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USE OF MOLECULAR INVERSION PROBES AND PYROSEQUENCING FOR SENSITIVE DETECTION OF *MYCOBACTERIUM TUBERCULOSIS*

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Nucleic acid-based detection of *Mycobacterium tuberculosis* infections has the potential to improve the analysis of the tuberculosis epidemiology and patient care by increasing the specificity and sensitivity of diagnosis. One potential diagnostic sequence, the DR locus, is present in all isolates of *M. tuberculosis* complex bacteria. It encodes no known gene product but is useful for molecular typing of *M. tuberculosis* because of its fortuitous absence in non-tuberculosis strains of mycobacteria. The DR locus contains a variable number of short direct repeats interspersed with non-repetitive spacers and is commonly used as a target for the spoligotyping method, a technique based on the detection of the presence or absence of distinct spacers between the repeats. In this study, we attempted to combine the specificity of molecular inversion probe (MIP) technology with the sensitivity of modified pyrosequencing readout in order to detect a short conserved 18 bp sequence included in DR locus in 25 isolates of *M. tuberculosis*. Additional sensitivity was obtained by introducing modifications in pyrosequencing methodology; by these means we achieved to detect 500 fg of *M. tuberculosis* DNA.

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