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**中国大陆学者发表的结核病英文文章摘要**

**（30篇）**

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**(tuberculosis[Title/Abstract]) AND (English[Language]) AND (China[Affiliation])**

**1. Clin Infect Dis. 2025 Jul 21:ciaf404. doi: 10.1093/cid/ciaf404. Online ahead of print.**

Safety, feasibility and rifapentine plasma concentration in Chinese children

with 1 month of daily rifapentine plus isoniazid for tuberculosis infection.

Liu W(1)(2), He T(1)(3), Zhan S(1)(2), Qin H(1)(2), Zeng J(1)(2), Li W(3), Lu

S(1)(2), Zhang P(1)(2).

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**BACKGROUND:** One month of daily rifapentine plus isoniazid (1HP) is a new regimen

for tuberculosis infection (TBI) to lower the incidence of active TB. But it had

not been prescribed for Chinese children and optimal dosage of daily rifapentine

for children remains controversial. We aim to assess the feasibility and safety

of 1HP in young Chinese children with TBI, and to provide evidence for

extrapolating dosing strategies to children.

**METHODS:** An open-label, prospective, single-arm clinical trial was conducted

among eligible participants (aged ≤ 14 years old). Completion rate, safety and

Rifapentine concentrations of 1HP regimen were analyzed.

**RESULTS:** Eighty children were enrolled in our study. 98.75% (79/80) of

participants completed the treatment, with only one case (1.25%) in 6-14 years

group of non-completion because of rash. 6.25% (5/80) experienced grade ≥3

adverse events (AEs), with no serious adverse events (SAEs) or deaths reported.

The relationship between rifapentine concentration (mg/L) and time (days) in

children stratified by age and weight demonstrated lowest rifapentine

concentration in participants less than 2 years old and less than 15kg when

compared to the other subgroups.

**CONCLUSIONS:** 1HP regimen is safe and feasible for young Chinese children with

tuberculosis infection. Weight-based daily rifapentine (10-15 mg/Kg) might not

be enough for young children, particularly for those younger than 2 years old

and less than 15kg.

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Infectious Diseases Society of America.

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**2. Clin Radiol. 2025 Jun 27;88:107004. doi: 10.1016/j.crad.2025.107004. Online**

**ahead of print.**

The diagnostic model from semi-supervised cross modality transformation improved

the distinguished ability of X-rays for pulmonary tuberculosis.

Zhou J(1), Ke H(2), Yang C(3), Zhang SJ(4), Sun WW(5), Chen L(6), Zhang ZM(7),

Fan L(8).

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**BACKGROUND:** Early diagnosis of tuberculosis is particularly difficult in

resource-poor areas. Traditional chest X-rays (CXR) have limited accuracy, while

CT scans are costly and involve radiation exposure. The study aims to improve

the diagnostic accuracy of routine X-rays for pulmonary tuberculosis to

approximate the performance of CT scans through building Artificial Intelligence

(AI) model, suitable for primary healthcare settings lacking CT facilities.

**METHODS:** In this study, datasets from our hospital and two open-source datasets,

namely the Shenzhen Hospital dataset (CHNCXR) and the Montgomery County dataset

(MC), were included. A semi-supervised cross-modality transformation

computational model was employed to independently train deep learning models

based on X-ray and CT images. Transfer learning was utilized for pre-training on

ImageNet, and the model performance was evaluated using 5-fold cross-validation.

**RESULTS:** In the evaluated patients, MX'(final augmented X-ray model) shows a

standout performance in diagnosing pulmonary tuberculosis (PTB) using chest

X-rays, with a 6% increase in high precision and a 1.8% increase in specificity,

significantly surpassing the original X-ray model MX(X-ray model). Although MX'

has a lower sensitivity (0.778) compared to MX (0.815), its overall balance

makes it highly suitable for initial screenings. The model's ability to

prioritize accuracy and specificity highlights its potential for effective

deployment in clinical scenarios with follow-up testing options.

**CONCLUSIONS:** The novel diagnosis model based on the AI method strikes a

meaningful balance between precision and accessibility. This makes MX' a

practical alternative in resource-limited settings, offering a more efficient

and scalable solution for tuberculosis diagnosis and screening.

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PMID: 40695011

**3. Int J Biol Macromol. 2025 Jul 19;320(Pt 4):146122. doi:**

**10.1016/j.ijbiomac.2025.146122. Online ahead of print.**

Deciphering the bidirectional catalytic mechanism of HGPRT from Mycobacterium

tuberculosis: Functional mapping of key active-site residues.

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As the number of tuberculosis cases worldwide has increased, the enzyme

hypoxanthine-guanine phosphoribosyltransferase from Mycobacterium tuberculosis

(MtHGPRT) has emerged as a promising target for drug development because of its

role in purine salvage and nucleotide homeostasis. However, the bidirectional

catalytic mechanism remains poorly understood, posing challenges for rational

drug design. Here, residue-specific functional mapping via systematic

mutagenesis coupled with molecular dynamics reveals key residues governing the

forward and reverse catalysis. D123 stabilizes

α-D-5-phosphoribosyl-1-pyrophosphate binding in the forward reaction, whereas

V124 and K154 enhance purine ring stability in the reverse reaction. In

addition, D126, V176, L181, and D182 regulate substrate coordination and active

site conformation. Cross-species validation confirmed the conserved roles of

D123 and V124. These findings provide a structural blueprint for enhancing our

understanding of the catalytic mechanism of MtHGPRT and offer insights into drug

design targeting HGPRT-related diseases and anti-tuberculosis therapies.

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PMID: 40692061

**4. Int J Rheum Dis. 2025 Jul;28(7):e70311. doi: 10.1111/1756-185X.70311.**

Noncanonical Differentiation of Memory B Cells Drives Latent Tuberculosis

Infection Reactivation Upon Tumor Necrosis Factor-Alpha Inhibitor Therapy: An

Integrative Transcriptomic Study.

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Zhang Y(1), Gu J(1).

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China.

**AIM:** Tumor necrosis factor inhibitors (TNFi) are widely used for the treatment

of autoimmune diseases, with latent tuberculosis infection (LTBI) reactivation

being a significant unresolved issue. The pathogenic mechanisms are not fully

understood. Integrated transcriptomic analysis could provide insights into

monitoring tuberculosis progression after TNFi therapy and help reduce LTBI

reactivation.

**METHODS:** We selected six transcriptomic datasets from studies related to TNFi

treatment and tuberculosis. Pathway enrichment, pseudotime, and transcription

factor analyses were performed to explore the underlying mechanisms.

**RESULTS:** Our analysis revealed distinct transcriptional changes in memory B

cells during tuberculosis progression and TNFi therapy. In active tuberculosis

(ATB), ROR1+ memory B cells were identified in a noncanonical differentiation

trajectory, characterized by downregulation of B cell-related genes (e.g., CD22,

EBF1, MS4A1), reduced translational capacity, and suppression of immune response

pathways, accompanied by upregulation of oxidative phosphorylation, which

highlighted metabolic alterations during tuberculosis progression. A similar

subtype also emerged in TNFi-treated patients, suggesting that metabolic

reprogramming of memory B cells may disrupt immune balance, thereby contributing

to LTBI reactivation and ATB development following TNFi therapy.

**CONCLUSIONS:** The study integrates bioinformatics and single-cell RNA sequencing

to reveal the role of memory B cells in ATB progression and TNFi treatment,

offering insights into TNFi-associated TB susceptibility and potential

therapeutic targets.

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**5. Infect Drug Resist. 2025 Jul 14;18:3527-3534. doi: 10.2147/IDR.S529466.**

**eCollection 2025.**

Phenotyping Nontuberculous Mycobacterial Lung Disease: Comparative Analysis of

Clinical and Imaging Features in a TB-Endemic Setting.

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**OBJECTIVE:** To systematically analyze clinical features and imaging

characteristics of nontuberculous mycobacterial pulmonary disease (NTM-PD)

patients in a tuberculosis specialty setting, establishing diagnostic and

management references.

**METHODS:** We conducted a retrospective analysis of 204 NTM-PD cases admitted to

our tuberculosis department from January 2018 to December 2023, evaluating

clinical manifestations, mycobacterial speciation, and radiological patterns.

