

Application of Advanced Whole Genome Sequencing Technology for Tuberculosis Outbreak Investigation

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Abstract

Tuberculosis (TB) is an *aerosol-transmissible* disease caused by the *Mycobacterium tuberculosis* complex. Blocking the transmission chain is one of the key strategies to stop TB. The global tuberculosis control has entered the genomic era. For facilitating TB control, we used whole genome sequencing (WGS) to obtain single nucleotide polymorphism (SNP) information of *M. tuberculosis* to improve discriminative limitations of conventional genotyping methods and to strengthen the delineation of transmission networks. Based on a confirmed multidrug-resistant TB (MDR-TB) outbreak, we define SNPs differences for TB outbreak investigations. To confirm an outbreak, the transmission events between cases within clusters were calculated using thresholds of ≤ 5 (definite) and ≤ 15 (probable) SNPs difference between isolates. Depending on cost-effectiveness, an algorithm was established using mycobacterial interspersed repetitive units-variable number tandem repeat (MIRU-VNTR) and WGS as the primary and secondary genotyping, respectively. However, WGS still needs to be combined with classical epidemiological methods to improve outbreak investigations.

Keywords: Tuberculosis, *Mycobacterium tuberculosis* complex, whole genome sequencing, outbreak investigation

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