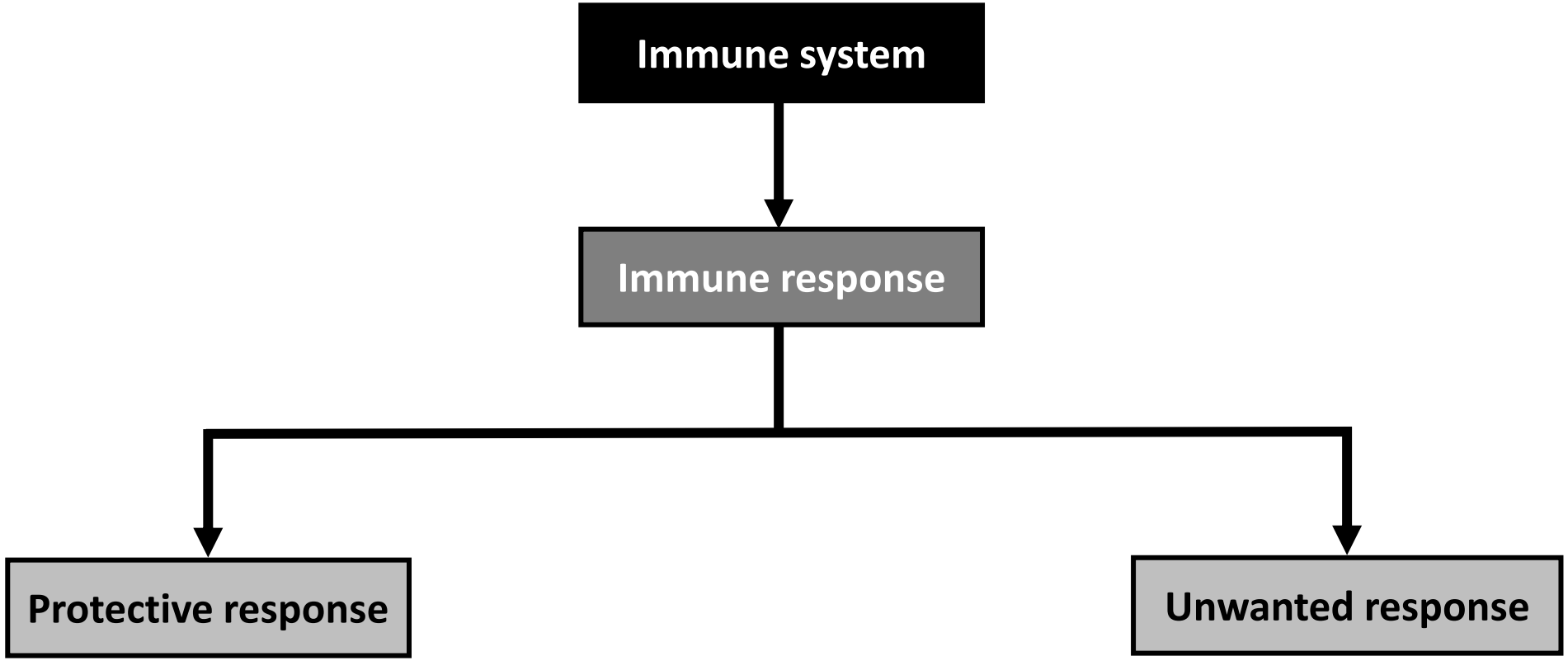
Pathophysiology I

Chapter (2): Immune system

- Branches of immune system
- Components of the immune system
  - Myeloid cells
  - Lymphocytes
  - Cytokines
- Innate immunity
- Adaptive immunity

Immune System

- very complex system
- Large number of cells and molecules
- protects the body from pathogens and foreign substances

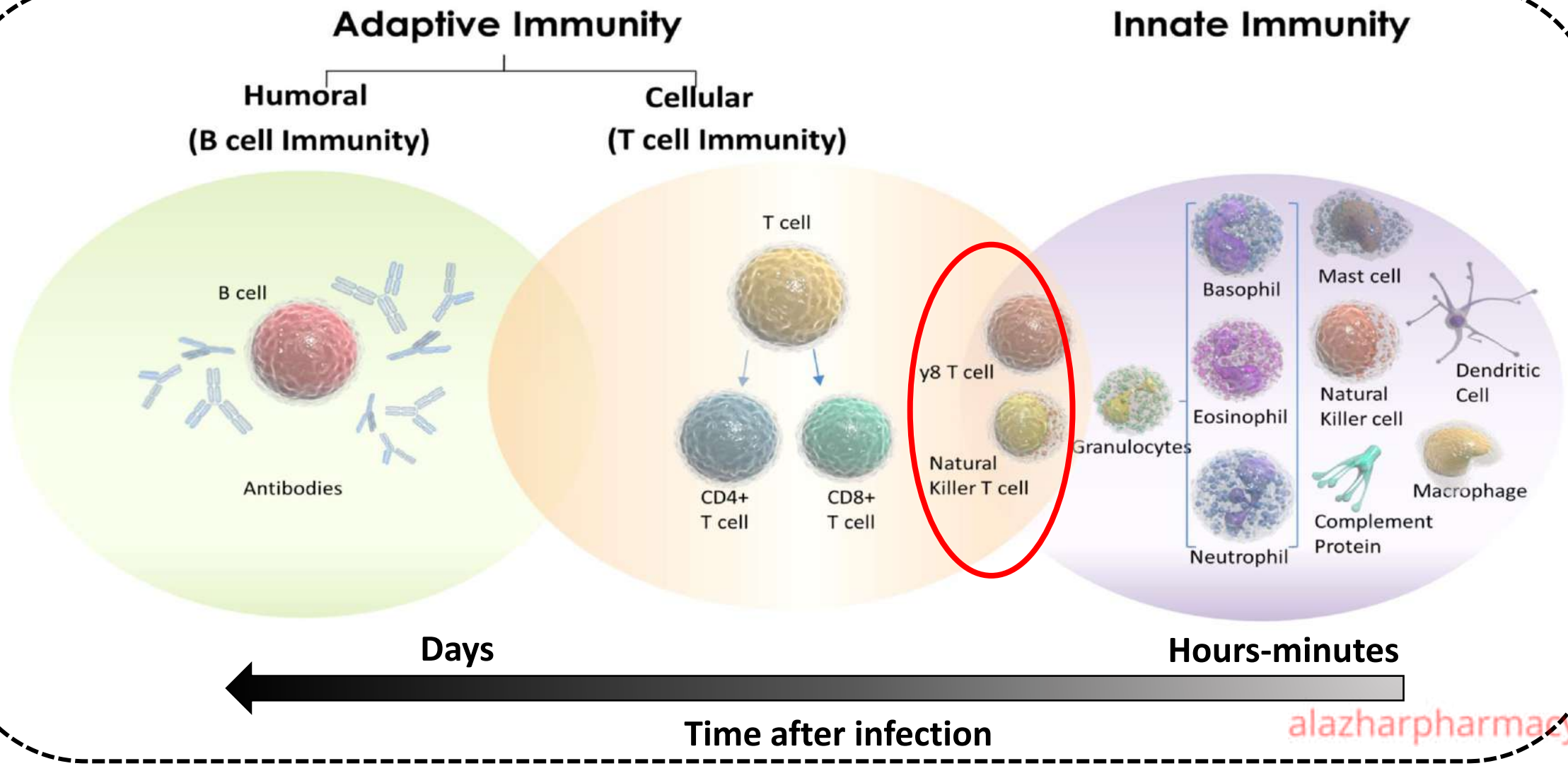


- Pathogens: Bacteria, viruses
- Cancer

- Autoimmune diseases
- Allergy

Immune System

- **Branches of immune system**

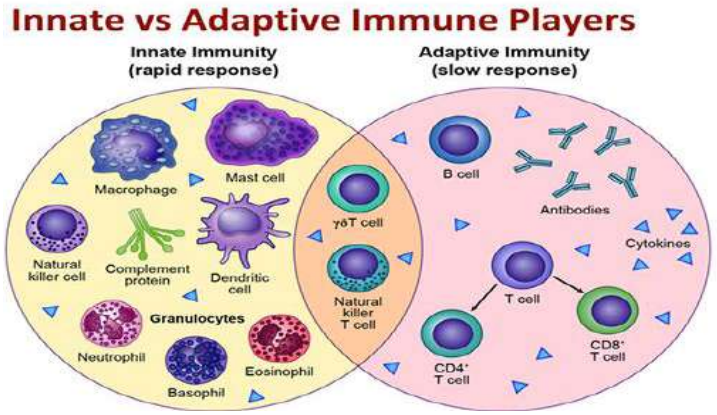


Immune System

TABLE 13.1 FEATURES OF INNATE AND ADAPTIVE IMMUNITY

FEATURE	INNATE	ADAPTIVE
Time of response	Immediate (minutes/hours)	Dependent upon exposure (first: delayed, second: immediate d/t production antibodies)
Diversity	Limited to classes or groups of microbes	Very large; specific for each unique antigen
Microbe recognition	General patterns on microbes; nonspecific	Specific to individual microbes and antigens (antigen/antibody complexes)
Nonself recognition	Yes	Yes
Response to repeated infection	Similar with each exposure	Immunologic memory; more rapid and efficient with subsequent exposure
Defense	Epithelium (skin, mucous membranes), phagocytes, inflammation, fever	Cell killing; tagging of antigen by antibody for removal
Cellular components	Phagocytes (monocytes/macrophages, neutrophils), NK cells, DCs	T and B lymphocytes, macrophages, DCs, NK cells
Molecular components	Cytokines, complement proteins, acute-phase proteins, soluble mediators	Antibodies, cytokines, complement system

Immune System



Hematopoietic stem cells

Multipotent progenitor cells

HSC

MPP

Hematopoiesis

Myeloid Lineage

Lymphoid Lineage

CMP

CLP

CILP

Macrophages

Granulocytes

Dendretic cells

Neutrophils

Eosinophils

Basophils

BCP

TCP

NKP

B cells

T cells

NK cells

ILC1

ILC2

ILC3

Immune System

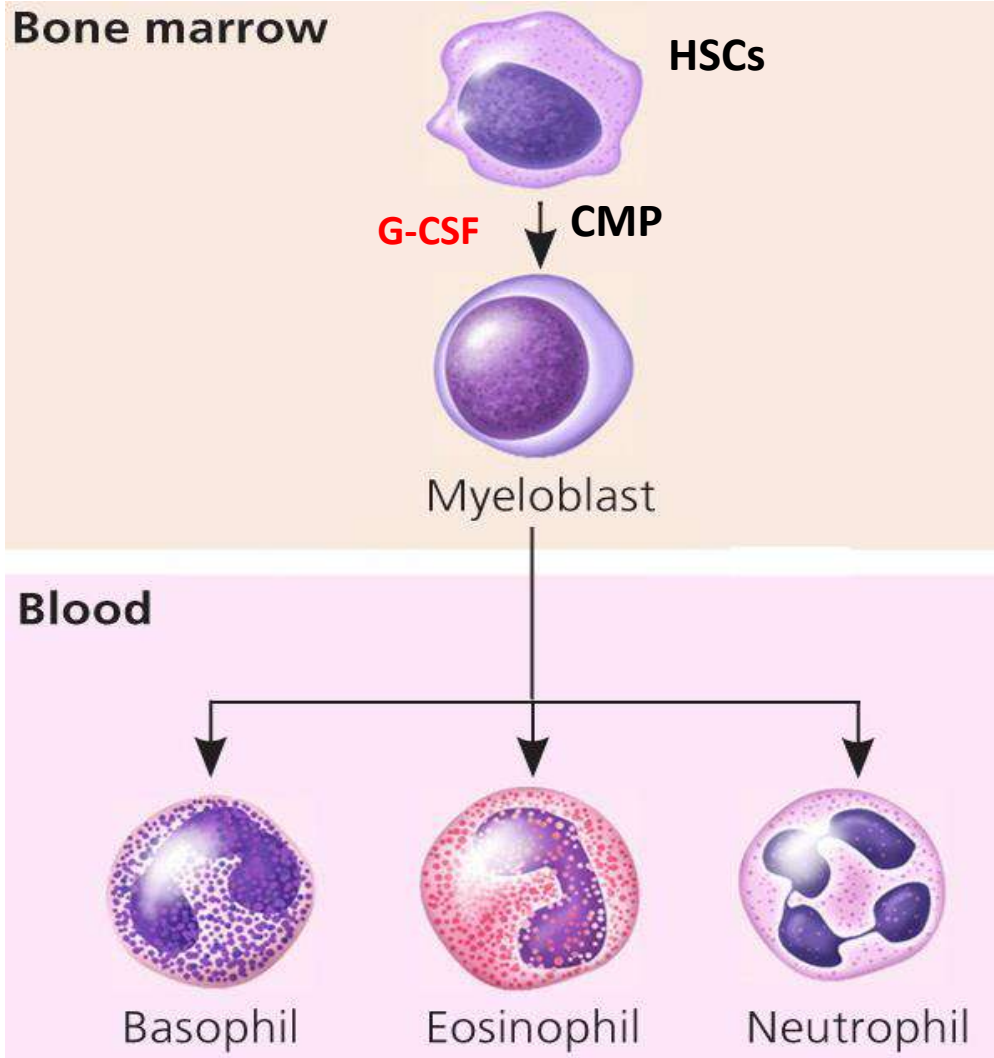
Innate immune system

a. Myeloid lineage cells

1. Granulocytes (polymorphonuclear leukocytes)

- **Neutrophils have three strategies for directly attacking microorganisms: generation of neutrophil extracellular traps, phagocytosis, release of cytokines**

- **Eosinophils and Basophils are important against parasites, which are too large to be ingested by macrophages and neutrophils.**



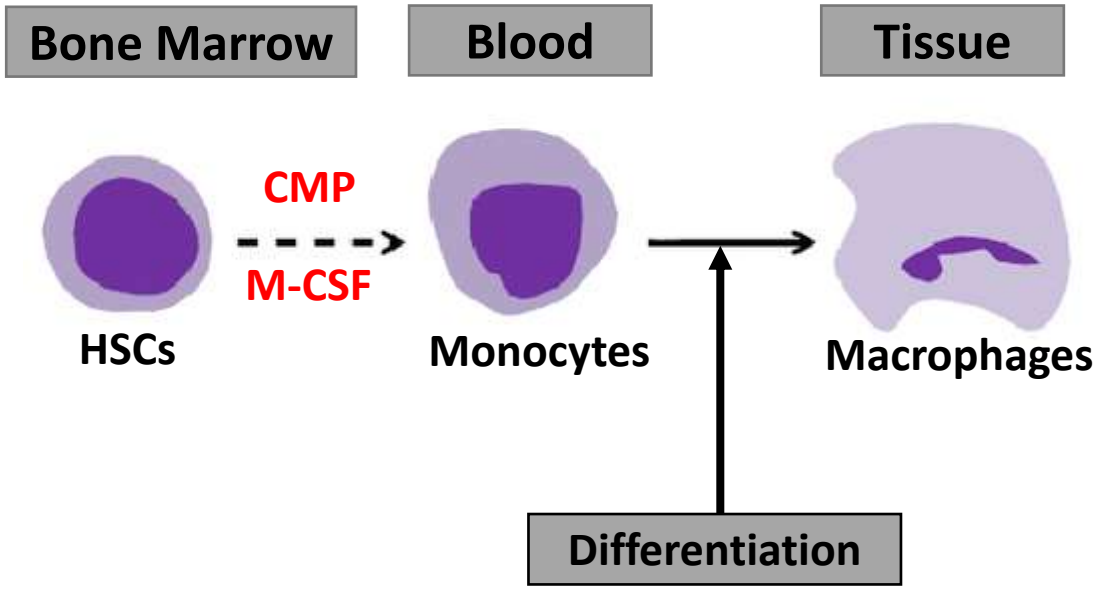
CMP: Common myeloid progenitor
G-CSF: Granulocyte colony-stimulating factor

