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**中国大陆学者发表的结核病英文文章摘要**

**（27篇）**

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**1. Diagn Microbiol Infect Dis. 2025 Jun 5;113(2):116946. doi:**

**10.1016/j.diagmicrobio.2025.116946. Online ahead of print.**

Establishment and evaluation of a diagnostic model for severe pulmonary

tuberculosis.

Wang Y(1), Hu P(2), Tang S(3), Zhang Z(4), Li Q(5).

**Yin Wang, Peilei Hu, Shuorun Tang, Zhuo Zhang, Qian Li\***

**\* Qian Li，Electronic address: 54690173@qq.com.**

Author information:

(1)Department of Tuberculosis Internal Medicine Ⅲ, Hunan Chest Hospital, No. 519

Xian Jiahu Road, Yuelu District, Changsha 410006, China.

(2)Department of Clinical Laboratory, Hunan Chest Hospital, Changsha 410006,

China.

(3)Department of Medical Administration, Hunan Chest Hospital, Changsha 410006,

China.

(4)Department of Medical Imaging, Hunan Chest Hospital, Changsha 410006, China.

(5)Department of Tuberculosis Internal Medicine Ⅲ, Hunan Chest Hospital, No. 519

Xian Jiahu Road, Yuelu District, Changsha 410006, China. Electronic address:

54690173@qq.com.

**BACKGROUND:** Diagnosing severe pulmonary tuberculosis (PTB) remains challenging

because of the absence of reliable biomarkers, delaying management and risk

prediction. This study aimed to identify key risk factors for severe PTB and

develop a predictive model for early assessment and intervention.

**METHODS:** Between January 2022 and December 2023, 182 patients with PTB were

included and categorized as having non-severe PTB (n = 112) or severe PTB (n =

70), defined as active PTB involving three or more lung fields on chest

radiography. Demographic data, hematological parameters, vascular endothelial

growth factor (VEGF), and inflammatory markers were analyzed and compared. Risk

factors for severe PTB were identified using regression models. Significant

variables were used to construct a diagnostic nomogram, with predictive

performance evaluated via receiver operating characteristic (ROC) curve

analysis.

**RESULTS:** The analysis identified a history of diabetes (odds ratio [OR] =

3.258), a higher systemic inflammation response index (SIRI; OR = 2.742), and

higher VEGF (OR = 1.011) and IL-6 levels (OR = 1.069) as independent risk

factors for severe PTB. A diagnostic nomogram was subsequently developed using

these factors. ROC analysis demonstrated that the model achieved an area under

the ROC curve of 0.866 (P < 0.001), sensitivity of 80 %, specificity of 83.04 %,

and Youden index of 0.630, significantly outperforming the individual factors (P

< 0.05). An independent validation confirmed its robustness.

**CONCLUSIONS:** A predictive model incorporating diabetes, SIRI, VEGF, and IL-6

enables reliable early risk assessment of severe PTB, facilitating targeted

interventions and improving clinical outcomes.

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**2. Microb Pathog. 2025 Jun 8;206:107794. doi: 10.1016/j.micpath.2025.107794. Online ahead of print.**

Application of antimicrobial drugs in Mycobacterium tuberculosis and research

progress.

Wang Y(1), Cao D(1), Liu G(2).

**Ying Wang, Daxing Cao, Guihua Liu\***

**\* Corresponding author. E-mail address: 13757068467@163.com (G. Liu).**

Author information:

(1)Department of Infectious Diseases, Changxing County People's Hospital,

Huzhou, 313100, China.

(2)Department of Infectious Diseases, Changxing County People's Hospital,

Huzhou, 313100, China. Electronic address: 13757068467@163.com.

Treatment regimens for Tuberculosis (TB) primarily rely on first-line drugs such

as isoniazid, rifampicin, ethambutol, and pyrazinamide. Although these drugs

have been pivotal in the treatment of drug-resistant tuberculosis, their high

costs limit widespread use in low- and middle-income countries. However, the

emergence of multidrug-resistant TB and extensively drug-resistant TB

necessitates the development of new anti-TB drugs and therapeutic strategies. In

terms of treatment, new drugs such as bedaquiline, delamanid, and pretomanid

have shown significant efficacy against MDR-TB and XDR-TB. Combination therapies

have substantially improved cure rates and reduced treatment duration. Despite

these advancements, drug resistance and adverse effects remain substantial

challenges. Understanding the resistant genes and biochemical mechanisms of M.

tuberculosis, developing drugs that disrupt its biofilms, optimizing drug

combinations, and personalizing treatments are crucial for reducing tuberculosis

mortality and controlling its spread, thus achieving WHO's goal of global

tuberculosis eradication. Future research should focus on improving drug

accessibility and affordability, and making significantly contributions to

global public health goals.

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**3. Eur J Pharm Sci. 2025 Jun 8:107160. doi: 10.1016/j.ejps.2025.107160. Online**

**ahead of print.**

Population pharmacokinetic and exposure-response study of a novel

anti-tuberculosis drug to inform its dosage design in phase III clinical trial.

Kong W(1), Liang H(1), Zhang Y(2), Li L(3), Li Y(3), Yan X(4), Liu D(5).

**Weijie Kong, Hao Liang, Yi Zhang, Lei Li, Yongguo Li, Xiaoyu Yan\*, Dongyang Liu\***

**\* Corresponding authors. E-mail addresses: xiaoyuyan@cuhk.edu.hk (X. Yan), liudongyang@vip.sina.com (D. Liu).**

Author information:

(1)Drug Clinical Trial Center, Peking University Third Hospital, Beijing, China;

Department of Nephrology, Peking University Third Hospital, Beijing, China.

(2)Drug Clinical Trial Center, Peking University Third Hospital, Beijing, China.

(3)Shanghai Jiatan Biotech Ltd., a subsidiary of Guangzhou JOYO Pharma Ltd.,

Shanghai, China.

(4)School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong,

Hong Kong SAR, China. Electronic address: xiaoyuyan@cuhk.edu.hk.

(5)Drug Clinical Trial Center, Peking University Third Hospital, Beijing, China;

Institute of Medical Innovation, Peking University Third Hospital, Beijing,

China. Electronic address: liudongyang@vip.sina.com.

Although bedaquiline (BDQ) received conditional approval for multi-drug

resistance tuberculosis (MDR-TB), a black box warning was added due to QT

prolongation risk. WX-081, a promising second-in-class drug that finished phase

II clinical trial, exhibited comparable anti-TB activity and better cardiac

safety. The accumulation of its active metabolite WX-081-M3 leads to QT

prolongation, whereas the relationships between dosage, exposure and response

have not been established. Accordingly, the dosage design for phase III study is

challenging. Here, the first population pharmacokinetic (PPK) and

exposure-response (E-R) analysis were conducted for WX-081. 1610 WX-081 and 1580

WX-081-M3 concentrations were collected from 24 healthy volunteers and 48

tuberculosis patients for PPK study. The pharmacokinetic parameters and sputum

culture conversions of 20 MDR-TB patients receiving BDQ and WX-081 were used for

E-R analysis. The absorption of WX-081 was well described by a

three-compartments transit model, while the distribution and elimination

profiles of WX-081 and WX-081-M3 were captured by three- and two-compartments

models, respectively. E-R analysis demonstrated that the clinical efficacy of

WX-081 is comparable with BDQ and can be evaluated by average concentration at

steady state (Cavg,ss) of WX-081. According to the simulation results of

different regimens, the dosage of 450 mg once daily (QD) for 1 week and

subsequent 300 mg QD for 1 week followed by 150 mg QD for 22 weeks was

recommended considering both efficacy and safety. Our study revealed the PK and

efficacy profiles of WX-081 for the first time and proposed a dose optimization

strategy to facilitate its clinical development.

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**4. Eur J Med Res. 2025 Jun 20;30(1):499. doi: 10.1186/s40001-025-02783-1.**

Analysis of the onset characteristics and diagnosis of 217 cases of renal

tuberculosis.

Li C(1)(2), Zhu G(3), Liu J(4), Wang Y(5), Zhang Y(6), Zheng H(7), Fan Z(4), Yin

H(4), Wang Q(4), Li W(8).

**Chongbin Li\*, Guiyun Zhu, Jianzhen Liu, Yani Wang, Ying Zhang, Hao Zheng, Zhengchao Fan, Hang Yin, Qian Wang, Wei Li\***

**\*Correspondence: Chongbin Li，lichongbin.good@163.com ；Wei Li，26200407@hebmu.edu.cn**

Author information:

(1)Department of Urology, The Second Hospital of Hebei Medical University,

Shijiazhuang, 050000, China. lichongbin.good@163.com.

(2)Department of Urology, Hebei Chest Hospital, Shijiazhuang, 050041, China.

lichongbin.good@163.com.

(3)Department of Pathology, Hebei Chest Hospital, Shijiazhuang, 050041, China.

(4)Department of Urology, Hebei Chest Hospital, Shijiazhuang, 050041, China.

(5)Molecular Biology Laboratory, Hebei Chest Hospital, Shijiazhuang, 050041,

China.

(6)Department of Radiological Imaging, Hebei Chest Hospital, Shijiazhuang,

050041, China.

(7)Department of Ultrasound, Hebei Chest Hospital, Shijiazhuang, 050041, China.

(8)Department of Urology, The Second Hospital of Hebei Medical University,

Shijiazhuang, 050000, China. 26200407@hebmu.edu.cn.

**OBJECTIVES:** To explore the latest characteristics and diagnostic methods of

renal tuberculosis, and to improve the new recognition and diagnostic level of

renal tuberculosis.

