Cell Mediated Immunity (CMI)

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Cell-Mediated Immunity (CMI)

Cell Mediated Immunity

- **Cell-mediated immunity** (**CMI**).

- T cells (lymphocytes) bind to the surface of other cells (Antigen Presenting Cells) that display the antigen and trigger a response

Antigen Presenting cells

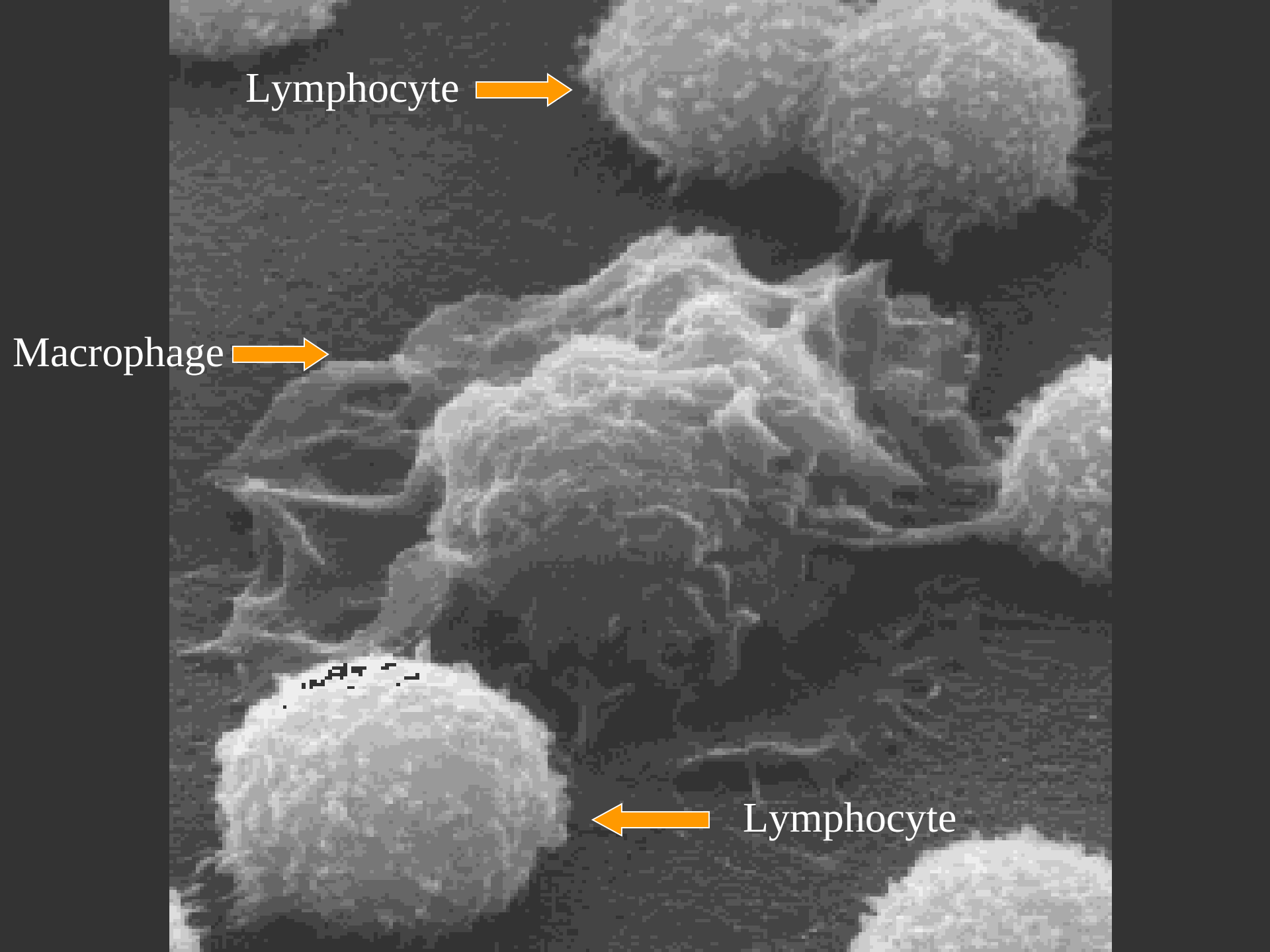
Monocytes : Peripheral blood

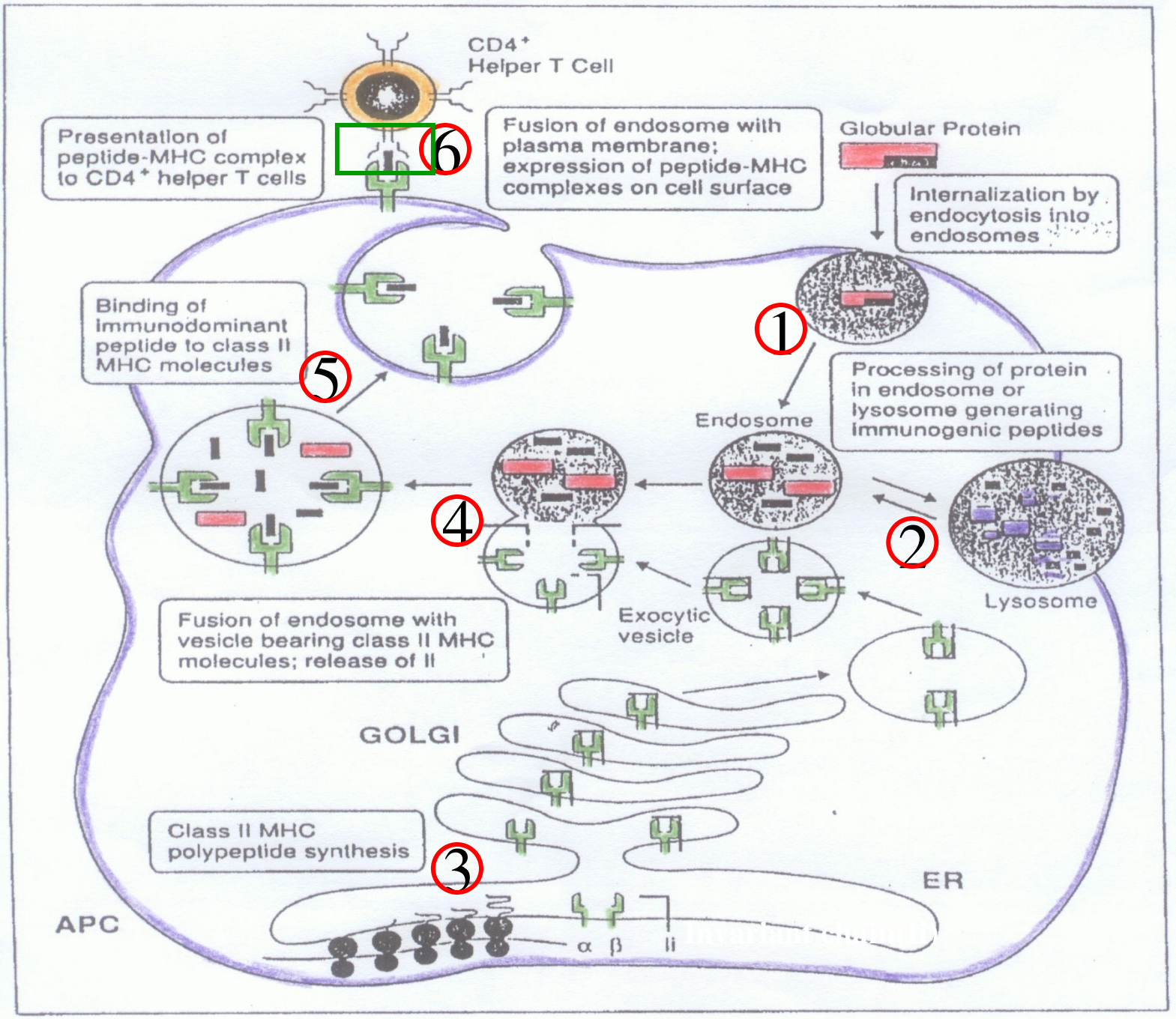
Macrophages : Tissues

Dendritic cells : Lymphoid tissues

