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Science and Technology Facilitates Tuberculosis Prevention and Control: Current Situation, Progress and Countermeasures

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Abstract

Tuberculosis (TB), a chronic communicable disease caused by the pathogen Mycobacterium tuberculosis, has harassed the human being for long-term and remains to be one of the major public health problems facing the world as well as the leading cause of death from a single infectious agent. We are falling short of TB control targets set by the World Health Organization (WHO) and United Nations (UN). To achieve the ambitious targets of global TB prevention and control, there is an urgent need for immediate action as well as science and technology breakthroughs (e.g., a new vaccine and drug) to rapidly reduce TB incidence worldwide. This study summarizes the current progress on global and China's TB prevention and control, and analyzes the contribution of science and technology in TB prevention and control. Based on the above analysis, we propose the following thought and advice on strengthening TB prevention and control through science and technology:Strengthening the basic research of TB, developing new TB vaccines and drugs, developing new diagnostic techniques for TB, and perfecting the system to support and strengthen the safeguard measures. The purpose of this study is to promote the policy layout and practice innovation of scientific prevention and control of TB in China, thus speeding up the realization of goals set by the WHO End TB Strategy.

Keywords

Mycobacterium tuberculosis, tuberculosis, tuberculosis prevention and control, science and technology, prevention and control measures

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Science and Technology Facilitates Tuberculosis Prevention and Control: Current Situation, Progress and Countermeasures

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Abstract: Tuberculosis (TB), a chronic communicable disease caused by the pathogen *Mycobacterium tuberculosis*, has harassed the human being for a long time and remains to be one of the major public health problems facing the world as well as a leading cause of death from a single infectious agent. We are falling short of TB control targets set by the World Health Organization (WHO) and the United Nations (UN). To achieve the ambitious targets of global TB prevention and control, there is an urgent need for immediate action as well as science and technology breakthroughs (e.g., a new vaccine and drug) to rapidly reduce TB incidence worldwide. This study summarizes the current progress on global and China's TB prevention and control, and analyzes the contribution of science and technology to TB prevention and control. On the basis of the above analysis, we propose the following advice on strengthening TB prevention and control through science and technology: strengthening the basic research of TB, developing new TB vaccines and drugs, developing new diagnostic techniques for TB, and perfecting the system to support and strengthen the safeguard measures. The purpose of this study is to promote the policy layout and practice innovation of scientific prevention and control of TB in China, thus speeding up the realization of the goals set by the WHO End TB Strategy. **DOI:** 10.16418/j.issn.1000-3045.20211116002-en

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Tuberculosis (TB), an ancient chronic communicable disease caused by *Mycobacterium tuberculosis* (Mtb), has been seriously threatening human health, particularly the poor and the vulnerable. TB has killed more than 1 billion people in the past 2000 years and kills about 1.5 million people worldwide every year. The World Health Organization (WHO) has put forward the End TB Strategy (2016–2035), and the United Nations (UN) has also set the goals of containing TB and ending the TB epidemic by 2035 in Transforming Our World: The 2030 Agenda for Sustainable Development. The deadlines set for these two goals are less than 14 years and 9 years from now, respectively [1–3]. However, given the current trends and technologies, the goal of eliminating TB may come into reality after 160 years in 2182 [4].

The most powerful weapon against infectious diseases is science and technology. Therefore, the eventual defeat of TB, an intractable chronic communicable disease, depends on scientific development and technological innovation. The priorities listed in Global Tuberculosis Report 2020 released by WHO include a vaccine to lower the risk of infection, a vaccine or new drug treatment to cut the risk of TB disease in the approximately 2 billion people already infected, etc. [5]. If no urgent action is taken to develop the relevant technologies, the goals of containing TB worldwide may not be achieved. This study summarizes the current progress in global and China's TB prevention and control, further analyzes the contribution of science and technology in TB prevention and control. Moreover, this study puts forward the following recommendations on strengthening TB prevention and control through science and technology, including strengthening basic research on TB, developing new TB vaccines and drugs, developing new diagnostic techniques for TB, and perfecting the system to support and strengthen the safeguard measures. This study aims at promoting the policy layout and practice innovation of scientific TB prevention and control in China, thereby accelerating the realization of the goals in the End TB Strategy.

