**LUNG CANCER RESEARCH FOUNDATION**®
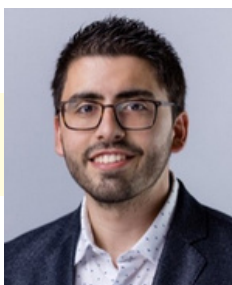
# RESEARCH GRANTS AWARDED IN 2023

# LEADING EDGE RESEARCH

### FRANCISCO EXPÓSITO, PHD
Yale University

*Investigating novel synthetic lethal vulnerabilities in EGFR-driven lung cancer*

*2023 William C. Rippe Award for Distinguished Research in Lung Cancer*

This project aims to understand how the loss of SETD2 hinders EGFR-driven tumor growth to leverage these findings to create new precision treatments for the treatment of patients with EGFR-mutant tumors.

### BENJAMIN MORRIS, PHD
University of Texas M.D. Anderson Cancer Center

*Deep whole genome sequencing of circulating tumor DNA for studying evolution and therapy resistance in small cell lung cancer*

This project will use cancer DNA collected from small blood draws to study how SCLC evolves following treatment and identify changes in cancer DNA and gene expression that drive resistance. The study will determine if resistant tumors are composed of one population of resistant cells or if multiple, hard to treat populations emerge after treatment to drive resistance.

# UNDERSTANDING RESISTANCE

### TREVER G. BIVONA, MD, PHD
University of California San Francisco

*Characterization and therapeutic targeting of a tumor-tumor microenvironment network promoting resistance to targeted therapy in lung cancer*

The overall goal of this project is to create an entirely new approach to treat lung cancer by developing a suite of precision therapies that are distinct in their mechanism of action against the tumor ecosystem and improve the effectiveness of current therapies against mutant EGFR, KRAS, and ALK as combination therapies, while critically maintaining safety and quality of life for patients. The work accomplished in this project could yield molecular treatments that better control, or potentially cure, lung cancer safely through improved precision medicine in the relatively near future.

### ANN PENDERGAST, PHD
Duke University School of Medicine

*Uncovering novel vulnerabilities to treat SCLC therapy resistance*

Small cell lung cancer (SCLC) is a highly aggressive neuroendocrine lung cancer that is typically metastatic upon diagnosis. The overall 5-year survival rate for SCLC patients is only ~7%, and has remained unchanged for over 30 years. Therefore, there is an urgent need to define the molecular mechanisms that promote metastatic SCLC in order to identify effective treatment strategies to treat this deadly cancer. The Pendergast laboratory recently found that pharmacologic inhibition of ABL kinases with ABL-specific inhibitors impairs SCLC metastasis in mouse models, resulting in prolonged animal survival. This proposal will evaluate whether ABL kinase inhibition sensitizes SCLC to therapies targeting stress response pathways, and/or to metabolic inhibitors.

# EARLY DETECTION & PRE-NEOPLASIA

## DARREN CHIU, MD, MMSC
Boston University

*The Spatial B Cell Landscape in Lung Squamous Premalignant Lesions*

Bronchial premalignant lesions (PMLs) develop in the airway from cellular and molecular changes, and they are precursor lesions of lung squamous cell carcinoma. While some PMLs progress to cancer, some of them regress spontaneously or remain stable. The presence and distribution of B cells in lung cancer has been associated with prognosis and survival, however, the role of B cells in the lung premalignancy is poorly understood. Using single cell sequencing technology and multiplex multiomic imaging, the study will identify B cell subpopulations in bronchial PMLs and characterize the spatial microenvironment that recruits and modulates B cells associated with PMLs severity and progression. The findings are expected to reveal new biomarkers for early diagnosis or interception of lung cancer.
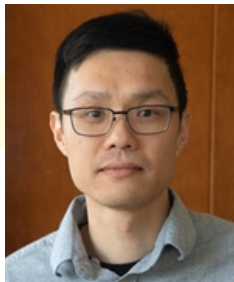
> " *LCRF funding was instrumental in allowing me to complete and publish the  project I was working on at the time. The project has fostered cross-institutional collaborations and a clinical trial. It provided support at a critical juncture so I can continue doing research. Now it serves as a springboard for me to compete for Federal funding with the results and publications I generated."*
>
> *Victoria Wang, MD, PhD*
> *University of California, San Francisco*
> *Two-time LCRF grantee*

# MINORITY CAREER DEVELOPMENT AWARDEES

## LLOYD BOD, PHD
Massachusetts General Hospital

*Harnessing B cell specific checkpoint molecules in lung cancer*

*2023 James B. Dougherty, MD Award for Scientific Merit*

Immunotherapy has transformed the paradigm of lung cancer treatment, yet its efficacy remains restricted, benefiting only a minority of patients—typically, two to four individuals out of every ten. Dr. Bod's research focuses on unraveling the functions of B cells, a critical component of the immune system. These cells are abundant in lung tissue and hold the capacity to assist T cells in their anti-cancer activities while directly combatting cancer cells themselves. This translational project's objective is to leverage genomics to identify and assess new molecules present on B cells, which could serve as innovative immunotherapy targets, thereby paving the way for new therapeutic strategies in lung cancer.

## LUIS PRIETO, PHD
Mayo Clinic

*Impact of senescent cells on lung tumorigenesis*
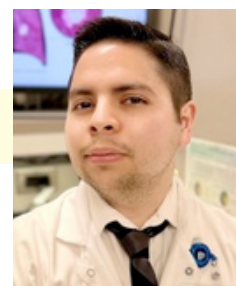
This study focuses on naturally occurring senescent (aging) cells to determine if they promote late-life development of lung cancer. Aging cells accumulate and promote the development of lung tumors by suppressing immune T cells. The next step will be to use treatments aimed at killing senescent cells to see if this effects the formation and/or growth of tumors.

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