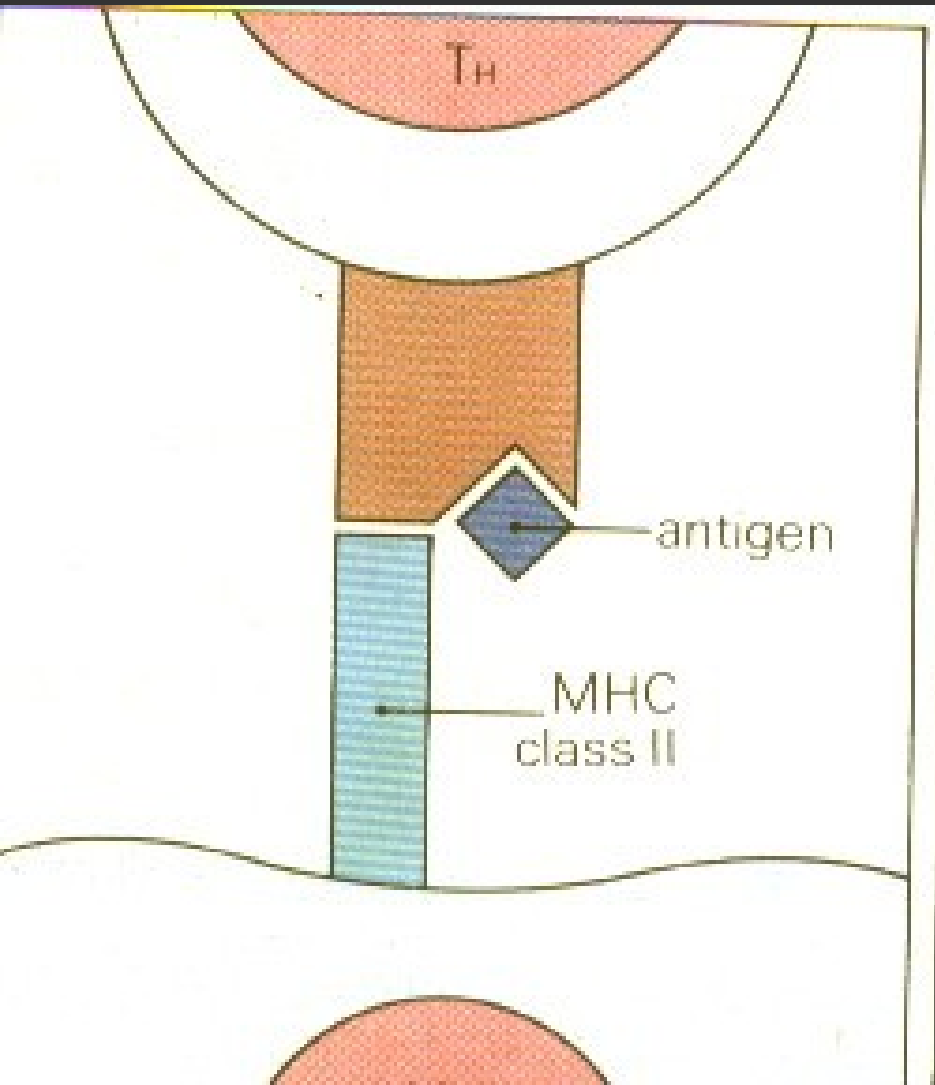
Langerhans cells : Epidermis

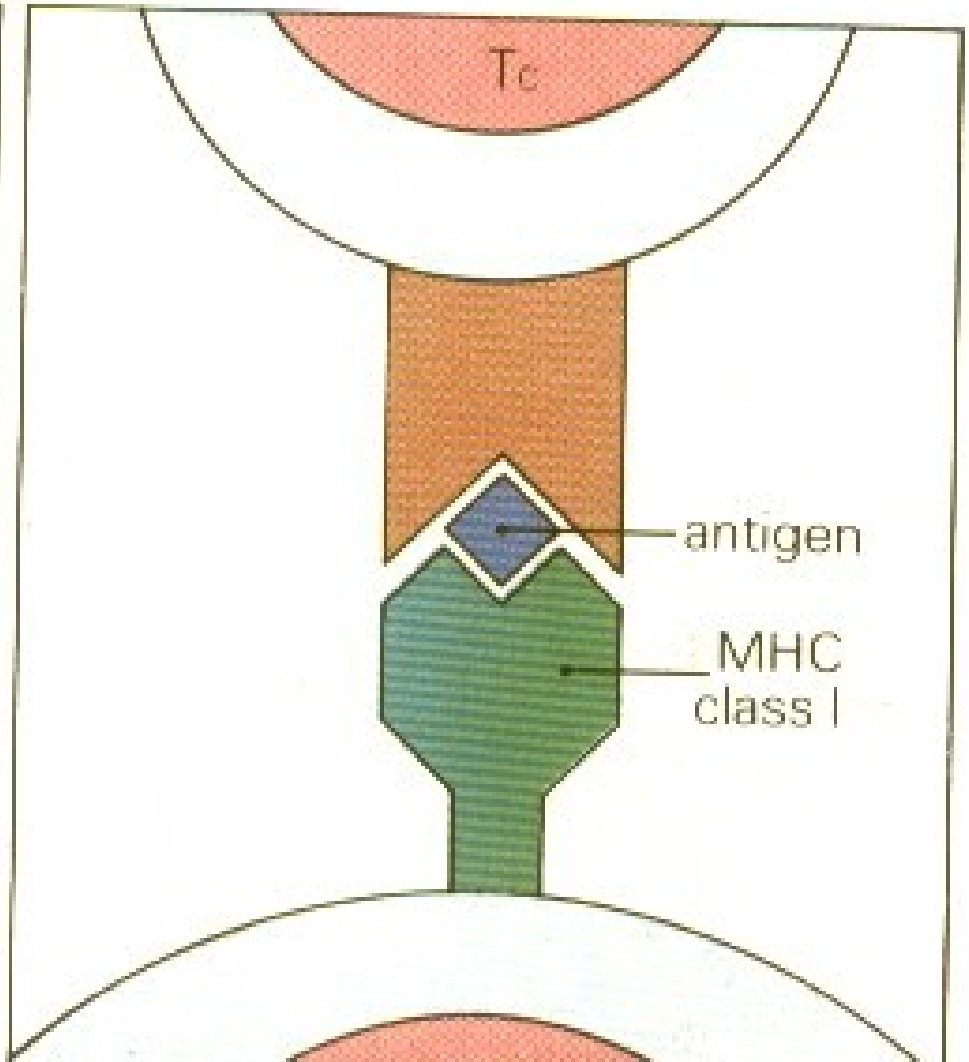
B-cells : Lymphoid tissue, Blood


Lymphocyte
Macrophage
Lymphocyte

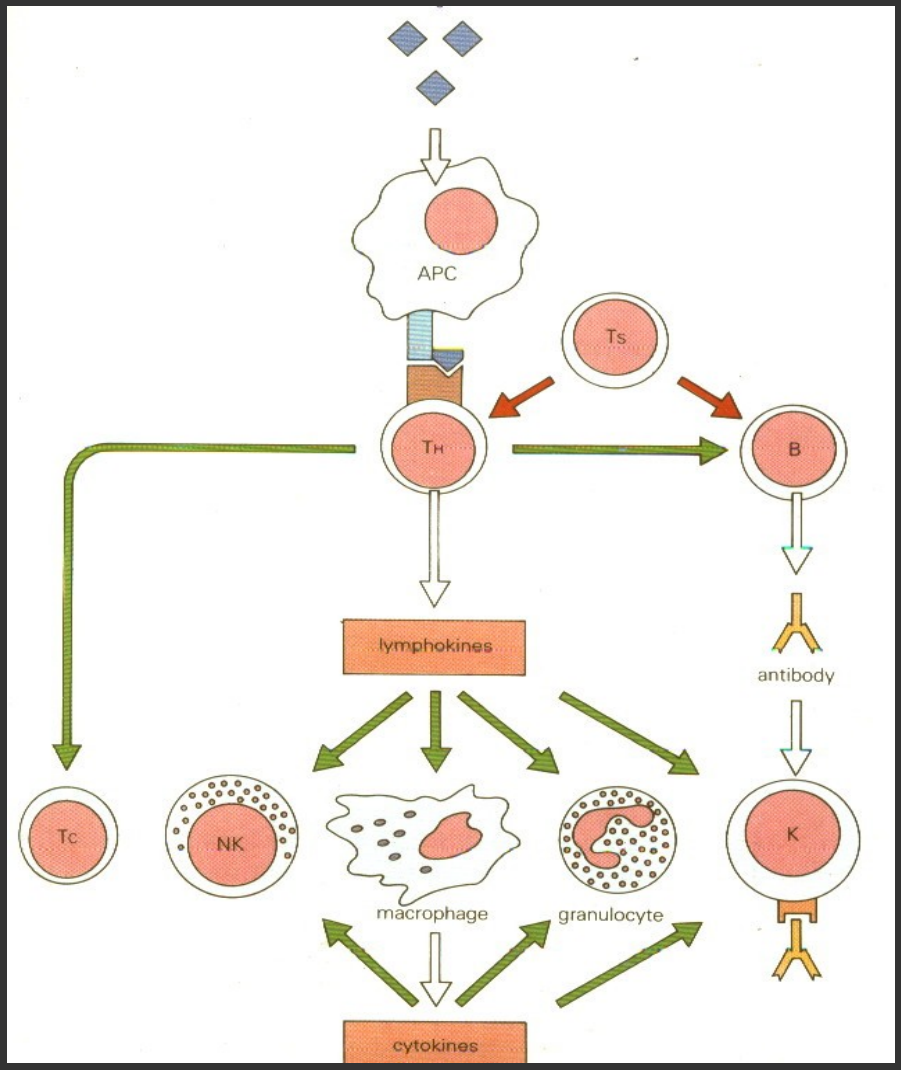

CD4+
Helper T Cell
Presentation of peptide-MHC complex to CD4+ helper T cells
6
Fusion of endosome with plasma membrane; expression of peptide-MHC complexes on cell surface
Globular Protein
Internalization by endocytosis into endosomes
Binding of immunodominant peptide to class II MHC molecules
5
1
Processing of protein in endosome or lysosome generating immunogenic peptides
Endosome
4
2
Lysosome
Exocytic vesicle
Fusion of endosome with vesicle bearing class II MHC molecules; release of Ii
GOLGI
Class II MHC polypeptide synthesis
3
ER
APC
α β Ii

