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

PRINCIPAL INVESTIGATOR: Jarred Younger, PhD

CONTRACTING ORGANIZATION: University of Alabama at Birmingham
BIRMINGHAM, AL 35294-0001

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5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Since the last annual report, we have received HRPO IRB approval and initiated advertising, recruitment, participant screening, participant enrollment, and the study protocol.

All start up subtasks have been completed. The study treatment compounds have been purchased, and the blinded capsules have been created and prepared into randomized lines.

To date, 131 potential participants have filled out the online screening questionnaire, 70 of those have been screened by telephone, and 6 participants have enrolled into the study. 23 other potential participants have been identified as meeting initial eligibility requirements, and every effort will be made to enroll these during the next reporting period.

Advertisement, recruitment, screening, and enrollment are ongoing as we work toward the Milestones: 120 potential participants screened by telephone, 40 GWI participants enrolled, First participant successfully completes 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
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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 the University of Alabama at Birmingham, we are recruiting 40 male veterans diagnosed with GWI. Each participant will receive three 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:**

- **What were the major goals of the project? & What was accomplished under these goals?**

- Task 1: Team review and progress meetings

  50% Completed.

  Milestone: Agreement on eligibility criteria, screening protocol and procedure – Completed

  Milestone: Consent form and human subjects protocol finalized – Completed

  (Note: Progress reviews and medical reviews will continue as the protocol is ongoing. All other subtasks in the SOW have been completed for task 1.)

- Task 2: Submission of Documents for Regulatory Approvals

  100% Completed.

- Task 3: Start up

  100% Completed.

  Milestone: Protocol ready to begin—Completed

- Task 4: Advertisement

  40% Completed. New recruitment tools have been launched and are actively ongoing. A recruiting event was held in March 2016 at the Birmingham Jefferson Civic Center (BJCC) in Birmingham, Alabama. Radio advertisements (subtask 1) were aired May 2, 2016-May 27, 2016 and August 8, 2016-September 8, 2016, and a third round is scheduled for January 2017. The recruitment webpage (subtask 2) has been published, and 131 individuals have filled out the online screening questionnaire linked from the webpage.

  Milestone: 120 potential participants screened by telephone—57.5% Completed. Seventy potential participants have been screened by telephone at this time, and 11 more individuals are scheduled to be screened by telephone.

  (Note: Birmingham VA recruitment (subtasks 3, 4, & 5) will be initiated in 2017 or as needed.)

- Task 5: Screen GWI participants for study

15% Completed. Six individuals have signed consent and enrolled into the study. One participant has been randomized; one has been excluded based on screening lab tests, and the remaining four are pending randomization. Twenty-three more potential participants have been determined to meet initial eligibility requirements and are pending in-person screening visits and enrollment.

Milestone: First participant enrolled—Completed

- Task 6: Run protocol

  0% Completed.

  (Note: Task progress is ongoing and is dependent on the completion of Task 5.)

- Task 7: Assays

  0% Completed.

  (Note: Task progress is dependent on the completion of Tasks 5 & 6.)

- Task 8: Analysis

  0% Completed.

  (Note: Task progress is dependent on the completion of Tasks 6 &7.)

- Task 9: Preparation of Final report and Publications

  0% Completed.

  (Note: Task progress is dependent on the completion of Tasks 6, 7, & 8.)

- **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?**

  The focus during the next reporting period will be on **Task 4: Advertisement** and **Task 5: Screen GWI participants for study.** As noted above, advertisement is ongoing, and an additional round of radio advertisements is scheduled for late winter/early spring to help drive recruitment forward. Screening and enrollment are ongoing as well. Every effort is being made to enroll the potential participants identified as meeting initial eligibility requirements as a result of our prescreening process and to work toward protocol completion.

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 OR PROBLEMS:**

Nothing to report.

6. **PRODUCTS:**

- **Publications, conference papers, and presentations**
  - **Journal publications.**

    Nothing to report.
  - **Books or other non-periodical, one-time publications.**

    Nothing to report.
  - **Other publications, conference papers, and presentations.**

    Donovan, E.K., Massey, R.L., & Younger, J.W. (2016, October*) Diagnostic overlap of Gulf War Illness, Myalgic Encephalomyelitis/ Chronic Fatigue syndrome, and Fibromyalgia in Gulf War Veterans.* Poster presented at the University of Alabama at Birmingham (UAB) Pain Symposium 2016, Birmingham, AL, USA.

    Massey, R.L., Donovan, E.K., & Younger, J.W. (2016, July) *Effects of Botanical Microglia Modulators in Gulf War Illness: A Novel Screening Approach.* Poster presented at the University of Alabama at Birmingham (UAB) Summer Expo 2016, Birmingham, AL, USA.
- **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**

  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 continues to review telephone screens and consult with Emily on potential participant eligibility and inclusion criteria as well as other project questions during a weekly meeting. Dr. Younger has also advised on additional recruitment and advertising methods. He continues to conduct informative broadcast sessions in an effort to increase community

	awareness and participant recruitment.

Name	Lisa Smoot
Project Role	Coordinator
Research Identifier	
Nearest person month worked	5 CM
Contribution to Project	Lisa has assisted with recruitment and pre-screening efforts by maintaining the UAB LISTSERV to send out newsletters and updated study recruitment materials to interested individuals and support groups. Also, she prepared and submitted UAB IRB annual review and HRPO/ORP continuing review documents.

Name	Emily Donovan
Project Role	Coordinator
Research Identifier	
Nearest person month worked	10 CM
Contribution to Project	Emily has maintained recruitment efforts by communicating with VA support group and community leaders for recruiting purposes. She has reviewed 131 prescreening questionnaires and has conducted 70 telephone prescreenings to identify 31 potential participants eligible for an in-person screening visit. She has conducted in-person screenings for 6 individuals, with even more scheduled in upcoming months.

8. **SPECIAL REPORTING REQUIREMENTS:**

None.

9. **APPENDICES:**

None.