Immune System

Innate immune system

a. Myeloid lineage cells

2. Monocytes/Macrophages



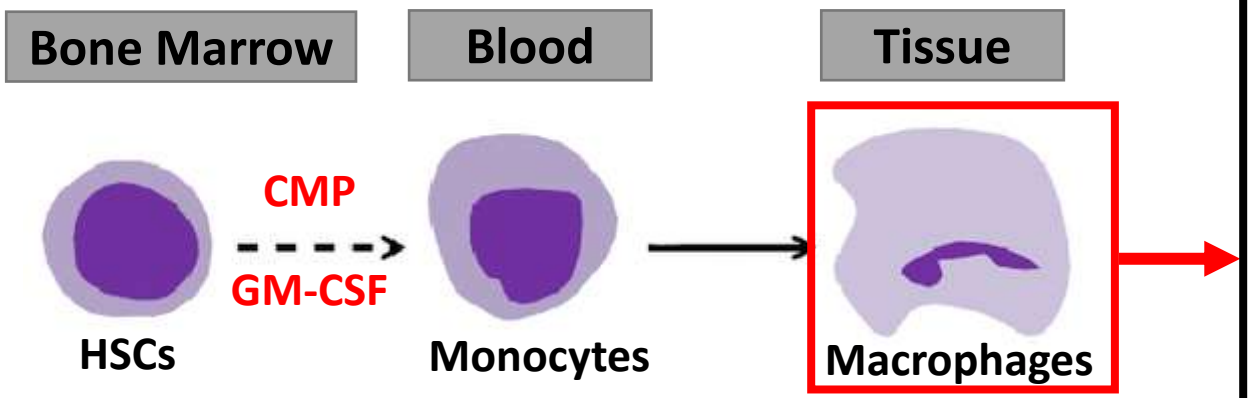
CMP: Common myeloid progenitor
M-CSF: Macrophage colony-stimulating factor

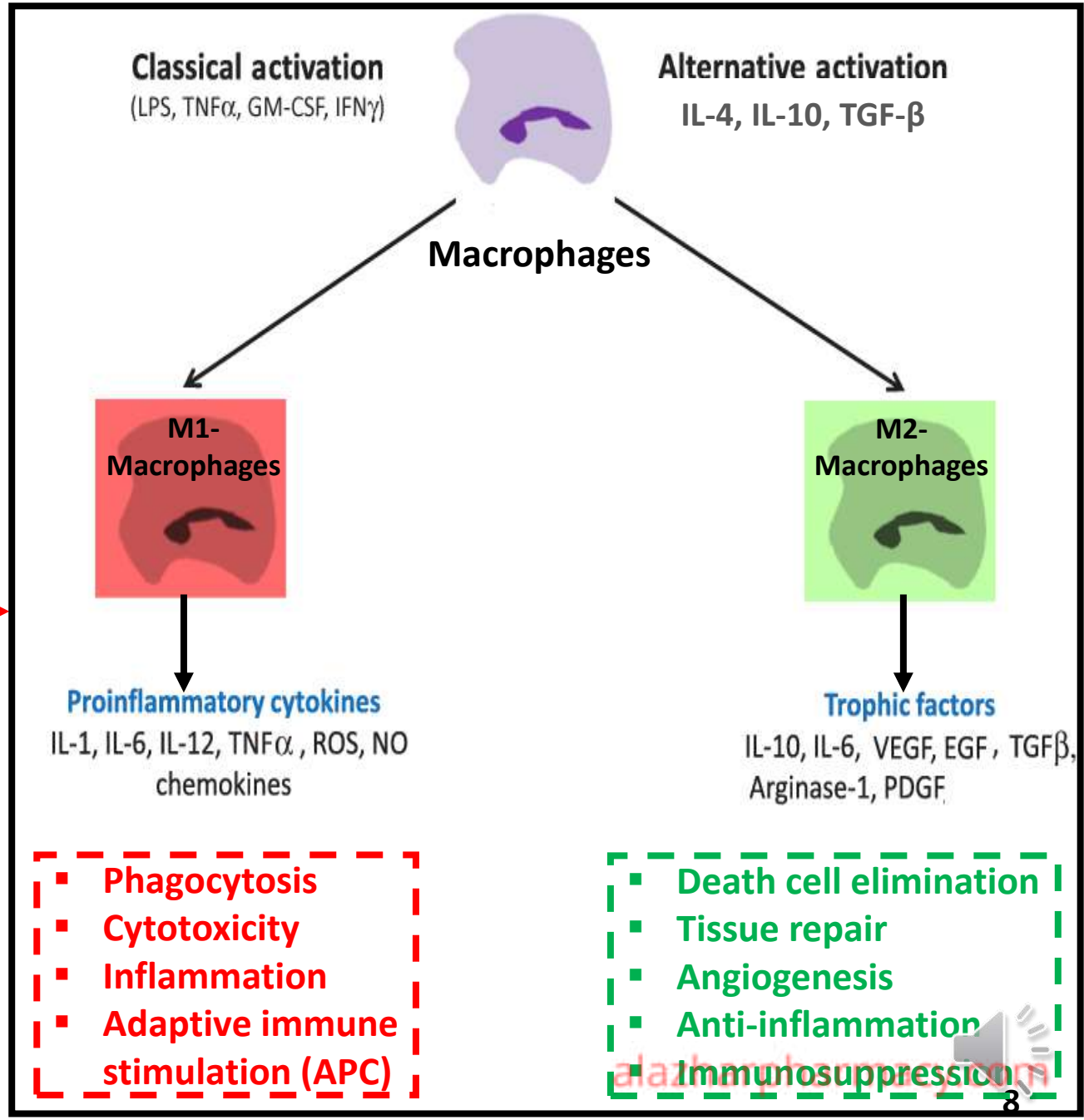
Immune System

Innate immune system

a. Myeloid lineage cells

2. Monocytes/Macrophages





VEGF: Vascular endothelial growth factor
EGF: Epidermal growth factor
PDGF: Platelet-derived growth factor
TNF-α: Tumor necrosis factor-α
TGF-β: Transforming growth factor-β
APC: Antigen presenting cell

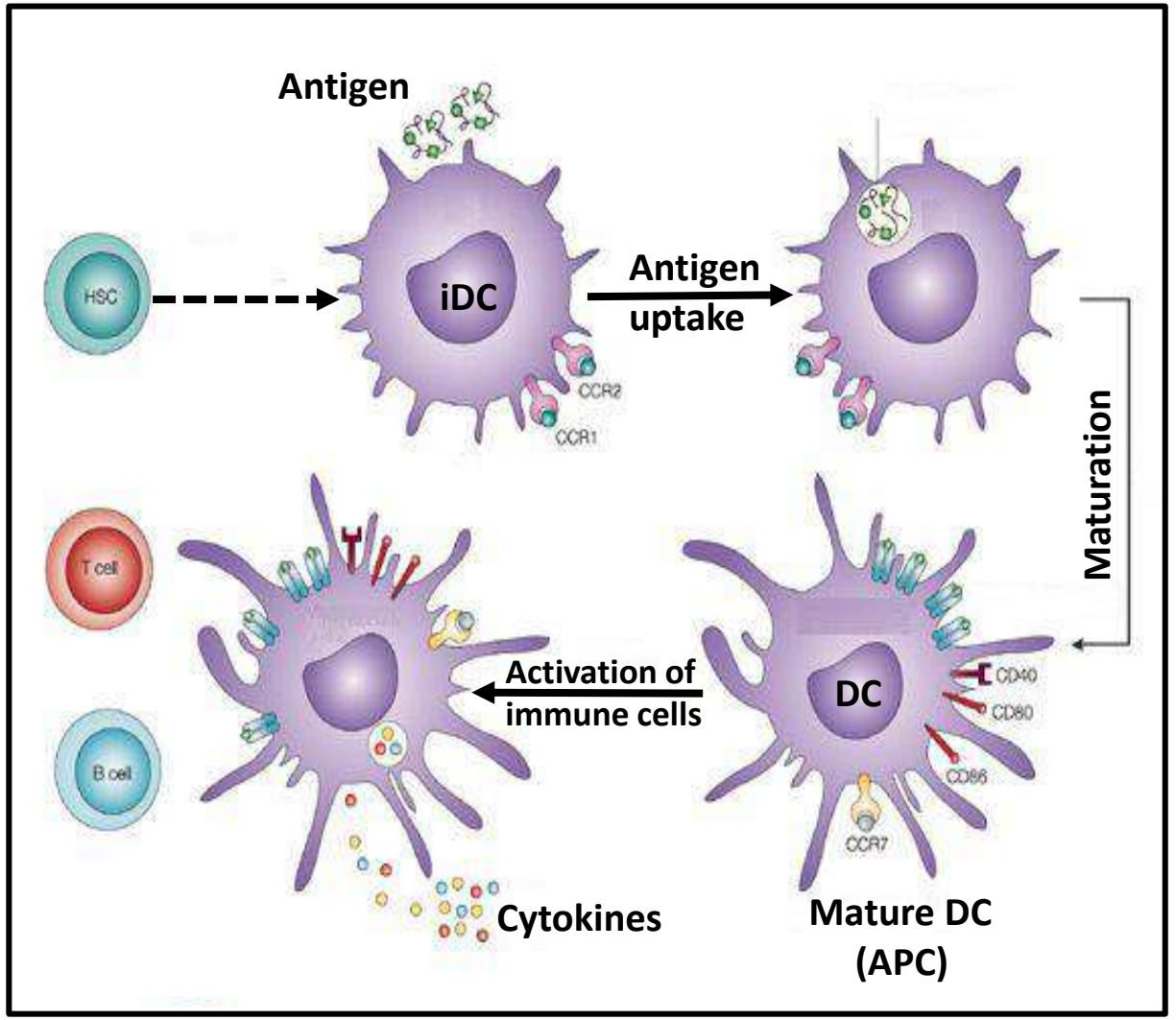
Immune System

Innate immune system

a. Myeloid lineage cells

3. Dendritic cells (DCs)

- **DCs are antigen-presenting cells (APCs).**
- **Found in an immature state in the blood. Once activated, they mature and migrate to the lymph nodes where they activate T cells and B cells.**

