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CELL MEDIATED AND HUMORAL IMMUNE SYSTEM

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CELL MEDIATED IMMUNE SYSTEM

Cell-mediated immune responses involve the destruction of infected cells by cytotoxic T cells, or the destruction of intracellular pathogens by macrophages (more...) The activation of naive T cells in response to antigen, and their subsequent proliferation and differentiation, constitutes a primary immune response

Cellular immunity protects the body through:

T-cell mediated immunity or T-cell immunity: activating antigen-specific cytotoxic T cells that are able to induce apoptosis in body cells displaying epitopes of foreign antigen on their surface, such as virus-infected cells, cells with intracellular bacteria, and cancer cells displaying tumor antigens;

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History

In the late 19th century Hippocratic tradition medicine system, the immune system was imagined into two branches: humoral immunity, for which the protective function of immunization could be found in the humor (cell-free bodily fluid or serum) and cellular immunity, for which the protective function of immunization was associated with cells. CD4 cells or helper T cells provide protection against different pathogens. Naive T cells, which are immature T cells that have yet to encounter an antigen, are converted into activated effector T cells after encountering antigen-presenting cells (APCs)

These APCs, such as macrophages, dendritic cells, and B cells in some circumstances, load antigenic peptides onto the MHC of the cell, in turn presenting the peptide to receptors on T cells. The most important of these APCs are highly specialized dendritic cells; conceivably operating solely to ingest and present antigens. Activated effector T cells can be placed into three functioning classes, detecting peptide antigens originating from various types of pathogen: The first class being

1) Cytotoxic T cells, which kill infected target cells by apoptosis without using cytokines, 2) Th1 cells, which primarily function to activate macrophages, and
2) 3) Th2 cells, which primarily function to stimulate B cells into producing antibodies.

Macrophage and natural killer cell action: enabling the destruction of pathogens via recognition and secretion of cytotoxic granules (for natural killer cells)
and phagocytosis (for macrophages);

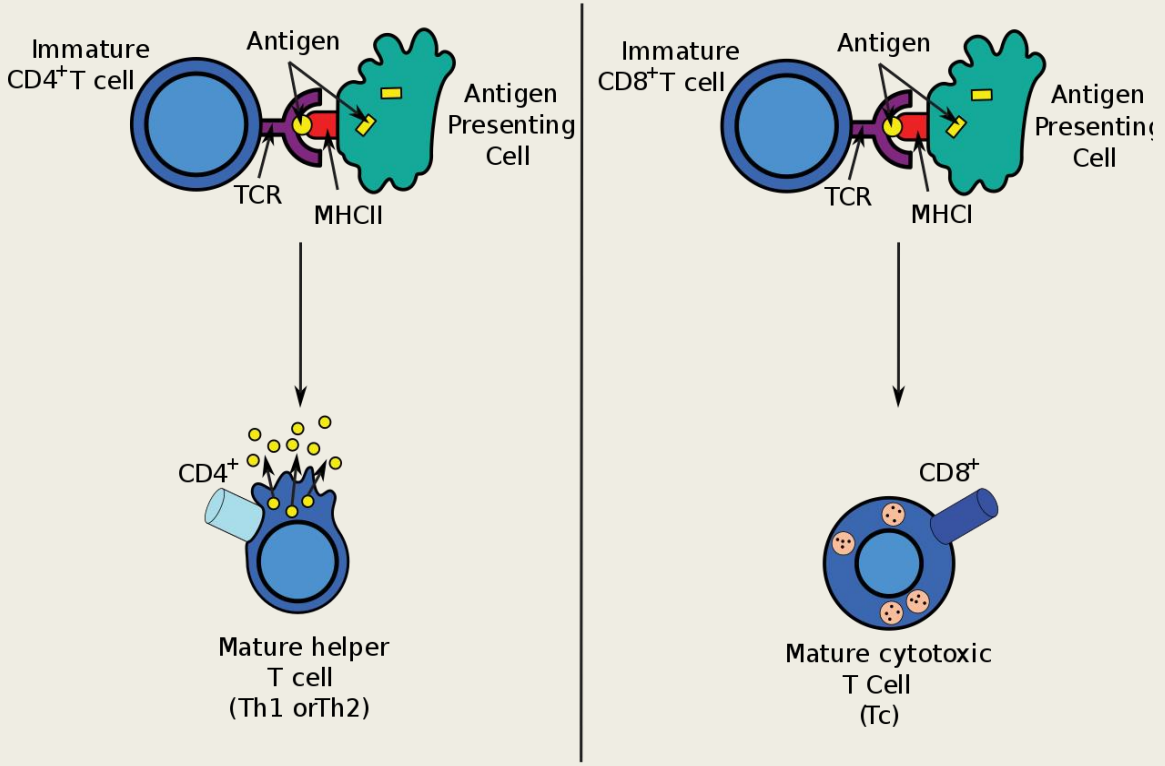
And Stimulating cells to secrete a variety of cytokines that influence the function of other cells involved in adaptive immune responses and innate immune responses.

