Genome editing of haematopoietic stem and progenitor cells to uncover novel therapeutics for Aplastic Anaemia and other Bone Marrow Failure Syndromes.

Dr Yih-Chih Chan

Flavorite Fellowship 2017 - 2020

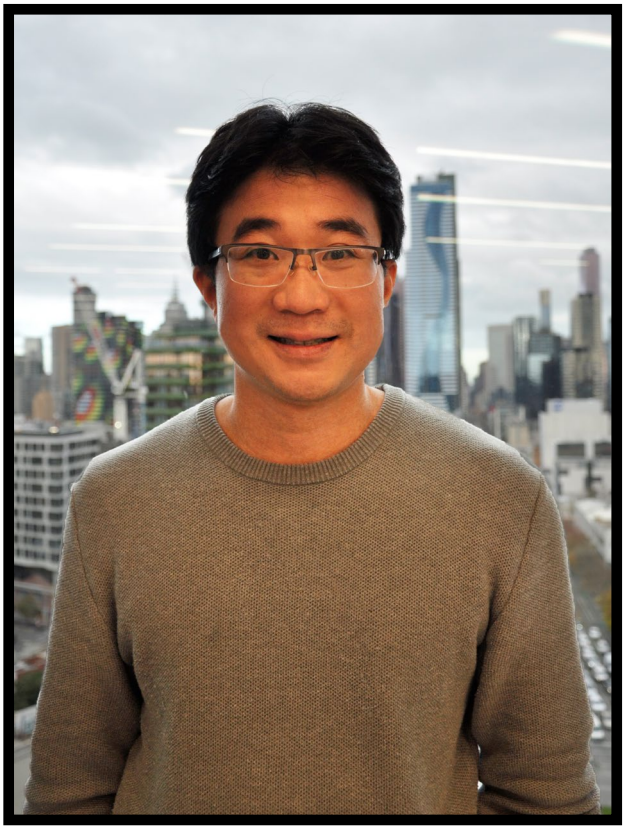
Dr Yih Chih Chan is a senior postdoctoral researcher at the Peter MacCallum Cancer Centre with expertise in both laboratory research and computational biology. He completed his PhD at the University of Auckland, NZ, in Molecular Medicine and Pathology, investigating regulation of immune cells in inflammatory diseases. Following his PhD, he took up a postdoctoral fellow at King's College London, UK, studying the role of the immune system in a non-allergic subtype of asthma. For the past 5 years, he has been working in Professor Mark Dawson's group at the Peter MacCallum Cancer Centre, focussing on the epigenetic regulation of blood disorders. In 2017, he was awarded the Maddie Riewoldt's Vision Flavorite Fellowship to discover novel therapeutic avenues to treat Bone Marrow Failure Syndromes.

Dr Chan explains, "In Bone Marrow Failure Syndromes, the body is unable to generate certain blood cell types. There are many different types of mature blood cells which are all thought to be derived from blood stem cells through sequential steps, known as differentiation, in a hierarchical manner. One of the main goals of this project is to understand the epigenetic process involved in each step of normal blood development."

The fascinating area of research that Dr Chan is currently focussed in is epigenetics. Within a single person, every cell, whether it is cells from the skin, eyes, heart or brain, have the exact DNA sequence. Despite the same genetic makeup, all these cells look and function very differently, and this control is termed epigenetics. Epigenetics is the precise control of the genetic sequence, to tell a cell to turn on or off particular genes which in turn affects how a cell behaves and function. Epigenetics research is therefore very complicated, but at the same time very powerful with enormous potential.

By understanding the epigenetic regulators of normal blood development, Dr Chan hopes to discover the main determining factors that generate each specific cell type, and therefore also understand what may have gone wrong in Bone Marrow Failure Syndromes. This understanding will also provide tools to assist with new ways in overcoming this group of diseases.

Dr Chan's project involves both complex bioinformatics analysis and cutting-edge laboratory research techniques. He has isolated different populations of cells that correspond to each main blood cell type and has looked at their gene expression profiles using next generation sequencing. This has enabled his team to compare and find differences in each of the different blood cell types. He has then used a variety of genome editing tools to see if he can control how a cell behaves by turning on or off specific genes. "We are beginning



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to unravel the complexity of blood development; we have identified key epigenetic genes that are required for long-term blood stem cells and important epigenetic complexes in the different cell types. Using this knowledge, we hope to be able to use the same signals to control cell fate decisions and allow us to direct cells to become a specific blood cell type that is absent in disease. If we can manipulate cell fate at will, this will be an incredibly powerful tool and provide new therapeutic avenues to achieve our ultimate goal of finding a cure."

Dr Chan believes the advances in science and technology in the last decade have been truly amazing. The advent of next generation sequencing technology has provided unprecedented insights into the genetics, gene expression and epigenetic regulation of cells. "This has provided us with a massive amount of information, even from just a single cell!"