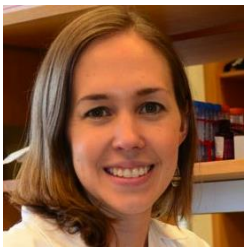
GRANT SNAPSHOT

2014 Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Kathryn Wellen, PhD
Institution:	University of Pennsylvania
Research Project:	*Understanding metabolic control of the pancreatic cancer epigenome*
Award Period:	July 1, 2014 – June 30, 2016
Amount:	$200,000

Biographical Highlights



Dr. Wellen graduated from the College of William and Mary in 2000. She received her PhD from Harvard University in 2006, working on obesity-linked inflammation and diabetes. Her postdoctoral work was conducted with Craig Thompson, MD, at University of Pennsylvania, where she sought to identify mechanisms linking changes in cellular metabolism with signaling pathways. Dr. Thompson is a member of the Pancreatic Cancer Action Network's Scientific Advisory Board. She started her independent laboratory at the University of Pennsylvania in 2011. Dr. Wellen was nominated for this award by Celeste Simon, PhD, recipient of a 2013 Innovative Grant from the Pancreatic Cancer Action Network. Dr. Wellen's current research focuses on elucidating mechanisms of metabolic control over the cancer cell epigenome.

Project Overview

Epigenetics is a process by which cells carefully regulate how and when particular genes get expressed. Deregulation of cellular epigenetics is essential for normal cells to transform into cancer cells. The mechanisms that cause epigenetic alterations in cancer cells are poorly understood, however, and insight into these mechanisms would facilitate the design of more specific therapeutics. Recently, evidence has emerged showing that epigenetic modifications are regulated by cellular metabolites (substances produced by nutrient breakdown in the cell).

The most commonly mutated gene in pancreatic cancer, KRAS, is thought to influence metabolic pathways within the cancer cells. Dr. Wellen and colleagues showed that expression of mutant KRAS indeed changes levels of metabolites in the pancreas cells, even during precancerous stages of progression. Dr. Wellen's proposed research plan will address the hypothesis that mutant KRAS causes cells to shift the balance of cellular metabolites, resulting in an altered epigenetic state that facilitates tumor cell growth. This hypothesis is based on findings that changes in the availability of one particular metabolite – acetyl-CoA – has dramatic effects on one type of epigenetic modification known as histone acetylation. The objective of Dr. Wellen and her colleagues' work is to investigate the mechanisms linking KRAS activation to the regulation of histone acetylation and to functionally test the importance of KRAS-driven acetyl-CoA production and histone acetylation on gene expression, tumor development, and tumor growth. Results of this study could pave the way toward innovative new strategies to target pancreatic cancer, exploiting the interface between metabolism and epigenetics.