General Internal Medicine and Clinical Innovations



Review Article ISSN: 2397-5237

Cell Mediated Immunity

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Abstract

Cell mediated immunity is by definition associated with the cellular immune response. It is a complex series of events that allows for protection against intracellular pathogens such as virus as well as bacteria. It does not involve antibody production as a rule although antibody may serve in an ancillary activation role. It is one of the two branches of immunity in the animal body. The other being antibody production.

Definition

Cell mediated immunity (CMI) does not by definition involve a large-scale antibody response to an antigen. Rather it is mediated by cells and the chemical signals that are sent out. These chemical signals may act directly as effector molecules such as tumor necrosis factor, or they may stimulate other cytokines of the complement system. Antibody may be involved as a bridge or effector molecule, or as part of a specific activation scheme. The initial response is the generation of an antigen-specific effector cell. This is the initiation of CMI. Cell mediated immunity is directed primarily at invading microbes including bacteria and virus, but also against cancer cells. CMI also has a role in transplant rejection.

Origin and overview

Since at least the time of Jenner, the immune system has been thought of as two arms. The humoral branch which can provide protection by immunization with the development of specific antibody to pathogens, and the cell mediated branch which functions by cell activation and communication [1,2]. This gives the normal mammalian immune response much flexibility as it responds to various pathogens. Immature T cells (that have not as yet encountered antigen) are converted or "activated" to effector T cells after coming into contact with antigen presenting cells (APC) [3]. APC includes B cells, macrophages and dendritic cells. During these encounters, antigenic sub-parts or peptides which are protein based are placed into contact with the major histocompatibility complex (MHC) of the cell. These complexes are then "presented" to peptide receptors on T cells. These T cells may be from one of several classes. T helper (2) cells stimulate mature B cells to differentiate into plasma cells and produce specific antibody; Cytotoxic T cells interact directly with a pathogen and by apoptosis kill the target cell. This is a direct interaction. Thirdly, are the T helper (1) cells which activate macrophages and may also stimulate cytokine production [4,5].

Effector cells

Cytotoxic CD8+ T cells

These cells migrate through the body and are critical for the elimination of virus and bacteria which may exist in the cytoplasm of cells. They react to cells which display MHC I complexes. They will release molecules that kill target cells directly [6].

Th1 cells

These cells express CD4+. These cells will matriculate through tissues and will recognize MHC II/Peptide complexes as recognized and displayed on macrophages. Gamma interferon is produced and is encountered by the macrophages. This tends to enhance the killing ability of the macrophages. This cell also has chemokine receptors (CXCR3A, CCR5) which allow for enhanced mobility to inflammation sites or areas [5].

Th2 cells

These cells also express CD4+. However, in this case they migrate to the lymph nodes where they encounter activated B cells that are expressing microbial peptide MHC on their surface. This is a result of the B cell essentially phagocytizing at least some protein fragment from the microbe, if not the whole organism, and are now expressing and displaying the processed microbial peptides by MHC II. Th2 cells, upon encounter with B cells (with the peptide-MHC II on their surface) will produce IL-4 and IL-5. These cytokines induct target B-cells to differentiate into plasma cells with the result of antibody production [7]. This is the best example in immunology of "collaboration" between humoral and cell-mediated immunity [5,7].

Immune Memory. Immune memory or as it is referred to in some of the older literature as the anamnestic response T memory cells are produced. They circulate in the blood (effector T memory) or are found in tissues (resident T memory). They may be either T8 or T4 cells. T memory cells (CD8) may be activated by virus and engage a inflammatory cytokine response. Circulating T memory cells are found associated with macrophages in the mucosa. The most important response that is elicited is the humoral immune response. This response is activated to a much faster extent, and to a greater degree that primary response to an antigen. This is due to the programming of these memory T cells. The anamnestic response also applies to non-specific immunity where antigen is responded to more rapidly [8,9].

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Keywords: cells, immunity, interleukin, effector molecule

Received: March 07, 2022; Accepted: March 18, 2022; Published: March 21, 2022

Gen Int Med Clin Innov, 2022 doi: 10.15761/GIMCI.1000210 Volume 7: 1-2

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Gen Int Med Clin Innov, 2022 doi: 10.15761/GIMCI.1000210 Volume 7: 2-2