Cell-mediated immunity is directed primarily at microbes that survive in phagocytes and microbes that infect non-phagocytic cells. It is most effective in removing virus-infected cells, but also participates in defending against fungi, protozoans, cancers, and intracellular bacteria. It also plays a major role in transplant rejection

Apoptosis (from Ancient Greek ἀπόπτωσις, apóptōsis, "falling off") is a form of programmed cell death that occurs in multicellular organisms. Biochemical events lead to characteristic cell changes (morphology) and death. These changes include blebbing, cell shrinkage, nuclear fragmentation, chromatin condensation, chromosomal DNA fragmentation, and global[vague] mRNA decay. The average adult human loses between 50 and 70 billion cells each day due to apoptosis. For an average human child between the ages of 8 and 14, approximately 20–30 billion cells die per day

FIG:Antigen presentation stimulates T cells to become either "cytotoxic" CD8+ cells or "helper" CD4+ cells.

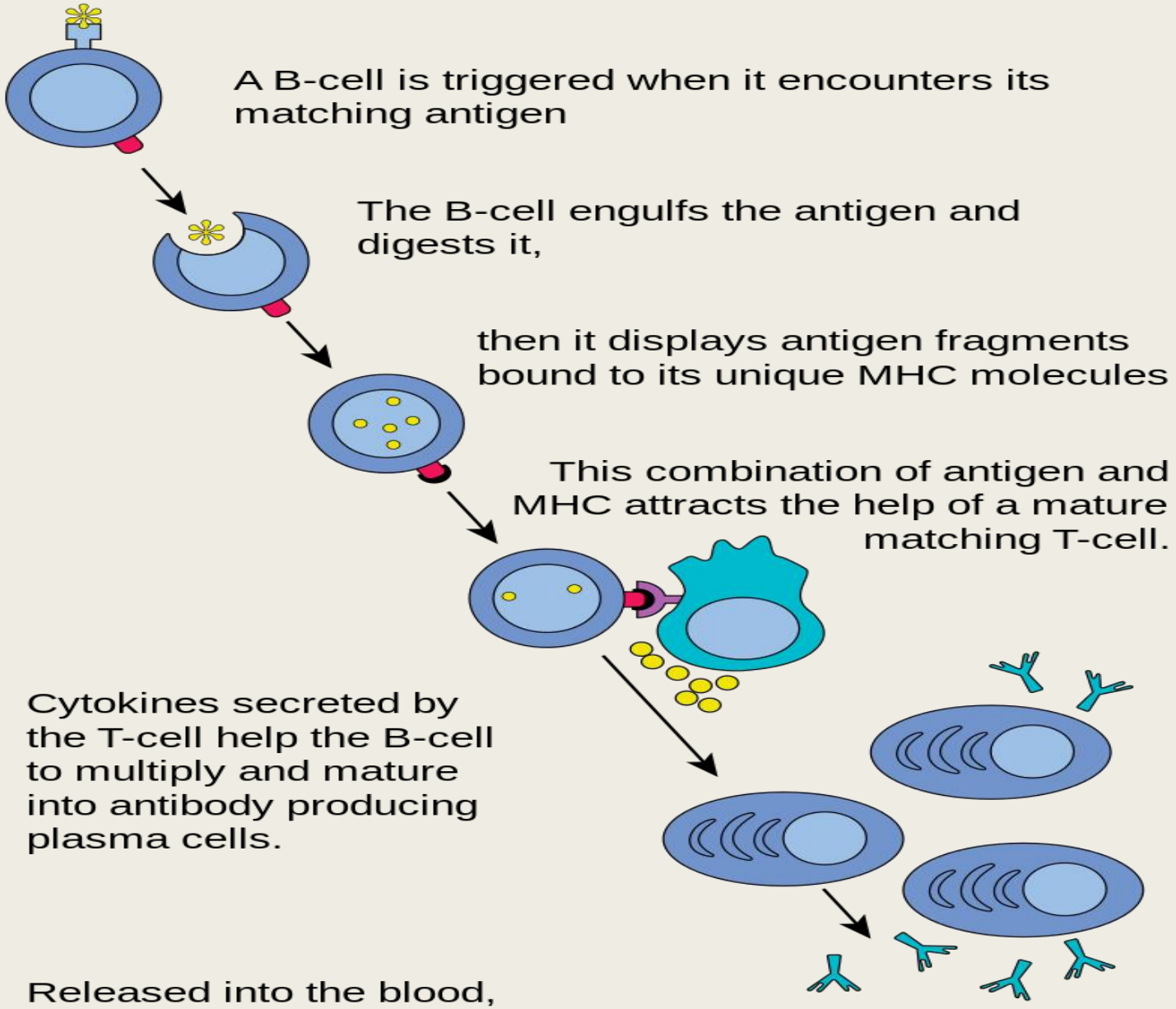
A cytotoxic T cell (also known as TC, cytotoxic T lymphocyte, CTL, T-killer cell, cytolytic T cell, CD8+ T-cell or killer T cell) is a T lymphocyte (a type of white blood cell) that kills cancer cells, cells that are infected (particularly with viruses), or cells that are damaged in other ways



