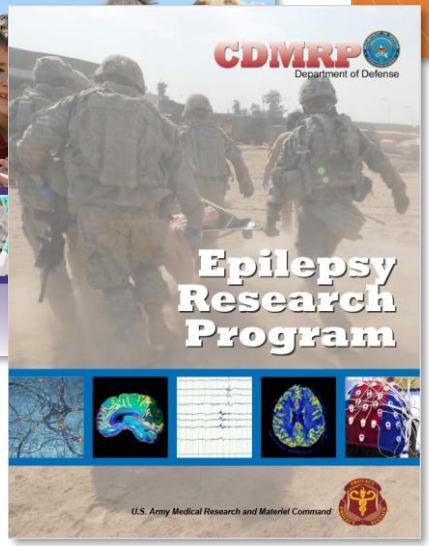
CDMRP Department of Defense

Neuroscience Programs at CDMRP









Alcohol and Substance Abuse Disorder Research Program (ASADRP)

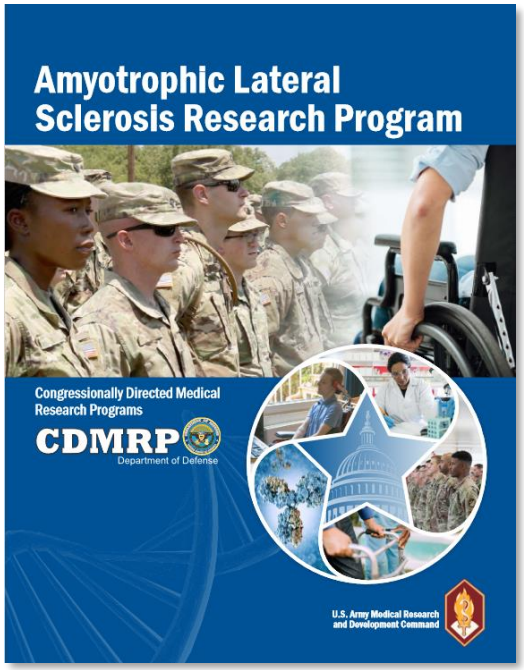
Vision: Improve the clinical outcomes of alcohol, opioid, and other substance use disorders

Mission: To explore integrated approaches to address alcohol and substance use disorders, and reduce the number of opioid and other substance use related deaths, through multidisciplinary, team based research efforts that translate basic knowledge into enhanced clinical pharmacological treatment protocols and enhanced quality of life for Service Members, Veterans, and the American public

FY21 Focus Areas

- Improved formulations to treat opioid use disorder with comorbid substance use
- Improved formulations to treat opioid use disorder with comorbid PTSD and other psychological disorders
- New formulations and/or combination of existing medication to improve treatment compliance, prevent relapse, and reduce risk of misuse
- Stronger, longer-duration formulations to counteract opioid (including fentanyl analogs) overdose
- Novel medications and immunotherapies to treat ASUD
- New medication targets for the treatment of ASUD

Amyotrophic Lateral Sclerosis Research Program (ALSRP)



Vision: Improve treatment and find a cure for ALS

Mission: Fund innovative and impactful research to develop new treatments for ALS.

Program Priorities

Preclinical Treatment Discovery → Preclinical Treatment Validation → Clinical Development

THREE NEW TREATMENTS NOW IN CLINICAL TRIALS

Humanized Anti-CD40LG IgG Antibody: Blocks damaging inflammation in motor neurons
https://clinicaltrials.gov/ct2/show/NCT04322149

GDNF-Expressing Neural Progenitor Cells: Transplanted cells secrete GDNF which protects and stimulates neurons
https://www.clinicaltrials.gov/ct2/show/NCT01348451

Pimozide: Strengthens electrical connections between nerves and muscles
https://clinicaltrials.gov/ct2/show/NCT03272503

FOUR NEW TREATMENTS IN PRECLINICAL ADVANCED DEVELOPMENT

Riluzole + Elacridar combination enhances the effectiveness of Riluzole treatments

