GRANT SNAPSHOT

2013 Samuel Stroum – Pancreatic Cancer Action Network – AACR Fellowship

Grantee:	Andrew Aguirre, MD, PhD
Institution:	Dana-Farber Cancer Institute
Research Project:	*Validation of Novel KRAS Synthetic Lethal Targets in Pancreatic Cancer*
Award Period:	July 1, 2013 – June 30, 2014
Amount:	$45,000

Biographical Highlights

Andrew Aguirre is a fellow in hematology/oncology at Massachusetts General Hospital and Dana-Farber Cancer Institute. He was an undergraduate at the University of Michigan and then earned MD and PhD degrees from Harvard Medical School. His graduate work focused on developing mouse models of pancreatic ductal adenocarcinoma in the laboratory of Dr. Ronald DePinho. Andrew completed a residency in internal medicine at the Massachusetts General Hospital. He is devoted to a career as a physician-scientist, with a clinical and research focus on gastrointestinal malignancies, particularly pancreatic cancer. He is currently a postdoctoral research scientist under the mentorship of Dr. William Hahn at Dana-Farber Cancer Institute and the Broad Institute, and is utilizing functional genomics approaches to identify novel therapeutic strategies in pancreatic cancer.

Project Overview

Previous studies have revealed that the gene *KRAS* is mutated in the majority of pancreatic cancer cases. *KRAS* gene mutation leads to the expression of a hyperactive KRAS protein that is a driving factor in the development and progression of the disease. Therefore, blocking the expression or activity of this protein is a tempting strategy to slow or stop the growth of the tumor. However, previous efforts have been unsuccessful at directly targeting mutant KRAS.

Dr. Aguirre and colleagues have utilized a genome-wide screening approach to identify which other genes can be blocked to selectively kill *KRAS* mutant cells. The aptly named *Project Achilles* seeks to discover the “Achilles heel” vulnerability of pancreatic cancer cells that have *KRAS* mutation. So far, Dr. Aguirre and colleagues have systematically turned off the expression of numerous genes and determined which ones, in the presence of *KRAS* mutation, lead to the death of pancreatic cancer cells, but do not affect cells that have normal *KRAS*. For his Fellowship grant funded in memory of Samuel Stroum, Dr. Aguirre proposes to further analyze these candidate genes, and determine whether they are indeed effective at slowing or stopping the growth of pancreatic cancer cells in a dish or in a mouse model of the disease. Finally, Dr. Aguirre will find out whether small pieces of genetic material can be delivered into mouse pancreatic tumors to target the genes found to most impact the growth and survival of the *KRAS* mutant cells. Through this technology, Dr. Aguirre and colleagues ultimately hope to establish the translational potential of therapeutic gene silencing in human pancreatic cancer.