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Identifying Immune Drivers of Gulf War Illness Using a Novel Daily Sampling Approach

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Institution Receiving Award: STANFORD UNIVERSITY

Program: GWIRP

Proposal Number: GW110044

Funding Mechanism: Investigator-Initiated Research Award

Partnering Awards:

Award Amount: \$900,642.00

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PUBLIC ABSTRACT

Gulf War Illness (GWI) is a debilitating disease that is estimated to affect at least 175,000 Veterans in the United States. The condition impacts many systems of the body, causing pain sensitivity, profound fatigue, cognitive dysfunction, chronic headaches, gastrointestinal problems, and other symptoms. The underlying pathology of GWI is still unclear, posing a severe obstacle to both the diagnosis and treatment of the disorder. The combination of widespread and debilitating symptoms, unpredictable prognosis, poor treatment options, and medical stigma cause considerable distress to patients. In order to make gains in curing GWI, it is essential that we develop objective, physiologic-based tests for the disorder, and identify physiological targets for treatments.

We hypothesize that a large percentage of GWI patients are suffering from a low-level inflammatory state that occurs in the brain and spinal cord. Through the process of inflammation, chemicals are produced that cause neurons to operate irregularly, leading to symptoms such as pain sensitivity and fatigue. The inflammation that underlies GWI may not be adequately captured by conventional autoimmune and inflammatory blood tests. One reason for this is that many of the immune factors that can drive the symptoms of GWI are not included in conventional tests of inflammation. Another reason is that the immune factors are too low in concentration to trigger flags on traditional tests but can still drive the symptoms because the targets are overly sensitized.

We have developed a new approach for testing the immune system in chronic diseases such as GWI. Our technique takes advantage of the fact that GWI sufferers have symptoms that vary in severity from day to day. By collecting blood daily, we can measure inflammatory processes on severe symptom days, moderate symptom days, and low symptom days. Therefore, we can find immune factors that "track" with the ups and downs of symptom severity. We also expand the immune factors tested well beyond those typically measured in the clinic. Using the daily sampling approach and comprehensive list of tests, we have created a sensitive measure for detecting abnormal immune system function in chronic multisymptom illnesses. We have already applied this technique successfully to screen for immune targets in fibromyalgia and chronic fatigue syndrome. The process was safe and easily tolerated by the participants. We found a number of inflammatory factors in the blood of those individuals that strongly correlated with pain and fatigue. The markers of inflammation were elevated on days when the patients reported high symptom severity and suppressed on days when the patients reported low severity. Because of the high degree of symptom overlap between those diseases and GWI, we strongly suspect that the same approach would help us better understand GWI.

In this study, we will track 40 GWI patients for 25 days. Each day, participants will submit a small blood sample for analysis of inflammatory factors. Also, participants will provide ratings of their GWI symptoms every day on a handheld computer. We will use the data to build a statistical model that will predict daily symptom severity using only the immune measurements. Our main goal with this research is to identify a small set of biological markers that are most associated with GWI symptoms. The successful completion of this

project would improve the clinical care of GWI in three ways:

1. Add credibility to GWI by confirming that biological factors are directly tied to symptoms.
2. Lead to the development of blood screening tools for objectively diagnosing GWI.
3. Identify immune targets so that specialized treatment for GWI can be developed.

The results of this study will help us to better understand the underlying pathobiology of GWI and may ultimately lead us to identify new treatment targets for GWI. This study is, therefore, a low-risk way to positively impact the lives of individuals with GWI.

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