CuATSM helps prevent misfolding in mutant Superoxide Dismutase enzymes in ALS

MicroRNA Mir-155 Antagonists reduce Mir-155 production reducing inflammation

Apilimod clearing toxic protein aggregates in ALS

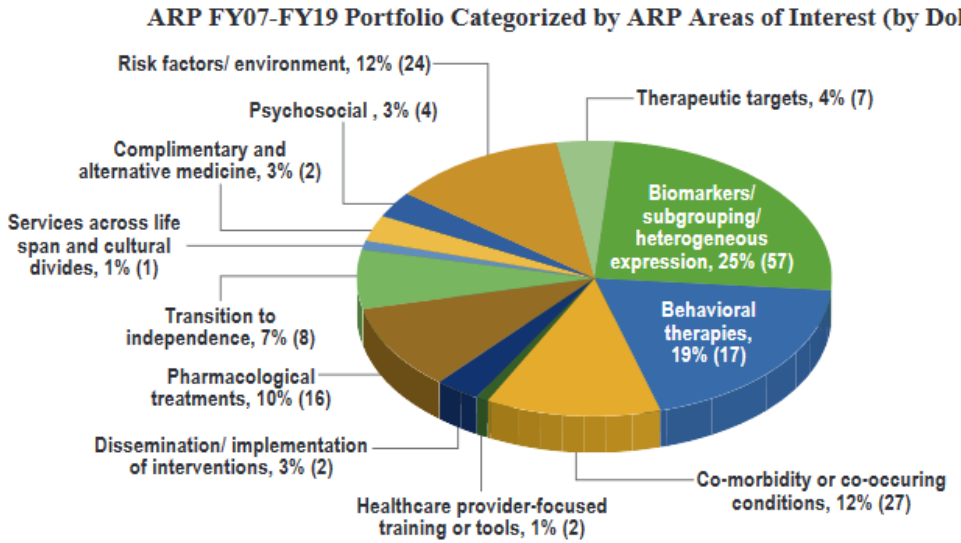
ALSRP HAS FUNDED THROUGH FY20 → **59** DRUG DISCOVERY AWARDS; **25** DRUG DEVELOPMENT AWARDS

Autism Research Program (ARP)

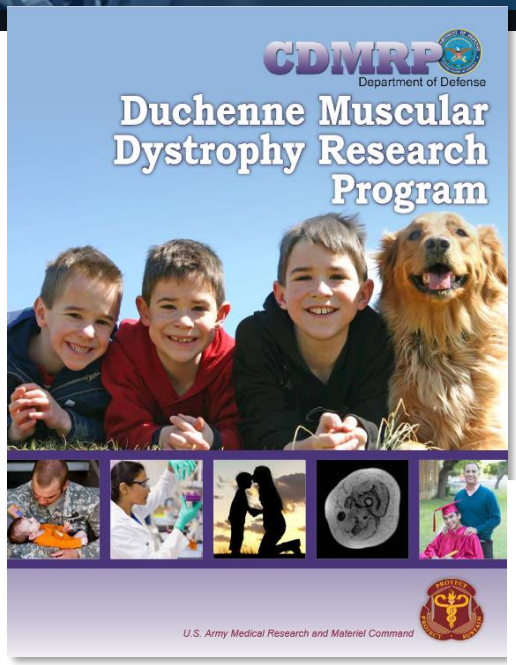
Program Priorities

Vision Improve the lives of individuals with ASD now

Mission: Promote innovative research that advances the understanding of ASD and leads to improved outcomes for Service members, their families, and the American public.



Duchenne Muscular Dystrophy Research Program (DMDRP)

