

Lec.9:Humoral and Cell-Mediated Immune Responses

The immune system distinguishes two groups of foreign substances. One group consists of antigens that are freely circulating in the body. These include molecules, viruses, and foreign cells. A second group consists of self cells that display aberrant MHC proteins. Aberrant MHC proteins can originate from antigens that have been engulfed and broken down (exogenous antigens) or from virus-infected and tumor cells that are actively synthesizing foreign proteins (endogenous antigens). Depending on the kind of foreign invasion, two different immune responses occur:

Humoral immunity

Humoral immunity : an immune response 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. Its aspects involving antibodies are often called **antibody-mediated immunity**.

The humoral response (or antibody-mediated response) involves B cells that recognize antigens or pathogens that are circulating in the lymph or blood .

The response follows this chain of events:

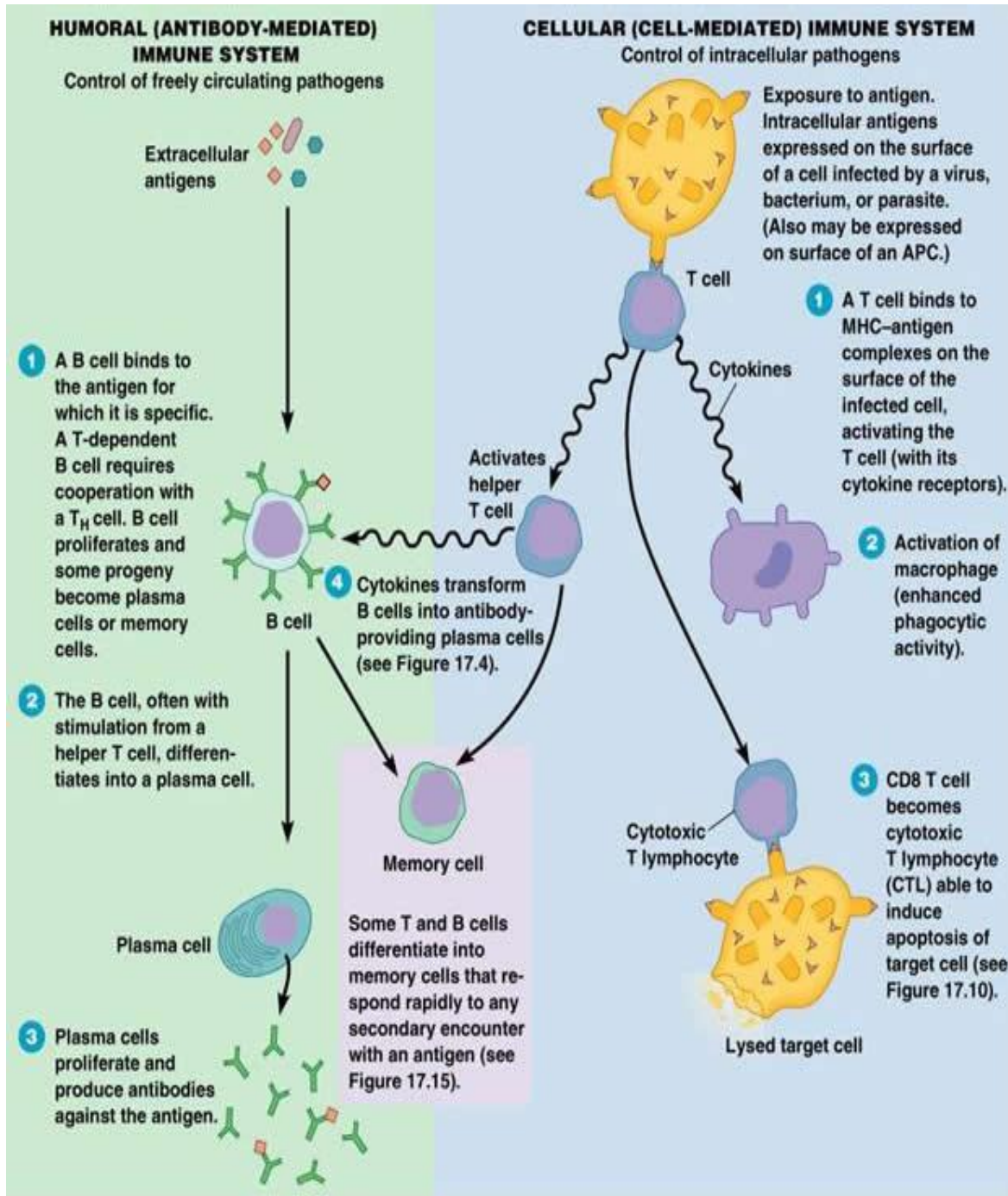
1. Antigens bind to B cells.
2. Interleukins or helper T cells costimulate B cells. In most cases, both an antigen and a costimulator are required to activate a B cell and initiate B cell proliferation.
3. B cells proliferate and produce plasma cells. The plasma cells bear antibodies with the identical antigen specificity as the antigen receptors of the activated B cells. The antibodies are released and circulate through the body, binding to antigens.
4. B cells produce memory cells. Memory cells provide future immunity.

Cellular immunity

Cellular immunity is an immune responses mediated by activated antigen specific T lymphocytes. This type of immune response that does not involve antibodies, but rather involves the activation of phagocytes, antigen-specific cytotoxic T-lymphocytes, and the release of various cytokines in response to an antigen.

