New results from a GWIRP-funded brain-imaging study in Boston provide the first direct evidence of neuroinflammation in veterans with GWI. Based on early GWIRP-funded study results, a focus on identifying and confirming or denying the presence of persistent neuroinflammation in GWI has been a key GWIRP goal. These results provide the first objective evidence confirming the relevance of neuroinflammation in GWI and that treatments should indeed be targeted at countering this neuroinflammation.¹

Another key area of GWIRP-funded research has been related to role of the gut-brain axis in GWI. A GWIRP-funded study also from Boston and also just published assessed the relationships between GWI, GI symptoms, gut microbiome and inflammatory markers in GWV from the Boston Gulf War Illness Consortium (GWIC). Results showed significantly different gut microbiome patterns among the GWI and control groups, including greater plasma levels of an inflammatory cytokine (TNF-RI) in the GWI+GI group, which was associated with significantly more reported chemical weapons exposure during the Gulf War and which reported significantly greater chronic pain, fatigue and sleep difficulties. Studies with larger samples sizes are needed to confirm these initial findings, which would be expected to suggest gut-related treatment targets.²

A GWIRP-funded study from Northern California published in November 2019 tested the safety, tolerability, and efficacy of KPAX002—a combination of methylphenidate hydrochloride plus a micronutrient formula designed to support mitochondrial function— another key area of significant GWI focus for treating GWI. The results were a 25% reduction in severity of multiple GWI symptoms including fatigue, cognitive symptoms, sleep problems, and pain, with an acceptable side effect profile. A larger randomized, double-blinded, placebo-controlled trial is necessary to determine if the observed pilot study benefit can be replicated in a larger sample size.³

Key areas of focus for GWIRP funding have also been unraveling GWI’s underlying pathobiology and improving definition and diagnosis, all with an eye towards treatment development. A GWIRP-funded study from San Diego published in July 2019 showed that despite differing exposure histories, significant, objective differences between GWI and Chronic Fatigue Syndrome (ME/CFS) were found (“a metabolic phenotype of GWI was clearly distinguished

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from controls”), which show that common clinical symptoms like fatigue can have different chemical mechanisms and different diagnostic implications. Larger confirmation is needed.

As GWIRP-funded treatment target identification and treatment development have showed significant advances – including through the two Gulf War Illness Consortia (GWIC) at Boston University and Nova Southeastern University; the Boston Biorepository, Recruitment, and Integrative Network (BRAIN); and the newly-funded (FY18) Gulf War Illness Clinical Trials and Interventions Consortium (GWICTIC) – the GWIRP fine-tunes its funding strategy annually. The goals are to fund preclinical research to inform treatment targeting, fund high-risk/high-reward potential-treatment pilot studies, and then speed those that show success into larger clinical studies than can provide the statistical significance to translate successful treatments into the clinic for GWI patients. As the steady stream of peer-reviewed published study results continue to show, the GWIRP’s strategy is clearly working.

A research publication from VA’s Millennium Cohort Study Team early this year concluded that, “Gulf War veterans’ increased risk of CMI/GWI persisted across the study period, highlighting the continued importance of screening and improving treatment options among this population.” And, an October 2019 publication by VA WRIISC researchers concluded that, “Establishment of a standard case definition, prioritized GWI research funding for the characterization of the pathophysiology of the condition, and rapid replication and adaptation of early phase, single site clinical trials could substantially advance research progress and treatment discovery for this condition.” These VA findings and recommendations strongly support the GWIRP’s active funding strategy, which is sharply focused on GWI’s pathobiology, definition and diagnosis, and a clear treatment development “pipeline.”

Finally, in early 2019 through a collaboration between the National Institutes of Health (NIH), CDC, VA, DoD GWIRP, and the GWI community, Common Data Elements (CDE) have been developed for GWI. “The goals of this effort are to increase the efficiency and effectiveness of clinical research studies and treatment, increase data quality, facilitate data sharing and aggregation of information across studies, and help educate new clinical investigators.” The GWIRP’s enforced use of these CDEs is expected to add valuable data to ongoing efforts to refine the GWI case definition and develop objective GWI markers.

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