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**中国大陆学者发表的结核病英文文章摘要**

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**1. Diagn Microbiol Infect Dis. 2025 Sep 8;114(1):117103. doi:**

**10.1016/j.diagmicrobio.2025.117103. Online ahead of print.**

The auxiliary diagnostic performance of creation tuberculin skin test for

mycobacterium tuberculosis compared with QuantiFERON-TB Gold Plus: A diagnostic

accuracy study.

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**BACKGROUND:** For bacteriologically negative suspected tuberculosis, immunological

testing provides important diagnostic evidence. The traditional tuberculin skin

test has poor specificity. QuantiFERON-TB Gold Plus (QFT-Plus, the latest

generation of Interferon-Gamma Release Assays) and creation tuberculin skin test

(C-TST) offer higher specificity and are less affected by non-tuberculous

mycobacteria and BCG vaccine. However, the efficacy of QFT-Plus and C-TST in

suspected tuberculosis remain unclear. We compared the performance of the

QFT-Plus with the C-TST in auxiliary diagnosing tuberculosis in individuals with

suspected tuberculosis.

**METHODS:** The subjects were 137 patients suspected of tuberculosis, including 74

pulmonary tuberculosis (PTB) patients and 63 non-active pulmonary tuberculosis.

All participants underwent both QFT-Plus and C-TST testing.

**RESULTS:** The sensitivities of QFT-Plus and C-TST in diagnosing PTB were 93.15 %

and 86.49 %, respectively. The specificities of QFT-Plus and C-TST in diagnosing

PTB were 40.35 % and 41.27 %, respectively. When QFT-Plus and C-TST were

combined, the specificity increased to 58.73 %. The Area Under the Curves of

Receiver Operating Characteristic in QFT-Plus and C-TST were 0.79 vs 0.67 (p <

0.05), respectively. In addition, the median IFN-γ level of TB2 tubes in the PTB

group of QFT-Plus was significantly higher than that of TB1 tubes.

**CONCLUSIONS:** QFT-Plus and C-TST demonstrated diagnostic value in helping

clinicians identify PTB and rule out non-patients to a certain extent, and the

two methods had moderate agreement. The combined diagnosis statistically

improved the specificity in auxiliary diagnosing PTB. Furthermore, the QFT-Plus

appears more advantageous than C-TST for auxiliary diagnosing of tuberculosis.

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**ahead of print.**

Pathogenic phosphorylation of linear ubiquitin machinery causes inflammasome

sensor degradation.

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Fang Y(1), Zhang X(1), Li B(4), Pang Y(2), Wang J(4), Zhang L(5), Liu CH(6),

Chai Q(7).

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Host immune cells are equipped with cytosolic sensors to detect invading

pathogens and initiate anti-infectious responses. However, how pathogens

undermine host intracellular surveillance for persistent infection is not fully

understood. Here, we identify that Mycobacterium tuberculosis protein kinase

PknG subverts inflammasome sensor NLRP3-mediated cytokine release and pyroptosis

by targeting host linear ubiquitin chain assembly complex (LUBAC).

Mechanistically, PknG phosphorylates the LUBAC subunit HOIL-1L to prevent it

from engaging in LUBAC formation, thereby suppressing linear ubiquitination of

inflammasome adaptor ASC to dampen NLRP3 inflammasome assembly. Meanwhile, this

phosphorylation stabilizes and activates HOIL-1L, which, in turn, exerts

ubiquitin ligase activity to mediate K48-linked ubiquitination of NLRP3 for

degradation. Disrupting the kinase activity or HOIL-1L-interacting region of

PknG facilitates host NLRP3-dependent anti-Mtb immunity in mice. Thus, the

bacterial kinase disrupts host linear ubiquitin machinery and coopts its

ubiquitin ligase subunit to constitute an inter-species enzymatic cascade that

drives inflammasome sensor degradation for counteracting immune surveillance.

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**3. Infect Dis Ther. 2025 Sep 13. doi: 10.1007/s40121-025-01224-0. Online ahead of print.**

Analysis of Adverse Drug Reactions of Clofazimine Reported in the FDA Adverse

Event Reporting System from 2004 to 2025 Q1.

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**INTRODUCTION:** Clofazimine (CFZ) is an antimycobacterial agent used primarily for

leprosy and multidrug-resistant tuberculosis. Despite its long clinical history,

comprehensive pharmacovigilance data remain limited. This study aimed to analyze

CFZ-associated adverse events (AEs) reported in the FDA Adverse Event Reporting

System (FAERS), identifying and pharmacovigilance signals.

