CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120262

Project Title:
Functional and structural characterization of small chemical compounds that arrest glioma stem cell growth with high activity and specificity

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Glioma is a type of tumor that develops in the brain, and glioblastoma multiforme (GBM) is the most common, aggressive, and malignant form of glioma. Patients with GBM have a dismal prognosis, and most patients die within 15 months of being diagnosed. The current treatment for these tumors – surgical removal when possible followed by radiation and chemotherapy - is, unfortunately, ineffective at blocking eventual tumor regrowth. The ultimate goal of this project is to identify novel drugs to treat these insidious tumors and prevent them from regrowing. We have generated a mouse model of GBM by creating mutations in genes that are frequently mutated in human GBM. 100% of these mice develop GBM that mimics the human disease. Using this mouse model, we identified a small population of tumor cells that we believe are responsible for tumor growth. This population of cancer cells was used in a large-scale chemical compound screen to identify compounds that block the growth of these cells. From this screen, we have identified many promising candidates. This application proposes experiments designed to thoroughly characterize these potential drugs, to first identify precisely how they arrest cancer cell growth. Because this is a difficult and costly process, we plan to focus on a few of the most promising compounds and to use this experimental outline as a platform for future development of the additional compounds not included in this application. Included in this proposal is the plan to chemically modify these candidates to improve their bioavailability and efficacy as therapeutic drugs. These studies will not only provide valuable information regarding the molecular mechanisms underlying tumorigenesis, but could also lead to breakthrough drugs for treating this terrible disease; the identification of drugs that affect this particular population of cells holds the promise of significantly impacting the long-term survival rate of GBM patients.