**METHODS:** We collected the medical records and postoperative histopathological

slides of 217 patients diagnosed and treated with renal tuberculosis in the

Department of Urology of Hebei Provincial Chest Hospital from March 25, 2013 to

February 6, 2024, and divided them into the typical group (145 cases) and the

atypical group (72 cases) according to their onset characteristics, and analyzed

the distribution of onset symptoms and the differences in the positive rates of

different examination methods between these two groups.

**RESULTS:** (1) Frequency, urgency and pain of urination were the main symptoms in

the typical group (66.82%), and local or systemic atypical symptoms in the

atypical group (33.18%), and the incidence rate of women in the atypical group

was higher than that in the typical group (P < 0.05). (2) In both groups, the

positive rate of CT diagnosis of renal tuberculosis was higher than that of

ultrasound and urography (P < 0.05), and there was no statistically significant

difference between the positive rates of T-SPOT.TB and PPD tests (P > 0.05). The

CT positivity rate in the typical group was higher than that in the atypical

group (P < 0.05). In the typical group GeneXpert MTB/RIF had a higher positive

rate than that of PCR TB-DNA, acid-fast staining and tuberculosis culture

(P < 0.05). However, in the atypical group and all patients in both groups,

there was no statistical difference between the positivity rates of GeneXpert

MTB/RIF and PCR TB-DNA (P > 0.05), both of which were higher than those of

acid-fast staining and TB culture (P < 0.05). The positivity rate of acid-fast

staining and tuberculosis culture was higher in the typical group than that in

the atypical group (P < 0.05). In the typical group, the positivity rate of LAM

antibody was higher than that of 38KDa and 16KDa (P < 0.05). However, in the

atypical group, there was no statistically significant difference between the

positivity rates of 38KDa and LAM antibodies (P > 0.05), and both were higher

than that of 16KDa antibodies (P < 0.05). (3) There was no significant

difference in pathological changes between the two groups, both of which were

dominated by granulomas and caseous necrosis, and the positivity of tissue PCR

TB-DNA was higher than that of antacid staining (P < 0.05), but there was no

statistically significant difference in the positivity of tissue PCR TB-DNA

between the two groups (P > 0.05). Cystoscopic biopsy was dominated by granuloma

and necrosis in the typical group and chronic inflammation in the atypical

group.

**CONCLUSIONS:** (1) In addition to renal tuberculosis with bladder irritation as

the main clinical manifestation, atypical renal tuberculosis is also an

important part of renal tuberculosis, which is characterized by systemic or

local atypical symptoms, and should be highly concerned. (2) CT, GeneXpert

MTB/RIF, T-SPOT.TB (or PPD test) and LAM antibody have higher sensitivity both

in typical and atypical renal tuberculosis, which can improve the diagnosis rate

of renal tuberculosis. (3) There is no significant difference in the pathologic

changes between typical and atypical renal tuberculosis, and PCR TB-DNA of the

tissues may help to improve the pathologic diagnosis of renal tuberculosis. In

atypical renal tuberculosis, bladder mucosal lesions are characterized by

chronic inflammation, and cystoscopic biopsy alone is of low diagnostic value.

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Integrative study of pulmonary microbiome and clinical diagnosis in pulmonary

tuberculosis patients.

Sun H(#)(1), Chen Q(#)(2), Zhang D(#)(1)(3), Hu L(#)(4), Li S(4), Lu M(1), Wang

Y(1), Su H(1), Gao Y(1), Guo J(1), Zhao Y(1), Du J(1), Liu C(5), Xia H(4), Xu

Y(1), Ge X(2), Yang Q(1)(3).

**Hongli Sun, Qiuyue Chen, Dong Zhang, Long Hu, Song Li, Minya Lu, Yao Wang, Huiting Su, Yi Gao, Jiayu Guo, Ying Zhao, Juan Du, Cun Liu, Han Xia, Yingchun Xu\*, Xiaojun Ge\*, Qiwen Yang\***

**\*Address correspondence to Yingchun Xu,****xycpumch@139.com****; Xiaojun Ge,****gxj\_199421@163.com****; Qiwen Yang,****yangqiwen81@vip.163.com****.**

Author information:

(1)Department of Clinical Laboratory, State Key Laboratory of Complex Severe and

Rare Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical

Sciences and Peking Union Medical College, Beijing, China.

(2)Department of Clinical Laboratory, The second Affiliated Hospital of Zunyi

Medical University, Zunyi, Guizhou, China.

(3)Key Laboratory of Pathogen Infection Prevention and Control (Peking Union

Medical College), Ministry of Education, Beijing, China.

(4)Department of Scientific Affairs, Hugobiotech Co., Ltd., Beijing, China.

(5)Department of Clinical Laboratory, The Affiliated Qingdao Third People's

Hospital of Qingdao University, Qingdao, Shandong, China.

(#)Contributed equally

This study investigated the diagnostic potential of mNGS for detecting MTB in

pulmonary tuberculosis patients. We analyzed pulmonary microbiome data to assess

its impact on mNGS diagnostic accuracy and explored the association between

microbiome profiles and clinical diagnosis. Bronchoalveolar lavage fluid samples

were collected from 236 patients with pulmonary infections, and the diagnostic

performance of mNGS was compared with traditional methods in detecting MTB.

Furthermore, the incidence of false negatives and false positives, as well as

the characteristics of the lung microbiota in TB patients, was analyzed to

improve the diagnostic precision of mNGS. We observed that among all detection

methods, mNGS showed the highest sensitivity (73.33%), followed by X-pert

(60.00%), culture (53.33%), RT-PCR (53.33%), and sputum smear (23.33%). Notably,

mNGS produced 3 false positive results in 236 samples, yielding a specificity of

98.54%. Analysis of the pulmonary microbiome revealed significant differences in

both α-diversity and β-diversity between patients with TB and uninfected

controls (P&lt;0.05). Shannon index and Chao1 index were identified as

significant predictors associated with MTB infection. ROC curve analysis

demonstrated an AUC of 0.765, indicating good discriminatory performance. This

study suggested that integrating wet-laboratory techniques with bioinformatics

analysis can further enhance the diagnostic accuracy of mNGS for TB.

Furthermore, microbiome analysis holds significant potential for the diagnosis

of MTB infection.

**IMPORTANCE:** This study focuses on the application of next-generation sequencing

(NGS) technology in detecting Mycobacterium tuberculosis in bronchoalveolar

lavage fluid and explores the impact of M. tuberculosis infection on the

pulmonary microbiome. By optimizing the methods and conducting microbial

analyses, the accuracy of metagenomic NGS for detecting M. tuberculosis has been

improved.

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**6. PLoS Pathog. 2025 Jun 17;21(6):e1013228. doi: 10.1371/journal.ppat.1013228.**

**eCollection 2025 Jun.**

TIGIT blockade improves anti-Mycobacterium tuberculosis immunity.

Zhou J(1), Yang Q(1), Xu H(1), Chen H(2), Jiang N(1)(3)(4), Ou Q(2), Qian M(1),

Lin X(1), Yang Y(1), Zhou F(1), Xu Y(1), Liu Q(1), Liu Y(1), Gao Y(1), Zhang

W(1)(4), Shao L(1), Ruan Q(1).

**Jingyu Zhou, Qingluan Yang, Haoxin Xu, Huaxin Chen, Ning Jiang, Qinfang Ou, Mengqing Qian, Xing Lin, Yixuan Yang, Feiran Zhou, Yuzhen Xu, Qianqian Liu, Yuanyuan Liu, Yan Gao, Wenhong Zhang, Lingyun Shao\*, Qiaoling Ruan\***

**\* Lingyun Shao，lingyun26@fudan.edu.cn; (LS) ；Qiaoling Ruan，**

**qlruan07@fudan.edu.cn (QR)**

Author information:

(1)Department of Infectious Diseases, Shanghai Key Laboratory of Infectious

Diseases and Biosafety Emergency Response, National Medical Center for

Infectious Diseases, Huashan Hospital, Fudan University, Shanghai, China.

(2)Department of Pulmonary Diseases, Wuxi Fifth People's Hospital, Wuxi, China.

(3)Department of Biostatistics and Computational Biology, SKLG, School of Life

Sciences, Fudan University, Shanghai, China.

(4)Shanghai Sci-Tech Inno Center for Infection & Immunity, Shanghai, China.

Despite the therapeutic benefit of immune checkpoint blockade in cancers, there

is no consensus on its effect in infectious diseases. Here we investigated

whether blocking the immune checkpoint T cell immunoreceptor with immunoglobulin

and immunoreceptor tyrosine-based inhibitory motif domains (TIGIT) increases T

cell immunity in active Mycobacterium tuberculosis infection. TIGIT expression

in both peripheral blood and lung lesions in tuberculosis patients was assessed,

and the correlation with clinical features analyzed. The functional status of

TIGIT+ and TIGIT-CD8+ T cell subsets in tuberculosis patients was analyzed by

flow cytometry and transcriptome analysis. To investigate the regulatory effect

of TIGIT, the function of CD8+ T cells in tuberculosis patients and bacterial

load in a tuberculosis mouse model were assessed after in vitro and in vivo

TIGIT blockade. In active tuberculosis patients, TIGIT expression on CD8+ T

cells in the peripheral blood was significantly upregulated and positively

correlated with disease severity. TIGIT expression in lung lesions was

significantly higher in patients with pulmonary tuberculosis than in patients

infected with other pathogens. TIGIT+CD8+ T cells exhibited higher activation

and differentiation levels, increased expression levels of cytokines and

cytotoxic molecules, and showed gene expression features of natural killer-like

cytotoxic effector CD8+ T cells. TIGIT blockade increased the ability of human

CD8+ T cells to produce effector molecules and kill intracellular bacteria in

vitro. Importantly, blocking TIGIT reduced lung bacterial burden in mice

infected with M. tuberculosis. The findings reveal that in active tuberculosis

patients, activated CD8+ T cells express TIGIT and blocking TIGIT enhances CD8+

T cell function and promotes clearance of M. tuberculosis. The findings also

suggest that TIGIT limits T cell immunity in tuberculosis and implicate TIGIT

blockade as a novel strategy for tuberculosis therapy.

