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Pathogenicity and Antimicrobial Resistance of Mycobacterium Tuberculosis: A Review Article

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Abstract

Mycobacterium tuberculosis (Mtb) induced tuberculosis (TB), is a severe public health problem world widely because of its intricate pathobiology and increasing antimicrobial resistance. Mtb possess a repertoire of virulence factors that can enable it to remain alive within cells, escape the immune system to form granulomas (multi-cellular aggregates), establish latency, and reactivate disease, which complicates the control and elimination of this disease. Concurrently, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB has made conventional antimicrobial therapy dramatically less effective, with prolonged treatment durations and worse clinical outcomes. Resistance arises through chromosomal mutations, efflux pump-- mediated resistance, and by phenotypic drug tolerance as well as due to limited penetration of drugs across the hydrophobic mycobacterial cell wall. Advances in molecular diagnostics, whole genome surveillance and development of new therapies such as a few host-directed therapies and also the experimental anti-virulence strategies have led to an improved understanding about TB pathogenesis and resistance dynamics too. This review highlights the emerging disease-causing of Mycobacterium tuberculosis and offers an overview of currently growing sources of antimicrobial resistance and treatment management issues, seeking to steer possible future direction for TB control and management.

Keywords: Pathogenicity, Antimicrobial Resistance, Mycobacterium tuberculosis

Introduction

Tuberculosis caused by the pathogen Mtb, remains within the top 10 leading causes of death from an infectious agent, and continues to be a global health challenge, despite the many advancements in the development active preventive vaccines and antimicrobial treatment paradigms. Despite the detailed and broad approaches undertaken over the past decades, recent estimates have shown that TB remains one of the leading causes of morbidity and mortality, especially in low and middle countries where high burden of comorbid conditions and social determinants of health further hamper the response to disease prevention, diagnosis, and treatment (Nasiri & Venketaraman, 2025). This complex process includes a dynamic interplay of Mtb virulence factors and host defense mechanisms that facilitate Mtb survival, acquisition of antibiotic tolerance and can also lead to immune escape and treatment failure. Hence, knowledge regarding virulence mechanism of the pathogen and modifications of antimicrobial therapy protocols are needed to formulate proper measures of control (Rahman et al., 2025).

The mechanism behind the pathogenicity of Mtb is characterized by a specific dormant lifestyle, followed by survival and evasion of host immune mechanisms and chronic disease. The bacterium possesses inter-cellular pathogen specialized virulence factors such as secretion of immunomodulatory proteins, lipid-rich cell envelope components and metabolic flexibility to survive within macrophages and evade host antimicrobial mechanisms (Nasiri & Venketaraman, 2025). The granuloma, a well-known hallmark of TB pathophysiology, has a dual role: while the granuloma contains the spread of infection (i.e., bacilli), it also provides a niche for Mtb where replication is favoured (immune pressure is low) and can become latent and therefore evade immune clearance. The evolution of immune evasion in the host adds complexity to the rendering of sterilizing immunity and partly accounts for the high burden of latent TB infection that we estimate affects billions globally. Therefore, chronic infection thus provides a strong reservoir for future disease expression and transmission highlighting the need for a better understanding of Mtb host–pathogen interactions (Ehlers & Schaible, 2013).

Abstract Mtb employs a sophisticated array of virulence factors during TB pathogenesis and primes itself to survive in a toxic host environment. These are cell wall-associated glycolipid molecules that confer resistance to oxidative stress and impede phagosome-lysosome fusion, immune-modulatory proteins such as ESAT-6 and CFP-10 that deregulate host immune signaling, and effector molecules that modify host cell metabolic programs. (Mboowa, 2025). In recent years, molecular immunology approaches have provided insights into these mechanisms and the methods by which Mtb can exploit autophagy, cytokine responses, and pathways of macrophage cell death to facilitate intracellular persistence and inhibit appropriate host responses. This is crucial information for discovering new therapeutic targets that can block the ability of this bacterium to outrun the immune system of its host (Nasiri & Venketaraman, 2025).

