

AWARD NUMBER: W81XWH-14-1-0620

TITLE: Direct Test for Neuroinflammation with [11C]DAP-713-PET Scanning

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REPORT DATE: December 2017

TYPE OF REPORT: Final

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

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE December 2017			2. REPORT TYPE Final		3. DATES COVERED 29 Sep 2014 - 28 Sep 2017	
4. TITLE AND SUBTITLE Direct Test for Neuroinflammation with [¹¹ C]DAP-713-PET Scanning					5a. CONTRACT NUMBER	
					5b. GRANT NUMBER W81XWH-14-1-0620	
					5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Pomper, Martin; Haley, Robert E-Mail: mpomper@jhmi.edu					5d. PROJECT NUMBER	
					5e. TASK NUMBER	
					5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Johns Hopkins University 733 N Broadway, MRB Suite 117 Baltimore, MD 21205					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 This project concerns the non-invasive detection of inflammation in the brains of individuals suffering from the Gulf War Illness (GWI). We are using quantitative positron emission tomography (PET) using [¹¹ C]DPA-713 (DPA). DPA binds to the translocator protein (TSPO), which is located on the outer mitochondrial membrane and is an established biomarker of neuroinflammation. We showed that DPA-PET was able to show a statistically significant trend of increased radiopharmaceutical binding from historical controls to Gulf War veteran controls to individuals with GWI. This pilot study lays the groundwork for a publication and larger study in this patient population. We have also added three additional historical controls and are in the process of adding them to the analysis.						
15. SUBJECT TERMS None Listed						
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			
Unclassified	Unclassified	Unclassified	Unclassified	17	19b. TELEPHONE NUMBER (include area code)	

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1. INTRODUCTION:

This project concerns the non-invasive detection of inflammation in the brains of individuals suffering from the Gulf War Illness (GWI). We used quantitative positron emission tomography (PET) using [¹¹C]DPA-713 (DPA). DPA binds to the translocator protein (TSPO), which is located on the outer mitochondrial membrane and is an established biomarker of neuroinflammation. The study has so far enrolled 11 Gulf War veterans and 10 elderly healthy men. The study is a collaboration between Johns Hopkins University and the University of Texas Southwestern Medical Center, where a carefully vetted population of individuals with GWI exists. PET imaging was performed at Johns Hopkins with analysis performed at both sites. Subject recruitment and analysis are ongoing.

2. KEYWORDS:

molecular imaging; PET; Gulf War Illness; DPA-713; distribution volume; neuroinflammation

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Tasks are verbatim from the approved SOW. Progress on each Subtask is provided in italics.

Task 1. To identify, contact, and screen subjects for study. The performance expectation of the PI (Dr. Pomper) will be, by the end of month 24, completing the recruitment of 32 qualified study participants, including 16 GWI subjects of a specific syndrome variant group and 16 matched controls.

Subtask 1a. To identify and contact study subjects (months 1-12). All subjects are Gulf War veterans who previously provided permission to be contacted by Dr. Haley's study team for future study participation. The UT Southwestern team led by Dr. Haley and Deborah Modesette will be responsible for this subtask. Average quarterly targets (for quarters 1-4) are 16 contacts (8 GWI and 8 controls), assuming ~ **50%** of which would be qualified for subsequent imaging studies after screening.

RESPONSE: Subjects were identified on a rolling basis with 16 subjects identified and recommended for contact by Dr. Haley's team, all of whom we attempted to contact, and many repeatedly. We received IRB approval on 10/21/14 and were funded on 7/31/15 to begin.

Subtask 1b. To screen study subjects (months 4-24). Interested participants for subtask 1a will undergo informed consent and a screening interview/procedures with Dr. Haley's study team, in collaboration with the study team lead by Dr. Pomper at Johns Hopkins Medical Institutions (JHMI), to ensure eligibility for positron emission tomography (PET) and magnetic resonance

(MR) imaging. The eligibility requirements are detailed in the narrative. During the first year, quarterly targets (for quarters 2 – 4) are 5 qualified participants, such that a total of 15 (8 GWI and 7 controls) can be imaged. During the second year, quarterly targets (for quarters 5 – 8) are 4 to 5 qualified participants, such that a total of 17 (8 GWI and 9 controls) can be imaged in year 2 (~11 subjects) and year 3 (~ 6 subjects). The initial screen will be performed at UT Southwestern by Dr. Haley and Deborah Modesette, as noted above, with the imaging aspects of the screen performed by Drs. Pomper and Coughlin and Ms. Kwanisai at Johns Hopkins.

