



**Name of Institution:** University of New South Wales, Lowy Cancer Research Centre

**Project Title:** *Therapeutically Targeting a Solute Carrier Transporter in the Stroma of Pancreatic Cancer*

**Principal Investigator:** Associate Professor Phoebe Phillips

**Grant:** Round 2 Innovation Grant 2016

**Background:**

There has been very little improvement in pancreatic cancer patient survival in the last 30 years, and as a consequence sadly eight Australians lose their battle to pancreatic cancer every day and more than 3,000 new pancreatic cancer cases are diagnosed each year in Australia. It is shattering and unacceptable for pancreatic cancer patients that the best chemotherapy available only prolongs life by an average of 16 weeks.

It has been shown that pancreatic cancer cells recruit normal pancreatic cells to support their growth and spread. Yet, these critical 'helper cells', known as pancreatic stellate cells have been ignored in current treatment strategies.

Pancreatic stellate cells produce an extensive scar tissue which makes up to 90% of the tumour, and increases tumour growth/chemo-resistance and blocks drug delivery to tumours.

Assoc. Prof Phillips' aim was to identify a therapy which shuts down the tumour-promoting activity of pancreatic stellate cells using a clinically relevant mouse model of pancreatic cancer.

**The Research:**

This grant allowed Assoc. Prof Phillips and her team to test a **novel cutting-edge gene therapy** designed to decrease the activity of pancreatic stellate cells in a clinically relevant mouse model of pancreatic cancer. Her novel work has uncovered a protein in pancreatic stellate cells, which when inhibited decreases pancreatic stellate cell growth and blocks their ability to **'feed'** pancreatic cancer cells key nutrients, which shuts down their tumour-promoting activity.



Exciting pre-clinical results in mice showed Assoc. Prof Phillips' novel approach resulted in a >50% reduction in pancreatic tumour growth. A/Prof Phillips believes she has uncovered a novel way to inhibit pancreatic stellate cell survival, decrease scar tissue, and inhibit tumour cells by shutting off their food supply from pancreatic stellate cells.

**The Impact:**

Nanomedicine is an urgently needed alternative to tackle pancreatic cancer and can inhibit any tumour-promoting gene by delivering cutting-edge gene therapy drugs (siRNA).

As a result of the Project, A. Prof Phillips successfully identified a novel therapy with both anti-tumour and anti-pancreatic stellate cells properties. Further more, as a result of the Project, A. Prof Phillips:

- (a) found a protein in pancreatic stellate cells, which when inhibited decreases pancreatic stellate cells growth and blocks their ability to 'feed' pancreatic cancer cells nutrients required for their survival, hence shutting down there tumour-promoting activity;
- (b) successfully decreased the activity of pancreatic stellate cells using her novel cutting-edge nanomedicine gene therapy in a clinically relevant mouse model of pancreatic cancer; and
- (c) identified a way to deliver highly specific gene therapy to pancreatic stellate cells using her nanomedicine to overcome the drug delivery barrier (scar tissue) that exists in pancreatic cancer.

A. Prof Phillips' exciting results:

- demonstrated that this approach significantly reduced pancreatic tumour growth by >50%.
- showed the tumours were less able to metastasise or spread to other organs in the body; and

Given the significant government funding A. Prof Phillips recently secured to continue developing this novel therapy, she hopes to be able to increase survival of patients with pancreatic cancer in the future using this novel approach.

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

**(a) A. Prof Phillips has been awarded additional research funding for this or related studies:**

- National Health Medical Research Council (**NHMRC**), *Metabolically Reprogramming the Stroma to Starve Pancreatic Tumours*. Project Grant Chief Investigators: Phillips P, McCarroll J, Goldstein D, Holst J, Morton J. 2018 – 2020 - **\$598,000**



