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Editorial: Modern molecular era of the mycobacterial world: Insights into diagnosis and transmission of mycobacteria and associated diseases

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Editorial on the Research Topic

Modern molecular era of the mycobacterial world: Insights into diagnosis and transmission of mycobacteria and associated diseases

Mycobacterium is a genus of actinobacteria with its own family, the Mycobacteriaceae. There are 265 mycobacterial species in this genus that have been identified thus far (www.bacterio.net/mycobacterium.html accessed on 17th Feb 2023). The pathogens in the Mycobacterium (*M*) genus, including *M. TB* complex, *M. leprae*, slow-growing mycobacteria (SGM), and rapid-growing mycobacteria (RGM), are known to cause infections in humans (1–3).

Non-tuberculous mycobacteria (NTM) are widely distributed in the environment and can infect animals and humans, according to the published literature (4–6). Even though saprophytes make up the majority of NTM, about one-third of NTM have been linked to illnesses that affect humans (Ratnatunga et al.). It is still unclear exactly how these mycobacterial infections are transmitted. Understanding the dynamics of transmission of mycobacterial infections can help to plan a strategy to lessen the burden of mycobacteria and stop the spread of mycobacterial infection.

It has been noted that 10 million people fall ill with tuberculosis (TB) worldwide, and a total of 1.6 million people die from TB (7); thus, drug-resistant TB remains a public health crisis. *M. tuberculosis* is proficient in altering the immune response for its own survival, leading to disease or latent infection. The molecules and mechanisms utilized to accomplish the survival of bacteria inside the host are not fully understood. Early and effective treatment of these infections is very important to prevent transmission within the population. There is an urgent need for fast and reliable point-of-care (POC) diagnostic methods for effective case management. Currently, the used methods for screening and diagnosis are clinical, immunological, microscopic, radiographic, and bacterial culture. In

addition, recent advances in molecular diagnostic methods, including loop-mediated isothermal amplification (LAMP), line probe assay (LPA), cartridge-based nucleic acid amplification test (CBNAAT), fully automated (GeneXpert) platform, and whole-genome sequencing (WGS), have been employed to diagnose and characterize tuberculosis and non-tuberculosis infections. Another technique for classifying and identifying mycobacteria uses the mass spectrometer (MS) and matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF) technologies.

The other main mycobacterial disease affecting humans is leprosy caused by *M. leprae*. The transmission of leprosy has not been understood fully. In recent advancements in molecular biology, the molecular marker has been used for the detection of the viability of *M. leprae* and transmission in the community.

This Research Topic presents original research articles and case studies that focused on recent developments in molecular biology and immunology in respect to diagnostic techniques, the transmission aspect of mycobacteria, the use of medication to treat mycobacterial infection, and the evaluation of drug resistance patterns, as well as the understanding of immune responses in the host against the bacteria, cell subsets at the local site, and how immune responses can stimulate the outcome of disease.

For NTM, Zhou et al. reported the first case of M. senegalense infection in a human after laparoscopic cholecystectomy was observed in China. M. senegalense infection in humans is extremely rare, especially in immunocompetent individuals. It is also difficult to detect M. senegalense infection because its symptoms are non-specific, and routine diagnostic tests are less sensitive. By using a molecular PCR followed by next-generation sequencing (NGS), the DNA sequences of M. senegalense in patient tissue samples were identified. M. senegalense infection was treated with quadruple therapy with clarithromycin, moxifloxacin, rifampicin, and oxycycline for 60 days, and it was noted that patient's wound healed remarkably.

In the field of tuberculosis, Mtafya et al. prospectively assessed the monitoring of the treatment response of a tuberculosis (TB) patient with TB bacteriology and novel tuberculosis–molecular bacterial load assay (TB-MBLA). The authors assessed bacteriologically confirmed cases for TB and assessed the symptoms and bacteriological resolution using smear microscopy, culture, and TB-MBLA over a six-month treatment. A decrease in TB-MBLA positivity reflected a fall in the bacillary load. Low-baseline bacillary load patients were more likely to be bacteriologically negative by month 2 and 6 of treatment, respectively. Mtafya et al. showed a high percentage agreement of clinical symptoms with bacteriological positivity for TB at diagnosis, which weakens rapidly during the early weeks of anti-TB therapy. These findings provide new evidence that relying solely on TB symptoms for diagnosis or monitoring may mislead the treatment decisions of some patients and the final treatment outcomes. These findings advocate for more investment in bacteriological tests to improve the accuracy of TB diagnosis and treatment monitoring in routine healthcare settings.

