

Name of Institution: Pancreatic Cancer Translational Research Group, Lowy Cancer Research Centre, UNSW Australia

Project Title: Elucidating the mechanism by which MutY-Homolog knockdown kills pancreatic cancer cells

Principal Investigator: Dr George Sharbeen

1) Summarise what the aim of your research was.

Pancreatic cancer is the most lethal cancer and is projected to become the second-leading cause of cancer-related deaths by 2030. This dismal forecast is largely due to a lack of development of more effective therapeutic treatments for pancreatic cancer. Our laboratory focuses on identifying new targets in pancreatic cancer and developing methods to inhibit these targets, using nanotechnology and clinically-relevant mouse models of pancreatic cancer. One target we have identified is a DNA repair protein which, when inhibited in pancreatic cancer cells, reduces their survival and increases the efficacy of cancer drugs currently used in the clinic. In order to effectively translate this target to the clinic, a full understanding of how inhibiting this target kills pancreatic cancer cells and sensitises them to cancer drugs is required. This research project sought to determine this mechanism.

2) What have the outcomes been to date?

We have shown that inhibition of our target can kill pancreatic cancer cells by inducing DNA damage. These important findings have formed the foundation to test this target in a clinically-relevant mouse model of pancreatic cancer. This work has high potential to provide a potent new therapeutic target for pancreatic cancer that could improve patient survival by reducing tumour growth and increasing pancreatic cancer cell sensitivity to existing cancer drugs.

3) What are the next steps?

We are currently using cutting-edge DNA sequencing technology to further probe the effect of inhibiting our target on DNA mutation in pancreatic cancer cells. Our work supported by Avner will form the foundation of larger NHMRC and Cure Cancer Australia funding applications. Results generated by this support have already been used to apply for an early career grant for Dr Sharbeen from Tour de Cure (outcomes to be announced).



4) What has it meant to have grant funding from the Avner Pancreatic Cancer Foundation?

Without funding from Avner, this critical research would not have been possible. The findings from this project will form the foundation of a publication and will contribute to a body of evidence that will help translate our at-the-bench work into a clinical target for pancreatic cancer. In the current climate of competitive research funding, it is particularly difficult for early career researchers to obtain seed funding to establish their own research and to develop as independent research leaders. The funding from Avner has also helped Dr Sharbeen establish this essential track-record of funding acquisition (as a lead chief investigator) and provided him with the opportunity to continue producing high quality research. Nationally, pancreatic cancer research is poorly funded, so this grant has also allowed us to build capacity in pancreatic cancer research workforce by employment of a research assistant.