**2025年第35周**

**中国大陆学者发表的结核病英文文章摘要**

**（27篇）**

**PubMed Publication date: 2025/8/25---2025/8/31**

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

**1. Bioorg Chem. 2025 Aug 21;164:108898. doi: 10.1016/j.bioorg.2025.108898. Online**

**ahead of print.**

Alterisocoumarins A-M: Isocoumarins with anti-inflammatory and anti-tuberculosis

activities from a mangrove endophytic fungus Alternaria sp. HN-17.

Wang G(1), Yuan Y(2), Mu R(3), Xue Z(3), Zhang Y(3), Xie D(3), Chen Y(4).

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Fifteen new isocoumarin derivatives 1-3, (±)-4, (±)-5, 6-10, (+)-11, (+)-12, and 13, together with eleven known analogues (-)-11, (-)-12, and 14-22 were isolated from the mangrove endophytic fungus Alternaria sp. HN-17. Their structures were unambiguously established by 1D/2D NMR and HRESIMS spectra, and electronic circular dichroism (ECD) calculations. Alterisocoumarin A (1) possesses a rare 6/6/6/5 tetracyclic skeleton featuring a γ-butyrolactone-fused dibenzo-α-pyrone core, while 2 and 3 have an unusual chlorinated furan ring system. In bioassay, compounds 1, (-)-4, 10, and 18 displayed good anti-inflammatory activity with IC50 values ranging from 10.68 to 28.05 μM than positive control (L-NMMA:

32.83 μM). Moreover, 1 exerts anti-inflammatory effects by down-regulated

expression the NF-κB and MAPK pathways. In addition, compounds 21 and 22 showed

notable anti-tuberculosis activities by inhibiting MptpA, MptpB and PTP1B. The

molecular docking results showed that compound 22 binds deeply in the active

cavity of PTP1B.

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DOI: 10.1016/j.bioorg.2025.108898

PMID: 40848709

**2. Int J Gen Med. 2025 Aug 14;18:4469-4480. doi: 10.2147/IJGM.S538660. eCollection 2025.**

Effect of Bdq-Containing Regimen and Molecular Detection of Bdq Resistance among

Pre-XDR-TB Patients with Unfavorable Outcomes.

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Mao Z(2)(3), Zeng J(2)(3), Lu S(1)(2)(3), Fang M(2)(3).

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**PURPOSE:** The objective of this study was to evaluate the efficacy of bedaquiline

(Bdq)-containing regimens in pre-extensively drug-resistant tuberculosis

(pre-XDR-TB) patients in Shenzhen, China, and to investigate the association

between Bdq resistance and unfavorable outcomes.

**METHODS:** Data were collected from 84 pre-XDR-TB patients categorized into Bdq (n

= 46) and non-Bdq (n = 38) groups. Individuals in the Bdq group were treated

with Bdq alongside individualized background drugs. Commonly used drugs (>50% of

patients) in both groups were linezolid (Lzd), clofazimine (Cfz), cycloserine

(Cs) and pyrazinamide (Pza). Treatment outcomes were classified as cure,

treatment completion, treatment failure, loss to follow-up, or death. Logistic

regression analysis was conducted to determine independent predictors of

treatment success using potential risk factors, including age, sex, body mass

index (BMI), TB treatment history, and other factors. Whole-genome sequencing

(WGS) was conducted on clinical isolates from 4 patients with unfavorable

outcomes and 4 patients with favorable outcomes in the Bdq group.

**RESULTS:** Favorable treatment outcomes were observed in 89.13% (41/46) of the Bdq

group and 52.63% (20/38) of the non-Bdq group (P = 0.0005). Univariate and

multivariate analyses identified Bdq was an independent factor associated with

treatment success (odds ratio [OR] = 11.572, 95% CI: 2.183-61.343, P = 0.004).

WGS identified an atpE\_Ala63Pro mutation conferring Bdq resistance in one

patient with an unfavorable outcome. Additional resistance mutations included

Rv0678\_Arg156fs (Bdq and Cfz resistance) and rplC\_Cys154Arg (Lzd resistance).

**CONCLUSION:** Bdq-containing regimens significantly improved the treatment

outcomes among pre-XDR-TB patients. The emergence of resistance mutations

highlights the importance of routine drug resistance monitoring and rational

drug use. Expanding access to Bdq and other novel drugs at affordable prices is

vital for improving the success of pre-XDR-TB treatment.

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DOI: 10.2147/IJGM.S538660

PMCID: PMC12361352

PMID: 40837941

**3. Case Rep Infect Dis. 2025 Aug 9;2025:8814569. doi: 10.1155/crdi/8814569.**

**eCollection 2025.**

Treatment of Tuberculous Meningitis With Contezolid in a Patient With Complex

Comorbidities: A Case Report and Literature Review.

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Central nervous system (CNS) tuberculosis (TB) is a severe manifestation of

Mycobacterium tuberculosis (MTB) infection, characterized by high mortality.

Contezolid, a novel oxazolidinone antibiotic, exhibits in vitro activity against

MTB and may offer a safety advantage over linezolid, a first-generation

oxazolidinone frequently linked to myelosuppression and neuropathy. Clinical

data on contezolid in CNS tuberculosis remain scarce. We report a middle-aged

man with chronic renal allograft dysfunction who was receiving long-term

hemodialysis and subsequently developed severe CNS TB complicated by multiple

coinfections, diabetes mellitus, and pancytopenia. An individualized multidrug

regimen that included contezolid was successfully employed, suggesting its

potential utility in complex CNS TB. This report highlights therapeutic

considerations for similar patients and underscores the need for further

research on the role of contezolid in TB treatment.

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John Wiley & Sons Ltd.

DOI: 10.1155/crdi/8814569

PMCID: PMC12357779

PMID: 40823118

**4. Ann Ital Chir. 2025 Aug 10;96(8):1028-1038. doi: 10.62713/aic.3961.**

Comparison Between the Efficacy of Oblique Lumbar Debridement Using an

Expandable Channel Combined With Posterior Percutaneous Internal Fixation and

Traditional Anterior-Posterior Surgery for Single-Segment Lumbar Tuberculosis.

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**AIM:** Lumbar tuberculosis can cause spinal instability and neurological deficits,

often requiring surgery. Traditional anterior-posterior surgery is effective but

highly invasive, leading to greater trauma and longer recovery. Minimally

invasive techniques, such as oblique lumbar debridement with posterior

percutaneous fixation, may reduce surgical damage and improve recovery. However,

their efficacy remains unclear. This study compares this minimally invasive

approach with conventional surgery to assess its feasibility as an alternative

treatment.

**METHODS:** A retrospective analysis was conducted on 156 patients diagnosed with

single-segment lumbar tuberculosis between July 2016 and October 2019. Patients

were divided into a minimally invasive group (Min group, n = 76), treated with

the oblique lumbar approach combined with Posterior Percutaneous Pedicle Screw

Fixation (PPPSF), and a conventional Open group (n = 80). All patients received

standard anti-tuberculosis therapy (isoniazid, rifampicin, pyrazinamide, and

ethambutol) for at least two weeks preoperatively and continued for 10-12 months

postoperatively, adjusted based on drug sensitivity testing. Nutritional support

and bracing for three months post-surgery were also provided. Surgical and

postoperative metrics were evaluated, including operative time, intraoperative

blood loss, length of abdominal incision, postoperative drainage volume and

postoperative hospital stay. Functional outcomes were assessed using the visual

analogue scale (VAS) and oswestry disability index (ODI), while serology markers

such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and

creatine phosphokinase (CPK) levels were measured. Radiographic parameters,

including the Cobb angle and sagittal vertical axis (SVA), were also evaluated.

