GRANT SNAPSHOT

2014 Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	David DeNardo, PhD
Institution:	Washington University in St. Louis
Research Project:	*Origins and Impact of Macrophages in Pancreatic Cancer*
Award Period:	July 1, 2014 – June 30, 2016
Amount:	$200,000

Biographical Highlights

Dr. DeNardo earned a bachelor's degree in biology from Willamette University in Salem, Oregon, and then went on to receive his PhD from Baylor University in Houston. He underwent his postdoctoral training at the University of California, San Francisco, and then was recruited to Washington University in St. Louis as an assistant professor in 2011. Dr. DeNardo has a strong background in studying tumor immunology and in studying tumor-associated macrophages, and has assembled the expertise needed for key research areas for this application.

Project Overview

A key feature of pancreatic tumors is a dense microenvironment of various cell types that surround and are integrated among the cancer cells. One of the prominent cell types is tumor-associated macrophages, or TAMs. Studies conducted in genetically engineered mouse models that are programmed to develop pancreatic cancer have demonstrated that TAMs are critical drivers of tumor progression, metastasis (spread), and drug resistance. In addition, the presence of high numbers of these TAMs has been shown to correlate with poor clinical outcomes in patients with pancreatic cancer. Therefore, TAMs are considered an attractive target for slowing or stopping the growth of pancreatic tumors.

The classical assumption has been that TAMs are recruited from cells in the blood, which are continuously generated in the bone marrow. This assumption has been the basis for several clinical trials targeting macrophage recruitment. However, using novel techniques to track these immune cells, Dr. DeNardo and his colleagues found that pancreatic tumors are often heavily infiltrated with macrophages derived from cell division rather than being recruited from the blood. He thus hypothesizes that resident proliferating TAMs are critical early mediators of tumor inflammation and drivers of tumor metastasis. Dr. DeNardo and his research team will test this hypothesis using a combination of 1) mouse models of pancreatic cancer in combination with unique cellular tracing to follow TAMs, and 2) assessment of proliferating TAMs in human pancreatic cancer tissue samples to determine their impact on patient outcomes. Results from these studies may be critical for guiding patient selection or identifying alternative targets to improve responses to macrophage-targeted therapies.