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Next-generation sequencing-based user-friendly platforms for drug-resistant tuberculosis diagnosis: A promise for the near future

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ABSTRACT

Since 2002, there has been a gradual worldwide 1.3% annual decrease in the incidence of tuberculosis (TB). This is an encouraging statistic; however, it will not achieve the World Health Organization's goal of eliminating TB by 2050, and it is being compounded by the persistent global incidence of drug-resistant tuberculosis (DR-TB) acquired by transmission and by treatment pressure. One key to effectively control tuberculosis and the spread of multiresistant strains is accurate information pertaining to drug resistance and susceptibility. Next-generation sequencing (NGS) has the potential to effectively change global health and the management of TB. Industry has focused primarily on using NGS for oncology diagnostics and human genomics, but the area in which NGS can rapidly impact health care is in the area of infectious disease diagnostics in low- and middle-income countries. To date, there has been a failure as a community to capitalize on the potential of NGS, especially at the reference laboratory level where it can provide actionable information pertaining to treatment options for patients. The rapid evolution of knowledge about the genetic foundations of tuberculosis drug resistance makes sequencing a versatile technology platform for providing rapid, accurate, and actionable results for treating this disease. No "plug-and-play" and "end-to-end" NGS solutions exist that provide clinically relevant sequence data from the *Mycobacterium tuberculosis* complex genome from primary clinical samples (e.g., sputum) in high-burden country reference laboratories, which is where they are most needed. However, such a system-based solution is underdeveloped by Foundation for Innovative Diagnostics (FIND), in collaboration with partners from academia, non-governmental organizations, and industry. The solution is modular and is designed and developed to perform targeted amplicon sequencing directly from a patient's primary sputum sample. This solution will initially allow reference laboratories to perform reflex NGS that provides a rapid and comprehensive analysis of a patient's *M. tuberculosis* complex drug resistance profile, thereby facilitating optimization of a patient's treatment, improving treatment outcomes, and reducing the spread of DR-TB. Such a system could also enable countries to implement culture-free drug resistance surveillance programs, which could bypass the need for expensive culture facilities, decrease a country's dependence on external laboratories, and significantly expand the map of global surveillance capabilities. In

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addition, the introduction of such a system will provide a foundation for NGS to be used for genotypic testing for human immunodeficiency virus-infected patients, surveillance of other diseases, in-country capability for outbreak discovery and management, and a host of other diagnostic benefits that are currently limited to high-income countries.

Conflicts of interest

The authors have no conflicts of interest to declare.

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