GRANT SNAPSHOT

2013 Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	Timothy Wang, MD
Institution:	Columbia University
Research Project:	*Dclk1 in pancreatic tumorigenesis*
Award Period:	July 1, 2013 – June 30, 2015
Amount:	$200,000

Biographical Highlights

Dr. Wang is the Silberberg Professor of Medicine and Chair of the Division of Gastroenterology at Columbia University Medical Center. He graduated from Williams College, received his MD from Columbia College of Physicians & Surgeons, followed by clinical training at Washington University, St. Louis and Harvard/Massachusetts General Hospital. Dr. Wang is a member of the American Society for Clinical Investigation and Association of American Physicians, chair of the Research Policy Committee for the American Gastroenterology Association, and a Senior Deputy Editor for *Cancer Prevention Research*. He is the principal investigator of a National Cancer Institute Tumor Microenvironment Network program, and Director of Research for the Columbia University Pancreas Center. His research is primarily focused on the role of inflammation and stem cells in gastrointestinal cancer. He was the first to show that overexpression of interleukin-1β was sufficient to induce gastric carcinogenesis, and Barrett's esophagus, and chronic pancreatitis in mice. He is the author of more than 200 peer-reviewed publications.

Project Overview

There is not yet a consensus in the field about which types of cells within the pancreas have the capacity to become cancer cells. Different from embryonic stem cells, cancer stem cells are the cells from which the tumor originates. Decades of research has shown that an activating mutation in the gene K-Ras promotes pancreatic cancer initiation and progression. However, in genetically engineered mouse models of pancreatic cancer, mutation of K-Ras alone is insufficient to drive cancer formation. Instead, K-Ras mutation has to occur in cells that also have an inactivating mutation in a tumor-suppressor gene, such as p53, facilitating cancer-like changes in the cells.

Dr. Wang plans to investigate whether a protein called doublecortin like kinase-1 (Dclk1) can serve as an identifier of pancreatic cancer stem cells. Moreover, he hypothesizes that the introduction of mutant K-Ras into cells that already express Dclk1 may lead to tumor growth and progression, even in the absence of mutant p53 or other altered tumor suppressor genes. To address this, Dr. Wang and his colleagues will compare the progression of tumors in mice with pancreatic cells expressing (a) Dclk1 and mutant K-Ras, (b) Dclk1, mutant K-Ras, and mutant p53, or (c) mutant K-Ras and mutant p53. The research team will also assess Dclk1 expression in human and mouse pancreatic cancer tissue samples. Finally, if Dclk1 expression is indeed necessary for the initiation of pancreatic tumors, Dr. Wang will determine whether blocking the expression or activity of this protein could stop or slow the growth of tumors. The identification of Dclk1 cells as the potential origin of pancreatic cancer, and Dclk1 as a potential therapeutic target, might offer novel insights into the pathogenesis of pancreatic cancer.