**METHODS:** We conducted a retrospective pharmacovigilance analysis of the FAERS

database from 2004 to 2025 Q1. ASCII-format data were imported into R 4.4.2 and

deduplicated using FDA guidelines. Reports Listing CFZ as the primary suspect

drug were identified using generic and brand names. AEs were coded using MedDRA

27.1. Disproportionality analyses, including reporting odds ratio (ROR),

proportional reporting ratio (PRR), Bayesian confidence propagation neural

network (BCPNN), and empirical Bayesian geometric mean (EBGM), identified

signals of disproportionate reporting. Subgroup analyses examined sex

differences, while time-to-onset (TTO) analyses characterized latency patterns.

**RESULTS:** A total of 1287 CFZ-related AE reports were identified, with 995

(77.3%) classified as serious. Death (11.6%) and hospitalization (18.1%) were

the most frequent serious outcomes. The majority of reports originated from the

United States (59.4%). Demographic analysis showed higher reporting among

females (49.6%) and patients aged 18-64 years (46.5%). Disproportionality

analyses identified 135 preferred terms with positive safety signals. The most

prominent signals included QT prolongation (ROR ~ 37.61), drug resistance

(ROR ~ 17.31), skin hyperpigmentation (ROR ~ 13.07), and respiratory failure

(ROR ~ 7.46), ranging from moderate to strong signal intensity. Subgroup

analyses revealed significant sex differences in specific AE signals. TTO

analysis indicated varied latency distributions across System Organ Class (SOC)

and preferred term levels.

**CONCLUSION:** Our pharmacovigilance assessment of FAERS data from 2004 to 2025 not

only identified multiple serious and consistent safety signals associated with

clofazimine such as prolonged QT intervals but also revealed a life-threatening

AE respiratory failure. Although the analysis of these AEs cannot directly

reflect causal relationships due to the nature of the FAERS data from

spontaneous reporting, our findings highlight the critical importance of

continuous pharmacovigilance, targeted clinical monitoring, and consideration of

sex-based risk differences to ensure the safe use of clofazimine in clinical

practice.

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**4. PLoS One. 2025 Sep 12;20(9):e0331264. doi: 10.1371/journal.pone.0331264.**

**eCollection 2025.**

Evaluation of the Xpert MTB/XDR test for detection of isoniazid,

fluoroquinolones, and second-line injectable drugs resistance to Mycobacterium

tuberculosis-Anhui Province, China.

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**INTRODUCTION:** The emergence of drug-resistant tuberculosis (DR-TB) has posed

significant challenges to TB control. This study assessed the diagnostic

performance of the Xpert MTB/XDR test for detecting drug resistance in TB

patients.

**METHODS:** This study analyzed 276 samples collected from clinically suspected

MDR-TB patients in Auhui Chest Hospital from 01/03/2022-01/03/2023. The Xpert

MTB/XDR test was evaluated for its ability to detect resistance to isoniazid

(INH), ethionamide (ETH), fluoroquinolones (FLQ), and second-line injectable

drugs (SLIDs) compared with phenotypic drug susceptibility testing (pDST).

Specimens were investigated by Sanger sequencing, where the MTB/XDR test and

pDST results were inconsistent. Afterward, the clinical performance of the Xpert

MTB/XDR test was also evaluated with the composite reference test

(pDST + sequencing).

**RESULTS:** The sensitivity of the Xpert MTB/XDR test against pDST in detecting

resistance to INH and FLQ using 276 samples was 95.77% (95% CI: 91.83-98.16) and

93.83% (95% CI: 86.18-97.97), respectively. In contrast, a lower sensitivity of

the MTB XDR test in predicting SLIDs and ETH resistance (sensitivity < 75%)

compared with pDST was demonstrated in this study. The specificity for detecting

all drugs was greater than 90%. Thirty-three samples were retested by

sequencing, which identified mutations predicting INH and FLQ resistance,

determining whether resistant or not by combining pDST and sequencing results.

When considering pDST + sequencing, the sensitivity and specificity of the

MTB/XDR assay for INH and FLQ drug targets increased, especially the detection

specificity of FLQ has reached 100% (95% CI: 97.95-100).

**CONCLUSION:** The Xpert MTB/XDR has high sensitivity and specificity in

drug-resistant tuberculosis patients, making it better suited to meet the needs

of rapid, sensitive, and accurate detection for drug-resistant tuberculosis in

resource-limited settings, and serving as a critical tool for achieving

personalized treatment and TB control.

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Generation of novel polyclonal antibodies against Mycobacterium tuberculosis

lipoarabinomannan, EspB, and Mtb8.

