



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP130212

Project Title:  
A molecularly targeted anticancer therapeutic strategy premised upon  
attack of aberrant Wnt pathway responses

Award Mechanism:  
Individual Investigator

Principal Investigator:  
Lum, Lawrence

Entity:  
The University of Texas Southwestern Medical Center

### Lay Summary:

The disregard of cancerous cells for environmental cues that enforce the orderly renewal of tissues in the adult body is a hallmark of every cancer type. The Wnt genes (pronounced "Wint") encode a large family of cell-to-cell signaling molecules that are essential to embryonic development and the regeneration of tissues lost from everyday wear and tear or traumatic injury. A number of genetic changes associated with cancer insidiously reprogram cells to continuously engage cell growth-promoting responses associated with Wnt stimulation regardless of whether or not these proteins are present. Free of this constraint on proliferation, these cells form tumors and can metastasize to other organ sites to disseminate disease throughout the body. Despite general consensus that Wnt-mediated signaling is essential to the formation of many cancers, there currently do not exist any drugs targeting this cellular process in clinical use. We have identified two previously unanticipated strategies for disabling Wnt signaling using chemicals thus enabling tests to determine the utility of this strategy as an anti-cancer therapeutic option. In this proposal we target genetic changes associated with forms of lung and colon cancer, and leukemia using next generation inhibitors of this pathway with drug-like properties that we have developed. The outcome of these studies will form the strategy for moving these chemical agents forward into clinical use in cancer management.