

# **Cell Signaling and Cell Receptors**



## **Learning Objectives:**

- ❖ List the modes of cell signaling.
- ❖ Define the term “Hormones”, classify hormones, and describe hormonal responses.
- ❖ List the types of lymphocytes and describe antigen receptors.
- ❖ Define the terms “Major Histocompatibility Complex” and “Human Leukocytes associated Antigen” and describe their role in immunity.
- ❖ Describe the mechanism of action of T-helper & T-cytotoxic cells in immunity.

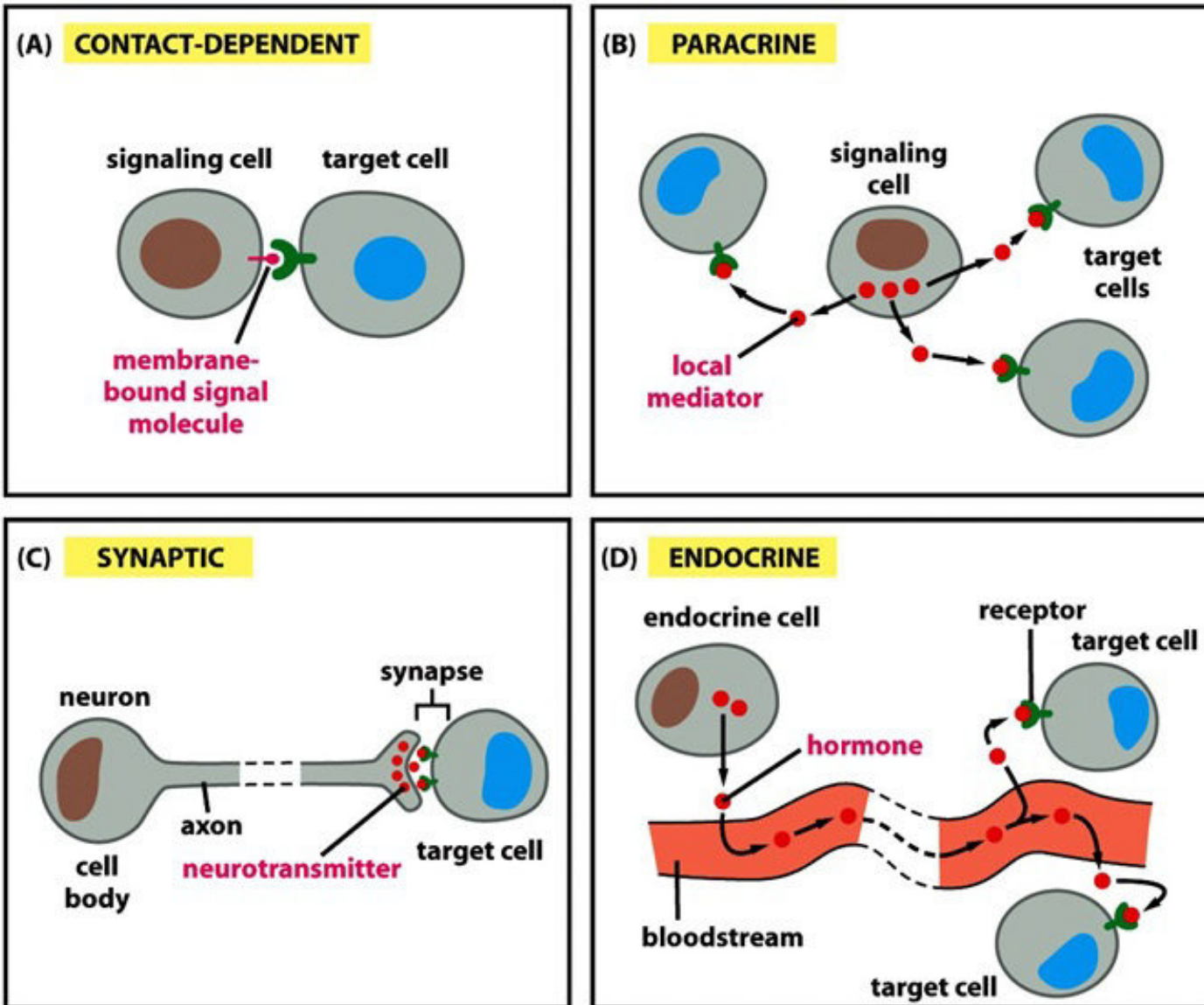
## Cell Signaling

- ❖ How do cells receive and respond to signals from their surroundings?
- ❖ Prokaryotes and unicellular eukaryotes are largely independent and autonomous.
- ❖ In multicellular organisms there is a variety of signaling molecules that are secreted or expressed on the cell surface of one cell and bind to receptors expressed by other cells. These molecules integrate and coordinate the functions of the cells that make up the organism.
- ❖ Sophisticated mechanisms control which signal molecules are released from a specific type of cell, at what time and concentration they are secreted, and how these signals are interpreted by the target cells.
- ❖ Some signalling molecules act over long distances, some act only on the immediate neighbour cells
- ❖ Most cells in higher organisms are both emitters and receivers of signals.

## Cell Signaling – *Modes of Cell-Cell Signaling:*

- ❖ **Direct cell-cell or cell-matrix** (integrins and cadherins).
- ❖ **Indirect:** Secreted molecules.
- ❖ **Endocrine signaling:** The signaling molecules are *hormones* secreted by endocrine cells and carried through the circulation system to act on target cells at distant body sites.
