A high resolution picture of tuberculosis transmission obtained from direct-from-sputum whole-genome sequencing.

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Abstract:

Whole-genome sequencing of M. tuberculosis (MTB) directly from clinical specimens (dWGS) will suppose a major breakthrough in tuberculosis diagnosis and control. To date, different strategies have been followed to sequence MTB from sputum samples and accurately predict drug-resistance. However, dWGS of MTB has never been used in genomic epidemiology. Here, we test and optimize both the laboratory and computational protocols to implement a dWGS pipeline able to produce a detailed genomic analysis from sputum samples in a week. We used dWGS on clinical specimens of 27 TB patients to evaluate its performance for drug-resistance prediction and genomic epidemiology. We were able to predict full drug resistance profiles and epidemiological links for the 28 out of the 37 specimens analyzed. In these samples, the agreement between dWGS and WGS from matching cultures was of 100% for both drug-resistance prediction and epidemiological clusters. In our work, we evaluate the state-of-the-art of dWGS for MTB and provide a cost-effective diagnostic algorithm for tuberculosis based on dWGS. We demonstrate that dWGS is a powerful tool to conduct high-precision genomic epidemiology in real time.