1 Development trends of TB

1.1 Current status of TB in China and the world

According to the Global Tuberculosis Report 2021 issued by WHO, there are 9.87 million newly diagnosed TB patients worldwide in 2020 and the estimated incidence rate shows a downward trend [6]. However, due to the impact of

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COVID-19 pandemic, a large number of TB patients are not diagnosed and treated in time, which leads to an increase in TB deaths from 1.408 million in 2019 to 1.494 million in 2020. This is the first increase in the past 15 years (Table 1). Meanwhile, drug-resistant TB is still a severe global public health crisis [6]. About 500 thousand rifampicin-resistant TB (RR-TB) patients are reported worldwide in 2019 and 78% of them are multidrug-resistant TB (MDR-TB) patients. Moreover, the treatment success rate is 85% for drug-susceptible TB worldwide but only 57% for MDR/RR-TB. Notably, the COVID-19 pandemic has greatly reduced the accessibility of health care and the visits of TB patients. According to the model estimates, the global TB prevention and control may be set back for 5–8 years due to the outbreak of COVID-19 [5].

As one of the major countries harassed by TB for years, China has become one of the 30 countries with high burdens of TB, drug-resistant TB and TB/AIDS (HIV). The estimated number of new TB patients in China is 842 thousand in 2020, which ranks only second to India after ranking the third in 2019 [6] (Table 1). The burden of drug-resistant TB is particularly heavy in China. It is estimated that the new RR-TB patients may be as high as 65 thousand per year, which ranks the second worldwide. Moreover, more than 70% of the drug-resistant TB patients have not been diagnosed in China, which may pose high risks for human-to-human transmission and great challenges for TB control [5]. In addition, there is a large population with latent TB infection in China. A total of 365 million people has been infected with Mtb, which ranks the second in the world [7]. These patients may develop into active TB in their lifetime and thus it is of great significance to adopt early and precise intervention against these latent infection cases.

1.2 Goals and current situations of TB prevention and control in the world

In 2014 and 2015, WHO member countries' strategic goals and the UN agenda for ending TB prevalence all include specific milestones for reducing TB incidence and mortality, and for eliminating catastrophic costs among TB patients and their households [1,2]. On the first WHO Global Ministerial Conference on TB in 2017, the Moscow Declaration to End TB [7] was adopted. The UN General Assembly held the first-ever high-level meeting on TB in 2018, which was attended by heads of different countries and governments as well as other leaders. The meeting agreed on a political declaration, and reaffirmed and added new commitments to Transforming Our World: The 2030 Agenda for Sustainable Development and the End TB Strategy. Global targets were set for the first time for the funding for TB prevention, treatment and research, as well as for the number of Mtb infections and patients treated [3].

The specific goals set by WHO and the UN for ending global TB prevalence are as follows: the mortality and incidence of TB in 2030 should decrease by 90% and 80%, respectively, as compared with those in 2015; the mortality and incidence in 2035 should decrease by 95% and 90%, respectively [1–3]. Although there have been some political declarations and great goals, the current progress is slow. The newly diagnosed TB patients are still maintained at a stable level every year in the recent five years. According to the Global Tuberculosis Report 2021, most of the WHO member countries and the high TB burden countries did not achieve the 2020 milestones of the End TB Strategy. Moreover, the COVID-19 pandemic has also caused tremendous negative effect on TB prevention and control (Figure 1) [6].