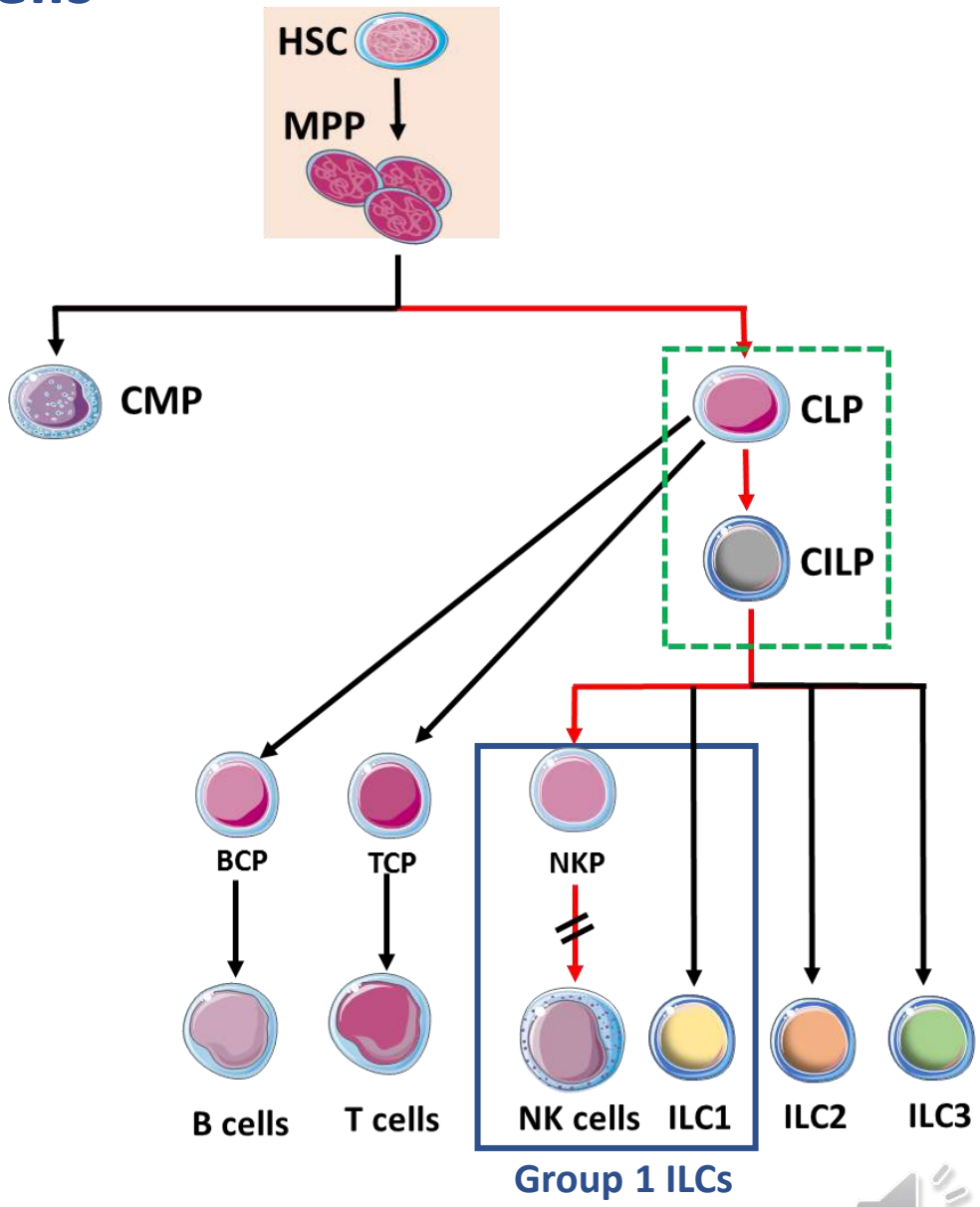


Natural Killer (NK) cells

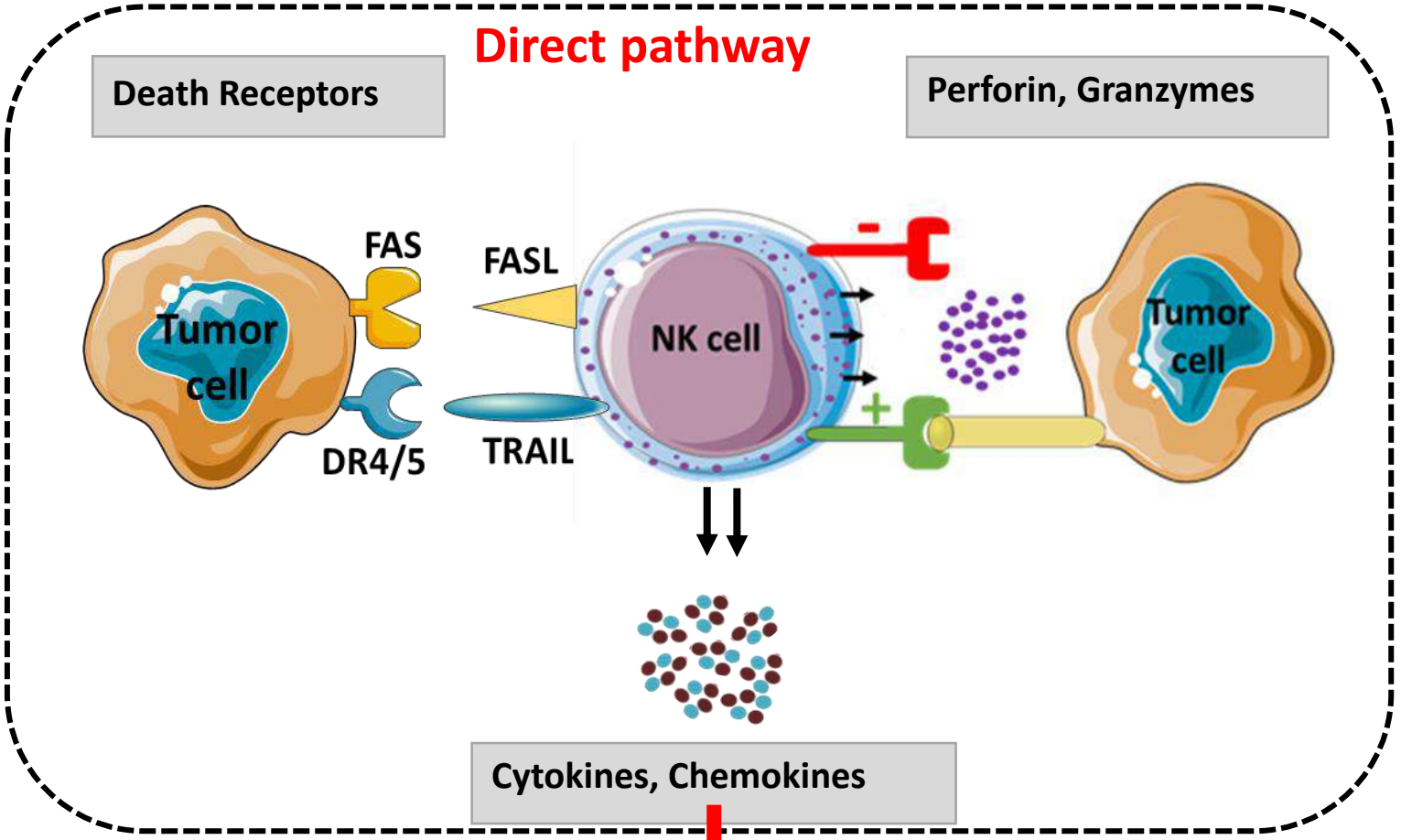
Innate immune system

b. Lymphoid lineage cells: Natural killer cell

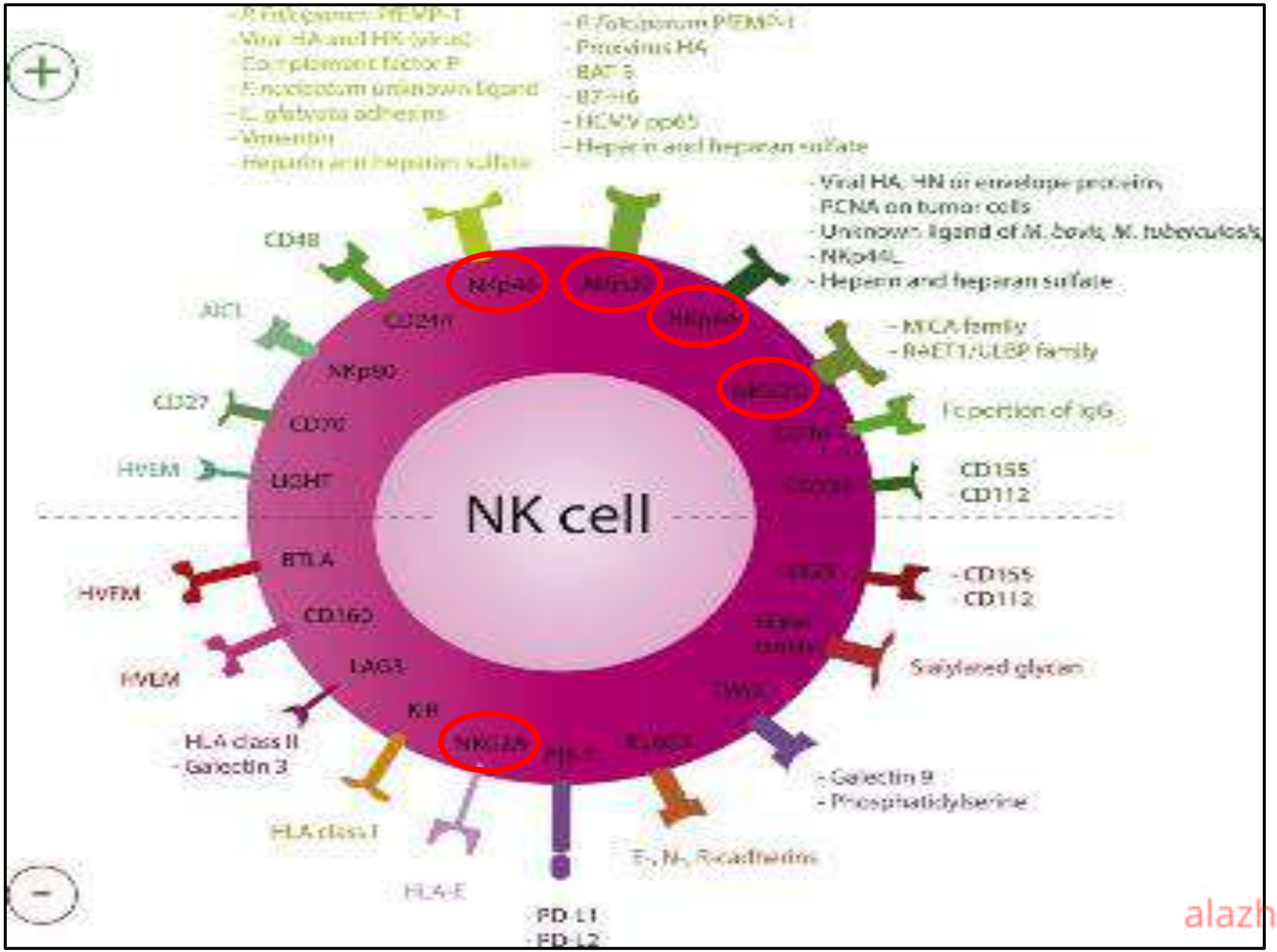
- **Cytotoxic innate lymphoid cells.**
- **Recognize and kill virus-infected cells and tumors.**



