Identifying novel drug targets in *Acinetobacter baumannii* 5075 using *in vitro* and *in vivo* fitness profiling

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Summary

My master's research focuses on a major health issue in Aotearoa: skin and soft tissue infections. *Acinetobacter baumannii*, is a bacterium that often causes these infections within our community. These infections can be difficult to treat because this bacterium is often resistant to multiple antibiotics. The aim of my research, supported by Te Niwha, was to understand which bacterial genes help *A. baumannii* to survive in an abscess and biofilm model, and to identify potential targets for new treatments that are effective, accessible, and able to support equity in healthcare.

Skin infections disproportionately affect Māori peoples, and antibiotic resistance can worsen health inequities. By aiming to identify new treatment options and improve understanding of how *A. baumannii* survives, my research contributes to better health outcomes and supports future tools that can benefit communities across Aotearoa.

This project used laboratory models designed to mimic real skin infections. I examined genes considered essential to *A. baumannii* in a murine skin abscess model and a biofilm environment where bacteria tend to persist in a community. One key gene identified as essential to *A. baumannii* was ABUW_1371, encoding the YaaA protein. This protein is involved in protecting bacteria from oxidative stress, damage caused by reactive oxygen species produced by the immune system and other external factors.

Preliminary findings show that when ABUW_1371 is disrupted, there is a significantly reduction in the bacterial load in the abscess model compared to wild type. This signifies that ABUW_1371 (protein YaaA) helps the bacteria to survive during infection. This makes this gene a promising candidate for further investigation as a potential therapeutic target. Additionally, my research involved optimising and refining multiple laboratory methods for working with *A. baumannii*. These established protocols will support future research within the current research group for work related to this pathogen.

Researchers studying bacterial infections and antibiotic resistance could use these findings to prioritise genes for future drug development. Over time, this research could contribute to new treatment strategies that make infections easier to treat. Additionally, clinicians and public health organisations could also benefit from this research, by driving the development of therapies that reduce the severity or duration of skin infections. Improving the efficacy of treatments for skin infections will directly affect Māori, who are disproportionately affected, reducing inequities in infection-related health outcomes.

The next step of my research involves confirming the role of the ABUW_1371 gene in more detail. This includes continuing the murine abscess assay, examining oxidative stress tolerance of the mutant, and understanding how the protein functions. If the gene continues to show promise, future research could include collaborating with biotechnology or chemistry groups to explore therapies that target this gene. Ongoing engagement with clinicians, Māori health groups, and the community will continue to ensure that this research remains relevant in improving health outcomes in Aotearoa.