



CANCER PREVENTION & RESEARCH  
INSTITUTE OF TEXAS

Award ID:  
RP130515

Project Title:  
Using microbial pathogens to probe weaknesses in human lung cancer

Award Mechanism:  
High Impact/High Risk

Principal Investigator:  
Alto, Neal

Entity:  
The University of Texas Southwestern Medical Center

Lay Summary:

Lung cancer is the most frequent cause of cancer deaths worldwide. Because most chemotherapeutic agents are non-specific and operate throughout the patient, it is critical to develop strategies that reduce overall toxicity and are highly specific at inhibiting cancer-causing pathways. To address this unmet need, I propose a new paradigm: cancer growth and proliferation can be selectively inhibited through cellular expression of bacterial toxins. It is now clear that bacteria have evolved over millions of years to potently and specifically inhibit human cell survival pathways of infected cells, but spare unintended targets. Therefore to unlock the potential of pathogenic bacteria to be used as tools to discover weaknesses in cancer, I have engineered a library of over 300 bacterial toxins, which will be used in high-throughput assays that are designed to cause death in Non Small Cell Lung Cancer (NSCLC) cells. Importantly, this strategy will complement ongoing efforts to identify new genes required for lung cancer cell survival with one major advantage: bacterial toxin activity will reveal novel rationale for drug design based on high potency and specificity while limiting side effects commonly observed in current therapeutic interventions.