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TITLE: Molecular Studies to Identify Mechanisms That Underlie Symptom Improvement in Microbiota Transfer Therapy Patients

PRINCIPAL INVESTIGATOR: Stephen J Walker

CONTRACTING ORGANIZATION: Wake Forest University Health Sciences, Winston Salem, NC

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this study is to perform molecular analysis (transcriptomic and metabolomic assays) on samples (whole blood, serum, and stool) derived from 84 adults with autism spectrum disorder (ASD) undergoing microbiota transfer therapy (MTT), and 84 adult controls, from an on-going CDMRP-funded clinical trial (James Adams, PI; Arizona State University) to identify mechanisms that underlie symptom improvement following MTT. Due to the onset of the coronavirus pandemic, recruitment at the ASU site has been severely curtailed since March 2020, and so sample collection and transfer to me has been limited to a portion of the initial 35 ASD sample sets, and 11 control sample sets. Because these samples need to be assayed in batches, although we have begun sample processing, we have not yet begun the molecular assays. We expect to get the assays underway in the Fall of this year (2021) and will likely request a no-cost extension to complete the work in 2023.

15. SUBJECT TERMS

Autism spectrum disorder, gastrointestinal, microbiota transfer therapy, transcriptomics, microbiome, metabolomics

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1. INTRODUCTION

The purpose of this study is to perform molecular analysis (transcriptomic and metabolomic assays) on samples (whole blood, serum, and stool) derived from 84 adults with autism spectrum disorder (ASD) undergoing microbiota transfer therapy (MTT), and 84 adults without ASD (controls), from an on-going CDMRP-funded clinical trial (James Adams, PI; Arizona State University) to identify mechanisms that underlie symptom improvement following MTT. In the subjects with ASD that receive MTT, whole blood, serum, and stool are collected at three time points: (1) baseline, (2) after 8 weeks, and (3) after 16 weeks, and assayed for gene expression and metabolite changes that occur over time. Profiles derived from whole blood, serum, and stool samples from individuals without ASD and who do not undergo MTT serve as 'normal' baseline transcriptomic and metabolomic profiles.

2. KEYWORDS

Autism spectrum disorder, gastrointestinal, microbiota transfer therapy, transcriptomics, microbiome, metabolomics

3. ACCOMPLISHEMENTS

- **What were the major goals of this project?**
  There are 7 tasks detailed on the SOW associated with this project. Task 1 requires procurement of the appropriate IRB and HRPO approvals. Tasks 2 and 3 describe sample processing, Tasks 4 and 5 describe acquisition of the molecular (transcriptomic and metabolomic) datasets; Task 6 describes metabolomic data analysis and visualization; Task 7 describes integrated omics data analysis.

- **What was accomplished under these goals?**
  To date, only Task 1: "Secure IRB and HPRO approvals to receive and use the specimens (human anatomical substances - HAS)" has been completed. Although part of the initial sample sets from 46 individuals (35 individuals receiving MTT and 11 controls) have been received in the PI's laboratory, samples processing, molecular assays, and data analyses described in Tasks 2-7 have not yet begun.

- **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?**
  Throughout the course of the next reporting period, we expect to receive most, if not all, of the remaining study samples. Throughout the period we will be processing the samples on hand and, as sufficient numbers of samples have been prepared and qc'd for batch assay, we will initiate the molecular data generation and analyses.

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

- **Changes in approach and reasons for change**
  Nothing to report.

- **Actual or anticipated problems or delays and actions or plans to resolve them**
  This project is entirely dependent on getting study samples (whole blood, serum, and stool) from Dr. Adams' clinical trial and therefore the delays Dr. Adams has experienced since March 2020 in being able to enroll and follow-up with participants in his study have impacted our ability to begin sample processing and data generation. Now that most of the relevant restrictions are easing, we anticipate that we can bring this project fully back online and begin receiving, processing, and assaying samples throughout the second reporting period (May 2021 through May 2022). We expect to ask for one year extension at the end of the second reporting period to complete the Tasks outlined in the SOW.

- **Changes that had a significant impact on expenditures**
  The inability to perform the lab work outlined in Tasks 2-5 over this last year has resulted in a significant reduction in expenditures during this reporting period. We anticipate that we will get back on track with expenditures in the second reporting period.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
  Nothing to report.

6. PRODUCTS

- **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 this project?**
  - **Name:** Stephen Walker
  - **Project Role:** PI
  - **Researcher ID:** 0000-0002-0732-2366
  - **Nearest person month worked:** 2
  - **Contribution to project:** Dr. Walker is responsible for project oversight and management.
  - **Funding Support:** this award

  - **Name:** Trang Simon
  - **Project Role:** Technician IV
  - **Researcher ID:** n/a
  - **Nearest person month worked:** 2
  - **Contribution to project:** Ms. Simon is responsible for sample handling/processing.
  - **Funding Support:** this award

- **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?**
  - **Organization Name:** Arizona State University
  - **Location of Organization:** Tempe Arizona
  - **Partner's contribution to the project:** Dr. James Adams provides samples (whole blood, serum, and stool) from participants in his CDMRP-funded clinical trial for this project.

8. SPECIAL REPORTING REQUIREMENTS

Nothing to report.

9. APPENDICES

Nothing to report.