

Department of Defense Congressionally Directed Medical Research Programs

Gulf War Illness Research Program

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CDMRP Department of Defense

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Who is the CDMRP?



DEPARTMENT OF DEFENSE

DEPARTMENT OF THE ARMY

ARMY MEDICINE
Serving To Heal...Honored To Serve

ARMY MEDICAL COMMAND

MEDICAL RESEARCH AND MATERIEL COMMAND

CDMRP
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

U.S. Army Medical Research and Materiel Command

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Partnerships

Advocates

- ❖ Demonstrate need
- ❖ Participate at all levels
- ❖ Passion and perspective





Congress

- ❖ Add funds to budget
- ❖ Targeted guidance



IMPROVE HEALTH (CURE)

Researchers

- ❖ Innovation and gaps
- ❖ Risk/Benefit
- ❖ Identify research likely to create paradigm shifts





DOD

- ❖ Program management
- ❖ Regulatory and budget requirements
- ❖ Institute of Medicine model



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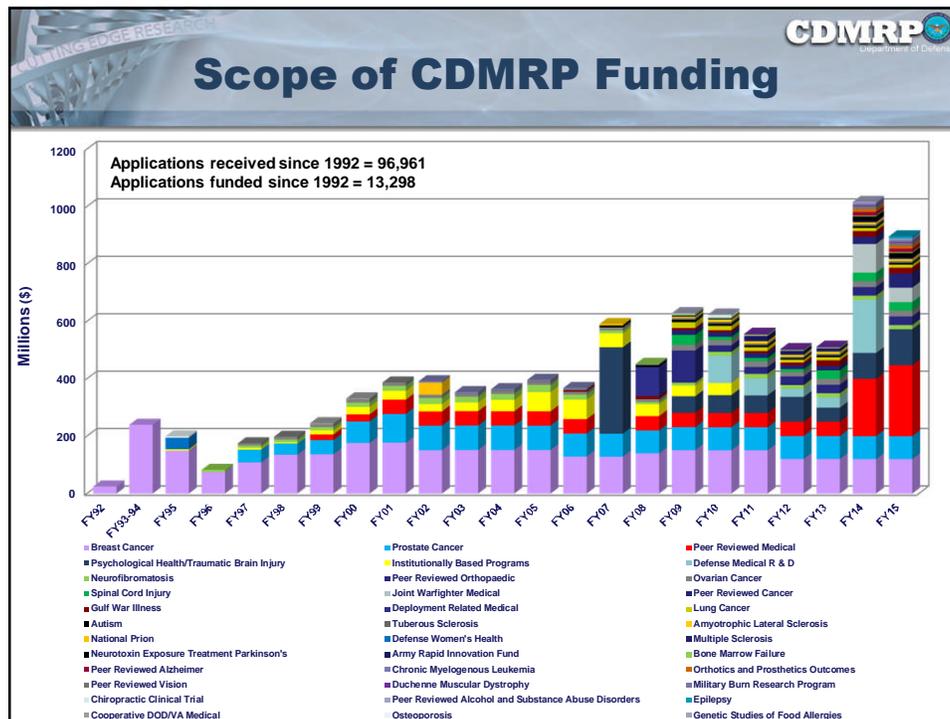
History of the CDMRP

- ◆ **In the early 1990s, grassroots advocacy efforts heightened political awareness of breast cancer**
- ◆ **Congress appropriated \$210M to the FY93 DoD budget for a new Breast Cancer Research Program (BCRP)**
- ◆ **USAMRMC was directed to manage the BCRP**
- ◆ **The Army sought the advice of the National Academy of Sciences Institute of Medicine (IOM), which resulted in:**
 - ❖ **A two-tier review process**
 - ❖ **A new model for research – incorporating patient advocates into program policy, investment strategy, and research focus**
- ◆ **From 1996–2014, additional research programs were added by Congress and USAMRMC for administrative management by CDMRP**



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FY08 National Defense Authorization Act

HR 1585 Conferees directed the Secretary of the Army to utilize the authorized funding... to undertake research on Gulf War Illnesses. Conferees also directed that activities under the Gulf War Illnesses program include:

- ◆ Studies of treatments for the complex of symptoms known as “Gulf War Illness”
- ◆ No studies based on psychiatric illness and psychological stress as the central cause
- ◆ Competitive selection and peer review to identify research with the highest technical merit and military value

