



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160307

Project Title:
Targeting Metastatic Pathways

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Over 90% of cancer-related deaths are due to metastasis and are not from the primary tumor. Presently, however, no treatment options are specific for metastatic sites. In large part, this lack of therapeutic development has been due to the complex and multi-step nature of tumor cell metastasis, which requires multiple genes to be up- or down-regulated. The principal aim of this grant is to explore one particular approach to intervening in metastatic tumor behavior through targeting a "master controller" of such behavior. In recent years, DNA mutations have been found to work in concert with much more widespread changes in cancer cells' chromatin (DNA+surrounding proteins). Such "epigenetic" alterations in the chromatin structure determines which genes are activated and which are silenced, and cancer cells are now known to undergo severe epigenetic changes at all stages of carcinogenesis. We have identified a specific protein, Aiolos, normally expressed only by blood cells; when expressed by lung cancer cells, it confers certain blood cell-like characteristics to the lung epithelium, particularly the ability to spread throughout the body via the blood stream. Aiolos appears to be a broad epigenetic controller; thus, we propose that this protein coordinates a widespread pro-metastatic gene expression profile. In this proposal, we will design strategies to countermand the effects of this protein through identification of upstream and downstream controllers of metastatic behavior. Additionally, we will create a synthetic editor of Aiolos-induced epigenetic markings. If successful, we will be able to specifically target a large number of metastasis-related genes simultaneously and alter tumor cell behavior.