CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120393

Project Title:
Preclinical Development of Texaphyrin-Platinum Conjugates

Award Mechanism:
Individual Investigator

Principal Investigator:
Sessler, Jonathan

Entity:
The University of Texas at Austin

Lay Summary:

Platinum chemotherapy is a frontline therapy for many cancers, including non-small cell lung cancer, mesothelioma, and ovarian cancer. For treatment with cisplatin, patients typically receive anti-nausea medication. They are also hydrated with physiological fluids so as to minimize the extent of kidney toxicity. The reason for this treatment protocol is that cisplatin, while effective, is highly non-selective and very toxic. This makes it difficult to administer a curative dose. This problem is compounded when the patient has developed a platinum resistant cancer. This happens all too often and is major contributing factor to the low (5-20%) 5-year survival rates in many cancers treated with platinum. There are many mechanisms of resistance involved, with the major ones being i) poor Pt uptake or retention and ii) inactivation of p53 mediated apoptosis (the process by which the cancer cells undergo programmed cell death when exposed to a drug). The Sessler group at the Univ. of Texas (UT) Austin has specialized in developing cancer-specific anticancer agents (called texaphyrins) for the last 20 years. Recently, in conjunction with platinum biologist Prof. Siddik (Subcontractor) at MD Anderson Cancer Center, they have created a texaphyrin-platinum hybrid designed to deliver large amounts of platinum specifically to a cancerous site. This lead system proved free of Pt resistance in cell culture studies. Initial animal studies, carried out in collaboration with Prof. Van Den Berg (Co-PI) of UT Austin's Department of Pharmacy, established that mice are capable of tolerating twice the amount of our texaphyrin-platinum hybrid when compared to the conventional platinum drug. This is a very promising result that is expected to lead to improved clinical outcomes, including greater survival rates. The goals of this study are to i) advance this first generation system towards clinical trials, ii) understand its mechanism of action, and iii) generate yet-improved drug leads.