DoD Gulf War Illness Research Program (GWIRP)

Each year, the Department of Defense's office of the Congressionally Directed Medical Research Programs (CDMRP) assesses scientific opportunities to advance research in specific areas. The investigators supported by individual programs are making significant progress against targeted diseases, conditions, and injuries. This list is not intended to be a full representation of accomplishments, but rather a sampling of the broad portfolio of research and advances resulting from congressional appropriations.

Year	GWIRP Research Contributions	Additional Information and Hyperlinks
2006	Dr. Beatrice Golomb from the University of California, San Diego, investigates whether the vitamin-like antioxidant coenzyme Q10 confers significant benefit for Gulf War illness symptoms and improves physical function when compared to placebo.	• Golomb BA, Allison M, et al. 2014. Coenzyme Q10 benefits symptoms in Gulf War veterans: Results of a randomized double-blind study. Neural Comput 26(11):2594-2651.
2008	Dr. Lisa Conboy from the New England School of Acupuncture, Inc. found that acupuncture provided improvement on the Physical Functioning Subscale (PFS) of the SF-36 in Veterans with GWI. Effects were observed following 4–6 months of treatment.	• Conboy L, St John M, Schnyer R. 2012. The effectiveness of acupuncture in the treatment of Gulf War Illness. Contemp Clin Trials 33(3):557-62. • GWIRP Video Highlight
2008	Dr. James Baraniuk of Georgetown University found a unique alteration in brain structure and function in GWI-affected Veterans. Moreover, specific responses to exertion were identified that were able to classify GWI individuals into subgroups.	• Rayhan RU, Stevens BW, et al. 2013. Increased brain white matter axial diffusivity associated with fatigue, pain and hyperalgesia in Gulf War Illness. PLoS One 8(3):e58493. • Rayhan RU, Stevens BW, et al. 2013. Exercise challenge in Gulf War Illness reveals two subgroups with altered brain structure and function. PLoS One 8(6):e63903. • GWIRP Research Highlight
2008	Drs. Nancy Klimas of the South Florida Veterans Affairs Foundation for Research and Education, Inc. and Gordon Broderick of Nova Southeastern University completed an integrative study of immune signaling molecules in GWI, CFS, and normal subjects at rest and during exercise, and they created a model of immune system and hormonal interactions that correctly distinguishes GWI and CFS subpopulations.	• Broderick G and Craddock TJ. 2013. Systems biology of complex symptom profiles: Capturing interactivity across behavior, brain and immune regulation. Brain Behav Immun 29:1-8. • Broderick G, Ben-Hamo R, et al. 2013. Altered immune pathway activity under exercise challenge in Gulf War Illness: An exploratory analysis. Brain Behav Immun 28:159-69. • Smylie AL, Broderick G, et al. 2013. A comparison of sex-specific immune signatures in Gulf War Illness and chronic fatigue syndrome. BMC Immunol 14:29.
2008	Dr. Ronald Bach from the Minnesota Veterans Medical Research and Education Foundation found that CRP, leptin, and BDNF levels are significantly higher in blood from Gulf War Veterans with multiple symptoms of chronic pain, chronic fatigue, and cognitive impairment. Further proteomic analysis revealed a coordinately expressed set of 18 CRP-related proteins in the plasma of Gulf War Veterans. This set of potential pro-inflammatory biomarkers was found to correlate with levels of the stress-related antigen Protein C.	• Johnson GJ, Leis LA, et al. 2013. Elevated platelet count, CRP and thromboxane analog-induced platelet aggregation in subjects with Gulf War Veterans' Illnesses: Evidence of a chronic inflammatory state? Blood Coagul Fibrinolysis 24(7):736-741. • GWIRP Research Highlight, 2011 • GWIRP Research Highlight, 2013

