**Name of Institution:** The Garvan Institute of Medical Research

**Project Title:** *Harnessing a novel 'tunable' immune check point to enhance the immunogenicity of anti-pancreatic ductal adenocarcinoma*

**Principal Investigator:** Associate Professor Shane Grey

**Grant:** Round 3 Innovation Grant 2017

**Background:**

As a result of the genomic analysis of thousands of samples, the team at the Garvan Institute has previously found a genetic 'volume control' switch that they believe allows for the 'tuning' of the immune system to be more or less aggressive. This project tested the idea in mice that 'T cells' can be tuned to increase the ability of the immune system to find, infiltrate, and kill Pancreatic Cancer cells.

**The Research:**

The team first used genome editing methods to generate different variants of a specific gene in mice, to compare immune response. They then tested these novel engineered mouse lines in various immune models to assess the speed, veracity and sensitivity of the immune system to different infectious challenges.

Next, they tested the anti-Pancreatic Cancer activity of the activated gene's immune system using mouse models of the disease. They compared the amount of spread (metastasis) of the cancer in these mice compared to mice with another version of the gene.

**The Findings:**

A/Prof Grey's team found that specific genetic 'versions' can tune the immune system in mice to a more aggressive setting. In testing the anti-Pancreatic Cancer activity of the activated gene's immune system, they were able to show that there is less spread (metastasis) of the cancer in a mouse model.

**What does this mean for Pancreatic Cancer?**

The most important findings from this project are that the Garvan team has identified novel genetic variants that enhance immunity. Secondly, they have shown that tuning immunity with this gene results in improved cancer outcomes in mice. They found that genetically-tuned mice lack any evidence of cancer

metastasis. This indicates that tuning patient immunity via this specific gene could represent a breakthrough technology in cancer.

A/Prof Grey hopes that this research will eventually lead to the genetic switch being reset in patients with Pancreatic Cancer, to make their own immune system much better at hunting down and destroying their cancer cells. Plans have begun to establish an *in vitro* (test tube) human T cell model to test whether engineering a specific human T cell will enhance its ability to target and kill a cancer cell.