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.

This project has two goals. The first one is to study a new antibody-drug conjugate in MET-altered lung cancer models. The researcher also plans to evaluate MET mutations that occur as a resistance mechanism. Knowing which mutations are driving resistance could potentially direct treatment.

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.

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.
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, we 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.

“The Spatial B Cell Landscape in Lung Squamous Premalignant Lesions”

DARREN CHIU, MD, MMSC
Boston University

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 PIETRO, 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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