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2008	Dr. Fiona Crawford of the Roskamp Institute developed a novel PB+PER exposure model in which delayed cognitive dysfunction presents, beginning at around 100 days post-exposure. Proteomic and lipidomic results from this model provided strong evidence for disruption of lipid metabolism in response to Gulf War agent exposure.	• Abdullah L, Crynen G, et al. 2011. Proteomic CNS profile of delayed cognitive impairment in mice exposed to Gulf War agents. Neuromolecular Med 13(4):275-288. • Abdullah L, Evans JE, et al. 2012. Lipidomic profiling of phosphocholine containing brain lipids in mice with sensorimotor deficits and anxiety-like features after exposure to Gulf War agents. Neuromolecular Med 14(4):349-361. • Abdullah L, Evans JE, et al. 2013. Chronic elevation of phosphocholine containing lipids in mice exposed to Gulf War agents pyridostigmine bromide and permethrin. Neurotoxicol Teratol 40:74-84. • Ojo JO, Abdullah L, et al. 2014. Exposure to an organophosphate pesticide, individually or in combination with other Gulf War agents, impairs synaptic integrity and neuronal differentiation, and is accompanied by subtle microvascular injury in a mouse model of Gulf War agent exposure. Neuropathology 34(2):109-27. • GWIRP Research Highlight
2008	Drs. Stephen Lasley and James O'Callaghan found that prior exposure to the stress hormone, corticosterone (CORT) "primed" the immune system of DFP-treated animals to mount an exaggerated response. These observations led to the creation of a murine neuroinflammation model of GWI based on combined exposure to physiological stress and a nerve agent.	• O'Callaghan JP, Kelly KA, et al. 2015. Corticosterone primes the neuroinflammatory response to DFP in mice: potential animal model of Gulf War Illness. J Neurochem 133(5):708-21. • GWIRP Research Highlight
2009	Dr. Beatrice Golomb from the University of California, San Diego found a prolonged phosphocreatine recovery time in Veterans afflicted with GWI as compared to non-deployed controls. This recovery time delay is suspected to be the result of mitochondrial dysfunction.	• Koslik HJ, Hamilton G, and Golomb BA. 2014. Mitochondrial dysfunction in Gulf War Illness revealed by 31Phosphorus Magnetic Resonance Spectroscopy: A case-control study. PLoS One 9(3):e92887.
2010	Dr. Brian Cooper of the University of Florida found that chronic exposure to chlorpyrifos, permethrin, and pyridostigmine bromide results in alterations of pain thresholds and vascular nociceptor function in a rat model. This dysfunction could cause widespread pain and contribute to the development of CNS symptoms that have been identified in Gulf War Veterans.	• Nutter TJ and Cooper BY. 2014. Persistent modification of Nav1.9 following chronic exposure to insecticides and pyridostigmine bromide. Toxicol Appl Pharmacol 277(3):298-309. • Jiang N, Nutter TJ, and Cooper BY. 2013. Molecular and cellular influences of permethrin on mammalian nociceptors at physiological temperatures. Neurotoxicology 37:207-19. • Nutter TJ, Jiang N, and Cooper BY. 2013. Persistent Na+ and K+ channel dysfunctions after chronic exposure to insecticides and pyridostigmine bromide. Neurotoxicology 39:72-83.
2010	Dr. David Rabago designed a 26-week, three-arm randomized controlled trial to study whether nasal irrigation with xylitol or saline is effective in the treatment of chronic rhinosinusitis and fatigue symptoms in GWI patients. Based on the Sino-Nasal Outcome Test (SNOT-20) scores, nasal irrigation with saline appeared to be a promising intervention.	• Hayer SD, Rabago DP, et al. 2015. Effectiveness of nasal irrigation for chronic rhinosinusitis and fatigue in patients with Gulf War Illness: Protocol for a randomized controlled trial. Contemp Clin Trials 41:219–26.

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2011	Dr. Alvin Terry found impaired axonal transport in the brains of living rats after treatment with chlorpyrifos, a well-known OP insecticide. The inhibition of transport was evident even 30 days after the OP dosing had ceased indicating repeated exposures to the pesticide chlorpyrifos, at doses below those associated with acute toxicity, can result in persistent alterations in axonal transport.	• Hernandez CM, Beck WD, et al. 2015. Repeated exposure to chlorpyrifos leads to prolonged impairments of axonal transport in the living rodent brain. Neurotoxicology 47:17-26. • GWIRP Research Highlight
2012	Two major multi-institutional research efforts by leading GWI investigators were initiated. Dr. Kimberly Sullivan of Boston University was awarded a consortium award for her collaborative project entitled "Brain-Immune Interaction as the Basis of Gulf War Illness Consortium (GWIC)." The objective of this study is to provide a cohesive understanding of the pathobiological mechanisms responsible for the symptoms of GWI in order to provide a targeted and efficient basis for identifying beneficial treatments and diagnostic markers. Dr. Mariana Morris of Nova Southeastern University was awarded a second consortium award for her collaborative project entitled "Understanding Gulf War Illness: An Integrative Modeling Approach." This project will integrate clinical understanding of the disease process with basic research efforts using a novel combination of animal and mathematical models.	• CDMRP News Release
2012	Dr. Lisa Pierce found a persistent increase in the expression of a specific microRNA (miRNA), miR-124, in the hippocampus of a GWI rat model. Dr. Pierce believes in vivo inhibition of miR-124 function in the hippocampus could be a promising and novel therapeutic approach to improve cognition, emotion regulation, and neuroendocrine dysfunction in GWI.	• Pierce LM, Kurata WE, et al. 2016. Long-term epigenetic alterations in a rat model of Gulf War Illness. Neurotoxicology 55:20-32.