MIRU-VNTR typing: the new international standard for TB molecular epidemiology

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Harmonized and reliable typing of pathogenic bacteria permits easy identification of locally or internationally circulating clones, which is essential for optimal epidemiological surveillance and disease control. This is especially true for diseases such as tuberculosis, with worldwide distribution and global emergence of drug-resistant strains. Mycobacterial interspersed repetitive unit-variable number of tandem repeat (MIRU-VNTR) typing [1-2] has become a major method for fast and high-resolution genotyping of Mycobacterium tuberculosis complex isolates. A system based on 15 to 24 loci has been proposed for international standardization by an international consortium including 10 European and American laboratories [3]. In population-based studies, standard MIRU-VNTR typing was shown to have an equal to slightly better predictive value than the previous gold standard IS6110 RFLP for the study of TB transmission, in settings with epidemiological characteristics representative of those of many developed countries. PCR-based interrogation of up to 24 independent and well-calibrated markers facilitates prompt and reliable molecular-guided elucidation of complex situations involving potential outbreak cases, mixed infections or re-infections [4-9]. As a result, this method is being internationally adopted, often in combination with spoligotyping, as the new reference method for TB molecular epidemiology, e.g. by the US CDC, large European research and epidemiological surveillance consortiums and National or Regional reference Centers.

In addition to their use for tracing TB transmission at the strain level, MIRU-VNTR markers can also provide useful predictions for classifying strains into genetic lineages [3, 7, 10], although these markers are intrinsically less deterministic than classical phylogenetic markers such as LSPs or SNPs. Such phylogenetic predictions are facilitated by the availability of freely accessible, on-line strain identification databases such as MIRU-VNTRPlus (http://www.miru-vntrplus.org) and TB-lineage (http://www.cs.rpi.edu/~bennek/tbinsight/tblineage).

Finally, new tools and services have become available, which facilitate quality-controlled implementation and use of this technique. These tools comprise MIRU-VNTR Calibration,
Validation and Typing kits for use on capillary electrophoresis-based DNA Analyzers. Their availability for easier and more efficient real-time genotyping will hopefully contribute to improved molecular-guided TB control and surveillance.

Selected references


