CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110383

Project Title:
Dependence of small cell lung cancer on the basic helix-loop-helix transcription factors Ascl1 and NeuroD1

Award Mechanism:
Individual Investigator

Principal Investigator:
Cobb, Melanie H

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Lung cancer is one of the most common and deadly cancers worldwide. Small cell lung cancer (SCLC) accounts for about 20% of lung cancer. Lung cancer is designated as SCLC based on appearance and growth behavior. It grows aggressively and has poor prognosis long term due to development of drug resistance. New targeted SCLC therapies are needed. We propose to exploit the dependence of SCLC on two related proteins, NeuroD1 and Ascl1, that regulate gene transcription. These transcription factors are required during lung development but not in adults. SCLCs share some properties with cells that secrete hormones and neurotransmitters, thus are classified as neuroendocrine cancers. Many SCLC and other neuroendocrine tumors require Ascl1 or NeuroD1 to continue to grow. Therefore, the genes and signaling pathways controlled by these factors serve as rich leverage points for discovery of novel drugs for SCLC and other neuroendocrine tumors. To this end, we propose genetic, cell biological, and biochemical studies in cells and animals to identify downstream events controlled by Ascl1 and NeuroD1 in SCLC that are required for tumor growth and survival. In addition, the structural requirements of these factors essential for their functions in promoting tumor survival and metastasis will be identified. Through these diverse approaches we will strive to develop novel therapeutic strategies for primary and chemo-resistant SCLC. Results of our research should have broader disease importance because Ascl1 and NeuroD1 are improperly expressed and change genes expressed in other neuroendocrine tumors and cancers, such as tumors in the nervous system (e.g. glioblastoma), thyroid, prostate, and gut.