Commentary

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Immunological Pathways in Pulmonary Tuberculosis: Host-pathogen Interactions

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Introduction

Pulmonary tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains one of the most significant infectious diseases worldwide, accounting for considerable morbidity and mortality. Despite being a preventable and treatable disease, TB continues to pose major global health challenges due to delayed diagnosis, treatment resistance and complex host-pathogen dynamics. The lungs are the primary site of infection, where Mtb encounters a sophisticated immune environment that determines disease progression, latency, or clearance. The immunological landscape of pulmonary TB is shaped by a delicate interplay between host defense mechanisms and microbial strategies for survival. The host immune system mounts both innate and adaptive responses to contain infection, while Mtb employs mechanisms to evade immune recognition and persist within macrophages. Understanding these immunological pathways is essential for improving diagnostics, developing novel vaccines and designing effective host-directed therapies [1].

Description

Innate immunity represents the first line of defense against pulmonary TB. Alveolar macrophages are the initial host cells that phagocytose Mtb, but instead of being eliminated, the pathogen can manipulate phagosomal maturation to establish a niche for survival. Pattern recognition receptors (PRRs), including toll-like receptors (TLRs) and nucleotide-binding oligomerization domain (NOD)-like receptors, detect Mtb components and initiate inflammatory signaling. This leads to the recruitment of neutrophils, dendritic cells and natural killer (NK) cells, which contribute to early containment. However, excessive neutrophil infiltration can exacerbate tissue damage, while NK cells play a dual role by releasing cytokines and enhancing macrophage killing. The balance between protective and pathological innate responses often determines the course of infection [2].

Adaptive immunity is crucial in shaping long-term outcomes of TB infection. CD4+ T helper cells, particularly the Th1 subset, play a central role by secreting interferon-gamma (IFN-γ), which activates macrophages to enhance bactericidal functions. Cytotoxic CD8+ T cells contribute by directly killing infected cells and producing granulysin to restrict bacterial growth. Regulatory T cells (Tregs), however, may suppress protective immune responses, enabling persistent infection. The hallmark of TB is granuloma formation, a structured immune response composed of macrophages, epithelioid cells, giant cells and lymphocytes. Granulomas aim to contain infection but may also provide a protective niche for Mtb survival, reflecting the paradox of host-pathogen interactions in TB. Cytokine networks are pivotal in orchestrating immune responses against pulmonary TB. Tumor necrosis factor-alpha (TNF-α) and interleukin-12 (IL-12) are critical for granuloma maintenance and Th1 polarization, respectively. Interleukin-10 (IL-10) and transforming growth factor-beta (TGF-β), on the other hand, exert immunosuppressive effects that facilitate pathogen persistence [3].

Dysregulation of cytokine responses can lead to either uncontrolled bacterial proliferation or excessive tissue pathology, both of which worsen disease outcomes. Emerging evidence also highlights the role of Th17 cells and IL-17 in promoting neutrophil recruitment and protective immunity, although their exact contribution remains context-dependent. The dynamic interplay between pro-inflammatory and anti-inflammatory cytokines underscores the complexity of TB immunopathogenesis. Mtb has evolved sophisticated strategies to evade host immunity, ensuring long-term persistence. These include inhibition of phagolysosome fusion, modulation of antigen presentation and interference with host cell apoptosis pathways. The pathogen can alter macrophage metabolism, shifting it toward a lipid-rich state that favors bacterial survival within foamy macrophages [4].

These mechanisms allow Mtb to establish latent infection, which affects nearly one-quarter of the global population. Reactivation of latent TB, often triggered by immune suppression, exemplifies

the delicate balance between host defenses and pathogen persistence. Addressing these evasion strategies is crucial for the development of effective therapeutic and vaccine strategies. Future directions in TB research emphasize harnessing host immunity to improve disease management and prevention. Identification of novel immune biomarkers may facilitate early diagnosis and better differentiation between latent and active TB. Next-generation vaccines aim to elicit stronger and longer-lasting T cell responses to overcome Mtb evasion mechanisms. Host-directed therapies that modulate immune pathways and metabolic processes offer promising adjuncts to conventional antimicrobials. Ultimately, integrating immunological insights with translational research holds the potential to transform TB control on a global scale [5].

Conclusion

The immunological pathways involved in pulmonary tuberculosis highlight the intricate host-pathogen interactions that govern disease outcomes. While innate and adaptive immunity collaborate to restrict infection, Mtb counters with evasion strategies that enable persistence and latency. Granuloma formation, cytokine regulation and cellular cross-talk exemplify the dual roles of immune responses in both protection and pathology. Advances in immunology and molecular biology continue to unravel the complex mechanisms underlying TB, offering opportunities for novel interventions. A deeper understanding of these pathways will be key to improving TB control strategies, vaccine design and host-directed therapies.

Acknowledgment

None.

Conflict of Interest

None.

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