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- NHMRC, *The Use of Gene Silencing Nanodrugs to Inhibit Lung Cancer Growth*. Chief investigators M Carroll J, Phillips PA, Quinn J. 2018 – 2020 - **\$454,950**
- Cancer Australia, *Therapeutically Targeting a Solute Carrier Transporter in the Stroma of Pancreatic Cancer*. Project Grant Chief Investigators: Phillips P, McCarroll J, Goldstein D, Holst J, Morton J. July 2017 – 2020 - **\$511,000**
- Cancer Australia. *Reprogramming the Tumour Microenvironment With the Use of Nanomedicines for the Treatment of Pancreatic Cancer*. Project Grant Chief Investigators: Phillips P, McCarroll J, Goldstein D, Morton J. July 2017 – 2020 - **\$500,000**
- Tour de Cure. *Nanomedicine-Based Treatment to Inhibit Pancreatic Cancer Growth and Metastases*. Project Grant Chief Investigators: Phillips P, McCarroll J, Davis T, Goldstein D, Morton J, Sharbeen G. 2018, **\$200,000**
- Tour de Cure. *Targeting MUTY-Homolog to Reduce Pancreatic Tumour Chemoresistance and Metastatic Spread*. Project Grant Chief Investigators: Sharbeen G, Phillips P, McCarroll J, Goldstein D. 2018, **\$80,000**

### **(b) A. Prof Phillips has published the following journal article:**

- *MutY-Homolog (MYH) inhibition reduces pancreatic cancer cell growth and increases chemosensitivity*. Sharbeen G, Youkhana J, Mawson A, McCarroll J, Nunez A, Biankin A, Johns A, Goldstein D, Phillips P. *Oncotarget*. 2017 Feb 7;8(6):9216-9229.

### **(c) A. Prof Phillips won the following award**

- Research Excellence Award from the University of New South Wales Sydney, Faculty of Medicine in 2017.

### **(d) A. Prof Phillips has presented findings in respect of the Project**

- Australian Gastroenterology Week (AGW), 2017
  - *Therapies personalised to the stroma in pancreatic cancer*
  - *Nanomedicine as a therapy to target 'undruggable' genes in pancreatic cancer*.
- Adult Cancer Program Seminar Series, Lowy Cancer Research Centre, UNSW Sydney, 2017. *Novel Therapeutic Targets in Pancreatic Cancer*.
- US-Australian Emerging Cancer Biomedical Technologies Workshop held at Virginia Tech Research Center in Arlington, Virginia, USA June, 2017. *Modulating Pancreatic Tumours using RNAi based Nanomedicines*.
- Translational Cancer Research Network Seminar Series and Prince of



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Wales Hospital. *The Future of Pancreatic Cancer treatment: A Pre-clinical View from the Laboratory.*

- EACR-AACR-SIC 2017 Special Conference: *The Challenges of Optimising Immuno and Targeted Therapies*, Florence, 24-28 June 2017. A Akerman, G Sharbeen, J Holst, J Youkhana, S Naim, J Liu, J McCarroll, D Goldstein, M Erkan, PA Phillips. *Targeting a Solute Carrier to Reprogram Tumour-Promoting Stromal Cells In Pancreatic Cancer.*

### **(e) Anouschka Akerman (PhD Student) won the following award and made the following presentations**

- The prestigious Campion-Ma-Playoust Memorial Award for the Best Oral Presentation, *Targeting a Solute Carrier to Reprogram Tumour-Promoting Stromal Cells in Pancreatic Cancer* from the Australian Society for Medical Research (ASMR) National Scientific Conference, Sydney, 2017.
- Adult Cancer Program Seminar Series, Lowy Cancer Research Centre, UNSW Sydney, 2017. *Metabolically reprogramming pancreatic stellate cells in pancreatic cancer.*
- Prince of Wales Hospital PhD Student Seminar Series, 2017, *Metabolically reprogramming pancreatic stellate cells in pancreatic cancer.*

### **Feedback provided by Assoc. Prof Phoebe Phillips**

*Thank you Caroline and the Avner Foundation Team for all your hard work, this grant has had a huge impact on my career and research funding. I recommend that you continue to involve researchers in your advocacy to community and politicians.*

*Also, congratulations on your first symposia this year – I really enjoyed being the convenor and based on the positive feedback I received, I encourage you to make this an annual event. This event was successful in creating at least two new collaborations for my team and I am sure many more collaborations will form following such an interactive symposium.*