GRANT SNAPSHOT

2014 Celgene Corporation – Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	George Miller, MD
Institution:	New York University School of Medicine
Research Project:	*Regulation of Pancreatic Tumorigenesis by Necroptosis*
Award Period:	July 1, 2014 – June 30, 2016
Amount:	$200,000

Biographical Highlights

Dr. Miller is an Associate Professor at NYU School of Medicine with appointments in the Departments of Surgery and Cell Biology. He performs roughly 100 complex operations in patients with liver, bile duct, or pancreatic cancer annually. Nevertheless, 80% of his effort is dedicated to basic and translation research in these diseases. He received his medical degree from McGill University in Quebec, then underwent his research and clinical fellowship training at NYU and Memorial Sloan-Kettering.

His lab is studying inflammation and the inflammation-cancer paradigm within the liver and pancreas. He is interested in numerous aspects of the biology of the pancreatic tumor microenvironment and its influence on causing mutations in cancer cells. He has been awarded several competitive grants, and has published exciting work in high impact journals.

Project Overview

Cancer cells are widely believed to die via a controlled organized process called “apoptosis,” a method of programmed cell death which produces cellular fragments called apoptotic bodies that get engulfed by specialized cells to avoid inflammation. Chemotherapies are thought to promote apoptosis whereas evasion of apoptosis is widely regarded as a basic modality cancer cells use for survival. By contrast, necrosis is a haphazard form of cell death – often the result of acute traumatic injury – and has widely been regarded as the biologic foil to apoptosis.

“Necroptosis” is a recently described novel method of cell death which denotes organized cellular necrosis. Necroptosis requires the co-activation of proteins called RIP1 and RIP3 kinases as its key machinery which co-associate to form the “necrosome” complex. However, the importance of necroptosis in limiting cellular viability and proliferation in pancreatic cancer has not been investigated. Dr. Miller and his colleagues’ preliminary work suggests that pancreatic cancer cells express the intermediates necessary for necroptosis and die more commonly via necroptosis than apoptosis. Further, chemotherapy treatment accelerates necroptotic cell death. Based on these data, the research team postulates that necroptosis is a central mechanism governing pancreatic cancer cellular demise. Since the role of necroptosis in limiting tumor progression has not been thoroughly investigated in pancreatic cancer, this proposal could have impact on both understanding pancreatic cancer cell biology and on the development of novel therapeutics.