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PERSONALIZED MEDICINE FUTURE PERSPECTIVE APPROACH FOR THE DIAGNOSIS OF TUBERCULOSIS

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ABSTRACT

Tuberculosis is a bacterial infectious illness that is spread mostly by communicable droplets from one person to another. Drug-resistant patients and substandard drug authorization Mycobacterium tuberculosis is one of the two major obstacles to tuberculosis (TB) management in endemic areas, such as India and the rest of the world. Precision medicine, also known as customized medicine, is based on the diversity of systems biology and using predictive techniques to assess health risk and build tailored health plans to assist patients in reducing risk, preventing disease, and treating it with precision. Only active pulmonary tuberculosis is contagious. TB continues to be a significant source of illness and mortality in many low- and middle-income nations, and drug-resistant TB is a major problem in many areas. Furthermore, several novel TB diagnostics methods, such as quick molecular testing, have been developed, and there is a demand for simpler point-of-care tests. Personalized medicine ushers in a new age in healthcare. In the subject of Mycobacteriology, personalized medicine may be used in a variety of ways, including prevention, diagnosis, improved therapy, and prognosis. To change an independent proposition in mycobacterial disorders, a genetic inclination and a protein affliction investigation are presented. Patients' results should be turned into accurate diagnostic tests and focused therapy in order for personalized medicine to be used successfully by the healthcare system.

KEYWORDS: Tuberculosis, Personalized medicine, Mycobacteriology, molecular tests, genetic inclination.

INTRODUCTION

Tuberculosis (TB) is the leading cause of death worldwide due to a single microbiological pathogen (Mycobacterium tuberculosis) (1). According to the World Health Organization (WHO), roughly 10 million people contracted tuberculosis for the first time in 2018, and 1.5 million people died from the disease. (1). Despite the enormous burden tuberculosis places on healthcare systems, particularly in developing countries, research on new tuberculosis prevention and diagnostic tools, as well as novel medicines, has only lately acquired traction. Robert Koch discovered the cause of tuberculosis (TB), an airborne infectious disease caused by Mycobacterium tuberculosis complex organisms, in 1882. In 2016, tuberculosis (TB) continues to be a major source of morbidity and mortality, especially in low- and middle-income nations (2).

M. tuberculosis is a lung infection that can cause disease in any section of the body. Furthermore, tuberculosis can manifest itself in a variety of ways, ranging from asymptomatic infection to a deadly condition (3). Patients with tuberculosis can be classed as having latent tuberculosis infection (LTBI), which is asymptomatic and non-communicable, or active tuberculosis disease, which is transmissible (in active pulmonary TB) and can be diagnosed with culture-based or molecular diagnostics. Patients with active tuberculosis experience general symptoms such as fever, weariness, loss of appetite, and weight loss, while those with pulmonary illness may experience a persistent cough and hives(3).

Isoniazid, rifampicin, pyrazinamide, and ethambutol are the four first-line antimicrobials used to treat tuberculosis. It is possible to develop resistance to any medicine. Multidrug-resistant tuberculosis (MDR-TB), which is defined as M. tuberculosis that is resistant to at least isoniazid and rifampicin, is a well-known disease that has been recorded in almost every country (2).

Comprehensively drug-resistant TB illness is resistant to not just isoniazid and rifampicin, but also any fluoroquinolone and any of the three injectable second-line aminoglycosides, resulting in much more severe disease symptoms. For LTBI and active TB disease, as well as drug-sensitive and drug-resistant TB disease, diagnostic and treatment options differ. TB is one of the top ten causes of death worldwide and the leading cause of mortality due to a single infectious agent. The bacterium M. tuberculosis mostly affects the lungs, which is known as pulmonary tuberculosis, but it can also affect other regions of the human body, which is known as extra-pulmonary tuberculosis. According to a global TB announcement for 2019, nearly 10 million people worldwide were infected with tuberculosis, with an average of 130 cases per 100,000 people (4).

In the Indian context, the clinical burden of tuberculosis is not evenly distributed across the country; Uttar Pradesh, which accounts for 17% of the Indian population, accounts for 20% of cases, with 187 cases per 100,000 people. Similarly, the Indian native groups (tribes) were found to be severely afflicted by tuberculosis (TB), with 703 cases per 100,000 people (5), over three times the Indian norm and beyond five times the global average.