The cell-mediated response involves mostly T cells and responds to any cell that displays aberrant MHC markers, including cells invaded by pathogens, tumor cells, or transplanted cells. The following chain of events describes this immune response:

1. Self cells or APCs displaying foreign antigens bind to T cells.
2. Interleukins (secreted by APCs or helper T cells) costimulate activation of T cells.
3. If MHC-I and endogenous antigens are displayed on the plasma membrane, T cells proliferate, producing cytotoxic T cells. Cytotoxic T cells destroy cells displaying the antigens.
4. If MHC-II and exogenous antigens are displayed on the plasma membrane, T cells proliferate, producing helper T cells. Helper T cells release interleukins (and other cytokines), which stimulate B cells to produce antibodies that bind to the antigens and stimulate nonspecific agents (NK and macrophages) to destroy the antigens.



Comparison between humeral and cellular immunity

	Humeral immunity	Cellular immunity
Main cells	B lymphocytes	T lymphocytes
Maturation	Generated and matured in bone marrow	Originate in bone marrow and complete development in thymus
Protect against	Extracellular microbes and their toxins <ol style="list-style-type: none"> 1. toxin induced diseases 2. infections (virulence related to polysaccharide capsule) 	Intracellular microbes <ol style="list-style-type: none"> 1. viruses 2. parasites (leishmania) 3. bacteria (mycobacteria, listeria) 4. kill tumor cells
%age of lymphocytes	10-20% circulating peripheral lymphocyte population	60-70%
Location in lymph nodes	Superficial cortex	Paracortical areas
Location in spleen	White pulp	Periarteriolar sheaths
Receptors	B-cell antigen receptor complex consisting of mainly IgM and IgD immunoglobulins	In 95% T cells à alpha/beta TCR In minority à gamma, T cells
Accessory surface molecules	Ig α , Ig β , Fc receptors, CD40, CD21	CD3 molecular complex Dimer of Σ chain CD4, CD8, CD2, CD28 integrins

End result of activation	Differentiation of B cells into antibody secreting cells called plasma cells	Secrete locally acting proteins called cytokines
Hypersensitivity reactions	I, II, III are antibody mediated	IV is cell mediated
Role of MHC molecules	Antigen receptor recognizes whole unprocessed proteins and has no requirement for presentation by MHC protein	Antigen receptor recognizes only processed peptides in association with MHC protein
Regulator of antibody synthesis	No	Yes
Onset	Rapid	Delayed type hypersensitivity
Antibodies	Formed	Not formed
Evaluation	From plasma level of antibodies	Skin test for development of delayed type of hypersensitivity
Cells involved	Ab synthesis requires 3 cells: <ol style="list-style-type: none"> 1. t lymphocytes 2. b lymphocytes 3. macrophage 	<ol style="list-style-type: none"> 1. macrophage 2. helper T cells 3. natural killer T cells 4. cytotoxic T cells

Cytokines

Cytokines are a large, diverse family of small proteins (usually smaller than 30 kDa) that function as messenger molecules that can communicate signals from one cell type to another and instruct the cell receiving the signal to proliferate, differentiate, secrete additional cytokines, migrate or die (act as intercellular messengers).

Cytokines regulate the nature, intensity and duration of the immune response by exerting a variety of effects on lymphocytes and/or other cells. Influencing both innate and adaptive immune responses.

Types of cytokines

They are released by cells and affect the behavior of other cells, and sometimes the releasing cell itself. There are many types of Cytokines, including:

- **Chemokines** are a type of cytokines that call in cells to the site of infection using a chemical message is a process referred to as chemotaxis.
- **Interferons** are proteins that inhibit viruses from replicating. If a cell gets invaded by a virus, it releases interferons. This signals other cells to put up their shields so the virus does not spread. So, interferons interfere with the spread of a virus. Interferons also activate natural killer T-cells. These cells further the fight against the virus by destroying infected cells.
- **Interleukins** are proteins that regulate immune and inflammatory responses. They are produced mainly by white blood cells . interleukins create communication between leukocytes. These functions include the growth ,maturation and activation of immune cells
- **Lymphokines** are cytokines that are produced by lymphocytes. Lymphokines have many roles, including the attraction of other immune cells, including macrophages and other lymphocytes, to an infected site and their subsequent activation to prepare them to mount an immune response.
- **Tumour necrosis factor** are cytokines that can cause cell death (apoptosis), induce tumor cell apoptosis and cachexia .

but generally not hormones or growth factors (despite some terminologic overlap). All those types of cytokines are produced by a broad range of cells, including immune cells like macrophages, B lymphocytes, T lymphocytes and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells; a given cytokine

may be produced by more than one type of cell (the two principal producers of cytokines are **helper T cells** (Th cells) and **macrophages**).

Cytokines	Action
Interferon family	Antiviral proteins
Chemokine family	Direct cell migration, adhesion and activation
Tumour necrosis factor family	Regulate inflammatory and immune responses
Interleukin family	Variety of actions dependent upon interleukin and cell type
Haematopoietins	Promote cell proliferation and differentiation
Transforming growth factor beta family	Regulation of immune cells

Cytokines bind to specific receptors on target cells.

The interaction of a cytokine with its receptor on a target cell can cause changes in the expression of adhesion molecules and chemokine receptors on the target membrane, thus allowing it to move from one location to another. Cytokines can also signal an immune cell to increase or decrease the activity of particular enzymes or to change its transcriptional program, thereby altering and enhancing its effector functions.

Cytokines that act on cells some distance away from the secreting cell, such that they must pass through the bloodstream before reaching their target, are referred to as **endocrine** .

Those that act on cells near the secreting cell, such that the cytokine merely has to diffuse a few ingstroms through tissue fluids or across an immunological synapse, are referred to as **paracrine**.

Sometimes, a cell needs to receive a signal through its own membrane receptors from a cytokine that it, itself, has secreted. This type of signaling is referred to as **autocrine**.