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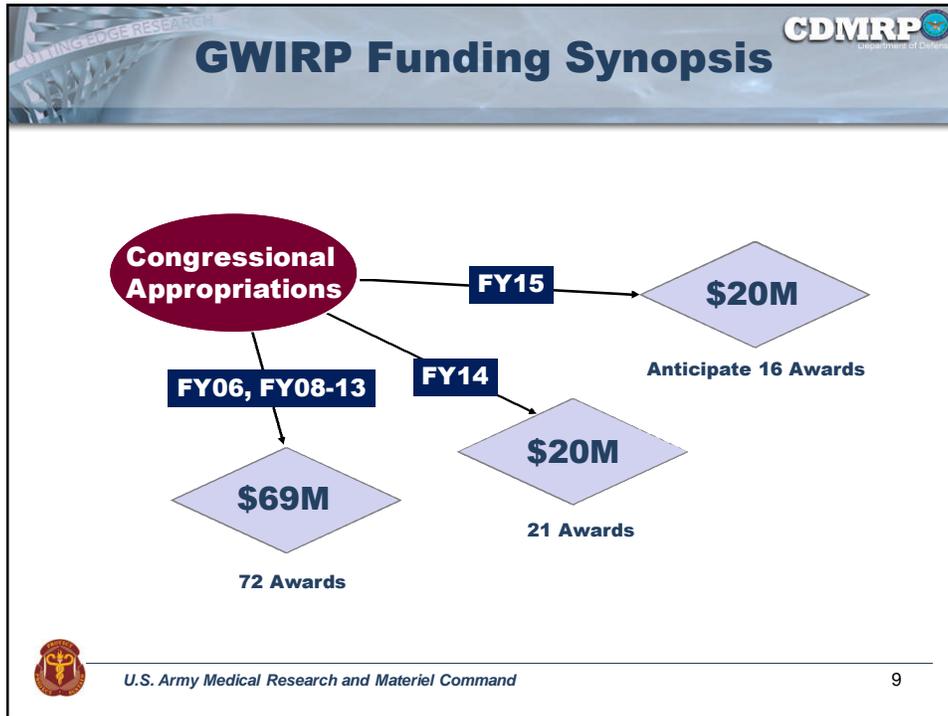
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Gulf War Illness Research Program

U.S. Army Medical Research and Materiel Command

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

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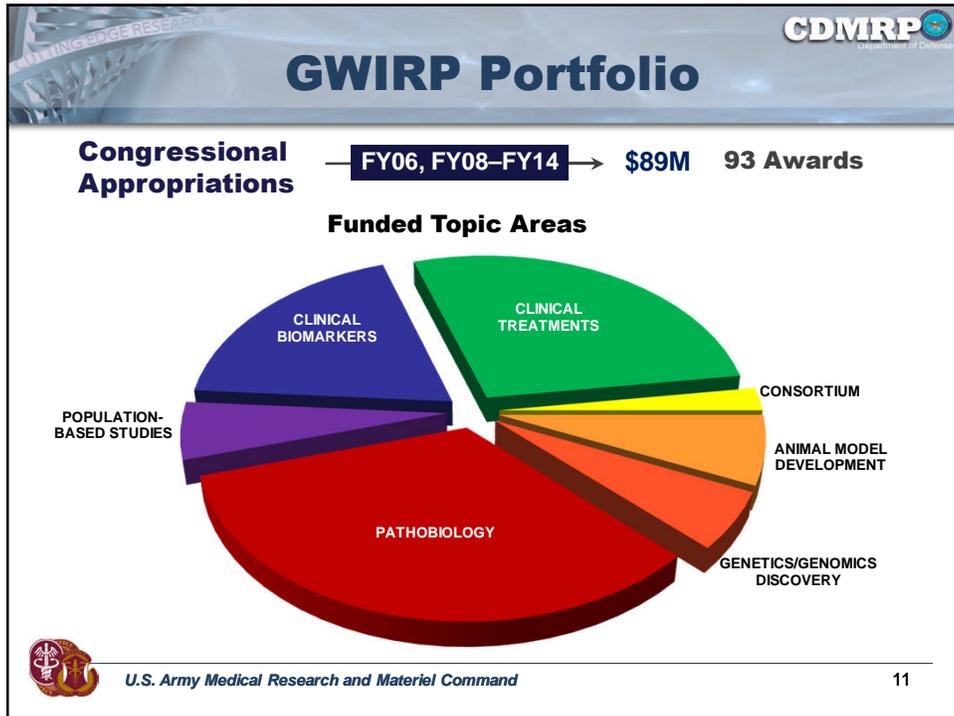
Award Mechanism Summary

