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Mini Review

Role of T-Helper cells (CD4⁺ T Cells) in human immune system against some microbial infection: A mini review

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Abstract

The human immune system consists of innate and adaptive immune responses which both provide protective immunity to microbial infection. The adaptive immune system consists of T and B cell which act as second line defense through production of neutralizing antibody by B cells and cytotoxic activity of CD8⁺ T cells. The CD4⁺ T-cell performs a central role in the immune responses. These cells also known as T4 or helper/inducer T lymphocytes recognize antigens presented by antigen presenting cells (APC) such as macrophages and monocytes. Once antigens such as bacteria and viruses are presented, CD4⁺ T lymphocytes orchestrate the body's antigen-specific immune response by Coordinating B-lymphocyte production of antibodies to these antigens, producing cytokines and induction of cytotoxic T-lymphocytes. The paper was aimed to review the role of T-helper cells (CD4⁺ T cells) in human immune system against some microbial infections.

More Information

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Introduction

There are two types of immune system in human for protection against pathogens. One of the immune systems is called the innate immune system. The innate immune system constitutes the first line of host defense during infection and, therefore, plays a crucial role in the early recognition and subsequent triggering of a pro-inflammatory response to the invading pathogens [1]. The second type of immune system is the adaptive (acquired) immunity. Unlike innate immunity, adaptive immunity is highly specific, has immunologic memory, and can respond rapidly and vigorously to a second antigen exposure [2]. The adaptive immune system, on the other hand, is responsible for the elimination of pathogens in the late phase of infection and in the generation of immunological memory [3]. This immune response can be antibody mediated (humoral), cell mediated (cellular), or both [4]. Cell-mediated immunity involves specialized white blood cells called T cells that act against microbe-infected cells and foreign tissues. They also regulate the activation and proliferation of other immune system cells such as macrophages, B cells, and other T cells. Humoral immunity, or antibody-mediated immunity, involves the production of glycoprotein antibodies by plasma cells derived from B cells. CD4⁺ T cells along with CD8⁺ T cells make up the majority of T-lymphocytes (T-cells) [2].

CD4⁺ T lymphocytes are a specialized subpopulation of T cells that recognize antigenic peptides in the context of MHC class II molecules. Historically, CD4⁺ T cells have been regarded as 'helper' T (Th) cells, since CD4⁺ T-cell help is required for both the induction of neutralizing antibodies by mature B cells and for the maintenance of effective cytotoxic T cell (CTL) responses. CD4⁺ T cells after being activated and differentiated into distinct effector subtypes play a major role in mediating immune response through the secretion of specific cytokines. The CD4⁺ T cells carry out multiple functions, ranging from activation of the cells of the innate immune system, B-lymphocytes, cytotoxic T cells, as well as non-immune cells, and also play critical role in the suppression of immune reaction, hence it plays vital role in immunity against pathogens such as bacteria and viruses [5].

T helper Cells (CD4⁺ T Cells)

T-helper (TH) cells, also known as CD4⁺ T cells are a

specialized subpopulation of T cells that recognize antigenic peptides in the context of MHC class II molecules. Historically, CD4+ T cells have been regarded as 'helper' T (Th) cells, since CD4+ T-cell help is required for both the induction of neutralizing antibodies by mature B cells and for the maintenance of effective cytotoxic T cell (CTL) responses. In the mid-1980s functional attributes were discovered that allowed CD4+ T cells to be subdivided into dichotomous subpopulations of Th1 and Th2 cells [6]. Th1 cells are defined by their property to produce IFNg, TNFa and IL-2 cytokines, and play critical roles in antitumor immunity [7] and immune responses to many virus infections including lymphocytic choriomeningitis virus (LCMV) [8], influenza virus [9], vesicular stomatitis virus (VSV) [10], polio virus [11], and murine g herpes virus [12]. Besides helper functions, Th1 cells also have important effector functions. For example, in addition to their immune-regulatory activities, both IFNg and TNFa cytokines mediate direct anti-viral activities as observed in murine infections of LCMV [13], herpes simplex virus (HSV) [14], vaccinia virus [15], measles virus (MV) [16] and Friend virus (FV) [17]. Th1 cells may also have cytotoxic potential as observed in a number of viral infections, including dengue virus [18], hepatitis B virus (HBV) [19], Measles Virus [20], human herpes virus 6 [21], Human Immunodeficiency Virus (HIV) [22] and Epstein-Barr virus (EBV) [23].