**RESULTS:** The cohort comprised 118 males and 86 females (mean age 65.34 ± 13.23

years), predominantly rural residents (63.24%). Common comorbidities included

previous pulmonary tuberculosis (58.33%), chronic obstructive pulmonary disease

(41.67%), and bronchiectasis (36.76%). Primary clinical manifestations were

productive cough (78.92%), dyspnea (25.98%), and hemoptysis (24.5%).

Mycobacterium avium complex (MAC) accounted for 59.80% of isolates, followed by

Mycobacterium abscessus (MABS) (16.67%). Radiological analysis revealed right

upper lobe (86.54%) and left upper lobe (82.69%) predominance, with multilobar

involvement (≥3 lobes) in 73.08% cases. Characteristic imaging features included

nodular opacities, pleural thickening (63.46%), cavitary lesions (54.81%), and

bronchiectasis (51.92%).

**CONCLUSION:** NTM-PD primarily affects elderly populations with chronic

respiratory symptoms, demonstrating extensive pulmonary involvement across

multiple lobes. The disease exhibits characteristic radiological triad of

nodules, cavitations, and bronchiectasis, with MAC being the predominant

pathogen in this cohort.

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**6. J Clin Tuberc Other Mycobact Dis. 2025 Jul 4;40:100548. doi:**

**10.1016/j.jctube.2025.100548. eCollection 2025 Aug.**

A method for purifying and concentrating Mycobacterium tuberculosis in sputum

specimens: The double-membrane filtration and concentration method (DMFCM).

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101149, China.

**BACKGROUND:** Tuberculosis (TB) is an infectious disease that poses a global

hazard to public health. Clinically, the small number and low concentration of

Mycobacterium tuberculosis (M.tb) in some specimens make TB difficult to detect

in the laboratory and affect the sensitivity of diagnosis.

**METHODS:** M.tb in clinical sputum specimens was purified and concentrated using

the double membrane filtration concentration method (DMFCM), which was compared

with existing methods and evaluated for application.

**RESULTS:** DMFCM removes 40-80% of impurities from 80.53% of specimens while

concentrating M.tb by up to 3.366 times. In microscopy examination, compared

with the direct smear method (DSM), the sensitivity with DMFCM of the test was

increased from 58.33% to 73.61%. For quantitative real-time PCR (qPCR), the

positive rate of the sputum specimens treated with the DMFCM (37/42) was higher

than that treated with centrifugation (35/42). In terms of cultures, treatment

of sputum specimens with DMFCM reduced the time required to determine a positive

result to 75% of the time required compared to the MGIT 960 liquid cultures, and

increased the rate of positivity.

**CONCLUSIONS:** The M.tb in the culture solution after DMFCM treatment is purer and

more concentrated, which can effectively improve the positive rate of detection.

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PMCID: PMC12272938

PMID: 40688754

**7. J Thorac Dis. 2025 Jun 30;17(6):3619-3630. doi: 10.21037/jtd-2024-2071. Epub**

**2025 Jun 9.**

Diagnostic performance of Xpert MTB/RIF in lymph node tuberculosis in a general

hospital.

Jin W(#)(1), Yin X(#)(1), Wang M(2), Fang T(1), Ni J(3), Zhou C(4), Yang W(5),

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**BACKGROUND:** In general hospitals, tuberculosis (TB) is an important infectious

cause of lymphadenopathy, but its etiological diagnosis rate is very low. This

study aimed to determine the performance of Xpert MTB/RIF(Xpert) in

differentiate tuberculous lymphadenopathy from other causes.

**METHODS:** A retrospective pairing study was carried out from August 2015 to July

2024. A total of 229 participants were involved. Microbiological reference

standard (MRS) and composite reference standard (CRS) were used as two

standards. All patients underwent biopsy measurement and specimens were examined

using histopathology, acid-fast bacilli (AFB), liquid culture with/without

Xpert. The baseline information, diagnostic methods and time were compared

between two groups. The diagnostic values including sensitivity, specificity,

accuracy (ACC), Kappa value and area under the curve (AUC) were compared.

**RESULTS:** This study included a total of 229 participants, of whom 150 were in

the no Xpert group and 79 in the Xpert group. The median age was 44 [31-58]

years, with female proportion of 60.0%. The most common sites of lymphadenopathy

are the neck (66%), mediastinum (17%), and abdomen (7%). In patients with lymph

node tuberculosis (LNTB), MRS was achieved in 35.4% of cases, while 60.0%

fulfilled CRS criteria. No significant differences were observed in MRS

percentage or pathology positivity rates between the two groups. The median time

from biopsy to diagnosis was significantly shorter in the Xpert group compared

to the no Xpert group {2 days [interquartile range (IQR), 1-9 days] vs. 7 days

(IQR, 5-15 days)}. In comparison to CRS, the sensitivity, specificity and AUC of

Xpert were 57.1% [95% confidence interval (CI): 42.2-72.1%], 100%, and 0.786

(95% CI: 0.711-0.861), respectively. The sensitivity of the combined culture and

Xpert significantly increased (71.4%, 95% CI: 57.8-85.1%). In comparison to MRS,

Xpert shared same sensitivity with culture while specificity was paralleled. The

combination of any two procedures yielded better results than single one, with

the combined Xpert and pathology yielding 90.0% (95% CI: 83.4-96.6%), combined

culture and pathology yielding 87.7% (95% CI: 80.5-94.8%), and combined culture

and Xpert yielding 91.7% (95% CI: 80.6-100%).

**CONCLUSIONS:** Xpert can accelerate the microbiological diagnosis time and reduce

the misdiagnose of lymph node granulomatous lesions. The application of Xpert

combined with culture or pathology may be the best pattern for the diagnosis of

LNTB in general hospital.

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**8. Front Immunol. 2025 Jul 4;16:1567167. doi: 10.3389/fimmu.2025.1567167.**

**eCollection 2025.**

miR-107-enriched exosomes promote ROS/wnt/autophagy, inhibit intracellular

mycobacterial growth and attenuate lung infection.

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Shen L(2), Shen H(3)(4), Wang F(1).

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Exosomes, known as small membrane vesicles of endocytic origin produced by most

cell types, exist in a variety of body fluids including plasma. The roles of

exosomes in immune responses against Mycobacteria tuberculosis (Mtb) infection

remain poorly characterized. Here, we found that miR-107 highly expressed in

exosomes from plasma of TB patients but not healthy control (HC) subjects.

Consistently, such miR-107-high exosomes were also detected in both the

extracellular fluid released by mycobacterial-infected macrophages and the

plasma of mycobacterial-infected mice. Interestingly, adding the miR-107-high

plasma exosomes or the miR-107 mimics to infected THP-1 macrophages inhibited

intracellular mycobacterial growth. Consistently, while nanoscale and

fluorescence imaging revealed that miR-107 could be transferred inter-cellularly

via exosomes, miR-107-enriched exosomes from miR-107 overexpressing cells also

inhibited mycobacterial growth in THP-1 macrophages and primary

monocytes/peripheral blood mononuclear cells (PBMC). Mechanistically,

miR-107-high exosomes increased ROS production; miR-107 regulated Wnt pathway by

targeting Wnt16 and promoted autophagy in THP-1 macrophages. Furthermore,

treatment of infected mice with miR-107-enriched exosomes reduced mycobacterial

infection in lung tissues. Our results raise a possibility to explore

miR-107-high plasma exosomes for a potential surrogate marker for TB. Findings

suggest that exosomes enriched with miR-107 or other bio-active molecules may

potentially serve as an attractive approach for treatment of infection.

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**9. BMC Infect Dis. 2025 Aug 1;25(1):973. doi: 10.1186/s12879-025-11312-8.**

Surveillance and analysis of drug resistance and drug resistance levels in

multidrug resistant tuberculosis on the tropical islands of China.

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**OBJECTIVE:** Multidrug-resistant tuberculosis (MDR-TB) remains a major public

health challenge in China. Hainan, China's largest tropical island, possesses

distinct socio-geographical features. However, the drug resistance patterns and

molecular epidemiology of MDR-TB in this region have not been fully elucidated.

