Escape Mechanisms of Mycobacterium Tuberculosis

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Definition

Tuberculosis, an infectious disease caused by *Mycobacterium tuberculosis* (MTB), mainly affects the respiratory system. It was demonstrated in 2019 that tuberculosis is the leading cause of mortality due to a single infectious agent. MTB is an intracellular parasite that mainly attacks macrophages and inhibits their apoptosis. One of the most disturbing matters in the treatment of MTB is the increasing resistance to current first-line antibiotics, resulting in long-term infection in humans and causing a series of pathological changes and clinical manifestations. A further understanding of the immune escape mechanisms of MTB is of major importance for the prevention, diagnosis, and treatment of tuberculosis.

1. Introduction

Statistics from the CDC and WHO show that ~10.0 million people around the world become infected with TB and there are 1.3–1.6 million TB-related deaths every year. Despite the availability of a vaccine for nearly 100 years, the global infection rate with *Mycobacterium tuberculosis* (MTB) is still approximately one in three people. However, the pathogen is eliminated in only 10% of people, allowing it to easily escape during the process of infection and remain dormant in old lesions, making the infection hard to control[1]. Therefore, it is urgent to elucidate the pathogenesis of MTB and the principles of immune evasion for the diagnosis and treatment of TB. We introduce the pathogenesis, escape mechanism, and treatment options for MTB in the following. It has been shown that the pathogenicity is associated with the toxicity of its components, metabolites of the bacterium, and the immune damage to its components. The occurrence of immune escape mainly occurs in the interaction between bacteria and macrophages. MTB, through the combination of surface receptors and macrophages, triggers a series of reactions that inhibit lysosomal acidification and maturation, free radical damage and inhibition, and other mechanisms to escape the host's immune response.

2. Pathogenesis of Mycobacterium Tuberculosis

The capsule, lipid, and protein of MTB have specific pathogenicity. The main components of the capsule are polysaccharide, lipids, and proteins. It is the presence of complex capsules that makes it possible for bacteria to infect people and live in them for more than a decade. The presence of the capsule in bacteria has been shown to prevent desiccation, promote adherence, and provide resistance to host immunity, including complement-mediated killing or down-regulation of the production of pro-inflammatory cytokines[2]. The role of lipids in MTB goes far beyond providing a carbon source. Recent reports have revealed that lipid utilization by MTB is more complex than was previously thought. MTB imports and utilizes fatty acids and cholesterol to convert both these lipids into bacterial end-products that mediate bacterial pathogenesis. These bacterial lipid end-products regulate bacterial replication, drug tolerance, and virulence[3]. As for protein, it is antigenic, and the combination of wax D can provoke a hypersensitivity reaction, cause tissue necrosis and systemic poisoning symptoms, and play a specific role in the formation of tuberculous nodules.

3. Immune Escape of Mycobacterium Tuberculosis

The immune response and the immune escape mechanisms after MTB infection is complicated, which makes it possible for bacteria to survive for a long time. First, MTB inhibits the maturation and acidification of phagolysosomes by regulating enzymes and other metabolic pathways, thus reducing the

immune action of the host against MTB. On the one hand, it can regulate the maturation of phagolysosomes *via* modulating bacterial proteins such as early secretory antigen-6/culture filtrate protein and ATP1/2 (secretion ATPase1/2, secreted secA1/2 protein), cytokine interferon (IFN)-α[4][5][6], IL-10[7], and the fusion of phagosomes with lysosomes. MTB inhibits the maturation of phagocytosis by suppressing the acidification of phagosomes and then persists in the relatively lower acidic environment (pH ~6.2)[8]. Second, it has been shown that, from the aspects of genes or the intrinsic structure of MTB, it inhibits oxidative stress and the function of reactive oxygen and reactive nitrogen intermediates. The interrelationship between the MTB gene cluster Rv0014c-Rv0019c [PknA (encoded by Rv0014c) and FtsZ-interacting protein A (FipA) (encoded by Rv0019c)] and FtsZ and FtsQ from the division cell wall cluster also contribute to the escape of MTB from oxidative stress [9]. Third, MTB inhibits the apoptosis and autophagy of the host cell to fulfill its latent infection. With regard to miRNAs, studies in this field have found that miR-30A suppresses the elimination of intracellular MTB and this is achieved by inhibiting autophagy. Conversely, non-coding RNAs (microRNAs, piRNAs, circRNAs and lncRNAs) regulate the host response against MTB infection[9]. Finally, several trace elements such as iron, hydrogen, and calcium ions in macrophages playing an essential role in the formation of lysosomes. Ions can inhibit lysosome formation in the interaction of cytokines and affect the ion balance and energy metabolism.