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**7. PLoS One. 2025 Jun 17;20(6):e0322913. doi: 10.1371/journal.pone.0322913.**

**eCollection 2025.**

The characteristics of latent tuberculosis infection and its influencing factors

in hospitalized patients in Suzhou, Jiangsu, China.

Zhou Y(1), Lv X(1), Zhu S(2), Xu P(1)(2).

**Yanyang Zhou, Xing Lv, Shuai Zhu, Ping Xu\***

**\* Ping Xu，573311485@qq.com**

Author information:

(1)Suzhou Medical College of Soochow University, Suzhou, Jiangsu, China.

(2)Department of Clinical Laboratory, The Fifth People's Hospital of Suzhou,

Suzhou, Jiangsu, China.

**OBJECTIVE**: China is a country with a high burden of tuberculosis (TB). It is

vital to reduce the number of new cases of TB in China. We aimed to examine and

investigate the distribution and affecting factors of the latent tuberculosis

infection (LTBI) detection rate in hospitalized patients in Suzhou, Jiangsu

Province.

**METHODS:** We analyzed the link between LTBI and patients' information, disease

diagnosis, and blood routine indices of hospitalized patients at the Fifth

People's Hospital in Suzhou from January 1, 2018, to March 31, 2024.

**RESULTS:** Results indicated that of the 6692 patients included in the study,

39.05% of them were diagnosed with LTBI. Multivariate analysis revealed that

sex, AIDS status, testing time, age, lymphocyte count, and neutrophil count were

influencing factors for the detection of LTBI ( p < 0.05). However, hepatitis B,

diabetes, hypertension, silicosis and monocyte count did not significantly

influence LTBI detection.

**CONCLUSION:** Sex, AIDS status, testing time, age, lymphocyte count, and

neutrophil count were influencing factors for the detection of LTBI.

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**8. Eur J Med Res. 2025 Jun 16;30(1):483. doi: 10.1186/s40001-025-02768-0.**

Exploring T-cell metabolism in tuberculosis: development of a diagnostic model

using metabolic genes.

Ding S(1), Huang C(1), Gao J(2), Bi C(3), Zhou Y(4)(3), Cai Z(5)(6).

**Shoupeng Ding, Chunxiao Huang, Jinghua Gao, Chun Bi, Yuyang Zhou, Zihan Cai\***

**\*Correspondence: Zihan Cai，zihancai001@163.com**

Author information:

(1)Department of Laboratory Medicine, Gutian County Hospital, Gutian, 352200,

China.

(2)Center for Precision Medicine, The People's Hospital of Chuxiong Yi

Autonomous Prefecture, Chuxiong, 675000, China.

(3)Oncology and Laboratory Immunology Research Innovation Center, Siyang

Hospital, Siyang, 237000, China.

(4)Department of Medical Laboratory, Siyang Hospital, Siyang, 237000, China.

(5)Department of Medical Laboratory, Siyang Hospital, Siyang, 237000, China.

zihancai001@163.com.

(6)Oncology and Laboratory Immunology Research Innovation Center, Siyang

Hospital, Siyang, 237000, China. zihancai001@163.com.

**OBJECTIVES:** The early diagnosis and immunoregulatory mechanisms of active

tuberculosis (ATB) and latent tuberculosis infection (LTBI) remain unclear, and

the role of metabolic genes in host-pathogen interactions requires further

investigation.

**METHODS:** Single-cell RNA sequencing (scRNA-seq) was applied to analyze

peripheral blood mononuclear cells (PBMCs) from 7 individuals, including 2

healthy controls (HC), 2 LTBI patients, and 3 ATB patients. We identified

T-cell-associated metabolic differentially expressed genes (TCM-DEGs) through

integrated differential expression analysis and machine learning algorithms

(XGBoost, SVM-RFE, and Boruta). These TCM-DEGs were then used to construct a

diagnostic model and evaluate its clinical applicability.

**RESULTS:** The analysis revealed significant immunological alterations in TB

patients, characterized by markedly elevated monocyte/macrophage populations

(p < 0.001) accompanied by reduced T and NK cell counts. Notably, LTBI cases

demonstrated an intermediate CD4+/CD8+ T-cell ratio, indicative of dynamic

immune homeostasis. The TB cohort exhibited increased inflammatory T-cell

populations, while CD8+ T-cell-mediated MHC-I and BTLA signaling pathways were

identified as key regulators of immune clearance and modulation. Transcriptomic

profiling identified five metabolically significant differentially expressed

genes (FHIT, MAN1C1, SLC4C7, NT5E, AKR1C3; p < 0.05) that effectively

distinguish between latent tuberculosis infection (LTBI) and active tuberculosis

(TB). The machine learning-driven diagnostic framework demonstrated remarkable

consistency across independent validation cohorts (GSE39940, GSE39939),

exhibiting AUC values spanning 0.867-0.873. Molecular subtyping analysis

delineated two distinct TB phenotypes: an immune-activated M1

macrophage-dominant subtype and a CD8 + T-cell infiltrated immunophenotype.

Clinical validation substantiated the differential expression patterns of

T-cell-related metabolic differentially expressed genes (TCM-DEGs; p < 0.05),

while the nomogram predictive model achieved exceptional discriminative capacity

(C-index = 0.944), demonstrating superior clinical applicability through

decision curve analysis.

**CONCLUSIONS:** Our findings reveal that TCM-DEGs critically regulate TB

progression through immune-metabolic reprogramming and cell-cell communication

networks. The developed diagnostic model and molecular subtyping strategy enable

precise TB-LTBI differentiation and inform immunotherapy optimization.

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**10.1186/s12941-025-00807-6.**

Impact of sublineage diversity on intrinsic susceptibility of Beijing genotype

Mycobacterium tuberculosis.

Li H(#)(1), Zhang G(#)(1), Ma Z(#)(1), Guo H(2), Shang Y(1), Yao C(1), Li S(3),

Pang Y(4), Pan J(5).

**Haoran Li, Guyue Zhang, Zichun Ma, Haiping Guo, Yuanyuan Shang, Cong Yao, Shanshan Li\*, Yu Pang\*, Junhua Pan\***

**\*Correspondence: Shanshan Li lss9011@126.com; Yu Pang，pangyupound@163.com; Junhua Pan，panjunhua0809@163.com**

Author information:

(1)Department of Bacteriology and Immunology, Beijing Chest Hospital, Capital

Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute,

Postal No 9, Beiguan Street, Tongzhou, 101149, Beijing, People's Republic of

China.

(2)Microbiological Laboratory, Shangqiu City Center for Disease Control and

Prevention, Shangqiu, 476000, Henan, People's Republic of China.

(3)Department of Bacteriology and Immunology, Beijing Chest Hospital, Capital

Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute,

Postal No 9, Beiguan Street, Tongzhou, 101149, Beijing, People's Republic of

China. lss9011@126.com.

(4)Department of Bacteriology and Immunology, Beijing Chest Hospital, Capital

Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute,

Postal No 9, Beiguan Street, Tongzhou, 101149, Beijing, People's Republic of

China. pangyupound@163.com.

(5)Department of Bacteriology and Immunology, Beijing Chest Hospital, Capital

Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute,

Postal No 9, Beiguan Street, Tongzhou, 101149, Beijing, People's Republic of

China. panjunhua0809@163.com.

(#)Contributed equally

Tuberculosis (TB) remains a significant global health issue, with drug-resistant

TB posing a major challenge. The genetic lineage of Mycobacterium tuberculosis

(Mtb) is known to influence various aspects, including drug resistance. Still,

the relationship between different lineages and drug resistance levels,

especially in the context of the Beijing genotype, requires further exploration.

This study aimed to investigate the disparities in drug resistance among diverse

lineages of Mtb. We analyzed 193 clinical isolates from drug-resistant TB

patients, among them 91.2% were MDR/pre-XDR-TB. Samples were collected from

patients at specific hospitals between 2014 and 2020. The isolates were

subjected to smear microscopy, sputum culture, minimum inhibitory concentration

(MIC) testing, and whole-genome sequencing (WGS). The MIC distributions and

resistance levels of drugs like INH, AMK, RIF, EMB, and FQ were analyzed, and

the association between lineages and drug resistance was determined using

statistical tests. Our results showed significant differences in the MIC

distributions and resistance levels of INH and AMK between lineages 2.2 and 2.3.

Lineage 2.3.2 was a protective factor for high-level INH resistance, and lineage

2.3 was a protective factor for high-level AMK resistance. The L2.3.6 strain had

a high proportion of high-level resistance to INH and AMK. This study provides

evidence for the evolution and spread of the modern Beijing genotype of Mtb. It

suggests that L2.3.6 will have the potential to become the main sublineage of

tuberculosis for the spread of drug-resistant tuberculosis and the necessity of

pedigree testing of drug-resistant strains in clinical treatment.

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**10. Int J Mycobacteriol. 2025 Apr 1;14(2):145-152. doi: 10.4103/ijmy.ijmy\_33\_25.**

**Epub 2025 Jun 20.**

Causes and Management of Chest Computed Tomography Lesions Progression in

Pulmonary Tuberculosis during Antituberculosis Treatment.

