

AWARD NUMBER: W81XWH-20-1-0738

TITLE: Gut Microbiome as a Predictor of Response to Chemotherapy in Metastatic Colorectal Cancer

PRINCIPAL INVESTIGATOR: Vikas Dudeja

CONTRACTING ORGANIZATION: University of Alabama, Birmingham, AL

REPORT DATE: October 2021

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development 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 2021		2. REPORT TYPE Annual		3. DATES COVERED 15Sep2020-14Sep2021	
4. TITLE AND SUBTITLE: Gut Microbiome as a Predictor of Response to Chemotherapy in Metastatic Colorectal Cancer				5a. CONTRACT NUMBER W81XWH-20-1-0738	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Vikas Dudeja E-Mail:dudejavikas@gmail.com, vdudeja@uabmc.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Alabama at Birmingham 701 20 th Street South Birmingham, AL 35294-0001				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development 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 The overall goal of this project is to evaluate whether gut microbiome can help predict response to cytotoxic chemotherapy in patients with metastatic colorectal cancer. Briefly, patients with measurable metastatic colorectal cancer will be enrolled. Gut microbiome samples will be collected before initiation of chemotherapy and after 8 cycles of chemotherapy. The study has following objectives. Primary Objectives: 1. Does gut microbiome composition at presentation predict response of metastatic colon and rectal cancer to the standard of care chemotherapy? Secondary Objectives: 1. What is the effect of chemotherapy treatment on gut microbiome? 2. Does change in gut microbiome correlate with response to chemotherapy? 3. Does tumor mutational composition correlate with gut microbiome? 4. Does gut microbiome composition at presentation predict progression free survival?					
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			19b. TELEPHONE NUMBER (include area code)
Unclassified	Unclassified	Unclassified	Unclassified	12	USAMRMC

TABLE OF CONTENTS

	<u>Page</u>
1. Introduction	4
2. Keywords	4
3. Accomplishments	4
4. Impact	6
5. Changes/Problems	7
6. Products	8
7. Participants & Other Collaborating Organizations	10
8. Special Reporting Requirements	12
9. Appendices	12

1. INTRODUCTION:

The overall goal of this project is to evaluate whether gut microbiome can help predict response to cytotoxic chemotherapy in patients with metastatic colorectal cancer. Briefly, patients with measurable metastatic colorectal cancer will be enrolled. Gut microbiome samples will be collected before initiation of chemotherapy and after 8 cycles of chemotherapy. The study has following objectives.

Primary Objectives:

1. Does gut microbiome composition at presentation predict response of metastatic colon and rectal cancer to the standard of care chemotherapy?

Secondary Objectives:

1. What is the effect of chemotherapy treatment on gut microbiome?
2. Does change in gut microbiome correlate with response to chemotherapy?
3. Does tumor mutational composition correlate with gut microbiome?
4. Does gut microbiome composition at presentation predict progression free survival?

2. KEYWORDS:

Colorectal cancer, chemotherapy, gut microbiome

3. ACCOMPLISHMENTS:

What were the major goals of the project?

The major goals of the project for the 1st year at UAB were:

- 1) Review and approval of the human studies by IRB and HRPO
- 2) Review and approval of animal studies by IACUC and ACURO
- 3) Recruitment of the 1st 13 subjects

The major goals of the project for the 1st year at the U Miami were:

- 1) Review and approval of the human studies by IRB and HRPO
- 2) Review and approval of animal studies by IACUC and ACURO
- 3) Recruitment of the 1st 7 subjects at the UAB

What was accomplished under these goals?

Despite hurdles imposed by the pandemic and the move of the initiating PI from U Miami to UAB, we have made significant progress.

At this time at the UAB site, we have achieved the following

1. Single site approval of the study
2. HRPO approval of the study
3. IACUC approval of the study
4. ACURO approval of the study
5. Hiring of the clinical research coordinator

At this time at the U Miami site, we have achieved the following

1. IACUC approval of the study
2. IRB approval of the study
3. IRB modification submission for the single site

We did face some significant challenges due to pandemic and other issues. For instance, we had gotten separate IRB approval for UAB and U Miami. However, after achieving these we were informed that DOD has moved to the single site IRB management. Thus, we had to go back to our IRBs and get approval for single site, which significantly delayed the launch of this study. However, we have recovered from this delay. The study is open at UAB and few patients have already been recruited and the U Miami is currently in their last stages of approval.

What opportunities for training and professional development has the project provided?

N/A

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?

Goals for the next reporting period

1. Recruitment of 32 patients in next 1 year.
2. Use of stool samples from 1st 8 patients in animals to understand the effect of stool transplantation on the tumor growth.
3. Microbiome analysis of patient samples.

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

We did face some significant challenges due to pandemic and other issues (transfer of the initiating PI from U Miami to UAB). For instance, we had gotten separate IRB approval for UAB and U Miami. However, after achieving these we were informed that DOD has moved to the single site IRB management. Thus, we had to go back to our IRBs and get approval for single site, which significantly delayed the launch of this study. However, we have recovered from this delay. The study is open at UAB and few patients have already been recruited and the U Miami is currently in their last stages of approval.

Changes that had a significant impact on expenditures

N/A

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

N/A

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:

- **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: Vikas Dudeja
Project Role: PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.2

Contribution to Project: Overall guidance, design and direction of the project
Funding Support: Billed to the grant

Name: Ana Karen Gutierrez Garcia
Project Role: Post doctoral fellow
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3

Contribution to Project: writing IACUC protocol, setting up models
Funding Support: Billed to the grant

Name: Utpreksha Vaish
Project Role: PI
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3

Contribution to Project: IRB, HRPO, develop systems
Funding Support: Billed to the grant

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

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: