GRANT SNAPSHOT

2009 Larry Kwicinski – Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Maxence V. Nachury, PhD
Institution:	Stanford University School of Medicine
Research Project:	Role of the Primary Cilium in the Initiation of Pancreatic Cancer
Award Period:	July 1, 2009 – June 30, 2011
Amount:	$100,000

Biographical Highlights

Dr. Nachury received his PhD in Molecular and Cellular Biology from the University of California, Berkeley in 2001 and completed his postdoctoral studies in tumor biology and angiogenesis at Stanford University and Genentech. Currently, he is an Assistant Professor at Stanford University School of Medicine, Department of Molecular and Cellular Physiology. Dr. Nachury's research focuses on the primary cilium, a once-obscure cellular organelle recently "re-discovered" for its role in a number of signaling pathways. Defects in cilium biogenesis have been found to lead to a variety of hereditary disorders. The goal is to characterize these disorders at the molecular and cellular levels to gain insight into the basic mechanisms of primary cilium biogenesis and to discover novel ciliary signaling pathways.

Dr. Nachury has had a longstanding interest in pancreatic cancer since losing his maternal grandmother to the disease 20 years ago. His recent move to Stanford Medical School enables him to bring together a range of experts in cancer research, cell biology and biochemistry in order to foster a synergistic understanding of diseases linked to the primary cilium.

Project Overview

In this funded project, which is being supported in memory of Larry Kwicinski, Dr. Nachury aims to define the connection between the loss of primary cilia, Kras and the development of pancreatic ductal adenocarcinomoa (PDAC). Mutations in the Kras oncogene are present in nearly all cases of PDAC. In fact, Kras appears to serve as a master switch in the transformation of the thin layer of tissue (the epithelium) of the pancreas and the acquisition of PDAC. Remarkably, research demonstrates that mutations in the Kras oncogene alone are sufficient to initiate major molecular pathways of disease progression. However, the general mechanisms by which Kras signaling recruits these diverse oncogenic pathways is not clearly understood.

Previous research by Dr. Nachury suggests that the primary cilium suppresses the development of PDAC but that its assembly is restrained during the initiation and progression of the disease. These initial observations will be further explored in the funded project. The general approach is twofold. First, to examine whether the loss of the primary cilium contributes to and accelerates the development of PDAC; that is, to determine if there is a causal relationship between the loss of this organelle and the development of pancreatic cancer. Second, to characterize the mechanism by which Kras suppresses cilium assembly and the molecular consequences of this loss. The long-term objective is to develop targeting strategies that will restore the assembly of primary cilia in patients with pancreatic cancer.