



Name of Institution: The University of New South Wales, Pancreatic Research Group, Ingham Institute for Applied Medical Research

Project Title: *Circulating Pancreatic Stellate Cells in Pancreatic Cancer*

Principal Investigator: Professor Minoti Apte OAM

Grant: Round 1 Innovation Grant 2015

Background:

Pancreatic cancer has very poor outcomes due largely to the fact that it tends to spread (metastasise) early. Prof Apte's previous research has focussed on pancreatic stellate cells being non-cancerous cells within the microenvironment surrounding pancreatic cancer cells. Her previous research found these pancreatic stellate cells:

- in metastatic cancer deposits;
- had spread to distant sites from the original (primary) cancer; and
- help cancer cells to grow and spread (metastasise) to other sites in the body.

Prof Apte postulated that these pancreatic stellate cells can be captured in circulation as they spread from the primary cancer. The aim of this research was therefore to isolate these circulating stellate cells and investigate how they might influence cancer progression and respond to cancer treatments.

The Research:

1. **Develop a reliable isolation technique for the detection of circulating pancreatic stellate cells:** Prof Apte successfully developed a reliable isolation technique for the detection of circulating pancreatic stellate cells.
2. **enumerate and characterise circulating tumour cells and circulating pancreatic stellate cells:**
 - (a) **in prospectively---collected blood samples from patients before and after chemotherapy/surgery:** Prof Apte recruited eight patients and isolated the first ever circulating pancreatic stellate cells from their patient blood samples.
 - (b) **in an orthotopic model of pancreatic cancer before and after treatment with therapy targeting HGF/c---MET pathway, with and without gemcitabine:** Prof Apte successfully:
 - developed a technique for the collection of blood from the portal vein;
 - isolated circulating tumour and pancreatic stellate cells from the mouse model;



- demonstrated that there were larger numbers of circulating tumour cells found in portal vein blood compared to cardiac puncture samples; and
- demonstrated that the volume of the primary pancreatic tumour correlates directly with the number of portal vein circulating tumour cells.

The Impact:

Prof Apte reported that the most important research finding produced by this Project funded by the Avner Pancreatic Cancer Foundation thus far is that circulating pancreatic stellate cells can indeed be isolated in the blood of patients with pancreatic cancer. Furthermore, as these pancreatic stellate cells are likely important in the formation of metastases, Prof Apte's findings open the door to a new avenue of research in the prevention of pancreatic cancer metastases.

Prof Apte effectively isolated circulating tumour cells in the portal vein blood of pancreatic cancer carrying mice. She positively demonstrated that the number of circulating tumour cells in the portal vein is higher than that found in cardiac puncture samples and that the number of such cells in the portal vein correlates with the size of the tumour. Prof Apte has reported that this is also an important finding as it lends further strength to the concept of portal vein sampling in the clinical setting to maximise the probability of successfully obtaining circulating tumour cells for analysis.

As a result of this Project funded by the Avner Pancreatic Cancer Foundation:

(a) Prof Apte has been awarded additional research funding for this or related studies:

- Hirshberg Foundation, Pancreatic Cancer –targeting Stromal--- Tumour Interactions to Inhibit Tumour Growth and Metastasis (2016-2017) - **\$26, 130**; and
- Accelerator Grant awarded by the Avner Pancreatic Cancer Foundation in 2017 based on the preliminary data produced as a result of this Project - **\$735,815**.

(b) Prof Apte has published the following journal article:

Circulating Pancreatic Stellate (Stromal) Cells in Pancreatic Cancer-a Fertile Area for Novel Research. Pang TCY, Xu Z, Pothula S, Becker T, Goldstein D, Pirola RC, Wilson JS, Apte MV. *Carcinogenesis*. 2017 Jun 1;38(6):588-591. doi: 10.1093/carcin/bgx030



(c) Prof Apte and her team have won the following awards:

- Cancer Institute NSW, Professor Rob Sutherland *Make a Difference Award* (Outstanding Researcher Award) August 2016 - **\$20,000**; and
- Dr Tony Pang, PhD student continued research on this Project in 2017 and was awarded the prestigious *GESA Young Investigator Award* for his presentation at the annual scientific meeting of the Gastroenterological Society of Australia (GESA) held in August 2017.

(d) Prof Apte has presented her findings, *Circulating Pancreatic Stellate Cells in Pancreatic Cancer* at the Australia New Zealand Hepatic, Pancreatic and Biliary Association Annual Scientific Meeting in 2016.

Feedback provided by Professor Minoti Apte OAM:

We thank the Foundation for supporting pancreatic cancer research. This Project has led to the first ever successful isolation of circulating pancreatic stellate cells in a pancreatic cancer patient as well as in a mouse model of pancreatic cancer. These findings open a new area of investigation for the prognostication and the treatment of pancreatic cancer.