2 Contribution of science and technology to TB prevention and treatment

2.1 Achievements and challenges of TB prevention and control through science and technology in China

TB patients may bring about heavy burdens for their families. A national survey reveals that the average out-of-pocket financial burden for each TB patient is more than CNY 15 000 and about 1/4 TB patients become poor due to this disease. Therefore, TB prevention and control have become a major challenge to the Healthy China initiative [8]. The CPC Central Committee and the State Council of China have paid additional attention to TB prevention and control and included it into the Outline of the Healthy China 2030 Plan in 2016. This is also an important step for China to fulfill its commitment to achieving the targets in Transforming Our World: the 2030 Agenda for Sustainable Development [9]. Additionally, China has issued a series of policies and taken

Table 1 Global and China's TB burden from 2016 to 2020

	2016		2017		2018		2019		2020	
	New TB patients (10 thousand)	Number of deaths (10 thousand)	New TB patients (10 thousand)	Number of deaths (10 thousand)	New TB patients (10 thousand)	Number of deaths (10 thousand)	New TB patients (10 thousand)	Number of deaths (10 thousand)	New TB patients (10 thousand)	Number of deaths (10 thousand)
Globe	1 040.0	167.4	1 000.0	160.0	1 000.0	145.1	1 000.0	140.8	987.0	149.4
China	89.0	4.2	88.4	4.0	88.6	3.6	83.3	3.3	84.2	3.2

Data source: WHO *Global Tuberculosis Report* (2017–2021)(https://www.who.int/teams/global-tuberculosis-programme/tb-reports)

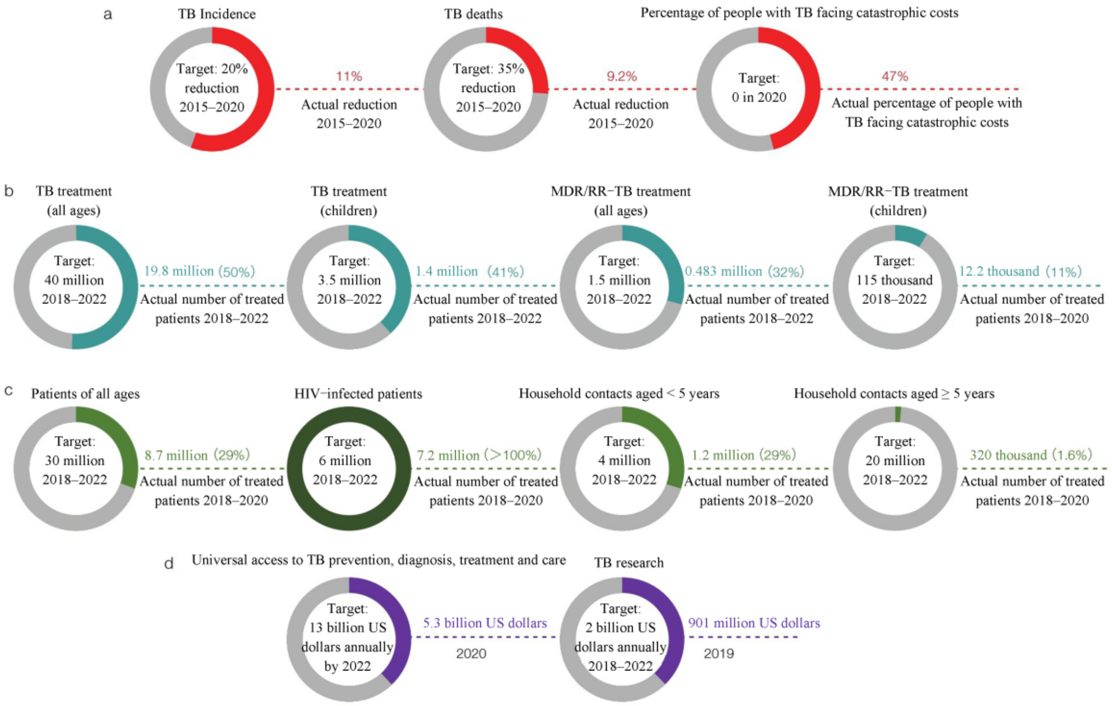

Figure 1 Current situation and milestone progress towards targets set by WHO End TB Strategy and UN's political declaration on fight against TB [6].(a) WHO End TB Strategy: 2020 milestones; (b) UN high-level meeting on TB: Treatment targets; (c) UN high-level meeting on TB: TB preventive treatment targets; (d) UN high-level meeting on TB: Funding targets