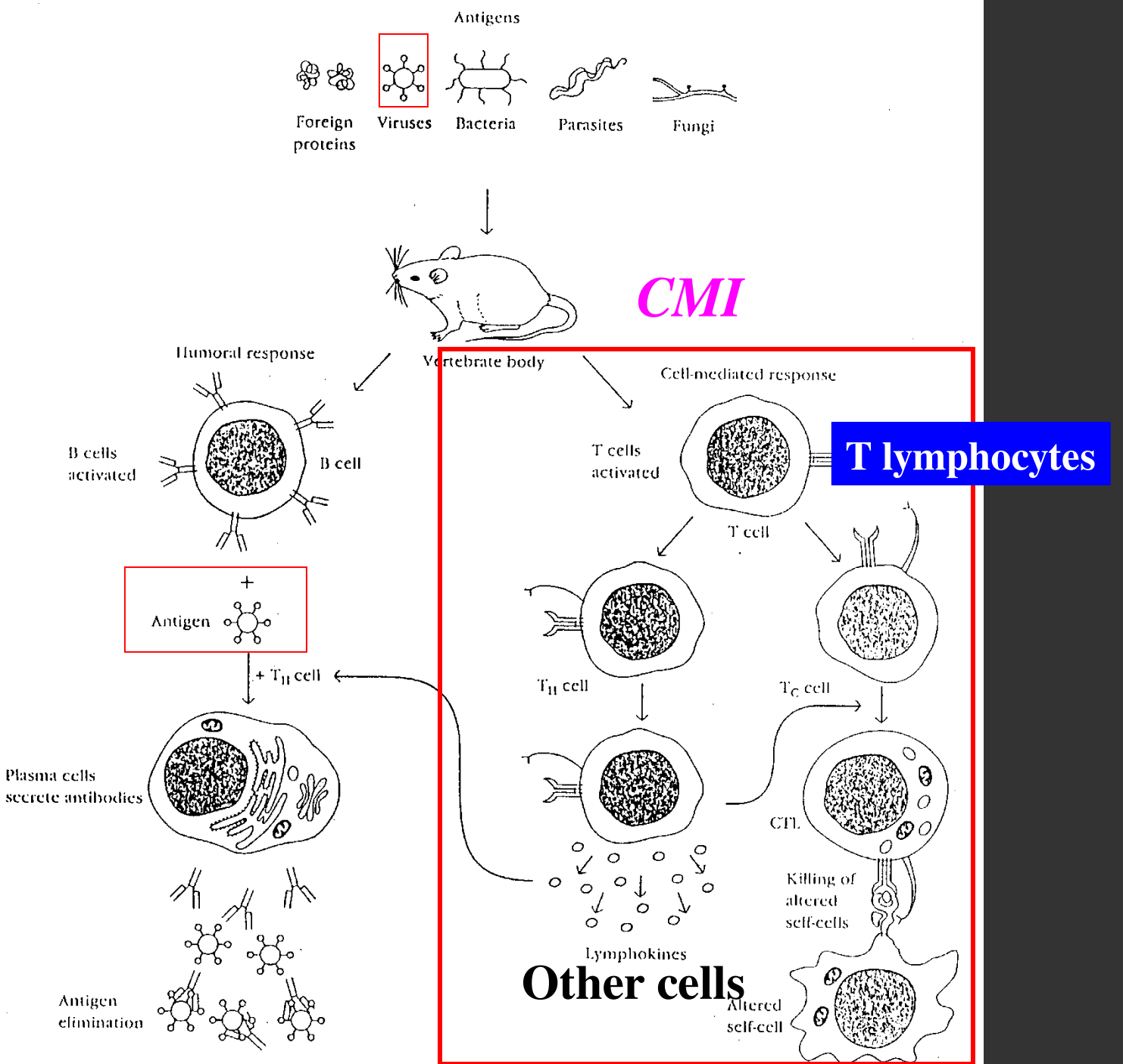
T cell Activation
Antigen Presentation





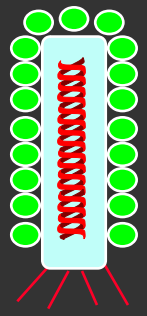
T cell Activation
Antigen Presentation




Antigens
Foreign proteins
Viruses
Bacteria
Parasites
Fungi
CMI
Humoral response
Vertebrate body
Cell-mediated response
B cells activated
B cell
T cells activated
T cell
T lymphocytes
Antigen
+ T_H cell
T_H cell
T_C cell
Plasma cells secrete antibodies
CTL
Killing of altered self-cells
Lymphokines
Other cells
Antigen elimination
Altered self-cell

