

Immunopathological Insights into Pulmonary *Mycobacterium tuberculosis* Infection Using a Humanized Mouse Model

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Introduction

In recent years, humanized mouse models have emerged as powerful tools for studying infectious diseases, including TB. By engrafting human immune cells or tissues into immunodeficient mice, these models offer a unique opportunity to investigate host-pathogen interactions and immune responses in a more physiologically relevant context. Humanized mouse models of pulmonary Mtb infection provide a platform for dissecting the immunopathological mechanisms underlying disease progression, identifying biomarkers of disease severity and evaluating novel therapeutic interventions. Pulmonary Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains a significant global health burden, with millions of new cases reported each year. Understanding the immunopathology of Mtb infection is crucial for developing effective strategies for disease control and management. While animal models have provided valuable insights into TB pathogenesis, traditional models often fail to fully recapitulate the complex immunological responses observed in human infection. This review aims to provide an overview of the immunopathology of pulmonary Mtb infection in humanized mouse models, highlighting key findings and insights gained from these studies. We will discuss the advantages and limitations of humanized mouse models for studying TB, the immunological responses elicited during Mtb infection and the implications for developing new diagnostic and therapeutic approaches. By synthesizing the current literature, this review seeks to advance our understanding of TB immunopathology and inform future research directions in the field [1,2].

Description

Traditional animal models, while valuable, often fail to fully capture the intricacies of human immune responses to Mtb due to species-specific differences in immune cell function and lung architecture. In recent years, humanized mouse models have emerged as promising tools for studying TB immunopathology in a more physiologically relevant context. These models involve engrafting human immune cells, tissues, or hematopoietic stem cells into immunodeficient mice, thereby generating a system that allows for the study of human-specific immune responses to Mtb infection. Humanized mouse models offer several advantages, including the ability to investigate host-pathogen interactions, evaluate immune responses and test potential therapeutics in a controlled experimental setting. These granulomas serve as sites of immune cell recruitment, activation and interaction, influencing the outcome of infection and disease progression. Furthermore, humanized mouse models allow for the study of specific immune cell subsets involved in TB immunopathology. For example, the role of CD4⁺ and CD8⁺ T cells in

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controlling Mtb infection, the contribution of innate immune cells such as macrophages and dendritic cells to granuloma formation and the dynamics of B cell responses in modulating the host immune response can be investigated in detail [3].

One of the key advantages of humanized mouse models is their ability to recapitulate key features of human TB immunopathology in the lungs. Upon infection with Mtb, humanized mice develop granulomatous lesions, a hallmark of TB pathology, characterized by the aggregation of immune cells, including macrophages, T cells and B cells, around infected lung tissue. By manipulating the composition of human immune cells engrafted into the mice, researchers can dissect the contributions of different cell types to TB pathogenesis and immunity. Pulmonary Tuberculosis (TB) remains a global health threat, with an estimated 10 million new cases reported annually. Despite extensive research efforts, understanding the complex immunopathology of *M. tuberculosis* (Mtb) infection, particularly in the lungs, remains a challenge [4].

Humanized mouse models allow researchers to assess the impact of these cytokines on granuloma formation, bacterial control, tissue damage and overall disease severity. Moreover, humanized mouse models offer a platform for evaluating novel therapeutic interventions for TB. By testing candidate drugs, vaccines, or immunomodulatory agents in humanized mice infected with Mtb, researchers can assess their efficacy, safety and potential mechanisms of action. This preclinical evaluation provides valuable insights into the translational potential of therapeutics, guiding their further development and optimization for clinical use [5].

Conclusion

In conclusion, humanized mouse models offer a valuable experimental platform for studying the immunopathology of pulmonary Mtb infection. By recapitulating key features of human TB immunology in a controlled experimental setting, these models provide insights into host-pathogen interactions, immune responses and potential therapeutic strategies. Continued research efforts aimed at refining humanized mouse models, elucidating TB immunopathology and translating experimental findings into clinical practice hold promise for advancing our understanding of TB and improving disease control and management strategies. Despite these advantages, humanized mouse models also have limitations that must be considered. The engraftment efficiency of human immune cells, the longevity of the engraftment and the complexity of the immune responses generated in the mice can vary between different models and experimental conditions. Furthermore, ethical considerations, cost constraints and technical challenges associated with maintaining humanized mouse colonies impose practical limitations on their widespread use.

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Conflict of Interest

There are no conflicts of interest by author.

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