Patients with tuberculosis have received the same standard therapy for the past five decades, despite differences in human immunology, pharmacokinetics, and pathophysiology, as well as differences in the novel microorganism, Mycobacterium tuberculosis. Treatment was either sporadic or based on the results of phenotypic drug susceptibility testing, which might take weeks or months to complete. Patient tailoring was largely restricted to altering body weight in pediatrics (6).

In M. tuberculosis complex strains, drug resistance is entirely mediated by genomic variations, primarily single nucleotide polymorphisms (SNPs) and tiny insertions/deletions (indels). Resistance genes are not acquired through plasmids or horizontal gene transfer (7).

As a result, resistant phenotypes of M. tuberculosis complex strains have a clear genetic correlation, which implies SNPs may be used to predict resistance with a high degree of precision, and are projected to eventually replace phenotypic drug susceptibility testing (DST) (7). Advances in next-generation sequencing (NGS) technology have made it possible to cross-question all resistance-related variations in the genomes of clinical M. tuberculosis complex strains.

We have now reached an exciting era of medicine, with significant improvements in the field of system biology, and there is a strong belief that tuberculosis sufferers would benefit greatly from these advancements (8 -9).

PERSONALIZED MEDICINE

Personalized medicine concepts are applicable to newly developed and transformative health-care approaches. Tailored health care is based on the variability of systems biology and employs predictive technologies to assess health risks and create personalized health plans to assist patients in reducing risks, preventing disease, and treating it precisely when it occurs. With the Veterans Administration providing individualized, proactive patient-driven care to all veterans, personalized health care is gaining popularity (10). In other cases, rather than the patient's genetic markup, personalized health care might be adjusted to the markup of the disease-causing agent; examples include drug-resistant bacteria or viruses (11).

"Genetic medicine" should not be confused with "personalized medicine." Genetics is the study of how a gene or a combination of genes is passed down through generations. It is a topic that has been around for more than 50 years. It investigates the influence of specific genes on health. Other genes, as well as environmental factors such as nutrition and toxicity exposure, can influence genetic diseases, which appear to be "simple" inherited conditions (12). Single nucleotide polymorphism (SNP) genotyping over the entire genome is now possible, allowing for genome mapping and the discovery of novel correlations that would be impossible to find using a candidate gene approach.

PERSONALIZED MEDICINE IN TUBERCULOSIS

In recent years, advances in biomedical research and the application of cutting-edge biological tools have transformed the medical sciences, making the task of capturing population genetic variations easier than ever. As a result, understanding of the relationship between human genes and various diseases, as well as therapy based on individual genetic composition (personalized medicine), has begun to evolve and is now being employed for various disorders. Chemotherapy is the sole technique to treat tuberculosis under the current protocol. Individual genetic variation in TB patients' responses to drugs (e.g. efficacy of drug metabolism) has been seen, justifying individual genetic diversity in TB patients' responses to drugs (e.g. effectiveness of drug metabolism) (13). Furthermore, differences in the drug sensitivity of the infected mycobacterium strain can influence treatment efficacy (for example, infection with drug-resistant M. tuberculosis, which is classified as MDR or XDR). Both of these characteristics (individual drug absorption ability in humans and infection with drug-resistant

mycobacterium) define TB treatment efficacy, and thus help to contribute for success of eradication programme.

Human genetic factors play a significant part in easing these two features, since various genes in humans have been identified that are involved in explaining susceptibility to mycobacterial disease. For example, a mutation in a gene that codes for the chemokine (C-C motif) ligand-2 (CCL2) (14), which is important for monocyte and T-cell recruitment, may increase the risk of developing tuberculosis. Similarly, a human tumor necrosis factor gene polymorphism has been linked to a decreased response to TB treatment (15).

Furthermore, a genome-wide association research discovered new loci that may increase the chance of dormantly infected people developing active tuberculosis (16).

