



Research

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GRANT SNAPSHOT

2009 Paul Mitchell – Pancreatic Cancer Action Network – AACR Career Development Award

Grantee:	Marina Pasca di Magliano, PhD
Institution:	University of Michigan Health Systems, Ann Arbor
Research Project:	Notch Signaling in Pancreatic Cancer Initiation and Progression
Award Period:	July 1, 2009 – June 30, 2011
Amount:	\$100,000



Biographical Highlights

Dr. Pasca di Magliano holds a joint appointment at the University of Michigan in the Divisions of Surgical Oncology, Section of General Surgery, and Cell and Developmental Biology. She earned her B.S. in 1996 at University of Napoli, Italy, before going on to receive her PhD in 2002 at the Institute for Molecular Pathology in Vienna, Austria, and completing postdoctoral training at University of California Diabetes Center in San Francisco. Her research

focuses on the formation and progression of pancreatic cancer, with a focus on signaling pathways that are activated during carcinogenesis and how these signaling pathways mediate the interactions of tumor cells with components of the tumor stroma (non-tumor cells that expand in response to tumor-cell-derived stimuli, and allow the tumor to grow, invade surrounding tissues and metastasize). Her work also explores the link between inflammation and pancreatic cancer.

Dr Pasca di Magliano became aware of the impact of pancreatic cancer when a childhood friend's mother succumbed to the disease at a very young age. Years later, after hearing a talk about pancreatic cancer, she decided to dedicate her research career to this field.

Project Overview

Pancreatic cancer develops through a series of precursor lesions known as Pancreatic Intraepithelial Neoplasia or PanINs. PanINs are characterized by the presence of a mutated form of the Kras gene and, in advanced lesions, by loss of tumor suppressor genes. Cell signaling pathways that are important during embryonic development but are normally inactive in most adult cells are reactivated in PanINs and in pancreatic cancer.

In this project, which is funded in memory of Paul Mitchell, Dr. Pasca di Magliano focuses on the role of the Notch signaling pathway in pancreatic cancer. Previous research shows that genes that constitute the Notch pathway get reactivated at high levels in pancreatic cancer. However, more research is needed to more fully understand the role that Notch signaling has on the onset and progression of pancreatic cancer.

Dr. Pasca di Magliano plans to more fully examine this relationship to determine whether inhibition of Notch signaling would block tumor development and progression in pancreatic cancer.

Moreover, she will study the interactions between Notch signaling and other signaling pathways that are important for pancreatic cancer initiation and progression, and use genetic strategies to regulate the Notch signaling pathway. In order to identify new potential therapeutic targets, it is essential to understand the contribution of different genes to cancer formation. Inhibition of Notch signaling is currently being tested in clinical trials for other human malignancies but its potential for preventing and/or treating pancreatic cancer remains unknown. The funded project is expected to not only enhance understanding of the biology of pancreatic cancer, but also have strong therapeutic implications.