measures for TB prevention and control in recent years, which has continuously reduced TB prevalence in China (except for a slight rebound due to the impact of COVID-19 in 2020) [6,10] (Table 1). In addition to the management measures, the ultimate achievement of the goals of TB prevention and control depends on the overall improvement of science and technology. According to the National Medium- and Long-term Program for Science and Technology Development (2006–2020), the National Science and Technology Major Project "Prevention and Treatment of AIDS, Viral Hepatitis and Other Major Infectious Diseases" approved by the State Council and led and organized by National Health Commisstion and the Health Bureau of Logistic Support Department of the Central Military Commission of China was launched in 2008. This project has achieved significant progress during the 11th, 12th, and 13th Five-Year Plan periods. ① TB diagnosis. A number of new bacteriological, immunological, and molecular biological techniques for diagnosing TB have been developed, which have shortened the time for detecting Mtb from 4–8 weeks to less than 6 hours, and increased the detection rate of Mtb in sputum from 25% to 50% [①]. Moreover, the newly developed recombinant Mtb fusion protein was applied in the screening of latent infection cases, which improved the detection level among the target population [11]. ② TB treatment. Because of the large number of TB patients and the serious drug resistance, a series of diagnostic products were developed and treatment protocols were optimized for diagnosis and sustainable treatment, which decreased the mortality rate of MDR-TB by 9% and made China a leading country in this field [②]. ③ Research on TB vaccines. The TB vaccines AEC/BC02 and Vaccae independently developed in China are among the 14 research projects on TB vaccines worldwide [5].

Despite the achievements mentioned above, there is still a long way to go towards the goal of ending TB by 2035, and the tasks of TB prevention and treatment in China are confronted with some major challenges, such as the lack of effective prevention measures. There is only one kind of vaccine to prevent TB, which is the Bacillus Calmette-Guerin (BCG). Because of its limited protective efficacy for adults, breakthroughs are still required for developing new TB vaccines. China has a large population with latent TB infection, which suggests an urgent need of appropriate immunological intervention. Moreover, no effective screening method is

① Ministry of Science and Technology of the People's Republic of China. Press Conference of National Science and Technology Major Project "Prevention and Treatment of AIDS, Viral Hepatitis and Other Major Infectious Diseases" (2018-03-27)[2021-11-29]. http://www.most.gov.cn/xwzx/twzb/fbh18032701/index.html.

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available to identify people susceptible to TB, and the immunological mechanism of pathogen eradication among the infected population remains unclear. Therefore, early screening and effective protection measures cannot be carried out effectively. Currently, the treatment of drug-resistant TB patients depends on anti-TB medicines, whereas the treatment success rate of existing drugs for drug-resistant TB patients is only 50% [12]. It is urgent to explore more effective TB treatment methods, such as new therapeutic vaccines based on novel mechanisms and strategies.

2.2 Progress and prospect of research in TB prevention and treatment

The basic research and applied research as well as the development and application of innovative techniques may provide a solid theoretical basis and strong technical support for the prevention and treatment of TB. Here, the progress in TB research is briefly introduced, including the progress in basic research on TB, the discovery of new targets for TB prevention and control, the development of new TB vaccines, the research and development of new anti-TB medicines, and new clinical treatment protocols for TB.

2.2.1 Basic research on TB and discovery of new targets for TB prevention and treatment

The understanding of Mtb infection, disease onset, and immune defense mechanism of hosts, as well as the discovery of new targets and markers, are crucial for developing new methods for TB prevention and treatment. The progress in the basic research on TB in recent years are introduced in three aspects as follows.