Postoperative complications were also documented.

**RESULTS:** The Min group demonstrated significantly shorter operation time,

smaller incisions, reduced blood loss, shorter hospital stays, and lower

postoperative drainage and CPK levels compared to the conventional Open group (p

< 0.05). There was no significant difference in VAS, ODI, ESR and CRP levels

between the two groups at different times after surgery (p > 0.05). Radiographic

assessments revealed no significant differences in the Cobb angle or SVA at any

postoperative time point (p > 0.05). However, the Min group exhibited a

significantly higher rate of Grade 1 spinal fusion (59 vs. 38 cases, p < 0.05).

Although postoperative complications were lower in the Min group (14.5% vs.

18.8%), the difference was not statistically significant (p = 0.474).

**CONCLUSIONS:** Oblique lumbar debridement with PPPSF represents a viable

alternative to traditional anterior-posterior surgery for single-segment lumbar

tuberculosis, offering reduced surgical trauma and accelerated postoperative

recovery.

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DOI: 10.62713/aic.3961

PMID: 40820626

**5. Biomed Environ Sci. 2025 Jul 20;38(7):819-828. doi: 10.3967/bes2025.071.**

Spatio-Temporal Pattern and Socio-economic Influencing Factors of Tuberculosis

Incidence in Guangdong Province: A Bayesian Spatiotemporal Analysis.

Wu HZ(1), Li X(2), Wang JW(1), Jian RH(3), Hu JX(2), Hu YJ(3), Xu YT(3), Xiao

J(2), Jin AQ(4), Chen L(5).

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**OBJECTIVE:** To investigate the spatiotemporal patterns and socioeconomic factors

influencing the incidence of tuberculosis (TB) in the Guangdong Province between

2010 and 2019.

**METHOD:** Spatial and temporal variations in TB incidence were mapped using heat

maps and hierarchical clustering. Socioenvironmental influencing factors were

evaluated using a Bayesian spatiotemporal conditional autoregressive (ST-CAR)

model.

**RESULTS:** Annual incidence of TB in Guangdong decreased from 91.85/100,000 in

2010 to 53.06/100,000 in 2019. Spatial hotspots were found in northeastern

Guangdong, particularly in Heyuan, Shanwei, and Shantou, while Shenzhen,

Dongguan, and Foshan had the lowest rates in the Pearl River Delta. The ST-CAR

model showed that the TB risk was lower with higher per capita Gross Domestic

Product (GDP) [Relative Risk ( RR), 0.91; 95% Confidence Interval ( CI):

0.86-0.98], more the ratio of licensed physicians and physician ( RR, 0.94; 95%

CI: 0.90-0.98), and higher per capita public expenditure ( RR, 0.94; 95% CI:

0.90-0.97), with a marginal effect of population density ( RR, 0.86; 95% CI:

0.86-1.00).

**CONCLUSION:** The incidence of TB in Guangdong varies spatially and temporally.

Areas with poor economic conditions and insufficient healthcare resources are at

an increased risk of TB infection. Strategies focusing on equitable health

resource distribution and economic development are the key to TB control.

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DOI: 10.3967/bes2025.071

PMID: 40820248

**6. Biomed Environ Sci. 2025 Jul 20;38(7):810-818. doi: 10.3967/bes2025.020.**

Increased Tertiary Lymphoid Structures are Associated with Exaggerated Lung

Tissue Damage in Smokers with Pulmonary Tuberculosis.

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XY(1), Sun YC(1).

**Yue Zhang, Liang Li, Zi Kang Sheng, Ya Fei Rao, Xiang Zhu, Yu Pang, Meng Qiu Gao, Xiao Yan Gai\*, Yong Chang Sun\***

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**OBJECTIVE:** Cigarette smoking exacerbates the progression of pulmonary

tuberculosis (TB). The role of tertiary lymphoid structures (TLS) in chronic

lung diseases has gained attention; however, it remains unclear whether

smoking-exacerbated lung damage in TB is associated with TLS. This study aimed

to analyze the characteristics of pulmonary TLS in smokers with TB and to

explore the possible role of TLS in smoking-related lung injury in TB.

**METHODS:** Lung tissues from 36 male patients (18 smokers and 18 non-smokers) who

underwent surgical resection for pulmonary TB were included in this study.

Pathological and immunohistological analyses were conducted to evaluate the

quantity of TLS, and chest computed tomography (CT) was used to assess the

severity of lung lesions. The correlation between the TLS quantity and TB lesion

severity scores was analyzed. The immune cells and chemokines involved in TLS

formation were also evaluated and compared between smokers and non-smokers.

**RESULTS:** Smoker patients with TB had significantly higher TLS than non-smokers (

P < 0.001). The TLS quantity in both the lung parenchyma and peribronchial

regions correlated with TB lesion severity on chest CT (parenchyma: r = 0.5767;

peribronchial: r = 0.7373; both P < 0.001). Immunohistochemical analysis showed

increased B cells, T cells, and C-X-C motif chemokine ligand 13 (CXCL13)

expression in smoker patients with TB ( P < 0.001).

**CONCLUSION:** Smoker TB patients exhibited increased pulmonary TLS, which was

associated with exacerbated lung lesions on chest CT, suggesting that cigarette

smoking may exacerbate lung damage by promoting TLS formation.

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DOI: 10.3967/bes2025.020

PMID: 40820247

**7. Biomed Environ Sci. 2025 Jul 20;38(7):792-809. doi: 10.3967/bes2025.041.**

Independent and Interactive Effects of Air Pollutants, Meteorological Factors,

and Green Space on Tuberculosis Incidence in Shanghai.

Ye Q(1), Chen J(2), Ji YT(1), Lu XY(1), Deng JL(1), Li N(1), Wei W(1), Hou

RJ(1), Li ZY(1), Xiang JB(1), Gao X(3), Shen X(2), Yang CG(4).

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**OBJECTIVE:** To assess the independent and combined effects of air pollutants,

meteorological factors, and greenspace exposure on new tuberculosis (TB) cases.

**METHODS:** TB case data from Shanghai (2013-2018) were obtained from the Shanghai

Center for Disease Control and Prevention. Environmental data on air pollutants,

meteorological variables, and greenspace exposure were obtained from the

National Tibetan Plateau Data Center. We employed a distributed-lag nonlinear

model to assess the effects of these environmental factors on TB cases.

