Award ID:
RP140399

Project Title:
Targeting Hypoxia in Breast Cancer With Highly Potent Small- Molecule Anticancer Prodrugs

Award Mechanism:
Individual Investigator

Principal Investigator:
Pinney, Kevin G

Entity:
Baylor University

Lay Summary:

While a number of new therapies are available to breast cancer patients, all too many will succumb to the disease, particularly for late stage metastatic presentation. Studies have shown increased cancer metastasis and a poor prognosis for individuals whose tumors have regions of low oxygen levels (hypoxia). Tumor hypoxia also represents an opportunity as a target for the selective delivery of anticancer agents. Our ultimate goal is to eliminate the mortality associated with metastatic breast cancer through treatment regimens with drugs that are designed to be non-cytotoxic until they reach hypoxic regions in tumors and become activated as highly potent anticancer agents. Success will lead to safer and more effective treatments for breast cancer patients who present with hypoxic, metastatic breast tumors. For this type of hypoxia-targeted therapy, it is highly desirable to utilize anticancer agents that are extremely potent against breast cancer, thus once they are selectively delivered to the malignant breast cancer cells they will be powerful enough to control or potentially reverse the course of the disease. We have discovered small-molecule benzosuberene- and dihydronaphthalene-based compounds that are among the most potent anticancer agents in their structural class. These anticancer agents will be synthesized as prodrug conjugates and investigated for their ability to selectively release the active anticancer agents and to delay tumor growth in hypoxic breast cancer animal models using state-of-the-art imaging. This project represents a collaboration between investigators with expertise in synthetic organic chemistry, biochemistry/cell biology and cancer imaging. In particular, success of this research will provide a new class of chemotherapeutics, which could rapidly be developed by a biotechnology company for near term clinical trials in Texas. This promises benefit both to the Texas economy, but most importantly, immediate hope for breast cancer patients.