Furthermore, anti-TB medications are known to cause hepatotoxicity, and the generation and elimination of hazardous metabolites are dependent on the activity of human enzymes such as N-acetyl transferase-2, cytochrome P450 oxidase, glutathione S transferase, interlukin-12, interferon-gamma, and others. Studies have indicated that mutations in these genes can modify enzyme activity and increase/decrease the risk of hepatotoxicity, as well as contribute to the prognosis of tuberculosis (17).

FUTURE PERSPECTIVE OF PERSONALIZED MEDICINE TO UPGRADE CLINICAL COUNSEL AND RESULTS (PREVENTION, DIAGNOSIS, TREATMENT AND MONITORING)

DIAGNOSIS

The presence of a positive adaptive immune response to M. tuberculosis in the tuberculin skin test or a positive reaction in an interferon-release assay in the absence of active TB is required for the diagnosis of inactive or latent infection with M. tuberculosis (LTBI) with the risk of progression to active disease(18).

The disease prevalence determines the positive anticipated values of adaptive immune responses to M. tuberculosis. The value of the tuberculin skin test and the interferon-release assay for the possibility of evaluating future TB has been demonstrated to be very limited in countries with low TB prevalence (e.g. Western Europe) in recent years (progression rates of 2/100patients year).

A new master plan for calculating the probability of disease succession (18-19) is required to reduce the number of people who need to be treated to stop a case of tuberculosis (19) and to effectively direct the delivery of preventive chemotherapy to at-risk groups (20). Recently, a transcriptome approach in South African teenagers with LTBI revealed a pattern of 16 gene transcripts that could distinguish between healthy individuals and those who progressed to active disease (21).

The development and application of molecular techniques has revolutionized M. tuberculosis diagnostics, allowing for more rapid detection of drug resistance and the initiation of appropriate treatment for MDR-TB patients (Multidrug resistant TB). For example, rapid molecular tests such as Cepheid's automated, cartridge-based Xpert MTB/RIF (Mycobacterium tuberculosis/Rifampicin) or Hain Lifescience's GenoType MTBDR plus (containing probes specific for MTB complex as well as probes for common rifampin resistance conferring mutations) and MTBDRsl (is a rapid test for detecting resistance to second-line TB drugs) have experience support from the WHO for their execution and are used in many context across the world (22-23; 24).

TREATMENT

Therapeutic drug monitoring (TDM) is a hot topic in TB therapy management. Estimating medication concentrations in patients' blood may result in improved potency and dosing in difficult-to-treat patients by adjusting drug dosages based on drug plasma concentrations (25) and may reduce the toxicity of second-line treatments in particular. TDM, in particular, minimizes the risk of sub-therapeutic drug concentrations in functional immunotherapy. As a result, it may be able to prevent the development of supplemental drug resistance (26).

Blood samples are examined using either a single analyte approach (27) or a multi analyte approach (particularly in regimens including multiple second-line medicines) utilizing high performance liquid chromatography and tandem mass spectrometry (28). This assay is only available at a few specialized centers due to its difficulty. The collection and delivery of dried blood spots may ease sample logistics for TDM at sites without this specific infrastructure (29). So far, five different antimicrobial medications have been used on dried blood spots (30).

The interest from TDM, as well as the reference values for drug concentrations, should be left ambiguous. There are few studies that show a link between TDM and treatment outcomes or acquired drug resistance (31-33). The claimed interrelations were frequently based on regression or multivariate analysis rather than those reference values (25; 31-33).

Biomarkers that act as proxies to assess therapeutic success or failure early in the course of treatment would be of interest to patients with chronic respiratory

disorders (34). TB-specific transcriptional patterns, primarily interferon-driven, and their modifications upon therapy initiation in individuals with susceptible TB, for example, have been observed (35-37).

In patients with susceptible TB, transcriptional alterations that can be observed as soon as 2 weeks after starting medication were studied (38). Furthermore, the dynamics of biological markers (e.g., peripheral T-regulatory cells, exhaustion T cells) and inflammatory proteins (e.g., vascular endothelial growth factor, interferon-inducible protein 10) during therapy were described (39-40).

Biomarkers or compound indicators, such as blood markers, radiological assessment by chest X-ray, CT (computed tomography), or positron emission tomography-CT, and clinical scores, could eventually aid in customizing the duration of therapy for patients with persistent respiratory infections (34; 41-42).

