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Review And Analysis of Essential Protein Targets of *Mycobacterium leprae* for Novel Anti-leprosy Drug Development

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Abstract
Leprosy, caused by *Mycobacterium leprae*, remains a significant public health concern in several parts of the world in spite of the availability of multidrug therapy. The emergence of drug resistance and the prolonged duration of treatment highlight the urgent need for novel therapeutic strategies. Due to its highly reduced genome and obligate intracellular lifestyle, *M. leprae* relies on a limited set of essential proteins for survival, persistence, and pathogenicity, making these proteins attractive targets for drug discovery. This review provides a comprehensive analysis of key essential protein targets involved in critical biological processes such as cell wall biosynthesis, energy metabolism, DNA replication, transcription, translation, and stress response mechanisms. Particular emphasis is placed on enzymes and regulatory proteins that are indispensable for bacterial viability and show minimal homology with human proteins, thereby reducing the risk of host toxicity. By integrating current knowledge from genomics, proteomics, and computational drug discovery studies, this review highlights promising targets that could facilitate the development of selective and effective antileprosy agents. The identification and validation of these essential proteins may accelerate the design of novel therapeutics and contribute to improved management and eventual eradication of leprosy.

Keywords
Leprosy, *Mycobacterium leprae,* Multidrug Therapy, Proteins

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INTRODUCTION:
Mycobacterium leprae is the causative agent of leprosy, a chronic infectious disease that predominantly affects the skin, peripheral nerves, eyes, and upper respiratory tract in humans. It is a slow-growing, acid-fast, rod-shaped bacterium with a strong preference for cooler regions of the body, such as the skin and peripheral nerves. The disease has a long incubation period, often spanning several years, which makes early diagnosis difficult. As the infection progresses, *M. leprae* invades Schwann cells of peripheral nerves, leading to nerve damage that manifests as loss of sensation, muscle weakness, and, in advanced cases, irreversible deformities and disabilities. Transmission occurs mainly through prolonged and close contact with untreated individuals, typically via respiratory droplets from the nose and mouth, although the bacterium is significantly less contagious than commonly perceived[1].

The etiological role of *Mycobacterium leprae* in leprosy was first established in 1873 by the Norwegian physician Gerhard Armauer Hansen, representing one of the earliest demonstrations that

a specific microorganism could cause a human disease. This landmark discovery transformed the understanding of leprosy, shifting it away from myths, superstition, and social stigma toward a scientifically defined and medically manageable condition. Hansen's work laid the foundation for modern leprosy research, ultimately enabling the development of effective diagnostic approaches and multidrug therapy, which has significantly reduced the global disease burden and improved patient outcomes[2].

Recent advances in genomics and immunology have greatly improved the understanding of *Mycobacterium leprae*, revealing extensive gene decay, host dependence, and mechanisms underlying immune evasion and nerve damage. Identification of key antigens and virulence factors has strengthened diagnostic approaches and informed vaccine and therapeutic research, supporting ongoing efforts to improve early detection and control of leprosy[3].

Mycobacterium leprae is a slender, rod-shaped, acid-fast bacterium measuring approximately 1-5 µm in length. It possesses a thick, lipid-rich cell wall that is characteristic of the genus *Mycobacterium*. This complex cell envelope is composed of peptidoglycan, arabinogalactan, and mycolic acids, which together provide structural rigidity and resistance to environmental stress. The high lipid content contributes to the organism's slow growth rate and intrinsic resistance to many antimicrobial agents[4].

Unlike many bacteria, *M. leprae* exhibits an extremely reduced genome, resulting in metabolic dependency on the host cell. Due to extensive gene decay, it lacks many essential metabolic pathways, which explains its obligate intracellular nature. The organism shows a preference for cooler body regions such as the skin, peripheral nerves, nasal mucosa, and extremities, which aligns with its optimal growth temperature of approximately 30°C. The waxy cell wall also plays a role in immune evasion by limiting antigen presentation and reducing recognition by host immune cells. These structural features collectively contribute to the persistence and chronic nature of leprosy[5].

