LUNG CANCER RESEARCH FOUNDATION
Living. Breathing. Science.®

INVESTING IN THE FUTURE OF RESEARCH

LCRF funds novel **lung cancer research** that might otherwise go unfunded.

To date, we have funded **383** research grants, totaling **$36 million**.

Photo: Marcus Goncalves, MD, PhD
Weill Cornell Medical College
2017 LCRF Grantee

"Funding from the LCRF made a big impact on my career early on. It helped me explore new scientific ideas that serve as the foundation for the studies that we do today in the lab, obtain additional funding and pursue approaches to translate our research into the clinic for patients."

Katerina Politi, PhD
Cancer Biologist and Associate Professor
Yale Cancer Center
Chair, LCRF Scientific Advisory Board
Two-time LCRF grantee

The Lung Cancer Research Foundation (LCRF) is the leading nonprofit organization focused on funding innovative, high-reward research with the potential to extend survival and improve quality of life for people with lung cancer. LCRF's mission is to improve lung cancer outcomes by funding research for the prevention, diagnosis, treatment and cure of lung cancer.

Through its Scientific Grant Program, LCRF funds projects across the spectrum of basic, clinical and translational research. To date, LCRF has funded 383 research grants totaling $36 million, the highest amount provided by an organization dedicated to funding lung cancer research.

LCRF provides critical seed funding to investigators, helping establish proof of concept evidence to pave the way for additional funding from government and other sources.

ETIOLOGY/PATHOGENESIS

MICHAEL ZIMMERMANN, PhD

European Molecular Biology Laboratory

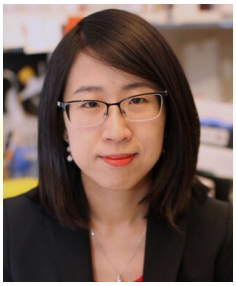
Identifying risk factors for lung cancer predisposition through systematic evaluation of environmental carcinogens' activation by the respiratory tract microbiota

2020 James B. Dougherty, MD Award for Scientific Merit

The human body harbors trillions of microbes (known as the human microbiome), which collectively encode many more genes than the human genome. These microbial communities colonizing different body surfaces play an essential role in human health and response to environmental factors. Numerous studies have linked changes in the microbiota composition to different diseases, such as the metabolic syndrome and cancer. Based on these observations and the fact that lung cancer prevalence was linked to altered respiratory tract microbiome compositions, Dr. ZImmermann hypothesizes that microbial strains with certain metabolic traits can be identified as predisposition risk factors for lung cancer.

CHENGCHENG JIN, PhD

University of Pennsylvania



Targeting the IL-1beta pathway for lung cancer treatment

Chronic inflammation is closely associated with lung cancer and plays a critical role in tumor progression, and metastases. However, the source of such inflammation has not been clearly defined and the contribution of specific cellular and molecular component of the immune system is yet to be elucidated. Interleukin 1beta (IL-1beta) has emerged as a key mediator of tumor-associated inflammation. Dr. Jin hypothesizes that selectively targeting the lung microbiota or the responding IL-1beta pathway can rewire the TME to reduce pro-tumorigenic inflammation while boost the anti-tumor immunity both at the baseline and in response to immunotherapies. The overarching goal of this study is to decipher the molecular mechanism by which active IL-1beta is generated in the lung TME, and to understand how IL-1beta shapes the tumor-associated immune response to affect lung cancer progression and response to immunotherapies.

ALICE BERGER, PhD

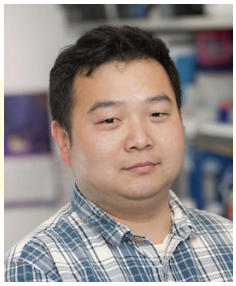
Fred Hutchinson Cancer Research Center

Novel strategies for therapeutic target discovery in lung cancer

Recent advances in understanding the human genome have led to successful new "precision oncology" for the treatment of lung cancer, such as the use of EGFR-targeted therapies in EGFR-mutant lung cancer. Discovering and applying these therapies has motivated a continued search for novel drug targets in these and other lung cancers. The foundation of these searches are high-throughput methods for genetic screening, but traditional target discovery experiments can only query a single gene's involvement in cancer. Some genes with redundant functions would not be identified in these studies. The goal of this project is to identify genetically redundant genes in the human genome and to identify gene pairs that are required for resistance to EGFR-targeted therapies. This work will directly help the tens of thousands of patients with EGFR-mutant non-small cell lung cancer.