**RESULTS:** Increased TB risk was linked to PM 2.5, PM 10, and rainfall, whereas NO

2, SO 2, and air pressure were associated with a reduced risk. Specifically, the

strongest cumulative effects occurred at various lags: PM 2.5 ( RR = 1.166, 95%

CI: 1.026-1.325) at 0-19 weeks; PM 10 ( RR = 1.167, 95% CI: 1.028-1.324) at 0-18

weeks; NO 2 ( RR = 0.968, 95% CI: 0.938-0.999) at 0-1 weeks; SO 2 ( RR = 0.945,

95% CI: 0.894-0.999) at 0-2 weeks; air pressure ( RR = 0.604, 95% CI:

0.447-0.816) at 0-8 weeks; and rainfall ( RR = 1.404, 95% CI: 1.076-1.833) at

0-22 weeks. Green space exposure did not significantly impact TB cases.

Additionally, low temperatures amplified the effect of PM 2.5 on TB.

**CONCLUSION:** Exposure to PM 2.5, PM 10, and rainfall increased the risk of TB,

highlighting the need to address air pollutants for the prevention of TB in

Shanghai.

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DOI: 10.3967/bes2025.041

PMID: 40820246

**8. Stem Cell Res Ther. 2025 Aug 29;16(1):469. doi: 10.1186/s13287-025-04596-9.**

Antimicrobial peptide PK34 modification enhances the antibacterial and

anti-inflammatory effects of bone-derived mesenchymal stem cells in

Mycobacterium tuberculosis infection.

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ZJ(6)(7), Li Q(8)(9).

**Xin-Yu He, Jia-Qi Wang, Yao Chen, Ting-Xun Yuan, Xiang Zhao, Yi-Jing Sun, Yi-Ming Liu, Zhong-Yan Wang, Yan-Bing Cai, Wei Gao, Chun-Ping Cui, Zheng-Jun Yi\*, Qian Li\***

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**BACKGROUND:** New therapeutic strategies are needed to treat tuberculosis (TB).

The antimicrobial peptide PK34 has a good ability to clear Mycobacterium

tuberculosis (Mtb) and is not prone to drug resistance and adverse reactions.

Mesenchymal stem cells (MSCs) can also be used as an adjunctive therapy for the

treatment of TB. However, there have been no studies combining the two for the

treatment of Mtb infection.

**METHODS:** We aimed to construct bone-derived mesenchymal stem cells secreting the

antimicrobial peptide PK34 (named Plent-PK34-BMSCs) and to investigate their

roles in both in vitro and in vivo Mtb H37Rv infection models.

**RESULTS:** We successfully constructed Plent-PK34-BMSCs that secrete and express

the antimicrobial peptide PK34, and demonstrated that PK34 modified MSCs

significantly enhanced their in vitro and in vivo antibacterial ability and

cytoprotective effects. The cytokine results showed that Plent-PK34-BMSCs

increased the levels of anti-inflammatory factors IL-4 and IL-10 in the cell

supernatant, decreased the levels of pro-inflammatory factors IL-6 in the serum

of the mice. In addition, lung tissue analysis results showed that mice treated

with Plent-PK34-BMSCs had reduced infiltration and congestion of inflammatory

cells in lung tissue, significantly reduced lung injury, and exhibited better

preservation of lung structure.

**CONCLUSIONS:** PK34 modification enhanced the therapeutic efficacy of MSCs in Mtb

infection models, and Plent-PK34-BMSCs transplantation has the potential to

treat TB.

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DOI: 10.1186/s13287-025-04596-9

PMCID: PMC12395748

PMID: 40877966 [Indexed for MEDLINE]

**9. BMJ Open. 2025 Aug 28;15(8):e092267. doi: 10.1136/bmjopen-2024-092267.**

Mediating role of health locus of control in supportive care needs and health

promoting behaviours among patients with tuberculosis in China: a

cross-sectional study.

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**OBJECTIVES:** To explore the mediating role of health locus of control in the

relationship between supportive care needs and health promoting behaviours among

patients with pulmonary tuberculosis.

**DESIGN:** A cross-sectional study.

**SETTING:** This survey was conducted in three tuberculosis-designated hospitals in

Xi'an, China, between March and May 2020.

**PARTICIPANTS:** A total of 294 participants completed the questionnaires.

**OUTCOME MEASURES:** The participants completed a self-designed socio-demographic

questionnaire, the Multidimensional Health Locus of Control scale, the

Supportive Care Needs Scale for Patients with Tuberculosis and the Health

Promoting Lifestyle Profile II. SPSS V.26.0 and Mplus were used for data

analysis.

**RESULTS:** The patients' supportive care needs had a negative association with

their health promoting behaviours (r=-0.58, p<0.001). The supportive care needs

were negatively related to internal health locus of control (r=-0.43, p<0.001),

and positively related to chance health locus of control (r=0.44, p<0.001) and

powerful others health locus of control (r=0.20, p<0.001). Health-promoting

behaviours had a significantly positive correlation with internal health locus

of control (r=0.49, p<0.001) and a negative correlation with chance health locus

of control (r=-0.36, p<0.001). Both internal health locus of control and chance

health locus of control acted as mediators between supportive care needs and

health promoting behaviours, while powerful others health locus of control did

not.

**CONCLUSION:** Health locus of control mediated the relationship between supportive

care needs and health promoting behaviours. A high level of internal health

locus of control and a low level of chance health locus of control may help to

improve health-promoting behaviours. Given the cross-sectional design of this

study, future experimental interventions targeting health locus of control are

needed to establish causal relationships with supportive care needs and health

promoting behaviours.

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DOI: 10.1136/bmjopen-2024-092267

PMID: 40876888 [Indexed for MEDLINE]

**10. BMC Infect Dis. 2025 Aug 25;25(1):1063. doi: 10.1186/s12879-025-11487-0.**

Plasma exosomal miR-122-5p\_R-1, miR-23b-3p\_R + 1, and miR-15a-5p\_R-1 are

associated with multidrug-resistant tuberculosis.

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**BACKGROUND:** Patients with multidrug-resistant tuberculosis (MDR-TB) who are

resistant to at least both rifampicin and isoniazid, lack effective treatment

options in clinic. The gold standard for the diagnosis of MDR-TB is drug

sensitivity test, which is time-consuming and has a relatively low positive

detection rate. Screening early diagnostic biomarker for MDR-TB is urgent need

in clinical practice.

**METHODS:** A total of 33 patients with MDR-TB, healthy controls and drug-sensitive

tuberculosis (DS-TB) were included in this study. Total plasma exosomal RNA was

extracted from the subjects, and the MDR-TB plasma-specific exosomal miRNAs were

obtained by Illumina sequencing.

**RESULTS:** There were 644 and 647 differentially expressed miRNAs in the plasma

exosomes of MDR-TB patients obtained by sequencing and biogenic analysis

compared with DS-TB patients and healthy controls, respectively. Differential

miRNAs are mainly involved in the biological function of regulation of

transcription and protein binding, and enriched in the pathways in cancer and

MAPK signaling pathway. Moreover, seven plasma exosomal miRNAs in MDR-TB

patients were significantly different from those in DS-TB patients and healthy

controls. Among them, three of the miRNAs (hsa-miR-122-5p\_R-1,

hsa-miR-23b-3p\_R + 1, and hsa-miR-15a-5p\_R-1) were found to be in target

relationship with MDR-TB related genes (NTRK2, KIDINS220, NCKAP1, MAPK9, NFAT5,

ATF6 and SLC11A2) by target gene prediction analysis. Further the bioinformatic

analysis showed that hsa-miR-122-5p\_R-1 targets the protein PGLYRP2, a

diagnostic biomarker identified in our previous study.

