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TITLE: Identification of Epigenetic Signatures as Biomarkers of Gulf War Illness

PRINCIPAL INVESTIGATOR: Dr. Anthony P. Malanoski

CONTRACTING ORGANIZATION: Naval Research Laboratory

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14. ABSTRACT

The objective of this research proposal is to use integrated approaches to investigate epigenetics changes of GWI and correlate the epigenetic changes with GW-relevant exposures (PB, pesticides, sarin) to identify the biological indicators in GWI pathogenesis in a well-established cohort of Gulf War veterans from the large multi-site DOD-funded Boston Gulf War Illness Consortium (GWIC) (GW120037). The most significant accomplishments in the initial year was developing protocols and obtaining approval of human subject research plans so that samples could be received. A meeting with contributors from the University of Boston occurred to finalize experimental plans. Supplies and equipment were ordered to facilitate experimental plan.

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Table of Contents

Introduction

The objective of this research proposal is to use integrated approaches to investigate epigenetics changes of GWI and correlate the epigenetic changes with GW-relevant exposures (PB, pesticides, sarin) to identify the biological indicators in GWI pathogenesis in a well-established cohort of Gulf War veterans from the large multi-site DOD-funded Boston Gulf War Illness Consortium (GWIC) (GW120037). Identified epigenetic changes associated with GWI could potentially provide additional treatment options for veterans with GWI by targeting these changes. It is the aim of this study to identify epigenetic risk factors for GWI by combining the extensive data collection efforts of the Boston GWIC with the epigenetics expertise of the Naval Research Laboratory investigators.

To achieve the objective of this proposed research, the following specific aims will need to be addressed.
Specific Aim 1: Identify DNA Methylation patterns specific to GWI
Specific Aim 2: Discover the changes in microRNA profiles associated with GWI
Specific Aim 3: Apply high performance computing (HPC) bioinformatics approaches to characterize GWI pathogenesis from multiple analytical modalities

Keywords: DNA Methylation, microRNAs, Gulf War Illness, bioinformatics

Accomplishments

This research uses integrated approaches to investigate epigenetics changes of GWI and correlate the epigenetic changes with GW-relevant exposures (PB, pesticides, sarin) to identify the biological indicators in GWI pathogenesis in a well-established cohort of Gulf War veterans from the large multi-site DOD-funded Boston Gulf War Illness Consortium (GWIC) (GW120037). The most significant accomplishments in the initial year was developing protocols and obtaining their approval of human subject research plans so that samples could be received. A meeting with contributors from the University of Boston occurred to finalize experimental plans. Supplies and equipment were ordered to facilitate experimental plan. A more detailed outline of statement of work tasks and accomplishments related to each follows.

Major Task 1: Collect blood samples from archive study participants

The samples were identified from the Boston GWI consortium biorepository but final transfer was not executed in FY 18 due to the lateness of arrival of funds. Arrangements for 60 samples to be shipped were completed in FY 19. After communication the managers of the consortium biorepository it was identified that they were still in the process of collecting samples for the repository. Ongoing delays have also occurred do to miscommunication on details of contracts. These have largely been resolved and arrangements for the final samples should be completed by the middle of FY 19.

Major Task 2: Determine DNA Methylation patterns

The first task that has been completed under this task in the second year of the project was development of the protocol to process the samples. The protocol was tested using none study samples to ensure effectiveness and has been applied to the samples that are on hand. A sequencing facility to have the samples processed at was identified and a contract was set in place. The initial samples have not yet been set but plans are to have them sent in the beginning of FY 19. Further samples will be processed and sent for sequencing in batches as they are received.

Major Task 3: Examine microRNA profiles

The majority of the subtasks for this task are also goals for the second and third year of the project. Protocol development is also complete for this task. The samples on hand have been processed and are ready for processing with the technology to sequence the microRNAs that was identified in the previous FY. This work will be carried out on site.

Major Task 4&5: Integrated bioinformatics analysis & Reporting

These tasks require large portions of task 2 and 3 to be completed before starting and will not begin until the third year of the project so no progress has been made on this task in the first year of the project.

There is nothing to report regarding opportunities for training and professional development.
No results were disseminated to communities of interest as none are far enough along to warrant it.

In the next year of the project that samples will have been transferred and work will proceed on processing samples and submitting to high throughput sequencing. It is anticipated that this portion of the work will be largely completed for in the upcoming year. As results of sequencing are received the analysis and bioinformatics processing of results will also be completed.

Impact

Nothing to Report.

Changes/Problems

The most significant difficulty was obtaining the samples from the biorepository. There were several miscommunications about requirements to place the order to transfer samples resulting in significant delays. Further communication with the biorepository has also identified that they do not have all the samples required for this study collected yet and are still in the process of collecting them. This was not communicated clearly at the initial submission of the proposed work and is leading to a revision of the timeline to delay final tasks. It is anticipated that all experimental work will be completed during the performance period of the third FY if all the samples are delivered from the biorepository. The final analysis may take longer than this and a no cost etention of the performance period may be required to allow completion of this task.

No other significant changes of problems were encountered in the second year of the project.

Products, Inventions, Patent Applications, and/or Licenses

Publications

Nothing to Report

Technologies or techniques

Nothing to Report

Inventions, patent applications

Nothing to Report

Participants & Other Collaborating Organizations

Name: Dr. Anthony P. Malanoski
Project Role: Principal Investigator
Researcher Identifier: 0000-0001-6192-888X
Nearest person Month worked:5
Contributions to Project: Coordinated efforts, communicated with collaborators to obtain samples

Name: Dr. Tomasz Leski

Project Role: Research Biologist
Researcher Identifier: 0000-0001-7688-9887
Nearest person Month worked:5
Contributions to Project: Developed experimental protocols, obtained necessary supplies for project.

There have been no significant changes to active sources of support.

Organization: Boston University School of Public Health (BU)
715 Albany Street, T4W
Boston, MA 02118
Site PI: Kimberly Sullivan
Partner's contributions are collaborative in form.
The source of the samples if the biorepository established by Dr. Sullivan's ongoing work. She provided expertise and did required work on her side to existing IRB protocols to allow for transfer of samples from the biorepository to NRL.
Organization: Nova Southeastern University
3301 College Avenue
Fort Lauderdale, FL 33314
Partner's contributions are collaborative in form and involved the actual selection o f samples from biorepository that will be transferred to NRL.

Special Reporting Requirements

Nothing to report

Appendices

No appendices attached to this report.