(1) Epidemiology and genomic characteristics of drug-resistant TB. Systematic analysis of the epidemiology and genomic characteristics of drug-resistant Mtb strains is helpful for understanding the development trend of Mtb resistance and providing new drug-resistant molecular markers and new drug targets. ① Epidemiological analysis of drug-resistant TB. Zhao et al. [13] have reported that drug-resistant TB is prevalent in China after conducting a survey on drug-resistant TB in China. The percentages of MDR-TB cases in the new and recurrent TB cases were 5.7% and 25.6%, respectively, and about 8% of the MDR-TB cases were also extensively drug-resistant TB (XDR-TB) cases. ② Genomic characteristics of drug-resistant Mtb strains. The research group of Bi Lijun sequenced the whole genome and transcriptome of 161 drug-resistant Mtb isolates from clinical trials. After analyzing the data, they discovered 72 new drug-resistant-associated genes and 28 intergenic regions (IGRs), which provided a batch of new drug resistance markers and drug targets for the establishment of new TB drug resistance detection methods and the drug research and development [14].

(2) Mechanisms of immune responses to TB. The interaction between Mtb and host immune system determines the outcome of infection. The major achievements in this research field are as follows. ① The immune escape mechanism of Mtb. The research groups of Liu Cui Hua, Gao George Fu, and Qiu Xiao Bo jointly reported the novel mechanism for PtpA, a Mtb effector protein, in promoting intracellular survival of pathogens by inhibiting innate immunity through host ubiquitin [15]. They unraveled the mechanism of the Mtb surface protein Rv1468c in recruiting host ubiquitin to trigger host xenophagy, thus regulating the intensity of inflammatory immune response of hosts [16]. Moreover, they revealed the new mechanism of PknG, a Mtb effector protein, in suppressing innate immunity through exerting unusual ubiquitinating enzyme activity and promoting pathogen intracellular survival by blocking autophagic flow via different domains and kinase activity [17,18]. The research groups of Ge Baoxue and Rao Zihe discovered a mechanism of the host E3 ubiquitin ligase ANAPC2 in damaging host immune responses via the ubiquitination of Mtb Rv0222 [19]. ② The immune mechanism of hosts for anti-Mtb infection. Khan et al. [20] revealed that Mtb infection can activate type I interferon/iron axis, inhibit bone marrow formation and impair protective trained immunity, which is against the protective trained immunity induced by BCG, suggesting a new immune escape strategy for pathogens in bone marrow-derived macrophages. Ji et al. [21] analyzed the correlation between type I interferon and TB susceptibility, further proving that IL-1α is an important regulator for TB susceptibility driven by type I interferon *in vivo*. Scheuermann et al. [22] analyzed the dynamic changes and interacting molecules of platelets in lung tissues during the pathogenesis of TB, suggesting that it was possible to reshape pulmonary immune responses by regulating innate immune responses.

(3) Action mechanisms and structures of TB drug targets. Important progress has been made in the action mechanisms and structures of TB drug targets in China and other countries. For example, the research group led by Zhang Ying reported RpsA, the first target of the first-line drug pyrazinamide for TB, and further revealed the molecular mechanism of pyrazinamide in killing Mtb with RpsA by inhibiting protein translation of Mtb, shedding light on further selection of drug candidates for TB [23]. Rao Zihe and his colleagues analyzed the structures of EmbA-EmbB and EmbC-EmbC complexes, targets of ethambutol and further confirmed the drug target and molecular mechanism of ethambutol, providing a theoretical basis for optimizing ethambutol and developing new Emb-targeting drugs [24]. Rempel et al. [25] confirmed that Rv1819c was the transport protein for vitamin B12 (cobalamin), suggesting that Rv1819c may serve as an ideal target for TB drugs. Moreover, they analyzed the three-dimensional crystal structure of Mtb Rv1819c. Guo et al. [26] revealed the three-dimensional image of bedaquiline inhibiting the activity of adenosine triphosphate (ATP), shedding light on the structural modification on TB drugs.

