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Molecular Diagnosis of Tuberculosis

Globally, there are 8 million new *Mycobacterium tuberculosis* (TB) cases and 2 million deaths associated with TB infection per year[1, 2]. *M. tuberculosis* primarily infects the lungs and is transmitted via respiratory droplets (the most contagious form) though it can affect any part of the body. Social risk factors associated with TB include imprisonment, alcohol and drug misuse, and homelessness.

Once infected, most individuals enter into a state of latency with no clinical manifestations and are not contagious. This state can reactivate at a later stage, particularly if the individual becomes immunocompromised. However, the remaining individuals (~5%) develop a primary active infectious disease.

Given the infectious nature of TB, accurate and early diagnosis is a critical step in its management and control. Treatment of TB and atypical *Mycobacterium* infection is difficult and long, involving a course of antibiotics, which may cause serious side effects. If a woman contracts TB during pregnancy, early diagnosis key in preventing premature births. In addition, if the mother is infectious postpartum, there is a risk of infecting the new born baby.

Overall, the accuracy of nucleic acid based tests have been shown to be far superior when applied to respiratory samples as opposed to other body fluids[1]. Studies have shown that well designed in-house assays were, for pulmonary TB, much better at ruling out TB than the commercial tests evaluated[1].

Assays designed ‘in-house’ for TB have statistically shown no improvement associated with a range of different nucleic acid extraction methods or different end point nucleic acid detection[3]. However, the use of a nested molecular amplification was shown to be critical to sensitivity[3]. A nested molecular amplification detection assay for TB is both fast and sensitive, but culture remains the gold standard for TB diagnosis and is crucial for assessing viability and thus infectivity[4]. Additionally TB microscopy is a mainstay for determining TB infectivity where a smear positive sample indicates active, and hence infectious, TB.

At Micropathology Ltd we use an ‘in-house’ nested molecular amplification assay for TB that has been continually improved over the past 15 years to take into account new sequence data as it became available. This assay has consistently given excellent results in external quality

assurance schemes. As a consequence we have been included in external quality assessment pilot schemes for panels before general release.

In addition, our TB assay also detects the *Mycobacterium avium* complex. While humans are the only known reservoirs for *M. tuberculosis,* comparatively *M. avium* is capable of causing disease in other animals such as birds and pigs. The *Mycobacterium avium* complex (MAC) also consists of *M. intracellulare* and these are difficult to distinguish, the complex is the most common atypical *Mycobacterium* associated with human disease. MAC primarily infects immunocompromised patients and rarely healthy individuals; it is ubiquitous in the environment.

Micropathology Ltd also have separate tests that can detect other members of the *Mycobacterium* genus in addition to TB rifampicin resistance.

References

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