CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP130312

Project Title:
Development of optogenetic tools for cellular and in vivo manipulation of cancer pathways

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Rice, Luke

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

To determine if a protein might be a good target for new cancer therapies, researchers must first evaluate the protein's role in cancer development using cell culture and in vivo mouse models. To do so, cancer cells are often engineered to turn on or off the production of a target protein as a way to artificially set its level within the cell. This lets researchers conduct critical experiments – turning on levels of a protein suspected to be cancer-promoting, or turning off a protein to simulate the effects of applying a new inhibitory drug – that provide essential data needed to decide if a target merits embarking on the long and costly road of drug development. Currently, most ways to achieve this control require that cells or animals be given chemicals to turn expression on or off. While useful, these approaches have key limitations: it is very difficult to apply such chemicals only to a portion of a tumor, or quickly remove them after they are applied. To address these problems, we developed a new system that replaces chemical controllers with blue light, letting us selectively illuminate an area and control action by simply turning light on or off. We've accomplished this by engineering a natural sensory protein called EL222, normally used by ocean bacteria to look for blue light, into a new and powerful tool that can work in cancer cells. With this system, we have obtained exciting data showing that we can use EL222 to turn on protein expression over 200-fold when we shine blue light onto cells grown in laboratory incubators. We propose a series of experiments to demonstrate that our light-driven system can be broadly useful for cancer research, including tests of our ability to control protein expression in human tumors grown in in vivo mouse models. If successful, our approach opens new and powerful ways to validate new cancer proteins at the earliest stages of drug discovery, helping focus research efforts on the best new targets.