2.2.2 Development of new TB vaccines

BCG, the only licensed TB vaccine, is insufficient to contain the global TB prevalence. Although BCG can provide moderate or good protection for infants and prevent severe TB, it does not protect adolescents and adults, the major population among which TB is transmitted. Therefore, it is in great need to develop new more effective TB vaccines. Currently, at least 14 vaccine candidates are under clinical development [5]. Tait et al. [27] reported that the results of a phase IIb clinical trial of the novel protein-adjuvant vaccine M72/AS01E which showed about 50% protection for people with latent TB infection. This vaccine has been approved for use in some low-income countries. In addition, several TB vaccines are in the preclinical stage. Some studies have attempted to improve immune protection by changing the vaccination routes. A study found that 9 out of 10 macaques with Mtb infection did not develop active TB after receiving intravenous BCG, with 6 out of 10 macaques showing no detectable levels of infection [28]. Another study showed that single-dose mucosal immunization with chimpanzee adenovirus-based vaccine accelerated TB control and limited its rebound after antibiotic cessation [29]. Although these studies provide new insights for improving the efficacy of TB vaccines, the available candidate vaccines seldom show antigenic and immunological diversity. Consequently, there is an urgent need to develop new vaccines that work in multiple ways, especially new TB vaccines that prevent initial infection (before exposure) or the development of disease (after exposure).

2.2.3 Research and development of new TB drugs

The research and development of new TB drugs are lagging behind worldwide. With the growing attention to infectious diseases in recent years, China and other countries have been developing new TB drugs under research or on clinical trials. At present, the cure rate of susceptible TB is about 85%, while that of drug-resistant TB is only 34%–55%. In addition, the treatment of drug-resistant TB patients requires at least 9–20 months of second-line drug therapy. Therefore, the research and development of new drugs for drug-resistant TB patients have always been a major concern worldwide. Three new drugs (bedaquiline, delamanid, and pretomanid) have been approved in some regions for the treatment for drug-resistant TB. However, these drugs have such limitations as inadequate efficacy and high toxicity, which can only be used as a part of combination regimens. Some TB drugs are still in preclinical and clinical trials. For example, WQ-3810, a new fluoroquinolone drug against drug-resistant developed by Ouchi et al. [30], can act on Mtb DNA helicases. Telacebec (Q203) is another new TB drug, which is developed by de Jager et al. [31]. It targets Mtb cellular energy metabolism through inhibiting the cytochrome bc1 complex. The preliminary results from phase II clinical trials on Telacebec showed that it had good *in vitro* and *in vivo* anti-Mtb activity. Although significant progress has been achieved, the resistance to TB drugs is inevitable. Therefore, more effective and low-toxicity anti-TB drugs are required to cope with the unceasing emergence of drug-resistant TB.

2.2.4 New clinical treatment protocols for TB

In the current stage when the research and development of TB drugs lags far behind clinical demand, the optimization of clinical treatment protocols for TB is one of the effective measures to improve TB prevention and control. The major progress is as follows. Abidi et al. [32] systematically compared the effectiveness of a standardized short regimen (9–12 months) and a traditional long regimen (18–20 months or longer). They found that the treatment success rate of the short regimen (80.0%) was higher than that of the long regimen (75.3%). Conradie et al. [33] reported a regimen with three oral drugs (bedaquiline, delamanid, and pretomanid) in South Africa for patients with XDR/MDR-TB. The results showed that the treatment completion rate of this regimen was higher, with the treatment success rate of 90%, which was not inferior to the traditional regimen. Franke et al. [34] reported a short-term clinical cohort study involving 1 109 patients with drug-resistant TB in multiple countries by using bedaquiline and (or) delamanid. The results showed that 85% of the patients turned negative in sputum test within six months of treatment, compared with 73% for HIV-infected people and 84% for non-HIV-infected people.