- ❖ **Synaptic signaling:** is performed by neurons that transmit signals electrically along their axons and release neurotransmitters at synapses, which are often located far away from the cell body.
- ❖ **Paracrine signaling:** The signaling molecules released by one cell act on neighboring target cells (*neurotransmitters*).
- ❖ **Autocrine signaling:** Cells respond to signaling molecules that they themselves produce (response of the immune system to foreign antigens, and cancer cells).

## Cell Signaling – *Modes of Cell-Cell Signaling:*



## Receptor Functions – *Hormone Receptors:*

- ❖ **The endocrine system** = organs secreting messengers (hormones) directly into the blood. It forms a very important communication system between organs & cells.
- ❖ Messages are slow compared with the nervous system. They are important in maintaining homeostasis all over the body.
- ❖ **Variability of hormonal responses:**
  - **More than 50 different endocrine products** have been identified.
  - Hormones can be **classified biochemically** as follows:
    - ✓ **Steroid hormones**; e.g. cortisol, estrogens, androgens
    - ✓ **Peptide hormones**; e.g. insulin, glucagon, pituitary hormones.
    - ✓ **Amino acid derivatives**, e.g. thyroxin, epinephrine (catecholamines).
  - **High specificity:**
    - ✓ Each hormone interacts with its own specific receptor protein located in or on the target cell.
    - ✓ Receptors for different hormones, on the same cell, initiate different types of responses because they are linked to different cellular response mechanisms.
    - ✓ The same hormone can be coupled to very different intracellular responses in different cell types.

