CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140685

Project Title:
Modulation of Autophagy: Phase II Study of Vorinostat Plus Hydroxychloroquine vs. Regorafenib in Refractory Metastatic Colorectal Cancer (mCRC)

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Colorectal cancer is a leading cause of cancer death in the United States and Texas. Patients with distant metastases have a 5-year survival rate of 13%, indicating the need for better treatments to improve survival in patients with advance colorectal cancer. For the past ten years, scientific evidence has shown treatments that inhibit factors that promote the blood supply (angiogenic inhibition) leads to improved survival in patients suffering with advance colorectal cancer. However, the benefit of angiogenic inhibition is modest once patients have failed initial angiogenic inhibition. Therefore, we need to discover other pathways in colorectal cancer proliferation that we can target so patients can live longer. Cancer cells can become immortal when the natural process of programmed cell death, known as apoptosis, is diminished. Pre-clinical colon cancer models have shown that vorinostat can induce apoptosis, a process that is further enhanced by preventing autophagy (or degradation of the cell) with hydroxychloroquine, a cheap anti-malarial drug. Combining vorinostat with hydroxychloroquine is tolerable in early phase clinical trials and preliminary data shows efficacy of this combination in patients with advance colorectal cancer. This proposal will help determine the efficacy of autophagy inhibition with vorinostat and hydroxychloroquine when compared to regorafenib, a predominant anti-angiogenic inhibitor, the current approved therapy albeit very modest benefit, in a randomized phase II clinical trial of patients with advance colorectal cancer once they have failed or refractory to all therapies used to treat their cancer. Along with efficacy, we will evaluate toxicity and identify biomarkers that correlate with efficacy of both classes of agents in patients with advance colorectal cancer. Findings from this study will identify a new class of cost effective therapy that improves survival for patients with refractory advance colorectal cancer.