**CONCLUSIONS:** We suggest that hsa-miR-122-5p\_R-1, hsa-miR-23b-3p\_R + 1, and

hsa-miR-15a-5p\_R-1 are closely related to MDR-TB.

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DOI: 10.1186/s12879-025-11487-0

PMCID: PMC12376478

PMID: 40855526 [Indexed for MEDLINE]

**11. Sci Rep. 2025 Aug 26;15(1):31348. doi: 10.1038/s41598-025-15754-7.**

Higher proportion of coagulative necrosis and PD-L1(+) immune cells in splenic

tuberculosis.

Dai J(#)(1), Liu L(#)(1), Liu J(1), Liu Y(1), Wu R(1), Zhou J(2), Chen W(3).

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Due to its low incidence and non-specific clinical manifestations, early

diagnosis of splenic tuberculosis (STB) is extremely challenging. Pathology is

the gold standard for disease diagnosis. The spleen's unique structural and

functional characteristics may confer distinct pathological features and immune

microenvironment in STB. However, no relevant study has been reported to date.

Here, we collected seven cases of STB and compared their clinical and

pathological characteristics with those of pulmonary tuberculosis (PTB). CT

scans revealed that STB primarily manifests as significant enlargement of the

spleen, with multiple round-shaped low-density shadows visible within. Compared

to the PTB group, the positive rates for molecular detection and acid-fast

staining were significantly lower in the STB group, while the proportion of

coagulative necrosis was substantially higher. Granulomas, caseous necrosis,

abscesses, fibrous proliferation, collagen degeneration, and granulation tissue

formation did not show significant differences between the two groups. We

further compared infiltrating immune cells and found that the numbers of T

cells, CD8+ T cells, and macrophages were significantly higher in the STB group

than those in the PTB group, but there was no statistical difference compared to

normal spleen tissue, suggesting that tuberculosis infection may not have a

significant impact on the immune response in STB cases. The number of PD-L1+

immune cells in the STB group was significantly higher than that in the PTB

group and normal spleen tissue, while the number of PD-1+ immune cells did not

differ significantly among the three groups. In summary, STB has unique

pathological features and immune microenvironment, with a higher incidence of

coagulative necrosis and an extreme immune suppression state.

© 2025. The Author(s).

DOI: 10.1038/s41598-025-15754-7

PMCID: PMC12381082

PMID: 40858649 [Indexed for MEDLINE]

**12. Microbiol Spectr. 2025 Aug 26:e0003025. doi: 10.1128/spectrum.00030-25. Online ahead of print.**

Improved detection of isoniazid-heteroresistant Mycobacterium tuberculosis

subpopulations by droplet digital PCR compared to MeltPro TB assay.

Li H(#)(1), Wang N(#)(2), Yang M(#)(1), Shang Y(1), Wang Y(1), Tan C(2), Wen

S(1), Guo Y(2), Pang Y(1).

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Drug resistance in Mycobacterium tuberculosis (Mtb), especially isoniazid (INH)

resistance, challenges tuberculosis control. This study evaluated droplet

digital PCR (ddPCR) against the traditional MeltPro TB assay. A total of 77

INH-resistant samples from Beijing Chest Hospital, China, underwent ddPCR, drug

susceptibility testing, and Sanger sequencing. Of the 73 valid samples, MeltPro

detected 55 INH-resistant and 18 heteroresistant samples; ddPCR found 55

high-frequency mutations, 11 of the 18 heteroresistant by MeltPro as

heteroresistant, and 6 of the 7 below limit as sensitive, 1 as Nocardia. Using

ddPCR as a secondary screening tool for MeltPro results can screen false

positives in MeltPro, improving INH resistance detection accuracy (98.63% vs.

89.04%). DdPCR technology performs excellently in tuberculosis drug resistance

detection and provides strong technical support for the accurate diagnosis and

treatment of tuberculosis.

**IMPORTANCE:** Tuberculosis has emerged as a significant threat to global health,

bringing numerous new cases and a large number of deaths annually. Isoniazid

(INH), as a first-line treatment drug, plays a crucial role. However, the

emergence of its drug resistance poses a tough challenge for tuberculosis

control. Currently, the methods for detecting INH resistance and

heteroresistance have limitations like the slow speed of traditional culture

tests and the insufficient sensitivity of molecular methods. Therefore,

improving the diagnostic efficacy of the detection results for INH resistance is

crucial for the treatment of tuberculosis.

DOI: 10.1128/spectrum.00030-25

PMID: 40856496

**13. Infect Immun. 2025 Aug 25:e0006325. doi: 10.1128/iai.00063-25. Online ahead of print.**

Host-directed therapeutic targets in macrophages and their ligands against

mycobacteria tuberculosis.

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Although current combination regimens of antibiotics have significantly improved

tuberculosis (TB) cure rates, substantial challenges persist in the global

effort to end TB. These include poor patient compliance, the emergence of

drug-resistant strains due to prolonged treatments, and the persistence of

latent TB infections. Host-directed therapies (HDTs) have emerged as a promising

complementary strategy, leveraging the modulation of host immune responses to

combat Mycobacterium tuberculosis (Mtb). Unlike conventional antibiotics, HDTs

can enhance therapeutic outcomes by boosting host defense mechanisms, reducing

treatment duration and dosage, and minimizing the risk of resistance

development. Notably, several HDTs have shown significant efficacy against

multidrug-resistant (MDR) Mtb strains, while also mitigating excessive

inflammation and lowering relapse rates-achievements that remain elusive with

antibiotic regimens alone. This review provides a comprehensive overview of

recent advancements in HDTs, focusing on druggable targets and the mechanisms by

which these therapies restore or enhance immune functions disrupted by Mtb. By

integrating insights into macrophage polarization, metabolic modulation,

autophagy promotion, and cell death regulation, HDTs offer innovative and

multifaceted approaches to TB treatment. Furthermore, the potential for HDTs to

synergize with existing antibiotics underscores their relevance in overcoming

current therapeutic limitations. This synthesis aims to inspire further research

and development, with the ultimate goal of advancing HDTs as a transformative

solution for TB management.

DOI: 10.1128/iai.00063-25

PMID: 40853278

**14. Cell. 2025 Aug 22:S0092-8674(25)00922-5. doi: 10.1016/j.cell.2025.08.008. Online ahead of print.**

Stereo-seq V2: Spatial mapping of total RNA on FFPE sections with high

resolution.

Zhao Y(1), Li Y(2), He Y(1), Wu J(3), Liu Y(4), Li X(5), Li Z(1), Yuan Q(1), Li

J(1), Zhang X(1), Hu X(1), Wu G(1), Qiu Y(1), Yuan J(1), Huang X(1), Xu M(1),

Yang M(1), Guo J(1), Cao T(1), Chen Q(1), Li D(1), Zhang J(6), Zhou X(1), Jiang

X(1), Zhu F(4), Dong X(7), Xiang R(4), Pan H(7), Han L(7), Deng Z(8), Deng H(9),

Zhang Y(10), Liu M(10), Wu Q(11), Wang G(12), Zhai J(11), Tan W(13), Liu X(14),

Wang Z(14), Li S(1), Duan T(1), Liu L(15), Chen A(1), Liu H(16), Chen C(17),

Liao S(18), Xu X(19).