To sum up, the research on TB has received increasing attention and achieved impressive progress. We are also pleased to see that a series of original and leading research results with great influence have been produced in China in recent years. However, it should be noticed that the scientific and technological support for TB prevention and control is still insufficient in China, while the technological supply is far from enough. Therefore, it is necessary to strengthen the overall research layout on TB in China, so as to better assist TB prevention and treatment through science and technology.

3 Thoughts and recommendations on TB prevention and treatment through science and technology

Despite the progress in TB prevention and control in the world, countries, and regions, efforts should be made to further strengthen the measures to prevent and treat TB through science and technology. As a major country harassed by TB, China is still confronted with the challenges in TB prevention and treatment. The main challenge is that the scientific and technological innovation based on new mechanisms, theories and strategies is still insufficient. To thoroughly implement the national strategy for people’s life and health, to achieve breakthroughs in the prevention and control of TB via science and technology during the 14th Five-Year Plan period, and to provide strong support for building up the science and technology of China, we need to perfect the top-level design as soon as possible, develop systematic layout of science and technology, make efforts to tackle key problems, and develop new technologies and new methods for TB control with independent intellectual property rights. This study puts forward five suggestions for the prevention and treatment of TB through science and technology in China.

3.1 Reinforcing basic research on TB

The pathogenesis of TB is complex and closely related to host immunity and metabolism, while there is still a lack of comprehensive and in-depth understanding of the pathogenesis of TB. It is suggested to strengthen the research on the dynamic regulation mechanism of Mtb-host interaction and on the protective immune mechanism against TB, so as to provide new strategies and targets for the development of TB vaccines and drugs. Moreover, TB is associated with autoimmune diseases (e.g., pulmonary nodules and inflammatory bowel disease), metabolic diseases (e.g., diabetes), and tumors. People with such diseases are often susceptible to TB. Therefore, TB and the comorbidities may have common mechanisms of pathogenesis. The studies of common mechanisms for pathogenesis of TB and the comorbidities may reveal the molecular markers of TB, thus providing new markers for screening high-risk people with latent infection. Moreover, such studies may also provide new common prevention and treatment methods for TB and the comorbidities.

3.2 Developing new TB vaccines

TB vaccines can be used to prevent TB and may be utilized as immunotherapy agents to shorten the treatment time of TB or reduce the risk of reoccurrence, thereby reducing the development and spread of drug-resistant TB. Moreover, TB vaccines can also be used against drug-resistant TB. By preventing TB, the vaccines can reduce the need for antibiotics, thereby preventing the emergerce of drug-resistance. The End TB Strategy calls for about 250 million US dollars a year to advance the development of TB vaccines. However, the average annual investment was only 95 million US dollars in 2005–2017 [5]. Given the continual TB prevalence and serious drug resistance to Mtb, it is urgent to clarify the immune response characteristics of lung mucosa to Mtb infection, especially the protective immune mechanism against Mtb infection, and to develop new TB vaccines with high efficacy and safety based on new theories, strategies, and targets. Meanwhile, more efforts should be made to explore new immunological evaluation methods for vaccines and develop new strategies to improve the protective efficacy and durability of vaccines.