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The unique cell wall of Mycobacterium tuberculosis (Mtb) creates a barrier to

hydrophilic drugs, which is crucial for its survival and pathogenicity. However,

the immune reactivity elicited by its components remains incompletely

understood. We aimed to assess the antibody responses induced by Mtb H37Rv cell

wall components and to develop and characterize antigen-specific polyclonal

antibodies (pAbs). Rabbits were immunized with these components. Immune serum

reactivity was tested against various Mtb antigens. Specific polyclonal

antibodies (pAbs) were purified by affinity chromatography. The results showed

that immune serum reacted with lipoarabinomannan (LAM), ESAT-6 secretion

system-1 (Esx-1) secreted protein B (EspB), and Mtb8, but showed no reactivity

with other tested Mtb antigens. LAM-, EspB-, or Mtb8-specific pAbs were

subsequently affinity-purified. The affinity-purified LAM pAb, EspB pAb, and

Mtb8 pAb each demonstrated high specificity and sensitivity, showing no

cross-reactivity with non-target antigens. They recognized antigens in

culture supernatants and cells from diverse mycobacterial strains, including

both slow-growing mycobacteria (SGM) and rapid-growing mycobacteria (RGM). In a

sandwich ELISA using LAM pAb as the capture antibody and

biotinylated LAM-specific monoclonal Abs (BJRbL01-Bio, BJRbL03-Bio, BJRbL20-Bio,

BJRbL52-Bio, or BJRbL76-Bio) as detection antibodies, the assay detected SGM but

did not react with RGM species. EspB pAb recognized EspB in both cell lysate and

culture supernatant fractions, where full-length and mature EspB are

predominantly found, respectively. Mtb8 pAb reacted with monomeric and

polymeric forms of Mtb8. In conclusion, we successfully generated novel pAbs

against LAM, EspB, and Mtb8, providing promising research tools for

investigating these critical molecules. KEY POINTS: Rabbit antibodies against

Mtb H37Rv cell wall components target LAM, EspB, and Mtb8 Novel LAM-, EspB-, and

Mtb8-specific pAbs were generated and characterized Broad mycobacterial

reactivity and specific target detection confirm pAb utility.

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Mycobacterial tyrosine phosphatase PtpB affects host cytokine expression by

dephosphorylating ERK1/2 and STAT3.

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Mycobacterium tuberculosis (Mtb) tyrosine phosphatases PtpA and PtpB have been

widely reported to affect host immunity response and bacterial intercellular

survival. However, a comprehensive investigation into the impact of PtpA and

PtpB on host phosphorylation, specifically in their roles as tyrosine

phosphatases, has not yet been reported. In this study, we first conducted the

potential dephosphorylation substrates map of PtpA and PtpB within the host. Our

findings demonstrated that PtpB significantly decreased the phosphorylation

levels of ERK1/2 and STAT3. Subsequent analysis indicated that PtpB modulated

the production of cytokine TNF and IL-1β by dephosphorylating ERK1/2 and

preventing its nuclear translocation. PtpB also reduced IL-6 and IL-1β

expression by dephosphorylating STAT3. The in vivo experiment demonstrated

increased bacterial survival and reduced cytokine expression in

PtpB-overexpression strain. Consequently, our findings demonstrate that Mtb

tyrosine phosphatases PtpA and PtpB play critical roles in the global tyrosine

phosphorylation landscape within the host. Specifically, PtpB modulates cytokine

expression through the dephosphorylation of ERK1/2 and STAT3.

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**Online ahead of print.**

Effects of anti-tuberculosis drugs on the proliferation and differentiation of

alveolar stem cells.

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Tuberculosis (TB), a disease caused by Mycobacterium tuberculosis (Mtb), not

only inflicts damage on lung epithelium but also poses a challenge to the

regenerative capacity of the lung. Using lung organoid culture techniques, we

assessed the effects of anti-Mtb drugs on the proliferation and differentiation

of type II alveolar (AT2) cells. We found that rifampicin, pyrazinamide,

ethambutol, and levofloxacin decreased the organoid-forming efficiency (OFE) of

AT2 cells. Additionally, rifampicin and levofloxacin inhibited the size of

organoids derived from AT2 cells. Isoniazid, ethambutol, and levofloxacin

promoted type I alveolar (AT1) cell differentiation. Moxifloxacin considerably

promoted the OFE and clone diameter while exerting minimal effects on AT1 cell

differentiation. Furthermore, we performed metabolomics to elucidate the

molecular mechanisms underlying lung epithelial stem cell regeneration. The

differentially expressed metabolites were closely associated with energy

metabolism, which is essential for cell proliferation and differentiation.