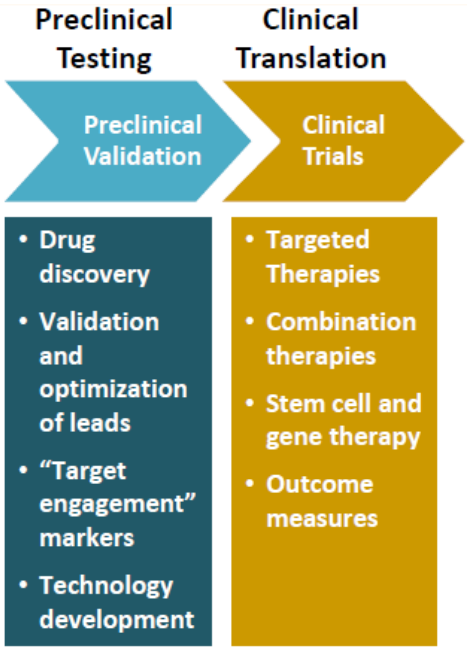


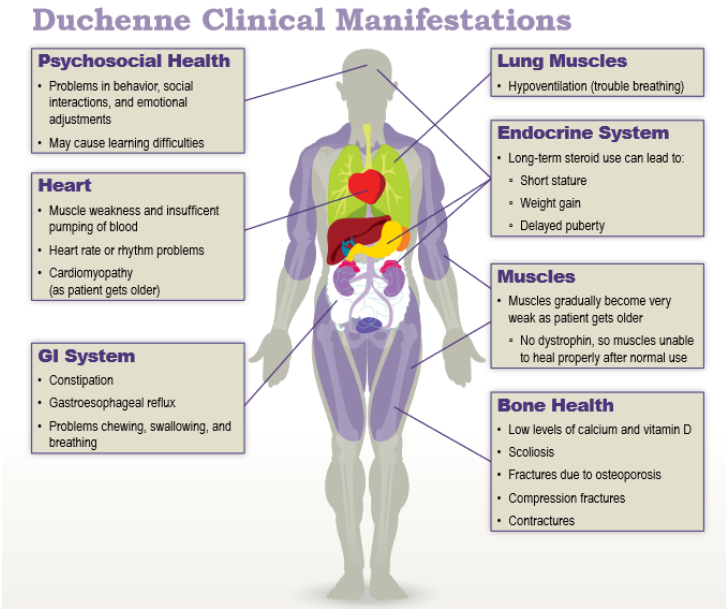
Program Priorities

- Support discovery and development of therapeutics, related devices, and tools
- Accelerate promising therapeutic ideas into clinical applications
- Advance basic research on the effect of Duchenne on the heart, bone, central nervous system, and gastrointestinal system
- Support research development

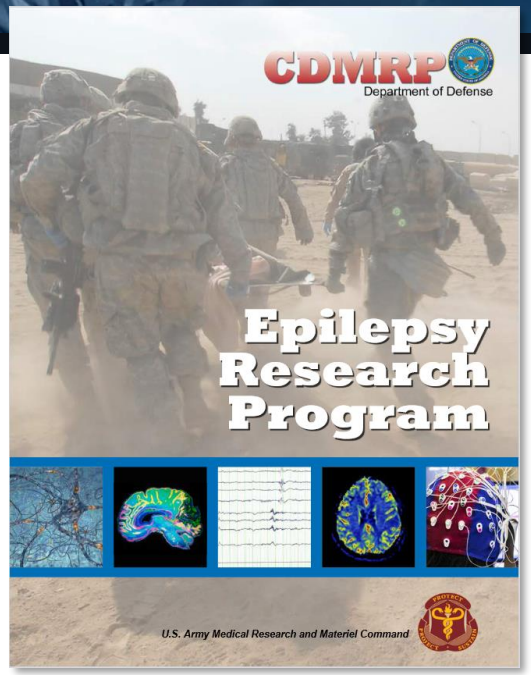
Vision: To preserve and improve the quality of life, and to extend the life span of all individuals with Duchenne

Mission: To better support the discovery and development of therapeutics, devices, and other inventions, and to promote their effective clinical testing.





Epilepsy Research Program (ERP)