RESPONSE: It provide challenging to meet our quarterly enrollment targets. We have subsequently replaced our team of study coordinators with a new team that is continuing to work in concert with Dr. Haley's team to continue recruitment. We have identified additional funding to undertake these tasks. To date we have enrolled 11 Gulf War veterans, two of whom were disqualified for having the recessive TSPO phenotype and would not be eligible for scanning. Among the final nine, four had GWI and five were controls that were in the same theater of engagement as those suffering from GWI.

Task 2. To perform [¹¹C]DPA-713 PET to study neuroinflammation in GWI and controls.

Subtask 2a. IRB amendments and HRPO approvals (months 1 – 3). The JHMI study team already has an existing protocol for undertaking DPA-PET, approved by the Johns Hopkins Institutional Review Board (IRB). Minor amendments will be made based on the proposed study. Work will be accomplished at Johns Hopkins by Drs. Pomper and Coughlin and Ms. Kwanisai. UTSouthwestern has an existing protocol for recruiting subjects and assisting with the statistical analysis of the data to be performed by Dr. Haley and will be approved for this proposal. The final JHU and UTSouthwestern IRB approvals will be sent to the DoD for HRPO review and approval.

RESPONSE: As noted above we received IRB approval to study the GWI cohort on 10/21/14.

Subtask 2b. Genotyping of patients (months 4 – 30). This must be performed in tandem with imaging on qualified subjects, i.e., patients and controls. Work will be accomplished at Johns Hopkins by Drs. Pomper and Coughlin.

RESPONSE: We enrolled our first subject for genotyping and subsequent scanning on 10/20/15, once funding was in place.

Subtask 2c. Imaging scans (months 4 – 30). For each qualified study participant, Dr. Haley (UT Southwestern) will work with the research coordinator at JHMI to schedule and arrange transportation. Participants will arrive at JHMI in the morning of the first of two study days and will travel home on the evening of study Day Two after completing all study portions, including MR and DPA-PET. Quarterly targets will follow that proposed in Task 1b, with the goal that all qualified subjects can be imaged on average within ~3 months. Work will be accomplished at Johns Hopkins by Drs. Pomper and Coughlin after the initial screening by Dr. Haley and Deborah Modesette at UT Southwestern.

RESPONSE: PET and MR scans were accomplished according to our revised work flow in the modified narrative on a rolling basis throughout the funding period. The numbers of patients involved are described in the RESPONSE to Subtask 1b above.

Subtask 2d. Data analysis (months 13 – 33). An established data analysis workflow has been developed at the JHMI site, as detailed in the narrative (**Fig. 6**). The normalization approach will be used to negate the genotype-dependency (and other confounding factors) existed in DPA-PET imaging. The regional normalized volume-of-distribution (V_t) will be obtained and compared between GWI subjects and controls, as well as

between GWI subjects and controls, as well as correlated to clinical symptoms. Analysis will be performed by Dr. Wang at Johns Hopkins using PMOD commercial image analysis software. We will perform a variety of analytical procedures with a focus on radiotracer kinetic modeling with gray matter normalization of results. The primary outcome variable will be the distribution volume of the radiotracer (V_T), taking into account the genotype of the patient. Standard statistical methods (t test, ANOVA and corresponding non-parametric tests, if appropriate) will be employed to assure significance of the results.

RESPONSE: We continue to analyze the PET data. Dr. Wang has left Johns Hopkins, with the data now being processed by our new physicist, Dr. Yong Du. Subsequent to provision of the modified SOW, we have learned that the normalization approach we proposed and have used on earlier subject populations is not effective, so we have been forced to exclude individuals with the recessive (T/T) TSPO phenotype. That is now a recognized limitation of study of this target. Statistical analysis was performed by Dr. Haley's group, with an interim report – demonstrating a statistically significant trend despite the small interim sample size – shown below.

Subtask 2e. Data presentation and publication (months 33 – 36). This will be performed in conjunction with subtask 3e, through the close collaboration between JHMI and UT Southwestern teams. Specifically, the neuroinflammation transmission aspects provided by DPA-PET will be presented both independently and synergistically, closely referencing GWI subjects' clinical symptoms and previously preclinical and clinical findings in GWI-related research. Leading this effort will be Dr. Haley at the UT Southwestern site and Dr. Pomper at Johns Hopkins.