ZHAN YAO, PhD

Memorial Sloan Kettering Cancer Center



Studies on the oncogenic function and mediation of drug resistance by ARAF in lung cancer

Despite the significant clinical benefit of epidermal growth factor receptor (EGFR, a receptor tyrosine kinase) inhibitors, primary and acquired resistance are commonly seen in lung cancer patients with EGFR activating mutations. Among those patients, ~20% tumors progress upon treatments by unknown mechanisms. By analyzing the genome sequencing data of the lung cancer patients with acquired resistance to EGFR inhibitors, Dr. Yao and his colleagues at MSKCC identified ARAF amplification as a new genetic event that may be responsible for the drug resistance. Current data suggest, in EGFR mutant lung tumors, ARAF amplification likely causes the drug resistance by activating RAS signaling.

Dr. Yao seeks to explore the detail functional consequences of ARAF activation of RAS in lung cancers and determine its role in the regulation of drug sensitivity. In addition, patient-derived xenograft models will be used to investigate therapeutic strategies for treating the ARAF-dependent drug resistance.

The cause, set of causes, or manner of causation of a disease or condition and its progression

WILLIAM LOCKWOOD, PhD
British Columbia Cancer Agency

SNF2 Histone Linker PHD RING Helicase as a novel tumor suppressor gene and risk factor in lung adenocarcinoma development

Through genetic analysis of lung tumors, Dr. Lockwood's group has recently uncovered the mutation of a gene that is located in a region linked to familial risk of lung cancer development. This gene is known to play a role in repairing damaged DNA, and he hypothesizes that its inactivation leads to increased gene mutations over time, increasing the risk of developing cancer. To test this, he will disrupt the gene in normal lung cells to determine if this allows them to transform into lung cancer. This study will determine whether this gene is associated with lung cancer susceptibility and development, and how this information can be used to improve screening aimed at the early detection of lung cancer in high risk patients.

JALAL AHMED, MD, PhD
Icahn School of Medicine at Mount Sinai

Targeting the tumor microenvironment to advance CAR T cell therapy for lung cancer

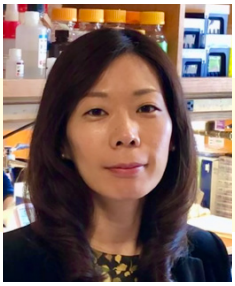
Chimeric antigen receptors (CARs) are engineered molecules that can redirect the killing activity of T cells to targets of interest and have had dramatic results in the treatment of other cancers such as leukemia. However, the application of this technology to lung tumors has remained challenging in part due to suppressive tumor microenvironments that are seen even at the earliest stages of human lung cancer.

Dr. Ahmed's study will work to demonstrate the potential of the CAR T platform to test novel combination therapies in lung cancer. His goal is to apply this model to further dissect the ways in which the tumor microenvironment blocks attack from immune cells, to test new CAR T cell combination therapies, and to test the safety and efficacy of several new CAR technologies that are under active development.

TARGETED THERAPIES

Drugs or other substances that block the growth and spread of cancer by interfering with specific molecules

HIDEKO ISOZAKI, PhD
Massachusetts General Hospital



Targeting APOBEC3A induction as a new therapeutic strategy to prevent acquired drug resistance in non-small cell lung cancer

The development of therapies that target oncogenic driver mutations has transformed the treatment of lung cancer. Despite notable progress in the design of successive generations of drugs with more potent activity and improved side-effect profiles, the inevitable development of acquired drug resistance continues to limit the clinical efficacy of these agents. Thus, there remains an urgent need for innovative therapeutic approaches to combat drug resistance. This project will test the hypothesis that preventing APOBEC-driven evolution of cancer cells treated with targeted therapies will prevent the development of acquired drug resistance.

