For Medical Research – Dr. Rytis Prekeris, Professor of Cell and Developmental Biology on the Anschutz Campus. The title of his proposal is ‘Mechanism of Midbody Inheritance and Signaling during Cell Proliferation and Differentiation’.

For Science and Engineering Research: Dr. Kai Yu, Assistant Professor of Mechanical Engineering at the CU Denver. The title of his proposal is ‘Liquid Crystal Elastomers as Artificial Muscles for Soft Robots’.

**BOB’S CORNER**

I am pleased to announce the two faculty members who have been chosen to submit their proposals for further consideration for funding to the Keck Foundation. We wish both well in their additional reviews by the Keck Foundation for awards to follow!

**RESEARCH CORNER**

The Fishbein laboratory focuses on developing biomarkers for prognosis and treatment of neuroendocrine tumors. Whereas precision medicine is a reality for the treatment of several cancers, significantly increasing progression-free survival in many cases, for neuroendocrine tumors (NETs) there are no prognostic or therapeutic precision targets. Our focus has been on NETs of the adrenal medulla and extra-adrenal ganglia called pheochromocytomas and paragangliomas (PCC/PGL), respectively. PCC/PGL are unique tumors in two ways. First, up to 40% of patients have a mutation in one of over 15 susceptibility genes in a variety of pathways. Second, the tumors hypersecrete catecholamines (or adrenaline) which can lead to hypertension, cardiovascular disease, stroke and even death. Once metastatic, PCC/PGL are associated with a 50% five-year survival rate and current treatments at best stabilize disease, but none are curative. Predicting who will develop metastatic disease has proven difficult as histopathologic scoring systems have not been validated. Patients with germline Succinate Dehydrogenase Subunit B (SDHB) mutations have an increased risk of malignant disease compared with the other susceptibility genes; but only half of patients with malignant PCC/PGL have an SDHB mutation. Thus, many patients have no known predictors. Given our inability to predict for and treat aggressive PCC/PGL and other NETs, it is critically important to identify molecular biomarkers to predict malignant disease and identify new therapeutic targets.

To this end, we have taken an integrative genomics approach across a variety of platforms both locally and through the collaborative effort with The Cancer Genome Atlas (TCGA) to analyze DNA and RNA from sporadic and hereditary PCC/PGL. Through these studies, we have identified several new drivers of tumorigenesis associated with clinically aggressive disease including somatic ATRX mutations and MAML3 fusion genes. We now are studying the functional consequences of these somatic alterations.
The gut microbiome seems to relate to almost every medical condition these days but its value in patients with cancer is a rapidly evolving area. In a recent issue of *Science*, the impact on cancer immunity may have important therapeutic implications.


The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients.

Matson V¹, Fessler J¹, Bao R², Chongsuwat T⁴, Zha Y⁴, Alegre ML⁴, Luke JJ⁴, Gajewski TF¹,⁴

**Author information**

1 Department of Pathology, University of Chicago, Chicago, IL 60637, USA.

2 Center for Research Informatics, University of Chicago, IL 60637, USA.

3 Department of Pediatrics, University of Chicago, IL 60637, USA.

4 Department of Medicine, University of Chicago, Chicago, IL 60637, USA.

**Abstract**

Anti-PD-1-based immunotherapy has had a major impact on cancer treatment but has only benefited a subset of patients. Among the variables that could contribute to interpatient heterogeneity is differential composition of the patients' microbiome, which has been shown to affect antitumor immunity and immunotherapy efficacy in preclinical mouse models. We analyzed baseline stool samples from metastatic melanoma patients before immunotherapy treatment, through an integration of 16S ribosomal RNA gene sequencing, metagenomic shotgun sequencing, and quantitative polymerase chain reaction for selected bacteria. A significant association was observed between commensal microbial composition and clinical response. Bacterial species more abundant in responders included *Bifidobacterium longum*, *Collinsella aerofaciens*, and *Enterococcus faecium*. Reconstitution of germ-free mice with fecal material from responding patients could lead to improved tumor control, augmented T cell responses, and greater efficacy of anti-PD-L1 therapy. Our results suggest that the commensal microbiome may have a mechanistic impact on antitumor immunity in human cancer patients.


**Precision medicine using microbiota.**

Jobin C¹.

**Author information**

1 Department of Medicine, Department of Infectious Diseases and Immunology, and Department of Anatomy and Cell Biology, University of Florida, Gainesville, FL 32611, USA.