RESPONSE: We are not yet ready to present these data. With our new team we will recruit to achieve a modified sample size of at least eight individuals with GWI and eight veterans with GW exposure. We will add this to our historical and healthy matched control populations to expand the three study groups noted in the interim analysis below. We believe that this will provide an adequate sample size for a publishable pilot cohort and will provide enough data to seek funding for a larger trial if the significance we have already demonstrated persists.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Major activities: This trial has enabled establishment of a collaboration between the Division of Nuclear Medicine and Molecular Imaging at Johns Hopkins and the Division of Epidemiology at UTSouthwestern. We have recruited patients and shuttled them from sites outside of Maryland to Johns Hopkins for imaging. The machinery is now in place to continue recruitment and imaging according to our now established workflow. We have also modified our PET imaging analysis by merely excluding individuals with the recessive TSPO phenotype and have submitted our results for interim analysis to UTSouthwestern who has completed those analyses.

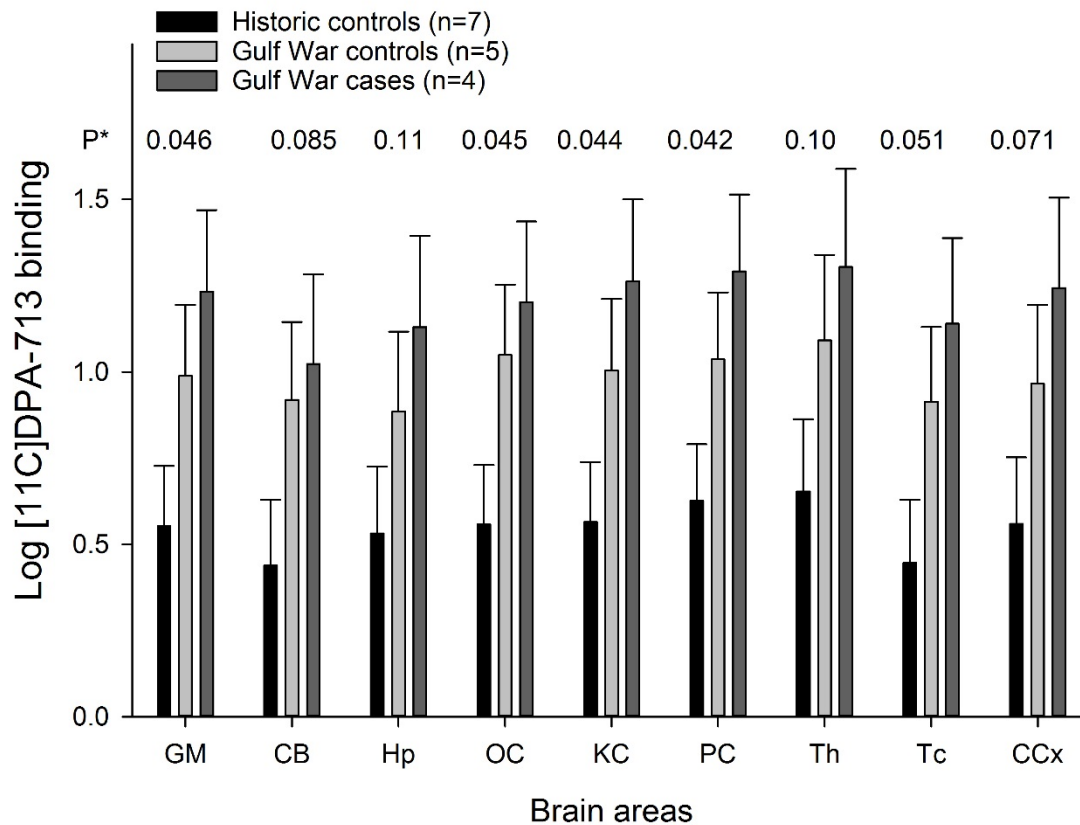
Specific objectives: As noted in the SOW our main objectives were straightforward but have been challenging to meet. We aimed to recruit veterans with GWI and veterans who served in the Gulf and did not develop GWI. We then intended to perform genetic testing for TSPO genotype followed by imaging with MR (for anatomic correlation with PET) and DPA-PET. Analysis of the imaging data followed by statistical analysis of the results were intended to follow. We have accomplished all of these objectives, although not yet on the intended scale.