This study aimed to assess the correlation between drug resistance genotypes and

phenotypic resistance levels in multidrug-resistant Mycobacterium tuberculosis

(MDR-MTB) strains collected from Hainan Island, using whole-genome sequencing

(WGS) and phenotypic drug susceptibility testing (DST).

**METHODS:** MDR-MTB strains isolated from patients on Hainan Island (2019-2021)

were analyzed. Minimum inhibitory concentrations (MIC) for 15 anti-TB drugs were

determined by broth microdilution (BMD). Whole-genome sequencing (WGS) was

performed using Illumina NovaSeq 6000. Genotypic resistance was predicted via

TB-Profiler, and correlations between resistance mutations and MIC levels were

assessed.

**RESULTS:** A total of 209 MDR-MTB strains were analyzed. Strains of lineage 2.2

exhibited significantly higher resistance to ethambutol (EMB) compared to

non-lineage 2 strains (P < 0.05). The sensitivity of WGS in predicting

resistance to first-line drugs isoniazid (INH), rifampicin (RIF), EMB, and

pyrazinamide (PZA) was 94.7%, 99.0%, 96.5%, and 80.8%, respectively. However,

specificity for EMB and PZA was lower at 60.2% and 79.4%. WGS also demonstrated

high sensitivity and specificity (> 95%) for second-line injectable

aminoglycosides (amikacin [AMK], capreomycin [CPM], and kanamycin [KM]), but

sensitivity for other second-line drugs except for fluoroquinolone drug

moxifloxacin (MOX, 94.4%) was below 80.0%. Notably, mutations in katG\_S315T,

rpoB\_S450L, and gyrA\_D94G were strongly associated with high-level resistance,

while mutations in fabG1, ahpC, embA promoters, and gyrA at codon 90 were linked

to low-level resistance.

**CONCLUSIONS:** This study quantitatively demonstrates the relationship between

specific drug resistance genotypes and resistance levels. It is the first to

characterize the regional resistance spectrum of MDR-MTB strains on Hainan

Island. These findings offer a novel foundation for MIC-based dose adjustment

and the optimization of treatment strategies in this region.  TRIAL

REGISTRATION: MR-46-23-020530. Date of registration:2023-07-03.

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**10. Emerg Microbes Infect. 2025 Dec;14(1):2534656. doi:**

**10.1080/22221751.2025.2534656. Epub 2025 Aug 1.**

Mixed infections and heteroresistance of Mycobacterium tuberculosis among

multidrug-resistant tuberculosis in China: a genomic epidemiology study.

Liu Y(1), Zhang Y(2), Lu X(1), Wu Z(2), Li M(1), Zhang R(1), Lu Y(1), Hou R(1),

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Mixed infection refers to the presence of multiple Mycobacterium tuberculosis

strains within one host, while heteroresistance denotes the coexistence of

drug-susceptible and drug-resistant strains or genotypes. Mixed infections and

heteroresistance with Mycobacterium tuberculosis can complicate drug resistance

diagnosis, treatment options, and transmission inference. We conducted a

population-based genomic epidemiological study of multidrug-resistant

tuberculosis (MDR-TB) in Shanghai, China, between January 1, 2005, and December

31, 2018, to evaluate the prevalence and impact of mixed infection and

heteroresistance on MDR-TB diagnosis and treatment outcomes. Demographic,

clinical, and laboratory data were collected, and factors associated with mixed

infections and heteroresistance were identified with multivariable logistic

regression analysis. Among the 936 MDR-TB patients in our study, 10.8% (101/936)

had mixed infections and 16.5% (154/936) exhibited heteroresistance, which was

more frequent with second-line anti-TB drugs (P < 0.01). There was a higher risk

of heteroresistance in older patients (≥60 years: aOR 1.91, 95% CI 1.02-3.57),

patients with diabetes (2.59, 1.36-4.91), and mixed infections (2.85,

1.67-4.88). Mixed infections and heteroresistance accounted for 22.6% (58/257)

of the strains with discrepancies between phenotypic and genotypic drug

susceptibility testing (DST). Strains with heteroresistance to EMB had a higher

discordance rate than those without (29.1% VS 17.2%, P < 0.05). Isolates that

were phenotypically susceptible but genotypically resistant harboured minority

or low-frequency resistance mutations and were more common in patients with

mixed infections and heteroresistance. In summary, mixed infections are

significantly associated with heteroresistance, and both mixed infections and

heteroresistance can lead to discrepancies between phenotypic and genotypic DST.

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PMID: 40748858 [Indexed for MEDLINE]

**11. Sci Rep. 2025 Jul 31;15(1):27988. doi: 10.1038/s41598-025-11949-0.**

RpoB mutation patterns in Rifampicin-resistant tuberculosis: a Jiangxi Province

study, 2021-2023.

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LS(1), Liang LC(1), Shu LH(1), Yang HQ(5).

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Antimicrobial resistance in Mycobacterium tuberculosis (M.tb) strains presents a

significant challenge to global tuberculosis (TB) control efforts. This study

was conducted to explore the distribution and prevalence of mutations at various

sites within the 81 bp Rifampicin (RIF) resistance-determining region (RRDR) of

the rpoB gene in M.tb, as detected by the Xpert MTB/RIF assay. This

retrospective analysis encompassed 9,867 non-repeating patients diagnosed with

TB between 2021 and 2023. Cases with RR detected by the Xpert were included in

further detailed analysis. The study utilized Chi-square tests or Fisher's exact

tests to identify statistically significant differences in demographic variables

and the prevalence of rpoB gene mutations between RResistant TB (RR-TB) and

non-RR-TB groups. Multiple logistic regression analysis was employed to examine

the relationship between probe types and demographic variables, with a P-value

of less than 0.05 considered statistically significant. Over the three-year

study period, M. tb was identified in 2,927 cases, with 485 being RR-TB. While

individuals aged ≥ 65 years constituted the largest absolute number of RR-TB

cases, the highest relative risk was observed in children aged 5-14 years

(OR = 2.68, 95% CI 1.16-6.22, P = 0.02) compared to the ≥ 65 reference group.

probe E missing emerged as the predominant mutation site, particularly prevalent

in pulmonary specimens and among individuals aged 55-64 years, with a

statistically significant difference (P < 0.001). An upward trend in probe B

mutations was also observed, reaching statistical significance (χ2 = 6.614,

P = 0.037).This molecular epidemiological study has identified the mutation

patterns within the rpoB gene that contribute to RR, as identified through the

use of Xpert technology over a three-year span in Jiangxi Province. The insights

gained are instrumental in informing individualized treatment regimens for RR-TB

patients by correlating mutation locations with resistance levels (e.g., probe E

mutations confer high-level resistance requiring second-line drugs, while probe

B mutations like D435Y may confer low-level "disputed" resistance). This

facilitates precision therapy, avoids unnecessary second-line treatments, and

reduces transmission. Future advancements in technology, such as large-scale

sequencing studies, could build upon these findings to further elucidate the

genetic variations at play. Ultimately, these discoveries could be corroborated

through rigorous in vitro and in vivo experimental research, reinforcing the

foundation of our understanding and response to antimicrobial resistance in

M.tb.

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PMID: 40745428 [Indexed for MEDLINE]

**12. Asia Pac J Clin Nutr. 2025 Aug;34(4):627-635. doi:**

**10.6133/apjcn.202508\_34(4).0014.**

Association between low vitamin B-12 status and latent tuberculosis infection

among adults.

Jiang L(#)(1), Yan T(#)(1), Zhang X(1), Liu C(2), Yan Q(1), Chai Y(1), Li Y(1),

Tan Y(1), Gao X(1), Wang Q(3).

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**BACKGROUND AND OBJECTIVES:** Tuberculosis (TB) remains a major public health

threat worldwide, but most of the presumed infected individuals remain

asymptomatic and contain Mycobacterium tuberculosis (MTB) in a latent

tuberculosis infection (LTBI), and some of them will progress to active

tuberculosis. Vitamin B-12 is crucial to maintain immune function, and play a

role in the metabolism of MTB, while few studies investigated the impact of

vitamin B-12 deficiency on tuberculosis. Therefore, we carried out the study to

explore the association between vitamin B-12 deficiency and LTBI using the

National Health and Nutrition Examination Surveys (NHANES).

