

Roskamp Institute Gulf War Illness Research Program
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The overarching goal of the Roskamp Institute GWI research program is to identify novel molecular targets and biomarkers for GWI. To that end we have developed a novel model of delayed cognitive impairment following exposure to PB+PER and are utilizing that model to explore GW-agent induced hippocampal dysfunction, genetic influences, disruption of immune/inflammatory mechanisms and proteomic response to GW-agent exposure.

We are applying state-of-the-art proteomic approaches, which we have established in-house, to the identification of molecular pathways triggered in response to GW agent exposure. These pathways are then being validated *in vitro* with standard molecular biology approaches, to determine their potential for therapeutic targeting. Studies of therapeutic intervention *in vivo* in the mouse model will fully characterize the neurobehavioral and neuropathological consequences of potential treatments.

Together with proteomic technology we are also applying lipidomic and metabolomic approaches to the identification of objective measures that distinguish veterans with GWI from Healthy Veterans, namely plasma biomarkers. Molecular ("omic") profiling in GWI mouse models will identify molecules correlating with neurological performance, and delineate biological functions that are specifically modulated following GW-agent exposure. Through clinical collaborations we will recruit GWI patients, healthy GW veterans, and GW-era veterans who were not deployed to the Gulf. We will similarly profile their plasma, and will compare the profiles across clinical subgroups and use the results from the mouse studies to identify the biological functions of most significance to GWI cognitive dysfunction. We will then explore the development of a plasma biomarker panel by using targeted investigations for the particular molecules of interest.

Identification of Biological Pathways Implicated in Hippocampal Dysfunction and Cognitive Impairment in Gulf War Illness (CDMRP; Crawford; 2009-2012)

Proteomic Immune Profiling for the Therapeutic Modulation of Cognitive Impairment in a Novel GWI Mouse Model (CDMRP; Ait-Ghezala; 2011-2014)

Identification of Plasma Biomarkers of Gulf War Illness Using "omic" Technology (VA; Crawford, *under review*).

Proteomic Approaches to Discover New Treatment Options for GWI (VA; Mullan, *under review*).