Yang S(1), Feng Y(2), Yang K(3), Pu J(1), Wang P(1).

**Shuangyin Yang, Yanmei Feng, Kuiliang Yang, Jie Pu, Pu Wang\***

**\*Address for correspondence: Prof. Pu Wang, E‑mail: wangpucqmu@163.com**

Author information:

(1)Department of Respiratory Medicine, The First Affiliated Hospital of

Chongqing Medical University, Chongqing, China.

(2)Department of Respiratory Medicine, Chongqing Emergency Medical Center,

Chongqing, China.

(3)The First Clinical College of Wuhan University, Wuhan, China.

**BACKGROUND:** Even with early antituberculosis (TB) treatment, some patients with

pulmonary TB (PTB) may experience progression of chest computed tomography (CT)

lesions. However, there is limited information on the causes and management of

this progression during treatment. This study was undertaken to improve clinical

understanding of the various causes and management strategies for the worsening

of chest CT lesions in patients with PTB.

**METHODS:** A retrospective analysis was performed on the medical records of 61 PTB

patients. We evaluated the radiological features, clinical characteristics,

laboratory findings, causes, and management of chest CT lesions progression in

PTB during anti-TB treatment and compared the characteristics of patients in the

paradoxical response (PR) group and the non-PR group.

**RESULTS:** The most common cause of the chest CT progression lesions was PR,

accounting for 50.8% (n = 31) of the cases. Other important causes included

insufficient anti-TB treatment (21.3%, n = 13), drug-resistant TB (8.2%, n = 5),

and comorbidities such as bacterial infections (8.2%, n = 5), fungal infections

(6.6%, n = 4), and lung cancer (4.9%, n = 3). Patients with PR were primarily

treated by continuing their anti-TB management, whereas those with non-PR due to

other causes received treatment targeting the underlying etiology. PR patients

were younger (Mann-Whitney U-test, P < 0.001; 95% confidence interval [CI]:

15.8-32.2)., had more asymptomatic cases (74.2% vs. 4.0%; χ2 test, P < 0.001;

odds ratio [OR]: 64.3, 95% CI: 12.5-330.2), showed higher Mycobacterium TB

culture positivity (64.5% vs. 30.0%; χ2 test, P = 0.015; OR: 4.2, 95% CI:

1.4-12.6), and had quicker lesion progression than the non-PR group (P = 0.004;

95% CI: 1.0-3.0).

**CONCLUSION:** PR is the major cause of chest CT lesion progression in PTB during

anti-TB. Continuation of anti-TB therapy can promote the absorption of lesions.

Differences between PR and non-PR patients can help clinicians in diagnosing and

guiding treatment strategies.

Copyright © 2025 International Journal of Mycobacteriology.

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**11. Open Life Sci. 2025 Jun 12;20(1):20251123. doi: 10.1515/biol-2025-1123.**

**eCollection 2025.**

Diagnosis of secondary tuberculosis infection in an asymptomatic elderly with

cancer using next-generation sequencing: Case report.

Huang J(1), Ren W(2), Hu W(3), Ni J(1).

**Jiahuan Huang, Wenbo Ren, Weishang Hu, Jianfang Ni\***

**\* Corresponding author: Jianfang Ni, e-mail: 815359023@qq.com**

Author information:

(1)Geriatric Medicine Center, Department of Geriatric Medicine, Zhejiang

Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical

College, Hangzhou, Zhejiang, China.

(2)Center for Rehabilitation Medicine, Rehabilitation & Sports Medicine Research

Institute of Zhejiang Province, Department of Rehabilitation Medicine, Zhejiang

Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical

College, Hangzhou, Zhejiang, China.

(3)Geriatric Medicine Center, Department No. 2 of Acupuncture & Massage,

Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou

Medical College, Hangzhou, Zhejiang, China.

In recent years, there has been a notable increase in the prevalence of tumors

and tuberculosis (TB), particularly among elderly and immunocompromised

populations. Early diagnosis and treatment are crucial for significantly

improving patient outcomes. However, traditional diagnostic methods exhibit

certain limitations. The rapid advancement of metagenomic next-generation

sequencing (mNGS) has shown promising applications in the field of infectious

diseases. We describe an 88-year-old male with multiple comorbidities, including

newly diagnosed localized prostate cancer, who presented asymptomatically.

Routine mNGS screening unexpectedly identified Mycobacterium tuberculosis,

suggesting that malignancy may foster immune conditions favoring latent TB

reactivation. This case emphasizes mNGS's role as a rapid, sensitive diagnostic

adjunct for occult infections in high-risk populations.

© 2025 the author(s), published by De Gruyter.

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**12. Front Microbiol. 2025 Jun 4;16:1582163. doi: 10.3389/fmicb.2025.1582163.**

**eCollection 2025.**

Epidemiological changes in tuberculosis and genotyping characteristics of

Mycobacterium Tuberculosis in Ningxia, China.

Liu G(1), Lv J(2), Chen L(2), Ma Y(1), Liu B(1), Jiang X(1).

**Guangtian Liu, Jufen Lv, Linlin Chen, Yinglong Ma\*, Bofei Liu\*, Xuefeng Jiang\***

**\*CORRESPONDENCE Yinglong Ma，liuzhiguo@icdc.cn ；Bofei Liu，lbf071138@163.com ；Xuefeng Jiang，Jiang\_xf2008@126.com**

Author information:

(1)The Fourth People's Hospital of Ningxia Hui Autonomous Region, Yinchuan,

China.

(2)The College of Public Health, Ningxia Medical University, Yinchuan, China.

**INTRODUCTION:** China is one of the three countries with the largest TB burden

globally, with an increased number of patients reported in 2021.

OBJECTIVE: In this study, we aimed to investigate the epidemiological profile of

tuberculosis (TB) and the genotype characteristics of Mycobacterium tuberculosis

(MTB) in the Ningxia Hui Autonomous Region, China.

**METHODS:** From 2005 to 2023, to provide a scientific basis for the precise

prevention and control of TB. Epidemiological data on TB in Ningxia were

obtained from the China Disease Control and Prevention Information System from

2005 to 2023. The temporal trend of TB incidence was assessed using a Joinpoint

regression analysis (Joinpoint 5.2.0), and spatial autocorrelation analyses were

performed using ArcGIS 10.8. Spoligotyping and McSpoligotyping based on 222

isolated MTB strains.

**RESULTS:** From 2005 to 2023, 51,345 patients with TB were reported in Ningxia.

The incidence of TB decreased from 48.22/100,000 in 2005 to 30.47/100,000 in

2023. Joinpoint analysis showed that the incidence of TB in all age groups

exhibited an overall decreasing trend. The incidences were significantly lower

among urban residents than among rural residents. A spatial analysis showed that

the southern mountainous area had a high incidence, with an average annual

incidence of more than 60/100,000 in the Xiji, Lund, and Haiyuan counties, and

this showed significant spatial clustering in 2007, 2009, 2014, 2016, and 2018.

Genotyping showed that Beijing was the main genotype in Ningxia, accounting for

80.63% of the total (78.26% in 2005-2012 and 83.18% in 2013-2023). A cluster

analysis showed that the Beijing type had strong intraregional transmission

characteristics. The overall incidence of TB in Ningxia, China, showed a

significant downward trend, but the prevalence was high in the southern

mountainous regions and rural populations. The high aggregation of Beijing-type

genotypes suggests a risk of intra-regional transmission and the need to

strengthen surveillance and transmission chain analyses.

**CONCLUSION:** TB incidence in Ningxia declined from 48.22 to 30.47/100,000

(2005-2023), yet remains high in southern mountainous regions. Persistent

Beijing-type M. tuberculosis strains dominate, suggesting sustained

transmission. Targeted interventions and further molecular studies are needed to

enhance control in endemic areas.

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DOI: 10.3389/fmicb.2025.1582163

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PMID: 40535020

**13. IJTLD Open. 2025 Jun 13;2(6):346-351. doi: 10.5588/ijtldopen.24.0684.**

**eCollection 2025 Jun.**

High incidence of TB at a psychiatric hospital.

Li X(1), Pang X(1), Mu C(1), Zhang F(1), Wang C(1), Zhang G(1).

**X Li, X Pang, C Mu, F Zhang, C Wang, G Zhang\***

**\*Correspondence to: Guoqin Zhang, E-mail: zhanggq\_cn@163.com**

Author information:

(1)Tianjin Center for Tuberculosis Control, Tianjin 300011, China.

**BACKGROUND:** Individuals with mental illness are susceptible to TB. This study

aimed to investigate a TB epidemic in a male psychiatric hospital to explore its

potential for institutional spread.

**METHODS:** From April 2022 to March 2023, 19 TB cases were diagnosed in a male

psychiatric hospital. Epidemiological investigations and screening of close

contacts were carried out.

**RESULTS:** A total of 400 psychiatric patients and 160 staff members were screened

for TB. The overall positive rate was 37.15%, with 43.09% among patients and

22.93% among staff. Ultimately, a total of 17 psychiatric patients (including 2

index cases, 5 active cases, and 11 confirmed cases) and 2 staff (1 active case

and 1 confirmed case) were diagnosed. The overall attack rate was 3.36%, with

4.20% in patients and 1.24% in staff. Whole-genome sequencing revealed that 3

drug-resistant patients from a third Department had mutations at two loci (rpoB

and rpsL) with fewer than 6 SNPs.

**CONCLUSION:** Strengthening surveillance and conducting comprehensive

epidemiological investigations for any occurrence of two or more TB cases is of

utmost importance. Additionally, enhancing diagnostic capabilities and ensuring

strict adherence to infection control protocols during patient care are

essential measures to prevent TB outbreak.