**Yu Zhao, Young Li\*, Ying He, Junqi Wu, Yi Liu, Xinxing Li, Zhaoxun Li, Qiaomei Yuan, Jialuo Li, Xinya Zhang, Xiaole Hu, Guifang Wu, Ying Qiu, Jie Yuan, Xin Huang, Mengru Xu, Mei Yang, Jing Guo, Tingting Cao, Qiuling Chen,Dandan Li, Jiajun Zhang, Xiaoxi Zhou, Xia Jiang, Fan Zhu, Xuan Dong, Rong Xiang, Hailin Pan, Lei Han, Ziqing Deng, Haohao Deng , Yan Zhang , Maoyuan Liu , Qin Wu , Gaoyang Wang, Jie Zhai , Weihong Tan , Xiawei Liu, Zehao Wang , Shanshan Li , Tianbi Duan , Longqi Liu , Ao Chen , Haiying Liu\*, Chang Chen\*, Sha Liao\*, and Xun Xu\***

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Performing total RNA profiling on formalin-fixed, paraffin-embedded (FFPE)

samples, the predominant sample conservation method in clinical practice,

remains challenging for current spatial transcriptomics techniques. Here, we

introduce Stereo-seq V2, which employs random primers to capture and sequence

RNAs in situ on FFPE sections and provides single-cell resolution. The

random-priming-based strategy offers unbiased transcript capturing and uniform

gene body coverage, which increase the sensitivity to marker genes, the

efficiency of non-polyadenylation (poly(A)) RNA profiling, and immune repertoire

coverage. We demonstrated the robust performance of Stereo-seq V2 on clinical

FFPE samples using triple-negative breast cancer (TNBC) sections and identified

tumor-specific alternative splicing events. In a Mycobacterium tuberculosis

(Mtb)-infected mouse model, we monitored gene expression dynamics of host and

pathogen transcriptomes simultaneously by utilizing Stereo-seq V2. We also

assembled immune repertoires and identified Mtb-specific BCR clones, which could

also be observed in human tuberculous lung samples. These results highlight

Stereo-seq V2's potential in biomedical research and personalized medicine.

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DOI: 10.1016/j.cell.2025.08.008

PMID: 40882628

**15. Vaccines (Basel). 2025 Aug 17;13(8):872. doi: 10.3390/vaccines13080872.**

Protective Efficacy of Subunit Vaccine Expressing Rv0976c Against Tuberculosis.

Zhou Z(1), Chen D(2), Chen F(1), Xu W(3), Pan Z(4), Xiang Z(1), Gao X(1), Li

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**OBJECTIVES:** The construction of subunit vaccines based on antigens that can

induce strong cellular immunity is a widely accepted strategy to develop new

tuberculosis vaccines. This study screens immunogens with potential for subunit

vaccine development from seven candidate antigens and then verifies their

vaccine efficacy.

**DESIGN:** C57BL/6 mice were immunized subcutaneously with purified PPE19, PPE50,

FadD21, Rv1505c, Rv1506c, Rv2035, and Rv0976c proteins formulated with Freund's

adjuvant to evaluate both the antigen-specific Th1 cellular immune responses and

IgG level. After the vaccination of mice with recombined pcDNA3.1 expressing

Rv0976c, intravenous or aerosol infection with M. tb were further challenged to

assess protective efficacy.

**RESULTS:** Purified PPE19, PPE50, FadD21, and Rv0976c proteins generated strong

antigen-specific Th1 cellular immune responses in mice. Compared to Ag85A,

Rv0976c also stimulated higher IgG antibody level in mice. In particular,

Rv0976c stimulated high and specific IgG antibody levels in serum from TB

patients. The vaccination of mice with DNA vaccines expressing Rv0976c, followed

by intravenous challenge with Bacillus Calmette-Guerin (BCG) Pasteur or M. tb,

resulted in significant levels of protection that are comparable to or better

than that afforded by the two leading antigens, Ag85A and PPE18.

**CONCLUSIONS:** These results indicated that Rv0976c was a better protective

antigen. Future studies to combine Rv0976c with other antigens and evaluate its

effectiveness as a booster of BCG or as a therapeutic vaccine are warranted.

DOI: 10.3390/vaccines13080872

PMCID: PMC12390289

PMID: 40872957

**16. Front Public Health. 2025 Aug 13;13:1572422. doi: 10.3389/fpubh.2025.1572422.**

**eCollection 2025.**

The influence and lag-effect of temperature and precipitation on the incidence

and mortality of tuberculosis, 2000-2021: an observational study.

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

particularly in low-and middle-income countries. Climate change may influence TB

burden through effects on human health, living conditions, and pathogen

transmission, yet its long-term impact remains underexplored.

**METHODS:** This observational study integrated data on temperature and

precipitation obtained from NCEI/NOAA, TB burden from the Global Burden of

Disease Study 2021, and socio-economic covariates from the World Bank open data

platform. We used quasi-Poisson regression to assess non-lagged associations and

applied distributed lag non-linear models to estimate lagged effects of climate

exposure on age-standardized incidence and mortality rates (ASIR and ASMR) of TB

from 2000 to 2021.

**RESULTS:** From 2000 to 2021, global TB age-standardized incidence rate and

age-standardized mortality rate declined annually by 2.15 and 4.18%,

respectively, with higher burdens in Africa and Southeast Asia. TB rates were

elevated in males and those over 50, while younger age groups (<5, 5-14) in

countries like the Philippines and Zimbabwe saw increases. A 1°C rise in

temperature reduced age-standardized incidence rate by 0.89% and ASMR by 1.61%,

while 1 mm increased precipitation raised age-standardized mortality rate by

1.80%, impacting males more. Higher temperatures increased TB rates in

South-East Asia and Western Pacific, while precipitation raised rates in Africa,

Eastern Mediterranean, and the Americas. Low and high temperatures showed

negative lag effects after 12-15 years, while high temperatures posed a

short-term risk for those aged 50+. 0 mm precipitation was protective after

10-15 years, while intermediate and humid precipitation levels had mixed

effects, including some negative impacts on mortality.

**CONCLUSION:** There is urgent need for tailored interventions that strengthen

healthcare infrastructure, enhance disaster preparedness, and address both

social determinants and climatic influences. By incorporating climate factors

into the understanding of TB trends, our study offers critical insights to guide

public health strategies in the era of climate change, contributing to more

effective approaches for achieving the SDG targets for TB elimination.

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DOI: 10.3389/fpubh.2025.1572422

PMCID: PMC12380760

PMID: 40880929 [Indexed for MEDLINE]

**17. Front Med (Lausanne). 2025 Aug 13;12:1621689. doi: 10.3389/fmed.2025.1621689.**

**eCollection 2025.**

Case Report: A case of tuberculous empyema causing rupture of the diaphragm was

misdiagnosed as diaphragmatic hernia.

