Platform Development for Patient Recruitment: The Cancer Microbiome and Metabolomics

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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.