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**14. Arthroplast Today. 2025 Jun 4;33:101722. doi: 10.1016/j.artd.2025.101722.**

**eCollection 2025 Jun.**

Application of 1-Stage and 2-Stage Total Hip Arthroplasty in Managing Active Hip

Tuberculosis Osteoarthritis of Varying Severity.

Wang YK(1)(2), Zhang YM(1), Bei Z(3).

**Ya-Kang Wang, Yu-Min Zhang, Zhang Bei\***

**\* Corresponding authors: Zhang Bei，E-mail address: 270296896@qq.com**

Author information:

(1)Department of Joint Surgery, Honghui Hospital, Xi'an Jiaotong University,

Xi'an, China.

(2)Key Laboratory of Biomedical Information Engineering of Ministry of

Education, Biomedical Informatics & Genomics Center, School of Life Science and

Technology, Xi'an Jiaotong University, Xi'an, P.R. China.

(3)Clinical Laboratory Medicine, Honghui Hospital, Xi'an Jiaotong University,

Xi'an, China.

**BACKGROUND:** Total hip arthroplasty (THA) has emerged as a valuable strategy for

managing hip tuberculosis (TB) osteoarthritis, but the optimal of 1-stage and

2-stage THA in patients with hip TB of varying severity levels surgical approach

remains debated. The purpose of this study was to investigate whether there were

differences in the effect of different surgical protocols on hip TB treatment.

**METHODS:** A retrospective cohort study was conducted on 43 patients who underwent

THA for hip TB at our institution between 2010 and 2020. Twenty-three patients

received a 1-stage THA, while 20 underwent a 2-stage procedure. Infection

control, functional status, complications and the blood loss and transfusion

volume were evaluated mean 4-year follow-up.

**RESULTS:** Both surgical approaches demonstrated favorable outcomes. No

significant differences were observed between the 1-stage and 2-stage groups in

terms of infection control (P = .35), functional improvement as measured by the

Harris Hip Score (P = .42), or complication rates (P = .61). The mean Harris Hip

Score improved significantly in both groups from baseline (P < .01 for both),

with a slightly higher score at 1 year in the 1-stage group (P = .04). The

differences in both blood loss and transfusion volume were statistically

significant (P < .01 and P = .01, respectively).

**CONCLUSIONS:** For patients with mild disease, 1-stage THA may be an appropriate

choice, while 2-stage THA is recommended for severe cases. Within their

respective indications, both approaches demonstrate good outcomes in terms of

infection control and functional restoration.

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**15. Infect Med (Beijing). 2025 May 17;4(2):100183. doi: 10.1016/j.imj.2025.100183.**

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Effect of glycemic control on lymphocyte subsets in the dissemination of

pulmonary tuberculosis: A retrospective analysis.

Lin Y(1), Chen X(2), Chen J(3), Wu D(2).

**Yujun Lin, Xiaohong Chen, Jiangwei Chen, Di Wu\***

**∗ Corresponding author. E-mail address: fkyywd@163.com (D. Wu) .**

Author information:

(1)Department of Respiratory and Critical Care Medicine, Fuzhou Pulmonary

Hospital of Fujian Province, Fuzhou 350008, Fujian Province, China.

(2)Department of Tuberculosis, Fuzhou Pulmonary Hospital of Fujian Province,

Fuzhou 350008, Fujian Province, China.

(3)The Medical Services Section, Fuzhou Pulmonary Hospital of Fujian Province,

Fuzhou 350008, Fujian Province, China.

**BACKGROUND:** Extrapulmonary tuberculosis (EPTB) complicates pulmonary

tuberculosis (PTB) management. Diabetes mellitus impairs immune function,

worsening tuberculosis (TB) outcomes.

**METHODS:** This retrospective study investigates the effect of glycemic control on

immune function and TB dissemination in 1,768 TB patients (2022-2024). Patients

were stratified by glycated hemoglobin (HbA1c) levels (≤ 6% vs. > 6%) and

fasting blood glucose (FBG) concentrations (< 7 vs. ≥ 7 mmol/L). Lymphocyte

subsets (CD3+, CD4+, CD8+ T cells, CD19+ B cells, and CD16+CD56+ natural killer

cells) were compared between glycemic control and TB groups. Multiple regression

and threshold effect analysis were conducted to assess the effects of HbA1c and

CD3+ T cells on TB dissemination and their critical values.

**RESULTS:** Poor glycemic control was associated with lower cell counts of all

lymphocyte subsets in patients with PTB (all p < 0.0001). Similar reductions

were observed in patients with concurrent PTB and EPTB (PTB + EPTB) when HbA1c

values > 6% (all p < 0.05). When HbA1c values ≤ 6% or FBG concentrations < 7

mmol/L, patients with PTB + EPTB showed lower immune cell counts than PTB (p <

0.05). Multiple regression indicated HbA1c increased TB dissemination risk (OR =

10.95), while CD3+ T cells showed protective effects. Threshold effect analysis

identified an HbA1c values ≥ 7.4% for metabolic control and CD3+ T cell

thresholds of 387/µL (immune deficiency) and 2,100/µL (immune overactivation).

**CONCLUSIONS:** Poor glycemic control impairs immune cells, while EPTB further

reduces immune cell numbers. Integrated glycemic management and immunological

monitoring help optimize treatment strategies and improve clinical outcomes,

particularly in patients at risk for EPTB.

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PMCID: PMC12173055

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**16. Front Oncol. 2025 Jun 3;15:1529049. doi: 10.3389/fonc.2025.1529049. eCollection 2025.**

Case Report: Epididymal NK/T-cell lymphoma and adrenal diffuse large B-cell

lymphoma are misdiagnosed as tuberculosis: two case reports and literature

review.

Ye D(1), Liu X(1), Yang Y(2), Yang Y(1), Fei Z(1), Liu H(1), Zhan Q(3), Xia

L(1).

**Dan Ye, Xuhui Liu, Yuexiang Yang, Yang Yang, Zhentao Fei, Huarui Liu, Qilin Zhan, Lu Xia\***

**\*CORRESPONDENCE Lu Xia，xialu@shaphc.org**

Author information:

(1)Department of Tuberculosis, Shanghai Public Health Clinical Center, Shanghai,

China.

(2)Department of Pathology, Shanghai Public Health Clinical Center, Shanghai,

China.

(3)Department of Hematology, Shanghai Public Health Clinical Center, Shanghai,

China.

Extranodal NK/T-cell lymphoma(ENKTCL) and diffuse large B-cell lymphoma(DLBCL)

are specific subtypes of non-Hodgkin lymphoma(NHL), which lack specific features

and are difficult to diagnose. The clinical features of lymphoma and

tuberculosis are similar, which are easy to be misdiagnosed and lead to delayed

treatment. This report describes two cases, one that of a 34-year-old man who

was diagnosed with epididymal tuberculosis because of fever, progressive

epididymal enlargement, positive T-cell Spot Test(T-SPOT), and epididymal

magnetic resonance imaging(MRI) suggesting possible epididymal tuberculosis. He

was treated with anti-tuberculosis therapy for 1 month, but the patient's

epididymis continued to grow. Needle biopsy pathology and immunochemical

examination showed an epididymal NK/T cell lymphoma, which gradually shrank

after chemotherapy. Meanwhile, a 77-year-old female patient was reported who was

diagnosed with adrenal tuberculosis because of fever, night sweats, abdominal

pain, positive QuantiFERON-TB Gold(QFT) test, and adrenal tuberculosis detected

by positron emission tomography/computed tomography(PET/CT). She received

anti-tuberculosis treatment for 2 weeks, but her symptoms were not improved.

Biopsy pathology and immunochemical examination showed adrenal diffuse large

B-cell lymphoma, which deteriorated rapidly after chemotherapy and she finally

died. In this report, epididymal NK/T cell lymphoma and adrenal diffuse large

B-cell lymphoma are rare, and the disease develops rapidly. The diagnosis

depends on pathological morphology and immunohistochemistry. Early detection,

diagnosis, and treatment are crucial for the prognosis of patients.

Copyright © 2025 Ye, Liu, Yang, Yang, Fei, Liu, Zhan and Xia.

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PMID: 40530019

**17. J Thorac Dis. 2025 May 30;17(5):3223-3237. doi: 10.21037/jtd-2025-604. Epub 2025 May 27.**

A systematic review and meta-analysis of artificial intelligence software for

tuberculosis diagnosis using chest X-ray imaging.

Han ZL(#)(1), Zhang YY(#)(2), Li J(#)(3), Gao S(#)(4), Liu W(5), Yang WJ(6)(7),

Xing ZH(1)(2)(6)(7).

**Zhi-Lin Han, Yu-Yang Zhang, Jian Li, Shan Gao, Wei Liu, Wan-Jie Yang\*, Zhi-Heng Xing\***

**\*Correspondence to: Wan-Jie Yang, BM. Email: yangwanjie0709@126.com; Zhi-Heng Xing, PhD. Email: 18920696025@189.cn.**

Author information:

(1)Department of Radiology, Haihe Hospital, Tianjin University, Tianjin, China.

(2)Haihe Clinical School, Tianjin Medical University, Tianjin, China.

(3)Artificial Intelligence Branch of the Commerce Statistics Chinese Society of

China Business, Beijing, China.

(4)Department of Nanchang Zhongke Institute of Mobile Medical Imaging, Nanchang,

China.

(5)Standardization Professional Branch of China Anti Tuberculosis Association,

Beijing, China.