## Receptor Functions – *Hormone Receptors – Cellular Response to Hormones:*

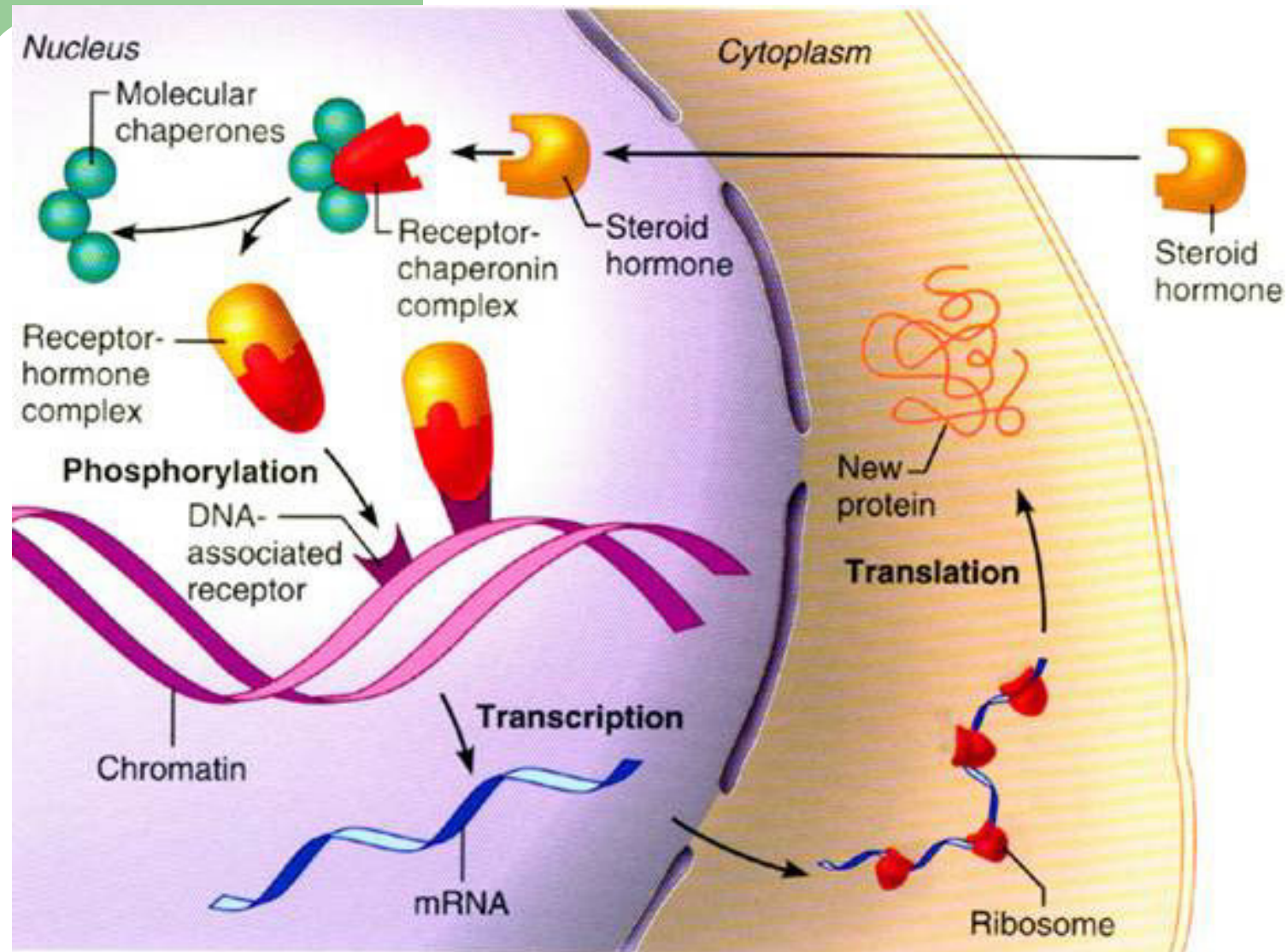
### ❖ **Steroids & Thyroid hormones:**

- They diffuse freely across the plasma membrane.
- They react with intracellular receptors, to form a receptor-hormone complex.
- The receptor-hormone complex binds to chromosomal sites to alter their ability to cause specific proteins to form (i.e. altering their transcriptional ability).

