CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160668

Project Title:
Pathogenesis and Early Progression of Lung Cancer

Award Mechanism:
Multi-Investigator Research Awards (Version 2)

Principal Investigator:
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Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

TITLE: Pathogenesis and Early Progression of Lung Cancer LAYPERSON'S SUMMARY In the United States, lung cancer is the leading cause of cancer, accounting for 30% of all cancer deaths. Texas is no exception, where lung cancer is equally sobering, due the state's unique demographics and the high prevalence of smoking in minority populations. Indeed, global trends, particularly in the developing world, imply a continued economic and personal cost of great proportion. Yet, intriguingly, amidst this bleakness is an opportunity for a transformation in preventative medicine and clinical care, born from recent high-profile discoveries and revolutions in molecular biology, data science, and clinical technologies. Investigators in our proposal have made integral contributions to all of these discoveries and have expertise in key technologies. Together these factors -- the pressing need to address lung cancer prevention and treatment, along with important recent discoveries and advances in molecular, computational and clinical science -- create the unparalleled opportunity for solving problems in lung cancer detection, diagnosis and clinical management. Providing solutions for a complex disease requires a collaborative and interdisciplinary approach. The common overall goals of our proposal provide a unifying foundation upon which our multi-disciplinary team can interact. Our proposal, Pathogenesis and Early Progression of Lung Cancer consists of investigators with deep scientific expertise and leverages the large volume of patients that visit three institutions in the Texas Medical Center (TMC) – UT MD Anderson Cancer Center (MDACC), Baylor College of Medicine (BCM), and Michael E. DeBakey Veterans Affairs Medical Center (VAMC). We expect this work will lead to significant advances in the diagnosis and treatment of lung cancer, by pursuing the following overarching themes (organized by project): a) discovering new layers of complexity among the populations of cells that comprise a tumor and the relationship of this complexity to patient outcome (Project 1); b) determining whether anti-tumor aspects of our immune system can be enhanced and used to predict outcome and improve treatment strategies (Project 2); c) using early changes in the genome of tumor cells to develop novel ways to diagnose metastasis to the lymph nodes, which serve as the gateway to more distant organs (Project 3); e) developing simple non-invasive blood tests for assessing risk of lung cancer development and implementing effective screening strategies and personalized treatments (Project 4). Adding to the significance of our overall application is the cohesive and inter-dependent nature of our projects. Knowledge and techniques to detect mutations in small portions of potentially complex mixtures of tumor cells (Projects 1 and 3), which could then be used for diagnosing the extent to which tumor has invaded the lymph nodes (Project 3). Complementing these investigations, detailed study of the

inflammatory process in tumors (Project 2) will be conducted with an ultimate goal of proposing translational treatment options based on the body's own native immune functions. For all projects, discovery of molecular events that are germane to the phenomena being studied become natural candidates for blood-based markers for early diagnosis and prediction of outcome patients with localized lung cancer (Project 4). While the specific proposals are designed for the study of lung cancer, the themes and paradigms that we will explore may be applied to other cancers. Tumor heterogeneity and genome-based diagnostics have been posited as important and possible, but only recently have revolutions in molecular biotechnology made them feasible. Leveraging the immune system to harness anti-tumor specificity is one of the most promising areas across the field of cancer research and has revolutionized lung cancer treatment. Finally, blood-based tests, or a liquid biopsy, based on circulating components from cancer cells or other markers have long been described as a holy grail of cancer detection and diagnosis, as well as prediction of tumor relapse, but only recently have become a distinct reality. Thus, successes of our project should impact research and patient prognosis for other cancer types, as well. Regardless of these bonus discoveries, however, ultimately our proposed project, if funded, will reduce the mortality of lung cancer and its burden on early stage patients and their families in Texas and the Nation.