However, this increasingly profound understanding of Mtb virulence is counteracted by widespread development and spread of drug-resistant strains making antimicrobial therapy less effective. The MDR-TB and XDR-TB Mtb strains have considerably increased concerns about their associated clinical importance and public health implications due to their high mortality rates, prolonged treatment regimens, and limited treatment choices available (Al-Asady & Ali, 2025). Genetic mutation causing impact on drug targets, Upregulated efflux pump, ultrastructural cell wall changes leading to drug less penetration or less efficacy are some mechanisms of resistance. These adaptations not only compromise existing first-line therapies (e.g., isoniazid and rifampicin) but also threaten the utility of more recent agents, which warrants further studies on alternative or add-on treatment strategies (Jowsey et al., 2024).

In response, the TB therapeutics pipeline has developed with deliveries of new optimized antimicrobial regimens including host-directed therapies and immunomodulatory and/or immunotherapy strategies, which is necessary to improve treatment efficacy while limiting resistance selection pressures. This will include rifapentine-based regimens delivered in shorter courses (non-inferior to standard therapy (Al-Asady & Ali, 2025; Lukas et al., 2025) for drug-sensitive TB that may improve adherence and reduce toxicity. Further, a number of host-directed therapies are being developed to modify inflammatory pathways (e.g., IL-1β or IL-17), autophagy, or immune exhaustion and may be either added to LBTIs to enhance bacterial clearance and/or decrease other immunopathology manifestations; however, these agents remain in early clinical development. However, besides these advances immunotherapy strategies like adjunctive cytokines or therapeutic vaccines also offer a possible way to enhance host response while contributing to durable responses (Lyu et al., 2025.(

Alternative means of controlling the spread of drug-resistant TB exclude pharmacological interventions with therapeutic and preventive strategies (such as bacteriophage therapy). Mycobacteriophages—viruses that infect and lyse mycobacterial species—demonstrate activity in granuloma-like, hypoxic and acidic conditions against virulent Mtb strains, potentially offering treatment value through mechanisms that differ from traditional antibiotics. Phage therapy and phage-derived agents are still experimental, however, their potential ability to lyse MTB while evading existing resistance mechanisms makes them a potential therapeutic avenue to investigate along with TB control efforts (Jeyasankar et al., 2024).

The inadequacies of current TB control efforts make an even stronger case for better diagnostic, therapeutic, and preventive tools. Fast, accurate Mtb infection and drug resistance detection is essential for control, yet continues to be a challenge decades later, particularly in contexts where traditional smear microscopy is of low sensitivity and where molecular diagnostics are not widely available. Development of diagnostic platforms such as genotypics-actuated surveillances, point-of-serve metallic testings, and animation intelligence-boosted imaging, to allow early interventions to minimize spread. That is exactly where genomic surveillance can assist, both in understanding transmission dynamics as well as gaining information on emerging resistance patterns that in turn guides public health response and optimizes therapeutic regimen. (Mboowa, 2025).

Pathogenesis of Mycobacterium tuberculosis

Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is a highly specialized intracellular pathogen, successful largely because of its ability to survive within the human host for extended periods of time. The pathogenesis of TB is therefore a complex, multi-step process that includes initial infection with mycobacteria, evasion of the immune system, intracellular survival and replication, formation of essential granuloma structures, the ability to persist in a state of latency, and ultimately, if the host becomes immunocompromised, the potential for reactivation (table 1). The understanding of these mechanisms is basic for the improvement of diagnostic strategies, therapeutic interventions, and vaccine development (Mohammadnabi et al., 2024).

