GRANT SNAPSHOT

2012 Bonnie L. Tobin – Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	Peter Espenshade, PhD
Institution:	Johns Hopkins University
Research Project:	*SREBP Pathway as a Target for Pancreatic Cancer Therapy*
Award Period:	July 1, 2012 – June 30, 2014
Amount:	$200,000

Biographical Highlights

Dr. Espenshade graduated summa cum laude with a degree in Molecular Biology from Princeton University in 1990. He received his PhD in 1997 from Massachusetts Institute of Technology where he worked on understanding how secretory vesicles form. For the past 15 years, Dr. Espenshade has investigated how cells measure the supply of essential molecules and adapt their physiology to changes in this supply. This work began as a postdoctoral fellow with Nobel laureates Drs. Michael Brown and Joseph Goldstein at UT-Southwestern Medical Center in Dallas with studies on regulation of cholesterol homeostasis and has expanded to include questions of how cells adapt to hypoxia. In 2002, Dr. Espenshade joined the Department of Cell Biology at Johns Hopkins University School of Medicine where he is now an Associate Professor. He is an Established Investigator of the American Heart Association and former Burroughs Wellcome Fund Career awardee.

Project Overview

Among the hallmarks of pancreatic tumors is the ability to grow and survive under very low oxygen and low nutrient conditions. Previous studies suggest that a process called autophagy overcomes the low nutrient availability. However, autophagy cannot compensate for low oxygen, since oxygen is necessary for the production of fat and cholesterol, key building blocks for all cells.

Dr. Espenshade therefore hypothesizes that pancreatic cancer cells circumvent the low oxygen conditions by turning on protein pathways necessary to make new fats and cholesterol. The membrane-bound transcription factor (a protein that controls new gene expression) sterol regulatory element binding protein (SREBP) is a master regulator of these mechanisms. In close collaboration with Anirban Maitra, MD (2004 Pancreatic Cancer Action Network – AACR Career Development Award recipient and member, Scientific Advisory Board), Dr. Espenshade will test whether low oxygen conditions directly activate SREBP, and then determine whether inhibition of SREBP prevents the development and growth of pancreatic cancer in several mouse models of the disease. The strategy of chemically inhibiting SREBP has been proven successful in models of heart disease, so drugs have already been developed that are known to be functional and safe.