**METHODS AND STUDY DESIGN:** A cross-sectional study was conducted by using data

from NHANES 2011-2012. Adults (aged ≥18 years) who had available data on serum

Vitamin B-12, serum Methylmalonic Acid (MMA) and QuantiFERON-TB Gold In-Tube

(QFT-GIT) results were included in the analysis. Multivariable logistic

regression was used to assess the association between Vitamin B-12 deficiency

and LTBI.

**RESULTS:** A total of 4773 subjects were included in the present study, of whom

479 were screened as LTBI. The LTBI group had a higher proportion of

participants with low Vitamin B-12 status. After adjusting for the possible

confounders, Vitamin B-12 deficiency was independently associated with a 37%

increased odds ratio of LTBI in the participants (OR: 1.37; 95% CI: 1.01-1.85).

Similar correlations remained in subjects aged ≥35 years and female subjects by

further stratified analysis.

**CONCLUSIONS:** Vitamin B-12 deficiency was significantly associated with higher

prevalence of LTBI in US adults. Maintenance of optimal Vitamin B-12 status has

potential benefits for LTBI prevention. Future studies are needed to assess the

roles and clinical implications of Vitamin B-12 in MTB infection.

DOI: 10.6133/apjcn.202508\_34(4).0014

PMCID: PMC12310438

PMID: 40738730 [Indexed for MEDLINE]

**13. mSystems. 2025 Jul 30:e0061625. doi: 10.1128/msystems.00616-25. Online ahead of print.**

Proteomic analysis of plasma unravels dynamic pathways and potential biomarkers

indicating disease stages following Mtb infection.

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Tuberculosis (TB) stages depend greatly on the interaction between Mycobacterium

tuberculosis (Mtb) and the host response. As a non-negligible source of active

tuberculosis (ATB), individuals with latent Mtb infection (LTBI) are insidious

and hard to be detected due to limited biomarkers. Further insight into the

pathogenic mechanisms associated with heterogeneous clinical outcomes after Mtb

infection benefits the prevention and control of TB epidemics. Therefore, this

study employed four-dimensional data-independent acquisition to quantify the

expression level of plasma proteins from healthy controls (HC), LTBI, and ATB,

with 15 participants in each group. Key proteins related to TB stages were

further assayed using parallel reaction monitoring (PRM) for validation in an

independent cohort, with a sample size of 20 individuals per group. Differential

abundance analyses showed a notable increase in the number of differentially

expressed proteins (DEPs) following Mtb infection, mainly involving carbohydrate

catabolism, metabolism of cholesterol and lipid, immune response and

inflammation, and complement and coagulation cascades. Protein-protein

interaction network suggested similar functional enrichment patterns as

aforementioned for core DEPs. Weighted gene co-expression network analyses

identified six modules, among which the brown module significantly correlated

with TB stages. Hub proteins in the brown module were enriched in lipid

metabolism and acute-phase response. Furthermore, PRM protein quantification

revealed that complement factor H (area under receiver operating characteristic

curves [AUC] = 0.708) had a better performance in differentiating LTBI and HC

than C4B (AUC = 0.625), while C4B (AUC = 0.917), MBL2 (AUC = 0.887), and SAA1

(AUC = 0.875) were helpful in differentiating ATB and HC. Also, SAA1 (AUC =

0.917) and matrix Gla protein (AUC = 0.905) favored the discrimination of ATB

from LTBI. Our work probes into the hub plasma proteins and pathways associated

with disease stages following Mtb infection, providing critical implications on

the diagnosis of TB stages.IMPORTANCEDistinct prognostic outcomes following

Mycobacterium tuberculosis (Mtb) infection result from host-pathogen

interactions, while the response mechanisms underlying such heterogeneous

phenotypes are far from understood. Through four-dimensional data-independent

acquisition and parallel reaction monitoring, our study linked specific plasma

proteomic profiles to various tuberculosis (TB) stages and corroborated relevant

pathways under various disease conditions. Of identified core proteins,

complement factor H formed a diagnostic classifier that distinguished latent Mtb

infection from healthy controls with good performance, and we also identified

C4B, MBL2, SAA1, and matrix Gla protein as potential proteomic signatures of

active tuberculosis. Additionally, this study further highlighted the critical

role of carbohydrate and lipid metabolism, immunological responses, and blood

coagulation in TB pathogenesis. Taken together, our findings feature a dynamic

landscape of plasma proteome following Mtb infection and provide additional

evidence on plasma biomarkers for TB diagnosis.

DOI: 10.1128/msystems.00616-25

PMID: 40736242

**14. NPJ Vaccines. 2025 Jul 29;10(1):173. doi: 10.1038/s41541-025-01216-8.**

A novel nanoparticle vaccine displaying multistage tuberculosis antigens confers

protection in mice infected with H37Rv.

Ding Y(#)(1), Li Y(#)(1), Wu Z(#)(2), Zhou Y(1), Guo Y(1), Tian S(1), Yu R(1),

Deng C(1), Wei R(1), Chen H(1), Li Y(1), Zhang X(1), Yu W(1), Jing C(1), Liu

S(1), Qin L(1), Lyu M(1), Zou Y(1), Yao Y(1), Tan L(1), Wu S(1), Liu W(3), Chen

X(4), Jin J(5).

**Yanbin Ding, Yuanyuan Li, Zhuhua Wu, Yu Zhou, Yan Guo, Siyu Tian, Rui Yu, Chunping Deng, Rui Wei, Hang Chen, Yan Li, Xiaokang Zhang, Wenjia Yu, Cai Jing, Shuyun Liu, Lili Qin, Meng Lyu, Yongjuan Zou, Yuanfeng Yao, Lu Tan, Shifen Wu, Weilong Liu\*, Xunxun Chen\*, Jing Jin\***

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Tuberculosis remains a major global health threat, as Bacillus Calmette-Guérin

(BCG), the only licensed vaccine, provides limited protection, particularly in

adolescents and adults. To address this limitation, a more effective

tuberculosis vaccine was developed using the SpyTag/SpyCatcher system to display

five clinically validated Mycobacterium tuberculosis antigens (Ag85A, ESAT-6,

CFP10, Rv2660c, and TB10.4) on self-assembling mi3 nanoparticles. These

nanoparticle-displayed antigens, formulated as 85A-NP, EC-NP, and RT-NP and

combined with a custom AS01E-biosimilar adjuvant, elicited stronger Th1-biased

immune responses in C57BL/6 mice than the corresponding recombinant proteins, as

evidenced by increased frequencies of polyfunctional CD4⁺ T cells producing

IFN-γ, IL-2, and TNF-α. In a murine aerosol challenge model, the mixed

nanoparticles formulation (85A-NP:EC-NP:RT-NP) conferred superior pulmonary

protection compared to single-antigen nanoparticles, recombinant protein

mixtures, an in-house M72-like vaccine and BCG. This modular platform enables

efficient multistage antigen incorporation and holds promise for next-generation

tuberculosis vaccine development.

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PMCID: PMC12307718

PMID: 40730746

**15. Proc Natl Acad Sci U S A. 2025 Aug 5;122(31):e2413946122. doi:**

**10.1073/pnas.2413946122. Epub 2025 Jul 29.**

A granulin-positive macrophage subtype in mycobacterial granulomas alleviates

tissue damage by limiting excessive inflammation.

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D(4), Luo S(3), Niu L(3), Sun T(3), Sun P(3), Qin L(5), Li W(5), Song S(4),

Takiff HE(6), Zhang S(7), Gao Q(1), Zhang Z(2)(8), Yan B(1)(3).

