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TITLE: Human Leukocyte Antigen in Gulf War Veterans: Association with Symptoms and Inflammatory Markers

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14. ABSTRACT During the initial year of the grant period, the primary emphasis has been on obtaining regulatory approval for study procedures, training staff and building a data repository, and initial identification and recruitment of study participants. We have obtained all regulatory approvals, created a data repository, and completed 40 acquisitions, with several additional acquisitions scheduled. We will continue to recruit at an accelerated pace to meet our recruitment goals and have identified additional recruitment avenues to maximize outreach.					
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1. **INTRODUCTION:**

GWI has affected a large number of veterans who served during the 1990-1991 Persian Gulf War. Despite extensive study, the pathogenesis and pathophysiology remain unclear. There is evidence of genetic effects and blood biomarkers that point to disruptions in immune system function as one underlying cause of GWI symptoms; however, studies evaluating immune system involvement in GWI have typically included small, non-representative samples. This project aims to evaluate GWI symptoms, genes associated with immune system functioning, and biomarkers of immune system dysfunction, inflammation, and autoimmunity in a large sample of Gulf War veterans with and without GWI to elucidate the relation of GWI to immune system dysfunction. If our hypothesis that GWI reflects immune system dysfunction resulting from genetic susceptibility coupled with environmental exposure(s) is supported, this will open new avenues of potential treatment, consistent with the burgeoning field of immunogenetics.

2. **KEYWORDS:** Gulf War Illness, Human Leukocyte Antigen, Genetics, Inflammation

3. **ACCOMPLISHMENTS:**

- **What were the major goals of the project?**

The major goal of this study is to evaluate immune genotype, inflammatory markers, and autoimmune involvement in a large sample of Gulf War veterans with and without GWI randomly selected from a list of 66,229 people in the State of Minnesota who served during the Gulf War from August 2, 1990 to April 11, 1991 (provided to us by the Department of Defense).

- **What was accomplished under these goals?**

The first 6 months of the study were dedicated to obtaining local IRB approval and HRPO approval, and hiring and training research staff, all of which was successfully completed in the expected timeframe. We also generated a random number list to identify GW era veterans for possible recruitment and completed our first acquisition, as expected, within the first 8 months of the study. We have successfully completed 40 acquisitions during this period. We have completed fewer acquisitions than planned due to limitations with our recruitment list including outdated contact information and non-GW veterans erroneously listed as GW era; we are working on alternative recruitment strategies to enhance recruitment of GW-era veterans. Finally, we created a data repository in this reporting period.

- **What opportunities for training and professional development has the project provided?**

Nothing to Report.

- **How were the results disseminated to communities of interest?**

Nothing to Report

- **What do you plan to do during the next reporting period to accomplish the goals?**

We plan to continue recruitment at an accelerated rate to meet the study goals. We have identified alternative strategies to identify GW era veterans and obtain updated contact information for individuals randomly selected from the list of over 66,000 people in Minnesota (provided to us by the Department of Defense) who served during the Gulf War. The new procedures are considerably more time-consuming than our original plan to send mass mailings to thousands of veterans with the original addresses provided; however, we are able to focus our recruitment efforts on those with valid contact information.

4. **IMPACT:**

- **What was the impact on the development of the principal discipline(s) of the project?**

Nothing to Report

- **What was the impact on other disciplines?**

Nothing to Report

- **What was the impact on technology transfer?**

Nothing to Report

- **What was the impact on society beyond science and technology?**

Nothing to Report

5. **CHANGES/PROBLEMS:**

- **Changes in approach and reasons for change**

- We had initially planned to mass mail recruitment letters to randomly selected GW era veterans. We have sent several hundred letters using the contact information provided on the list of MN GW-era veterans; however, the contact information provided was from the time of service (25 years ago) and therefore most of the letters did not reach their intended recipients. Consequently, we have modified our strategy as follows: we utilize a random number list to

identify potential participants and then utilize VA and VBA records to search for updated addresses and confirm GW-era service. This approach is much more time-consuming; however, it has proven to be more fruitful than our mass mailing approach. We have searched VA and VBA records for 3000 randomly selected veterans; of those, only 596 were found to have served during the Gulf War. Initial recruitment letters were sent to all 596; follow up phone calls have been made to those with known phone numbers.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

Our goal was to recruit 100 participants by the end of the first year; we have completed data acquisitions on 40 participants. The delay has been related to outdated contact information as previously described. In addition to our targeted random recruitment approach (described above) we have also obtained IRB approval to post flyers at local American Legions, VFWs, and in print to maximize recruitment and reach veterans we would otherwise be unable to locate.

- **Changes that had a significant impact on expenditures**

Nothing to Report

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to Report

6. **PRODUCTS:**

- **Publications, conference papers, and presentations**

Nothing to Report

- **Journal publications.**

Nothing to Report

- **Books or other non-periodical, one-time publications.**

Nothing to Report

- **Other publications, conference papers, and presentations.**

Nothing to Report

Website(s) or other Internet site(s)

Nothing to Report

Technologies or techniques

Nothing to Report

Inventions, patent applications, and/or licenses

Nothing to Report

Other Products

We have developed a database to facilitate data analysis and dissemination of research findings.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

Name:	<i>Lisa James</i>
Project Role:	<i>PI</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>2</i>
Contribution to Project:	<i>Study design and oversight; completion of regulatory documents; training of study staff</i>
Funding Support:	<i>DoD</i>

Name:	<i>Apostolos Georgopoulos</i>
Project Role:	<i>Co-I</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>2</i>
Contribution to Project:	<i>Oversight of database development and staff involved in DNA isolation</i>
Funding Support:	<i>DoD</i>

Name:	<i>Brian Engdahl</i>
Project Role:	<i>Co-I</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>2</i>
Contribution to Project:	<i>identification of study participants</i>
Funding Support:	<i>DoD</i>

Name:	<i>Laura Kalipe</i>
Project Role:	<i>Coordinator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>2</i>
Contribution to Project:	<i>Data acquisition and DNA isolation</i>
Funding Support:	<i>DoD</i>

Name:	<i>Matt Sanders</i>
Project Role:	<i>Research Fellow</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>1</i>
Contribution to Project:	<i>Database development</i>
Funding Support:	<i>DoD</i>

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Nothing to Report

- **What other organizations were involved as partners?**

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

Nothing to report

9. APPENDICES

Nothing to report