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TITLE: ProBIOPTIC: Protein Biomarkers to Inform Optimization of PTSD Therapeutics to Inform Clinical Trials

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This project aims to address the understanding of biological factors contributing to an individual's long-term outcomes following a traumatic event by investigating how blood biomarkers relate to posttraumatic stress disorder (PTSD) symptom presentation following a traumatic event in Service Members and Veterans (SMVs). Through novel analysis of brain derived exosomes from existing blood samples, we can measure brain related messaging and activities by their protein-rich cargo. Enhanced understanding of the biological underpinnings of PTSD symptom clusters will help identify targeted treatments for personalized interventions based on the dysregulated pathway identified, and can also serve as predictive biomarkers for PTSD. The project aims to determine protein profiles and protein networks associated with participants with PTSD compared to those without PTSD, using SOMAscan technology. It also aims to determine protein profiles and networks associated with each of the four PTSD symptom clusters, through SOMAscan technology, and hopes to validate these determined protein profiles. This study has obtained full approval and is awaiting the completion of legal agreements before analyses can begin.

15. SUBJECT TERMS
PTSD; SOMAscan; predictive biomarkers; treatment; protein profiles.

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1. INTRODUCTION:

This project aims to address the understanding of biological factors contributing to an individual's long-term outcomes following a traumatic event by investigating how blood biomarkers relate to posttraumatic stress disorder (PTSD) symptom presentation following a traumatic event in Service Members and Veterans (SMVs). Through novel analysis of brain derived exosomes from existing clinical date and blood samples, we can measure brain related messaging and activities by their protein-rich cargo. Enhanced understanding of the biological underpinnings of PTSD symptom clusters will help identify targeted treatments for personalized interventions based on the dysregulated pathway identified, and can also serve as predictive biomarkers for PTSD. The project aims to determine protein profiles and protein networks associated with participants with PTSD compared to those without PTSD, using SOMAscan technology. It also aims to determine protein profiles and networks associated with each of the four PTSD symptom clusters, through SOMAscan technology, and hopes to validate these determined protein profiles.

2. KEYWORDS:

PTSD; SOMAscan; predictive biomarkers; treatment; protein profiles.

3. ACCOMPLISHMENTS:

What were the major goals of the project?

This research project will determine the protein profiles and protein networks (from brain-derived exosomes) that are associated with participants with PTSD compared to controls without PTSD using the SOMAscan technology. It will also determine the protein profiles and protein networks (from brain-derived exosomes) that are associated with each of the four PTSD symptom clusters: intrusion symptoms (Criterion B), avoidance symptoms (Criterion C), negative alterations in cognitions and mood (Criterion D), and arousal symptoms (Criterion E) using the SOMAscan technology. Finally, the project will validate the protein profiles (from brain-derived exosomes) obtained via the SOMAscan technology (Aims 1 and 2) in circulating blood plasma using protein quantification methods (i.e., SIMOA, meso-scale diagnostics, and ELISA). These goals will be completed by utilizing de-identified blood samples which were previously collected from participants who took part in the CAPS-5 study, which assessed PTSD-related clinical data.

In order to accomplish the above goals, the project has three major tasks:
Major Task 1: Protocol Preparation and Approvals
Major Task 2: Coordinate Study Staff
Major Task 3: SOMAscans

What was accomplished under these goals?

Project has been approved as exempt by the WRNMMC IRB and has obtained OHRO approval, but is still awaiting a start letter (dependent on completion of a CRADA and an MTA); The project is also approved by the Johns Hopkins University (JHU) IRB. Goals achieved include:

Major Task 1: Protocol Preparation and Approvals:

1. Received full IRB approval of exempt status from WRNMMC (OCT2022) and JHU (MAR2023)
2. Obtained second-level OHRO approval through the DoD (JAN2023).
3. Discussions between USAMMDA, WRNMMC, CERV, and JHU regarding CRADA and MTA requirements. Drafts of both documents were distributed to the relevant parties by WRNMMC DRP Business Office. Feedback received from JHU and USAMMDA. Some feedback received but additional negotiations in progress with CERV before the final drafts will be sent out for review.
4. Ongoing monthly conference calls to discuss various logistics to approval and study set-up.

Major Task 2: Coordinate Study Staff:

1. CERV RA identified and will be hired once CRADA/MTA is established.
2. Staff training completed and ongoing.

Major Task 3: SOMAscans

- No associated accomplishments 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?

- Obtain CRADA and MTA in order to receive start letter.
- Hire research assistant for Cincinnati VA.
- Transfer blood samples from Cincinnati VA to JHU in order to begin exosome extraction and subsequent SOMAscan analysis.
- Transfer clinical data from Cincinnati VA to WRNMMC.
- Hire post-doctoral fellow for WRNMMC after SOMAscan analysis is underway.

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:

Nothing to report.

Changes in approach and reasons for change

Nothing to report.

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

Nothing to report

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

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals

Nothing to report.

Significant changes in use of biohazards and/or select agents

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.

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**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Dr. Sara Lippa
Project Role: Co-Principal Investigator
Researcher Identifier: ORCID ID 0000-0002-6352-7577
Nearest person month worked: 1
Contribution to Project: Dr. Lippa is the co-principal investigator of the study. She has completed all regulatory forms thus far, developed the protocol and other project-related documents, and coordinated with other entities and sites who will be involved with the project.

Name: Dr. Kimbra Kenney
Project Role: Associate Investigator
Researcher Identifier: ORCID ID 0000-0002-8138-7539
Nearest person month worked: 1
Contribution to Project: Dr. Kenney has assisted with study development and IRB protocol and CRADA/MTA initiation, submission, and review.

Name: Kathleen Chard, PhD.
Project Role: Associate Investigator
Researcher Identifier: N/A
Nearest person month worked: 1
Contribution to Project: Dr. Chard has assisted with regulatory forms for the study, as well as other project-related documents. She has also coordinated with other entities and sites who will be involved with the project.

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

COLLABORATIVE AWARDS: N/A.

QUAD CHARTS: See attached.

9. APPENDICES: N/A.