**Geyang Luo, Yanling Wen, Min Wang, Hao Wang, Duoduo Li, Mingfeng Liao, Dong Zeng, Sizhu Luo, Liangfei Niu, Tao Sun, Peng Sun, Liyi Qin, Weimin Li, Shu Song, Howard E Takiff, Shuye Zhang\*, Qian Gao\*, Zheng Zhang\*, Bo Yan\***

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Granulomas play a crucial role in the pathology of tuberculosis, but the immune

environment governing their formation remains largely unknown. To explore the

dynamic changes in the immune microenvironment during the formation of

tuberculous granulomas, we infected adult zebrafish with Mycobacterium marinum

and then examined uninfected and infected kidneys, as well as large and small

granulomas in the kidneys. Using single-cell RNA sequencing technology, we

identified two major macrophage subpopulations in the hematopoietic tissue

(kidney) of zebrafish under uninfected physiological conditions: monocyte

derived and tissue-resident macrophages. Interestingly, the infection induced

the emergence of epithelioid cells and a previously undescribed grna.2+

macrophage subpopulation. Depletion of grna.2+ macrophages with the

nitroreductase-metronidazole ablation system resulted in shortened zebrafish

survival after infection, increased bacterial load, and more granulomas,

especially necrotic granulomas. Depletion of grna.2+ macrophages also produced a

denser granuloma structure with fewer T cells. RNA-seq and flow cytometry

analysis revealed that depletion of grna.2+ macrophages led to upregulated

inflammatory signaling pathways, including tnfα and il1β, and increased

macrophage lytic cell death. Similarly, in samples from tuberculosis patients,

we also identified GRN-positive macrophages, which exhibit similar

anti-inflammatory functions. This subset of grna.2+ macrophages present in

developing granulomas can suppress excessive inflammatory responses to alleviate

macrophage lytic death, reduce tissue damage, promote T cell infiltration and

ultimately help control mycobacterial growth in vivo.

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PMID: 40729382 [Indexed for MEDLINE]

**16. BMC Infect Dis. 2025 Jul 28;25(1):950. doi: 10.1186/s12879-025-11356-w.**

Whole-genome sequencing for analyzing the transmission characteristics of

drug-resistant Mycobacterium tuberculosis in Ganzhou, China.

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**OBJECTIVE:** The study aimed to understand the drug resistance profile and

transmission characteristics of drug-resistant Mycobacterium tuberculosis (MTB)

in Ganzhou, China, to provide a scientific basis for developing prevention and

control strategies.

**METHODS:** DNA extracted from re-cultured positive strains underwent whole-genome

sequencing (WGS). The online platform SAM-TB was used to identify drug

resistance-related mutations in each strain, construct a phylogenetic tree, and

calculate the pairwise strain single-nucleotide polymorphism (SNP) distances. A

threshold of 12 SNPs between pairwise strains was set to identify transmission

clusters. Epidemiological investigations were conducted for patients within

these transmission clusters to analyze the characteristics of drug-resistant

tuberculosis (TB) transmission.

**RESULTS:** A total of 82 strains were analyzed. The most common mutations observed

for isoniazid, rifampicin, ethambutol, and streptomycin were katG (S315T,

32/61), rpoB (S450L, 13/37), embB (M306V, 5/12), and rpsL (K43R, 18/26),

respectively. Mutations were also observed in genes conferring resistance to

other drugs, including pncA (pyrazinamide), gyrA (ofloxacin), rrs, and eis

(aminoglycosides). The strains belonged to lineage 2 (75.61%, 62/82) and 4

(24.39%, 20/82). Three clusters containing 12 drug-resistant strains were

identified as transmission clusters, ranging in size from 2 to 8, with a

clustering rate of 14.63% (12/82). Notably, lineage 2 strains were more

prevalent in clustered cases than lineage 4 strains (19.35%, 12/62 vs. 0%, 0/20,

Fisher’s exact test, P = 0.033). The isoniazid resistance rate was significantly

higher in clustered strains (100%, 12/12) than in non-clustered strains (70.00%,

49/70) (Fisher’s exact test, P = 0.031). Two potential transmission chains of

drug-resistant TB were identified.

**CONCLUSION:** This study utilized WGS technology to provide important data on the

genetic mutation types and transmission dynamics of drug-resistant TB in

Ganzhou. WGS demonstrates significant potential in early prediction of drug

resistance in TB and identification of recent transmission events, offering

essential support for monitoring public health events and intervening in

drug-resistant tuberculosis.

SUPPLEMENTARY INFORMATION: The online version contains supplementary material

available at 10.1186/s12879-025-11356-w.

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PMCID: PMC12306122

PMID: 40722062

**17. Front Med (Lausanne). 2025 Jul 16;12:1611322. doi: 10.3389/fmed.2025.1611322.**

**eCollection 2025.**

Drug resistance patterns, trends, and risk factors for multidrug resistance of

tuberculosis in Wenzhou, China: a ten-year retrospective analysis (2014-2023).

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**OBJECTIVE:** Tuberculosis (TB), particularly drug-resistant tuberculosis (DR-TB),

remains a major public health threat in China. Despite global efforts,

multidrug-resistant tuberculosis (MDR-TB) complicates control strategies.

Wenzhou, a densely populated coastal city, lacks localized data on TB drug

resistance trends. This study analyzes DR-TB patterns (2014-2023) and identifies

MDR-TB risk factors to inform targeted interventions.

**METHODS:** A retrospective study included 10,993 TB patients from Wenzhou Central

Hospital. Sociodemographic and phenotypic drug susceptibility testing (pDST)

data were extracted from the Tuberculosis Information Management System (TBIMS)

of the Chinese Center for Disease Control and Prevention (China CDC) and

hospital databases. Resistance definitions followed World Health Organization

criteria. Trends in resistance rates and risk factors for MDR-TB were evaluated

using chi-square tests and multivariate logistic regression.

**RESULTS:** Among 10,993 patients, 20.41% had DR-TB. Resistance rates in new

patients were highest for isoniazid (12.15%) and streptomycin (10.89%), while

retreated patients showed higher resistance to isoniazid (34.61%) and rifampicin

(27.04%). The overall drug resistance rate of DR-TB decreased from 26.01% (2014)

to 19.31% (2023), driven by a decline in retreated cases (64.19%-28.57%),

whereas the proportion in new cases remained stable (∼18%). The proportion of

MDR-TB in retreated patients fell from 47.30% to 18.37%, but increased slightly

in new cases (2.51%-3.86%). Risk factors for MDR-TB included age <65 years (OR =

1.496-1.640), Han ethnicity (OR = 1.911), migrant status (OR = 1.296),

unemployment (OR = 1.819), and prior TB treatment (OR = 7.513).

**CONCLUSION:** Drug-resistant tuberculosis prevalence in Wenzhou declined over the

decade, largely due to improved management of retreated cases. However,

persistent primary DR-TB transmission among new patients highlights the need for

enhanced active screening and targeted interventions. High-risk groups,

including young people, individuals of Han ethnicity, migrants, unemployed

individuals, and retreated patients, require prioritized attention in TB control

strategies.

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**18. Front Public Health. 2025 Jul 16;13:1611459. doi: 10.3389/fpubh.2025.1611459.**

**eCollection 2025.**

Rifampicin-resistant tuberculosis in Fujian Province, Southeast China: a

retrospective analysis of drug resistance screening and treatment outcomes,

2019-2024.

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**BACKGROUNDS:** Rifampicin-resistant tuberculosis (RR-TB) remains a major challenge

to global TB control efforts. In Fujian Province, Southeast China, where RR-TB

prevalence has been notably high, understanding epidemiological trends and

treatment outcomes is crucial for optimizing interventions. This study aimed to

analyze RR-TB characteristics, resistance patterns, and treatment outcomes to

inform evidence-based control strategies.

**METHODS:** An observational study was conducted utilizing data from China's

National Tuberculosis Information Management System, focusing on

bacteriologically confirmed tuberculosis cases reported in Fujian Province

during 2019-2024. Epidemiological characteristics, drug resistance and outcomes

of RR-TB were described as frequency (n) and percentage (%). Risk factors for

unsuccessful outcomes were assessed using univariate and multivariate logistic

regression.

**RESULTS:** A total of 1,368 RR-TB patients were detected, with an overall

resistance rate of 3.7%. The RR rate showed a steady decline year by year (χ2

 = 76.214, p < 0.001), mainly due to the decrease in new TB cases (χ2  = 60.966,

p < 0.001). RR-TB patients exhibited higher co-resistance to isoniazid (71.9%

vs. 6.3%, p < 0.001) and ofloxacin (29.8% vs. 1.8%, p < 0.001) compared to

rifampicin-sensitive TB. Of 1,056 RR-TB patients initiated on treatment, 720 had

outcome data, revealing a low success rate (58.6%) due to high loss to follow-up

(31.1%) and mortality (9.3%). Multivariate analysis identified male sex

(AOR = 1.67, 95% CI: 1.11-2.52, p = 0.014), age ≥45 years (AOR = 2.27, 95% CI:

1.58-3.26, p < 0.001), high-risk group status (AOR = 1.42, 95% CI: 1.04-1.94,

p = 0.026), and occupation as farmer/worker (AOR = 2.17, 95% CI: 1.10-4.26,

p = 0.025) as independent risk factors of unsuccessful treatment.

