

Platform Development for Patient Recruitment: The Cancer Microbiome and Metabolomics

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**Faculty**

Co- investigators:

<b>Name</b>	<b>Title</b>	<b>Institution</b>	<b>Department</b>	<b>Area of Expertise for this Project</b>	<b>E-mail / Phone</b>
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**Abstract**

Immune checkpoint inhibitors (ICIs) are playing a rapidly increasing role in the treatment of human malignancies. While these therapies are changing treatment paradigms, not all tumors respond to treatment, and resistance generally develops over time. Recent studies in both preclinical and clinical settings have shown that the human microbiome influences response to immunotherapy. Evolving data have shown that several tryptophan metabolites regulate immune cells and antitumor immune response. *Plasma levels of tryptophan metabolites depend on nutrition, but might also be regulated by tumor cells*

or the microbiome. Understanding associations between the microbiome, and tryptophan metabolites, and treatment response/resistance might, therefore, be vital to fully realize the potential of immunotherapy. Studies evaluating these factors in cancer patients are currently limited, and are particularly scarce in diverse patient populations. We propose to develop a **new** microbiome and blood biobank in patients receiving ICIs at Boston Medical Center, and use this new resource to examine *via interdisciplinary approaches and investigators* (from microbiome biology, to cancer, to chemistry to computational) *new hypotheses* concerning associations between certain tryptophan metabolites, the microbiome, and response to immunotherapy in diverse patient populations. Our specific aims are as follows:

1. To develop a blood and microbiome biobank to define microbiome signatures that hallmark response or resistance to checkpoint inhibitors in head and neck, and non-small cell lung carcinoma (NSCLC) patients treated at Boston Medical Center (having sizable numbers of patients in each category).
2. To utilize the biobank to explore the association between circulating tryptophan metabolites and response to checkpoint inhibitors in the above cancers. In addition to building banks useful for multiple other applications, our proposed ARC studies will lay the ground for future mechanistic investigations, and possibly guide new paths to therapy.

## Summary

We propose developing a blood and microbiome biobank, and performing a multi-dimensional analysis of microbiome and metabolic biomarkers of sensitivity and resistance in head and neck and NSCLC patients receiving treatment with checkpoint inhibitors at Boston Medical Center, an academic institution that serves a unique and unstudied population comprising 70% under-represented minorities. Our proposed ARC will collaborate closely with “Systems Biology Approaches to Microbiome Research ARC”, particularly for microbiome objectives of this project, and will leverage their expertise and developed methods and software to analyze and understand microbiome data. As described in our section on “Future Directions,” we anticipate that we will expand our platform and analyses to other cancer types, as well as to patients beyond Boston Medical Center.

## Trainees

pre- or post?	Name	PI’s Name	Program/Department
PhD student	Yue (Jason) Zhao	Dr. Evan Johnson	Bioinformatics

## pre-ARC Meetings and Workshops

Date	Discussion Topic/ Title of Talk	Discussion Leaders/ Presenters	Location/ Program or Meeting Title (e.g.,ASH, Russek Day etc)
1/31/2019	Discussion about objectives, approaches, and operational work flow of microbiome and IO therapy project	Dr. Kulke, Dr. Evan Johnson, Kiana Mahdavian, and Casey Simon-Plumb	BMC

3/19/2019	Discussion about ARC project and ARC grant proposal	Dr. Ravid, Dr. Kulke, Kiana Mahdaviani	BU Medical Campus
3/29/2019	Discussion about collaboration on metabolomics objectives of the ARC grant proposal	Dr. Norman Lee, Dr. Stephen Whelan and Kiana Mahdaviani	BU Charles river campus
4/8/2019	Discussion about tryptophan metabolite targeted metabolomics and IO therapy project	Dr. Norman Lee, Dr. Stephen Whelan, Dr. Kulke and Kiana Mahdaviani	BMC
4/10/2019	Discussion about development of a blood and microbiome biobank in collaboration with the Uganda Cancer Institute.	Dr. Kulke, Dr. Evan Johnson, Kiana Mahdaviani	BMC
4/24/2019	Discussion about ARC project and ARC grant proposal	Dr. Ravid, Dr. Kulke, Kiana Mahdaviani	BU Medical Campus

**Distribution of ARC participants (Core and non-core members):** Please list % of faculty from Charles River Campus vs. Medical Campus vs. other participants (e.g., industry), and within each % in different departments.

