CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100890

Project Title:
Advanced (Pre-IND) Preclinical Development of a Novel, Highly Promising, Human Therapeutic Protein For the Treatment of Hepatocellular Carcinoma

Award Mechanism:
Individual Investigator

Principal Investigator:
Georgiou, George

Entity:
The University of Texas at Austin

Lay Summary:

Hepatocellular carcinomas (HCC) account for most liver cancers and constitute one of the highest mortality malignancies. Only 10-20% of these cancers are operable and mean survival rates for the rest is only 8 months. There are between 250,000 and one million deaths globally from HCC per year and the most recent therapeutic for liver cancer, only increased survival by 3 months. Chemotherapy has not resulted in prolonged survival, nor has combination chemotherapy been more effective. Thus, there is a clear unmet need for developing novel and effective chemotherapeutic agents for HCC. About 80% of liver cancers and a large fraction of melanomas have lost the ability to synthesize the amino acid L-Arginine a necessary protein building block. Extensive studies have revealed that depletion of L-Arginine in serum results in selective tumor killing while leaving normal tissues unharmed. The Georgiou team at UT Austin has employed state of the art protein engineering techniques to develop a novel therapeutic enzyme that destroys L-Arginine in serum. Georgiou and coworkers further carried out pharmacological optimization of this enzyme for L-Arginine depletion therapy of cancer. This candidate therapeutic enzyme (termed TEA20) is non-immunogenic, stable and has proven efficacious in preclinical studies. The objective of the present grant is to pursue the advanced preclinical development of this drug leading to it testing in humans in a clinical trial. Further improvements in the potency of this drug and also detailed investigations of the consequences of L-Arginine depletion on cancer cells will be carried out. FDA-compliant large scale production of this drug will be undertaken followed by rigorous toxicological analysis, as required in preparation for clinical trials.