Mtb transmission is mainly through inhalation of aerosolized droplets released by individuals with active pulmonary TB. Mtb is phagocytosed by the first line of host defense: resident alveolar macrophages, upon reaching the alveoli. Mtb is different from many other bacteria in the sense that it is able to replicate within macrophages by hijacking the normal phagosomal maturation process. Among them, Mtb blocks phagosome–lysosome fusion, disallows phagosome acidification, and survives reactive oxygen and nitrogen species by expression of antioxidant enzymes including, but not limited to, catalase-peroxidase (KatG), and superoxide dismutase (Nasiri & Venketaraman, 2025).

The Mtb cell wall — one of the most characteristic aspects of bacterial pathogenicity — is distinguished by the presence of mycolic acids in addition to an abundance of lipoarabinomannan (LAM), trehalose dimycolate, and other complex lipid constituents (2–5). Such factors are important for immune modulation, antimicrobial peptide resistance, and intrahost persistence. For example, lipoarabinomannan acts by targeting host signaling cascades, regulating pro-inflammatory cytokine generation, and clamping macrophage activation to promote bacterial viability in the cell. Intrinsic antibiotic resistance and mycobacterial slow bacterial growth is also significantly linked to the impervious nature of mycobacterial cell envelope (Mboowa, 2025).

Innate immune responses after initial infection induce the migration of other immune cells like monocytes, neutrophils, and dendritic cells to the infection site (1). Dendritic cell-mediated antigen presentation drives $CD4^+$ T helper 1 (Th1) cell activation with production of of both IFN-γ and TNF-α. These cytokines are necessary for the activation of macrophages and restriction of infection. However, rather than being killed, Mtb often achieves a state of equilibrium where bacterial proliferation is limited but not cleared (Nasiri & Venketaraman, 2025).

To achieve this immune containment, granulomas, a defining feature of TB pathology develop, which further allows for containment of TB. Granulomas are organized aggregates of macrophages, epithelioid cells, multinucleated giant cells, lymphocytes and fibroblasts. Granulomas can contain an infection and limit spread but also forming a supportive niche for bacteria to persist. Mtb have evolved mechanisms through either metabolic characteristics or adaptations in the granuloma, where they can regulate their oxygen consumption and enter a non-replicating or dormant state, and adaptive stress responses, such as that regulated by the DosR system, to survive in hypoxic, nutrient-limited, and acidic environments (Lyu et al., 2025).

Latent tuberculosis infection (LTBI) is the consequence of effective host immune control of Mtb without its complete clearance. Although the people with LTBI are asymptomatic, not contagious, they have living bacteria that can become active later in life. Immunosuppression (HIV infection, diabetes mellitus, malnutrition, aging, or immunosuppressive therapies) Reactivation Granuloma integrity is compromised during reactivation and permits the replication and dissemination of bacilli—especially in the lungs—which results in active tuberculosis (TB) disease (Nasiri & Venketaraman, 2025).

On a molecular level, Mtb utilize a broad complexity of virulence factors to modulate immune responses from the host. The ESX-1 secretion system (importantly involved in the export of early secreted antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10, PDB ID: 3CBQ)) is critical for providing access to the cytosol, disrupting the phagosomal membrane, and modulating host cell death pathways. They enhance tissue injury, dissemination of bacteria, and evasion of the immune system. Even more significantly, Mtb also commandeers the apoptosis and necrosis pathways for the advantage of bacterial persistence and spread [61].

Another important host-based factor that impacts TB pathogenesis is the heterogeneity of host responses to infection. As has been discussed, unregulated inflammation is a destructive process leading to cavitation by uncontrolled bacterial replication because of insufficient immune system activation. This delicate balance also recapitulates the dual nature (pathogenic and protective) of host immunity. Recent investigations in 2025 point to host genetics, immune checkpoints, and metabolic reprogramming as important modulators of disease outcomes (Lyu et al., 2025).