3.3 Developing new TB drugs

The treatment of drug-resistant TB depends on TB drugs. However, the cure rate of existing drugs for drug-resistant TB is still low, and the existing TB drugs may cause drug resistance to Mtb. China now faces the weak capacity in original TB drug development and low transformation rate of research achievements. In the future, the research and development of new TB drugs based on new mechanisms should be strengthened. In the research and development of new TB drugs, efforts should be made to improve the effectiveness against drug-resistant TB and reduce the occurrence of drug resistance. Host-directed immunotherapy drugs are one of the main research directions in the future. The host-directed immunotherapy drugs can eliminate immune escape and exhaustion caused by pathogens, improve the protective immune responses of hosts, and reduce the tissue damage caused by excessive inflammatory responses and immunopathological responses. It is expected that host-directed immunotherapy drugs may become one of the important therapies against drug-resistant TB, and the combination with traditional antibiotic TB drugs may shorten the course of treatment and reduce the occurrence of drug resistance. Therefore, it may be of great clinical value to strengthen the studies about host immune mechanism upon Mtb infection and develop host-based immunotherapy drugs against TB. Moreover, on the basis of the complex pathogenesis of TB and the characteristics of chronic infection, efforts can be made to explore the role and mechanism of Chinese herbal compound prescriptions and their components in TB prevention and treatment, and to investigate the new therapies with integrated Chinese and western medicine against TB.

3.4 Developing new diagnostic techniques for TB

Early and timely diagnosis of TB is crucial for treating patients as early as possible and reducing the spread of TB. TB diagnostic methods and techniques require further improvement, especially those for drug-resistant TB and latent TB infection. New diagnostic markers are urgently needed, including blood markers that can distinguish between active TB and latent TB infection and molecular detection targets of drug-resistant genes. In terms of diagnostic techniques, immediate and portable detection techniques with higher sensitivity and specificity remain to be developed. In addition, there is a lack of effective screening methods to identify people susceptible to TB. The available screening methods are mostly based on the association between mutation of a gene locus and TB incidence, while the immunological mechanism is unknown. Therefore, it is difficult to carry out early screening and further take effective protective measures. Meanwhile, since the mechanisms for TB susceptibility and pathogenesis are complex and affected by many factors, integrated analysis and comparison of multi-level omics (including genomics, proteomics, ubiquitination proteomics, and metabolomics) should be carried out from a systematic, integrated, and dynamic perspective. Moreover, we should explore the host markers capable of dynamically indicating the progression of Mtb infection, screen and verify the biological markers that can be used for rapid detection and diagnosis of TB and for indicating the incidence of latent infection, treatment, and prognosis of TB patients.

3.5 Perfecting the systems to support and reinforce safeguard measures

Science and technology are the basis for the WHO End TB Strategy, while TB control through science and technology requires innovative environment and resources.

(1) Creating a favorable environment for scientific research and technological innovation for TB. We should formulate policies to encourage new models of collaborative research and strengthen partnerships between government and social capitals. Moreover, we should support the sharing of intellectual property rights and resources (such as samples and data), and simplify and unify research review and product supervision procedures to carry out research consistently and efficiently and rapidly transform research achievements. In addition, financial and non-financial incentive measures should be adopted to stimulate innovation at all levels including basic research, technology development, and achievement transformation.

(2) Increasing financial investment in TB field. The basic research on TB, research and development of vaccines and drugs, and improvement of diagnostic techniques have long lacked enough funding support. Moreover, the attraction of the market is not enough to motivate enterprises to invest in TB field. Therefore, it is urgent for the government to increase stable support for the basic research on TB, support the unmet funding in the early stage of development of new techniques and methods for TB diagnosis and prevention, and encourage joint development of enterprises and other developers.

(3) Promoting the cultivation of innovative talents in TB field. The new techniques and methods for TB diagnosis, prevention, and control depend on a comprehensive understanding of the pathogenesis and immune mechanism. Therefore, it is suggested to promote talent cultivation for the basic research and technological innovation, and encourage, support, and cultivate well-trained innovative talents to continuously step up the original research on TB.

4 Conclusions

TB prevention and control in China are still confronted with major challenges, but also are embracing great opportunities. China's TB prevention and control through science and technology has a bright prospect in the 14th Five-Year Plan period. We should seize the opportunities, face the difficulties, and cooperate to accelerate the progress of TB prevention and control in China and contribute China's power and wisdom to the global goals for TB prevention and control.

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