HUMORAL IMMUNE SYSTEM

Humoral immunity or humoural immunity is the aspect of immunity that is mediated by macromolecules found in extracellular fluids such as secreted antibodies, complement proteins, and certain antimicrobial peptides. Humoral immunity is so named because it involves substances found in the humors, or body fluids. It contrasts with cell-mediated immunity. Its aspects involving antibodies are often called antibody-mediated immunity.

Humoral immunity refers to antibody production and the accessory processes that accompany it, including: Th2 activation and cytokine production, germinal center formation and isotype switching, and affinity maturation and memory cell generation. It also refers to the effector functions of antibodies, which include pathogen and toxin neutralization, classical complement activation, and opsonin promotion of phagocytosis and pathogen elimination.

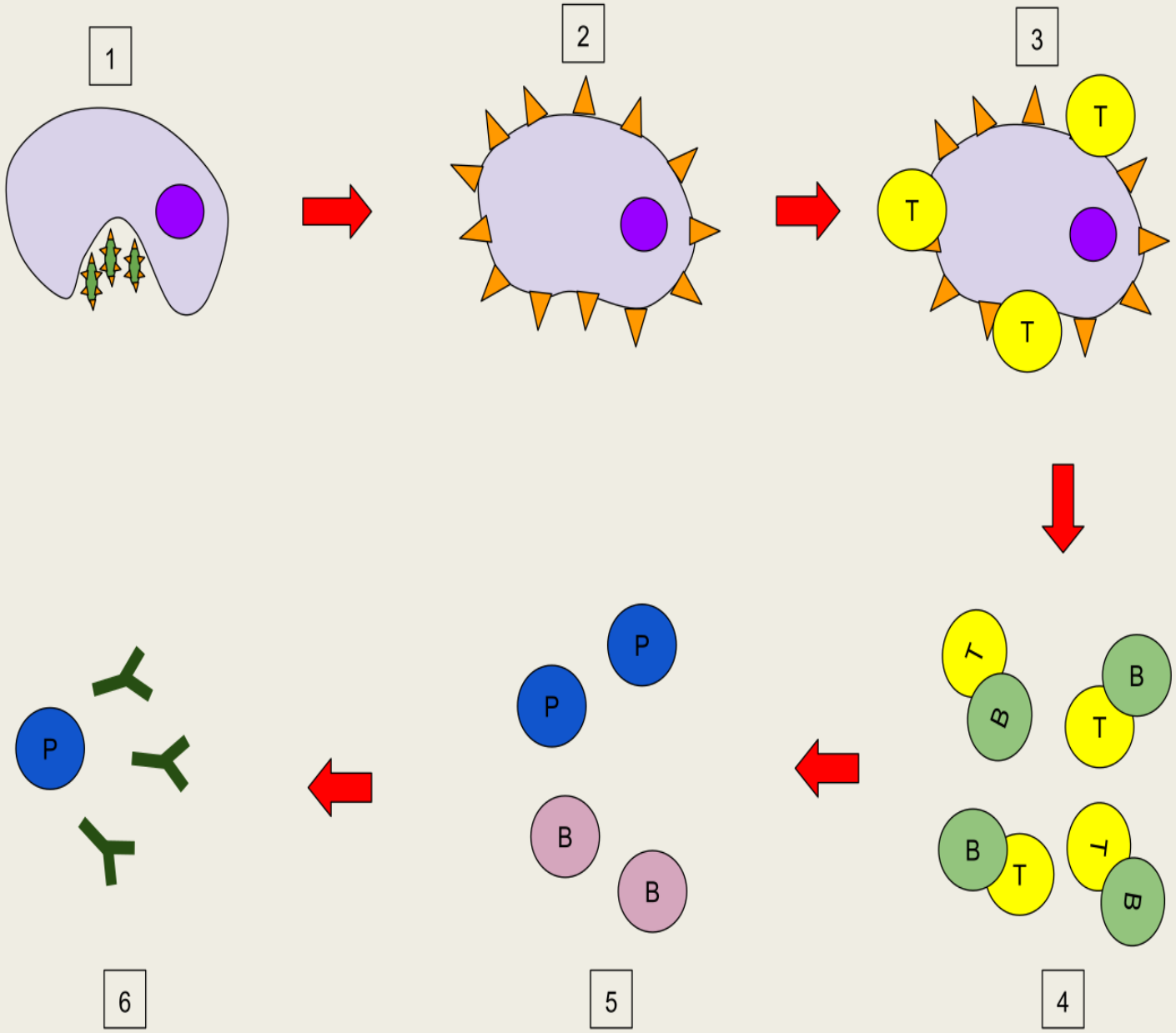


B cell activation is a large part of the humoral immune response

History

The concept of humoral immunity developed based on analysis of antibacterial activity of the serum components. Hans Buchner is credited with the development of the humoral theory.

In 1890 he described alexins, or "protective substances", which exist in the blood serum and other bodily fluid and are capable of killing microorganisms. Alexins, later redefined as "complement" by Paul Ehrlich, were shown to be the soluble components of the innate response that lead to a combination of cellular and humoral immunity, and bridged the features of innate and acquired immunity.