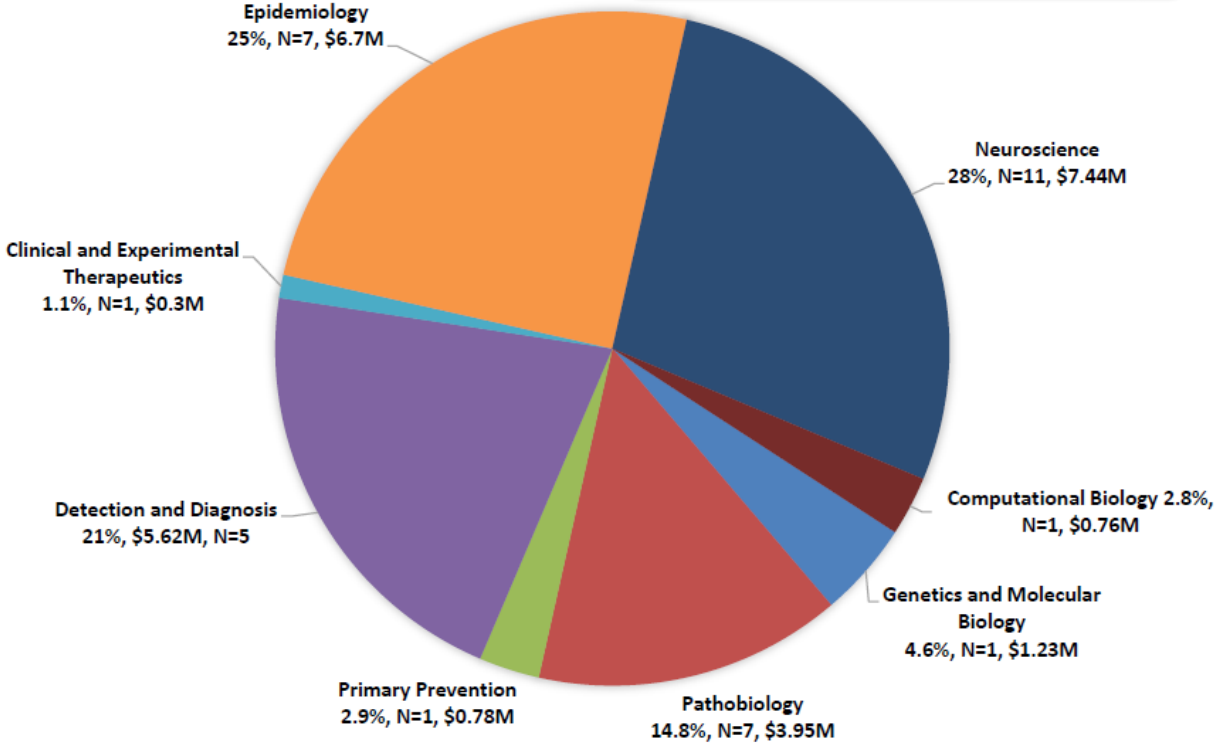


Vision: A time when post traumatic epilepsy can be prevented or managed.

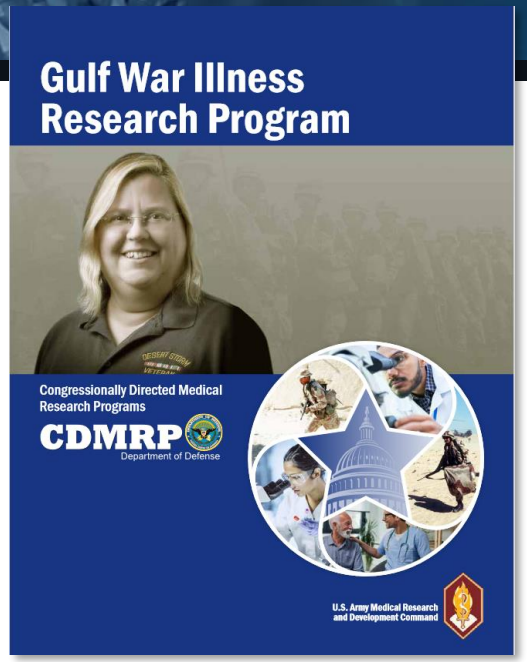
Mission: To understand the mechanisms of PTE and associated comorbidities to improve quality of life, especially in Service members, Veterans, and caregivers.

Program Priorities

- Innovative Research
- Longitudinal Studies
- Markers and Mechanisms
- Epidemiology
- Quality of Life



Gulf War Illness Research Program (GWIRP)



Vision Improved 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 the pathobiology and symptoms of disease.