**CONCLUSION:** Fujian Province has demonstrated a steady decline in rifampicin

resistance rates, primarily driven by reductions in new TB cases. However,

treatment inclusion rate and success rate remains suboptimal, highlighting the

need for targeted interventions-including enhanced adherence support, intensive

follow-up, and adverse event management-particularly for high-risk groups such

as older males and manual laborers. These findings can guide tailored strategies

to further reduce RR-TB burden in similar settings.

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**eCollection 2025.**

Risk Factors for Postoperative Neurologic Dysfunction in Patients with Spinal

Tuberculosis: A Retrospective Study.

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Lv J(1), Bai J(1), Wu Z(1), Feng Y(1).

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**PURPOSE:** Unexplained neurological dysfunction often occurs in patients after

spinal tuberculosis(STB) surgery; therefore, this study aimed to analyze the

causes of this dysfunction from the perspectives of the patient's preoperative

inflammatory state, carrier bacterial state, and increased degree of

autoimmunity.

**PATIENTS AND METHODS:** We collected 247 patients with STB and 270 patients with

degenerative diseases of the spine admitted from May 2015 to December 2024 at

the Second Hospital of Shanxi Medical University. According to the exclusion

criteria, 132 patients for each disease were included in this study. All

patients with spinal STB underwent one-stage posterior lesion removal. We used

the ASIA score to assess patients' neurological function and pain levels before

and after surgery. We also compared the patients' pre- and postoperative changes

in relevant inflammatory indicators, such as the ESR and PCT.

**RESULTS:** Postoperatively, one patient developed paraplegia with an ASIA grade of

A; 29 patients developed incomplete paraplegia with an ASIA score of grade B in

5 patients, grade C in 7 patients, and grade D in 17 patients. In the damaged

group, LYM% decreased from 35.52 ± 10.44 preoperatively to 14.36 ± 7.27

postoperatively. NEU% increased from 54.72 ± 11.85 preoperatively to 77.72 ±7.16

postoperatively. The WBC count increased from 5.97±1.65 preoperatively to 8.34 ± 2.71 postoperatively. The LNR decreased from 0.72 ± 0.31 preoperatively to 0.18 ± 0.11 postoperatively. Neurological dysfunction was somewhat recovered in the postoperative period (6 months to 2 years) in all patients.

**CONCLUSION:** In summary, this clinical study successfully established a

predictive model with significant prognostic value for postoperative

neurological dysfunction in patients with spinal tuberculosis. Notably, based on

the ranking of variable contributions, the use of antituberculosis drugs may

play a pivotal role in the development of postoperative neurological dysfunction

in spinal tuberculosis patients. A well-validated nomogram incorporating

acid-fast staining and piezosurgery use may facilitate preoperative risk

stratification. Prolonged exposure of the spinal cord to a highly inflammatory

environment may serve as a risk factor for intraoperative spinal cord injury in

these patients. Furthermore, identical or similar surgical procedures may yield

differential clinical outcomes across different disease subtypes and individual

patients.

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PMID: 40735649

**20. Vaccines (Basel). 2025 Jun 24;13(7):676. doi: 10.3390/vaccines13070676.**

Stopping Tuberculosis at the Gate: The Role of M. tuberculosis Adhesins in

Infection and Intervention.

Yang H(1)(2), Ma Y(1)(2)(3), Lei X(1)(2), Chai S(1)(2), Zhang S(1)(2), Su

G(1)(2), Li S(3), Du L(1)(2).

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The global burden of tuberculosis (TB), exacerbated by the rise of

drug-resistant Mycobacterium tuberculosis (M. tuberculosis), underscores the

need for alternative intervention strategies. One promising approach is to block

the infection at its earliest stage-bacterial adhesion to host cells-thereby

preventing colonization and transmission without exerting selective pressure.

Adhesins, surface-exposed molecules mediating this critical interaction, have

therefore emerged as attractive targets for early prevention. This review

outlines the infection process driven by bacterial adhesion and describes the

architecture of the M. tuberculosis outer envelope, emphasizing components that

contribute to host interaction. We comprehensively summarize both non-protein

and protein adhesins, detailing their host receptors, biological roles, and

experimental evidence. Recent progress in the computational prediction of

adhesins, particularly neural network-based tools like SPAAN, is also discussed,

highlighting its potential to accelerate adhesin discovery. Additionally, we

present a detailed, generalized workflow for predicting M. tuberculosis

adhesins, which synthesizes current approaches and provides a comprehensive

framework for future studies. Targeting bacterial adhesion presents a

therapeutic strategy that interferes with the early stages of infection while

minimizing the risk of developing drug resistance. Consequently, anti-adhesion

strategies may serve as valuable complements to conventional therapies and

support the development of next-generation TB vaccines and treatments.

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PMID: 40733653

**21. Vaccines (Basel). 2025 Jun 23;13(7):671. doi: 10.3390/vaccines13070671.**

Mycobacterium tuberculosis PPE18 Protein Bodies in Insect Cells: A Candidate

Tuberculosis Vaccine.

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**BACKGROUND/OBJECTIVES:** Mycobacterium tuberculosis is the causative agent of

tuberculosis and the leading cause of death from a single infection with the

microorganism. Tuberculosis remains globally one of the major diseases leading

to high mortality rates, with serious implications for public health and

economic development. Therefore, tuberculosis prevention and control is crucial

for global health and socio-economic stability. The development of effective

preventive vaccines remains an urgent task in the fight against tuberculosis.

**METHODS:** The Mycobacterium tuberculosis antigen PPE18 was fused to Zera, and

Bacmid was extracted and transfected into Sf9, which was purified and

characterized for the formation of nanoparticle protein bodies. BALB/c mice and

calves were immunized, and the immunogenicity of the nanoparticle vaccine was

assessed by serum antibodies and splenic lymphocytes.

**RESULTS:** Zera-71CA-mCherry can be expressed in Sf9 cells, forming 0.5-1.2 μm

protein bodies. Excising the mCherry sequence, Zera-71CA/Zera-PPE18 candidate

nanoparticle-immunized mice were able to elicit serum antibody levels and the

proliferation of splenic lymphocytes, and immunized calves were determined to

have high levels of serum antibody levels, and IFN-γ and TNF-α levels.

**CONCLUSIONS:** The results indicated that Zera-71CA/Zera-PPE18 recombinant

nanoparticles had good immunogenicity as a subunit vaccine in both BALB/c mice

and calves and are potential candidates for further development as effective

subunit vaccines.

DOI: 10.3390/vaccines13070671

PMCID: PMC12300796

PMID: 40733648

**22. Vaccines (Basel). 2025 Jun 21;13(7):669. doi: 10.3390/vaccines13070669.**

The Impact of Animal Models and Strain Standardization on the Evaluation of

Tuberculosis Vaccine Efficacy.

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Sheng X(2)(3)(4)(5), Huang Y(3)(4)(5), Wang J(3)(4)(5), Niu Q(3)(4)(5), Chen

G(3)(4)(5), Tian W(1), Zhao A(2)(3)(4)(5), Xu M(2)(3)(4)(5).

**Jiazheng Wei, Junli Li, Xiaochi Li, Weixin Du, Cheng Su, Xiaobing Sheng, Yang Huang, Jinsong Wang, Qun Niu, Guoqing Chen, Wei Tian\*, Aihua Zhao\*, Miao Xu\***

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Tuberculosis (TB) remains one of the most significant challenges to global

public health. Vaccine development is a critical strategy for the prevention and

control of TB. However, evaluating the protective efficacy of TB vaccines faces

numerous challenges, particularly in the selection of animal models and

bacterial strains. Variations in animal models, challenge strains, challenge

routes, and doses can significantly impact the outcomes of preclinical

evaluations. This article highlights the importance of standardizing preclinical

evaluation models, summarizes the animal models and challenge strains used in

novel TB vaccine candidates, efficacy studies, and discusses the advantages and

limitations of commonly used animal models in TB vaccine research. It also

points out the differential performance of various animal models in simulating

protection and pathology. Given the current limitations of using a narrow range

of challenge strains and the lack of standardized infection routes and doses,

this article calls for the establishment of more standardized challenge strains

and the development of standardized evaluation models to improve the reliability

and generalizability of new TB vaccine efficacy assessments.