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Tuberculous empyema (TE) is a chronic active infection caused by Mycobacterium

tuberculosis that invades the pleural cavity. Initially, fluid accumulates in

the pleural space, followed by an influx of neutrophils, which gradually

develops into purulent fluid. This process can eventually lead to pleural

thickening and calcification, restricting lung expansion and impairing lung

function. Additionally, empyema can extend outward through weaknesses in the

chest wall, forming abscesses in the soft tissues outside the thoracic cavity.

The combination of anti-tuberculosis medications and surgical intervention is a

crucial treatment approach for tuberculous empyema. We report a case of

tuberculous empyema that invaded the diaphragm, resulting in diaphragmatic

rupture and the formation of a subcapsular liver abscess, which was initially

misdiagnosed as a diaphragmatic hernia. The patient showed significant

improvement and was discharged following surgical treatment.

Copyright © 2025 Liu, Zhou, Li and Xu.

DOI: 10.3389/fmed.2025.1621689

PMCID: PMC12380699

PMID: 40880761

**18. Front Cell Infect Microbiol. 2025 Aug 13;15:1560870. doi:**

**10.3389/fcimb.2025.1560870. eCollection 2025.**

Development and evaluation of a multiplex molecular point-of-care assay for

direct identification of Mycobacterium tuberculosis and prioritized

non-tuberculous mycobacteria.

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HT(1), Zhang YF(3), Yang QW(1)(4), Xu YC(1)(4).

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**OBJECTIVE:** This study aimed to establish a multiplex molecular point-of-care

assay called fastNTM incorporating an ultra-fast sample pre-treatment for direct

identification of Mycobacterium tuberculosis complex (MTBC) and 8

non-tuberculous Mycobacteria (NTM) commonly prioritized in clinical settings,

and to evaluate its performance in 149 clinical confirmed mycobacterial-positive

samples.

**METHODS:** The study was divided into two stages: a pilot study to establish the

methodology and a clinical validation study to evaluate its performance. In the

pilot study, we established the fastNTM and analyzed its performance regarding

limits of detection, reproducibility, specificity and efficiency. The clinical

validation study was performed using 149 clinical confirmed

mycobacterial-positive samples, with 16S rRNA identification as the reference

standard. The complete process, from patient to result, was accomplished within

90 minutes.

**RESULTS:** Of the 149 positive clinical mycobacterial cultures analyzed, 136 were

within the designed targets. Among these 136 cultures, 133 samples were

correctly identified by fastNTM, achieving an accuracy rate of 97.79%.

**CONCLUSIONS:** This study demonstrates that fastNTM with its high accuracy rate

are capable to rapidly and effectively differentiate between MTBC and the major

NTM species.

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DOI: 10.3389/fcimb.2025.1560870

PMCID: PMC12380709

PMID: 40880634 [Indexed for MEDLINE]

**19. Front Med (Lausanne). 2025 Aug 12;12:1597849. doi: 10.3389/fmed.2025.1597849.**

**eCollection 2025.**

Case Report: Papillary renal cell carcinoma complicated by ipsilateral renal

tuberculosis.

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Zhang N(2), Yu B(1), Fu N(1).

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Papillary renal cell carcinoma (PRCC) complicated by ipsilateral renal

tuberculosis (TB) represents an exceptionally rare and complex clinical

condition. Renal TB is the most common form of urogenital TB, while PRCC is the

most prevalent histological subtype of non-clear cell renal cell carcinoma

(RCC). In this study, we present the first reported case of PRCC complicated by

ipsilateral renal TB, where the patient exhibited low back pain without

hematuria. Initial imaging studies indicated a space-occupying lesion in the

left kidney, raising suspicion of renal tumors. Subsequent postoperative

pathology, immunohistochemical staining, and tuberculosis PCR results confirmed

the diagnosis of PRCC complicated by ipsilateral renal TB.

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DOI: 10.3389/fmed.2025.1597849

PMCID: PMC12379642

PMID: 40873793

**20. Front Cell Infect Microbiol. 2025 Aug 11;15:1574824. doi:**

**10.3389/fcimb.2025.1574824. eCollection 2025.**

Predictive analysis of all-cause mortality of previously untreated pulmonary

tuberculosis patients complicated by hypertension.

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Y(6)(7).

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**OBJECTIVE:** To investigate the risk factors for all-cause mortality of previously

untreated pulmonary tuberculosis patients complicated by hypertension and

construct a predictive model.

**METHODS:** We retrospectively analyzed the clinical data of inpatients with

previously untreated pulmonary tuberculosis complicated by hypertension from

2019 to 2021 in Changsha Central Hospital. Patients' survival status and

cardiovascular events were collected through telephone follow-up. LASSO

regression was utilized to screen predictive variables, and binary logistic

regression identified mortality risk factors. A predictive nomogram model was

developed using R software, and its precision and reliability were verified.

**RESULTS:** Among the 1,014 patients, there were 100 (9.86%) deaths and 82 (8.09%)

cardiovascular events. LASSO regression screened out 13 predictive variables.

Multivariate logistic regression analysis revealed that smoking history, sputum

bacteriology, pleural effusion, coronary heart disease, and chronic kidney

disease were independent risk factors. Based on the training set data, a

nomogram prognostic model was developed, showing an AUC of 0.712 (95% CI:

0.777-0.847), with 50.0% sensitivity and 84.3% specificity. The model's fit was

confirmed through internal and external validations.

**CONCLUSION:** The prediction model constructed in this study has high predictive

ability and satisfactory clinical efficacy, and can provide an effective

individualized prediction tool for assessing all-cause mortality risk in

patients with previously untreated pulmonary tuberculosis complicated by

hypertension.

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DOI: 10.3389/fcimb.2025.1574824

PMCID: PMC12375569

PMID: 40861491 [Indexed for MEDLINE]

**21. Front Immunol. 2025 Aug 11;16:1601637. doi: 10.3389/fimmu.2025.1601637.**

**eCollection 2025.**

CD39 dynamics in tuberculosis: a potential biomarker of immune dysregulation and

T cell exhaustion.

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**BACKGROUND:** Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb),

remains a global health crisis complicated by immune dysregulation and T cell

exhaustion. CD39, an ectonucleotidase generating immunosuppressive adenosine, is

implicated in cancer and chronic infections, yet its spatiotemporal role in TB

pathogenesis remains unclear.

**METHODS:** Multiple publicly available datasets were utilized to evaluate CD39

across TB disease stages, diverse infectious diseases and anti-TB treatment.

Diagnostic accuracy was evaluated via ROC curves and combined signature

analysis. Immune cell infiltration were analyzed using CIBERSORTx. Cytokine

profiles and age-stratified associations were examined. Pathway enrichment

analysis was performed by GSEA. Single-cell analysis of non-human primate

granulomas assessed CD39's temporal dynamics, utilizing Monocle 3 for CD39+

T-cell trajectory analysis.