Wang et al. reported that prisons are regarded as a hotspot for TB disease and transmission, emphasizing that prevention strategies must focus on this hotspot to achieve the global target of ending TB (8). The present study observed a significant burden of TB in an incarcerated population in Qingdao, where 3.36% of inmates had pulmonary TB. The prevalence of TB found in this study was six times higher than the estimated prevalence for the general population (0.5% in 2010) (9). It is not only a risk to other prisoners and prison staff, but it also has the potential to put communities in danger of TB disease after their release from prison.

Worku et al. evaluated the drug sensitivity of M. tuberculosis and its association with the bacterial genotype and evaluated the performance of Xpert MTB/RIF (Xpert) in detecting resistance to rifampicin (RIF). The authors reported that the SIT 149 (T3-ETH) spoligotype was significantly associated with resistance to one or more drugs and multidrug resistance to TB, which was widespread in Ethiopia. The Xpert assay was observed to have high sensitivity and specificity in detecting rifampicin-resistant M. tuberculosis. Hence, this test can be applied widely.

Zhuang et al. analyzed the clinical characteristics of patients with central airway stenosis due to tuberculosis. The authors reported that despite receiving mostly adequate anti-tuberculosis chemotherapy, patients with TB can present with CASTB, involving severe scarring stenosis, bronchial occlusion, tracheobronchomalacia, and even destroyed lungs.

Sharma et al. evaluated the immune responses at the local site of infection and in the peripheral blood to improve the understanding of the immunological mechanisms involved in the containment and progression of TB. Significantly higher intracellular calcium levels, phosphorylation levels of ZAP-70, Erk1/2, and p-38 in CD3 and CD28 induced cells of pleural fluid as compared to the blood cells of the same patient with tuberculous pleural effusion (TPE). An alteration in the activation of the same events after stimulation with ESAT-6 and Ag85A was noted.

Adepoju et al. observed that frontline TB providers in private hospitals in Lagos struggled with assigning correct treatment outcomes for TB patients based on the NTBLCP guideline. The huge proportion of TB patients with missing end-of-treatment, month six follow-up results is of great concern. The result was a huge discrepancy between the reported and actual cure and completion rate data. Increased access to all the periodic follow-up AFB tests for TB patients on treatment and availability of the National TB Guideline for referencing could potentially improve the adherence of private TB service providers while assigning TB treatment outcomes.

In the field of leprosy, Turankar et al. reported that the molecular epidemiology of leprosy is important to study leprosy transmission dynamics and to enhance the understanding of leprosy in endemic areas by utilizing the molecular typing method. In this study, the authors observed the presence of viable M. leprae in inhabitant areas of leprosy patients. These viable bacilli might survive in the environment and might help to cause leprosy disease after repeated exposure to a susceptible host. A similar genotype in clinical and environmental samples indicates that the

environment could possibly act as a source of infection. The SNP and VNTR combination showed the M. leprae strain similarities and their differentiation in certain blocks of Purulia. Such studies with the combination of genetic markers may provide a tool to track the transmission link in the community.

Conclusion

The collection of papers in this Research Topic provides insight into the challenges associated with the diagnosis, prevention, and management of mycobacterial diseases. The importance of recent molecular techniques used for the rapid diagnosis and identification of specific species and the transmission aspect of mycobacterial disease is highlighted, from the individual to the community level. The completion of treatment is essential to stop the transmission of the disease and to facilitate its proper management. The advancement in molecular technology and recognition of the molecular marker in the *M. leprae* genome has added to the value of tracking community transmission.

Author contributions

RT and IS wrote this editorial and interpreted all the data, followed by analysis. ML and UG reviewed and edited the draft. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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