Recognition of biomarkers that direct when to start NTM-PD (non-tuberculous mycobacterial pulmonary disease) therapy and allow early prognosis of medication failure or success would be beneficial, however such biomarkers have not been investigated yet. The Aspergillus-specific IgG antibody has been found to change between colonization and infection with a sensitivity of 96 percent and a specificity of 98 percent for CPA (cardiopulmonary arrest) (43).

Given that INH (isonicotinic acid hydrazide) is one of the first-line treatments for tuberculosis and that there is a clear link between unrelated genotypes and drug metabolism in humans, the first step in personalized medicine should be genetic profiling of the NAT2 genetically polymorphic N-acetyltransferase 2 (NAT2) enzyme and, as a result, INH tweaking. In this regard, the following policy can be considered. First, a TB patient's acetylation phenotype could be categorized based on the allele of the NAT2 gene, and second, INH doses with suitable concentration and frequency could be resolved on and operated to regulate the acetylation phenotype.

In India, a database of NAT2 genotypes will be created, which may be utilized to develop similar precision medicine techniques for other disorders. For example, while maintaining the same daily dose per kilo body weight for both acetylation phenotypes, a patient with the slow acetylation phenotype (as determined by the NAT2 genotype) can receive INH in lower concentrations but with regular repeats, whereas a patient with the fast acetylation phenotype can receive the efficacious concentration with the currently determined repeats (44).