Recent insights into TB pathogenesis are also linked to the resurgence of evidence gained by exploring host-directed pathways during TB pathogenesis such as those involved in autophagy and lipid metabolism and exhaustion of immunity. It induces lipid droplet uptake in macrophages, which can be ordered at a and hare the sources of nutrients, and it also directly forces the repression of autophagic pathways that would otherwise be far more able to clear the pathogenic Mtb. Thus, these disease mechanisms further underscore Mtb pathogenesis and the ability of Mtb to take control of the biology of the host to promote its own survival (Nasiri & Venketaraman, 2025).

Table1. The biological function, role in pathogenesis and clinical implications of the main virulence factors of Mycobacterium tuberculosis

Virulence factor	**Biological function**	**Role in pathogenesis**	**Clinical implication**
Mycolic acids	Cell wall integrity and impermeability	Protects Mtb from host defenses and antibiotics	Contributes to intrinsic drug resistance
Lipoarabinomannan (LAM)	Immune modulation	Inhibits phagosome–lysosome fusion and macrophage activation	Promotes intracellular survival
ESX-1 secretion system (ESAT-6, CFP-10)	Protein secretion	Disrupts phagosomal membrane; enhances dissemination	Associated with virulence and tissue damage
KatG (catalase-peroxidase)	Oxidative stress defense	Neutralizes reactive oxygen species	Also linked to isoniazid activation/resistance
DosR regulon	Dormancy regulation	Enables survival under hypoxia and nutrient limitation	Facilitates latent TB infection
Efflux pumps	Drug extrusion	Reduces intracellular drug concentration	Contributes to multidrug resistance

Antibiotic Resistance

Background: Antimicrobial resistance (AMR) in Mycobacterium tuberculosis (Mtb) poses an enormous threat to global TB(tuberculosis) control, resulting in the ineffectiveness of standard therapeutic regimens and increased morbidity and mortality on a global scale. Tuberculosis (TB) remains one of the deadliest infectious disease killers globally and the slow rise of drug-resistant strains threatens to reverse progress in the global TB programme towards reducing the burden and mortality of the disease. Multidrug- and extensively drug-resistant (MDR- and XDR-) TB calls for immediate solutions outside the classic treatment paradigms and a comprehensive understanding of the mechanisms of resistance (Dheda et al., 2017).

MDR-TB is considered to be resistance to at least INH and RIF, the most effective first line anti-TB drugs (table 2). Chromosomal mutations that modify sites targeted by antibiotics, or pathways used to activate drugs will also lead to the survival of Mtb in the presence of therapeutic concentrations of these drugs, such resistance is classified as Mdr. Rifampicin (RIF) is a first line antituberculosis drug that targets the βsubunit of RNA polymerase, whose expression is encoded by the rpo B gene, and the main mechanism of RIF resistance is the mutation of the rifampicin-resistance–determining region (RRDR) in rpoB. Likewise, the pro-drug INH is activated by the katG-encoded catalase–peroxidase, and mutations in katG or the inhA promoter decrease activation and binding of the drug, leading to resistance. Such genetic modifications disrupt drug action whilst maintaining fundamental bacterial fitness, and they can arise under the selective pressure of inappropriate or inadequate treatment (Ye et al., 2021).

Resistance has extended to second-line agents including fluoroquinolones and injectable aminoglycosides (amikacin, kanamycin) that are essential drugs to treat MDR-TB. Mutations in fluoroquinolone resistance genes (gyrA and gyrB) and mutations in ribosomal RNA or modifying enzymes conferring aminoglycoside resistance have been identified via genomic studies in MDR isolates. Such molecular adaptations represent an evolutionary response to chronic antibiotic pressure, highlighting one mechanism through which Mtb can gradually acquire resistance determinants to several drug classes (Falzon et al., 2013).