Significant results: We showed that DPA-PET was able to show a statistically significant trend of increased radiopharmaceutical binding from historical controls to Gulf War veteran controls to individuals with GWI (see figure). This is the first time a molecular imaging technique, with a specific cellular target in mind, has been applied to this population. Despite the small number of individuals studied we were able to demonstrate a significant trend. A detailed description of the statistical analysis follows: We used the SAS GLM procedure with the MANOVA option to perform a repeated-measures ANOVA to test for differences in [¹¹C]DPA-713 binding among the 3 clinical groups consisting of: veterans with Gulf War illness-syndrome 2 (GWIS2), well veterans controls, and historic non-veterans controls. Among the nine veterans, four veterans had GWIS2 and five veterans were well veteran controls. The repeated measures were the following nine brain areas: gray matter (GM), cerebellum (CB), hippocampus (Hp), occipital cortex (OC), frontal cortex (FC), parietal cortex (PC), thalamus (Th), temporal cortex (Tc), and cingulate cortex (CCx). The prior hypothesis was for an increasing trend in binding from historic controls to veteran controls to GWI veterans, so for the primary hypothesis test the group measure was entered into the analysis as an ordinal variable, TSPO genotype was included as a dichotomous confounding variable (C/T genotype vs C/C genotype; T/T genotype excluded), and a Wilks lambda 1-tailed exact test was applied. Since the results in the nine brain regions were expected (and found) to be highly correlated, no multiple comparisons correction was used. A secondary hypothesis test involved combining the historic and veterans control groups into a single control group to be compared with the GWI veteran group. Because of the relatively small numbers of subjects in the groups, all analyses employed exact tests.

The results of the primary hypothesis test showed a statistically significant trend of increasing [¹¹C]DPA-713 binding across the 3 groups ($P = 0.038$, see the figure). The secondary hypothesis test comparing the GWI veterans to the combined controls was not statistically significant ($P = 0.22$).

In future analyses involving larger samples sizes in all groups, we will subdivide the veteran control group into those who were and those who were not deployed to the Gulf War theater of operations during the 1991 Gulf War. The present pilot study had 4 deployed veteran controls and only 1 nondeployed veteran control. Interestingly, the binding of the 1 nondeployed control was close to the mean of the historic control group, suggesting that the deployed controls, though showing no signs of GWI, may have an intermediate level of neuroinflammation between the nondeployed controls and the GWI veterans. Since the sample sizes are small in this pilot study, we were not able to test this hypothesis.

[11C]DPA-713 binding of Gulf War illness Cases compared with Historic Controls and Gulf War Veteran Controls



*P values are 1-tailed test for an increasing trend, controlling for TSPO genotype (no multiple comparisons correction because of high correlation among areas).

Test for overall repeated-measures 3-group effect by Wilks' Lambda 1-tailed exact test, $p = 0.038$.

Test for overall repeated-measures 2-group effect (GW cases vs All controls) by Wilks' Lambda 1-tailed exact test, $p = 0.22$.

Repeated-measures analyses performed with the Manova option of SAS Proc GLM (v. 9.4)

Other achievements: There has been a significant training component to this study, as noted below.

Commentary: The only goal we have not met is our full complement of study subjects. Because our study protocol remains in place and because we have identified additional funding beyond that provided by the DoD to continue, we are confident that we will be able to recruit and scan a sufficient number of veterans to provide preliminary data to justify a more definitive study. Such a study may involve imaging of neuroinflammation beyond TSPO, using other radiopharmaceuticals that we are developing in parallel programs. We have also added a group of age-matched healthy

controls as a third group from our historical dataset of subjects imaged with DPA. Although not part of the original proposal, our usual comparator when studying a new population has been age-matched controls. As can be seen in our interim analysis there is a difference in radiopharmaceutical uptake between such controls and individuals who served in the Gulf War. Those with GWI show a trend to even higher levels of uptake, corresponding to yet greater brain microglial activation, a surrogate for brain injury and repair.

there is nothing significant to report during this reporting period, state "Nothing to Report."

This project was directly undertaken by a junior team of researchers (an assistant professor from the Department of Psychiatry leading an assistant professor from the Division of Medical Imaging Physics and several research study coordinators) at Johns Hopkins who worked with the group at UT Southwestern. New collaborations were forged and new leadership skills obtained. The research study coordinators had not previously worked with individuals from the military. One of the junior faculty noted above has recently been promoted to associate professor (Dr. Du), while the other (Dr. Coughlin) is under consideration, in part, on the basis of skills obtained during this project. We recruited two new study coordinators and a program manager to this study as we noted challenges with recruitment. All required substantial training after onboarding and all are now seasoned members of the study team.

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We will soon be generating an abstract and publication of the aforementioned work, however, to do so we feel we will need to recruit four more individuals with GWI and three more veterans with GW exposure who do not have GWI to travel to Johns Hopkins. We are actively pursuing that goal at present.

