CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
DP150074

Project Title:
Inhibitors of Hydrogen Sulfide Biosynthesis: Preclinical Development of Novel Colorectal Cancer Therapies

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
Hellmich, Mark

Entity:
The University of Texas Medical Branch at Galveston

Lay Summary:

Texas ranks third among all the states for the highest incidence and expected deaths due to colorectal cancer. For advanced disease, chemotherapy with or without a drug called Cetuximab (which blocks epidermal growth factor receptor signaling) helps the patient live longer. However, up to 50% of patients with colorectal cancer have mutations in genes called KRAS or BRAF that make their tumor resistant to the drug Cetuximab. Currently, doctors do not recommend using the drugs like Cetuximab if the patient's tumor has one of these genetic mutations. Therefore, treatment options are limited for almost half of all patients with advanced colorectal cancer. We have recently discovered that an enzyme called cystathionine-beta-synthase or CBS, which produces the gas called hydrogen sulfide (H2S), is expressed at higher levels in colorectal cancer than normal tissue. Normally, H2S regulates blood pressure and the growth of new blood vessels. We have discovered that CBS-produced H2S stimulates the metabolism and growth of colon cancers. Importantly, if we reduce CBS levels in tumor cells or block the production of H2S, the tumor cell metabolism slows and their growth is inhibited. We are proposing to make new and better drugs that block CBS and H2S production, which can be used alone or in combination with existing anti-cancer drugs, to improve the lives of patients with colorectal cancers particularly those with tumors that express KRAS or BRAF mutations.