Altogether, our data suggest that anti-Mtb drugs exhibit diverse and specific

impacts on the growth and differentiation of AT2 cells. This may be directly

related to the effect of drugs on the energy metabolism of alveolar stem cells,

providing new insights and tools for the evaluation of anti-Mtb drugs.

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Hierarchical integration of mNGS, PCR, and other conventional methods for

precision TB diagnostics.

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This study systematically compared the diagnostic accuracy of seven assays for

detecting the Mycobacterium tuberculosis complex, including metagenomic

next-generation sequencing (mNGS), droplet digital polymerase chain reaction,

real-time quantitative polymerase chain reaction, EasyNAT MTC, GeneXpert

MTB/RIF, interferon-gamma release assay (IGRA), and acid‒fast staining (AFS). We

try to select appropriate combinations of tuberculosis (TB) detection methods

for regions with varying levels of medical resources, based on sensitivity,

cost-effectiveness, and operational feasibility. A retrospective analysis was

conducted on 141 samples collected from patients with suspected active TB at The

First Affiliated Hospital of Sun Yat-sen University between April 2022 and April

2024. Among these samples, there were 100 cases assigned to the case group and

41 cases to the control group, based on the tuberculosis diagnostic criteria.

Historical data for Xpert, IGRA, and AFS were collected, and parallel

experiments using mNGS, droplet digital PCR (ddPCR), real-time quantitative

polymerase chain reaction (RT-qPCR), and EasyNAT were conducted on all samples.

Diagnostic performance was evaluated by comparing it with the final clinical

diagnoses. Sensitivity, specificity, positive predictive value, negative

predictive value, and receiver operating characteristic (ROC) curve analysis

were conducted, along with DeLong tests for statistical comparison. Compared

with the final clinical diagnosis, mNGS demonstrated the highest sensitivity

(100%), followed by IGRA (79.2%), EasyNAT (79.1%), RT-qPCR (78.0%), ddPCR

(75.8%), Xpert (75.3%), and AFS (16.7%). The specificity was 100% for both Xpert

and AFS, followed by ddPCR (97.6%), RT-qPCR (95.1%), EasyNAT (92.7%), IGRA

(72.7%), and mNGS (75.6%). ROC analysis revealed a significantly greater area

under the ROC curve for mNGS (0.878) than for ddPCR (0.817, P = 0.031). DeLong

tests revealed statistically significant differences in diagnostic performance

between mNGS and ddPCR (P < 0.05) and between IGRA and AFS (P < 0.01). mNGS

uniquely identified the pathogens involved in co-infection and quantified

pathogen-specific sequencing reads. Through a comprehensive evaluation of the

diagnostic efficacy, cost-effectiveness, and timeliness of tuberculosis

detection methods, we propose corresponding combinations of TB testing

approaches for regions with different healthcare resources. For undeveloped

regions with limited resources, a combination of AFS +EasyNAT + chest X-ray is

recommended. Primary care facilities may additionally employ IGRA + RT-qPCR.

Intermediate-level hospitals can incorporate Xpert MTB/RIF for drug resistance

testing, while tertiary hospitals or specialized centers should, on the basis of

these fundamental tests, utilize mNGS for diagnosis and ddPCR for therapeutic

monitoring in patients with complex mixed infections.

**IMPORTANCE:** This study is the first to comprehensively evaluate the diagnostic

efficacy, cost-effectiveness, and timeliness of seven TB detection methods in a

single-center cohort. Our findings provide actionable solutions for optimizing

TB diagnostics in diverse healthcare ecosystems, aligning with the WHO's End TB

Strategy to ensure equitable access to rapid diagnostics.

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**eCollection 2025.**

A correlation analysis between nutritional status and physical function in the

elderly with pulmonary tuberculosis.

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T(1), Li Y(1), Long X(3), Zhang M(3), Yang X(2), Hu Y(1).

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**BACKGROUND:** Malnutrition is a significant risk factor contributing to the

progression of the elderly with pulmonary tuberculosis (TB). This study aimed to

evaluate the nutritional status of the elderly with pulmonary TB using the Mini

Nutritional Assessment (MNA) and explore the relationship between their

nutritional status and physical function.

**METHODS:** This was a cross-sectional survey study. Data collection was from July

2023 to March 2024. 532 the elderly with pulmonary TB who were admitted to a

tertiary infectious disease hospital in Chengdu were included in this analysis.

