GRANT SNAPSHOT

2010 Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Alec Kimmelman, MD, PhD
Institution:	Dana-Farber Cancer Institute
Research Project:	DNA Repair and the DNA Damage Response in Pancreatic Cancer
Award Period:	July 1, 2010 – June 30, 2012
Amount:	$200,000

Biographical Highlights

Dr. Kimmelman earned his MD and PhD from The Mount Sinai School of Medicine in New York and then remained to complete his internship in Internal Medicine and residency in Radiation Oncology. Subsequently, he joined Harvard Medical School, first as a clinical fellow, then instructor and more recently as Assistant Professor. Dr. Kimmelman also is an attending physician in Brigham and Women's Hospital and Dana-Farber Cancer Institute. He serves as an ad-hoc reviewer on the editorial boards of several leading scientific journals, including *Oncogene*, *Genes and Development*, and *Clinical Cancer Research*. His own research has been published in *Genomics, Oncogene*, *Molecular Cellular Biology*, *Cancer Research*, *Cancer Cell, Science*, and *Nature*.

Dr. Kimmelman's longstanding research interests derive from the recognition that the Ras oncogene and K-Ras mutations are a nearly universal event in pancreatic cancer. Also, as a practicing radiation oncologist specializing in gastrointestinal malignancies, he has unfortunately been witness to the devastating effect of pancreatic cancer. Work in his laboratory focuses on understanding the pathogenesis of pancreatic cancer and uses genetically engineered mouse models of pancreatic cancer, as well as cell culture based systems, to study the disease. One particular priority is to explore the DNA damage response in pancreatic cancer and how this may relate to therapeutic resistance. The ultimate hope is that these findings can be rapidly translated to the clinic.

Project Overview

Despite a better understanding of the molecular characteristics of pancreatic cancer cells, researchers have struggled to comprehend the failure of chemotherapy, radiation therapy, or targeted drugs to effectively treat this disease. Dr. Kimmelman shed light on this mystery by identifying pancreatic cancer cells' dependence on DNA repair proteins.

Dr. Kimmelman's experimental approach was an extensive screening method to identify which genes were pivotal to cancer cells' survival. He determined that silencing of several genes within the DNA repair family caused the death of pancreatic cancer cells. Cells are equipped with DNA repair proteins to fix damage to their DNA, caused either randomly, by external agents such as chemotherapy, or by the overall genomic instability caused by cancer. Dr. Kimmelman's preliminary data suggest that pancreatic cancer cells may be "addicted" to the activity of their DNA repair machinery, suggesting that the cells might be susceptible to its inhibition. Therefore, he proposes to further investigate the role of DNA repair machinery in pancreatic cancer, and determine whether proteins within this family could serve as a therapeutic target.