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a A novel molecular strategy for surveillance of multidrug resistant tuberculosis in high burden settings

In South Africa, transmission of drug-resistant TB (DR-TB) strains is a significant contributor to rising rates of multidrug-resistant tuberculosis (MDR-TB), as opposed to primary drug resistance – the development of drug resistance while on treatment. Hence, disruption of chains of transmission is a key factor in controlling and prevention of DR-TB. Intrinsic to any intervention to prevent transmitted DR -TB is the implementation of an early warning surveillance system to detect genotypic clusters among DR-TB isolates as an indication of transmission in the population. Genotyping of clinical isolates of *M. tuberculosis* has improved our understanding of the epidemiology and patterns of transmission of tuberculosis. Integrating genotyping with surveillance activities provides essential information needed to determine the relative frequency of *M. tuberculosis* strains in specific geographic areas, and the extent of spread of related strains in communities. Routine genotyping forms an important component of TB control programs in many low prevalence settings but is costly and labour intensive for high prevalence settings.

There are currently three main genotyping methods for *M. tuberculosis* including: 1) IS6110-restriction fragment length polymorphism (IS6110-RFLP); 2) spacer oligonucleotide typing (spoligotyping) and 3) mycobacterial interspersed repetitive units-variable number tandem repeats (MIRU-VNTR).

To date, genotyping in South Africa has been primarily used for research purposes in limited geographic areas. The Centre for Tuberculosis (incorporating the National TB Reference Laboratory) at the National Institute for Communicable Diseases (NICD) has recognized the need to establish a country level molecular surveillance system in South Africa to support the investigation of and public health response to MDR-TB. Therefore, the center conducted a study in collaboration with researchers from the United States, to determine the usefulness of a novel and simple genotyping approach, combining spoligotyping with *pnc*A sequencing (SpoNC), against two well-established methods: IS*6110*-RFLP and 24-loci MIRU-VNTR and the findings recently published in PloS One (see reference below). The discriminatory power of the SpoNC strategy was similar to the established methods (IS6110-RFLP and 24-loci MIRU-VNTR), and was able to detect important clonal strains that are relevant to the South African context rapidly and easily. SpoNC can be done directly from clinical samples without the need for prior culture, as well as from Ziehl-Neelsen-stained smear slides. Moreover, SpoNC is less costly in terms of consumables and labour as compared to either IS*6110*-RFLP or 24-loci MIRU-VNTR typing. Taken together, the results of our study support the value of SpoNC strategy for MDR-TB surveillance in a high burden setting. Based on these findings, the Centre for Tuberculosis has commenced with a tiered approach to MDR-TB transmission surveillance, involving SpoNC strategy as a first-line method, followed where relevant by 24-loci MIRU-VNTR typing. Further validation in different geographical settings is underway to ensure the system works well. This has begun in four districts with the target of one high burden district per province under surveillance for transmission clusters by end of 2017.

Further reading

Said HM, Kushner N, Omar SV, Dreyer AW, Koornhof H, Erasmus L, Gardee Y, Rukasha I, Shashkina E, Beylis N, Kaplan G, Fallows D, Ismail NA. A novel molecular strategy for surveillance of multidrug resistant tuberculosis in high burden settings. PLoS One. 2016 Jan 11;11(1):e0146106.

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