The nutritional status of the patients was evaluated using MNA, and they were

divided into well-nourished group (≥24 points) and abnormal-nourished group (<24

points). This study assessed physical function using the Berg Balance Scale

(BBS), the Timed Up and Go test (TUG), and the Five-Times-Sit-to-Stand Test

(FTSST). Clinical data and physical function of the two groups were compared,

and the correlation between nutritional score and physical function was

analyzed.

**RESULTS:** There were 109 cases (20.5%) in well-nourished group and 423 cases

(79.5%) in abnormal-nourished group. Compared with well-nourished group, the

abnormal group showed a decrease in the BBS scores [(52.55 ± 7.10) vs

(43.20 ± 16.29), p < 0.05], and an increase in the TUG [9.00 (7.00, 10.00) vs

9.00 (7.40, 12.00), p < 0.05] and the FTSST [12.00 (9.00, 14.75) vs 15.00

(10.00, 20.10), p < 0.05]. Correlation analysis showed that the nutritional

score of patients was positively correlated with the BBS scores (r = 0.474,

p < 0.001), and negatively correlated with the TUG (r = -0.200, p < 0.001) and

the FTSST (r = -0.501, p < 0.001).

**CONCLUSIONS:** Malnutrition is common in the elderly with pulmonary TB.

Nutritional status in these patients is associated with the BBS scores, the TUG,

and the FTSST.

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and source are credited.

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**ahead of print.**

Ultra-high field strength electroporation enables efficient DNA transformation

and genome editing in nontuberculous mycobacteria.

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Efficient DNA delivery is essential for genetic manipulation of mycobacteria and

for dissecting their physiology, pathogenesis, and drug resistance. Although

electroporation enables transformation efficiencies exceeding 10⁵ CFU per µg DNA

in Mycobacterium smegmatis and Mycobacterium tuberculosis, it remains highly

inefficient in many nontuberculous mycobacteria (NTM), including Mycobacterium

abscessus. Here, we discovered that NTM such as M. abscessus exhibit exceptional

tolerance to ultra-high electric field strengths and that hypertonic

preconditioning partially protects cells from electroporation-induced damage.

Using ultra-high electric field strength (3 kV/mm) electroporation, we achieved

dramatic improvements in plasmid transformation efficiency-up to 106-fold in M.

abscessus, 83-fold in Mycobacterium marinum, and 37-fold in Mycobacterium

kansasii-compared to standard conditions (1.25  kV/mm). Transformation

efficiency was further influenced by the choice of selectable marker. Ultra-high

field strength electroporation also markedly enhanced allelic exchange in M.

abscessus expressing Che9c RecET recombinases, increasing the recovery of gene

deletion mutants by over 1,000-fold relative to conventional electroporation. In

parallel, oligonucleotide-mediated recombineering for targeted point mutations

produced nearly 10,000-fold more mutants under ultra-high field conditions.

Together, these findings establish ultra-high field electroporation as a robust,

broadly applicable platform for genetic engineering of NTMs. This method

substantially enhances transformation efficiency and enables construction of

advanced genetic tools-including expression libraries and CRISPRi knockdown

libraries-in species that have historically resisted genetic

manipulation**. IMPORTANCE** Infections caused by nontuberculous mycobacteria (NTM),

including Mycobacterium abscessus, are increasing globally, yet genetic

manipulation of these pathogens remains technically challenging due to

inefficient DNA delivery and low gene editing success. The ultra-high electric

field strength electroporation strategy described here overcomes these barriers,

enabling dramatic improvements in both transformation and genome editing

efficiency. This advance paves the way for high-throughput functional genomics

in NTMs, including the construction of genome-wide knockout, CRISPRi knockdown,

and expression libraries. Broad adoption of this approach will accelerate

discovery of genetic determinants of virulence and drug resistance, facilitating

the development of antimicrobials and vaccines.

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**11. China CDC Wkly. 2025 Aug 22;7(34):1106-1113. doi: 10.46234/ccdcw2025.186.**

Auxiliary Diagnostic Value of the Interferon Gamma-Induced Protein 10 mRNA

Release Assay for Tuberculosis in People Living with HIV/AIDS - Beijing

Municipality, China, 2022-2024.

Yan H(#)(1), Duan H(#)(2), Han X(1), Sun J(1), Liang Q(2), Zhao Y(3), Ma Z(1),

Ding N(1), Ren M(1), Jiang T(1), Zhang T(1), Su B(1)(4).