**RESULTS:** CD39 was upregulated in active TB patients versus TB infection (TBI)

and healthy controls (HC), correlating with older age, disease severity, and

distinct expression patterns compared to other respiratory and systemic

infections. CD39 demonstrated superior diagnostic accuracy over IFN-γ in

distinguishing TB from TBI/HC and other respiratory diseases. Combining CD39

with TBX21 or GZMB further improved diagnostic specificity. High CD39 expression

correlated with suppressed Th1 and elevated Th2/Th17/regulatory cytokines,

alongside pronounced neutrophil infiltration. Age-stratified analysis revealed

complex age-dependent associations of CD39 expression with various immune cell

types. Single-cell analysis revealed declining CD39 transcriptional activity

during prolonged infection despite expanded cellular distribution, linked to

early T cell maturation followed by broader immunomodulatory shifts. Decreased

CD39 expression with anti-TB treatment correlated with improved immune cell

balance and resolved T cell exhaustion.

**CONCLUSION:** CD39 is a critical regulator of immune exhaustion and

neutrophil-driven inflammation in TB, with diagnostic and therapeutic potential.

Targeting CD39 may provide a novel therapeutic strategy for TB.

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DOI: 10.3389/fimmu.2025.1601637

PMCID: PMC12375674

PMID: 40861457 [Indexed for MEDLINE]

**22. Imeta. 2025 Jun 22;4(4):e70054. doi: 10.1002/imt2.70054. eCollection 2025 Aug.**

Gut microbiota and tuberculosis.

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SS(7), Manaithiya A(8), Xiao M(9), Ni R(2), An Y(2), Zhang M(2), Tian Y(2), Zhou

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G(18), Armanni A(18), Fumagalli S(18), Wang W(19), Cao C(20), Carpena M(21),

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB), remains a

significant global health challenge. Recent advancements in gut microbiota (GM)

research have shed light on the intricate relationship between GM and TB,

suggesting that GM alterations may influence host susceptibility, disease

progression, and response to antituberculosis drugs. This review systematically

synthesizes and analyzes the current research progress on the relationship

between GM and TB, focusing on six key aspects: (1) bidirectional effects

between GM dynamics and TB progression; (2) the interaction between GM and

anti-TB drugs; (3) GM and TB immune response; (4) GM as a potential target for

diagnosis and treatment of TB; (5) multi-omics and artificial intelligence (AI)

technologies in GM-TB research; (6) current challenges and future directions in

GM-TB research. We highlight the bidirectional nature of the GM-TB interaction,

where MTB infection can lead to GM dysbiosis, and changes can affect the host's

immune response, contributing to TB onset and progression. Advanced molecular

techniques, such as next-generation sequencing and metagenomics, along with AI,

play pivotal roles in elucidating these complex interactions. Future research

directions include investigating the relationship between GM and TB vaccine

efficacy, exploring GM's potential in TB prevention, developing microbiome-based

diagnostic and prognostic tools, and examining the role of GM in TB recurrence.

By addressing these areas, we aim to provide a comprehensive perspective on the

latest advancements in GM and TB research and offer insights for future studies

and clinical applications. Ultimately, the development of novel microbiome-based

strategies may offer new tools and insights for the effective control and

management of TB, a disease that continues to pose a significant threat to

public health.

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behalf of iMeta Science.

DOI: 10.1002/imt2.70054

PMCID: PMC12371273

PMID: 40860431

**23. Front Med (Lausanne). 2025 Aug 7;12:1637007. doi: 10.3389/fmed.2025.1637007.**

**eCollection 2025.**

Development and validation of a nomogram to predict atelectasis in adult lymph

node fistula tracheobronchial tuberculosis patients.

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**BACKGROUND:** Lymph node fistula tracheobronchial tuberculosis (TBTB) is a severe

respiratory condition that can result in complications such as airway stenosis

and atelectasis, posing significant clinical challenges, particularly in adults.

Currently, no standardized assessment tools are available to predict the risk of

atelectasis in these patients, highlighting the need to develop an effective

predictive model to guide early clinical intervention and personalized

treatment.

**METHODS:** A retrospective study was conducted involving 547 adult patients

diagnosed with lymph node fistula TBTB at our hospital between January 2017 and

December 2023. Diagnoses were confirmed by chest computed tomography,

bronchoscopy, and combined etiological or pathological examinations. After

applying the inclusion and exclusion criteria, 301 cases were included in the

final analysis. Patients were randomly assigned to a development group (n = 211,

70%) and a validation group. Following univariate and multivariable logistic

regression to identify significant predictors, we developed a nomogram. Model

validation included assessment of discriminatory ability [receiver operator

characteristic (ROC) analysis], calibration accuracy, and clinical utility

(DCA).

**RESULTS:** Among the 301 patients with lymph node fistula TBTB, the incidence of

atelectasis was 60.13% (181/301). Of those, 72.93% (132/181) had right lung

involvement, and 50.28% (91/181) specifically had atelectasis in the right

middle lobe. Independent predictors identified by multivariable logistic

regression included age, occupation as a farmer, mediastinal lymphadenopathy

with ring enhancement, and right middle lobe bronchial involvement. A risk

nomogram was developed using these predictors. The area under the curve (AUC) of

the nomogram was 0.824 (95% CI: 0.685-0.806) in the development group and 0.857

(95% CI: 0.702-0.877) in the validation group. Calibration plots based on 500

bootstrap resamples showed good agreement between predicted and observed

probabilities across both groups. DCA revealed that the model provided a net

clinical benefit within threshold probability ranges of 0.2-0.9 for the

development group and 0.15-0.85 for the validation group.

**CONCLUSION:** The predictive model and associated nomogram developed in this study

can accurately estimate the risk of atelectasis in adult patients with lymph

node fistula TBTB. This tool may assist clinicians in developing individualized

intervention strategies.

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DOI: 10.3389/fmed.2025.1637007

PMCID: PMC12367512

PMID: 40852365

**24. Front Chem. 2025 Aug 7;13:1631086. doi: 10.3389/fchem.2025.1631086. eCollection 2025.**

A naked-eye biosensing system based on one-pot RPA-CRISPR/Cas12a driver G4-hemin

self-assembly for Mycobacterium tuberculosis.

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**INTRODUCTION:** The rapid and accurate identification of Mycobacterium

tuberculosis (MTB) is essential for effective tuberculosis (TB) control.

However, conventional diagnostic methods for MTB suffer from limitations such as

low sensitivity, poor specificity, high cost, reliance on specialized

instruments, and complex, time-consuming procedures. To address these

challenges, there is an urgent need for a simple, rapid, and highly sensitive

detection method that can be deployed in point-of-care settings.

**METHODS:** We developed a one-pot biosensing system combining recombinase

polymerase amplification (RPA) and CRISPR/Cas12a-driven G4-hemin self-assembly

for the colorimetric detection of MTB. Glycerol was employed as a

phase-separation barrier to prevent interference between RPA amplification and

CRISPR/Cas12a trans-cleavage. A single-stranded DNA (ssDNA) probe, designed to

self-assemble with ssDNA-hemin into G4-hemin nanozymes upon

CRISPR/Cas12a-mediated cleavage, served as the reaction substrate. The

ssDNA-hemin further enhanced the catalytic activity of the generated G4-hemin

DNAzyme. The entire assay was completed in a single step within 60 min without

requiring complex instrumentation.

