Te Niwha

Research Project Impact Case Study

Signatures of vaccine-induced protection against Tuberculosis (TB)

Key researchers
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Introduction

Research Purpose:

Tuberculosis (TB) remains one of the most serious global infectious threats, killing more people annually than any other single cause infectious agent. There is ongoing TB transmission in Aotearoa New Zealand and the Pacific, and to meet this challenge, this project is part of a broader collaborative programme that has brought together internationally recognised TB-research leaders in Aotearoa to focus on TB diagnosis and prevention, through public health measures, vaccination and improving treatment options for antimicrobial resistant organisms. This sub-project aimed to take a bench-to-bedside approach to inform the development and testing of new, improved vaccines to prevent TB.

Research Approach:

This project aimed to correlate BCG vaccination-induced changes to the gene expression in the lung with changes to gene expression in the peripheral blood to identify markers of immune protection that can be easily measured in the clinic. Correlates of mucosal protection against *Mtb* infection that we can identify in the blood can be used for future vaccine development and evaluation.

Alignment with Te Niwha:

This collaborative proposal aligns with the Charter Principles, as work together to build new relationships amongst the different projects in this programme, as well as fostering established relationships that have been built over time and through shared experience. We have connections with those that will be involved with and affected by our research. Those involved in this proposal have all shown leadership within their respective areas and wish to participate together to develop this platform for the benefit of Aotearoa. We have developed future leaders by supporting research fellow Naomi Daniels in this project, and PhD students Riya Shajumon. Partnership with tangata whenua is being built, to ensure bi-directional learning and discussion with those who may be impacted by our research.

Results

We have developed a flow cytometry panel to analyse innate and adaptive immune activity after vaccination. We obtained ethical approval and developed a protocol and data analysis pipeline for the study. Sample collection and flow cytometry analysis of the data have been completed, RNA-sequencing is underway and analysis will be completed by PhD candidate Riya Shajumon in her final year. RNA-sequencing of samples from peripheral blood of mice vaccinated with BCG and challenged with Mtb by aerosol has been completed and fully analysed. The gene expression patterns of vaccinated mice were inversely correlated with those found in the lung; revealing that innate immune training signals can be detected in peripheral blood. Whether this holds true for human clinical samples remains to be determined.

Impact

This project has led to development of new collaboration between the University of Otago and Liggins Institute at the University of Auckland, that will facilitate moving pre-clinical research into the clinic. Using pre-clinical models we have greater capacity for discovery of correlates of protection against TB as we can easily control vaccination and TB exposure; however, it is critical to bring this research to the clinic. Specifically, this work is providing the knowledge foundation to contribute to the milestones of developing platforms to assess vaccine responses against infectious diseases of importance to New Zealand, such as TB, through improving protective outcomes for BCG vaccination. By identifying correlates that are detectable in easily accessible clinical samples (peripheral blood), we can design and test new TB vaccines, or new modes of vaccine delivery, that either improve immunity induced by BCG or replace the BCG vaccine.