LCRF funding supports advances *in lung cancer research such as:*

- Basic and clinical science driving development of targeted therapies.
- Identification of biomarkers for treatment resistance.
- Discovery of new immunotherapy treatments that prolong remission.
- Quadrupling advanced stage NSCLC 5-year survival rate in under 10 years.
- Support for world-wide research into all areas of unmet need in lung cancer.

READ MORE ABOUT LCRF-FUNDED RESEARCH AT LCRF.ORG/OUR-INVESTIGATORS

DISPARITIES

Preventable differences in opportunities to achieve optimal health that are experienced by disadvantaged populations

HILARY ROBBINS, PhD, MPH

International Agency for Research on Cancer

Risk prediction models to ensure equitable eligibility for lung cancer screening in minority populations

2020 William C. Rippe Award for Distinguished Research in Lung Cancer

Screening by low-dose CT (LDCT) can reduce lung cancer mortality, but research has largely neglected racial and ethnic minorities. Criteria for defining screening eligibility fail to acknowledge how lung cancer risk varies across racial and ethnic groups. This means a white individual and an African-American individual might have the same lung cancer risk, but only the white person might meet current guidelines for screening. The most promising solution is to base eligibility on individual risk calculated using a prediction model, but such models must be properly calibrated to perform just as well in racial/ethnic minorities as among whites. This study aims to develop lung cancer risk prediction tools so screening eligibility can be defined in a way that is fully equitable across racial and ethnic groups.

JOSHUA CAMPBELL, PhD

Vanderbilt University

Determining differences in immunotherapy outcomes and immunobiology in African American patients with NSCLC

Novel classes of cancer therapeutics work by activating the immune system, which in turn targets and kills cancer cells. These "immunotherapies" have had great success in treating some patients with advanced stage lung cancer. However, we do not fully understand why immunotherapy works for some lung cancer patients yet not for others. There is a major need to more fully characterize the immune system in lung cancer patients and determine the clinical and biological factors that are necessary for an immunotherapy to work effectively. This study will determine if there are significant differences in immunotherapy response and toxicity between African American (AA) patients and other populations and if molecular pathways associated with response to immunotherapy are similar or different between populations. Identifying molecular features associated with response in AA patients can lead to developiing new diagonostic biomarkers and potentially identify novel avenues of therapeutic development.

MARJORY CHARLOT, MD, MPH

University of North Carolina

Understanding the immune landscape of non-small cell lung cancer in African Americans

In the United States, 18% more deaths occur among Black men with lung cancer compared to White men with lung cancer. While recent advances in the treatment of lung cancer have led to significant improvements in survival, Black patients are less likely to be invited to participate in cancer research and as a result are less likely to have access to state-of-the art cancer treatments. Having a better understanding of lung cancer that includes the Black population and identifying opportunities to engage Black patients in research will likely help to reduce excess lung cancer deaths experienced by Black men. This project will study the immune landscape in tumor samples obtained from Black patients with lung cancer as well as strategies to enhance participation of Black patients with lung cancer in cancer research.

SUPPORTIVE CARE

NISHA MOHINDRA, MD

Northwestern University Feinberg School of Medicine

Development and implementation of 4R care sequences in patients with NSCLC receiving targeted therapies

This project's overall goal is to implement the systematic and innovative approach for care planning and delivery to improve side effect management, treatment adherence and supportive care for patients with non-small cell lung cancer (NSCLC) receiving targeted therapies. The improvement will be achieved via the 4R Care Sequence plans that will be used by patients, their caregivers and their care team. The 4R (Right Information and Right Treatment to the Right Patient at the Right Time) model is an innovative approach to personalized cancer care planning, team-based care delivery and patient /caregiver self-management for optimized outcomes and minimized treatment side effects and comorbidities.