Te Niwha

Research Project Impact Case Study

Mahi Tahi: Decreasing transmission and improving diagnosis of Tuberculosis to reduce health inequities

Short Research Title

Druggable vulnerabilities are widespread in drug-resistant strains of *M. tuberculosis*

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Introduction

Drug resistant strains of Mycobacterium tuberculosis threaten to make one of the worlds deadliest pathogens even more difficult to treat. Our prior work has demonstrated that drug-resistance in *M. tuberculosis* leads to cellular stress and creates vulnerabilities that could be a potential Achilles heel. Targeting these pathways with drugs could drastically improve treatment outcomes and prevent the evolution of drug-resistance. For our findings in laboratory isolates of *M. tuberculosis* to have clinical impact we need to determine whether the same principles apply to drug resistant strains found in the clinical, where there is an incredible amount of genetic and phenotypic diversity.

Results

Through this Te Niwha funded project our work has both (i) identified collateral vulnerabilities that are conserved in a wide range of phenotypically and genetically diverse drug resistant strains and (ii) demonstrated that strain specific collateral vulnerabilities are conserved in drug resistant clinical isolates. Furthermore, these collateral vulnerabilities are influencing the evolution of drug-resistant strains as they search for strategies to overcome these impaired pathways.

Impact

This ongoing body of work represent a paradigm shift in our understanding of drug-resistance in M. tuberculosis. It is having genuine impacts on how we design future treatment strategies by both providing experimental evidence to support the use of current regimens that have excellent efficacy against DR-strains and identifying highly vulnerable drug targets to initiate drug-discovery programmes with both national and international collaborators. The long term outcomes of this work will improve treatment outcomes for communities that are disproportionately affected by tuberculosis, both globally and in Aotearoa.