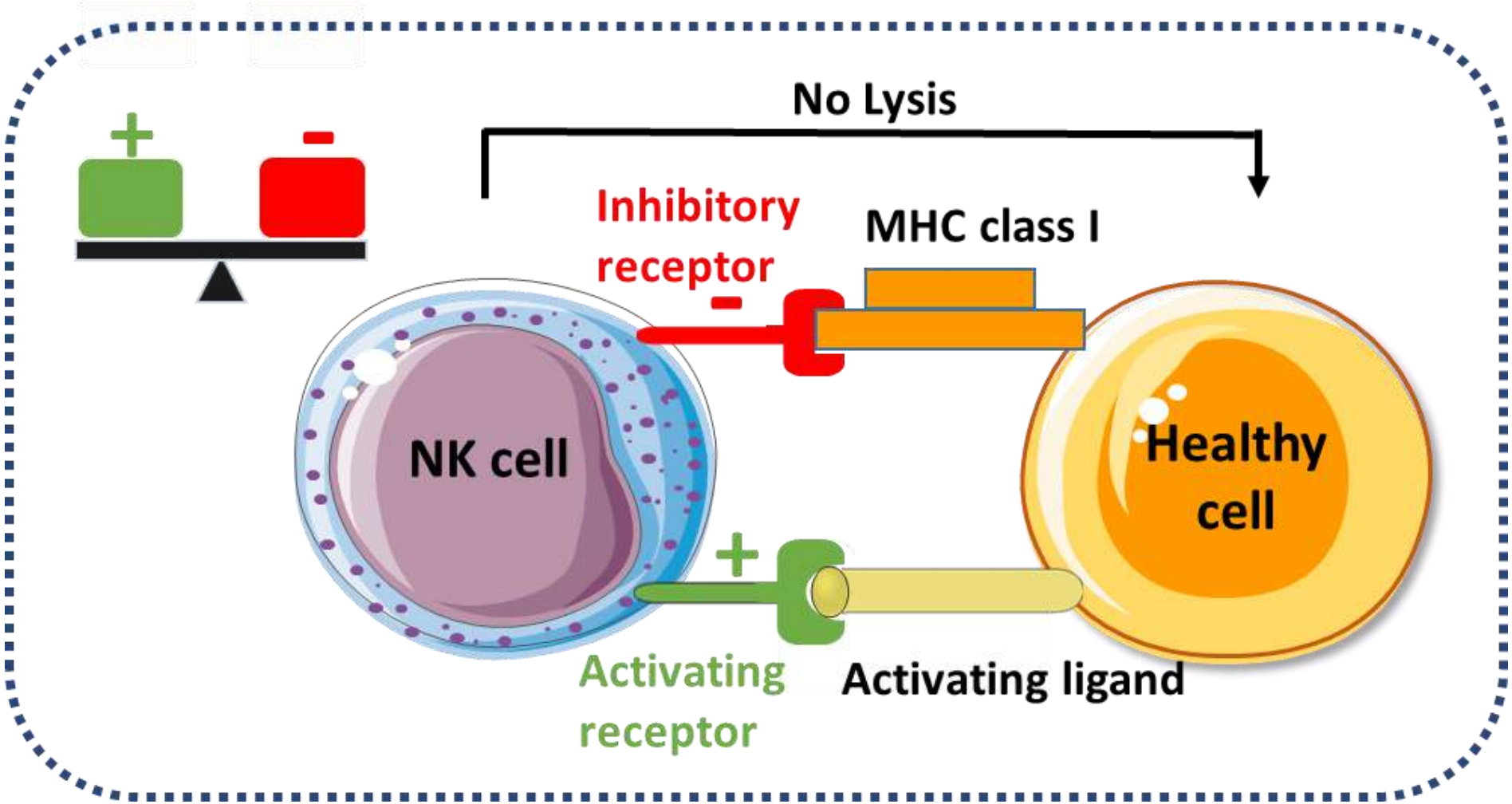
NK cells



NK cell receptors

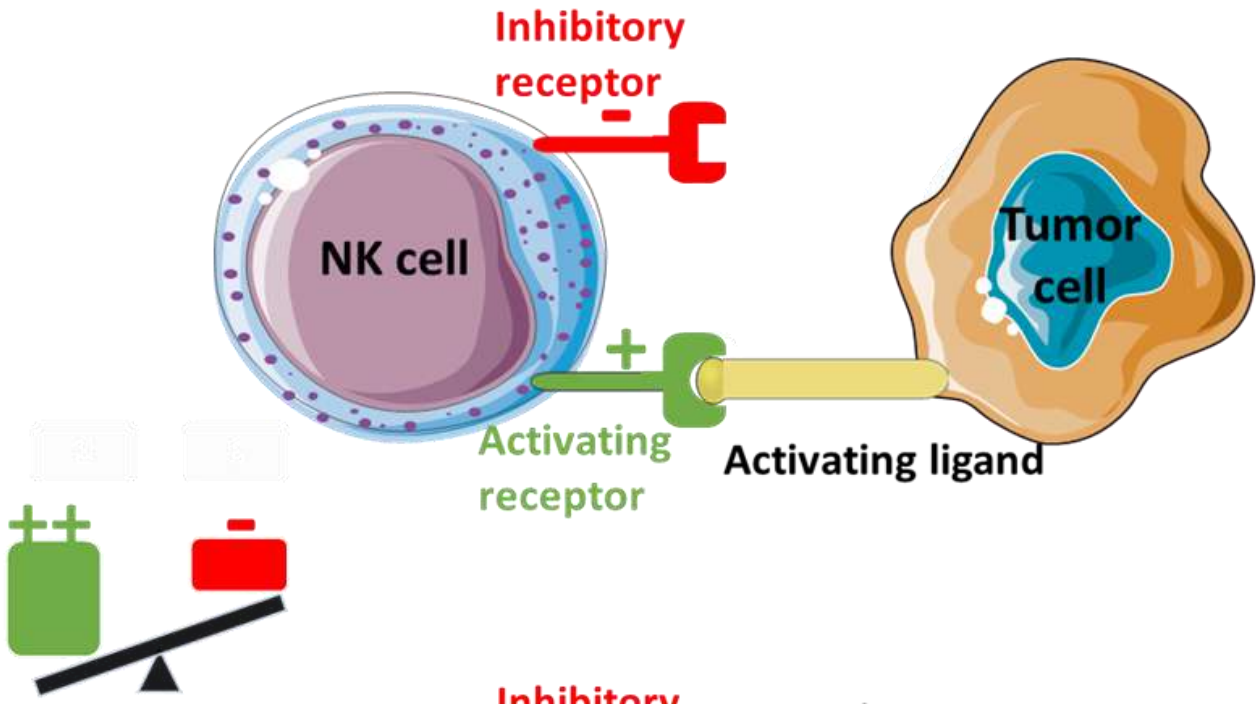


NK Cells

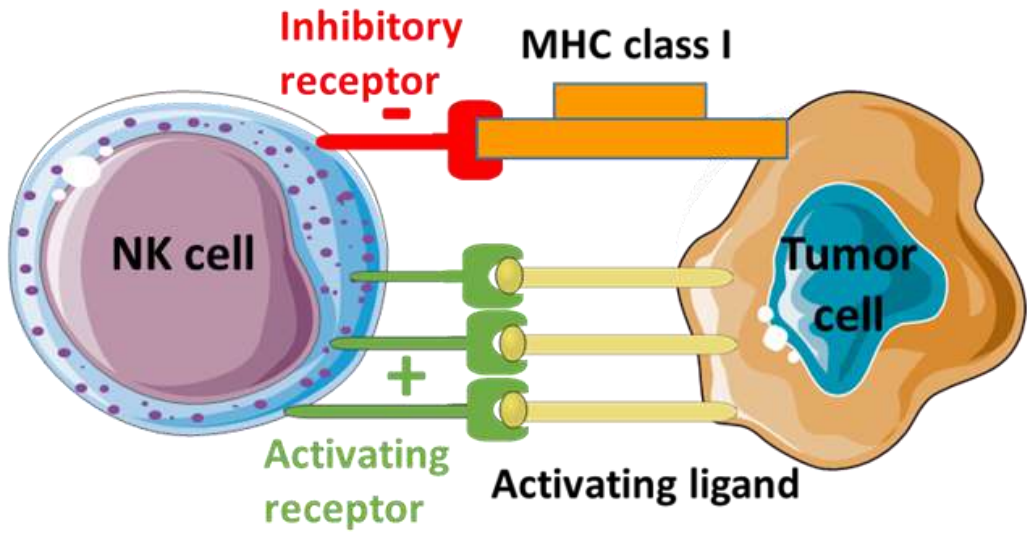


MHC: Major histocompatibility complex

NK Cells

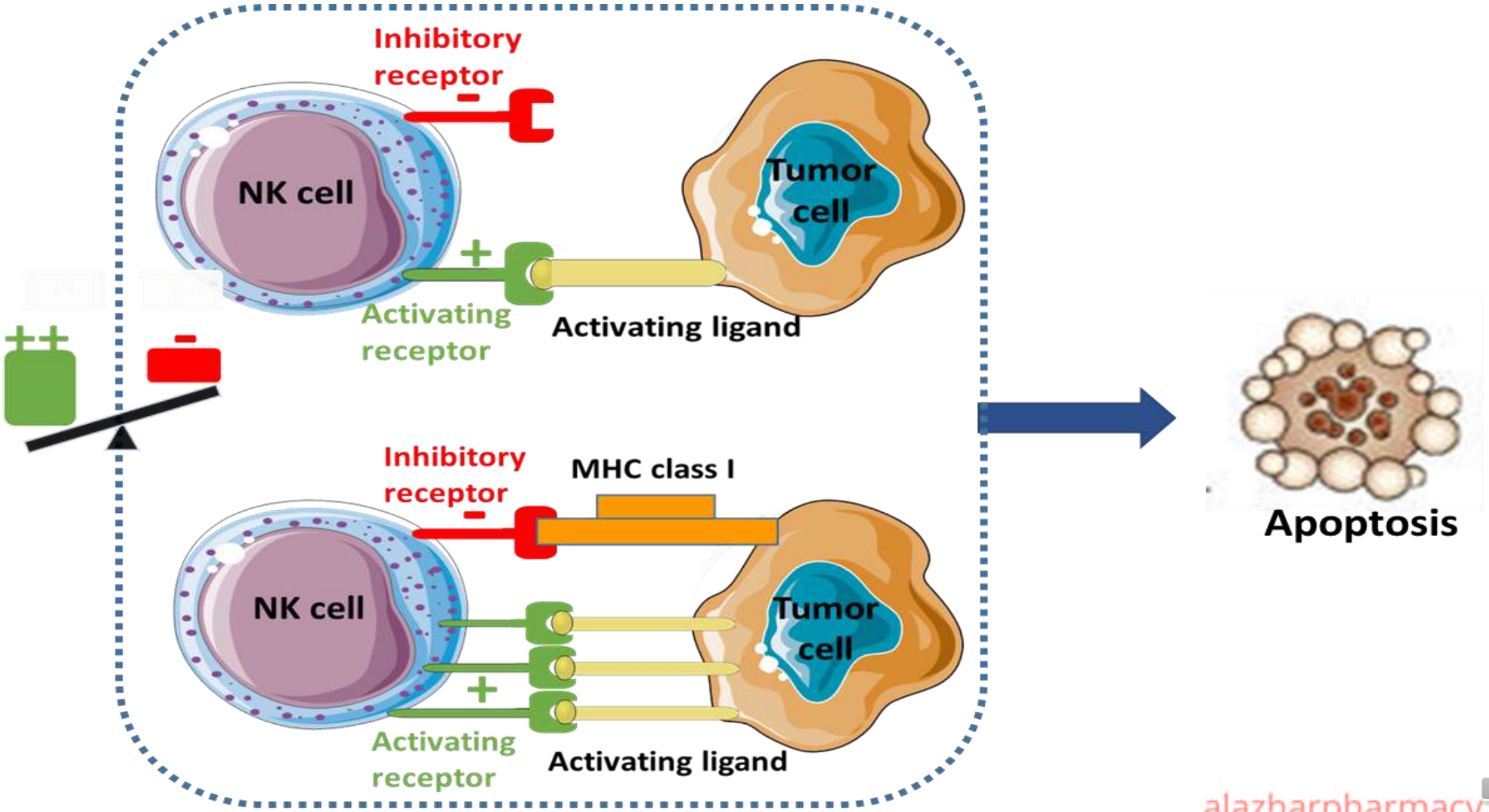


Missing-self recognition

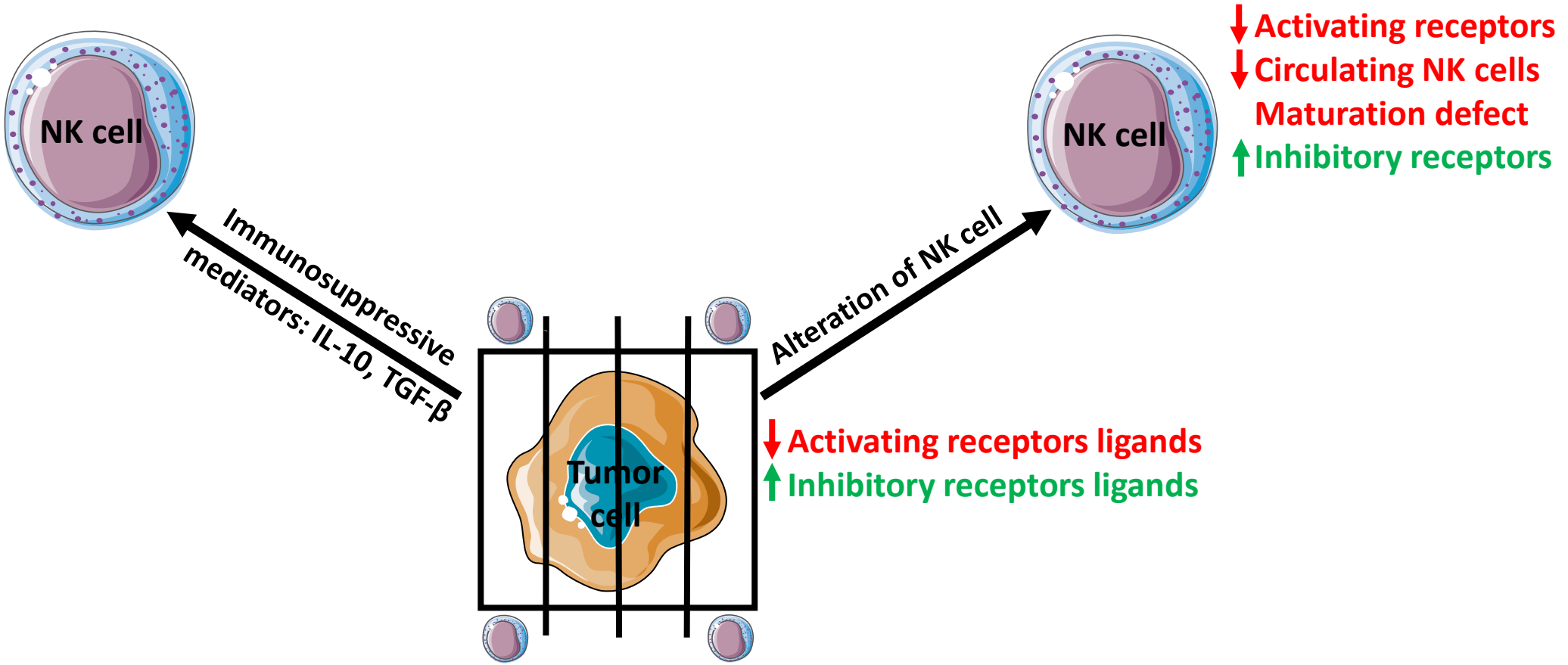


Stress-induced recognition

NK Cells



NK cells and Leukemia



Immune System

Adaptive immune cells

1. T lymphocytes (T cells)

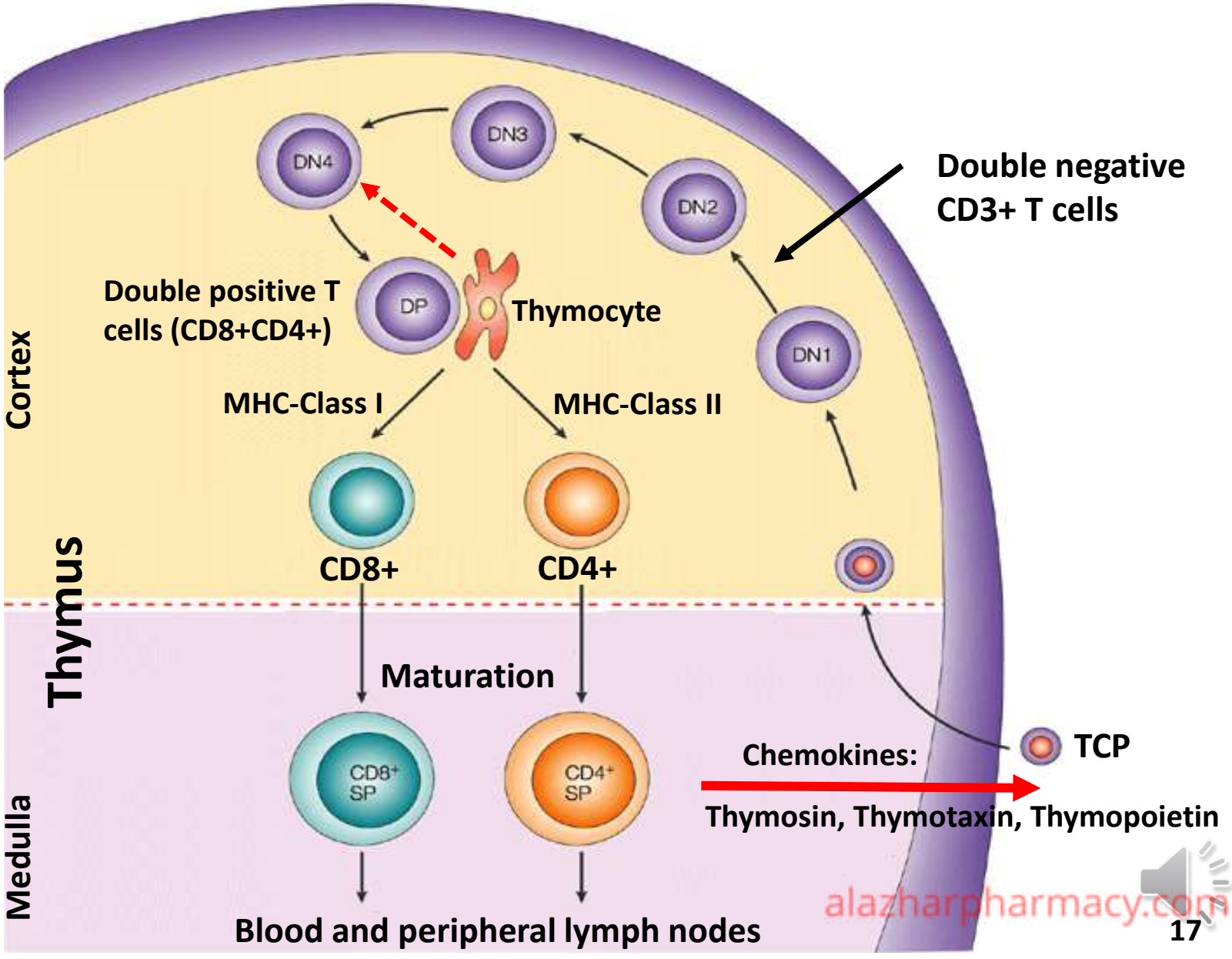
- CD3+CD8+: Cytotoxic T cells
  - Tregulatory cell: CD25+CD8+Treg
- CD3+CD4+: Helper T cells
  - Tregulatory cell: CD25+CD4+Treg