By contrast, Th2 cells secrete IL-4, IL-5, IL-9, IL-13 and IL-25 when activated in response to bacterial, helminth or parasitic pathogens such as *Clostridium tetani, Staphylococcus aureus, Streptococcus pneumonia, Pneumocystis carinii, Schistosoma mansoni,* and *Trichinella spiralis* [24]. Th2 cells provide help for B cells to produce IgM, IgA, IgE, and IgG iso-type antibodies, which form the effector molecules of the humoral immune response [25]. The Th1/Th2 paradigm introduced by Mossman and Coffman has been expanded by identification of other CD4+ T cell sub-populations. IL-17 secreting cells designated as Th17 cells [26,27] are important for resistance to extracellular bacteria and fungi, but may also contribute to allergic responses [28] and autoimmune pathogenesis in diseases such as multiple sclerosis, rheumatoid arthritis, psoriasis and inflammatory bowel disease [29]. Yet another sub-population of CD4+ T cells is the follicular helper T (Tfh) cell. Upon antigenic stimulation, Tfh produce IL-21 and home to B cell follicles where they are essential for the differentiation of B cells into germinal center B cells and antibody secreting plasma cells [30,31].

Activities of CD4+ T Cells

The CD4+ T-cell performs a central role in the immune response [32]. These cells also known as T4 or helper/inducer T lymphocytes recognize antigens presented by cells bearing HLA class 11 molecules such as monocytes. The CD4+ molecule helps to stabilize the binding of these T-lymphocytes to HLA 11 molecule on the antigen-presenting cell [33]. Once an antigen is recognized, CD4+ T lymphocytes orchestrate the body's antigen-specific immune response and specific functions of CD4+ T lymphocytes include the: Coordinating B-lymphocyte production of antibodies to these antigens; Producing cytokines and Induction of cytotoxic lymphocytes.

These crucial functions make CD4+ T lymphocytes critical elements of the immune system, and their dysfunction and destruction in HIV-1 infection seriously impairs the ability to respond to diverse pathogens [34].

CD4+ T cells contribute a myriad of activities in protective immunity against viruses that are initiated by infection or by vaccination. These activities can be broadly separated into distinct categories that include recruitment of key lymphoid cell populations into secondary lymphoid tissue or sites of pathogen infection, provision of help for expansion or function of other effector cells, or offering direct effector function through production of cytokines or cell-mediated cytotoxicity. One key activity of CD4+ T cells is recruitment of other lymphoid cells: CD4+ T cells can promote engagement of CD8+ T cells with dendritic cells (DCs) in secondary lymphoid tissue [35,36], cause influx of lymphoid cells into draining lymph node, and recruit innate or antigen-specific effectors to the site of viral replication [37]. Whether these CD4+ T cells are ever limiting in response to infection, and can thus serve as predictors of disease susceptibility, is not yet known. The role of CD4+ T cell help in CD8+ T cell priming, effector function, and memory has been extensively studied in recent years [38]. Although such help may not be as critical for viruses that offer many CD8 epitopes [39] and/or generate potent activating signals from DCs through strong Toll-like receptor engagement, it may be critical for pathogens that antagonize the immune response by down-regulating the activity of pro-inflammatory mediators. It is also likely to be essential for the development of memory CD8+ T cells that can be recalled upon challenge [40]. With chronic viral infections, the role and importance of CD4+ T cell help is even more profound. Under these conditions, CD8+ T cells rely on continued rounds of expansion for which CD4+ T cell cytokine production is critical [41]. That CD4+ T cell help is needed for high-affinity, neutralizing antibody responses by B cells has been known for decades, but more recent work has identified the follicular helper CD4+ T cells (Tfh) as the key subset that mediates this function [31,42]. Recent identification of cells with Tfh lineage markers and functional activity in circulation of human subjects [43] raises the possibility that quantifying this subset may be useful as a biomarker for future vaccine responses, particularly if coupled with analyses of CD4 specificity. Finally, increasing evidence supports the view that CD4+ T cells have direct roles as effectors in antiviral immunity either through provision of key antiviral cytokines or through direct cytotoxicity [44].

Conclusion

There are two types of immune system in human for

protection against pathogens. They are innate and adaptive (acquired) immune system. The acquired immune system is made up of T and B cells. CD4+ T cells along with CD8+ +T cells make up the majority of T-lymphocytes (T cells). The CD4+ T cells carry out multiple functions, ranging from activation of the cells of the innate immune system, B-lymphocytes, cytotoxic T cells, as well as non-immune cells, and also play critical role in the suppression of immune reaction, hence it plays vital role in immunity against pathogens such as bacteria and viruses.

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