### ❖ **Peptides & Catecholamines:**

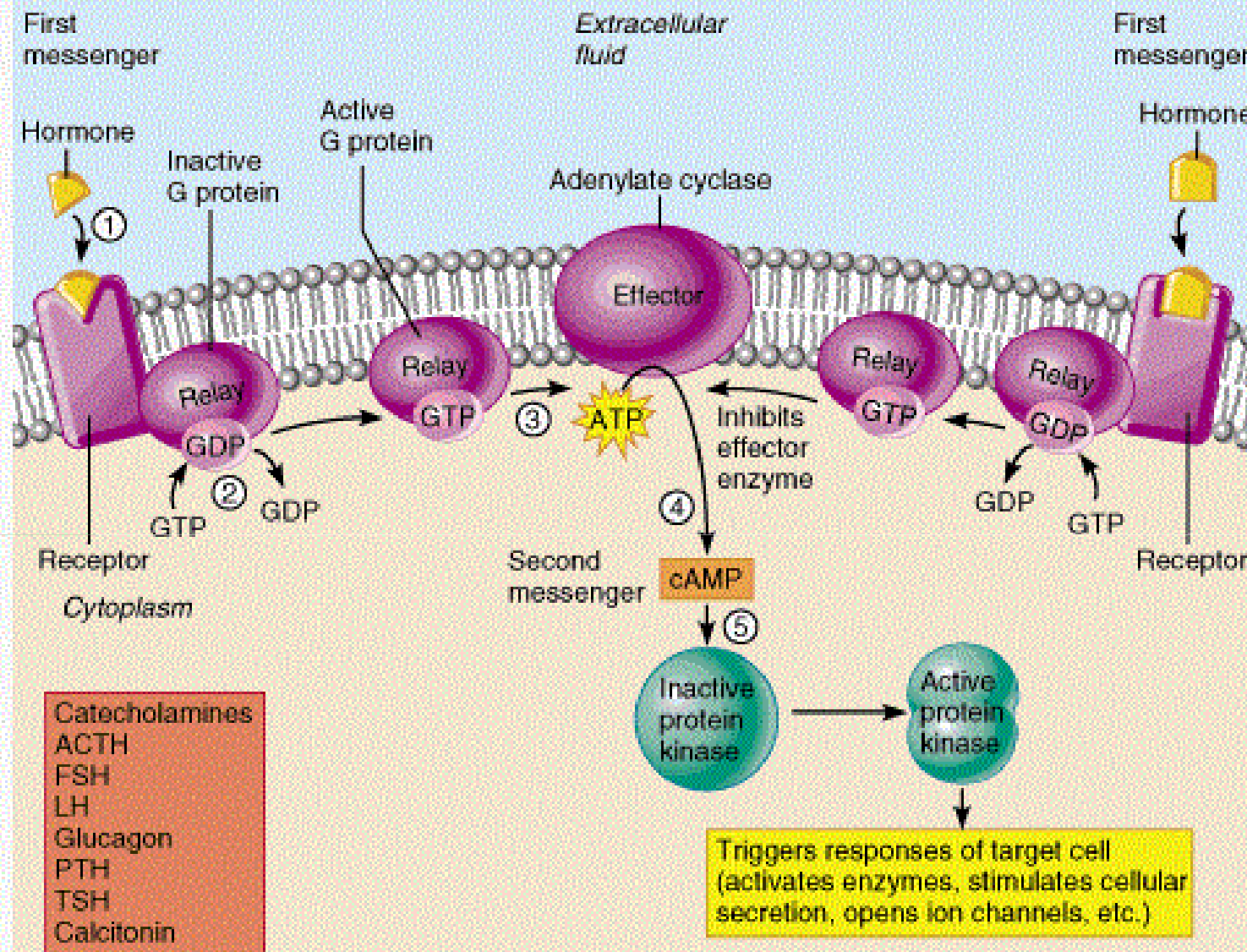
- Interact with cell surface receptors
- Receptors have:
  - ✓ An extracellular domain with a hormone-binding site.
  - ✓ An hydrophobic membrane-spanning domain.
  - ✓ An intracellular domain that initiates a cascade of intracellular reactions leading to a biological response.
- Cascade of intracellular reactions may involve an intracellular second messenger, which may be either *Cyclic AMP* or *Calcium-Calmodulin*
- Second messengers often cause phosphorylation of other proteins and alter their function in this way.





**Direct Gene Activation Mechanism of Steroid Hormones**





## Second-Messenger Mechanisms of Protein-Peptide Hormones

## Receptor Functions – *Antigens & Antigen Receptors:*

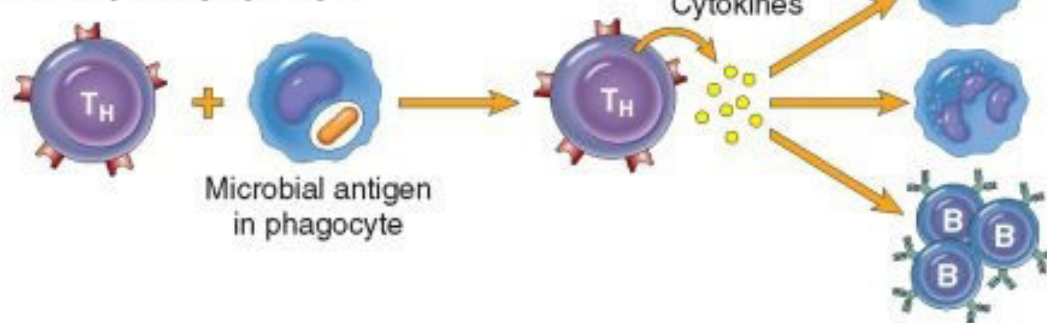
- ❖ The ‘**Lymphocytes**’; white blood cells called lymphocytes mediate the immune response to invaders and they are classified as:
  - **B cells:** antibody-producing cells responsible for *humeral immunity*.
  - **T cells:** responsible for *cell-mediated immune responses* and these are sub classified into: *Cytotoxic T cells* and *Helper T cells*.
- ❖ **Antigen Receptors:**
  - Every lymphocyte carries antigen receptors protein on its surface:
    - ✓ **B cells’ receptors are antibodies.**
    - ✓ **T cells’ receptors are similar, but not identical to antibodies.**
  - One lymphocyte may have 100,000 surface receptors, all identical for any one cell.
  - Variety of immune responses is achieved by having  $10^{12}$  lymphocytes, representing about  $10^{8\text{or}9}$  different specificities.