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**INTRODUCTION:** Diagnosing tuberculosis (TB) in HIV-infected individuals presents

significant challenges due to difficulties in obtaining specimens containing

adequate quantities of Mycobacterium tuberculosis (Mtb). This study aimed to

evaluate the diagnostic performance of the IP-10 mRNA assay independently and in

combination with established diagnostic tests for Mtb detection.

**METHODS:** The study cohort comprised 111 HIV-infected individuals who presented

with TB at Beijing Youan Hospital from 2022 to 2024. Participants were

categorized into confirmed TB, probable TB, or non-TB groups according to the

diagnostic criteria for tuberculosis (WS288-2017). The performance of the IP-10

mRNA release assay was evaluated by the STARD guidelines on blood samples

collected after enrollment.

**RESULTS:** The IP-10 mRNA release assay demonstrated significantly higher

sensitivity than interferon-γ release assays (IGRAs) and culture methods for

confirming pulmonary tuberculosis (PTB) diagnosis while maintaining comparable

specificity. Receiver operating characteristic (ROC) analysis revealed that the

diagnostic performance of the IP-10 mRNA release assay used in parallel with

Xpert MTB/RIF significantly exceeded that of the IP-10 mRNA release assay alone

(0.731 vs. 0.687, P=0.02). Among HIV-infected individuals, the IP-10 mRNA

release assay showed superior performance compared to IGRAs for diagnosing

extrapulmonary tuberculosis.

**CONCLUSIONS:** The IP-10 mRNA release assay exhibited excellent diagnostic

performance and demonstrates substantial potential as an auxiliary tool for

diagnosing TB in HIV-infected individuals. The combined application of IP-10.TB

and Xpert MTB/RIF further enhance diagnostic efficacy.

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Altered T Lymphocytes Mitochondrial Function and Inflammatory Factors of

Peripheral Blood in HIV Patients With Mycobacterial Infection.

Wang M(1), Dong X(2), Wan H(1), Shi J(1), Hui L(1), Chen W(1), Liu S(1), Yan

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To characterise T-cell immunity and inflammatory profiles in HIV patients with

mycobacterial co-infections. This study enrolled 41 HIV patients co-infected

with Mycobacterium tuberculosis (HIV-TB, n = 27) or non-tuberculous mycobacteria

(HIV-NTM, n = 14), along with 30 controls (20 HIV-monoinfected, 10

post-treatment) from a single centre. Flow cytometry quantified T-cell subsets

(CD3 + CD4+, CD3 + CD8+, CD28+ subsets), mitochondrial parameters (mass [MM],

low membrane potential [MMP-low%]) and cytokines (IFN-γ, IL-2/4/6/10/17A,

TNF-α). Co-infected groups showed reduced T-cell counts versus HIV-monoinfected

controls (p < 0.05). Elevated MMP-low% in CD3 + CD4+/CD28+ T cells indicated

mitochondrial dysfunction in co-infected patients (p < 0.05). HIV-TB patients

exhibited higher CD3 + CD4+/CD28+/CD8+ T-cell MM than HIV-NTM (p < 0.05), while

HIV-NTM demonstrated greater MMP-low% (p < 0.05). Proinflammatory cytokines

(IFN-γ, IL-6, IL-17A) inversely correlated with CD4+ counts and MM, but

positively with CD8 + CD28+ MMP-low%. MMP-low% in CD3 + CD4 + CD28+ T cells and

IL-2 differentiated IRIS/non-IRIS cases (p < 0.05), with combined AUC = 0.834

for IRIS prediction (p = 0.001). HIV/mycobacterial co-infection exacerbates

T-cell depletion and mitochondrial dysfunction, with HIV-NTM showing more severe

impairment. MMP-low% and IL-2 may serve as biomarkers for IRIS risk

stratification.

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**13. Front Mol Biosci. 2025 Aug 26;12:1613454. doi: 10.3389/fmolb.2025.1613454.**

**eCollection 2025.**

Insights into the protein ubiquitinome in the host‒pathogen interplay during

Mycobacterium tuberculosis infection.