Mycobacterium leprae has evolved specialised survival mechanisms that allow it to persist within host tissues for extended periods. One of the key strategies is its ability to survive and multiply inside macrophages and Schwann cells. Upon entry, the bacterium inhibits phagosome–lysosome fusion, thereby escaping intracellular degradation. Additionally, M. leprae modulates host immune signalling pathways by altering cytokine production. It suppresses pro-inflammatory cytokines such as IFN-γ while promoting anti-inflammatory cytokines like IL-10, enabling long-term intracellular survival. The expression of stress-response proteins such as heat shock proteins (Hsp18 and Hsp70) further enhances bacterial resilience under hostile conditions such as oxidative stress and nutrient deprivation. The bacterium also exhibits metabolic dormancy, allowing it to remain viable in a non-replicating state for prolonged periods. This dormancy contributes to latent infection and reactivation years after initial exposure, complicating eradication efforts[6].

Multidrug Therapy (MDT) for Leprosy

The current standard treatment for leprosy is Multidrug Therapy (MDT), consisting of dapsone, clofazimine, and rifampicin[7]. These drugs work together to prevent resistance and effectively kill *Mycobacterium leprae*. Their key features and evolution are summarized below.

Dapsone

- A bacteriostatic drug that inhibits folate synthesis in *M. leprae*.
- Kills bacilli within 3–6 months, but full clinical recovery may take 2–3 years.
- Mucosal lesions heal first, followed by skin improvements; nerve damage heals slowly.
- Generally, well tolerated but has known side effects.
- Resistance emerged in the 1960s, making monotherapy ineffective.

Rifampicin

- Introduced in 1970; the only bactericidal drug in MDT.
- Works by inhibiting RNA synthesis.
- Highly potent—just a few supervised doses can kill 99**.99%** of viable bacilli.
- Effective even against dapsone-resistant strains.
- Once-monthly 600 mg dosing is recommended by WHO.
- Rare side effects, but resistance can occur from RpoB gene mutations.

Clofazimine

- A fat-soluble dye with bacteriostatic and anti-inflammatory properties.
- Binds to GC-rich regions of bacterial DNA and modulates immune responses.
- Very slow-acting but resistance is rare.
- Causes red-brown discoloration of skin and secretions due to tissue accumulation.
- Useful in managing type 2 leprosy reactions (T2R).
- Not recommended as monotherapy[8].

Transmission Biology and Environmental Persistence

Transmission of leprosy occurs primarily through prolonged close contact with untreated individuals, particularly via respiratory droplets containing viable bacilli. Although less contagious than other infectious diseases, prolonged exposure significantly increases transmission risk. Environmental reservoirs such as soil and certain animals (notably armadillos) have been identified as potential sources of infection, particularly in endemic regions[9]. The ability of *M. leprae* to survive outside the human host for limited periods contributes to environmental persistence. Poor socioeconomic conditions, overcrowding, malnutrition, and limited access to healthcare further enhance transmission risk, reinforcing leprosy as a disease closely linked to poverty and social inequality [10],[11].

Target Proteins for Inhibiting the Growth of *M. leprae*

Mycobacterium leprae, the bacterium that causes leprosy, has a minimal genome and has lost many genes over time. As a result, it relies on only a few essential proteins to survive and grow. These proteins help the bacterium build its cell wall, produce energy, copy its DNA, and protect itself from stress inside human cells**.** As *M. leprae* has very little functional redundancy, disruption of these essential pathways can severely impair its growth. This makes its core metabolic, cell-wall, and stress-response proteins especially attractive targets for drug discovery. Moreover, many of these proteins are conserved across mycobacterial species, allowing insights from Mycobacterium tuberculosis research to guide structure-based and in-silico antileprosy drug development[12], [13]

- Phenolic Glycolipid-1
- Lipoarabinomannan
- Hsp70/ Hsp18 (heat shock protein)
- ML0405/ ML2331
- ESAT-6 (early secreted antigenic target-6)
- ESAT-6 (early secreted antigenic target-6)
- CFP-10 (culture filtrate protein)
- Major membrane protein-2

Phenolic Glycolipid-1

Phenolic Glycolipid-1 (PGL-1) is a distinctive lipid antigen found exclusively in *Mycobacterium leprae* and is absent in most other mycobacterial species. Structurally, it comprises a phenolic core attached to long-chain fatty acids and carbohydrate components, which together confer amphipathic properties. PGL-1 plays a central role in leprosy-associated nerve damage by specifically binding to laminin-2 receptors on Schwann cells, facilitating bacterial entry into peripheral nerves. Following invasion, *M. leprae* triggers demyelination and axonal injury, resulting in the irreversible neuropathy characteristic of the disease. In addition to its neurotropic effects, PGL-1 suppresses host immune responses by inhibiting macrophage activation through interference with Toll-like receptor signalling, leading to reduced nitric oxide production and enhanced bacterial survival. Importantly, PGL-1 also has significant diagnostic value, as circulating anti-PGL-1 IgM antibodies are widely used as biomarkers for early detection of leprosy, particularly in endemic areas. Experimental studies have further employed PGL-1-coated nanoparticles to investigate mechanisms of nerve tropism. Overall, PGL-1 exhibits strong immunomodulatory activity, combining immune evasion with targeted nerve invasion, and stands out as one of the most unique and critical virulence factors of *M. leprae[14],[15]*.

