Te Niwha

Research Project Impact Case Study

Improving the safety and effectiveness of leprosy treatment In Kiribati through enhanced surveillance of drug resistance and detection of factors predisposing to dapsone reactions

Short Research Title

Towards elimination: improving the effectiveness and safety of leprosy treatment in the Pacific

Key researchers

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Introduction:

Kiribati is a Pacific Island neighbour of Aotearoa New Zealand and has one of the highest rates of leprosy in the world. This stigmatised and neglected Mycobacterial disease can cause major disability and is both treatable and preventable. Sea level rise is causing an existential threat to Kiribati due to its low-lying geography. Migration of i-Kiribati people to countries such as Aotearoa New Zealand is likely to increase and thus there is a strong likelihood of reintroduction of this once-endemic disease to Aotearoa.

Successful treatment of leprosy is hindered by three important factors: 1) lack of widely available, sensitive and specific diagnostics, 2) a high incidence of reactions to the antimycobacterial drugs used for therapy (and thus treatment default) and 3) progressive antimicrobial resistance of *Mycobacterium leprae* strains. Currently, laboratory testing for leprosy is not available in Kiribati. Preliminary molecular testing of a small number of skin biopsy specimens using PCR and Sanger sequencing in Christchurch has revealed a prevalence of dapsone resistance in *M. leprae* isolates from Kiribati of 11% (one of the standard drugs used in leprosy therapy). This assay does not identify all genotypic markers of first-line drug resistance and thus the true prevalence of resistance may be substantially greater. An ongoing mass leprosy chemoprophylaxis campaign using rifampicin will likely provide additional selective pressure on rifampicin resistant strains. Two heritable factors dramatically increase the risk of dangerous haemolytic and hypersensitivity reactions to dapsone. These are deficiency of the enzyme glucose-6-phosphate dehydrogenase (G6PD) and presence of the HLA-B*13:01 gene respectively. These are known to be prevalent in certain neighbouring pacific countries but their prevalence in Kiribati is unknown.

This study aims to address these deficiencies in knowledge and diagnostic capability by focusing on three key domains of study:

1. More comprehensively assessing the baseline prevalence of resistance to rifampicin, dapsone and fluoroquinolones by using the novel multiplex Deeplex Myc-Lep assay for detection of multiple different resistance markers at multiple loci using *M. leprae* DNA isolated from skin biopsy specimens.

2. Determining the prevalence of the HLA-B*13:01 genotype and G6PD deficiency in the Kiribati population using cross-sectional surveying to establish whether pre-treatment testing is warranted to reduce the risk of dangerous dapsone reactions

3. Development of a practicable and cheap CRISPR-Cas assay for *M. leprae* that could be used in-country for immediate confirmatory testing for leprosy

This project is conducted in partnership with the National Leprosy Unit of Kiribati and the Pacific Leprosy Foundation and has a strong emphasis on alignment with Kiribati Ministry of Health & Medical Services priorities and accountability to the people of Kiribati. Work on the project is also strengthening pre-existing collaborations with the University of Sydney and Centenary Institute, Sydney, Australia. The project and collaborations aim to build research and clinical capacity in both Aotearoa New Zealand and Kiribati through provision of multiple training and leadership opportunities for two PhD candidates in Aotearoa New Zealand and one Masters and one postgraduate Public Health diploma student in Kiribati. Bidirectional knowledge transfer between Kiribati and Aotearoa New Zealand is engrained in study processes and results are fed back regularly at both local and national levels in Kiribati.

Results:

This Te Niwha-funded study is currently approximately halfway to completion with unequal progress across the three research domains.

Domain 1: After a lengthy optimisation and trouble-shooting phase, the Deeplex Myc-Lep assay is now working well in our laboratory workflow. We have just commenced batch testing of stored skin biopsy specimens from patients with proven leprosy to determine the baseline prevalence of rifampicin, dapsone and fluoroquinolone resistance. Results are not yet available. Once stored samples have been processed, we will turn our attention to prospectively-collected skin biopsies to monitor for development of rifampicin resistance precipitated by mass administration of rifampicin chemoprophylaxis.

Domain 2: Ethical approval for the G6PD deficiency and HLA-B*13:01 surveys has been granted conditionally by the University of Otago Ethics Committee and has just been approved formally by the Kiribati Ethics Committee. Whilst awaiting ethical approval, we have acquired the SD Biosensor bedside G6PD assay kit and have begun quality control processes. We are also optimising our HLA-B*13:01 assay using purified DNA from an HLA-B*13:01 positive patient purchased from a commercial provider, as well as negative controls. Sample collection is planned to commence in Kiribati in June.

Domain 3: Strong progress has been made towards development of a *M. leprae* CRISPR-Cas assay. PCR primers have been designed to amplify a conserved and high copy-number region of the genome. A CRISPR-Cas guide RNA has been designed to detect a target sequence within the amplified region. Sensitivity testing using serial dilutions has shown very high assay sensitivity for detection of *M. leprae*. Specificity testing using other non-leprae Mycobacterial strains is underway.

Two papers related to this project have been published thus far; one describing the performance of retrospective and prospective rifampicin-based leprosy chemoprophylaxis in Kiribati[1] and the second summarising the evidence for effectiveness of rifampicin-based chemoprophylaxis against leprosy[2].