Step 1: A macrophage engulfs the pathogen. Step 2: The macrophage then digests the bacterium and presents the pathogen's antigens. Step 3: A T helper cell binds to the macrophage and becomes an activated T helper cell. Step 4: The activated T helper cell binds to a B cell in order to activate the B cell. Step 5: When the B cells are activated, some B cells turn into plasma cells and are released in the blood, while other B cells become B memory cells that quicken response for a second exposure. Step 6: Plasma cells then secrete antibodies, which bind to antigens to fight the invading pathogens.

Major discoveries in the study of humoral immunity[3]

Substance	Activity	Discovery
Alexin(s) Complement	Soluble components in the serum that are capable of killing microorganisms	Buchner (1890), Ehrlich (1892) [2]
Antitoxins	Substances in the serum that can neutralize the activity of toxins, enabling passive immunization	von Behring and Kitasato (1890)[4]
Bacteriolysins	Serum substances that work with the complement proteins to induce bacterial lysis	Richard Pfeiffer (1895)[5]
Bacterial agglutinins and precipitins	Serum substances that agglutinate bacteria and precipitate bacterial toxins	von Gruber and Durham (1896), [6] Kraus (1897) [7]
Hemolysins	Serum substances that work with complement to lyse red blood cells	Belfanti and Carbone (1898) [8] Jules Bordet (1899) [9]
Opsonins	Serum substances that coat the outer membrane of foreign substances and enhance the rate of phagocytosis by macrophages	Wright and Douglas (1903)[10]
Antibody	Formation (1900), antigen-antibody binding hypothesis (1938), produced by B cells (1948), structure (1972), immunoglobulin genes (1976)	Founder: P Ehrlich[2]

Mechanism

In humoral immune response, first the B cells mature in the bone marrow and gain B-cell receptors (BCR's) which are displayed in large number on the cell surface.