**RESULTS AND DISCUSSION:** Under optimized conditions, the biosensing system

achieved ultrasensitive naked-eye detection of MTB with a limit of detection

(LOD) of 10 copies/μL, comparable to traditional four-step fluorescent assays.

Clinical validation using 104 patient samples demonstrated high concordance with

standard diagnostic methods. This approach combines the advantages of

recombinase polymerase amplification (RPA), CRISPR/Cas12a specificity, and

G4-hemin DNAzyme-based colorimetric signal amplification, enabling simple,

equipment-free visual detection. Given its speed, sensitivity, and ease of use,

this biosensing system holds significant promise for point-of-care MTB nucleic

acid testing in resource-limited settings.

Copyright © 2025 Yuan, Yuan, Huang, Li, Cai, Yang, Li, Chen and Min.

DOI: 10.3389/fchem.2025.1631086

PMCID: PMC12367758

PMID: 40851838

**25. Front Cell Infect Microbiol. 2025 Aug 7;15:1629703. doi:**

**10.3389/fcimb.2025.1629703. eCollection 2025.**

Stenotrophomonas tuberculopleuritidis sp. nov., a novel pathogenic

Stenotrophomonas species isolated from tuberculous pleurisy patient.

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**INTRODUCTION:** Stenotrophomonas represents a group of bacteria that exhibit

significant value in industrial and agricultural applications, while also posing

pathogenic risks to humans. 704A1T was isolated from a patient with tuberculous

pleurisy. Its 16S rRNA sequence showed the highest homology (99.72%) with a

Stenotrophomonas strain without defined species classification. It is necessary

to clarify the species 704A1T belonging to and its potential pathogenicity to

humans.

**METHODS:** Systematical evaluations including phenotypic and biochemical

characteristics, antibiotic susceptibility, genomic sequencing were conducted.

The pathogenicity and immunological characteristics were tested by intranasally

inoculated C57BL/6J mice.

**RESULTS:** 704A1T is Gram negative rod-shaped bacterium with flagella at single

extreme. Showing highly similar with S. maltophilia, 704A1T also displayed

distinct characteristic peaks in fatty acid profiling and MALDI-TOF analysis.

704A1T was resistance to 21 antibiotics, including four anti-tuberculosis drugs:

rifampicin, streptomycin, rifabutin, and cycloserine. The average nucleotide

identity (ANI) values of 704A1T compared to defined Stenotrophomonas species

ranged from 80.03% to 89.6%, below than both the commonly accepted 95%-96% ANI

threshold for prokaryote species and the 95% threshold suggested for

Stenotrophomonas. Though no mortality was observed, 704A1T could cause severe

consolidation in murine lung tissue and has the ability of hematogenous

dissemination.

**CONCLUSION:** Results supported the classification of 704A1T (=GDMCC 1.4133T) as a

novel species within the genus Stenotrophomonas, for which the name

Stenotrophomonas tuberculopleuritidis sp. nov. is proposed. 704A1T is a

multi-antibiotic resistance strain with potentially stronger pathogenicity than

S. maltophilia and requires more clinical attention. The isolation of 704A1T

underscored the importance of sustained surveillance and taxonomic clarity of

Stenotrophomonas species emerging from clinical environments.

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DOI: 10.3389/fcimb.2025.1629703

PMCID: PMC12367676

PMID: 40851804 [Indexed for MEDLINE]

**26. Front Cell Infect Microbiol. 2025 Aug 7;15:1641385. doi:**

**10.3389/fcimb.2025.1641385. eCollection 2025.**

Whole-genome sequencing and machine learning reveal key drivers of delayed

sputum conversion in rifampicin-resistant tuberculosis.

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Rifampicin-resistant tuberculosis (RR-TB) remains a major global health

challenge, with delayed sputum culture conversion (SCC) predicting poor

treatment outcomes. This study integrated whole-genome sequencing (WGS) and

machine learning to identify clinical and genomic determinants of SCC failure in

150 RR-TB patients (2019-2023). Phenotypic and genotypic analysis revealed high

rates of isoniazid resistance (74.0%) and rpoB mutations (97.3%, predominantly

Ser450Leu), with 90% of strains belonging to Lineage 2 (Beijing family). While

64.7% achieved 2-month SCC, 18.0% remained culture-positive at 6 months.

Univariate analysis linked 2-month SCC failure to smear positivity, resistance

to isoniazid, amikacin, capreomycin, and levofloxacin, and pre-XDR-TB status,

though only smear positivity (aOR=2.41, P=0.008) and levofloxacin resistance

(aOR=2.83, P=0.003) persisted as independent predictors in multivariable

analysis. A Random Forest model achieved robust prediction of SCC failure (AUC:

0.86 ± 0.06 at 2 months; 0.76 ± 0.10 at 6 months), identifying levofloxacin

resistance (feature importance: 6.37), embB\_p.Met306Ile (5.94), and smear

positivity (5.12) as top 2-month predictors, while katG\_p.Ser315Thr (4.85) and

gyrA\_p.Asp94Gly (3.43) dominated 6-month predictions. These findings underscore

smear positivity, levofloxacin resistance, and specific resistance mutations as

critical drivers of SCC failure, guiding targeted RR-TB treatment strategies.

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DOI: 10.3389/fcimb.2025.1641385

PMCID: PMC12367658

PMID: 40851801 [Indexed for MEDLINE]

**27. Front Cell Infect Microbiol. 2025 Aug 7;15:1640647. doi:**

**10.3389/fcimb.2025.1640647. eCollection 2025.**

Autophagy in mycobacterial infections: molecular mechanisms, host-pathogen

interactions, and therapeutic opportunities.

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Mycobacteria pose significant global health burdens, with Mycobacterium

tuberculosis complex causing tuberculosis-a leading infectious killer claiming

over 1.25 million lives annually-and NTM driving pulmonary and ulcerative

infections, particularly in immunocompromised populations. Autophagy, a

conserved cellular degradation pathway, serves as a critical mechanism of host

defense against mycobacteria by delivering bacteria to the lysosome. As a

response, mycobacteria have evolved intricate strategies to subvert or exploit

autophagy for survival. Consequently, autophagy exhibits a dichotomous role in

mycobacterial infection: functioning as a protective mechanism of host while

simultaneously serving as a virulence determinant hijacked by bacteria for their

survival. This review synthesizes current insights into the molecular mechanisms

mediating host-initiated autophagy during mycobacterial infection, as well as

the bacterial strategies for subverting or hijacking autophagic pathways. While

autophagy may be hijacked by mycobacteria, substantial evidence from numerous

studies demonstrates that autophagy-activating agents may be beneficial in

restricting mycobacteria infection, even with multidrug-resistant strains. This

review also systematizes promising agents that enhance autophagy to improve

bacterial clearance. By synthesizing the latest research findings, this article

aims to enhance our understanding of the intricate relationship between

autophagy and mycobacteria, paving the way for efficient host-directed therapies

(HDTs) against this severely harmful pathogen.

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DOI: 10.3389/fcimb.2025.1640647

PMCID: PMC12367789

PMID: 40851798 [Indexed for MEDLINE]