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

of manipulating and circumventing the host's immune system to establish

infection. Ubiquitination plays a crucial role in the host's response to

pathogens; however, the global alterations in protein ubiquitination during Mtb

infection remain poorly understood. To elucidate the regulatory roles of

ubiquitination in the immune response to Mtb, we investigated the ubiquitome of

human macrophages following Mtb infection. In our study, we identified a total

of 1,618 proteins exhibiting altered ubiquitination levels, with 1,182

lysine-ubiquitination sites in 828 proteins showing increased ubiquitination and

1,077 sites in 790 proteins displaying decreased ubiquitination. Bioinformatics

analyses revealed that most proteins involved in the immune response were

upregulated, including those associated with autophagy, lysosome, the NF-κB

signaling pathway, necroptosis, and ferroptosis. Furthermore, the ubiquitination

levels of numerous proteins involved in conserved physiological processes, such

as ribosome biogenesis, spliceosome function, nucleocytoplasmic transport, and

mRNA surveillance, were also altered, suggesting that these pathways may be

regulated by ubiquitination during Mtb infection. The extensive pool of

ubiquitinated proteins and sites identified in this study will serve as a

valuable resource for understanding the regulatory mechanisms of the

ubiquitination system in immune responses during Mtb infection.

Copyright © 2025 Feng, Lin, Huang, Li, Xu, Ye and Zhang.

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**eCollection 2025.**

Latent class analysis of inflammation and drug-induced liver injury phenotypes

in older tuberculosis patients: associations with anxiety, depression, and

insomnia.

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**INTRODUCTION:** Anxiety, depression, and insomnia are common among older patients

with tuberculosis (TB), yet their associations with inflammatory responses and

drug-induced liver injury (DILI) remain insufficiently explored. This study

aimed to identify distinct inflammation-DILI phenotypes in older TB patients and

examine differences in anxiety, depression, and insomnia across subgroups.

**METHODS:** In this cross-sectional study, 251 older TB patients were evaluated.

Serum inflammatory markers and liver function indicators were collected, along

with standardized assessments of anxiety, depression, and insomnia. Latent class

analysis (LCA) was employed to classify inflammation-DILI phenotypes, and

multinomial logistic regression was used to explore associations between

subgroup characteristics and mental health outcomes.

**RESULTS:** Three latent subgroups were identified: (1) moderate inflammation with

normal liver function (83.2%), (2) mild inflammation with abnormal liver

function (5.3%), and (3) severe inflammation with normal liver function (11.5%).

Compared with the moderate inflammation group, the severe inflammation group

exhibited significantly higher rates of anxiety, depression, and insomnia.

Alcohol consumption was a significant risk factor for severe inflammation (P <

0.05), while smoking was associated with mild inflammation and abnormal liver

function (P < 0.05).

**CONCLUSION:** Distinct inflammation-DILI phenotypes exist among older TB patients

and are associated with varying psychological symptom burdens. Monitoring

inflammatory markers, liver function, and mental health symptoms-especially

insomnia, anxiety, and depression-may facilitate more personalized care in this

vulnerable population.

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**15. Medicine (Baltimore). 2025 Sep 5;104(36):e44221. doi:**

**10.1097/MD.0000000000044221.**

Miliary tuberculosis and central nervous system infection caused by hematogenous

transmission from a primary subcutaneous tuberculous abscess: A case report.

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**RATIONALE:** We report an extremely rare case in which delayed diagnosis and

treatment of Mycobacterium tuberculosis infection primarily involving the

subcutaneous tissues of an extremity led to hematogenous dissemination of the

infection and subsequent deterioration of the patient.

**PATIENT CONCERNS:** An 82-year-old man presented to our hospital with a painful

mass on the right ankle for over a year, as well as persistent fever and

shortness of breath for >14 days. He received piperacillin/tazobactam followed

by meropenem, which failed to decrease his peak temperature.

**DIAGNOSES:** After performing chest computed tomography, acid-fast staining of the

abscess specimen, GeneXpert M tuberculosis/rifampin assay, and cerebrospinal

fluid tests, the patient was diagnosed with miliary pulmonary tuberculosis and

tuberculous meningitis hematogenously transmitted from a primary subcutaneous

tuberculous abscess.

**INTERVENTIONS:** Isoniazid, rifampin, levofloxacin, linezolid, and ethambutol were

administered through a nasogastric tube to treat the tuberculosis, and 5 mg of

dexamethasone was administered to reduce the inflammatory response.

**OUTCOMES:** The treatment was halted because of poor compliance, and the patient

died of respiratory failure within 1 month of returning home.

**LESSONS:** We suggest tuberculosis screening or biopsy recommendations for chronic

soft tissue swellings in high tuberculosis-burden areas, to avoid missed or

delayed diagnosis.

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**16. Evol Med Public Health. 2025 Jul 1;13(1):167-175. doi: 10.1093/emph/eoaf014.**

**eCollection 2025.**

Within-host population dynamics of extensively drug-resistant Mycobacterium

tuberculosis revealed by an over 3-year longitudinal study.

