

AWARD NUMBER: W81XWH-14-1-0623

TITLE: Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators

PRINCIPAL INVESTIGATOR: Jarred Younger, PhD

CONTRACTING ORGANIZATION: University of Alabama at Birmingham
Birmingham, AL 35294

REPORT DATE: October 2015

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE October 2015			2. REPORT TYPE Annual Report			3. DATES COVERED 30 Sep 2014 - 29 Sep 2015		
4. TITLE AND SUBTITLE Treating Gulf War Illness with Novel Anti-Inflammatories: A Screening of Botanical Microglia Modulators						5a. CONTRACT NUMBER		
						5b. GRANT NUMBER W81XWH-14-1-0623		
						5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) Jarred Younger, PhD Lisa Smoot, Lab Manager E-Mail: younger@uab.edu						5d. PROJECT NUMBER		
						5e. TASK NUMBER		
						5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Alabama at Birmingham-UAB AB 1170 1720 2 nd Avenue South Birmingham, AL 35294-0111						8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012						10. SPONSOR/MONITOR'S ACRONYM(S)		
						11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited								
13. SUPPLEMENTARY NOTES								
14. ABSTRACT On June 30, 2015, we obtained final IRB approval and an IND exemption determination from UAB IRB. All approved documents (consent form, human subject protocol and attachments) were forwarded to ORP HRPO for final approval on July 2, 2015. While awaiting final ORP HRPO approval we have worked to establish collaborations with Birmingham and Alabama VA support groups for recruitment purposes. We have also established a great rapport with the nursing staff at the UAB Clinical Research Unit (CRU) where the study will be conducted. We have selected personnel to run the study and started training on the UAB IRB process, regulatory document preparation, review and submission. Upon the receipt of the final IRB ORP HRPO approval, we will initiate recruitment advertising, participant screening, enrollment and the study protocol.								
15. SUBJECT TERMS Gulf War Illness, botanical, anti-inflammatory, biomarker, microglia, improvement, treatment								
16. SECURITY CLASSIFICATION OF:				17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON		
a. REPORT	b. ABSTRACT	c. THIS PAGE	USAMRMC					
U	U	U	UU	6	19b. TELEPHONE NUMBER (include area code)			

Table of Contents

	<u>Page</u>
1. Introduction.....	1
2. Keywords.....	1
3. Accomplishments.....	1
4. Impact.....	2
5. Changes/Problems.....	2
6. Products.....	2
7. Participants & Other Collaborating Organizations.....	3
8. Special Reporting Requirements.....	3
9. Appendices.....	3

1. INTRODUCTION:

The major aim of this research project is to identify the most promising botanical anti-inflammatories for the treatment of Gulf War Illness (GWI). A second, exploratory, aim is to identify biomarkers of GWI improvement. To accomplish those aims at UAB, we are recruiting 40 male veterans diagnosed with Gulf War Illness (GWI). Each participant will receive 3 different botanical compounds and placebo over a 300 day period. Each participant will also participate in a 30-day baseline period starting the first month to report their individual daily GWI symptom severity ratings. Analyses will then be conducted to identify the most effective botanical compound that reduced microglia hyper excitability. Ultimately, this information may be used to develop new treatments that specifically target the pathophysiological mechanisms of Gulf War Illness.

2. KEYWORDS:

Gulf War Illness, botanical, anti-inflammatory, biomarker, microglia, improvement, treatment

3. ACCOMPLISHMENTS:

(Note: We have successfully completed the institutional transfer from Stanford University to the University of Alabama at Birmingham-UAB. A revised SOW was submitted on September 24, 2014).

Current Objectives:

- Begin participant enrollment
- Begin the protocol and data collection

Task 1: Team review and progress meetings

25% Completed.

(Note: Final approval from USAMRMC ORP HRPO is on-going; upon final approval receipt participant enrollment will begin. The final meeting before starting the study protocol and medical reviews will be scheduled after ORP HRPO approval has been received. The completion of Task 1 *Milestones: Agreement on eligibility criteria, screening protocol and procedure; Consent form and human subjects protocol finalized* are dependent upon receipt of ORP HRPO final approval).

Task 2: Submission of Documents for Regulatory Approvals

100% Completed.

(Note: UAB IRB approval was received June 30, 2015 and all approved documents were submitted to USAMRMC ORP HRPO on July 2, 2015 for approval).

Task 3: Start up

30% Completed. We have selected the personnel to run the project.

(Note: The completion of Task 3 and *Milestone: Study protocol ready to begin* is dependent upon receipt of ORP HRPO final approval. Also, the purchase and blinding of the treatment compounds, scheduling the mock session and creation of the trial database /randomized lines will begin upon receipt of the ORP HRPO final approval).

Task 4: Advertisement

0% Completed. Task progress is dependent on the completion of Task 3.

(Note: The initiation of Task 4 and *Milestone: 120 potential participants screened by telephone* are dependent upon the receipt of ORP HRPO final approval).

Task 5: Screen GWI participants for study

0% Completed. Task progress is dependent on the initiation of Task 4.

(Note: The completion of Task 5 *Milestone: First participant enrolled* is dependent upon the receipt of ORP HRPO final approval).

Task 6: Run protocol

0% Completed. Task progress is dependent on the initiation of Task 5 and participant enrollment.

Task 7: Assays

0% Completed. Task progress is dependent on the completion of Tasks 5 & 6.

Task 8: Analysis

0% Completed. Task progress is dependent on the completion of Task 6 & 7.

Task 9: Preparation of Final report and Publications

0% Completed. Task progress is dependent on the completion of Tasks 6, 7, & 8.

4. **IMPACT:**

Nothing to report

5. **CHANGES OR PROBLEMS:**

We are currently awaiting final IRB approval from ORP HRPO. Upon receipt of that final approval, advertising for recruitment, participant screening and enrollment will begin. We anticipate enrollment will begin by mid-January 2016.

6. **PRODUCTS:**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

Name	Jarred Younger
Project Role	PI
Research Identifier	
Nearest person month worked	1.7 CM
Contribution to Project	Dr. Younger has prepared & reviewed documents for submission to UAB to complete the grant transfer process from Stanford University to UAB; and also to receive UAB IRB & ORP HRPO final approval. Dr. Younger has met with local VA support group leaders in an effort to establish a recruiting collaboration.

Name	Lisa Smoot
Project Role	Coordinator
Research Identifier	
Nearest person month worked	2.3 CM
Contribution to Project	Lisa has assisted Dr. Younger with the preparation, review and submission of documents to UAB to complete the grant transfer process from Stanford University to UAB; to receive final UAB IRB for approval. She has also forwarded UAB approved and requested documents to ORP HRPO for their final IRB approval. Lisa has identified local VA support groups and met with leaders to establish recruiting methods to initiate upon receipt of final ORP HRPO approval.

8. SPECIAL REPORTING REQUIREMENTS:

None.

9. APPENDICES:

None.