### B lymphocyte



Antibody secretion

### CD4+ helper T lymphocyte

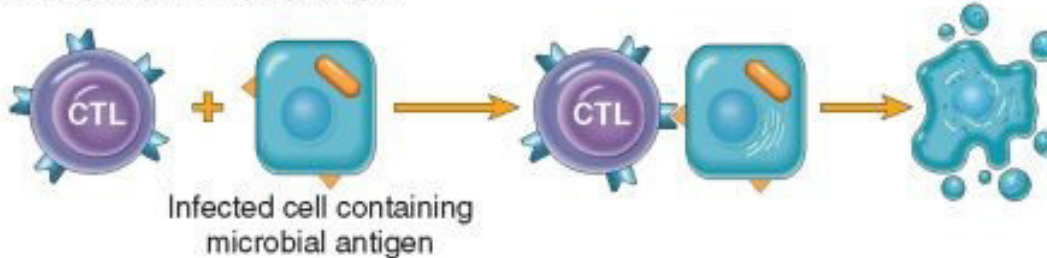


Activation of  
macrophages

Inflammation

Stimulation of  
B lymphocytes

### CD8+ cytotoxic T lymphocyte



Killing of  
infected cell

*The principal classes of lymphocytes and their functions in adaptive immunity*

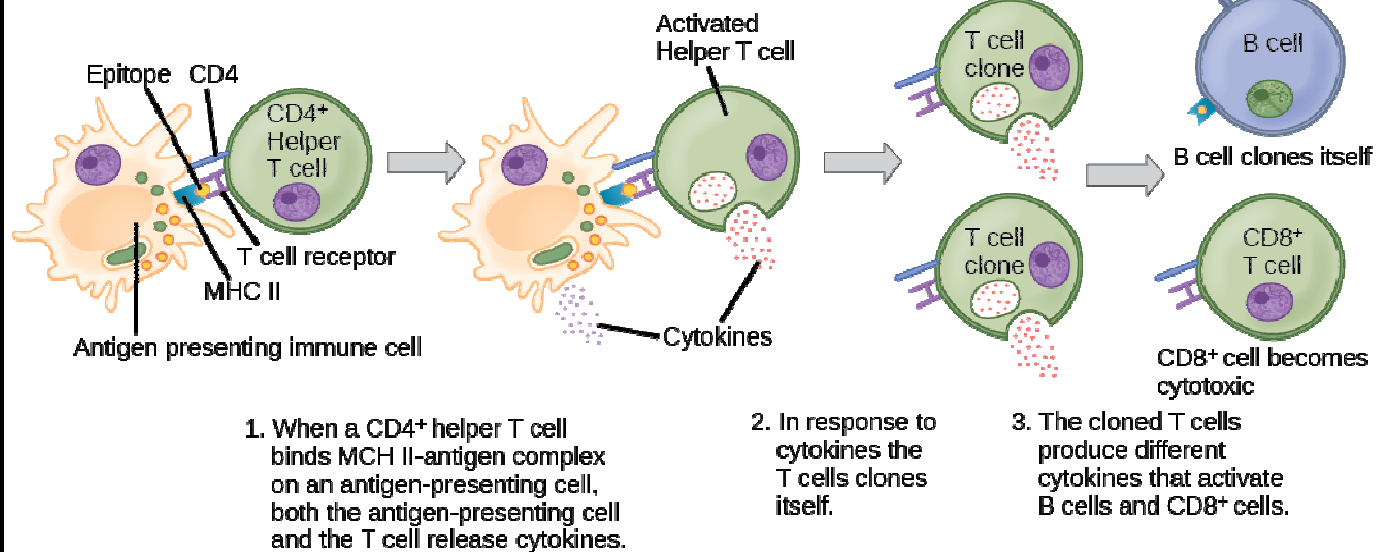
## *Antigens & Antigen Receptors – The Major Histocompatibility Complex (MHC):*