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PMID: 40733646

**23. Microorganisms. 2025 Jun 23;13(7):1456. doi: 10.3390/microorganisms13071456.**

Disorders of Gut Microbiota and Plasma Metabolic Profiles May Be Associated with

Lymph Node Tuberculosis.

Long Y(1)(2), Huang J(1), Zheng S(1), Bai S(1), Liu Z(1), Li X(1), Gao W(1), Ke

X(1), Tang Y(1), Yang L(2), Wang H(1), Li G(1).

**Yun Long, Jiamin Huang, Shasha Zheng, Shimeng Bai, Zhe Liu, Xue Li, Wenying Gao, Xue Ke, Yunyan Tang, Liang Yang, Haijiang Wang\*, Guobao Li\***

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The association of gut microbiota with lymph node tuberculosis (LNTB) remains

unexplored. This study employed metagenomic sequencing and plasma metabolomics

analyses to investigate the role of gut microbiota in LNTB patients. Significant

alterations in gut microbial diversity were observed in LNTB patients,

characterized by a notable reduction in bacterial taxa involved in short-chain

fatty acid (SCFA) synthesis, including Ruminococcus, Faecalibacterium,

Roseburia, and Blautia, compared to healthy individuals. KEGG pathway analysis

further revealed that gut dysbiosis could negatively impact SCFA biosynthesis

and metabolism. Plasma metabolomics demonstrated disruptions in metabolites

associated with SCFA synthesis and inflammation pathways in the LNTB group.

Integrated analysis indicated significant correlations between specific gut

microbiota (Blautia, Butyricicoccus, Coprococcus, Ruminococcus, Bacteroides,

Clostridium) and plasma metabolites, including α-benzylbutyric acid, acetic

acid, and succinic acid. Our findings demonstrate that gut microbiota dysbiosis

and related metabolic dysfunction significantly reduce SCFA production in LNTB

patients, potentially identifying novel therapeutic targets for LNTB management.

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PMCID: PMC12298930

PMID: 40731966

**24. Ther Adv Med Oncol. 2025 Jul 24;17:17588359251355058. doi:**

**10.1177/17588359251355058. eCollection 2025.**

Establishment and validation of a convenient and efficient screening tool for

active pulmonary tuberculosis in lung cancer patients based on common

parameters.

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Y(6), Du J(6), Li L(7)(3), Zhang T(8)(4).

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Street, Tongzhou District, Beijing 101149, China.

**BACKGROUND:** Coexistent pulmonary tuberculosis and lung cancer (PTB-LC) is a rare

type of disease with frequent under- and/or mis-diagnosis. Establishment of a

reliable screening model for PTB-LC holds considerable medical and economic

significance.

**OBJECTIVES:** We aimed to develop an efficient and convenient tool to identify

high-risk individuals for tuberculosis (TB) infection among LC patients based on

commonly available parameters in clinical practice.

**DESIGN:** This study consisted of a primary retrospective patient cohort for model

construction and verification, and a prospective patient cohort for prospective

validation.

**METHODS:** Patients with active PTB-LC and LC diagnosed in Beijing Chest Hospital

from 2018 to 2022 were collected and 1:1 matched according to time of admission

and were classified into a training set (n = 281) and testing set (n = 121).

Baseline information, clinicopathological features, imaging manifestations, and

blood testing results were collected and analyzed. Five machine learning

methods, including logistic regression (LR), random forest (RF), support vector

machine (SVM), decision tree (DT), and neural network (NN), were employed to

develop a screening model for PTB-LC.

**RESULTS:** Through multivariable analysis, gender, pleural effusion, cavitation,

monocyte count (MONO), and plasma adenosine deaminase (ADA) levels were

identified as independent predictors of PTB-LC and included in model

construction. LR, RF, SVM, DT, and NN were used to construct the screening or

pre-diagnosis models. The RF demonstrated the best performance with an area

under the curve of 0.966 in the training set, 0.817 in the testing set, and

0.805 in the prospective dataset. The accuracy, precision, recall, and F1 score

of the RF model of the training set were 0.88, 0.87, 0.89, and 0.88,

respectively, and these indicators of the testing set were 0.71, 0.75, 0.72, and

0.74, respectively, which were superior to those of other methods. The

prospective cohort further validated the good performance of the screening

model. We also established a nomogram with gender, pleural effusion, cavitation,

MONO, and serum ADA in assessing high-risk patients of developing TB infection.

Further TB-related diagnostic tests were recommended for these high-risk

patients.

**CONCLUSION:** The RF screening model constructed with gender, pleural effusion,

cavitation, MONO, and ADA may help identify high-risk patients of PTB-LC from LC

alone cases.

Plain Language Summary: A convenient screening model for TB infection from

patients with LC We used five machine learning methods in establishing a

screening model involving male gender, pleural effusion, cavitation, peripheral

monocyte and serum ADA in screening high-risk cases in developing tuberculosis

infection among lung cancer patients.

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**25. Front Med (Lausanne). 2025 Jul 14;12:1521011. doi: 10.3389/fmed.2025.1521011.**

**eCollection 2025.**

Case Report: A rare case of tuberculous otitis media mimicking chronic

suppurative otitis media - an ongoing challenge.

Shu C(1), You T(1), Huang M(1), Xu M(1), Zhang J(1), Peng Z(1)(2).

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Ear tuberculosis, a rare form of extrapulmonary tuberculosis caused by

Mycobacterium tuberculosis, predominantly affects the middle ear. The common

symptoms of ear tuberculosis include otorrhea, hearing loss, and facial nerve

paralysis, and if left untreated, it can lead to complete deafness. Diagnosing

ear tuberculosis can be challenging, as its symptoms often overlap with those of

otitis media, leading to potential misdiagnosis. Early diagnosis and appropriate

treatment are essential for a favorable prognosis. Delayed diagnosis or

inadequate treatment can result in severe complications, including irreversible

hearing loss and chronic ear problems. Therefore, raising awareness among

healthcare providers about the clinical features and diagnostic approach to ear

tuberculosis is critical for improving patient outcomes. This study presents the

case of a 28-year-old patient with tuberculous otitis media (TOM), presenting

with otorrhea, hearing loss, and facial paralysis. Additionally, a comprehensive

literature review of 492 records published over the past decade in PubMed and

the Web of Science databases was conducted. Our study summarizes the clinical

manifestations, diagnostic methods, and treatment strategies of 118 patients

with ear tuberculosis, offering valuable insights to support early diagnosis and

intervention, ultimately reducing the risk of adverse outcomes.

Copyright © 2025 Shu, You, Huang, Xu, Zhang and Peng.

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PMCID: PMC12301375

PMID: 40727526

**26. Antibiotics (Basel). 2025 Jun 20;14(7):625. doi: 10.3390/antibiotics14070625.**

Sentinel-Site-Based Surveillance of Mycobacterium tuberculosis Drug Resistance

and Epidemiology in Sichuan, China.

Wang Y(1)(2), Liu C(3), Zhao B(2), Ou X(2), Xia H(2), Song Y(2), Zheng Y(2),

Zhou Y(2), Xing R(2), Zhao Y(2), Zheng H(4).

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**OBJECTIVES:** To investigate epidemiological/drug-resistance characteristics and

identify potential factors related to drug-resistant and clustered tuberculosis

in Sichuan.

**METHODS:** A total of 295 Mycobacterium tuberculosis (MTB) isolates were collected

from surveillance sites in Sichuan from 2019 to 2021. The minimum inhibitory

concentrations (MICs) of 12 anti-TB drugs were acquired using the broth

microdilution method, followed by whole-genome sequencing (WGS) analysis.

**RESULTS:** Of 268 MTB isolates with both WGS and drug-susceptibility testing (DST)

results, 159 (59.3%, 159/268) strains belonged to the Beijing lineage (L2).