Impact

This project is expected to have immediate and longer-term scientific, infrastructure and social impacts. In the short term, we will be able to provide robust evidence on the prevalence of drug resistance in i-Kiribati *M. leprae* isolates which will directly guide national policy on empiric first-line *M. leprae* treatment as well as individual patient treatment decisions. Establishing the prevalence of the HLA-B*13:01 genotype and G6PD deficiency will determine whether pretreatment testing is warranted in this environment. The tools and training required for ongoing bedside G6PD testing will be provided as part of the project. In the longer term, the work on CRISPR-Cas assay development should lead to a practicable and cheap assay that can be used in-country for immediate confirmatory leprosy diagnosis.

The project will continue to enhance communication and co-operation with our colleagues in Kiribati as well as with other research collaborators in Australia, the United States and The Netherlands. At its completion, the project will have played an important role in postgraduate training and experience for two Aotearoa New Zealand-based PhD students and one i-Kiribati masters and one i-Kiribati postgraduate Public Health diploma student leading to improved infectious diseases research and clinical capacity in both countries. The project will also have contributed substantially to a bigger, ongoing programme of leprosy operational and research work in Kiribati that is having a marked societal impact through enhancing capacity in the Kiribati Leprosy Unit, raising awareness of leprosy both at population and Ministry level, and reducing stigma associated with leprosy. Ultimately, it is hoped that the scientific advances and capacitybuilding resulting from this study will accelerate leprosy elimination in Kiribati and reduce the likelihood of reintroduction of this scourge to Aotearoa New Zealand.

Following completion of this Te Niwha-funded project, translational research work in Kiribati will continue, focusing on the most effective means of reducing the burden of leprosy through enhanced chemoprophylaxis regimens and strategies. Further product development of the CRISPR-Cas assay will be undertaken to make this as robust and rapid as possible to maximise suitability for a resource-limited environment such as Kiribati. We plan to seek further funding for our research endeavours, including from the Leprosy Research Initiative in The Netherlands.

[1] Campbell PO*, Bauro T*, Rimon E, Timeon E, Bland C, Ioteba N, Douglas NM, Cunanan A, Chambers ST. Single-dose rifampicin leprosy chemoprophylaxis for household contats In Kiribati: an audit of a combined retrospective and prospective approach. Trop Med Infect Dis 2024, 9(3), doi: 10.3390/tropicalmed9030058

[2] Campbell PO, Douglas NM, Chambers ST. A review of the efficacy, safety and feasibility of rifamycin-based post-exposure chemoprophylaxis for leprosy. Trop Med Infect Dis 2025, 10(4), doi: 10.3390/tropicalmed10040084

Update – December 2025

Antimicrobial resistance (AMR) remains one of the most urgent health challenges facing the Pacific. Fiji in particular has seen rising rates of carbapenem-resistant *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa*, with several high-risk strains circulating within and between hospitals since 2016 without real-time genomic surveillance. This project directly addresses that gap by establishing the first fully functional AMR genomic surveillance system in Fiji and building the foundational capability to extend this model to other Pacific Island Countries.

Over the past reporting period, the project has achieved significant scientific and operational milestones. We successfully established MinION-based sequencing capacity at Fiji National University, enabling local generation of high-quality genomic data for priority pathogens. This has transformed Fiji's surveillance capability from retrospective and external-lab dependent processes to real-time, in-country genomic epidemiology. Training delivered to FNU staff has strengthened technical skills in DNA extraction, library preparation, QC, data analysis, and interpretation of AMR genotypes. This has contributed to a sustainable local workforce capable of supporting ongoing national surveillance.

A key achievement has been the implementation of national sample referral pathways, allowing isolates from CWMH, Lautoka, Labasa and selected private laboratories to be transported routinely to FNU for sequencing. This ensures that genomic surveillance is integrated into routine diagnostic workflows and supports early detection of outbreaks. Sequencing efforts have already revealed persistent high-risk clones among CROs, including *A. baumannii* ST2, *K. pneumoniae* ST6260, *E. coli* ST410, and *P. aeruginosa* ST773, with evidence of continued circulation across multiple hospitals since 2020 and earlier for *A. baumannii* ST2. These findings provide essential insight into transmission dynamics and the spread of mobile resistance elements, informing infection prevention and control strategies across Fiji.

The project also established a national Fiji Microbiology Network Group, creating a collaborative platform for harmonising laboratory protocols, strengthening data reporting, and building a cohesive national approach to AMR surveillance. Through this initiative, laboratories are now aligned on CLSI-based practices and are supported in transitioning toward standardised data submission for WHO GLASS.

This project further advanced Fiji's capacity to evaluate novel antimicrobials through the development of optimised susceptibility methods for CROs. This offers clinicians access to early evidence on treatment options for highly drug-resistant infections and positions Fiji as a regional contributor to antimicrobial discovery efforts.

Overall, this work has accelerated Fiji's progression towards becoming a Pacific AMR Reference Laboratory and regional hub for genomic epidemiology. The combination of local sequencing, harmonised laboratory networks, strengthened technical capacity and regional partnerships has already demonstrated clear scientific excellence, strong applied outcomes and significant public health impact. Over the coming year, we will expand the surveillance network, deepen regional collaboration, integrate sequencing outputs into national policy, and move toward full sustainability through cost-recovery frameworks and long-term institutional support.