GRANT SNAPSHOT

2012 George & June Block Family Foundation – Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	David Boothman, PhD
Institution:	University of Texas, Southwestern Medical Center
Research Project:	*NQO1-mediated 'Kiss of death' Targeted Therapy for Pancreatic Cancer*
Award Period:	July 1, 2012 – June 30, 2014
Amount:	$200,000

Biographical Highlights

Dr. Boothman received his PhD from the Department of Microbiology at the University of Miami. After a post-doctoral fellowship at Dana-Farber Cancer Institute, Harvard, 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, Case Comprehensive Cancer Center. Currently, Dr. Boothman is Professor of Pharmacology, Associate Director for Translational Research, Simmons Cancer Center, UT Southwestern at Dallas, where he also co-directs the "Program in Cell Stress and Cancer Nanomedicine." Dr. Boothman has served on numerous peer-review study sections and has published more than 120 peer-reviewed papers. He holds the Robert B. and Virginia Payne Professorship in Oncology. His laboratory focuses on changes in cellular features to promote cancer, cells with special abilities to form and reform tumors and resist treatment, and the microenvironment that surrounds and infiltrates tumors. Additionally, he is looking at a novel class of drugs that can be activated within the body to preferentially attack cancer cells and spare normal cells.

Project Overview

In his project generously funded by the George & June Block Family Foundation, Dr. Boothman is searching for ways to exploit characteristics unique to pancreatic cancer cells, to formulate a treatment strategy that selectively targets cancer cells without harming healthy cells. Pancreatic cancer cells express high levels of a protein called NAD(P)H:quinone oxidoreductase 1 (NQO1); in fact, NQO1 levels in pancreatic cancer cells can be 100-times higher than in normal pancreas. Thus, NQO1 is an attractive therapeutic target. Dr. Boothman has already tested a novel drug, called beta-lapachone (ß-lap), that is 'metabolically activated' into toxic reactive oxygen species by NQO1. Then, the drug induces cell death only in cancer cells expressing NQO1.

However, preliminary studies have indicated that some of the damage caused by ß-lap can be reversed or repaired in cancer cells. To circumvent this, Dr. Boothman proposes to study the combination of ß-lap with drugs that block DNA repair pathways, and determine if this increases effectiveness in pancreatic cancer cells and mouse models of the disease. Excitingly, ß-lap is currently in early Phase I clinical trials to test for side effects in humans, paving the way for future treatment regimens that include ß-lap alone or in combination.