CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120256

Project Title:
Identify signature profile for sensitivity/resistance to PI3K pathway inhibitors to predict response to therapy in Glioblastoma.

Award Mechanism:
Individual Investigator

Principal Investigator:
Yung, W. K. Alfred

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Cancer treatment is entering an era in which information from the human genome project is being translated most readily into personalized treatment. The Cancer Genome Atlas Network (TCGA) recently described a robust gene expression-based molecular classification of glioblastoma multiforme (GBMs) into 4 distinct subgroups, and the next step is to determine if the molecular characteristics can be translated to therapeutic responsiveness. To achieve this, we need to develop efficient approaches to identify the role and function of candidate genes/pathways that are altered and characterize these molecular subgroups. The goal of this project is to develop a systematic platform for identifying the determinants of resistance/sensitivity of tumors treated with PI3K pathway inhibitors and accelerate the translation of this data into clinical therapeutic developments. Glioma Stem Cells (GSCs), possibly originated from transformed neural stem/progenitor cells, are considered to be responsible for the initiation, propagation, and recurrence of gliomas. The wide and continuous histological spectrum of gliomas with regard to proportions of the various differentiated and anaplastic cells may be dictated by the heterogeneous phenotype of the underlying GSCs. The central hypothesis of this proposal is that GSCs are responsible for repopulating tumor growth and thus the origin of recurrence, and GSC is a better model to understand mechanism of resistance and sensitivity to targeted therapy Therefore, this project will utilize a panel of well characterized GSC lines derived from patient tumor samples to develop a systematic and rational platform for identification of the genetic determinants leading to tumor response or resistance to therapy and to identify and validate predictors of therapeutic responsiveness by GBM molecular subtype that could potentially lead to patient stratification and selection.