



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150334

Project Title:
Personalized Functionalization of Pediatric High Grade Glioma

Award Mechanism:
Individual Investigator Research Awards for Cancer in Children and Adolescents

Principal Investigator:
Deneen, Benjamin

Entity:
Baylor College of Medicine

Lay Summary:

A major effort in cancer research is focused on identifying genes directly responsible for promoting cancer progression (referred to here as "drivers"). The identification of driver genes and characterization of their function has been the moving force behind much of the recent progress in cancer treatment. Driver identification is particularly important for aggressive cancers such as pediatric high grade glioma (PHGG), which represents 10% of all pediatric brain tumors. Most children diagnosed with PHGG receive a dismal prognosis, as the disease carries a 5 year survival rate of <5%. Recent studies at the Baylor College of Medicine characterized the full spectrum of gene mutations present within PHGG tumor genomes. The challenge now is to develop efficient means to identify which of these mutant genes are directly responsible for PHGG. Discovery of such driver genes is a significant challenge given their large number and the fact that their activity is shaped by tumors' immediate surrounding environment within the body. To identify PHGG drivers, we will use a novel screening platform that employs (1) our robotics-driven collection of over 32,000 human genes, (2) an innovative strategy that enables rapid modeling of barcoded mutant genes based on the genomes of individual PHGG patient tumors and (3) a driver screening system for delivering these cancer gene candidates directly to the developing mouse brain. We will use these technologies to identify functional PHGG driver genes, providing unprecedented insight into driver gene networks responsible for this fatal disease. Moreover, these studies will illuminate new drug targets desperately needed by PHGG patients with no other effective treatment options. Our ultimate goal is to scale these efforts into a personalized clinical trial pipeline that would provide functional relevance of patient's tumor genome at the time of biopsy that would facilitate decisions on individualized patient therapy.