BBRAIN

Boston Biorepository, Recruitment and Integrated Network for GWI

Resource Site 1
Boston University School of Public Health*

Resource Site 4
San Francisco VA

NETWORK COORDINATING CENTER

Resource Site 2
Miami VA/NOVA Southeastern University*

Resource Site 3
Bronx VA

*Resource Site and Biorepository Storage Site

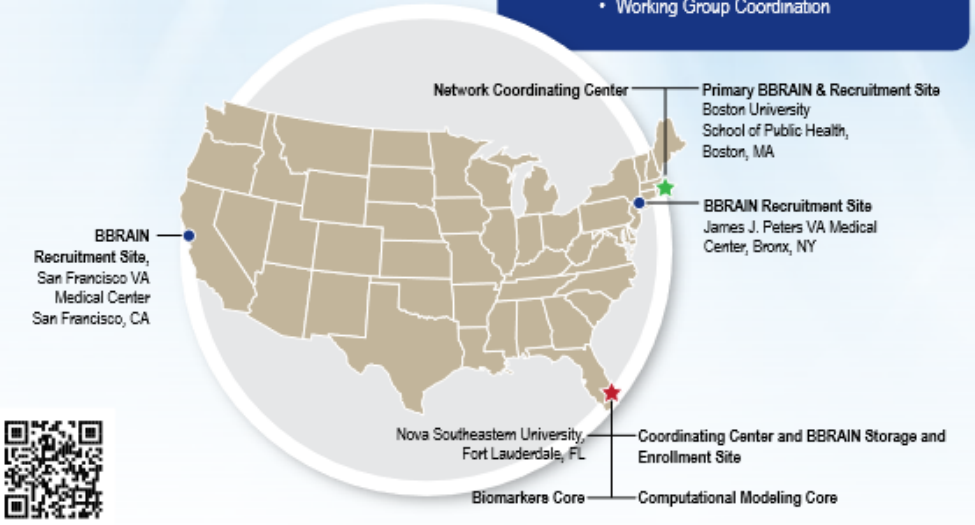
BBRAIN ORGANIZATIONAL STRUCTURE

Steering Committee
BBRAIN PI, RS, PIs, GWI Advocates

Retrospective Resource Sites

Network Coordinating Center

Network Coordinating Center Tasks
- Institutional Review Board Protocol/ Regulatory Coordination
- Biospecimen Collection, Tracking and Dissemination
- Data Management/Monitoring
- Statistical Management
- Resource Site Performance Evaluation
- Working Group Coordination



*For more details, see http://sites.bu.edu/bbrain/.

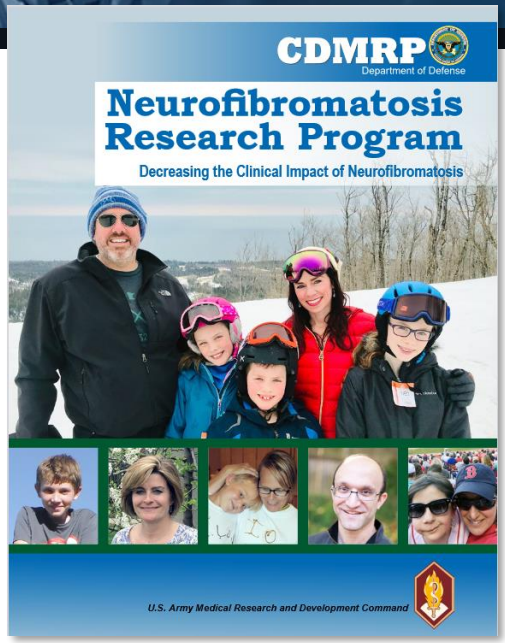
Multiple Sclerosis Research Program (MSRP)

Strategic Goals	Focus Areas	Investment
Understand, measure, and treat relapsing and progressive aspects of MS	Correlates of disease activity and progression in MS	$10.7M 15 Awards
Identify strategies for neuroprotection, repair and restoration of function, and ultimately improving symptoms and quality of life	Central nervous system regenerative potential in demyelinating conditions	$6.8M 11 awards
Elucidate the cause and pathophysiology of MS symptoms that have a high impact on quality of life and develop treatment strategies	Biology and measurements of MS symptom	$8.2M 19 awards
Identify the factors that contribute to MS etiology and disease course	Factors contributing to MS etiology, prodrome, onset and evolution (*New in FY20*)	N/A