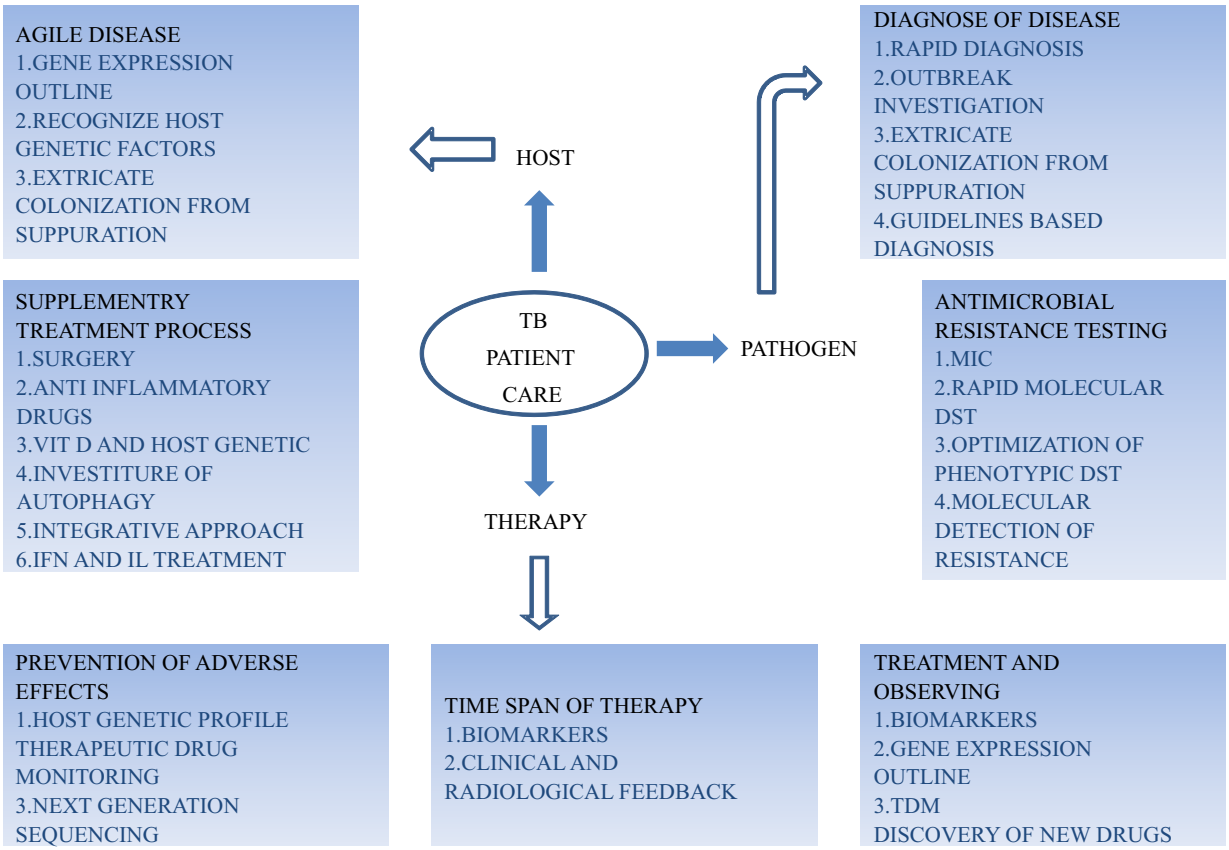

Fig. 1. Prevention and Treatment of TB

CONCLUSION

Precision medicine in the treatment of tuberculosis has been a hot topic in recent years. New therapeutic guidelines are authorizing tailored therapy based on drug susceptibility testing (DST) results, which is a good thing (45). Furthermore, DST should be used in conjunction with information on antibiotic pharmacokinetics (PK) and pharmacodynamics (PD). The Global Tuberculosis Network's pharmacology committee is advocating Therapeutic Drug Monitoring (TDM) as part of this oversight (46). It has become sufficiently easy to administer anti-TB medications with the TDM approach, certifying the right amount, decreasing adverse occurrences, and maximizing regimen efficacy. The next phase should be a modified controlled trial to compare TDM with supervision quality in order to demonstrate the benefits of precision dosing (47).

Given the fact that genotype-based dosage calculation for TB in the NAT2-INH system is quite simple, precision medicine in TB appears to be a foregone conclusion. Because the spread of MDR M. tuberculosis resistant to rifampicin and isoniazid is a major concern (48), customizing therapy might help to prevent MDR-TB from spreading.

Patients with persistent respiratory infections are more likely to stay in the hospital longer than patients with other medical problems. Individualized medicine also necessitates taking into account the mental and physical needs of patients by assuming personalized psychosocial assistance, physiotherapy, and rehabilitation. We have no doubt that tailored treatment will help independent people make better decisions. Patients and physicians, not machines, should, nonetheless, make personal decisions. Computerized algorithms will improve clinical decision-making; nevertheless, they are not intended to act as a substitute for the doctor-patient connection; instead, the eventual goal is to keep medicine confidential.

CONFLICT OF INTEREST: None

REFERENCES

1. World Health Organization. Global tuberculosis report 2019. World Health Organization; 2019.
2. World Health Organization. Global tuberculosis report 2015. World Health Organization; 2015.
3. Berry MP, Graham CM, McNab FW, et al. An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis. Nature. 2010; 466:973–977.
4. Wlodarska M, Johnston JC, Gardy JL, et al. A microbiological revolution meets an ancient disease: improving the management of tuberculosis with genomics. Clin Microbiol Rev. 2015; 28:523–39.
5. Thomas BE, Adinarayanan S, Manogaran C, et al. Pulmonary tuberculosis among tribals in India: A systematic review & meta-analysis. The Indian journal of medical research. 2015;141(5):614.
6. Horsburgh Jr CR, Barry III CE, Lange C. Treatment of tuberculosis. New England Journal of Medicine. 2015 26;373(22):2149-60.
7. Meehan CJ, Goig GA, Kohl TA, et al., Whole genome sequencing of Mycobacterium tuberculosis: current standards and open issues. Nature Reviews Microbiology. 2019;17(9):533-45.
8. Lange C, Alghamdi WA, Al-Shaer MH, et al., Perspectives for personalized therapy for patients with multidrug-resistant tuberculosis. Journal of internal medicine. 2018;284(2):163-88.
9. Olaru ID, Lange C, Heyckendorf J. Personalized medicine for patients with MDR-TB. Journal of Antimicrobial Chemotherapy. 2016 1;71(4):852-5.
10. Snyderman R. Personalized health care: from theory to practice. Biotechnology journal. 2012;7(8):973-9.
11. Altmann A, Beerenwinkel N, Sing T, et al., Improved prediction of response to antiretroviral combination therapy using the genetic barrier to drug resistance. Antiviral therapy. 2007 1;12(2):169.
12. Chang LJ, Chen SU, Tsai YY, et al., An update of preimplantation genetic diagnosis in gene diseases, chromosomal translocation, and aneuploidy screening. Clinical and experimental reproductive medicine. 2011;38(3):126.
13. Joshi JM. Tuberculosis chemotherapy in the 21st century: Back to the basics. Lung India: Official Organ of Indian Chest Society. 2011;28(3):193.
14. Feng WX, Flores-Villanueva PO, Mokrousov I, et al., (A/G) polymorphisms and tuberculosis susceptibility: a meta-analysis. The International journal of tuberculosis and lung disease. 2012 1;16(2):150-6.
15. García-Elorriaga G, Carrillo-Montes G, Mendoza-Aguilar M, et al. Polymorphisms in tumor necrosis factor and lymphotoxin A in tuberculosis without and with response to treatment. Inflammation. 2010;33(4):267-75.
16. Png E, Alisjahbana B, Sahiratmadja E, et al., A genome wide association study of pulmonary