- These cells are naïve cells

MHC: Major histocompatibility complex

CD: Cluster of Differentiation protein

- CD14
- CD56
- CD64
- CD19, 20

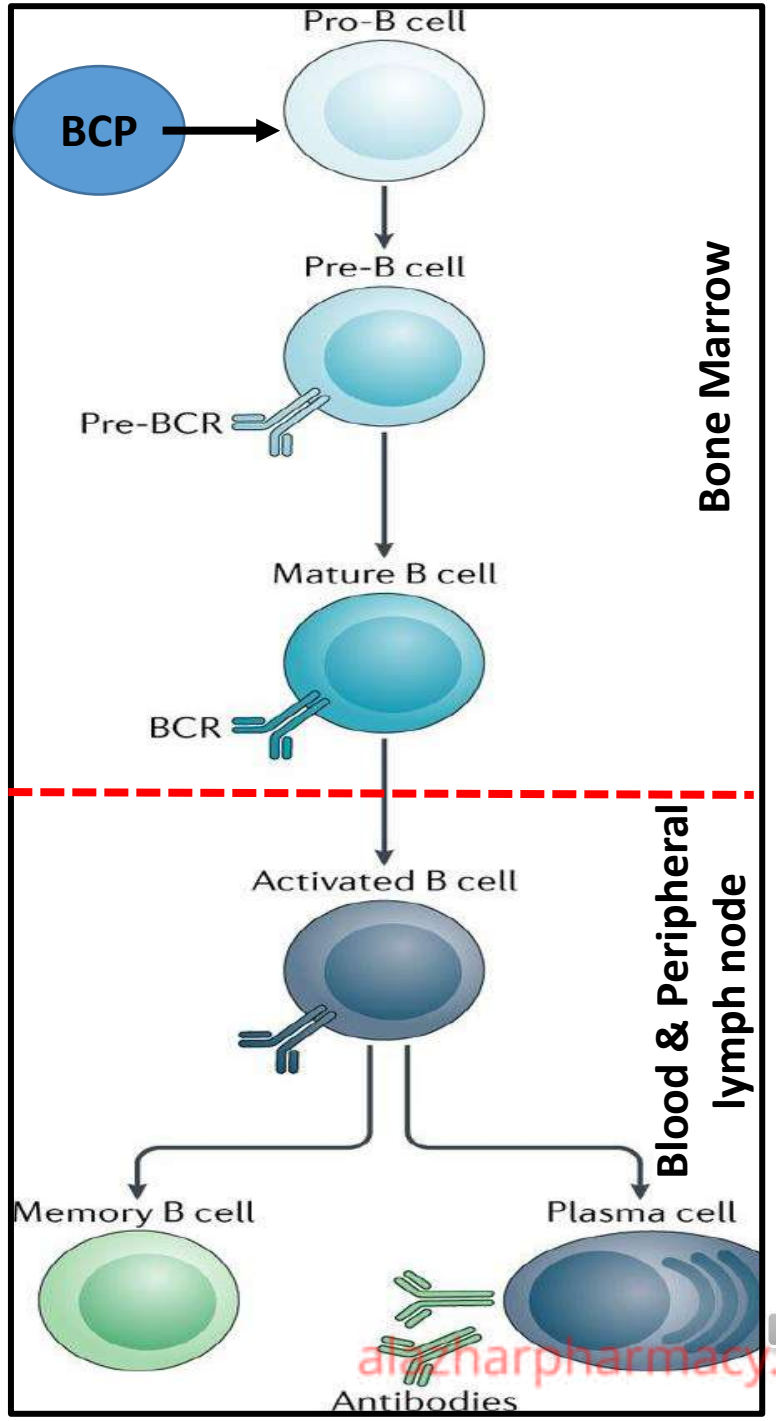


Immune System

Adaptive immune cells

1. B lymphocytes (B cells)

- Naïve B cells
- Memory B cells
- Plasma B cells

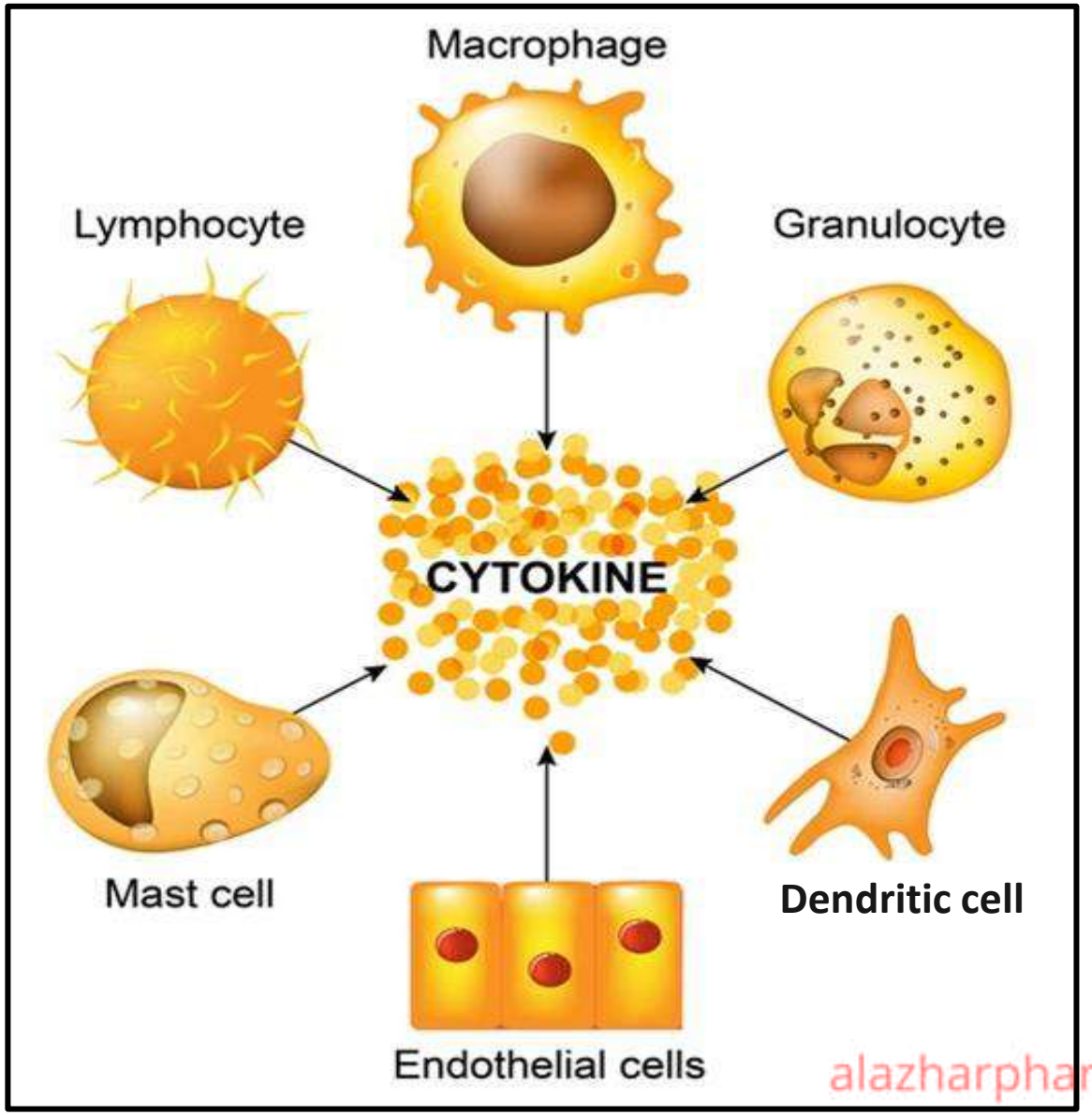


Immune System

Immune mediators

1. Cytokines
2. Complement proteins

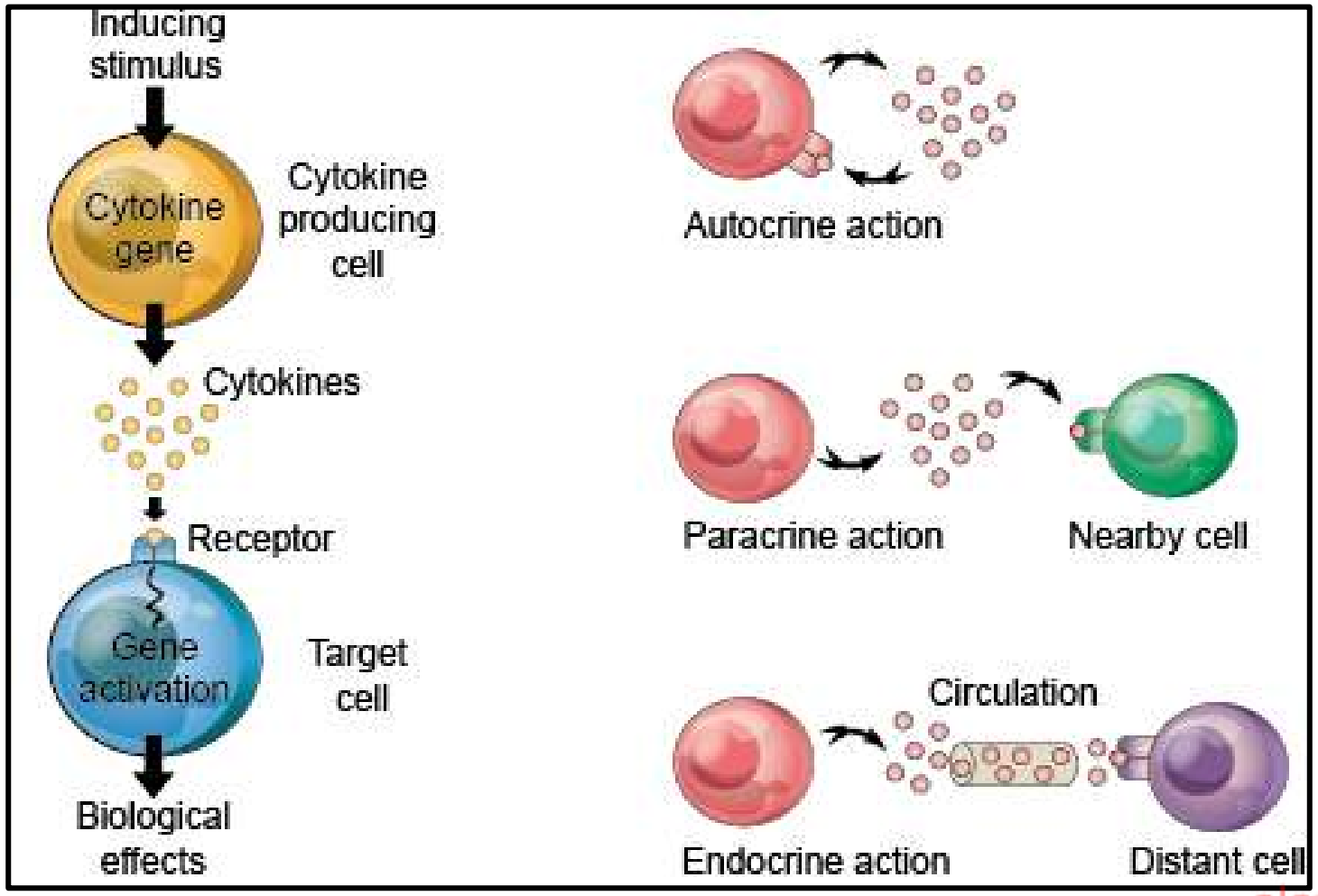
- One cell secretes different cytokines
- Different cells secrete the same cytokine



Immune System

Immune mediators

1. Cytokines

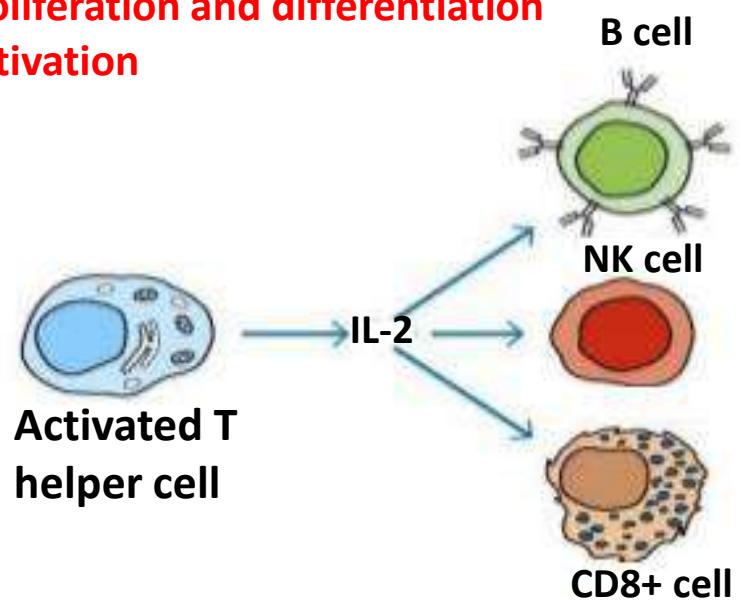


Immune System

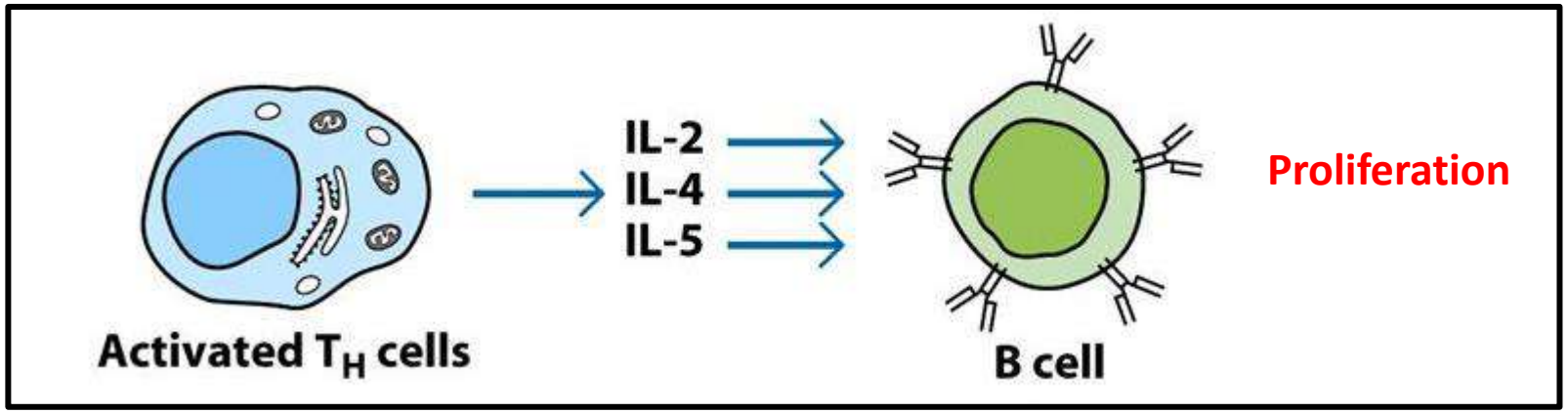
Immune mediators: Cytokines

1. Pleiotropic action

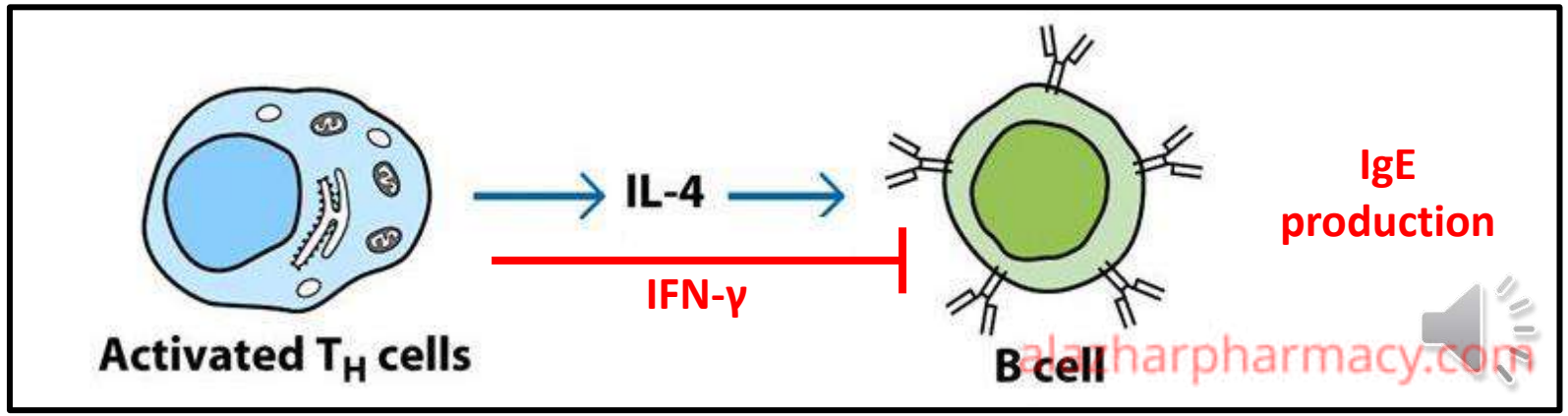
a. Proliferation and differentiation
b. Activation



2. Redundant action

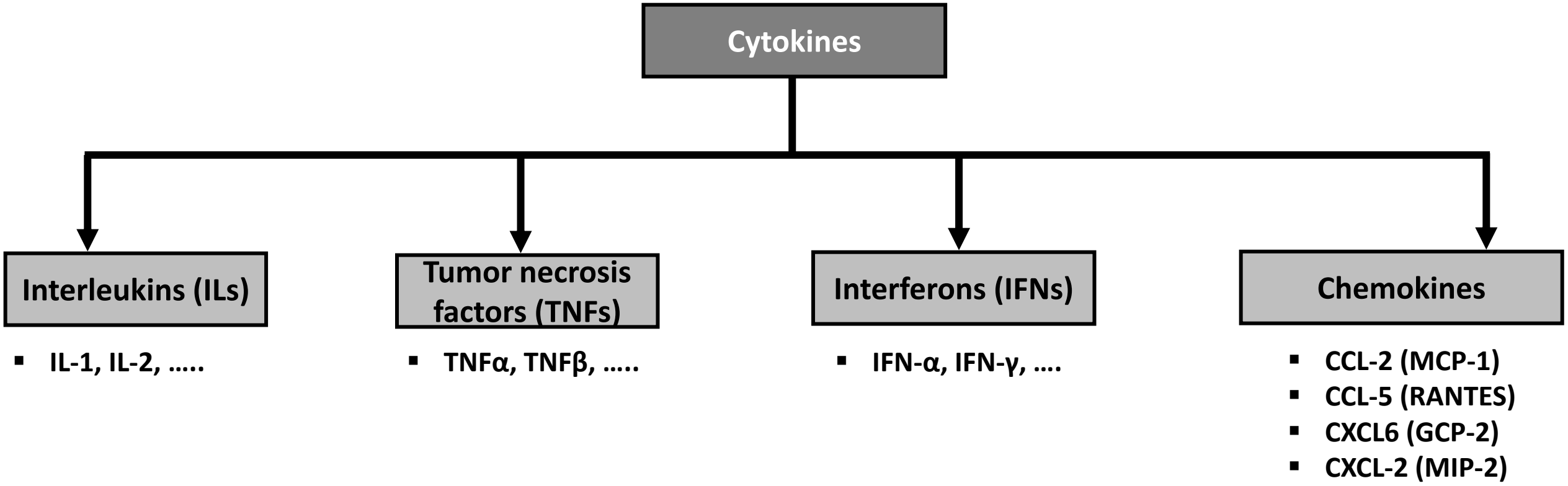


3. Antagonist action



Immune System

Immune mediators



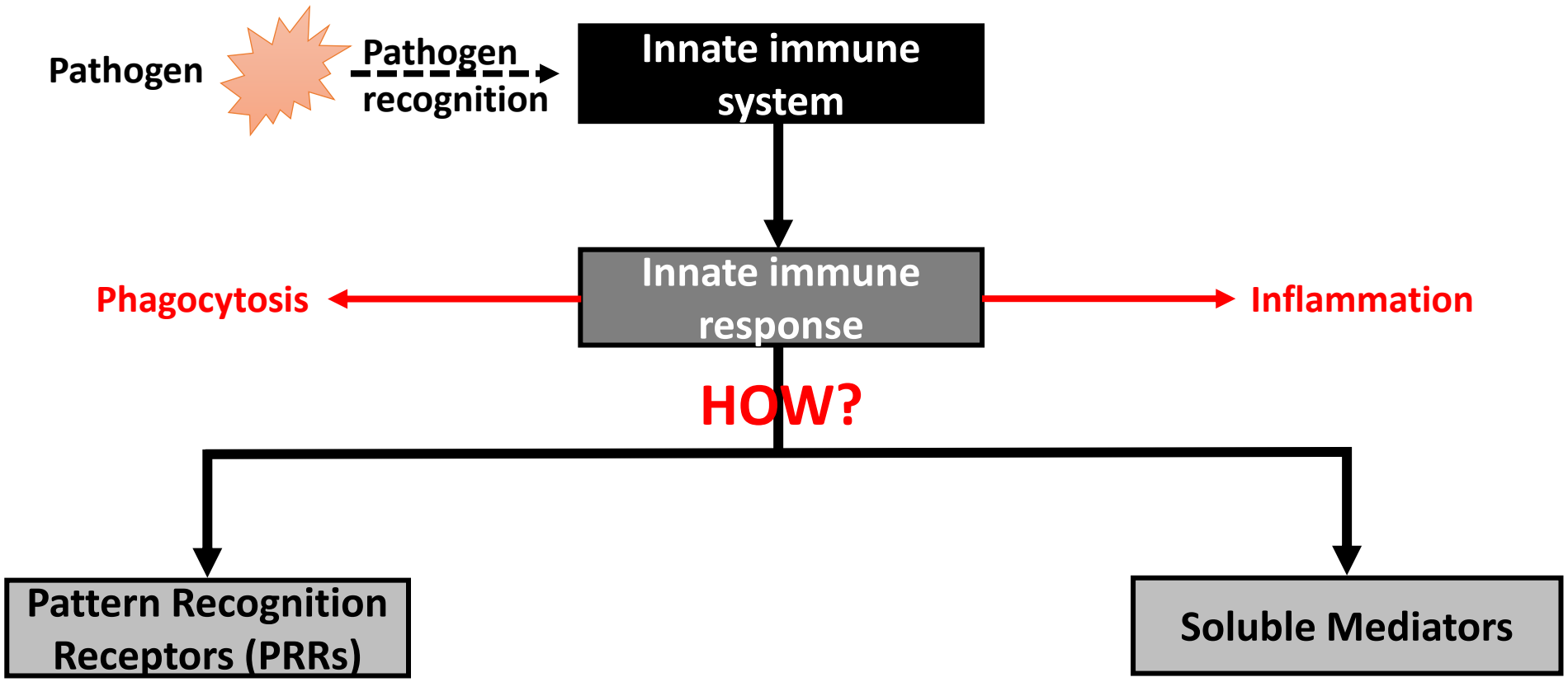
- IL-1, IL-2, …..
- TNFα, TNFβ, …..
- IFN-α, IFN-γ, ….
- CCL-2 (MCP-1)
- CCL-5 (RANTES)
- CXCL6 (GCP-2)
- CXCL-2 (MIP-2)

