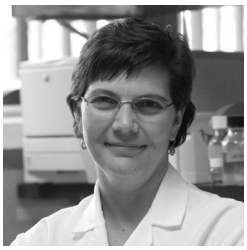
GRANT SNAPSHOT

2010 The Randy Pausch Family – Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	Diane Simeone, MD
Institution:	University of Michigan, Ann Arbor
Research Project:	Targeting Notch Signaling in Pancreatic Cancer Stem Cells
Award Period:	July 1, 2010 – June 30, 2012
Amount:	$200,000



Biographical Highlights

Dr. Simeone is Division Chief of Gastrointestinal Surgery, Professor of Surgery and Molecular and Integrative Physiology, Associate Chair for Research, Department of Surgery, and Surgical Director of the Multidisciplinary Pancreatic Cancer Clinic at University of Michigan. She holds the Lazar Greenfield Endowed Professorship in Surgery.

Dr. Simeone received her MD from Duke University Medical School in Durham, North Carolina and completed her General Surgery residency training at the University of Michigan Medical Center. She is the principal director of a research laboratory that is funded by the National Institutes of Health. Her basic science laboratory investigates mechanisms of pancreatic growth regulation and molecular events important in the development and progression of pancreatic adenocarcinoma.

Dr. Simeone is an associate member of the Early Detection Research Network, an NCI-funded initiative to identify and validate early detection biomarkers for the diagnosis of pancreatic cancer. She has been included in the Best Doctors of America (2005-2010), Best Surgeons in America (2007-2010) and America's Top Doctors for Cancer (2010). She is on the editorial boards of several leading scientific journals, including *Pancreatology* and *Journal of Gastrointestinal Surgery*, and serves as an advisor to multiple leading cancer research organizations.

Project Overview

Dr. Simeon is planning a clinical trial that specifically targets cancer stem cells (CSC) within a pancreatic tumor population. Her group has identified protein markers to differentiate these cells, which are highly aggressive and resistant to chemotherapy and radiation.

Dr. Simeon's studies show that CSCs depend on the activity of the molecule Notch, and are susceptible to its inhibition. Notch is a potent signaling molecule previously determined to function during embryonic development of various organs, including the pancreas, and recently identified as reactivated in pancreatic cancer. The proposed clinical trial will treat patients after surgery with the standard chemotherapy gemcitabine, in combination with a drug that targets Notch. Patients will be assessed for changes in disease-free and overall survival, and blood and tumor samples will determine if the presence or activity of CSCs decreases under these treatment conditions. This trial marks the first attempt to directly target the especially dangerous and resilient CSC population within pancreatic tumors.