GRANT SNAPSHOT

2014 Pancreatic Cancer Action Network – Rising Tide Foundation – Gateway Clinical Continuation Research Grant

Grantee:	David Boothman, PhD
Institution:	University of Texas Southwestern Medical Center
Research Project:	*Exploiting an NQO1 'kiss of death' for pancreatic cancer therapy*
Award Period:	July 1, 2014 – June 30, 2017
Amount:	$1,000,000

Biographical Highlights

Dr. Boothman received his PhD from the Department of Microbiology at the University of Miami. After a post-doctoral fellowship at the Dana-Farber Cancer Institute, Harvard, in the lab of Dr. Arthur B. Pardee, he joined the Department of Radiation Oncology, University of Michigan, as an Assistant Professor. In 1993, he moved to the Department of Human Oncology at the University of Wisconsin, Madison, and was promoted from Assistant to Associate Professor, with tenure. In 1998, he became Professor of Pharmacology and Radiation Oncology, Case Western Reserve University, where he served as Associate Director for Basic Science. Currently, Dr. Boothman is the Robert B. and Virginia Payne Professor of Oncology and Pharmacology, and Associate Director for Translational Research, Simmons Cancer Center, UT Southwestern at Dallas. He also co-directs the "Program in Cell Stress and Cancer Nanomedicine." His laboratory focuses on understanding cellular stress responses that promote cancer and resist treatment. His lab explores the roles of DNA damage and repair that alter metabolism and the tumor microenvironment. Dr. Boothman's project builds upon studies supported by his 2012 Pancreatic Cancer Action Network Innovative Grant, generously funded by the George & June Block Family Foundation. The new grant will be funded with the Rising Tide Foundation and Gateway for Cancer Research.

Project Overview

Previously, Dr. Boothman and his colleagues identified a protein, NAD(P)H:quinone oxidoreductase1 (NQO1), that is highly expressed in pancreatic cancer cells compared to normal tissue, including the pancreas. Dr. Boothman's novel treatment strategy involves exploiting NQO1 expression to metabolize the drug, β-Lapachone (β-Lap, clinical form ARQ761), that then leads to accumulation of hydrogen peroxide specifically in cancer cells. Excess hydrogen peroxide hyper-activates the DNA repair enzyme, PARP1, causing cell death.

Pre-clinical studies at UT Southwestern indicated that β-Lap was efficacious against pancreatic cancers in mice. Dr. Boothman and colleagues will investigate and develop noninvasive technology to examine the effects of β-Lap on glucose metabolism in various mouse models of pancreatic cancer alone and in combination with the chemotherapy drugs, gemcitabine and nab-paclitaxel. Importantly, this grant will support a clinical trial in collaboration with Dr. Shaalan Beg (UT Southwestern) and Dr. Daniel Laheru at Johns Hopkins to test β-Lap and gemcitabine/nab-paclitaxel in 20 patients to determine the safety and feasibility of this novel combination therapy.