Immune System

TABLE 13.2 CYTOKINES OF INNATE AND ADAPTIVE IMMUNITY

CYTOKINES	SOURCE	FUNCTION
Interleukin-1 (IL-1)	Macrophages, endothelial cells, some epithelial cells	Wide variety of biologic effects; activates endothelium in inflammation; induces fever and acute-phase response; stimulates neutrophil production
Interleukin-2 (IL-2)	$CD4^+$, $CD8^+$ T cells	Growth factor for activated T cells; induces synthesis of other cytokines; activates cytotoxic T lymphocytes and NK cells
Interleukin-3 (IL-3)	$CD4^+$ T cells	Growth factor for progenitor hematopoietic cells
Interleukin-4 (IL-4)	$CD4^+$ T_2H cells, mast cells	Promotes growth and survival of T, B, and mast cells; causes T_2H cell differentiation; activates B cells and eosinophils; and induces IgE-type responses
Interleukin-5 (IL-5)	$CD4^+$ T_2H cells	Induces eosinophil growth and development
Interleukin-6 (IL-6)	Macrophages, endothelial cells, T lymphocytes	Stimulates the liver to produce mediators of acute-phase inflammatory response; also induces proliferation of antibody-producing cells by the adaptive immune system
Interleukin-7 (IL-7)	Bone marrow stromal cells	Primary function in adaptive immunity; stimulates pre-B cells and thymocyte development and proliferation
Interleukin-8 (IL-8)	Macrophages, endothelial cells	Primary function in adaptive immunity; chemoattracts neutrophils and T lymphocytes; regulates lymphocyte homing and neutrophil infiltration
Interleukin-10 (IL-10)	Macrophages, some T-helper cells	Inhibitor of activated macrophages and DCs; decreases inflammation by inhibiting T_1H cells and release of IL-12 from macrophages
Interleukin-12 (IL-12)	Macrophages, DCs	Enhances NK cell cytotoxicity in innate immunity; induces T_1H cell differentiation in adaptive immunity
Type I interferons (IFN-α, IFN-β)	Macrophages, fibroblasts	Inhibit viral replication; activate NK cells; and increase expression of MHC-I molecules on virus-infected cells
Interferon-γ (IFN-γ)	NK cells, $CD4^+$ and $CD8^+$ T lymphocytes	Activates macrophages in both innate immune responses and adaptive cell-mediated immune responses; increases expression of MHC-I and MHC-II and antigen processing and presentation
Tumor necrosis factor-α (TNF-α)	Macrophages, T cells	Induces inflammation, fever, and acute-phase response; activates neutrophils and endothelial cells; kills cells through apoptosis

Innate immune response



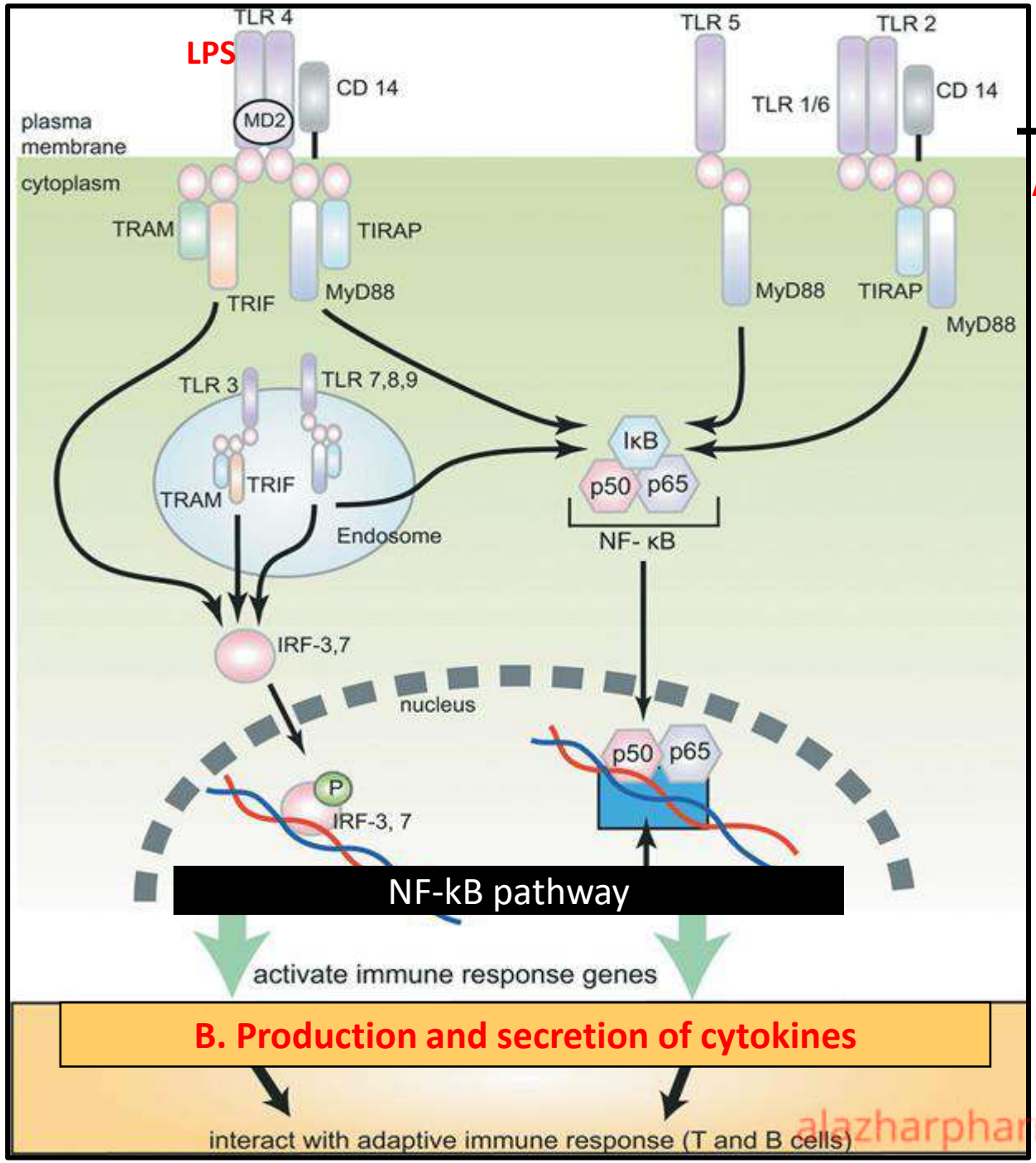
Innate immune response

Pathogen Recognition

1. Pattern recognition receptors (PRRs)
   - Their ligands are called Pathogen associated molecular patterns (PAMPs)

a. Toll-like receptors (TLRs)

b. Mannose receptors (MRs)



Innate immune response

Innate immune responses

Pathogen Recognition

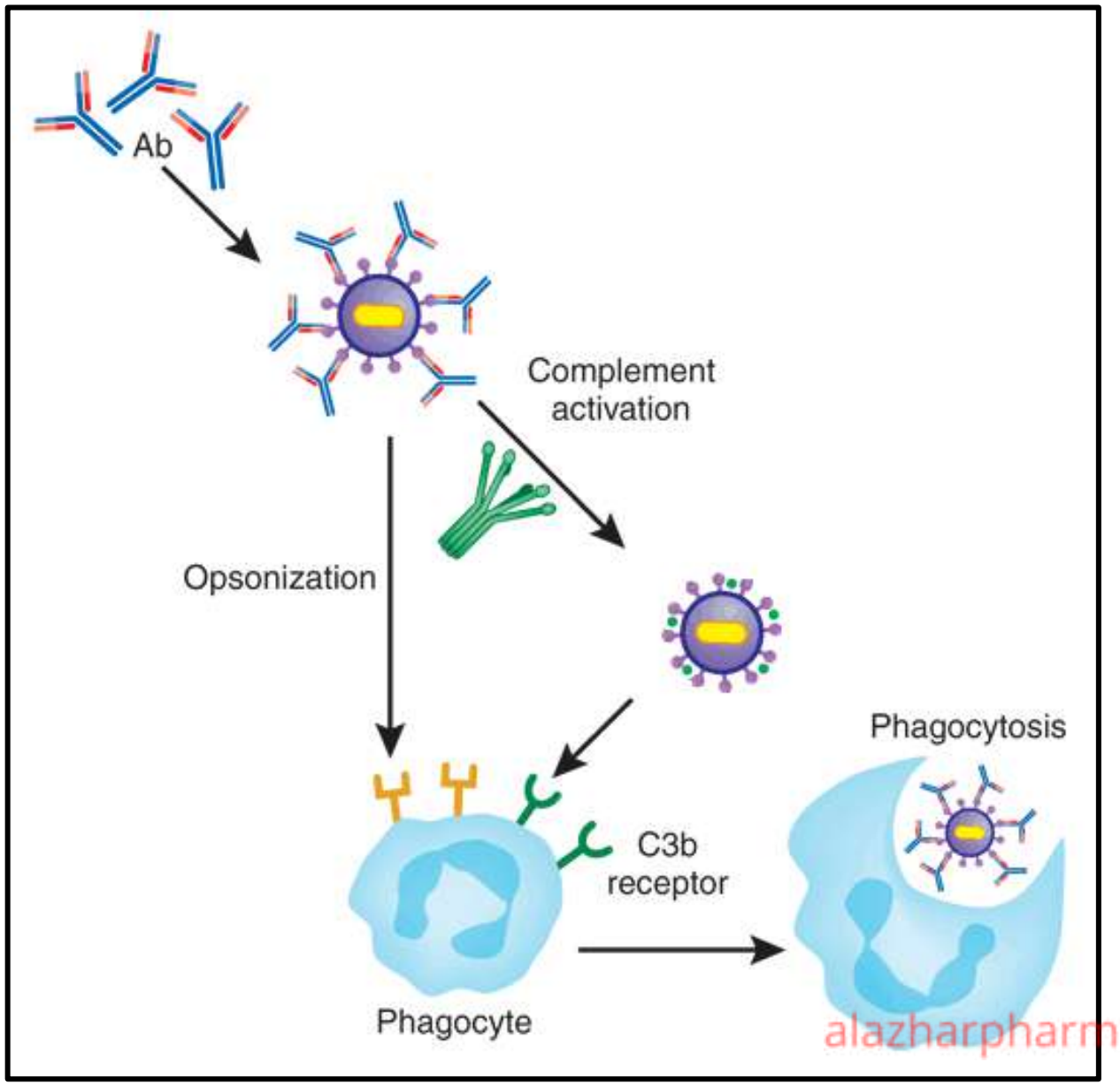
2. Soluble mediators

i. Opsonins: ***Opsonization process***

a. **Antibodies: IgM, IgG**
b. **Complement proteins**
c. **Mannose binding lectin (MBL)**

