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*

Key researchers

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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.

Research Activities

Findings in laboratory isolates of *M. tuberculosis* have demonstrated that drug resistant strains have genetic vulnerabilities. These vulnerabilities represent a potential Achilles heel, that if correctly targeted could have major clinical impacts on reducing treatment times. Here, we sought to determine if identified vulnerabilities translate to clinical isolates of M. tuberculosis where there is an incredible amount of genetic and phenotypic diversity. By using a combination of functional genomics, and computational approaches we demonstrated that these collateral vulnerabilities are present in clinical isolates and are influencing the evolution of drug-resistant strains.

Key achievements

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. The key ouput of this study is a manuscript that is currently at the second round of revisions at Nature Communciations. The appointed post-doc, Dr Wang, was also able to contribut to multiple other projects in this research group. Finally, we have also been able to leverage the data generated in this study to establish new collaborations and secure additional funding (*announcements are currently embargoed*).