GRANT SNAPSHOT

2013 Abby Sobrato – Pancreatic Cancer Action Network – AACR Innovative Grant

Grantee:	Yves Boucher, PhD
Institution:	Harvard Medical School
Research Project:	*Targeting Desmoplasia in Pancreatic Cancer to Improve Drug Efficacy*
Award Period:	July 1, 2013 – June 30, 2015
Amount:	$200,000

Biographical Highlights

Dr. Boucher did his undergraduate studies and graduate studies in Canada at the Université Moncton and Université Laval, respectively. After completing his PhD in Experimental Pathology, he performed his postdoctoral studies at Carnegie Mellon University in Pittsburgh, PA. Dr. Boucher joined the faculty of Harvard Medical School as an Instructor in 1991, and is currently an Associate Professor of Radiation Oncology. He is also a Principal Investigator and Director of the Morphology and Immunohistochemistry Core in the Edwin L. Steele Laboratory at Massachusetts General Hospital. Dr. Boucher's research over two decades has provided insight into (a) how the tumor vasculature and interstitial matrix affect drug delivery to cancer cells and (b) how interstitial matrix and vascular basement membrane remodeling influences cancer cell migration, and blood and lymphatic vessel invasion. He has recently begun examining strategies to improve drug delivery in pancreatic cancer.

Project Overview

The tumor microenvironment in pancreatic tumors is formed by a dense desmoplasia, or growth of fibrous connective tissue. The desmoplasia serves to protect the tumor. Due to its density, the desmoplasia exerts physical pressure on the blood vessels in pancreatic tumors, blocking blood supply and causing the cancer cells to exist in low-oxygen, or hypoxic, conditions. Because most chemotherapeutic drugs are administered intravenously, the poor blood supply to pancreatic tumors leads to insufficient drug delivery, contributing to the tumors' resistance to treatment.

Dr. Boucher proposes to attack the desmoplasia in pancreatic tumors by two approaches. First, he will test whether a medicine designed to treat high blood pressure, telmisartan, could open up some of the tumor blood vessels in a mouse model of pancreatic cancer. Also, a cell type known as macrophages may be able to chew up some of the desmoplastic tissue. Therefore, Dr. Boucher will treat the mice with a drug called FGK45 that stimulates a distinct macrophage subpopulation and causes an infiltration to the tumor. Dr. Boucher and his colleagues will perform experiments to determine whether telmisartan and FGK45 are successful at opening the blood vessels and recruiting macrophages to the tumor environment. Finally, the research team will introduce intravenous chemotherapeutic drugs to the mouse, with the expectation that relieving the pressure on the blood vessels and diminishing the desmoplasia will allow better drug delivery to the tumor itself, and therefore better effectiveness at killing the cancer cells. If any of these approaches is successful, these results will form the foundation for future clinical trials in pancreatic cancer led by their clinical collaborators.