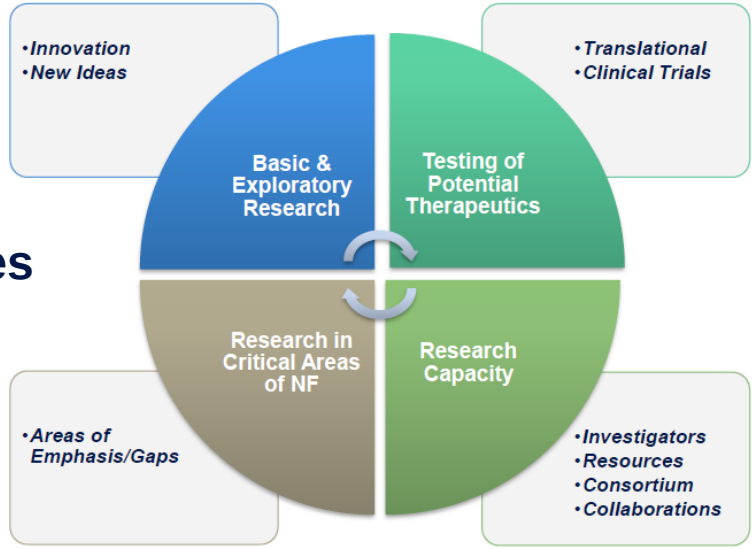
Vision: To prevent, cure, reverse, or slow the progression, and lessen the personal and societal impact of multiple sclerosis

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

Neurofibromatosis Research Program (NFRP)

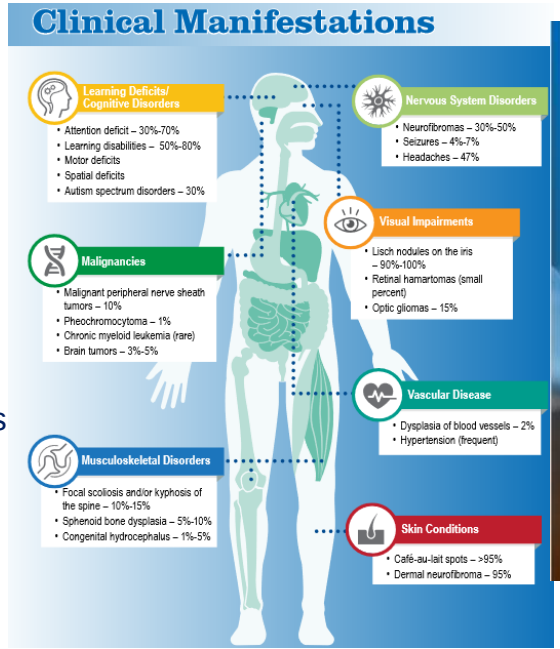


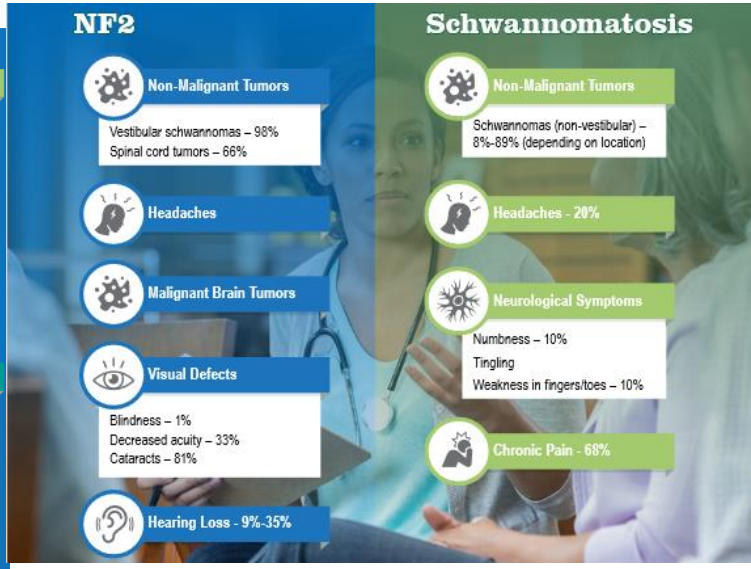
Program Priorities



Vision: Decrease the clinical impact of neurofibromatosis

Mission: Promote research directed toward the understanding, diagnosis, and treatment of NF1, NF2, and schwannomatosis to enhance the quality of life for persons with these disorders





