GRANT SNAPSHOT

2009 Seena Magowitz – Pancreatic Cancer Action Network – AACR Pilot Grant

Grantee:	George A. Calin, MD, PhD
Institution:	University of Texas, MD Anderson Cancer Center
Research Project:	Roles of MicroRNAs and Ultraconserved Genes in Pancreatic Cancers
Award Period:	July 1, 2009 – June 30, 2011
Amount:	$200,000

Biographical Highlights

Dr. Calin received both his MD and PhD degrees from Carol Davila University of Medicine in Bucharest, Romania, where he also served as an Assistant Professor in Gastroenterology. He completed cancer genomics training at University of Ferrara, Italy and then in 2000 became a postdoctoral fellow at Kimmel Cancer Center in Philadelphia, PA, where while working in Dr. Carlo Croce laboratory, made the discovery linking microRNA genes to cancer. Subsequently, he held research and teaching positions at Thomas Jefferson University, Philadelphia and Ohio State University, Columbus. Currently, Dr. Calin is an Associate Professor in Experimental Therapeutics at MD Anderson. Dr. Calin's research focuses on the roles of microRNAs and other non-coding RNAs in cancer initiation and progression, mechanisms of cancer predisposition, and new RNA therapeutic options.

Project Overview

One of the most unexpected and fascinating recent discoveries in molecular oncology involves the interplay between abnormalities in both protein coding genes (PCGs) and non-coding RNAs (ncRNAs), including short miRNAs and ultraconserved genes (UCGS) (which remain unmodified in sequence during millions of years of evolution), in causing the initiation, progression and spread of cancer. Growing evidence demonstrates that miRNAs can work as tumor suppressors (blocking the malignant potential) or oncogenes (activating the malignant potential). However, the pathogenetic mechanisms of the final steps of tumorigenesis (i.e., metastases in adjacent or distant sites) for pancreatic ductal adenocarcinoma (PDAC), which is the most lethal form of cancer in the Western world, is still largely unknown.

The long-term goal of this project, which is funded in memory of Seena Magowitz, is to decipher the roles of miRNAs and UCGs during the metastatic process of PDAC. To achieve this goal, three different types of investigations will be undertaken. First, the genome-wide expression of both miRNAs and UCGs will be profiled by microarray and real-time PCR from a set of normal and tumor samples from the same patients, and from enriched malignant cells dissected under the microscope. This will result in a list of differentially expressed ncRNA genes. Then, using computer-assisted experiments, the expression of these three categories of genes will be correlated and a list of negative correlations will be obtained, suggestive of gene expression regulation. Second, plans are to analyze interactions between miRNAs and UCGs, and miRNAs and messenger RNAs of protein coding genes, and find new regulatory networks of genes significant for PDAC tumorigenesis. Third, the proved interactor pairs will be tested in pancreatic cancer cells for biological effects, including cell death and proliferation, showing how important these regulatory networks are during pancreatic tumorigenesis. Results of the study will provide new insights into the molecular mechanisms and signal transduction pathways altered in PDACs, and also offer opportunities for identifying new molecular markers and potential therapeutic agents.