ii. Cytokines

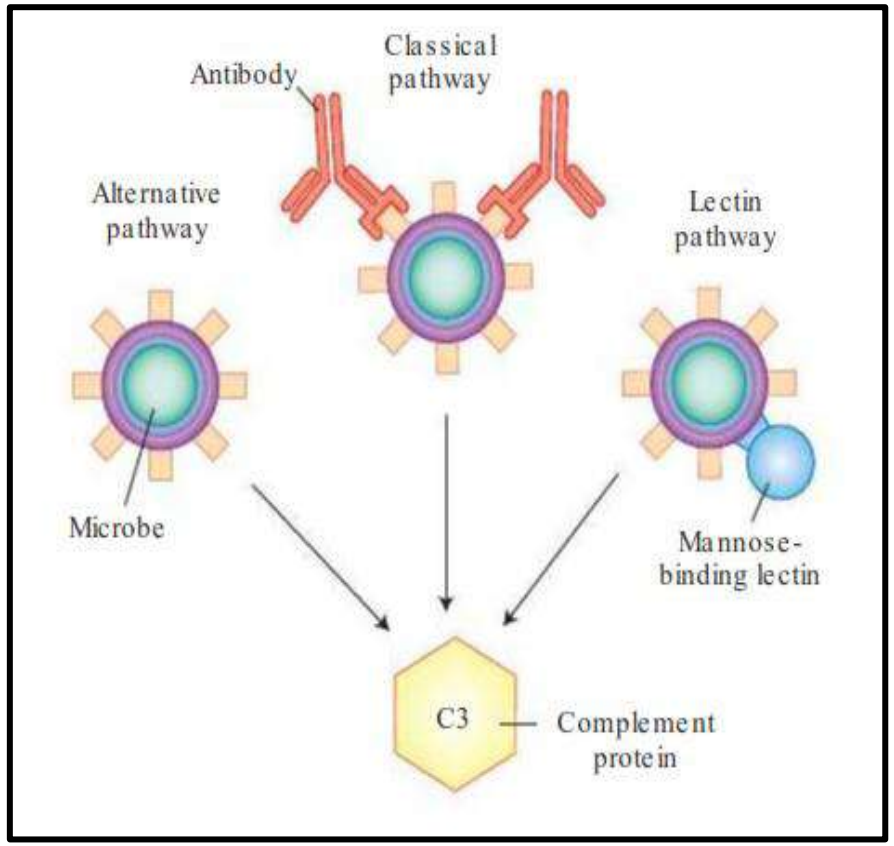
iii. Acute phase proteins



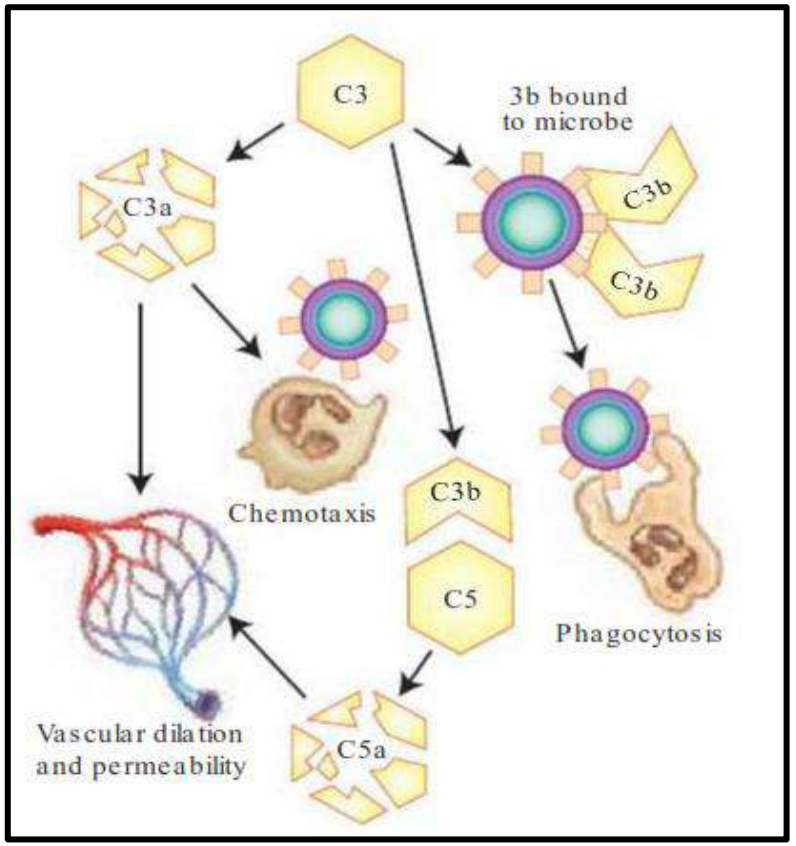
Innate immune response

Complement system

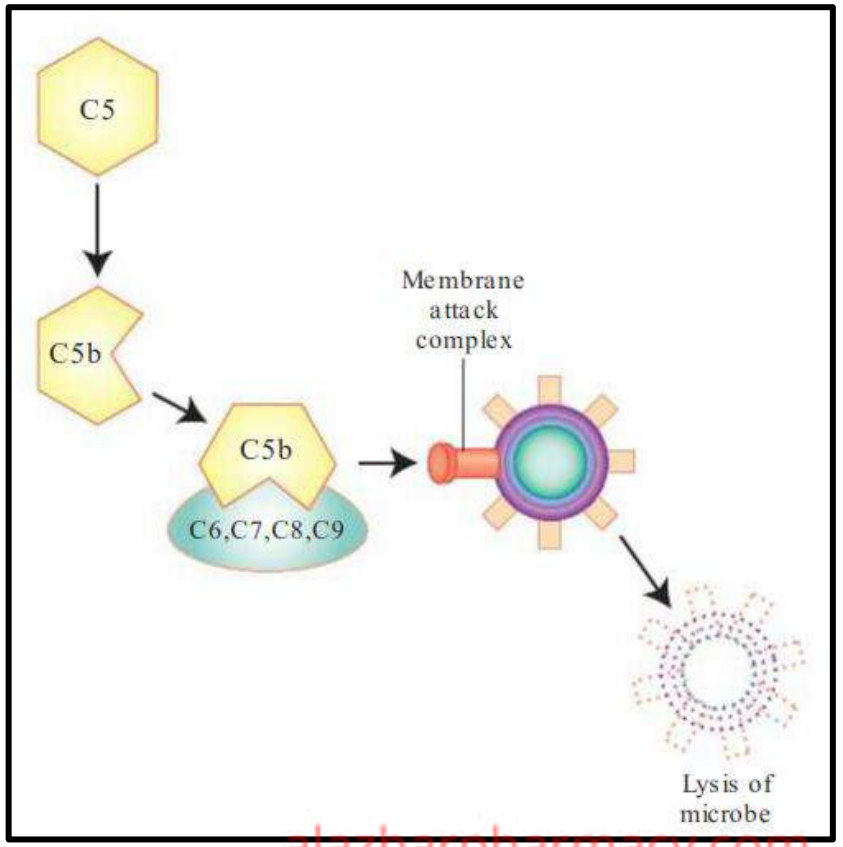
Initial activation phase



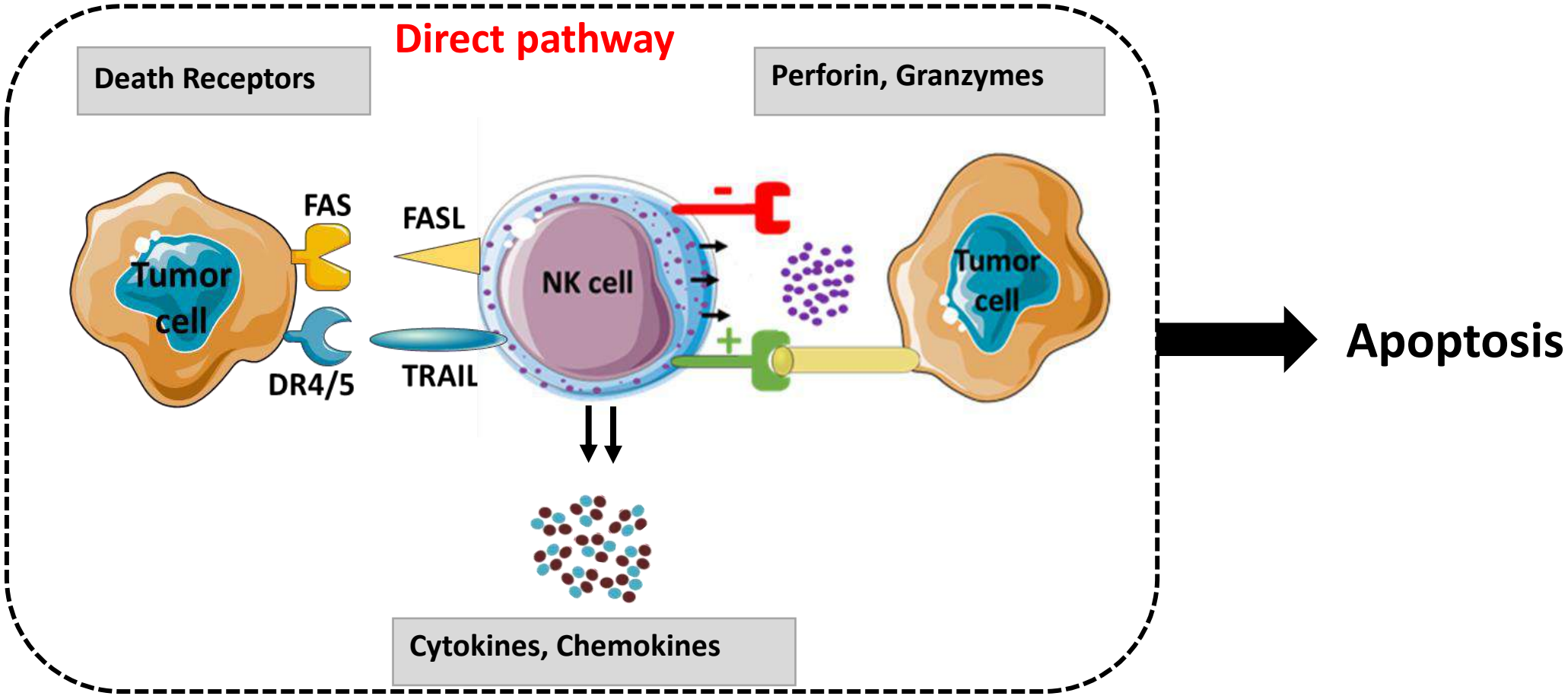
Amplification of inflammation phase



Membrane attack phase



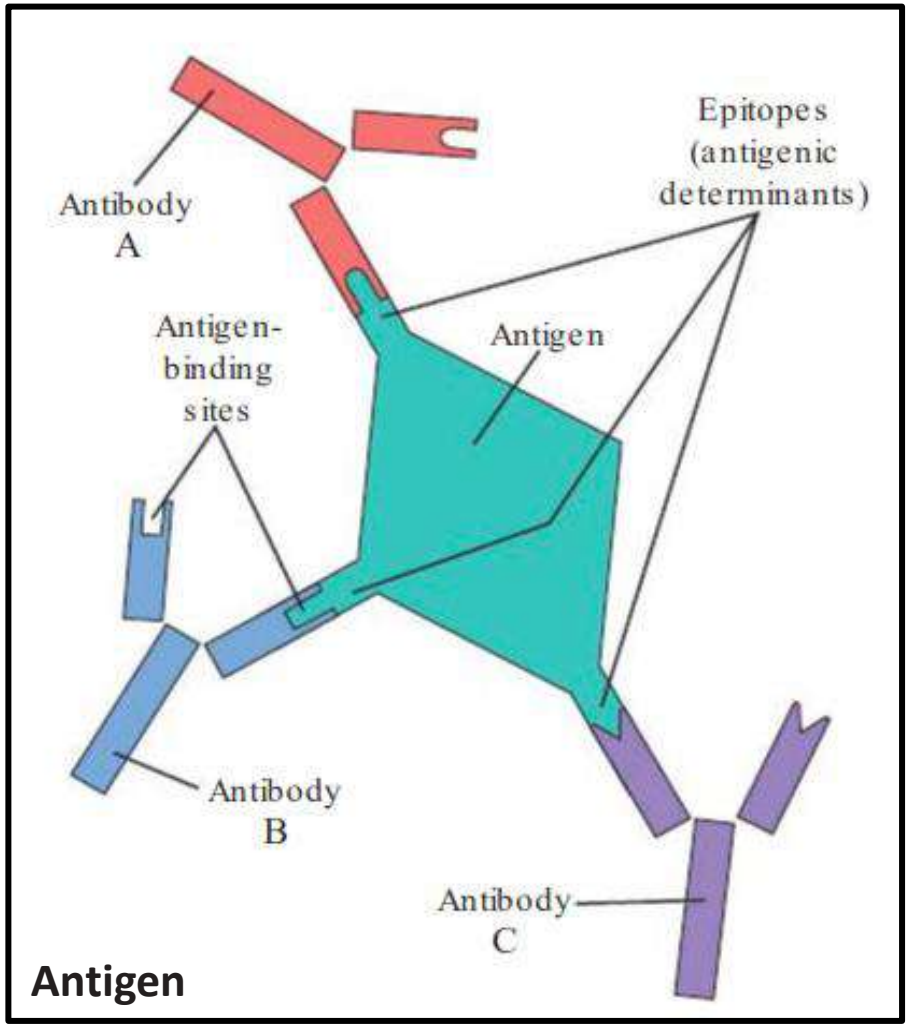
Innate immune response



Adaptive immune response

1. **Antigens**

   - **Haptens**



Antigen

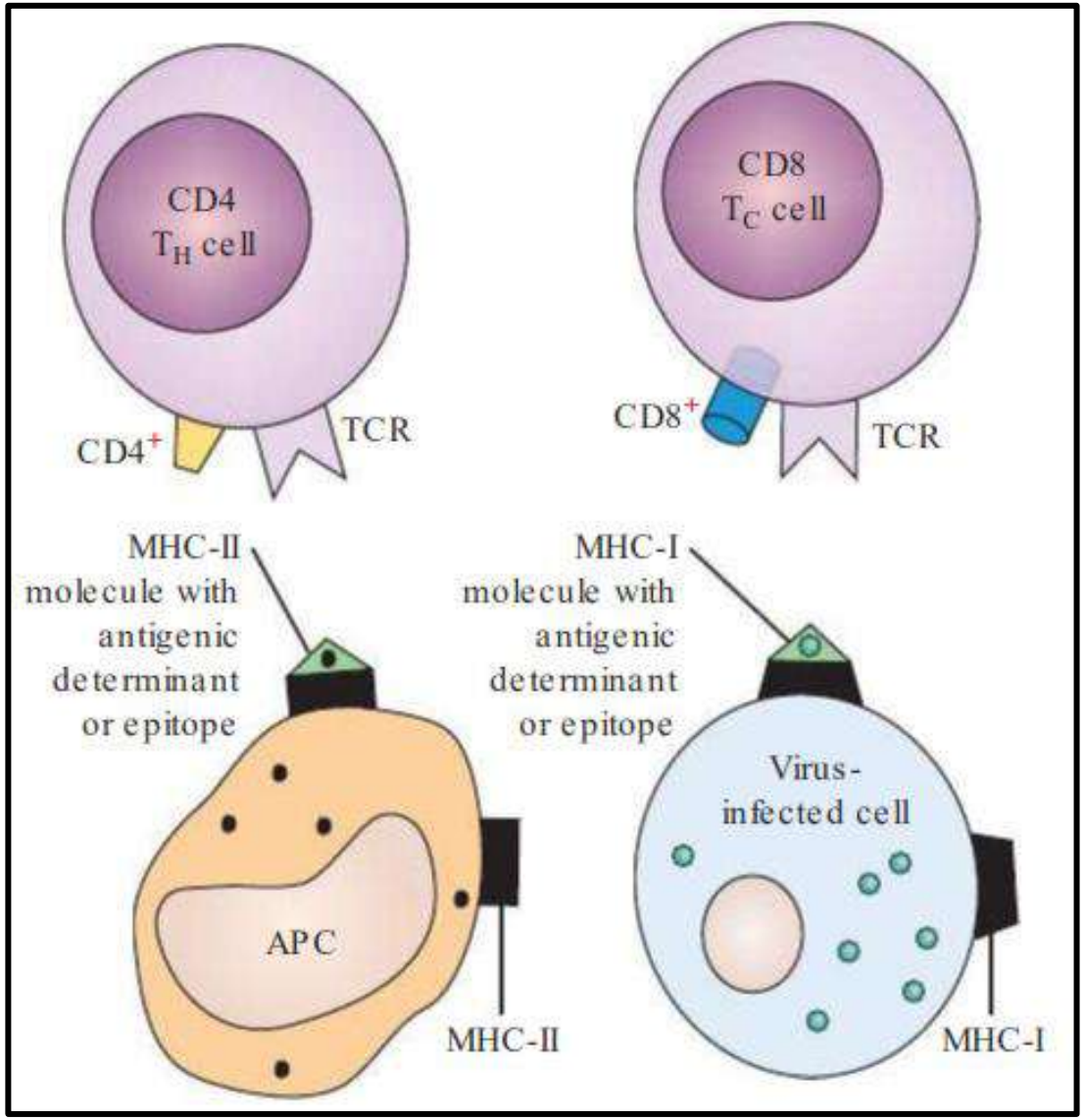
Adaptive immune response

2. MHC molecules: Human leukocytes antigens (HLAs)

- **Class I: HLA-A, B, C**
- **Class II: HLA-DR, DP, DQ**

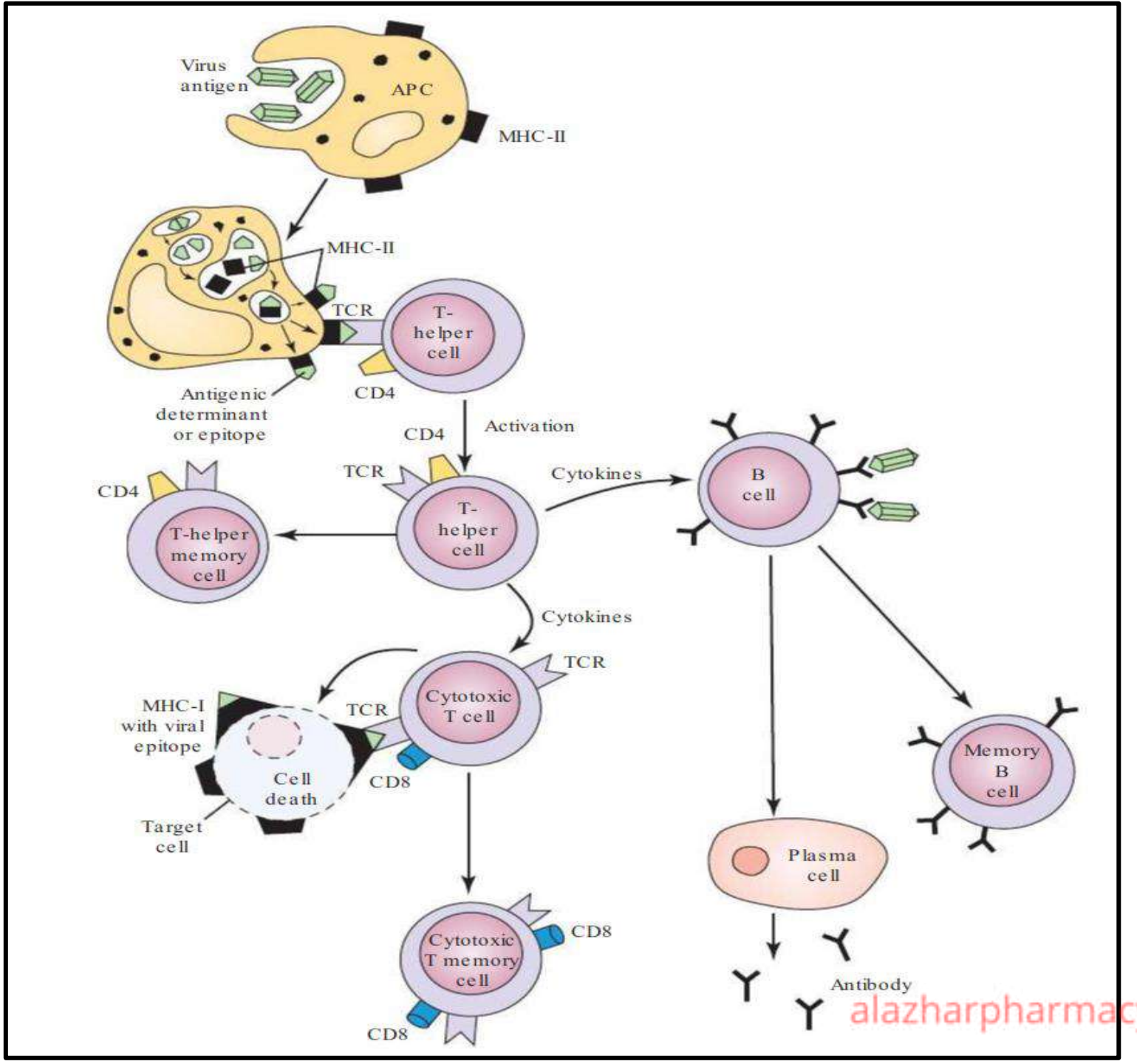
3. Antigen presenting cells (APCs): macrophages and DCs.

- **MHC-class II**



1. **Cell mediated immunity**

- **T helper cell (CD4+)**
  - **T helper 1**
  - **T helper 2**
  - **T helper 17**
- **Cytotoxic T cell (CD8+)**
- **Regulatory T cells**



Adaptive immune response

1. **Cell mediated immunity**

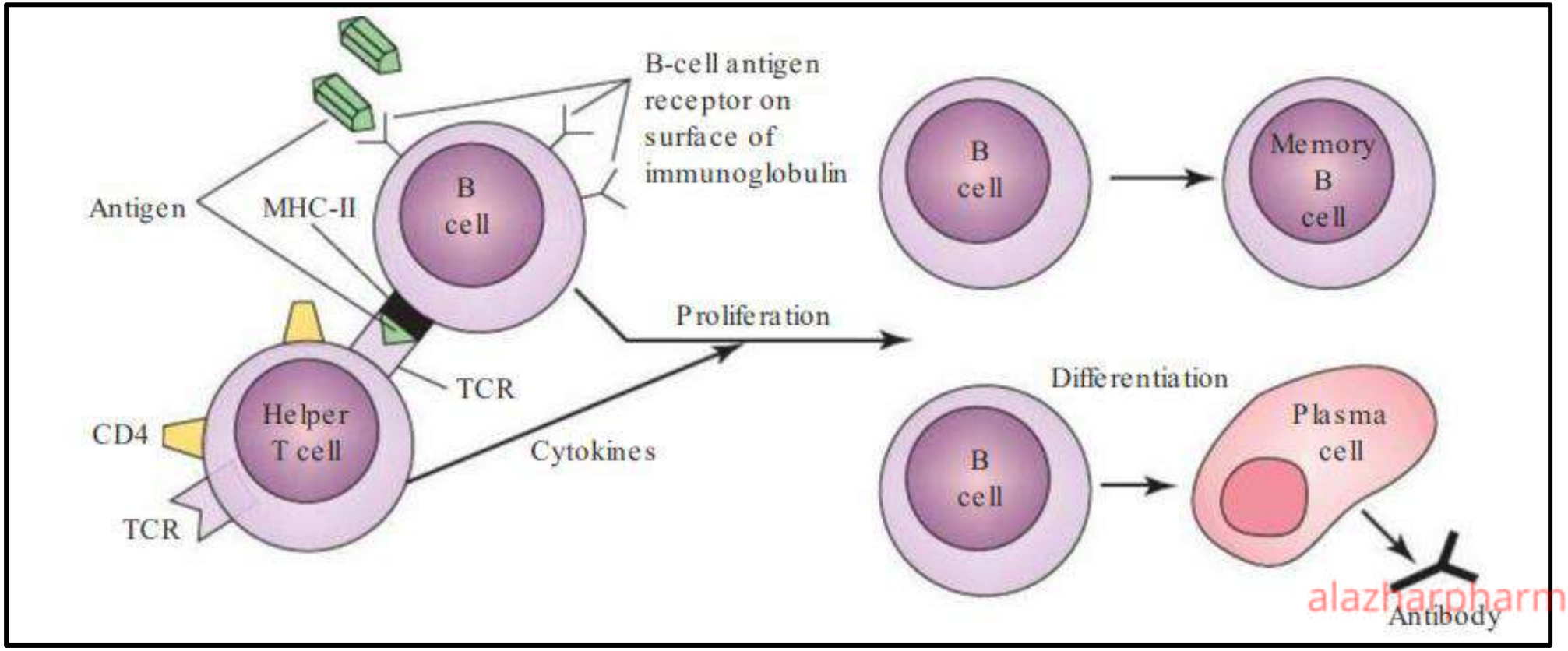
- **Regulatory T cells**
  - **CD4+ CD25+ FOXP3+ Tregs**
  - **CD8+ CD25+ FOXP3+ Tregs**

} **IL-10, IL-35, TGF-β**

Adaptive immune response

2. Humoral mediated immunity

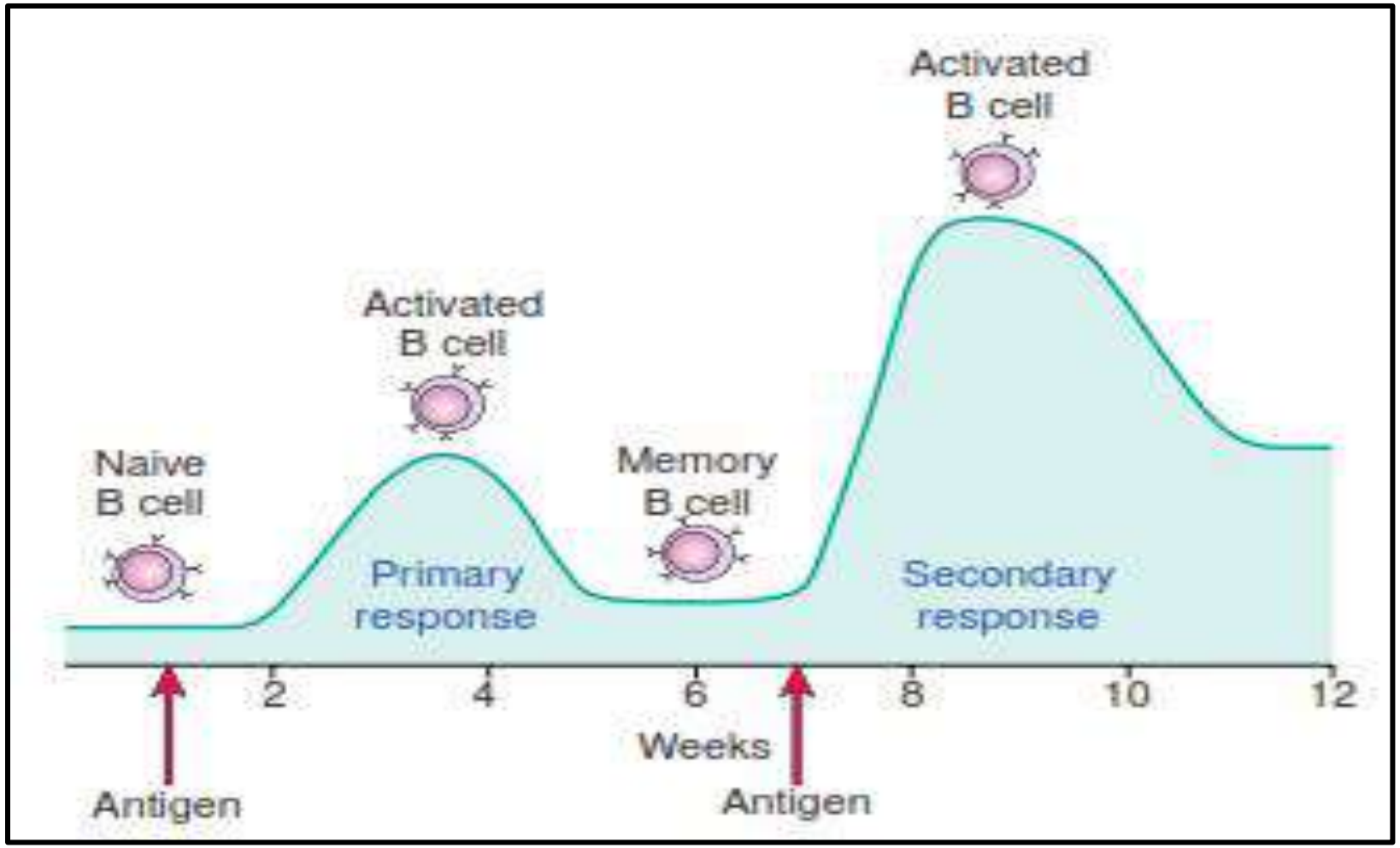