Isoniazid had the highest resistance rate (15.3%, 41/268), followed by

rifampicin (9.3%, 25/268). The sensitivity of WGS to predict drug resistance

varied from 75% to 97.6%, and the specificity was above 96.0% for all. rpoB

Ser450Leu (41.7%, 10/24) and katG Ser315Thr (70%, 28/40) were the most frequent

mutations in rifampicin and isoniazid resistance isolates, respectively. The

clustering rate in Sichuan was 9.3% (25/268), and patients ≤ 24 years old (aOR = 11.697; 95% CI: 0.817-167.463) had a greater risk of clustering.

**CONCLUSIONS:** Our findings prove that WGS is a promising tool for predicting drug

resistance to isoniazid, rifampicin, ethambutol, moxifloxacin and levofloxacin

in Sichuan. The higher resistance rate to isoniazid emphasizes the urgent need

for susceptibility testing surveillance and application management. Improving

the diagnosis, treatment and management of patients ≤ 24 years old may reduce

the transmission of MTB in Sichuan.

DOI: 10.3390/antibiotics14070625

PMCID: PMC12291903

PMID: 40723928

**27. Biomolecules. 2025 Jul 4;15(7):959. doi: 10.3390/biom15070959.**

Heparin-Binding Hemagglutinin-Induced Trained Immunity in Macrophages:

Implications for Antimycobacterial Defense.

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Tuberculosis (TB) is a major global health threat, with the current Bacillus

Calmette-Guérin (BCG) vaccine having limited efficacy against adult pulmonary

disease. Trained immunity (TI) is a form of innate immune memory that enhances

antimicrobial defense. It is characterized by the epigenetic and metabolic

reprogramming of innate immune cells and holds promise as a promising approach

to prevent TB. In this study, we investigated the capacity of heparin-binding

hemagglutinin (HBHA), a methylated antigen of Mycobacterium tuberculosis, to

induce TI in murine RAW264.7 macrophages, human-derived THP-1 macrophages, and

human peripheral blood mononuclear cells (hPBMCs). HBHA-trained macrophages

exhibited the enhanced expression of pro-inflammatory cytokines (IL-1β, IL-6,

TNF-α) following secondary lipopolysaccharide stimulation. The epigenetic

profiling indicated elevated levels of H3K4me1 and H3K4me3 histone marks at

cytokine gene loci. Further, metabolic analysis revealed heightened lactate

production and the increased expression of glycolytic enzymes. Functionally,

HBHA-trained macrophages exhibited improved control of intracellular

mycobacteria, as evidenced by a significant reduction in colony-forming units

following BCG infection. These findings elucidate that HBHA induces a functional

TI phenotype via coordinated epigenetic and metabolic changes, and suggest HBHA

may serve as a valuable tool for studying TI and its relevance to host defense

against mycobacterial infections, pending further in vivo and clinical

validation.

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**10.1016/j.jgar.2025.07.012. Online ahead of print.**

Global Prevalence of Tuberculosis and Drug-Resistant Forms: A 30-Year Analysis

from 1990 to 2019.

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**INTRODUCTION:** Tuberculosis (TB) remains a major global health threat.

Multidrug-resistant (MDRTB) and extensively drug-resistant TB (XDRTB) present

growing challenges.

**METHODS:** This study utilized Global Burden of Disease data to analyze

age-standardized prevalence rates (ASPR) and evaluate the global and national

prevalence trends of TB and its subtypes from 1990 to 2019.

**RESULTS:** Global TB prevalence is declining but MDRTB and XDRTB are rising

sharply. In 2019, TB ASPR was 23,085 per 100,000, falling 1.044% annually since

1990. Latent TB infection decreased 1.044% yearly to 22,906 per 100,000 in 2019.

Drug-susceptible TB fell 1.692% annually to 169 per 100,000 in 2019. MDRTB rose

6.008% yearly, reaching 8.6 per 100,000 in 2019. XDRTB increased 71.746% yearly

to 0.4 per 100,000. Rates varied widely between countries. ASPR tended to be

higher in males and poorer regions. Pace of change differed by sex,

socioeconomics and geography.

**CONCLUSIONS:** Substantial variations exist in TB prevalence and trends globally,

reflecting inequities. Findings provide comprehensive long-term TB assessments,

with rising multidrug resistance threatening progress and elimination goals.

Urgent targeted strategies are needed for high-risk groups, surveillance,

resources, commitment and political will, especially in disadvantaged

populations.

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Mycobacterial phthiocerol dimycocerosate induces Galectin-3 upregulation to

impair proinflammatory responses and favor immune evasion.

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Mycobacterium tuberculosis, a typical intracellular parasite that causes

tuberculosis, is ranked as the top infectious killer for humans in annual WHO

reports. Pathogenic mycobacterium has evolved numerous strategies to favor their

intracellular survival including a unique lipid-rich-cell-wall and granuloma

formation during infection. Phthiocerol dimycocerosate (PDIM) is a critical

virulence factor of mycobacteria including Mycobacterium marinum (Mm), which

manipulate host immune responses and granuloma induction and facilitate immune

evasion, but the mechanisms still remain unclear. We used an

AACT/SILAC-based-quantitative proteomic approach to determine PDIM-responsive

proteomics during Mm-infection. A major difference was the high abundance of

Gal-3 in WT\_Mm-infected cells not observed in PDIM-deficient infections. Gal-3

induction by PDIM-replete bacteria was primarily via Toll-like-receptor 2, and

also engaged TGF-β non-classical-pathway. Elevated Gal-3 in macrophages

prevented the turnover and translocation of NF-κB to effectively modulate the

profile of inflammatory cytokines. Gal-3 Silencing effectively reduced tissue

damage induced in mice by PDIM-expressing Mm. We found upregulated Gal-3 in the

serum and BALF of clinical tuberculosis cases, which decreased significantly

after effective chemotherapy. Our findings demonstrated that upregulated Gal-3

not only plays an important role in regulating host immune response and

granuloma formation, but also suggests that targeting-Gal-3 therapy could be a

promising anti-tuberculosis strategy.

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Non-targeted metabolomics and machine learning reveal metabolic dysregulation in

lymph node tuberculosis.

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**BACKGROUND:** Lymph node tuberculosis (LNTB) is the most prevalent form of

extrapulmonary tuberculosis; however, differentiating it from non-LNTB remains

challenging due to overlapping clinical features and suboptimal diagnostic

methods. Current diagnostic methods for LNTB lack both sensitivity and

specificity. This study aimed to characterize the metabolic differences between

LNTB and non-LNTB patients, elucidate the pathological mechanisms underlying

LNTB, and identify diagnostic biomarkers using machine learning models.

**METHODS:** Serum samples from 40 LNTB patients and 30 non-LNTB patients were

analyzed using ultra-high-performance liquid chromatography-mass spectrometry.

Differential metabolites were identified based on a variable importance in

projection >1, false discovery rate-adjusted p-value <0.05. Pathway enrichment

analysis was performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG).

Machine learning, including support vector machines and random forest, were

employed to screen for diagnostic biomarkers, which were validated by receiver

operating characteristic curves.

**RESULTS:** Among the 1294 detected metabolites, 89 exhibited significant

differences between the two groups. By integrating KEGG enrichment with

topological analysis, phenylalanine, tyrosine, and tryptophan biosynthesis

possessed the highest impact, followed by phenylalanine metabolism, and

aminoacyl-tRNA biosynthesis. Machine learning identified four biomarkers:

Leu-Ala [area under the curve (AUC) = 0.8292], evodiamine (AUC = 0.7558),

fenazaquin (AUC = 0.7175), and acetol (AUC = 0.7117). Leu-Ala demonstrated the

highest diagnostic accuracy, with a sensitivity of 73.5 % and specificity 86.7 %

at a cutoff value of 0.62.

**CONCLUSIONS:** Untargeted metabolomics revealed dysregulation in the biosynthesis

of phenylalanine, tyrosine, and tryptophan, phenylalanine metabolism, as well as

in aminoacyl-tRNA biosynthesis in LNTB. Additional, Leu-Ala was identified as a

novel diagnostic biomarker. The integrating of metabolomics with machine

learning presents a promising approach for LNTB detection, though larger

validation studies are necessary.

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