DNA technologies to combat tuberculosis

Every year approximately 300 people in BC are diagnosed with active tuberculosis (TB) disease.[1] To establish effective treatment, isolation precautions, and public health responses, a rapid and accurate diagnosis of TB is required. The definitive diagnosis of TB requires laboratory confirmation of *M. tuberculosis* in a clinical specimen.

The current process of laboratory detection starts with fluorescence microscopy for acid-fast bacilli (AFB). Detecting AFB is suggestive but not diagnostic for *M. tuberculosis* as half of AFB-positive specimens in BC result from nontuberculous mycobacteria; thus samples must undergo additional tests for *M. tuberculosis*. Mycobacterial culture is the gold standard for TB diagnosis: it is a sensitive method that can detect *M. tuberculosis* in AFB-positive and AFB-negative specimens.

Unfortunately, mycobacteria grow slowly and culture can take up to 6 to 8 weeks to provide results. Culture-based susceptibility testing requires another few weeks to complete, again due to the slow growth of *M. tuberculosis*. Overall, the entire process, from sample collection to final results usually takes 4 weeks or more to complete.

At the BC Public Health Microbiology and Reference Laboratory, DNA tests are available to help guide the treatment and public health management of TB. Rapid, high-throughput testing for *M. tuberculosis* is routinely conducted using an in-house real-time polymerase chain reaction (PCR) assay on all specimens that show AFB, as well as, upon request, any other specimens.[2] The TB PCR result allows patients who are being investigated for TB to begin treatment for TB (if they are positive for TB) or be released from airborne isolation (if they are negative for TB).

DNA sequencing can also predict antibiotic resistance to anti-TB drugs weeks earlier than culture-based testing.[3] By examining specific *M. tuberculosis* genes that confer antibiotic resistance, we can identify resistance mutations and allow patients to start appropriate antibiotic therapy earlier in the course of the infection.

Using one of the newest DNA sequencing platforms, the Illumina MiSeq, we are also able to sequence the entire genome of each *M. tuberculosis* isolate.[3] By comparing genetic sequences of each *M. tuberculosis* organism isolated, we can track the spread of TB in the province.[4] This information can help direct public health resources where they are needed most in order to further reduce the rates of TB in our province.

Recent advances in DNA technologies also include point-of-care devices for the rapid detection of *M. tuberculosis* and prediction of drug resistance. One such system is the Cepheid GeneXpert, which has been endorsed by the World Health Organization in the global battle against TB.[5] This is a lab-in-a-box system that can produce real-time PCR results to detect the presence of *M. tuberculosis* in clinical specimens with minimal laboratory manipulation. It also has the benefit of predicting rifampin resistance, which may indicate multidrug-resistant TB. Several hospitals in BC are now equipped with GeneXpert systems, allowing them to rapidly test for *M. tuberculosis* and other specific pathogens.

DNA technologies can provide rapid early detection and characterization of *M. tuberculosis*, enabling a rapid public health response, initiation of appropriate antimicrobial therapy, and informing provincial epidemiological analysis for a more effective public health response. We expect that these technologies, combined with effective clinical and public health policies and practice, will help substantially reduce TB incidence in our province over the coming decades.[6]

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This article is the opinion of the BC Centre for Disease Control and has not been peer reviewed by the BCMJ *Editorial Board.*

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