	FY06	FY08	FY09	FY10	FY11	FY12	FY13	FY14
GWIRP Appropriation	\$5M	\$10M	\$8M	\$8M	\$8M	\$10M	\$20M	\$20M
Number of funded awards								
Award Mechanism								
Early Idea	Exploratory Hypothesis Development Award	2						
	Idea Award		2					
More Mature Idea	New Investigator Award							4
	Investigator-Initiated Research Award	6	8	7	8	6	4	10
	Investigator-Initiated Research Expansion Award							6
Translational/Clinical	Innovative Treatment Evaluation Award			2	2	1	0	5
	Clinical Trial Award		2	0	0	1	0	1
	Consortium Development Award				3			
	Consortium Awards					2		
	Total Awards (Pre-applications)	8 (81)	12 (113)	9 (43)	13 (82)	8 (57)	6 (83)	16 (87)

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FY12 GWIRP Consortia

Understanding Gulf War Illness: An Integrative Modeling Approach
 Dr. Mariana Morris, Nova Southeastern University

- ◆ Characterization of multi-system dysfunction in mouse models of GWI using validation and direction from computational biology
- ◆ Integration of human and animal studies using computational modeling to identify mediators and test putative therapeutics
- ◆ Goal is to develop a translational model for rapid identification of targets and prediction of effective therapeutic interventions

Brain-Immune Interactions as the Basis of Gulf War Illness
 Dr. Kimberly Sullivan, Boston University

- ◆ Brings together researchers from 5 sites
- ◆ Series of clinical and preclinical studies to test for chronic brain-immune activation and chronic inflammation
- ◆ Goal is to identify brain-immune pathways that can be targeted for intervention



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 **GWIRP Research Outcomes**

- ◆ **Low-dose sarin exposure produces long-term changes in brain neurochemistry of mice**
 - ❖ FY06 IIRA Dr. Mariana Morris, Wright State University
 - ❖ Published in 2013 *Neurochemical Research* 38(1):108-116
- ◆ **Exposure to an organophosphate-based pesticide, individually or in combination with other GW agents, results in neuropathological changes in the brain**
 - ❖ FY08 IIRA Dr. Fiona Crawford, Roskamp Institute
 - ❖ Published in 2014 *Neuropathology* 34(2):109-27
- ◆ **Repeated exposures to pesticides, at doses below those associated with acute toxicity, result in persistent alterations in axonal transport in the brain**
 - ❖ FY11 IIRA Dr. Alvin Terry, Georgia Regents University
 - ❖ Published in 2015 *Neurotoxicology* 47:17-26
- ◆ **Epigenetic alterations in the hippocampus of rats exposed to GW chemicals and stress persist one year later**
 - ❖ FY12 IIRA Dr. Lisa Pierce, Tripler Army Medical Center, HI
 - ❖ Published in 2015 *FASEB J* 29:814.6

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 **GWIRP Research Outcomes cont.**

- ◆ **Altered immune pathway activity following exercise challenge in veterans with GWI**
 - ❖ FY08 IIRA Dr. Nancy Klimas, VA Medical Center, Miami
 - ❖ Published in 2013 *Brain Behav Immun* 8:159-169
- ◆ **Multisystem dysregulation results in an altered but stable homeostatic drive serving to sustain GWI**
 - ❖ FY09 IIRA Dr. Gordon Broderick, Nova Southeastern
 - ❖ Published in 2014 *PLoS One* 9(1):e84839
- ◆ **Veterans affected by GWI show prolonged post-exercise recovery of phosphocreatine, consistent with a role for mitochondrial dysfunction**
 - ❖ FY12 IIRA Dr. Beatrice Golomb, University of San Diego
 - ❖ Published in 2014 *PLoS One* 9(3):e92887
- ◆ **Presence of the stress hormone, corticosterone, exacerbates the neuroinflammatory response following a single dose of a sarin surrogate**
 - ❖ FY08 IIRA Dr. Stephen Lasley, University of Illinois/Dr. James O'Callaghan, CDC NIOSH
 - ❖ Published in 2015 *J Neurochem* 133(5):708-21