(6)Tianjin Institute of Respiratory Diseases, Tianjin, China.

(7)TCM Key Research Laboratory for Infectious Disease Prevention for State

Administration of Traditional Chinese Medicine, Tianjin, China.

(#)Contributed equally

**BACKGROUND:** Pulmonary tuberculosis (PTB) remains a global public health

challenge, with 10.8 million new cases reported in 2023. Early diagnosis is

crucial for controlling its spread, yet traditional sputum-based tests face

limitations in turnaround time and resource availability. Chest X-ray (CXR) is a

cost-effective diagnostic tool, but its use in high-tuberculosis (TB) burden

regions is restricted by a shortage of radiologists. Artificial intelligence

(AI)-based computer-aided detection (CAD) systems, leveraging deep learning,

offer a promising solution for automated PTB detection. However, variability in

diagnostic performance across AI tools and the need for scenario-specific

threshold adjustments remain challenges that need to be addressed. Our

meta-analysis evaluated the diagnostic accuracy of five AI-based PTB detection

products, aiming to provide insights for advancing AI applications in TB

screening and diagnosis.

**METHODS:** The PubMed, Embase, Web of Science, and Cochrane Library databases were

searched for literature related to CXR diagnosis of TB based on AI technology

published from the establishment day of the database to December 19, 2024. The

keywords were "artificial intelligence", "tuberculosis", "chest X-ray", and

"diagnosis". The literature search, screening, data extraction, quality

evaluation, and bias risk assessment were conducted independently by two

researchers, and Stata 17.0 software (StataCorp) was used to process and analyze

the data.

**RESULTS:** A total of 5,651 references were retrieved, and 21 references were

finally selected according to the inclusion and exclusion criteria. The

meta-analysis included five software solutions for CXR analysis: JF CXR-1 (JF

Healthcare, Nanchang, China), qXR (Qure.ai, Mumbai, India), Lunit INSIGHT CXR

(Lunit, Seoul, South Korea), CAD4TB (Delft Imaging, 's-Hertogenbosch,

Netherlands), and InferRead DR Chest (Infervision, Beijing, China). Their

sensitivity and specificity were as follows: JF CXR-1, 86.0% and 80.0%; qXR,

90.0% and 64.0%; Lunit INSIGHT CXR, 90.0% and 63.0%; CAD4TB, 91.0% and 60.0%;

InferRead DR Chest, 89.0% and 59.0%.

**CONCLUSIONS:** AI software has demonstrated excellent diagnostic performance in

assisting the CXR diagnosis of TB and can help clinicians to make rapid and

accurate decisions in screening and treating patients with TB.

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**18. J Thorac Dis. 2025 May 30;17(5):3318-3325. doi: 10.21037/jtd-2025-878. Epub 2025 May 28.**

Clinical outcomes of contezolid in treating complex tuberculosis: real-world

evidence from 11 patients.

Liu Y(1), Cui Z(2), Fu Y(2), Chan ED(3)(4)(5), Hu C(1).

**Ying Liu, Zixuan Cui, Yingxi Fu, Edward D Chan, Chunmei Hu\***

**\*Correspondence to: Chunmei Hu, Email: njyy003@njucm.edu.cn.**

Author information:

(1)Department of Tuberculosis, the Second Hospital of Nanjing, Nanjing

University of Chinese Medicine, Nanjing, China.

(2)Nanjing University of Chinese Medicine, Nanjing, China.

(3)Department of Medicine, Rocky Mountain Regional Veterans Affairs Medical

Center, Aurora, CO, USA.

(4)Department of Academic Affairs, National Jewish Health, Denver, CO, USA.

(5)Division of Pulmonary Sciences and Critical Care Medicine, University of

Colorado School of Medicine, Aurora, CO, USA.

**BACKGROUND:** Tuberculosis (TB) remains a major global health challenge,

especially among patients with drug intolerance or comorbidities that limit

treatment options. Although linezolid (Lzd), an oxazolidinone antibiotic, has

demonstrated good efficacy against Mycobacterium tuberculosis (MTB), its

long-term use is frequently associated with serious adverse effects such as

myelosuppression and peripheral neuropathy. Contezolid, a novel oxazolidinone

with a more favorable safety profile, has shown comparable in vitro activity

against MTB. However, clinical data on its use for TB treatment are limited.

This report seeks to provide a real-world experience on the use of contezolid in

the treatment of TB.

**METHODS:** A retrospective case series was conducted using medical records from

drug-susceptible TB patients admitted to the Second Hospital of Nanjing between

March 2022 and March 2024. Patients with a confirmed diagnosis of TB (based on

clinical, microbiological, or histopathological evidence), documented drug

susceptibility to background anti-TB medications, and who received a

contezolid-containing regimen for at least one month due to intolerance or

contraindications to standard anti-TB therapy were included in the study. The

information about the patient, including demographics and clinical data,

laboratory findings, treatment, and adverse events (AEs), was collected.

Treatment outcomes were assessed through sputum culture conversion, clinical

symptom improvement, and imaging findings. Safety evaluations were based on

laboratory tests and AEs grading according to World Health Organization (WHO)

criteria.

**RESULTS:** Of the 11 patients included in the study, six received a Lzd-containing

anti-TB regimen at the outset of the treatment. However, due to the emergence of

intolerable and severe AEs, which resulted in the cessation of the standard

regimen, the anti-TB regimen was modified to one that contained contezolid. The

remaining five patients elected to pursue the anti-TB regimen containing

contezolid due to relative contraindications associated with their general

condition and underlying disease. No serious AEs were observed in those

receiving contezolid. Ultimately, all 11 patients demonstrated clinical

improvement, achieved sputum culture converted to negative, and exhibited a

favorable prognosis.

**CONCLUSIONS:** In this small retrospective case series, contezolid was well

tolerated. In certain populations with particularly challenging forms of TB,

contezolid could be a valuable addition to anti-TB treatment regimens.

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**19. Medicine (Baltimore). 2025 Jun 13;104(24):e42750. doi:**

**10.1097/MD.0000000000042750.**

Repeat detection of Mycobacterium DNA in sputum for the diagnosis of pulmonary

tuberculosis.

Zan L(1), Ao J, Sun F.

**Lina Zan\*, Jiafu Ao, Feng Sun**

**\* Correspondence: Lina Zan, (e-mail: 18956890567@189.cn).**

Author information:

(1)Inspection Center, The People's Hospital of Bozhou, Bozhou, China.

This study explores the application value of real-time fluorescence quantitative

PCR for repeated detection of Mycobacterium DNA in sputum for the diagnosis of

pulmonary tuberculosis (TB). A total of 111 patients who were ultimately

clinically diagnosed with pulmonary tuberculosis and sought treatment at Bozhou

People's Hospital from January 2019 to March 2021 were selected. Mycobacterium

DNA in sputum was detected by quantitative real-time PCR. The patients with TB

were divided into Groups 1, 2, and 3 according to the number of sputum DNA

examinations for Mycobacterium TB after admission. Group 1 was tested once,

Group 2 was tested twice, and Group 3 was tested 3 times. There were 61 patients

with pulmonary TB in Group 1, 37 patients in Group 2 and 13 patients in Group 3.

Among the 111 patients with TB, the overall positive rate of sputum culture was

59.46% (66/111). The positive rates of TB-DNA in sputum of Groups 1, 2, and 3

were 49.18% (30/61), 70.27% (26/37), and 84.62% (11/13), respectively, and the

positive rate of TB-DNA in Group 1 was significantly lower than that in Group 2

and Group 3 (P < .05). Repeated detection of Mycobacterium TB-DNA in sputum can

improve the positive rate of TB patients, and 2 consecutive tests may be more

suitable for early diagnosis of TB patients.

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**20. Infect Drug Resist. 2025 Jun 10;18:2951-2961. doi: 10.2147/IDR.S523064.**

**eCollection 2025.**

The Association of Latent Tuberculosis Infection with Air Pollutant Exposure,

Meteorological and Other Factors: A Retrospective Study in Eastern China of

College Students.

Qiu B(#)(1), Xu Z(#)(1)(2), Miao R(1)(2).

**Beibei Qiu, Zhengyuan Xu, Ruifen Miao\***

**\*Correspondence: Ruifen Miao, Email ruifenmiao@126.com**

Author information:

(1)Department of Chronic Communicable Disease, Nanjing Municipal Center for

Disease Control and Prevention Affiliated to Nanjing Medical University,

Nanjing, People's Republic of China.

(2)School of Public Health, Nanjing Medical University, Nanjing, People's

Republic of China.

(#)Contributed equally

**OBJECTIVE:** The associations between meteorological factors, air pollutant

indicators, and latent tuberculosis infection (LTBI) have not yet been

confirmed. This study aimed to assess the association of meteorological factors,

air pollutant indicators, and other factors with LTBI among college students.

**METHODS:** We selected 5,193 freshmen randomly who originated from key

tuberculosis areas in nine colleges in Nanjing. We ranked the importance of

independent variables using Least Absolute Shrinkage and Selection Operator

(LASSO) regression and random forest models. We then conducted a multi-model

analysis after incorporating them into the prediction model. In addition, we

adopted a calibration curve to determine the quality of the model. A nomogram

was used to evaluate the possibility of using multiple models to predict LTBI

risk.

**RESULTS:** We found that higher outdoor PM10 concentrations (OR: 1.35; 95% CI:

1.10-1.65) was associated with LTBI. A history of allergies (OR: 1.37; 95% CI:

1.16-1.62) and coal-based fuels (OR: 1.44; 95% CI: 1.11-1.87) had a positive

correlation with the occurrence of LTBI. Taking vitamin D supplements (OR: 0.82;

95% CI: 0.69-0.98) could reduce the risk of LTBI. Besides, age (OR: 1.11; 95%

CI: 1.00-1.22) were significantly associated with strong positive populations.