tuberculosis susceptibility in Indonesians. BMC medical genetics. 2012;13(1):1-9.

17. Wang J, Tang S, Shen H. Association of genetic polymorphisms in the IL12-IFNG pathway with susceptibility to and prognosis of pulmonary tuberculosis in a Chinese population. European journal of clinical microbiology & infectious diseases. 2010;29(10):1291-5.
18. Zellweger JP, Sotgiu G, Block M, et al., Risk assessment of tuberculosis in contacts by IFN-γ release assays. A Tuberculosis Network European Trials Group study. American journal of respiratory and critical care medicine. 2015 15;191(10):1176-84.
19. Sester M, van Crevel R, van Leth F, et al. Numbers needed to treat to prevent tuberculosis. European Respiratory Journal. 2015 1;46(6):1836-8.
20. Gutsfeld C, Olaru ID, Vollrath O, et al. Attitudes about tuberculosis prevention in the elimination phase: a survey among physicians in Germany. PLoS One. 2014 13;9(11):e112681.
21. Zak DE, Penn-Nicholson A, Scriba TJ, et al., A blood RNA signature for tuberculosis disease risk: a prospective cohort study. The Lancet. 2016 4;387(10035):2312-22.
22. Rothenberg ME. Eosinophilia. New England Journal of Medicine. 1998 28;338(22):1592-600.
23. Meng Y, Lichtman AH, Bridgen DT, et al. Inhalation studies with drugs of abuse. NIDA Research Monograph. 1997 1;173:201-24.
24. Brigden ML. The monitoring of potential long-term complications in treated adult cancer patients. Annals of Saudi medicine. 1997;17(6):622-8.
25. Alsultan A, Peloquin CA. Therapeutic drug monitoring in the treatment of tuberculosis: an update. Drugs. 2014;74(8):839-54.
26. Srivastava S, Pasipanodya JG, Meek C, et al. Multidrug-resistant tuberculosis not due to noncompliance but to between-patient pharmacokinetic variability. The Journal of infectious diseases. 2011 15;204(12):1951-9.
27. Alffenaar JW, Bolhuis M, van Hateren K, et al., Determination of bedaquiline in human serum using liquid chromatography-tandem mass spectrometry. Antimicrobial agents and chemotherapy. 2015 1;59(9):5675-80.
28. Han M, Jun SH, Lee JH, et al. Method for simultaneous analysis of nine second-line anti-tuberculosis drugs using UPLC-MS/MS. Journal of Antimicrobial Chemotherapy. 2013 1;68(9):2066-73.
29. Chideya S, Winston CA, Peloquin CA, et al., Isoniazid, rifampin, ethambutol, and pyrazinamide pharmacokinetics and treatment outcomes among a predominantly HIV-infected cohort of adults with tuberculosis from Botswana. Clinical infectious diseases. 2009 15;48(12):1685-94.
30. Pasipanodya JG, McIlleron H, Burger A, et al. Serum drug concentrations predictive of pulmonary tuberculosis outcomes. The Journal of infectious diseases. 2013 1;208(9):1464-73.
31. Weiner M, Benator D, Burman W, et al., Tuberculosis Trials Consortium. Association between acquired rifamycin resistance and the pharmacokinetics of rifabutin and isoniazid among patients with HIV and tuberculosis. Clinical infectious diseases. 2005 15;40(10):1481-91.
32. Heyckendorf J, Olaru ID, Ruhwald M, et al. Getting personal perspectives on individualized treatment duration in multidrug-resistant and extensively drug-resistant tuberculosis. American journal of respiratory and critical care medicine. 2014 15;190(4):374-83.
33. Olaru ID, Lange C, Heyckendorf J. Personalized medicine for patients with MDR-TB. Journal of Antimicrobial Chemotherapy. 2016 1;71(4):852-5.
34. Zuur MA, Bolhuis MS, Anthony R, et al., Current status and opportunities for therapeutic drug monitoring in the treatment of tuberculosis. Expert opinion on drug metabolism & toxicology. 2016 3;12(5):509-21.
35. Bloom CI, Graham CM, Berry MP, et al., Detectable changes in the blood transcriptome are present after two weeks of antituberculosis therapy 2012.
36. Berry MP, Graham CM, McNab FW, et al., An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis. Nature. 2010;466(7309):973-7.
37. McNab FW, Berry MP, Graham CM, et al., Programmed death ligand 1 is over-expressed by neutrophils in the blood of patients with active tuberculosis. European journal of immunology. 2011;41(7):1941-7.
38. Riou C, Perez Peixoto B, Roberts L, et al., Effect of standard tuberculosis treatment on plasma cytokine levels in patients with active pulmonary