- ❖ “MHC” surface proteins on cells are an important part of our *biochemical individuality*, causing our own cells to become antigens in relation to some else’s system. *This makes transplants and grafts difficult.*
- ❖ MHC proteins also complex with foreign antigens (e.g. from infection), causing the foreign antigens to become even more antigenic in our system, stimulating the T cells much more strongly, and helping us to overcome the infection.
- ❖ In humans, MHC antigens are called **Human Leukocytes-Associated Antigen (*HLA Antigens*)**, *coded on chromosome 6*. They are important in pathology because *certain people have HLA antigens which seems to cause unusual disease conditions.*

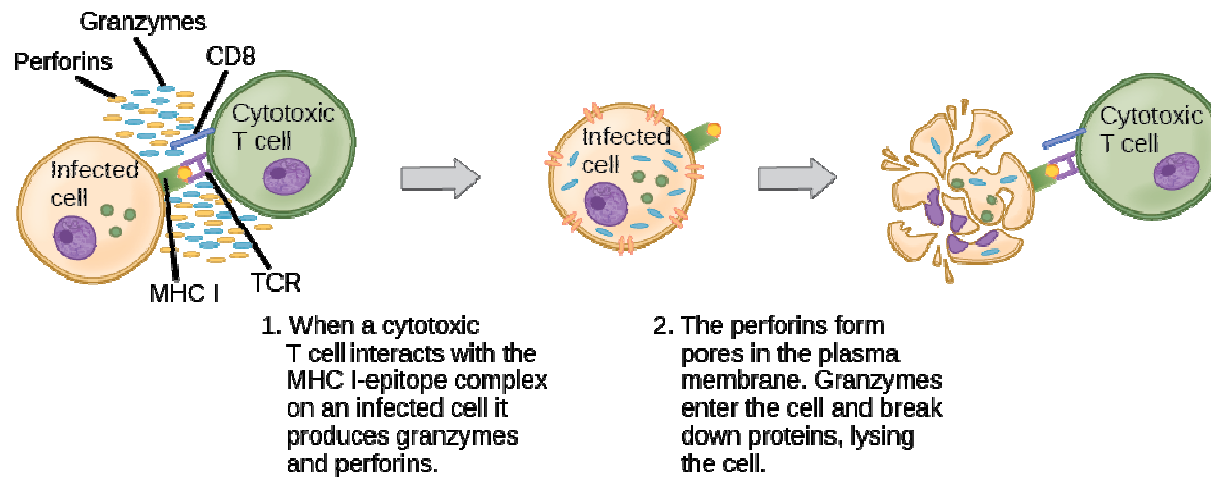
## ***Antigens & Antigen Receptors – The Major Histocompatibility Complex (MHC):***

- ❖ MHC genes inherited from both parents are expressed on cell surfaces.
- ❖ They are ***highly polymorphic***, which means that every individual is likely to have a different MHC complex from another one. This makes transplants even harder.
- ❖ They form two families of antigens, both of which are ***glycoproteins which resemble immunoglobulins***:
  - **Class I antigens:**
    - ✓ *All nucleated cells* have them.
    - ✓ *They complex with fragmented antigens from any agent* which infects any cell.
    - ✓ ***They activate cytotoxic T cells***, enabling them to recognize e.g. virus in future.
  - **Class II antigens:**
    - ✓ *B lymphocytes and macrophages* have them.
    - ✓ Foreign antigens are captured by ***antigen-presenting cells (APC), (B cells and macrophages)***, processed and fragmented, and presented on the cell surface in complex with MHC class II proteins.
    - ✓ ***They activate helper T Cells.***

### CD4<sup>+</sup> T cells



### CD8<sup>+</sup> T cells



***CD4<sup>+</sup> ( T Helper Cells ) & CD8<sup>+</sup> ( Cytotoxic Cells ) Role in Immunity***