Apart from the chromosomal mutations that confer inherited resistance to the drugs, Mtb also demonstrates what is termed tolerance and phenotypic adaptation that hinders treatment. Unlike classical resistance, where bacteria grow in the presence of antibiotics, tolerance is defined as the ability of bacteria to survive transient exposure to antibiotics without genetic change. Mtb has a unique slow growth rate and physiology which also contributes to antibiotic tolerance, since many antibiotics work on fast growing cells (Li et al., 2022). The less susceptibility of dormant or metabolically altered Mtb subpopulations to drug killing in granulomas leads to persistent infection even with long-term therapy. Such tolerant bacteria can resume growth after antibiotic concentrations are lowered, leading to treatment failure and recurrence (Aljeldah, 2020).

Mtb cell envelope is a key intrinsic component for drug resistance. The impermeability of their unique cell wall, which is largely composed of mycolic acids and layered with complex glycolipids, is characterized by low drug permeability and low rates of penetration of antibiotics. The barrier provides low permeability, which reduces the effective concentrations of many antimicrobials, particularly hydrophilic ones, within the bacterium requiring elevated doses or drug combinations to provide effects in the therapeutic range. Alongside a group of efflux pump systems dedicated to preventing passive elimination of antibiotics from the bacterial cytosol, this attribute renders mycobacteria intrinsically and acqui red resistant (Roque-Borda et al., 2025)

Mtb efflux pumps are an ancient adaptation to antibiotic stress that can be co-opted and turned on and off in response to rapid antibiotic pressure without the need for a genomic mutant to arise (Guo et al., 2025). This class of transmembrane proteins, which encompass several superfamilies, extrudes broad panels of drug molecules, leading to reduced intracellular concentrations and prolonged bacterial killing. Expression of efflux pumps can be induced by exposure to antibiotics and is associated with both intrinsic (nature) and adaptive (acquired) resistance mechanisms to drug therapy evidence. These mechanisms are precisely why single agent therapy or intermittent treatment may select a resistant subpopulation (Szumowski et al., 2013).

Beyond the standard categories of genetic resistance we also come to the issue of heteroresistance, when within a single patient you have a mixture of susceptible and resistant bacilli which adds yet another diagnostic and therapeutic challenge. When the resistant pathogens represent a very small proportion of the entire population, conventional assays can have a negative predictive value and this routinization of resistance under treatment can result in the low identified resistance and inappropriate therapy combined with their selective amplification through the so-called vicious circle associated with heteroresistance. This is a good example of the need for molecular diagnostics more sensitive than available currently to identify the presence of relatively subtle patterns of resistance to guide meaningful therapy (Ye et al., 2021).

At both ends of the AMR–TB crisis continuum, innovation is required to transform these needs into research priorities. Point-of-care and rapid diagnostics that can rapidly and accurately identify drug resistance (eg, GeneXpert and line probe assays) are important for early diagnosis and treatment of drug-resistant TB to prevent TB transmission. Parasite genetics — Resistance profiling can guide tailored regimens to better outcomes for patients and to reduce the selection of further resistant strains. New drugs, repurposed drugs and host-directed therapy are additional avenues that are being investigated to overcome conventional resistance mechanisms (Chauhan et al., 2021).

Table 2. Mode of action of antibiotic resistance in Mycobacterium tuberculosis

Drug class	**Key gene(s) involved**	**Mechanism of resistance**	**Clinical relevance**
Isoniazid (INH)	*katG*, *inhA*	Reduced pro-drug activation or target modification	Leads to MDR-TB when combined with rifampicin resistance
Rifampicin (RIF)	*rpoB*	Alteration of RNA polymerase β-subunit	Strong predictor of MDR-TB
Fluoroquinolones	*gyrA*, *gyrB*	DNA gyrase mutations	Defines pre-XDR and XDR-TB
Aminoglycosides	*rrs*, *eis*	Ribosomal alteration or drug modification	Limits second-line treatment options
Ethambutol	*embB*	Impaired arabinosyl transferase activity	Often co-exists with INH resistance
Multiple drugs	Efflux pump genes	Reduced intracellular drug concentration	Contributes to tolerance and stepwise resistance