tuberculosis. PloS one. 2012 14;7(5):e36886.

39. Wu YE, Peng WG, Cai YM, et al., Decrease in CD4+ CD25+ FoxP3+ Treg cells after pulmonary resection in the treatment of cavity multidrug-resistant tuberculosis. International Journal of Infectious Diseases. 2010 1;14(9):e815-22.
40. Singh A, Mohan A, Dey AB, et al. Inhibiting the programmed death 1 pathway rescues Mycobacterium tuberculosis–specific interferon γ–producing T cells from apoptosis in patients with pulmonary tuberculosis. The Journal of infectious diseases. 2013 15;208(4):603-15.
41. Ralph AP, Ardian M, Wiguna A, et al., A simple, valid, numerical score for grading chest x-ray severity in adult smear-positive pulmonary tuberculosis. Thorax. 2010 1;65(10):863-9.
42. Wejse C, Gustafson P, Nielsen J, et al., TBscore: Signs and symptoms from tuberculosis patients in a low-resource setting have predictive value and may be used to assess clinical course. Scandinavian journal of infectious diseases. 2008 1;40(2):111-20.
43. Page ID, Richardson MD, et al. Comparison of six Aspergillus-specific IgG assays for the diagnosis of chronic pulmonary aspergillosis (CPA). Journal of Infection. 2016 1;72(2):240-9.
44. Cordes H, Thiel C, Aschmann HE, et al. A physiologically based pharmacokinetic model of isoniazid and its application in individualizing tuberculosis chemotherapy. Antimicrobial agents and chemotherapy. 2016 23;60(10):6134-45.
45. Nahid P, Mase SR, Migliori GB, et al., Treatment of drug-resistant tuberculosis. An official ATS/CDC/ERS/IDSA clinical practice guideline. American journal of respiratory and critical care medicine. 2019 15;200(10):e93-142.
46. Alffenaar JW, Gumbo T, Dooley KE, et al., Integrating pharmacokinetics and pharmacodynamics in operational research to end tuberculosis. Clinical Infectious Diseases. 2020 10;70(8):1774-80.
47. Alffenaar JW, Akkerman OW, Kim HY, . Precision and personalized medicine and anti-TB treatment: is TDM feasible for programmatic use?. International Journal of Infectious Diseases. 2020 1;92:S5-9.
48. Seung KJ, Keshavjee S, Rich ML. Multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. Cold Spring Harbor perspectives in medicine. 2015 1;5(9):017863.

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