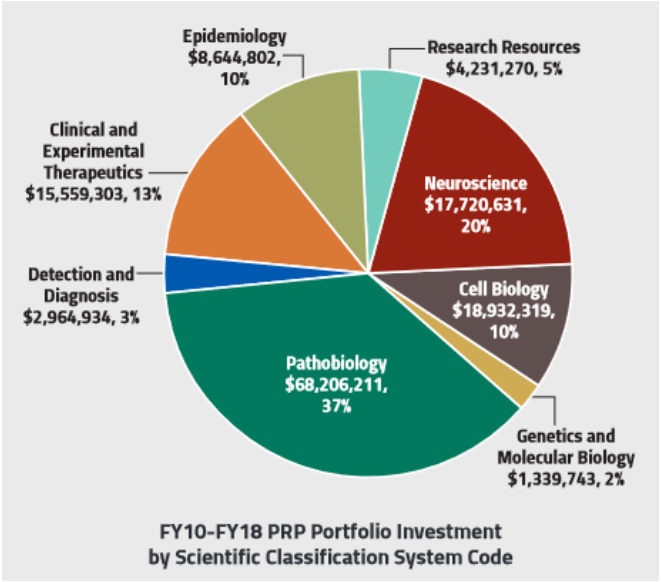
Neurotoxin Exposure Parkinson's Research Program (NTEPRP)

Program Priorities

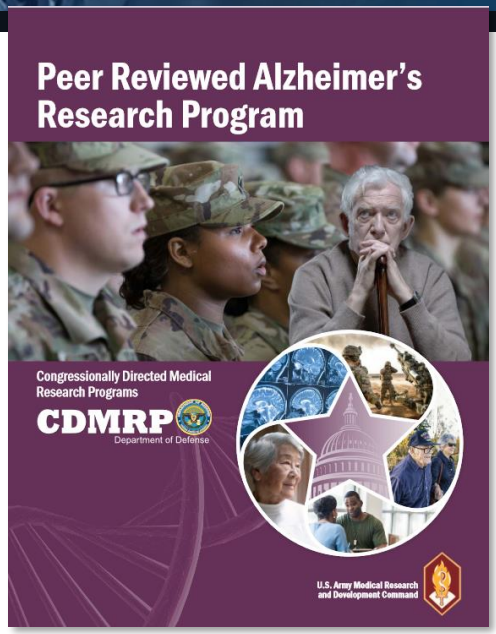
- Determine the biologic mechanisms of neurodegeneration in PD.
- Delineate how deployment, environmental, and occupational exposures in combination with gene - environment interactions impact the development and progression of PD.
- Understand the mechanisms of the cognitive, psychiatric, and other non-motor symptoms of PD.
- Determine how circuitry and synaptic mechanisms of PD, dopamine refractory motor symptoms, and treatment-associated dystonia influence PD progression.
- Identify the biological mechanisms of impact from exercise and other lifestyle modifications on neurodegeneration in PD.

Vision: to increase the understanding of Parkinson's disease (PD) and to develop treatments towards a cure

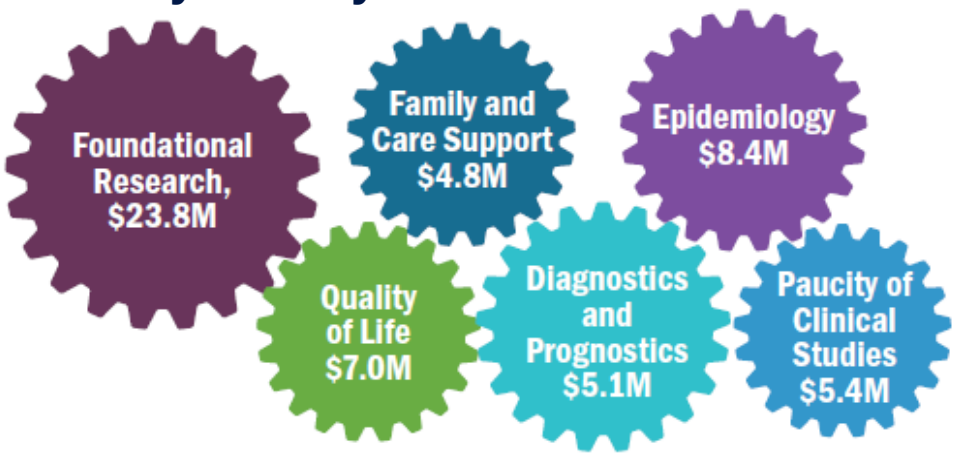
Mission: To support research investigating the underlying biologic mechanisms and therapeutic interventions of neurodegenerative effects caused by deployment, environmental, and occupational exposures.