These membrane-bound protein complexes have antibodies which are specific for antigen detection. Each B cell has a unique antibody that binds with an antigen. The mature B cells migrate from the bone marrow to the lymph nodes or other lymphatic organs, where they begin to encounter pathogens.

B cell activation

When a B cell encounters an antigen, the antigen is bound to the receptor and taken inside the B cell by endocytosis. The antigen is processed and presented on the B cell's surface again by MHC-II proteins.

B cell proliferation

The B cell waits for a helper T cell (TH) to bind to the complex. This binding will activate the TH cell, which then releases cytokines that induce B cells to divide rapidly, making thousands of identical clones of the B cell. These daughter cells either become plasma cells or memory cells. The memory B cells remain inactive here; later when these memory B cells encounter the same antigen due to reinfection, they divide and form plasma cells. On the other hand, the plasma cells produce a large number of antibodies which are released free into the circulatory system.

Antibody-antigen reaction

Now these antibodies will encounter antigens and bind with them. This will either interfere with the chemical interaction between host and foreign cells, or they may form bridges between their antigenic sites hindering their proper functioning, or their presence will attract macrophages or killer cells to attack and phagocytose them.

The complement system is a biochemical cascade of the innate immune system that helps clear pathogens from an organism. It is derived from many small blood plasma proteins that work together to disrupt the target cell's plasma membrane leading to cytolysis of the cell. The complement system consists of more than 35 soluble and cell-bound proteins, 12 of which are directly involved in the complement pathways.

The complement system is involved in the activities of both innate immunity and acquired immunity. Activation of this system leads to cytolysis, chemotaxis, opsonization, immune clearance, and inflammation, as well as the marking of pathogens for phagocytosis. The proteins account for 5% of the serum globulin fraction. Most of these proteins circulate as zymogens, which are inactive until proteolytic cleavage.

Three biochemical pathways activate the complement system: the classical complement pathway, the alternate complement pathway, and the mannose-binding lectin pathway. The classical complement pathway typically requires antibodies for activation and is a specific immune response, while the alternate pathway can be activated without the presence of antibodies and is considered a non-specific immune response. Antibodies, in particular the IgG1 class, can also "fix" complement.

Antibodies

Immunoglobulins are glycoproteins in the immunoglobulin superfamily that function as antibodies. The terms antibody and immunoglobulin are often used interchangeably. They are found in the blood and tissue fluids, as well as many secretions. In structure, they are large Y-shaped globular proteins. In mammals there are five types of antibody: IgA, IgD, IgE, IgG, and IgM. Each immunoglobulin class differs in its biological properties and has evolved to deal with different antigens. Antibodies are synthesized and secreted by plasma cells that are derived from the B cells of the immune system.

An antibody is used by the acquired immune system to identify and neutralize foreign objects like bacteria and viruses. Each antibody recognizes a specific antigen unique to its target.

By binding their specific antigens, antibodies can cause agglutination and precipitation of antibody-antigen products, prime for phagocytosis by macrophages and other cells, block viral receptors, and stimulate other immune responses, such as the complement pathway.

An incompatible blood transfusion causes a transfusion reaction, which is mediated by the humoral immune response. This type of reaction, called an acute hemolytic reaction, results in the rapid destruction (hemolysis) of the donor red blood cells by host antibodies. The cause is usually a clerical error, such as the wrong unit of blood being given to the wrong patient. The symptoms are fever and chills, sometimes with back pain and pink or red urine (hemoglobinuria). The major complication is that hemoglobin released by the destruction of red blood cells can cause acute kidney failure.