# GRANT SNAPSHOT

## 2009 Constance Williams – Pancreatic Cancer Action Network – AACR Pilot Grant

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| Grantee: | Brian Lewis, PhD |
| Institution: | University of Massachusetts Medical School |
| Research Project: | Involvement of micRNAs in Kras-Induced Pancreatic Tumorigenesis |
| Award Period: | July 1, 2009 – June 30, 2011 |
| Amount: | $165,000 |

## Biographical Highlights

Dr. Brian Lewis is a two-time grant recipient of the Pancreatic Cancer Action Network. He was awarded a Career Development Award in 2006 for his research on the relationship between notch signaling and pancreatic cancer. Dr. Lewis earned his PhD in human genetics and molecular biology from Johns Hopkins University, and completed postdoctoral training at the National Institutes of Health and Memorial Sloan-Kettering Cancer Center. In 2003, he joined the Program in Gene Function and Expression at the University of Massachusetts Medical School as an Assistant Professor. His lab focuses on identifying correlations between specific genetic changes, tumor behavior, and cell signaling pathways.

Dr. Lewis's involvement in pancreatic cancer research results from his recognition of the urgent need that exists in speeding scientific discovery and understanding, and making a positive difference in the lives of patients and families impacted by the disease.

## Project Overview

Pancreatic ductal adenocarcinoma (PDAC) develops through the progression of precursor lesions called pancreatic intraductal neoplasms (PanINs). As the disease progresses, these lesions show increasing structural, molecular and genetic alterations. The earliest known genetic alteration, present in 90% of PDAC cases, involves mutations in Kras2. The fact that Kras mutations occur early in pancreatic cancer lesions suggests that they contribute to pancreatic tumor formation.

MicroRNA (miRNA) is a class of small non-protein-coding RNAs that are altered in pancreatic cancer. Preliminary data suggest that an activated Kras molecule alters the expression of several miRNAs in primary pancreatic ductal epithelial cells, the presumed cell of origin for PanINs and PDAC. However, we have an incomplete understanding of how Kras gene mutations contribute to pancreatic tumor initiation and the role of miRNAs in this relationship.

Dr. Lewis's project, which is funded in memory of Constance Williams, is designed to answer the following two key questions. First, are miRNAs required for Kras to enhance the proliferation and survival of pancreatic ductal epithelial cells, and for the ability of these cells to form tumors? Second, do individual miRNAs mediate Kras-induced cell transformation and tumor development?

The findings from this project will generate new insights into the mechanisms by which Kras initiates the formation of pancreatic tumors, and the functional roles of microRNAs in this process. With this new knowledge, we will better understand the molecular mechanisms involved in pancreatic cancer. In addition to advancing knowledge about the biology of pancreatic cancer, an improved understanding of the connection between miRNAs and Kras-induced pancreatic tumorigenesis will help guide the development of new therapeutic approaches for the disease.