- **B cells**
  - **Primary response**
  - **Secondary response**



Adaptive immune response

2. Humoral mediated immunity

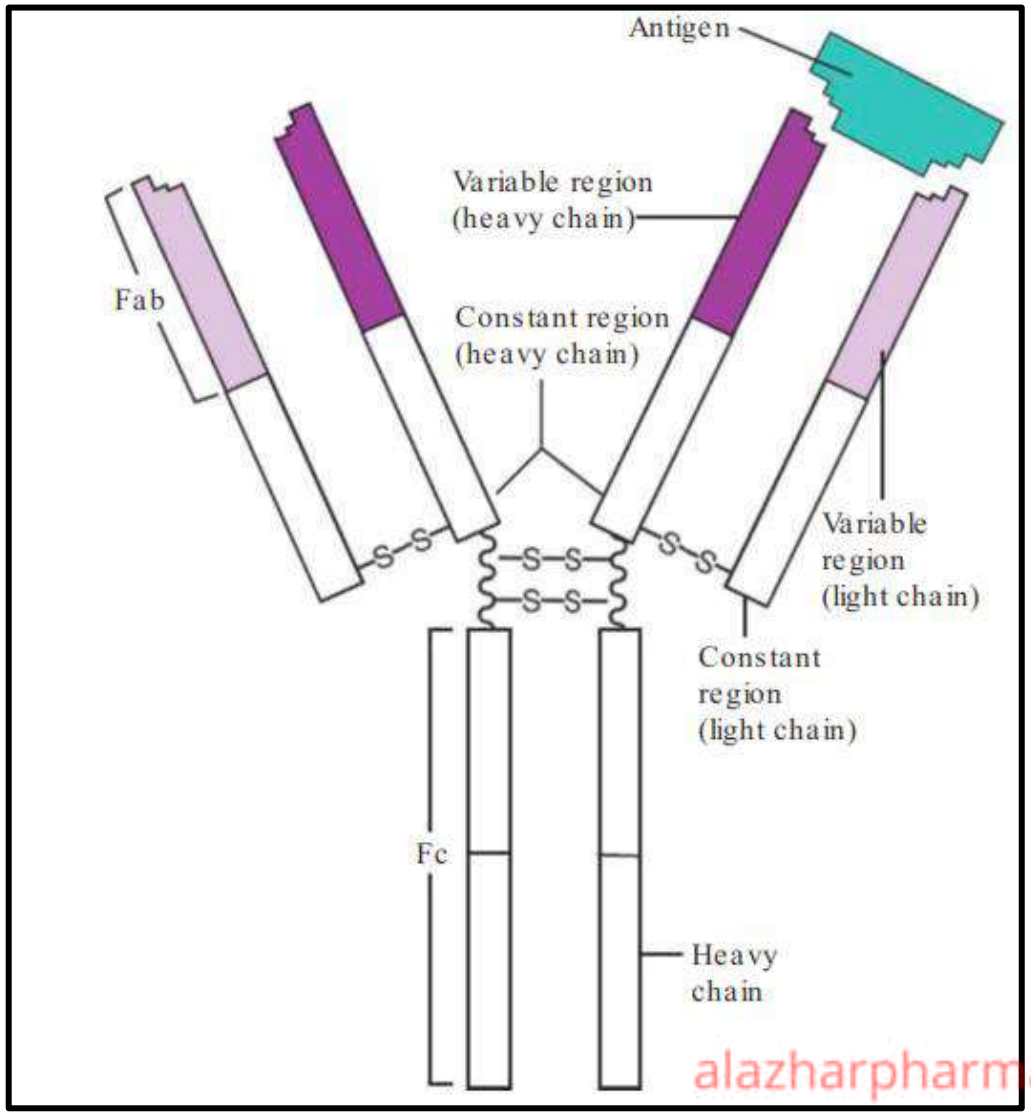
- B cells
  - Primary response
  - Secondary response



Adaptive immune response

2. Humoral mediated immunity

- **B cells**
  - **Antibodies**

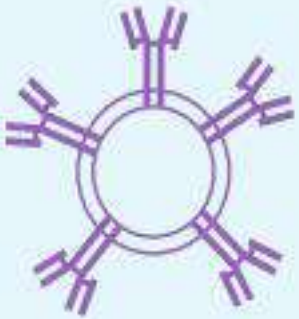


Adaptive immune response

2. Humoral mediated immunity

- B cells
  - Antibodies

TABLE 13.4 CLASSES AND CHARACTERISTICS OF Igs

FIGURE	CLASS	PERCENTAGE OF TOTAL	CHARACTERISTICS
	IgG	75.0	Displays antiviral, antitoxin, and antibacterial properties; only Ig that crosses the placenta; responsible for protection of newborn; activates complement and binds to macrophages
	IgA	15.0	Predominant Ig in body secretions, such as saliva, nasal and respiratory secretions, and breast milk; protects mucous membranes
	IgM	10.0	Forms the natural antibodies such as those for ABO blood antigens; prominent in early immune responses; activates complement
	IgD	0.2	Found on B lymphocytes; needed for maturation of B cells
	IgE	0.004	Binds to mast cells and basophils; involved in parasitic infections, allergic and hypersensitivity reactions

Adaptive immune response

- Active immunity
- Passive immunity