Lipoarabinomannan

Lipoarabinomannan (LAM) is a complex glycolipid component of the mycobacterial cell wall that is anchored to the membrane and extends outward as a highly branched polysaccharide structure. It is biosynthetically related to lipomannan and phosphatidylinositol mannosides; however, in *Mycobacterium leprae*, specific structural modifications confer distinct immunological characteristics. Functionally, LAM acts as a potent immunosuppressive molecule by inhibiting T-cell proliferation, suppressing interleukin-2 production, and scavenging reactive oxygen intermediates. These effects collectively impair macrophage activation and antigen presentation in the host, thereby promoting bacterial survival and contributing to the chronic nature of leprosy. Additionally, LAM is capable of mimicking host molecular patterns, which facilitates immune evasion and further protection against host defences. Although LAM is a conserved virulence factor among pathogenic mycobacteria, the variant present in *M. leprae* is less pro-inflammatory than that of *M. tuberculosis*, accounting for the characteristically slow and insidious progression of leprosy. Overall, LAM exhibits a dual role as both a protective shield against host immune mechanisms and an active modulator of immune responses, underscoring its central importance in the pathogenesis of leprosy[16],[17], [18].

Hsp70/ Hsp18 (heat shock protein)

Heat shock proteins, particularly Hsp70 and Hsp18, are stress-responsive molecular chaperones that

play a critical role in maintaining protein homeostasis in *Mycobacterium leprae* under adverse conditions such as oxidative stress, nutrient limitation, temperature fluctuations, and host immune pressure. In this pathogen, Hsp18, a small 18 kDa heat shock protein, primarily functions to prevent irreversible protein aggregation, while Hsp70 facilitates the proper folding, refolding, and stabilization of denatured or misfolded proteins, thereby ensuring bacterial survival during intracellular persistence. Beyond their housekeeping roles, these heat shock proteins are among the most highly immunogenic antigens of *M. leprae*, capable of eliciting strong T-cell–mediated immune responses in infected individuals. This immunogenicity links them to inflammatory processes, where heightened immune activation contributes to nerve inflammation, tissue damage, and the immunopathology observed in leprosy reactions. Notably, Hsp70 and Hsp18 exhibit significant structural and antigenic similarity to human heat shock proteins, leading to molecular mimicry and potential cross-reactivity, which may underlie autoimmune-like phenomena and exacerbate nerve injury. Additionally, Hsp18 has been reported to interact with anti-leprosy drugs, potentially influencing bacterial stress responses and treatment efficacy. Owing to their conserved nature, surface exposure during stress, and strong antigenicity, these proteins are also being explored as biomarkers for diagnosis and as promising vaccine or immunotherapeutic targets. Thus, Hsp70 and Hsp18 represent a paradox in leprosy pathogenesis: they are indispensable for bacterial adaptation and persistence, yet simultaneously render the pathogen vulnerable to host immune recognition, positioning them as central components in the ongoing host–pathogen arms race[19],[20], [21].

ML0405/ ML2331

ML0405 and ML2331 are *Mycobacterium leprae*–specific protein antigens that are absent in *Mycobacterium bovis* BCG and most environmental or non-pathogenic mycobacterial species, making them particularly valuable for leprosy-specific immune recognition. Their primary significance lies in their high diagnostic specificity, as both antigens induce strong interferon-gamma (IFN-γ) responses from antigen-specific T cells, enabling effective discrimination of leprosy from tuberculosis and other mycobacterial infections. In infected individuals, ML0405 and ML2331 stimulate robust cellular immune responses alongside detectable humoral responses, reflecting ongoing or early-stage infection and active antigen presentation. Importantly, these proteins are expressed during in vivo infection, further supporting their relevance as biomarkers rather than incidental antigens. Their exclusivity to *M. leprae* minimizes cross-reactivity, a major limitation of many conventional mycobacterial antigens, thereby improving diagnostic accuracy in endemic regions where multiple mycobacterial exposures are common. Experimental and clinical studies have demonstrated the successful incorporation of ML0405 and ML2331 into ELISA-based serological assays and IFN-γ release assays for early and subclinical leprosy detection, including among household contacts. Additionally, these antigens are being explored as components of multi-antigen diagnostic panels and as potential candidates for immunomonitoring disease progression and treatment response. Overall, ML0405 and ML2331 are highly immunogenic, *M. leprae*–exclusive sentinel markers that effectively bridge fundamental immunological research with translational diagnostic applications in leprosy control[22], [23].