Conclusion

The exceptional pathogenicity of Mtb coupled with the growing threat of antimicrobial resistance calls for continued basic and clinical research into TB. Understanding the molecular basis of host–pathogen interaction & disease pathobiology, developing better therapeutic and preventive strategies against TB will be crucial for mitigating the global burden of TB, curing & improving treatment & preventive outcomes, and ultimately for several nations to meet the TB elimination targets. Mycobacterium tuberculosis pathogenesis involves the interplay of host-derived and mycobacterial virulence factors. The global prowess of Mtb as a human pathogen is largely attributable to its adaptation to persist in macrophages, with some bacteria forming granulomas, entering a quiescent state and subsequently reactivating when the conditions permit. Identifying and characterising these pathogenic mechanisms will require novel and/or existing technologies; this work will be pivotal to overcoming barriers to development of improved diagnostics, more effective antimicrobial therapy, and novel host-directed interventions critical to long-term TB control and elimination. In summary,Mtb acquires antibiotic resistance through chromosomal mutations, physiological traits, cell envelope hurdles and efflux mechanisms that enabled the pathogen to survive under the stress of the antibiotics employed. The persistence spread of MDR and XDR TB globally underscores the role of active surveillance systems, resilient diagnostic tools and new therapeutic regimens to address drug-resistant TB and maximize patient management.

References

1. Al-Asady, I. N., & Ali, J. F. (2025). Host-pathogen interactions in *Mycobacterium tuberculosis*: Molecular mechanisms and implications for treatment. *International Journal of Medical Science and Dental Health, 10*(11), 73–80. https://doi.org/10.55640/ijmsdh-10-09-07