If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We intend to continue recruiting, scanning and analysis. We will include further historical controls as comparators. Although this is technically our final report, we intend to keep the Gulf War Illness Research Program apprised of our results, with the support received fully acknowledged. We also intend to interface with other GWI researchers interested in neuroimaging to combine our unique molecular imaging dataset with other potential markers of GWI that may be available within a biorepository for deeper analysis and leveraging of our data.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

At this point we have only interim results on a small sample size. However, if the initial trend is maintained, we will have demonstrated the ability to generate a quantitative biomarker for describing what has been considered by some a controversial and subjective illness. This could be the first of several such non-invasive, molecular imaging-based markers to emerge in the study of GWI.

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

We have shown the capacity for DPA-PET once again to reflect on microglial activity within the brain, non-invasively and quantitatively, and have added a new patient population to those who have been successfully imaged with this putative neuroinflammatory imaging agent. This will provide further motivation and rationale to use TSPO as a non-invasive biomarker of brain injury and repair and continue to animate the field of imaging in neuroinflammation.

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

We continually obtain requests for (a) cross-referencing of our Investigational New Drug application to enable use of DPA-PET elsewhere – as recently as several months ago; (b) toxicology data so that other centers can use DPA-PET; (c) help with analysis of DPA-PET data, etc. Many groups worldwide now use imaging agents targeting the translocator protein (TSPO) for assessment of neuroinflammation in human subjects – and increasingly turn to DPA, in part, due to our studies. Furthermore, we continue to develop other brain radiotracers for neuroinflammation, with targets other than TSPO, in part motivated by this project.

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Once completed this project will provide a way for those suffering from GWI to point to a quantitative measure of illness/inflammation within their central nervous system, as we have shown for individuals with other chronic neuroinflammatory processes, e.g., repetitive mild traumatic brain injury. This could prove valuable as a way to educate other soldiers and the military about the dangers of serving in affected areas. It may also alleviate the sense that such wounded soldiers are suffering from other entities that are not quantifiable and definitive and adds to the increasing body of knowledge – using neuropsychological testing and brain imaging – that GWI is an independently identifiable pathological process that has its own pathophysiology and potential road to treatment and recovery.

5. **CHANGES/PROBLEMS:** The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:

Please see above.

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

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Please see above.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Please see above. The main issue we confronted was the

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

N/A

Significant changes in use of biohazards and/or select agents

N/A

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”

- **Publications, conference papers, and presentations**
Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report at this time.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to report at this time.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report at this time.

- **Website(s) or other Internet site(s)**
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report at this time.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

As noted above, we have and continue to share our ability to analyze DPA-PET studies (Cornell, Stanford) and allow cross-referencing of our IND (Cornell, Stanford) to facilitate other investigators in this area.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Parallel programs in neuroinflammation are enabling us to generate new composition of matter (for imaging) that form the basis of several new invention disclosures. Such work, however, has been inspired by and performed in parallel to this GWI award.

- *outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*

- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

*Name: Mary Smith
 Project Role: Graduate Student
 Researcher Identifier (e.g. ORCID ID): 1234567
 Nearest person month worked: 5*

Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.

Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)

*Name: Martin Pomper, M.D., Ph.D.
 Project Role: Professor, co-Principal Investigator
 Nearest person month worked: 1
 Contribution to Project: Planning, strategy, analysis, manuscript review.*

*Name: Jennifer Coughlin, M.D.
 Project Role: Co-Investigator
 Nearest person month worked: 3
 Contribution to Project: Planning, strategy, analysis, manuscript review*

*Name: Hailey Rosenthal
 Project Role: Research Program Assistant
 Nearest person month worked: 3
 Contribution to Project: Recruitment/patient liaison*

*Name: Ala Lisok
 Project Role: Lab Coordinator*

Four new individuals in addition to those noted above became associated with the project mid-way:

Name: Sarah Frey
Project Role: Research Program Assistant
Nearest person month worked: 2
Contribution to Project: Recruitment/patient liaison

Name: Erica Marshall
Project Role: Research Program Assistant
Nearest person month worked: 2
Contribution to Project: Recruitment/patient liaison

Name: Yong Du, Ph.D.
Project Role: Research Associate
Nearest person month worked: 2
Contribution to Project: Physicist – data analysis

Name: Rehab Abdallah, MB BCh
Project Role: Clinical Research Program Manager
Nearest person month worked: 2
Contribution to Project: Oversee all research activity

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report.

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

Additional financial support for further imaging and recruitment has arisen through the Henry N. Wagner, Jr. endowment fund. That will pay for an additional seven to eight PET and MR studies and the effort for the study coordinators and rest of the team to enroll them.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: N/A

9. APPENDICES: N/A