Tuberculosis

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Contributor: vishwanath venketaraman

Dendritic cells are the principal antigen-presenting cells (APCs) in the host defense mechanism. An altered dendritic cell response increases the risk of susceptibility of infections, such as Mycobacterium tuberculosis (M. tb), and the survival of the human immunodeficiency virus (HIV). Thus, an understanding of the intricate pathways involved in the dendritic cell response are needed to prevent co-infections and co-morbidities in individuals with TB and HIV

Keywords: dendritic cells, ; Th1 CD4 T cells ; Th2 CD4 T cells ; Regulatory T cells ; HIV ; Tuberculosis

1. Introduction

TB is recognized as one of the top 10 leading infectious killers globally; it is also the most common opportunistic infection and a contributing cause of death for HIV patients. Globally, it is estimated that TB has 10 million incident cases and an estimated 1.9 million deaths[1]. According to the World Health Organization's Annual Tuberculosis Report in 2019, the highest estimated total incidence of TB was in Southeast Asia, with 4,370,000 incident cases. Africa was second to Southeast Asia with 2,450,000 incident cases. Thus, most cases and deaths are in developing countries. Individuals with other comorbidities and factors that suppress the immune system, such as uncontrolled diabetes, HIV infection, chronic renal failure, and use of immunosuppressive drugs, are at higher risk for contracting primary *M. tb* infection and undergoing reactivation of latent *M. tb* infection[2]. Furthermore, social determinants of health, including poverty, undernutrition, lack of access to anti-retroviral therapy (ART) for HIV, and smoking, lead to a higher *M. tb* disease burden and, thus, concentrate the disease in socio-economically disadvantaged countries[3]. In developing regions, such as Sub-Saharan Africa, limited access to ART increases the susceptibility to HIV and other co-infections most commonly seen with TB and HIV comorbidities[4]. Administration of ART reduces TB incidence by 67%[5], as well as mortality if ART is started early [6].

2. Pathophysiology of Tuberculosis

Initial infection with *M. tb* involves the inhalation of aerosolized infectious droplets containing the pathogen, which travel down the respiratory tract to infect the lungs' alveoli. Thereafter, *M. tb* can travel throughout the body via systematic and lymphatic circulation and infect other organs, such as the brain, kidney, bone, or apex of the lungs. Within 2–8 weeks, macrophages—specialized immune cells—mount an immune response by ingesting and destroying the *M. tb*. However, some of the macrophages aggregate and form a granuloma, an immune barrier that encloses and suppresses the *M. tb*, instead of completely clearing the infection[7]. In these granulomas, mature macrophages fuse to form multinucleated giant cells. Alongside macrophages, cells, such as dendritic cells (DCs), neutrophils, natural killer cells, fibroblasts, CD4 T cells, and cytotoxic CD8 T cells are also recruited to the granuloma via cytokine mediation, leading to further containment of the bacterium[8].

Inside the granuloma, effector responses, along with a lack of nutrients and oxygen, cause *M. tb* to become dormant and remain in a non-replicating state. The contained *M. tb* within a granuloma in the lungs is referred to as latent tuberculosis (LTBI). In immunocompromised individuals, a breakdown of immune responses can result in reactivation of *M. tb*[9]. An immune-compromised state promotes liquefaction of the caseum in the granuloma and bacterial replication, thereby promoting cavity formation and the release of *M. tb* to the exterior during coughing, causing spread of the infection to other parts of the lungs[10]. Active *M. tb* deflects the host defense mechanisms via cord factor, preventing fusion between the phagosome and lysosome and degradation of the bacterium[11].

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