Peer Reviewed Alzheimer's Research Program (PRARP)



Portfolio by Priority Area

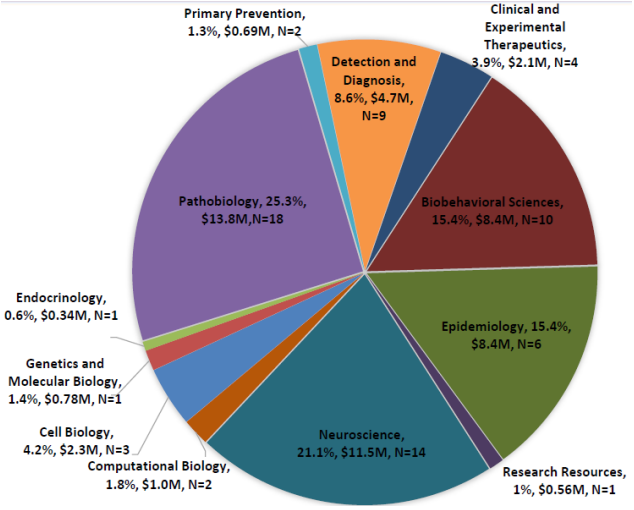


Vision: To address the long-term consequences of traumatic brain injury as WKH\ SHUWDLQV WR $O]KHLPHU¶V disease (AD) and related dementias (ADRD)

Mission: Devoted to (1) understanding the association between traumatic brain injury and AD/ADRD, and (2) reducing the burden on affected individuals and caregivers, especially in the military and Veteran communities

AD/ADRD in the Military

	Patients	Out-Patient Encounters	Hospital Bed Days
Active Service Members	244	679	961
Other DOD Beneficiaries	302,948	3M	3.29M



HIGH-IMPACT RESEARCH

Neuroscience-related Injury and Rehabilitation Research Programs and Topics

CDMRP Department of Defense

Research Program	FY21 $M
Alcohol and Substance Abuse Disorders	$4.0
Amyotrophic Lateral Sclerosis	$40.0
Autism	$15.0
Bone Marrow Failure	$7.5
Breast Cancer	$150.0
Chronic Pain Management	$15.0
Combat Readiness Medical	$10.0
Duchenne Muscular Dystrophy	$10.0
Epilepsy	$12.0
Gulf War Illness	$22.0
Hearing Restoration	$10.0
Joint Warfighter Medical	$40.0
Kidney Cancer	$50.0
Lung Cancer	$20.0
Lupus	$10.0
Melanoma	$30.0
Military Burn	$10.0
Multiple Sclerosis	$20.0

Research Program	FY21 $M
Neurofibromatosis	$20.0
Neurotoxin Exposure Treatment Parkinson's	$16.0
Orthotics and Prosthetics Outcomes	$15.0
Ovarian Cancer	$35.0
Pancreatic Cancer	$15.0
Peer Reviewed Alzheimer's	$15.0
Peer Reviewed Cancer (20 Topics)	$115.0
Peer Reviewed Medical (42 Topics)	$370.0
Peer Reviewed Orthopaedic	$30.0
Prostate Cancer	$110.0
Rare Cancers	$17.5
Reconstructive Transplant	$12.0
Scleroderma	$5.0
Spinal Cord Injury	$40.0
Tick-Borne Disease	$7.0
Traumatic Brain Injury and Psychological Health Research	$175.0
Tuberous Sclerosis Complex	$8.0
Vision	$20.0

TOTAL = $1.5B

For more information, please visit:

cdmrp.army.mil