2. Aljeldah M. M. (2020). Antibiotic sensitivity of *Mycobacterium tuberculosis* isolates; a retrospective study from a Saudi tertiary hospital. *Journal of Taibah University Medical Sciences*, *15*(2), 142–147. https://doi.org/10.1016/j.jtumed.2020.01.003
3. Chauhan, A., Kumar, M., Kumar, A., & Kanchan, K. (2021). Comprehensive review on mechanism of action, resistance and evolution of antimycobacterial drugs. *Life sciences*, *274*, 119301. https://doi.org/10.1016/j.lfs.2021.119301
4. Dheda, K., Gumbo, T., Maartens, G., Dooley, K. E., McNerney, R., Murray, M., … Lange, C. (2017). The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. The Lancet Respiratory Medicine, 5(4), 291–360. https://doi.org/10.1016/S2213-2600(17)30079-6
5. Ehlers, S., & Schaible, U. E. (2013). The granuloma in tuberculosis: dynamics of a host-pathogen collusion. *Frontiers in immunology*, *3*, 411. https://doi.org/10.3389/fimmu.2012.00411
6. Falzon, D., Gandhi, N., Migliori, G. B., Sotgiu, G., Cox, H. S., Holtz, T. H., Hollm-Delgado, M. G., Keshavjee, S., DeRiemer, K., Centis, R., D'Ambrosio, L., Lange, C. G., Bauer, M., Menzies, D., & Collaborative Group for Meta-Analysis of Individual Patient Data in MDR-TB (2013). Resistance to fluoroquinolones and second-line injectable drugs: impact on multidrug-resistant TB outcomes. *The European respiratory journal*, *42*(1), 156–168. https://doi.org/10.1183/09031936.00134712
7. Guo, Y., Yang, J., Wang, H., Sha, W., & Yu, F. (2025). Key resistance-associated mutations in multidrug-resistant tuberculosis: a genomic study from Shanghai, China, with a focus on aminoglycosides. *BMC microbiology*, *25*(1), 702. https://doi.org/10.1186/s12866-025-04446-x
8. Jeyasankar, S., Kalapala, Y. C., Sharma, P. R., & Agarwal, R. (2024). Antibacterial efficacy of mycobacteriophages against virulent Mycobacterium tuberculosis. *BMC microbiology*, *24*(1), 320. https://doi.org/10.1186/s12866-024-03474-3
9. Jowsey, W. J., Cook, G. M., & McNeil, M. B. (2024). Antibiotic resistance in *Mycobacterium tuberculosis* alters tolerance to cell wall-targeting inhibitors. *JAC-antimicrobial resistance*, *6*(3), dlae086. https://doi.org/10.1093/jacamr/dlae086
10. Li, H., Yuan, J., Duan, S., & Pang, Y. (2022). Resistance and tolerance of Mycobacterium tuberculosis to antimicrobial agents-How M. tuberculosis can escape antibiotics. *WIREs mechanisms of disease*, *14*(6), e1573. https://doi.org/10.1002/wsbm.1573
11. Lukas, K., Dang, M. T., Necas, C., & Venketaraman, V. (2025). Anti-TB Drugs for Drug-Sensitive and Drug-Resistant *Mycobacterium tuberculosis*: A Review. *Current issues in molecular biology*, *47*(9), 776. https://doi.org/10.3390/cimb47090776
12. Lyu, M. Y., Lai, H. L., Peng, H. R., Luo, H., Zhou, J., Ma, W. A., Zhang, C. Y., Ruan, H. X., Liu, Y., Chen, J., & Ying, B. W. (2025). Immunotherapy for tuberculosis: current strategies and future directions. *Military Medical Research*, *12*(1), 68. https://doi.org/10.1186/s40779-025-00655-7
13. Mboowa, G. (2025). Reimagining tuberculosis control in the era of genomics: The case for global investment in *Mycobacterium tuberculosis* genomic surveillance. *Pathogens, 14*(10), 975. https://doi.org/10.3390/pathogens14100975
14. Mohammadnabi, N., Shamseddin, J., Emadi, M., Bodaghi, A. B., Varseh, M., Shariati, A., Rezaei, M., Dastranj, M., & Farahani, A. (2024). Mycobacterium tuberculosis: The Mechanism of Pathogenicity, Immune Responses, and Diagnostic Challenges. *Journal of clinical laboratory analysis*, *38*(23), e25122. https://doi.org/10.1002/jcla.25122
15. Nasiri, M. J., & Venketaraman, V. (2025). Advances in host–pathogen interactions in tuberculosis: Emerging strategies for therapeutic intervention. *International Journal of Molecular Sciences, 26*(4), 1621. https://doi.org/10.3390/ijms26041621
16. Rahman F. (2024). Characterizing the immune response to *Mycobacterium tuberculosis*: a comprehensive narrative review and implications in disease relapse. *Frontiers in immunology*, *15*, 1437901. https://doi.org/10.3389/fimmu.2024.1437901
17. Roque-Borda, C. A., Vishwakarma, S. K., Ramirez Delgado, O. J., de Souza Rodrigues, H. L., Primo, L. M. D., Campos, I. C., de Lima, T. S., Perdigão, J., & Pavan, F. R. (2025). Peptide-Based Strategies Against Mycobacterium tuberculosis Covering Immunomodulation, Vaccines, Synergistic Therapy, and Nanodelivery. Pharmaceuticals, 18(10), 1440. https://doi.org/10.3390/ph18101440
18. Szumowski, J. D., Adams, K. N., Edelstein, P. H., & Ramakrishnan, L. (2013). Antimicrobial efflux pumps and Mycobacterium tuberculosis drug tolerance: evolutionary considerations. *Current topics in microbiology and*

immunology, *374*, 81–108. https://doi.org/10.1007/82_2012_300

19. Ye, M., Yuan, W., Molaeipour, L., Azizian, K., Ahmadi, A., & Kouhsari, E. (2021). Antibiotic heteroresistance in Mycobacterium tuberculosis isolates: a systematic review and meta-analysis. Annals of clinical microbiology and antimicrobials, 20(1), 73. https://doi.org/10.1186/s12941-021-00478-z