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GRANT SNAPSHOT

2013 Pancreatic Cancer Action Network – AACR Pathway to Leadership Grant

Grantee:	Costas Lyssiotis, PhD
Institution:	Harvard Medical School
Research Project:	*Exploration and Targeting of Metabolic Dependencies in Pancreatic Cancer*
Award Period:	July 1, 2013 – June 30, 2018
Amount:	$600,000

Biographical Highlights

Dr. Lyssiotis obtained his bachelor's degree in chemistry and biochemistry from the University of Michigan and his PhD in chemical biology at The Scripps Research Institute in La Jolla, CA. In 2010, he joined the laboratory of Lewis Cantley, PhD at Harvard Medical School as the Amgen fellow of the Damon Runyon Cancer Research Foundation. He is currently a senior postdoctoral fellow in Dr. Cantley's laboratory at Weill Cornell Medical College. His research is focused on understanding the biochemical pathways and metabolic requirements that enable pancreatic tumor growth and, in particular, how this information can be used to design targeted therapies to treat this dreadful disease. For the initial phase of the project outlined in his grant proposal, Dr. Lyssiotis will be co-mentored by Dr. Cantley and Alec Kimmelman, MD, PhD, recipient of a Career Development Award from the Pancreatic Cancer Action Network in 2010.

Project Overview

Like all cells in the body, pancreatic cancer cells depend on the nutrients we consume to grow and survive. Treating cancer by targeting the way that malignant cells take in and use such nutrients (their metabolism) has emerged as a highly promising therapeutic strategy. However, because normal cells and cancer cells often require the same energy sources and metabolic pathways, designing effective metabolism-based cancer therapies has been challenging. In 2012 and 2013, Dr. Lyssiotis was a lead author on two papers in the prestigious journals *Cell* and *Nature* uncovering new roles for the mutated protein K-Ras as a master regulator of pancreatic cancer metabolism. Importantly, these studies have revealed new therapeutic targets and suggested new ways to treat pancreatic cancer.

In this proposed project, Dr. Lyssiotis will further evaluate the dependence of pancreatic cancer cells on the nutrients glucose (sugar) and glutamine (a prevalent amino acid, or building block of proteins). Since K-Ras has proven to be an elusive target, Dr. Lyssiotis will explore therapeutic targets downstream of K-Ras. Specifically, he will focus on determining how mutant K-Ras instructs pancreatic cancer cells to break down these two essential nutrients and how the energy derived is used to build DNA and to defend against harmful reactive oxygen species. Dr. Lyssiotis aims to use his understanding of these newly identified pancreatic cancer-specific metabolism pathways to develop innovative targeted therapies that selectively eliminate diseased cells.