ESAT-6 (early secreted antigenic target-6)

ESAT-6 (Early Secreted Antigenic Target-6) is a low–molecular–weight (~6 kDa) secretory protein encoded within the Region of Difference 1 (RD1), and it shows strong homology to ESAT-6 of *Mycobacterium tuberculosis*. Functionally, ESAT-6 is a highly potent T-cell antigen that elicits robust interferon-gamma (IFN-γ) responses, indicating active cellular immune recognition and contributing to immunopathological processes. In the human host, ESAT-6 plays an important role in immune modulation by disrupting antigen presentation pathways, altering macrophage and dendritic cell function, and facilitating bacterial survival and dissemination. Mechanistically, ESAT-6 can damage host cell membranes and promote phagosomal escape, thereby enhancing intracellular persistence. A defining feature of ESAT-6 is its tight functional association with CFP-10 (Culture Filtrate Protein-10), with which it forms a heterodimeric secretory complex that is exported via the ESX-1 secretion system, a key virulence mechanism in pathogenic mycobacteria. This ESAT-6/CFP-10 complex amplifies host immune activation while simultaneously promoting tissue damage and bacterial spread. Clinically, ESAT-6 is widely used in interferon-gamma release assays (IGRAs) for tuberculosis diagnosis due to its absence in BCG strains, and analogous strategies are being investigated to assess its utility in leprosy diagnostics and immunomonitoring. Additionally, ESAT-6 has been explored as a candidate antigen in vaccine and immunotherapeutic

research, given its strong immunogenicity. Overall, ESAT-6 exhibits a dual character—acting both as a critical virulence factor that shapes host–pathogen interactions and as a valuable diagnostic and research tool—making it a double-edged molecule in leprosy pathogenesis and translational research[24],[25], [26].

CFP-10 (culture filtrate protein)

CFP-10 (Culture Filtrate Protein-10) is a small ~10 kDa secretory protein encoded within the Region of Difference 1 (RD1) locus, where it is co-expressed with ESAT-6 in pathogenic mycobacteria. These two proteins form a tightly associated heterodimeric complex that is exported through the ESX-1 type VII secretion system, a major determinant of mycobacterial virulence. Functionally, CFP-10 is a highly immunodominant antigen that elicits strong $CD4^+$ and $CD8^+$ T-cell responses, characterized by robust interferon-gamma (IFN-γ) production, thereby playing a role in granuloma formation and maintenance. In the human host, CFP-10 influences macrophage activation and cytokine signaling, contributing to both protective immunity and immunopathology associated with chronic infection. Due to its significant sequence homology with CFP-10 from *M. tuberculosis*, cross-reactivity can occur, which poses challenges for differential diagnosis but also reflects the evolutionary conservation of RD1-associated virulence mechanisms. A defining feature of CFP-10 is its functional synergy with ESAT-6, as the stability, secretion, and biological activity of each protein depend on the formation of the ESAT-6/CFP-10 complex, effectively allowing them to operate as a single virulence and immunological unit. Clinically, CFP-10 is widely used alongside ESAT-6 in interferon-gamma release assays for tuberculosis and is being evaluated for its applicability in leprosy diagnostics, immunomonitoring, and vaccine design. Overall, CFP-10 exhibits a dual nature as both a key mediator of host immune activation and a practical biomarker of infection, positioning it as an important target in the development of improved diagnostic and immunotherapeutic strategies[27],[28], [29].