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GWIRP Treatment Outcomes

- ◆ **Acupuncture may improve some GWI symptoms, including pain, fatigue, sleep quality, and cognitive symptoms**
 - ❖ FY08 CTA Dr. Lisa Conboy, New England School of Acupuncture, Inc.
 - ❖ Published in 2012 *Contemp Clin Trials* 33(3):557-562
- ◆ **Carnosine found to increase cognitive function and reduce gastrointestinal symptoms in veterans with GWI**
 - ❖ FY06 IIRA Dr. James Baraniuk, Georgetown University
 - ❖ Published in 2013 *Glob J Health Sci* 5(3):69-81
- ◆ **Coenzyme Q10 (CoQ10) found to reduce pain, fatigue, and cognitive symptoms in veterans with GWI**
 - ❖ FY06 IIRA Dr. Beatrice Golomb, University of San Diego
 - ❖ Published in 2014 *Neural Computation* 26(11): 2594-2651
- ◆ **Xylitol- and saline-based nasal irrigation may mitigate respiratory (chronic rhinosinusitis) and fatigue symptoms in GWI**
 - ❖ FY10 ITEA Dr. David Rabago, University of Madison, WI
 - ❖ Published in 2015 *Contemp Clin Trials* 41:219-226



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Ongoing Treatment Evaluations

- ◆ **Naltrexone and Dextromethorphan** (Dr. William Meggs, East Carolina University)
- ◆ **Intranasal insulin** (Dr. Julia Golier, Bronx Veterans Medical Research Foundation, Inc.*)
- ◆ **Inflammation reduction** (Dr. Ronald Bach, Minnesota Veterans Medical Research and Education Foundation*)
- ◆ **Methylphenidate plus a GWI-specific nutrient formula** (Dr. Jon Kaiser, K-PAX Pharmaceuticals, Inc.)
- ◆ **Portable vestibular stimulator** (Dr. Jorge Serrador, Veterans Biomedical Research Institute, Inc.*)



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Ongoing Alternative Therapies

- ◆ **Probiotic for bowel symptoms** (Dr. Ashok Tuteja, Western Institute for Biomedical Research)
- ◆ **Botanical anti-inflammatories** (Dr. Jarred Younger, University of Birmingham, AL)
- ◆ **Sauna detoxification** (Dr. David Carpenter, State University of New York, Albany)
- ◆ **Cognitive therapy for improvement of sleep quality** (Dr. Yoshio Nakamura, University of Utah)
- ◆ **Acupressure** (Dr. Vernon Lin, Cleveland Clinic)
- ◆ **Polyphenol Preparations** (Dr. Giulio Pasinetti, Mount Sinai School of Medicine, NY)
- ◆ **Yoga for pain management** (Dr. Peter Bayley, Palo Alto Institute for Research and Education)