**CONCLUSION:** Higher outdoor PM10 concentration, history of allergies, and use of

coal-based fuels were positively correlated with the occurrence of LTBI. Vitamin

D supplementation might reduce the risk of LTBI. Besides, older people were more

likely to contribute to strong positive results.

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Unique pathological features and drug resistance patterns in cutaneous

tuberculosis.

Liu Y(#)(1), Wu R(#)(1), Liu J(1), Dai J(1), Liu D(1), Liu Y(1), Liang Y(1),

Chen W(1).

**Yuejiao Liu, Runrui Wu, Junjun Liu, Jinlong Dai, Dongxu Liu, Yadong Liu, Yumei Liang\*, Wen Chen\***

**\*CORRESPONDENCE Yumei Liang，liangyumei309@126.com ；Wen Chen， dr.chen20160224@foxmail.com**

Author information:

(1)Chinese PLA Key Laboratory of Tuberculosis, Department of Pathology, The 8th

Medical Center, Chinese PLA General Hospital, Beijing, China.

(#)Contributed equally

Cutaneous tuberculosis (CTB), a rare manifestation of extrapulmonary

tuberculosis, often presents diagnostic challenges in clinical settings due to

its atypical presentation. The definitive diagnosis relies heavily on

pathological evaluation, which underscores the importance of understanding the

distinct pathological characteristics and drug resistance patterns of CTB, a

subject that has not been extensively explored previously. In this study, we

conducted a comparative analysis of 59 CTB samples and 59 pulmonary tuberculosis

samples, focusing on their clinicopathological features. Our findings reveal

that CTB can be characterized by subcutaneous irregular hypoechoic regions on

ultrasound, localized soft tissue swelling, and flaky low-density shadows on CT

scans, with MRI effectively determining the extent of bone and soft tissue

involvement. The two groups had no statistical difference in the positivity rate

for acid-fast staining and molecular detection. Notably, the incidence of

granulomatous lesions was higher in CTB compared to pulmonary tuberculosis, and

the high number of macrophages in the skin may be an important reason. However,

other parameters such as caseous necrosis, coagulative necrosis, inflammatory

necrosis, acute inflammation, hemorrhage, fibroplasia, and exudation showed no

significant differences between the two groups. Intriguingly, many significant

differences in drug resistance patterns were found between the CTB group and the

control group. But when comparing the secondary CTB group to the control group,

the only significant difference found was in resistance to RFP + INH + STR.

Overall, our study highlights unique pathological features and drug resistance

profiles in CTB, providing valuable insights for more accurate clinical

diagnosis and tailored therapeutic strategies.

Copyright © 2025 Liu, Wu, Liu, Dai, Liu, Liu, Liang and Chen.

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Household economic burden and catastrophic expenditures in non-resistant

tuberculosis patients: cross-sectional survey in Guizhou, China.

Ma X(1), Huang A(1), Chen H(1), Zhou J(1), He Y(1), Wang W(2), Du R(2), Guo

X(2), Zhao Q(2), Li J(1).

**Xiaoxue Ma, Aijue Huang, Huijuan Chen, Jian Zhou, Yuying He, Weibing Wang, Rong Du, Xueli Guo, Qi Zhao\*, Jinlan Li\***

**\*CORRESPONDENCE Qi Zhao，zhaoqi@shmu.edu.cn ；Jinlan Li，lijinlanpublic@126.com**

Author information:

(1)Guizhou Provincial Center for Disease Control and Prevention, Guiyang, China.

(2)School of Public Health, Fudan University, Shanghai, China.

**OBJECTIVES:** In accordance with the World Health Organization (WHO)'s "End TB

Strategy," which aims to eradicate catastrophic expenditures faced by

TB-affected families, we intend to thoroughly investigate and comprehend the

economic burden, catastrophic expenditures, and contributing factors pertaining

to non-drug-resistant tuberculosis patients' families in Guizhou Province. Our

goal is to formulate policy recommendations that can effectively alleviate the

financial strain on these patients and their families.

**METHODS:** The pulmonary tuberculosis cases, which were non-drug-resistant,

registered across the province during May-June 2020, and successfully treated at

the time of the survey, underwent questionnaire interviews conducted through

probability proportional sampling. Utilizing the WHO methodology, the household

economic burden borne by these patients was computed, with the mean and median

(interquartile range), abbreviated as "M (IQR)," employed to describe the

economic burden, and the proportion (%) used to depict catastrophic

expenditures. Further analysis of the factors influencing catastrophic

expenditures within these families was conducted using chi-squared (χ 2) tests

and binary logistic regression.

**RESULTS:** The average total out-of-pocket expenses (OOP) incurred by 2,283

non-drug-resistant pulmonary tuberculosis patients in Guizhou Province amounted

to 10,581.82 RMB ($1453.11), with a median expenditure of 5,277 RMB (IQR:

2,110-12,352 RMB). Notably, indirect expenses comprised 58.07% of the total

expenditure. Taking the time of diagnosis as the cut-off point, the majority of

these expenses occurred during the treatment phase, but the before diagnosis

stage also imposed a significant economic burden, averaging 3,191.58 RMB

($438.27). Among the 2,283 patients, 50.37% (1,150 patients) experienced

catastrophic events due to their medical expenses. Key risk factors for these

catastrophic events included poverty, employment status, before diagnosis

visits, hospitalization, mobility issues, and delayed diagnosis.

**CONCLUSION:** The economic burden imposed on households by tuberculosis patients

in the province remains considerable, with the indirect burden accounting for

the lion's share. The likelihood of catastrophic expenditures persists,

significantly influenced by factors such as poverty, hospitalization, delayed

diagnoses, and before diagnosis visits. Recommendations include reinforcing

targeted public health education, enhancing the diagnostic and therapeutic

capabilities of medical institutions, regulating their practices, curbing

unnecessary hospitalizations, and instituting a long-term framework aimed at

alleviating the indirect economic burden. By doing so, we can collaboratively

diminish the economic strain on patients and mitigate the risk of catastrophic

expenditures, ultimately striving for the achievement of zero catastrophic

expenditures among households.

Copyright © 2025 Ma, Huang, Chen, Zhou, He, Wang, Du, Guo, Zhao and Li.

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Bidirectional two-sample Mendelian randomization reveals causal link between

genetic blood metabolites and tuberculosis.

Shi Z(#)(1), Zhao C(#)(1), Yu X(#)(2), Zhao D(1), Li Y(3).

**Zhenyu Shi, Chenyi Zhao, Xiaowen Yu, Dingding Zhao, Yongqiang Li\***

**\*Correspondence: Yongqiang Li，liyongqiang@vip.henu.edu.cn**

Author information:

(1)Huaihe Hospital, Henan University, Kaifeng, People's Republic of China.

(2)Chongqing Key Laboratory of Traditional Chinese Medicine to Prevent and Treat

Autoimmune Diseases, Chongqing, People's Republic of China.

(3)Huaihe Hospital, Henan University, Kaifeng, People's Republic of China.

liyongqiang@vip.henu.edu.cn.

(#)Contributed equally

Tuberculosis (TB), caused by infectious agent Mycobacterium tuberculosis (Mtb)

seriously poses a great threat to health. An array of metabolites generated by

metabolic pathways are essential for Mtb pathophysiology. However, a specific

causal relationship between TB and human metabolites remains indistinct. This

study aimed to investigate the relationship between 1400 metabolites and TB by

Mendelian randomization (MR) analysis. In this study, a total of 1400

metabolites were utilized as exposure factors, while TB-related data served as

the outcomes. And TwoSampleMR package and R software were adopted to perform

this MR analysis. Various regression fitting methods were employed to conduct MR

analysis, including inverse variance weighted (IVW), MR-Egger, weighted median,

simple mode, and weighted mode. In addition, potential biases arising from

linkage disequilibrium and weak instrumental variables were considered.

Metabolites that failed to meet the criteria in both the heterogeneity and

pleiotropy tests were considered to have no substantial causal influence on the

results, ensuring the robustness and reliability of our analysis. IVW analysis

showed that six human metabolites exhibited a significant causal influence

(P < 0.05) on TB. Among them, dodecanedioate, myristoleate (14:1n5), and

1-(1-enyl-palmitoyl)-2-arachidonoyl-GPE(p-16:0/20:4) demonstrated a strong

causally positive effect on TB, indicating that with the increase of these

metabolites, TB progressed robustly. Glycerol 3-phosphate, sphingomyelin

(d18:1/20:2, d18:2/20:1, and d16:1/22:2), and 2-methylserine were significantly

negatively associated with TB, an increase in these metabolites inhibited TB

progression. This is the first time to reveal the causal effects of human

metabolites on TB through MR, and the metabolites may be potential biomarkers

candidate for TB diagnosis, and monitoring these metabolites might have great

clinic significance for TB diagnosis and treatment in the future.

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**Online ahead of print.**

Structural insight of a bi-functional isoprenyl diphosphate synthase Rv0562 from

Mycobacterium tuberculosis.

Wang Q(1), Yang Y(2), He B(1), Huang JW(3), Kuo CJ(4), Chen CC(5), Guo RT(6).