Major membrane protein-2

Major Membrane Protein-II (MMP-II), also known as the 22 kDa protein, is a prominent surface-exposed antigen of *Mycobacterium leprae* and represents one of the most immunodominant proteins recognized during leprosy infection. It is strongly antigenic and elicits robust responses from both arms of the immune system, stimulating antibody production as well as vigorous $CD4^+$ T-cell–mediated immunity. Functionally, MMP-II induces the release of key pro-inflammatory cytokines such as interferon-gamma (IFN-γ), tumor necrosis factor-α (TNF-α), and interleukin-2, which contribute to macrophage activation and bacterial control but may also drive inflammation-associated tissue and nerve damage in reactive forms of leprosy. In humans, MMP-II is consistently recognized across different clinical spectra of the disease, highlighting its dominance as an in vivo antigen. A notable feature of MMP-II is its successful expression in recombinant *Mycobacterium bovis* BCG systems, where it has been shown to enhance protective immune responses and inhibit *M. leprae* multiplication in experimental models. This has positioned MMP-II as a promising vaccine candidate, either alone or as part of multi-antigen formulations. Additionally, its strong and specific immunogenicity makes it useful for immunomonitoring disease progression and evaluating treatment efficacy. Overall, MMP-II functions as a frontline antigen that bridges host immune recognition with translational applications in vaccine development and immunodiagnostics, underscoring its importance in leprosy pathogenesis and control strategies[30],[31], [32].

Although current MDT regimens are effective in early stages, several limitations have been reported, including poor patient compliance, adverse drug reactions, and emergence of drug resistance. Studies have reported relapse rates of 5–10% in endemic regions, mainly due to rifampicin and dapsone resistance. Additionally, prolonged treatment causes hepatotoxicity, pigmentation, gastrointestinal disturbances, and immune suppression[33], [34]. Hence, there is an urgent need for alternative and complementary therapeutic strategies that can target the pathogen more efficiently while minimizing toxicity. Scaffold-based drug discovery offers a promising approach by identifying core chemical structures capable of interacting with essential proteins of *M. leprae*. These scaffolds can be optimized for enhanced efficacy, reduced toxicity, and improved pharmacokinetic profiles[35].

Antimicrobial Resistance in Leprosy

Antimicrobial resistance (AMR) in leprosy has emerged as a major concern worldwide. Mutations in genes such as **rpoB**, **folP1**, and **gyrA** are responsible for resistance to rifampicin, dapsone, and fluoroquinolones, respectively. Surveillance studies have reported multidrug-resistant *M. leprae* strains in endemic regions. The persistence of resistant strains compromises disease elimination programs and increases transmission risk. Moreover, the intracellular survival of *M. leprae* further complicates antibiotic efficacy, necessitating drugs

capable of penetrating host cells and maintaining intracellular activity[36].

Socioeconomic Burden of Leprosy

Leprosy imposes a significant socioeconomic burden due to disability, social stigma, and long-term healthcare costs. Affected individuals often suffer from unemployment, social exclusion, and psychological distress. Disability-adjusted life years (DALYs) related to leprosy remain high in endemic countries. Indirect costs such as productivity loss, rehabilitation, and long-term care further strain healthcare systems. Therefore, effective and affordable therapeutic alternatives are essential to reduce the disease burden and improve quality of life[37], [38].

Host–Pathogen Interaction in Leprosy

The interaction between *Mycobacterium leprae* and the host immune system determines disease outcome. Infection begins when the bacterium enters through the respiratory tract or broken skin and is phagocytosed by macrophages. It then preferentially infects Schwann cells in peripheral nerves using specific surface receptors such as laminin-2 and α-dystroglycan. Once inside Schwann cells, M. leprae reprograms host gene expression, inducing dedifferentiation and promoting a regenerative-like state that facilitates bacterial survival and dissemination. This unique interaction explains the nerve tropism seen in leprosy. The host immune response plays a decisive role in disease progression. Strong cell-mediated immunity restricts bacterial growth, whereas impaired immunity allows widespread dissemination. Thus, disease manifestation reflects a dynamic balance between bacterial virulence and host defence mechanisms[39].

Pathophysiology of Leprosy

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae*, an obligate intracellular pathogen with a predilection for peripheral nerves, skin, and reticuloendothelial tissues. The pathogenesis of leprosy is complex and primarily depends on the interaction between the host immune response and the pathogen. Unlike many other bacterial infections, *M. leprae* exhibits an exceptionally slow replication rate, with a doubling time of approximately 12–14 days, allowing it to evade early immune detection and persist within host cells[40]. The primary cellular targets of *M. leprae* are Schwann cells and macrophages. The bacterium enters Schwann cells through specific surface receptors such as laminin-2 and α-dystroglycan, leading to demyelination and nerve degeneration. Once internalized, *M. leprae* manipulates host cell signaling pathways to avoid lysosomal degradation and immune clearance. This immune evasion contributes to long-term infection and progressive nerve damage. The clinical spectrum of leprosy is determined by the host's immune response, particularly cell-mediated immunity (CMI)[41], [42]. Based on immunological response, leprosy is classified into two polar forms and intermediate borderline forms:

- **Tuberculoid leprosy (TT):** Characterised by a strong Th1-mediated immune response with high levels of interferon-gamma (IFN-γ) and interleukin-2 (IL-2). This form shows low bacterial load, well-formed granulomas, and limited nerve involvement.
- **Lepromatous leprosy (LL):** Characterised by a weak or absent cell-mediated immune response. High bacterial load is observed with widespread dissemination. Increased levels of IL-4, IL-10, and transforming growth factor-beta (TGF-β) suppress macrophage activation, allowing bacterial survival[43].

Between these two poles lie borderline forms that show immunological instability and frequent disease progression or reversal. Inflammatory mediators such as tumour necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and reactive oxygen species (ROS) play a crucial role in nerve damage. Chronic inflammation leads to demyelination, axonal degeneration, and fibrosis of peripheral nerves, ultimately resulting in sensory loss, deformities, and disability. Repeated inflammatory episodes, known as lepra reactions (Type 1 and Type 2 reactions), further aggravate nerve injury and tissue destruction. Thus, the pathophysiology of leprosy is not merely due to bacterial proliferation but is significantly influenced by immune dysregulation, inflammatory mediators, and host-pathogen interactions[44]. Clinically, leprosy presents as a spectrum of disease manifestations depending on the host's immune response. At one end is tuberculoid leprosy, characterised by strong cell-mediated immunity, few lesions, and minimal bacterial load. At the opposite end is lepromatous leprosy, marked by diffuse skin lesions, high bacillary load, and systemic involvement. Between these poles lie borderline forms that exhibit immunological instability and frequent shifts in disease severity. Acute inflammatory episodes known as lepra reactions (Type 1 and Type 2) significantly contribute to nerve damage and disability. This clinical diversity highlights the complexity of host–pathogen

interactions and underscores the importance of individualised therapeutic approaches.

Limitations of conventional drug therapy

Multidrug therapy (MDT), consisting primarily of rifampicin, dapsone, and clofazimine, remains the standard treatment regimen for leprosy. While MDT has significantly reduced disease prevalence worldwide, several limitations compromise its long-term effectiveness. One major limitation is the development of antimicrobial resistance. Mutations in the *rpoB*, *folP1*, and *gyrA* genes confer resistance to rifampicin, dapsone, and fluoroquinolones, respectively. Surveillance studies have reported an increasing incidence of multidrug-resistant *M. leprae* strains, particularly in endemic regions. Another critical challenge is the long duration of therapy, typically ranging from 6 to 12 months or longer in multibacillary cases. Prolonged treatment often results in poor patient compliance, incomplete adherence, and increased risk of relapse. Adverse drug reactions further complicate treatment outcomes. Dapsone is associated with hemolytic anaemia and hypersensitivity reactions, while clofazimine causes skin discolouration and gastrointestinal disturbances. Rifampicin may lead to hepatotoxicity and drug–drug interactions, especially in patients with coexisting conditions. Additionally, conventional antibiotics exhibit limited efficacy against dormant or intracellular bacilli. *M. leprae* residing within Schwann cells and macrophages remain metabolically inactive, rendering many antibiotics ineffective. This persistence contributes to relapse and continued transmission[45], [46]. Therefore, existing therapeutic regimens primarily suppress bacterial growth rather than achieve complete eradication. These limitations emphasise the urgent need for novel therapeutic strategies that can target dormant bacteria, modulate host immune responses, and minimise adverse effects[47].

CONCLUSION

Finding Mycobacterium leprae's essential protein targets is a critical first step in creating new, more potent antileprosy treatments. Due to its smaller genome and reliance on a limited number of essential metabolic and cellular pathways, M. leprae exhibits special vulnerabilities that can be deliberately exploited in the development of new drugs. Because they are essential for bacterial survival and persistence, proteins involved in cell wall biosynthesis, DNA replication, transcriptional regulation, energy metabolism, and stress adaptation stand out as especially promising candidates. By focusing on these vital proteins, particularly those that are not very similar to their human counterparts, therapeutic selectivity may be improved while host toxicity is reduced.

To turn these targets into clinically effective treatments, more research concentrating on resistance profiling, translational development, and experimental validation will be necessary. All things considered, systematic investigation of key protein targets has great potential to aid in the development of next-generation antileprosy medications and support long-term disease control tactics.

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