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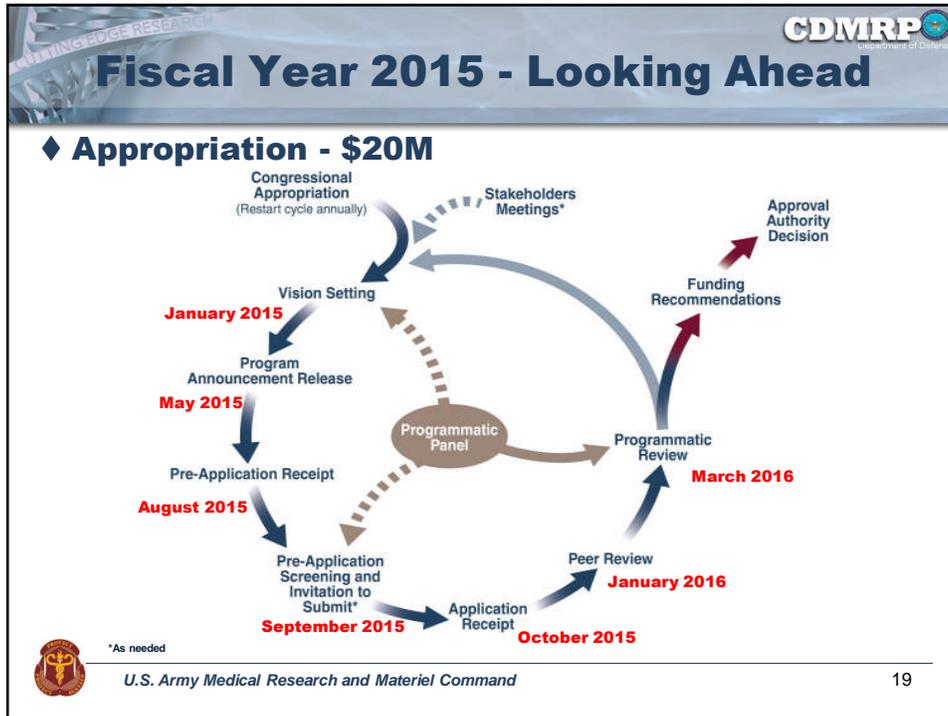
New FY14 Pilot Trials

Awarded in September 2015

- ◆ **D-cycloserine** (Dr. Rosemary Toomey, Boston University)
- ◆ **Vagus Nerve Stimulation** (Dr. Benjamin Natelson, Beth Israel Medical Center, NY)
- ◆ **Anti-inflammatory compound Anatabine** (Dr. Fiona Crawford, Roskamp Institute)
- ◆ **Low FODMAP (carbohydrate) diet** (Dr. Ashok Tuteja, Western Institute for Biomedical Research)
- ◆ **Liposomal Glutathione and Curcumin** (Dr. Nancy Klimas, South Florida Veterans Affairs Foundation for Research and Education, Inc.* / Dr. Richard Deth, Nova Sotheastern)
- ◆ **Mitochondrial cocktail** (Dr. Beatrice Golomb, University of San Diego)



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GWIRP FY15 Priority Areas

- ◆ Improve understanding of pathobiology and symptoms
- ◆ Improve definition and diagnosis
- ◆ Identification of effective treatments

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GWIRP FY15 Investment Strategy

Clinical Trial Awards:

- ❖ Clinical Trial Award (22%) 1 award @ \$4.0M
- ❖ Innovative Treatment Evaluation Award (18%) 3 awards @ \$3.4M

Innovation-based Awards:

- ❖ Investigator-Initiated Research Award (IIRA) (20%) 5 awards @ \$3.6M
- ❖ IIRA Expansion Award (17%) 3 awards @ \$3.0M

Population-based Award:

- ❖ Epidemiology Research Award (10%) 1 award @ \$1.9M

Investigator Award:

- ❖ New Investigator Award (13%) 3 awards @ \$2.4M



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FY15 GWIRP Programmatic Panel

<ul style="list-style-type: none"> ◆ Anthony Hardie, former Staff Sergeant USA (Chair) Florida Veterans for Common Sense ◆ Roberta F. White, Ph.D. (Chair Emeritus) Boston University School of Public Health ◆ Daniel Havlichek, M.D. Michigan State University ◆ Carlos Maldonado, Ph.D. Department of Veterans Affairs ◆ K. Jeffrey Myers, M.D.U.S. Department of Veterans Affairs 	<ul style="list-style-type: none"> ◆ Marni Silverman, Ph.D. Henry M. Jackson Foundation for the Uniformed Services University of the Health Sciences ◆ Andrea White, Ph.D. University of Utah ◆ David K. Winnett, Jr., Captain USMC Retired Veterans for Common Sense ◆ CAPT Mark Lyles, D.M.D., Ph.D. United States Naval War College ◆ Fiona Crawford, Ph.D. Roskamp Institute
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Finding and Funding the Best Research

RESEARCH PROGRAMS FUNDING OPPORTUNITIES CONSUMER INVOLVEMENT SEARCH AWARDS MEDIA CENTER ABOUT US

Enhanced Neuroinflammation in Gulf War Illness

Steve Lasley, Ph.D.,
University of Illinois College
of Medicine at Peoria

James O'Callaghan, Ph.D.,
Centers for Disease Control and Prevention -
National Institute for Occupational Safety and Health

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