

Title:

A cloud-based analytics platform for antimicrobial susceptibility testing of *Mycobacterium tuberculosis* from WGS data

Abstract:

Globally, the incidence of tuberculosis (TB) has been decreasing since 2005. However, drug-resistant strains of *Mycobacterium tuberculosis* (Mtb) are emerging worldwide, and are often associated with poor treatment outcomes, posing a significant threat to global TB control. Phenotypic drug susceptibility-testing (pDST) is too slow to inform treatment decisions and targeted molecular approaches fail to test for all resistances. Previous studies have shown that such methods can lead to underdiagnosis of drug resistance, resulting in inadequate treatment and higher mortality. These studies also demonstrate the superiority of whole-genome sequencing (WGS) in providing the complete susceptibility profile. As such, clinical laboratories are increasingly adopting WGS for diagnostics and surveillance of Mtb, and infectious diseases in general. Despite the promises WGS holds in clinical microbiology diagnostics, bioinformatics data analysis remains a bottleneck, restricting the effective implementation of NGS technologies in clinical settings.

We are developing an intuitive cloud-based analytics platform for predicting resistance to anti-TB drugs from WGS data. By identifying drug resistance-conferring variants and predicting treatment options following WHO guidelines, our platform will guide clinicians towards individualised TB therapies. This ensures patients are treated with sufficiently active drugs, have improved treatment outcomes, and prevents the selection of additional resistances. The platform additionally provides a phylogenetic classification of the strain and identifies transmission clusters and outbreaks. The clinician can inform the platform about treatment outcomes for patients with similar susceptibility profiles, to ultimately better inform patient diagnosis and treatment.

Mtb proves to be an ideal candidate for developing our platform due to its slow growth rate, the clonality of its genome and the high correlation between pDST and genomic variants. In the future, we plan to extend our analytics platform to other pathogens, further contributing to the fight against antimicrobial resistance.

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