**Qian Wang, Yu Yang\*, Biyu He, Jian-Wen Huang, Chih-Jung Kuo\*, Chun-Chi Chen\*, Rey-Ting Guo\***

**\*Corresponding authors. E-mail addresses: guoreyting@hubu.edu.cn (R.-T. Guo), ccckate0722@hubu.edu.cn (C.-C. Chen), yangyu@hubu.edu.cn (Y. Yang) and ck476@nchu.edu.tw (C.-J. Kuo).**

Author information:

(1)State Key Laboratory of Biocatalysis and Enzyme Engineering, Hubei Hongshan

Laboratory, School of Life Sciences, Hubei University, Wuhan 430062, PR China.

(2)State Key Laboratory of Biocatalysis and Enzyme Engineering, Hubei Hongshan

Laboratory, School of Life Sciences, Hubei University, Wuhan 430062, PR China.

Electronic address: yangyu@hubu.edu.cn.

(3)State Key Laboratory of Biocatalysis and Enzyme Engineering, Hubei Hongshan

Laboratory, School of Life Sciences, Hubei University, Wuhan 430062, PR China;

Zhejiang Key Laboratory of Medical Epigenetics, Department of Immunology and

Pathogen Biology, School of Basic Medical Sciences, Hangzhou Normal University,

311121 Hangzhou, PR China.

(4)Department of Veterinary Medicine, College of Veterinary Medicine, National

Chung Hsing University, Taichung, Taiwan. Electronic address: ck476@nchu.edu.tw.

(5)State Key Laboratory of Biocatalysis and Enzyme Engineering, Hubei Hongshan

Laboratory, School of Life Sciences, Hubei University, Wuhan 430062, PR China;

Zhejiang Key Laboratory of Medical Epigenetics, Department of Immunology and

Pathogen Biology, School of Basic Medical Sciences, Hangzhou Normal University,

311121 Hangzhou, PR China. Electronic address: ccckate0722@hubu.edu.cn.

(6)State Key Laboratory of Biocatalysis and Enzyme Engineering, Hubei Hongshan

Laboratory, School of Life Sciences, Hubei University, Wuhan 430062, PR China;

Zhejiang Key Laboratory of Medical Epigenetics, Department of Immunology and

Pathogen Biology, School of Basic Medical Sciences, Hangzhou Normal University,

311121 Hangzhou, PR China. Electronic address: guoreyting@hubu.edu.cn.

Mycobacterium tuberculosis (Mtb) is the causative agent of tuberculosis. Mtb

uses MK-9(II-H2), which consists of an isoprenyl side chain containing nine

isoprene units, with one being hydrogenated in the β-position, as an essential

element in the electron transport system. Rv0562 that can operate geranylgeranyl

diphosphate synthase (GGPPs) activity catalyzes the synthesis of MK-9(II-H2) by

condensing one molecule of DMAPP with eight molecules of isopentenyl diphosphate

(IPP) to form a C45 long-chain isoprenoid product. In this study, the structures

of Rv0562 were determined in the apo-form at a resolution of 2.54 Å and in

complex with IPP and Mg2+ at a resolution of 1.89 Å, revealing detailed

interactions between the enzyme and substrates. Moreover, the crystal structure

of the Rv0562-DM variant was determined at 2.27 Å resolution in complex with

polyethylene glycol (PEG), which occupies the substrate binding tunnel,

mimicking the long-chain product. The chain length determination mechanism of

Rv0562 is also probed through mutagenesis experiments. The obtained structures

help us understand how Rv0562 catalyzes isoprenyl chain elongation, showing

implications in developing new anti-Mtb treatments.

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Self-assembled ferritin nanoparticles using SpyCatcher/SpyTag multimerization of

Mycobacterium tuberculosis TB10.4 protein induce potent immunogenicity.

Guo F(1), Dong S(1), Song Y(1), Xiesihan G(1), Jiang H(1), Qian Z(1), Wang X(2),

Wang H(3), Xu T(4).

**Fangzheng Guo, Sihang Dong, Yamin Song, Ge Xiesihan, Hairui Jiang, Zhongqing Qian, Xiaojing Wang, Hongtao Wang\*, Tao Xu\***

**\*Corresponding authors. E-mail addresses: hongtaowang@bbmu.edu.cn (H. Wang), taoxu@bbmu.edu.cn (T. Xu).**

Author information:

(1)Anhui Province Key Laboratory of Immunology in Chronic Diseases, Laboratory

Medicine Experimental Center, Laboratory Medicine College, Bengbu Medical

University, Bengbu 233000, China.

(2)Anhui Province Key Laboratory of Clinical and Preclinical Research in

Respiratory Disease, Molecular Diagnosis Center, First Affiliated Hospital of

Bengbu Medical University, Bengbu, China.

(3)Anhui Province Key Laboratory of Immunology in Chronic Diseases, Laboratory

Medicine Experimental Center, Laboratory Medicine College, Bengbu Medical

University, Bengbu 233000, China.. Electronic address: hongtaowang@bbmu.edu.cn.

(4)Anhui Province Key Laboratory of Immunology in Chronic Diseases, Laboratory

Medicine Experimental Center, Laboratory Medicine College, Bengbu Medical

University, Bengbu 233000, China.. Electronic address: taoxu@bbmu.edu.cn.

Although Bacillus Calmette-Guérin (BCG) continues to play a role in alleviating

tuberculosis as a global public health crisis, its potential to cause

disseminated disease in immunocompromised individuals further limits its

widespread use. However, traditional subunit vaccines face the challenge of weak

immunogenicity. In this study, we employed the SpyCatcher/SpyTag system and a

ferritin (Fer) nanoparticle (NP) to construct an NP-based vaccine targeting the

non-region of difference antigen TB10.4. The construct comprises two components:

a SpyCatcher003-Fer vector and SpyTag003-TB10.4 antigen, expressed in

prokaryotic and eukaryotic systems, respectively. These components were

self-assembled into the tuberculosis nanovaccine candidate,

SpyCatcher-Fer-TB10.4 (SFT), in vitro. Compared with the monomeric TB10.4,

subcutaneous immunization with SFT-without an adjuvant-markedly enhanced cell

proliferation, promoted T lymphocyte activation, and stimulated multiple

TB-related cytokines, with responses comparable to or exceeding those induced by

BCG. These findings suggest that SFT is superior to conventional recombinant

proteins and holds promise for eliciting immunoprotective effects similar to

those of BCG in the future.

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Tuberculosis Verrucosa Cutis on Hands.

Zhu YC(1)(2), Liu ZH(2).

**Yan-Chu Zhu, Ze-Hu Liu\***

**\*Corresponding Author: Ze-Hu Liu, Email: zehuliu@zcmu.edu.cn**

Author information:

(1)Department of Dermatology, Hangzhou Third Hospital Affiliated to Zhejiang

Chinese Medical University, Hangzhou, ZheJiang Province, China.

(2)Department of Dermatology, Hangzhou Third People's Hospital, Hangzhou,

ZheJiang Province, China.

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**print.**

Antimycobacterial Muraymycins Isolated from Streptomyces sp. NRRL 30475 Using

OSMAC and Precursor-Feeding Strategies.

Zhou F(1)(2), Sun J(1), Zhang R(1), Peng H(1), Ren Y(3), Zhu Y(1), Sun Y(1), Van

Lanen SG(4), Chen W(3), Wang X(1)(5).

**Fengjuan Zhou, Jiawen Sun, Rui Zhang, Hanyang Peng, Yunyao Ren, Youjuan Zhu, Yongdi Sun, Steven G Van Lanen, Wei Chen\*, Xiachang Wang\***

**\*Corresponding Authors Xiachang Wang−J Email: xiachangwang@njucm.edu.cn ；Wei Chen− Email: njyy039@njucm.edu.cn**

Author information:

(1)Jiangsu Key Laboratory for Functional Substances of Chinese Medicine, Nanjing

University of Chinese Medicine, Nanjing 210023, China.

(2)Department of Pharmacy, Kunshan Hospital of Traditional Chinese Medicine,

Kunshan 215300, China.

(3)Department of Tuberculosis, the Second Hospital of Naning, Affiliated to

Naniing University of Chinese Medicine, Nanjing 210003, China.

(4)Department of Pharmaceutical Sciences, College of Pharmacy, University of

Kentucky, Lexington, Kentucky 40536, United States.

(5)Fujian Province Key Laboratory for the Development of Bioactive Material from

Marine Algae, College of Oceanology and Food Science, Quanzhou Normal

University, Quanzhou 362000, China.

Three mutant strains of Streptomyces sp. NRRL 30471 were screened with eight

different media based on "One Strain Many Compounds" (OSMAC) and

precursor-feeding strategies. Five new muraymycins, D5-D9 (4-8), together with

three known congeners were isolated and identified from Streptomyces sp. NRRL

30475 using an optimized BPM23A medium containing methionine, leucine, and

arginine (each 1.5 g/L). Structures of new compounds were elucidated using HR-MS

and NMR spectroscopic data. Muraymycin D6 (5) represents the first natural

muraymycin with phosphorylation at the 3'-OH of the ribofuranoside moiety.

Muraymycin D9 (8) features a unique dehydrocyclization of the carboxyl of a

valine with the epicapreomycidine imide of the peptide moiety, forming an

isopropyl hydantoin structure. Except for muraymycin D8 (7), which lacked the

ribofuranose, all isolated muraymycins (1-6 and 8) displayed potent

antimycobacterial activity against Mycolicibacterium smegmatis (MIC = 2-32

μg/mL). Specifically, the activities of 1-4 and 6 were even better than those of

the positive control isoniazid (MIC = 16 μg/mL). Moreover, muraymycins D1, D2,

D4, and D5 (1-4) had antimycobacterial effects against M. tuberculosis with MIC

values in the range of 8-16 μg/mL. This finding highlights muraymycin nucleoside

has potential for the development of antituberculosis antibiotics.

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