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**BACKGROUND AND OBJECTIVES:** Drug resistance is a major contributor to

tuberculosis (TB) deaths worldwide. Understanding the dynamics of in-host

evolution of Mycobacterium tuberculosis (MTB) drug resistance can help to

improve treatment success rates.

**METHODOLOGY:** The microevolution of drug-resistant MTB was studied in three

patients with long-standing, extensively drug-resistant TB (XDR-TB) by analyzing

whole genome sequences of serial isolates collected during treatment.

**RESULTS:** We identified three patterns of in vivo MTB microevolution during

long-term, ineffective treatment: (i) new drug-resistant subpopulations emerge

and compete with other subpopulations during treatment; (ii) drug resistance

profiles remaining stable without the emergence of new drug-resistant

subpopulations; and (iii) after a drug is stopped, new drug-resistant

subpopulations continue to emerge and compete with existing subpopulations.

**CONCLUSIONS AND IMPLICATIONS:** The microevolution of drug-resistant MTB within

patients on long-term ineffective treatment is complex. Subpopulations with

different resistance-conferring mutations can compete with each other and with

newly emerged subpopulations. Often, one subpopulation eventually dominates and

achieves long-term stability. This work deepens the understanding of MTB

microevolution in XDR-TB patients.

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**17. Front Endocrinol (Lausanne). 2025 Aug 21;16:1617292. doi:**

**10.3389/fendo.2025.1617292. eCollection 2025.**

Inhibition of CYP450 family 1 subfamily B member 1 (CYP1B1) expression in

macrophage reduces the inflammatory response in type 2 diabetes mellitus

combined with tuberculosis.

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Type 2 diabetes (T2DM) and tuberculosis (TB) both regulate inflammation and may

exert synergistic or antagonistic effects through shared immune pathways.

Previous studies have demonstrated that T2DM is a risk factor for TB. However,

at the level of gene regulatory networks, it remains unclear whether there are

key interaction nodes linking these two diseases. In this study, we integrated

bioinformatic analysis from the Gene Expression Omnibus (GEO) database and

performed differential gene expression analysis and weighted gene co-expression

network analysis (WGCNA). Furthermore, we applied machine learning techniques to

identify key genes among the commonly differentially expressed genes (DEGs). In

addition, this study employed siRNA in THP-1 cells to validate the cross-talk

genes selected through bioinformatic analysis. The THP-1 cells were treated with

high-concentration glucose (15.5 μM, Glu), Mycobacterium tuberculosis ESAT-6, or

Glu+ESAT-6. We identified a total of 23 common genes between TB and T2DM using

DEGs and WGCNA. Furthermore, expression patterns from external datasets revealed

three key cross-talk genes linking TB-T2DM: CYP1B1, SERPING1, and CHPT1.

Notably, only CYP1B1 was significantly upregulated in the THP-1 detection test,

compared to the unstimulated (control) group (P < 0.05). Moreover, CYP1B1

significantly reduced the expression of pro-inflammatory cytokines (TNF-α, IL-6, IL-1β, IL-10), M2 macrophage polarization markers (CD163, Arg-1), and chemokines (CXCL-10), and was associated with the NOD2 and TRAF6 signaling pathways (P < 0.05). These findings elucidate the regulatory mechanisms underlying the comorbidity of TB and T2DM, providing a theoretical basis for the development of precise combination therapies and novel therapeutic targets.

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**Online ahead of print.**

Host-directed immunotherapy to enhance treatment of Mycobacterium tuberculosis

infection.

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Tuberculosis (TB), caused by Mycobacterium tuberculosis (MTB), remains one of

the leading causes of morbidity and mortality worldwide, particularly in low-

and middle-income countries. The extensive use of antibiotics has led to the

emergence of multidrug-resistant and extensively drug-resistant MTB strains,

intensifying the challenges associated with TB treatment. In this context,

host-directed immunotherapy has emerged as a promising adjunct strategy that

aims to modulate the host immune response rather than directly targeting the

pathogen. By leveraging host-pathogen interactions, such approaches may enhance

immune clearance, reduce treatment duration, and limit tissue damage. This

review comprehensively summarizes current knowledge on host immune responses to

MTB infection, mechanisms of immune defense, recent advances in host-targeted

immunotherapeutic interventions and the challenges for TB treatment. A deeper

understanding of these host-directed therapies is crucial for combating MTB

infections and offers novel, resistance-independent treatment options to

counteract resistance issues in TB management. Combining host-directed therapies

with conventional antibiotics may improve treatment outcomes and reduce drug

resistance, though further optimization in terms of delivery systems, efficacy,

and safety remains necessary.

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