CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100674

Project Title:
Small-molecule differentiation agent to target glioma stem cells

Award Mechanism:
Individual Investigator

Principal Investigator:
Hsieh, Jenny

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

The human brain has many hidden mysteries at the molecular and cellular and whole organ levels. Among these, tucked into the deep recesses of the brain, is the neural stem cell, which undergoes self-renewal to give rise to the hundreds of thousands of specialized neuronal and glial cells that are necessary to maintain cellular homeostasis and memory function in the brain. Converging evidence indicates that neural stem cells (or “glioma stem cells”) are the targets of heritable changes that lead to cancer. The “glioma stem cell hypothesis” dictates that rare cells with indefinite proliferation potential drive the formation and growth of brain tumors and are targets of transformation, and if true, might explain why many of the currently available drugs can shrink metastatic tumors, but effects are usually transient and often do not appreciably extend lifespan. Thus, drugs targeting glioma stem cells might result in more long lasting responses and even cures. My laboratory has identified a novel small-molecule family of 3,5-disubstituted isoxazoles from a stem cell-based high throughput screen of the UT Southwestern chemical compound library that suspends growth and differentiates human glioblastoma multiforme brain tumor stem cells, currently thought to be the cellular culprit underlying one of the most devastating of human malignancies. Our CPRIT project is focused on examining the effects of isoxazoles in glioma stem cells, with the long-term goal of translating a greater understanding of glioma stem cells and neurogenic small molecules in brain cancer into new therapeutic strategies, agents, and drugs designed to stop the growth of tumor cells in the brain. Over the course of three years, we will test isoxazoles in rodent glioma stem cells in vitro, determine the molecular mechanism underlying isoxazole-mediated resistance, and begin in vivo efficacy studies of isoxazoles towards differentiation-based therapy.