4. Conclusions and Future Direction

MTB is one of the most prevalent infectious diseases, but although the existence of anti-tubercular drugs are available, this disease still kills millions of people each year. The current therapeutic strategies for MTB are still based on drugs; however, one of the greatest difficulties is the resistance to first-line treatment. Many investigations in this field have been conducted to further understand the immune mechanisms of MTB and to find druggable targets. The ultimate goal – full eradication of this disease – remains unresolved, and it seems that reaching this goal is very difficult but not impossible. In the future, effective tools and alternative biological chemicals should be put on the agenda to inhibit the infection, which is important for overcoming MTB resistance. Besides, in order to detect the symptoms and achieve early diagnosis, more focus should be put on further understanding of the biological interactions between MTB and humans. In addition, alternative drugs that could shorten the duration of cure, reduce costs, limit side-effects, and allow for immunodeficient patients are still very urgently needed.

References

1. Zhai W, Wu F, Zhang Y, Fu Y, Liu Z: The Immune Escape Mechanisms of Mycobacterium Tuberculosis. Int J Mol Sci 2019, 20(2).
2. Kalscheuer R, Palacios A, Anso I, Cifuente J, Anguita J, Jacobs WR, Jr., Guerin ME, Prados-Rosales R: The Mycobacterium tuberculosis capsule: a cell structure with key implications in pathogenesis. Biochem J 2019, 476(14):1995-2016.
3. Wilburn KM, Fieweger RA, VanderVen BC: Cholesterol and fatty acids grease the wheels of Mycobacterium tuberculosis pathogenesis. Pathog Dis 2018, 76(2). 4. Rohde K, Yates RM, Purdy GE, Russell DG: Mycobacterium tuberculosis and the environment within the phagosome. Immunol Rev 2007, 219:37-54.
4. Schuller S, Neefjes J, Ottenhoff T, Thole J, Young D: Coronin is involved in uptake of Mycobacterium bovis BCG in human macrophages but not in phagosome maintenance. Cell Microbiol 2001, 3(12):785-793.
5. Flynn JL, Chan J: Immune evasion by Mycobacterium tuberculosis: living with the enemy. Curr Opin Immunol 2003, 15(4):450-455.
6. Ma J, Yang B, Yu S, Zhang Y, Zhang X, Lao S, Chen X, Li B, Wu C: Tuberculosis antigen-induced expression of IFN-alpha in tuberculosis patients inhibits production of IL-1beta. FASEB J 2014, 28(7):3238-3248.
7. Chen Z, Wang T, Liu Z, Zhang G, Wang J, Feng S, Liang J: Inhibition of Autophagy by MiR-30A Induced by Mycobacteria tuberculosis as a Possible Mechanism of Immune Escape in Human Macrophages. Jpn J Infect Dis 2015, 68(5):420-424.
8. Sureka K, Hossain T, Mukherjee P, Chatterjee P, Datta P, Kundu M, Basu J: Novel role of phosphorylation-dependent interaction between FtsZ and FipA in mycobacterial cell division. PLoS One 2010, 5(1):e8590.
9. Wei L, Liu K, Jia Q, Zhang H, Bie Q, Zhang B: The Roles of Host Noncoding RNAs in Mycobacterium tuberculosis Infection. Front Immunol 2021, 12:664787.

Keywords

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