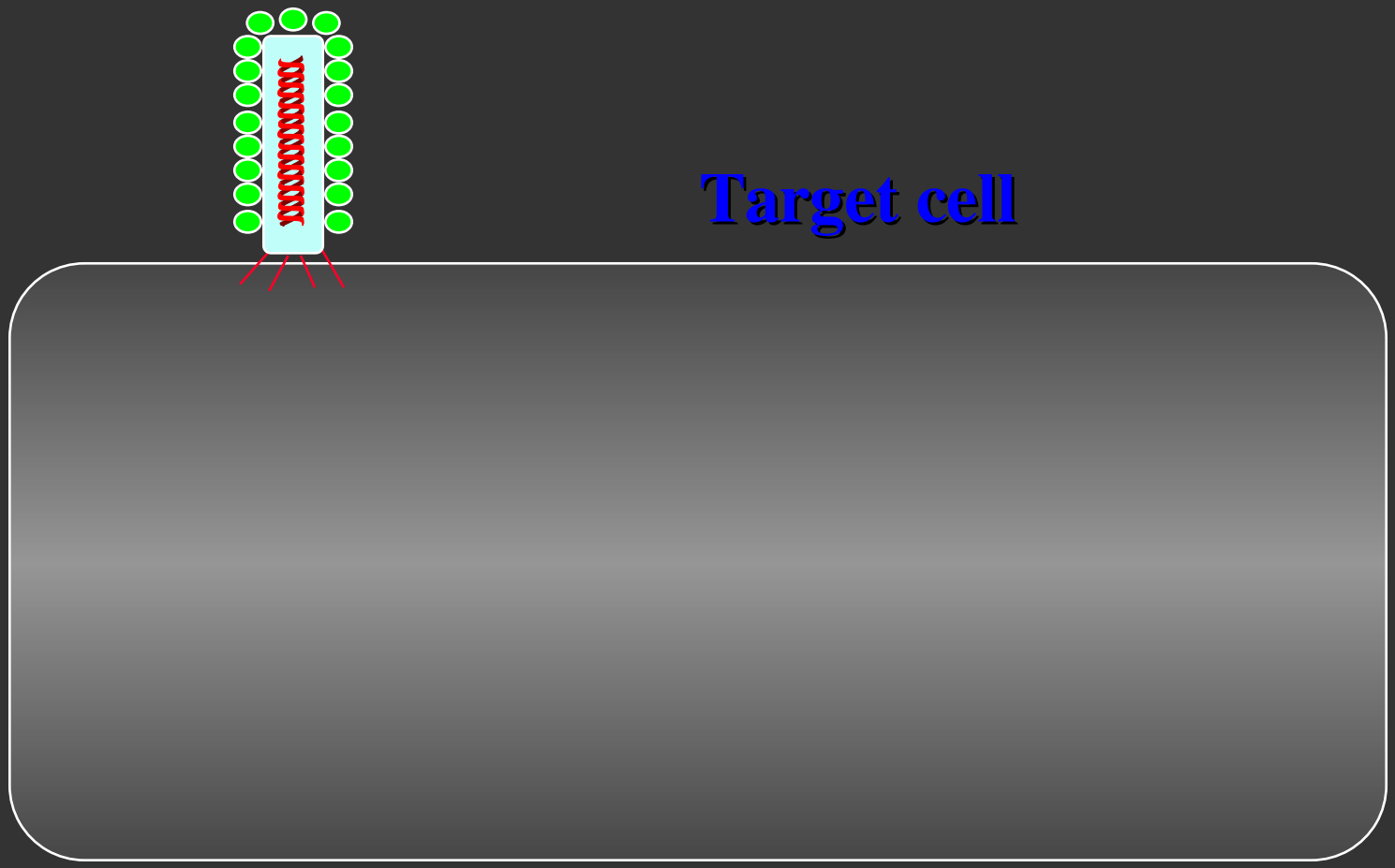
1 . Endogenous antigen

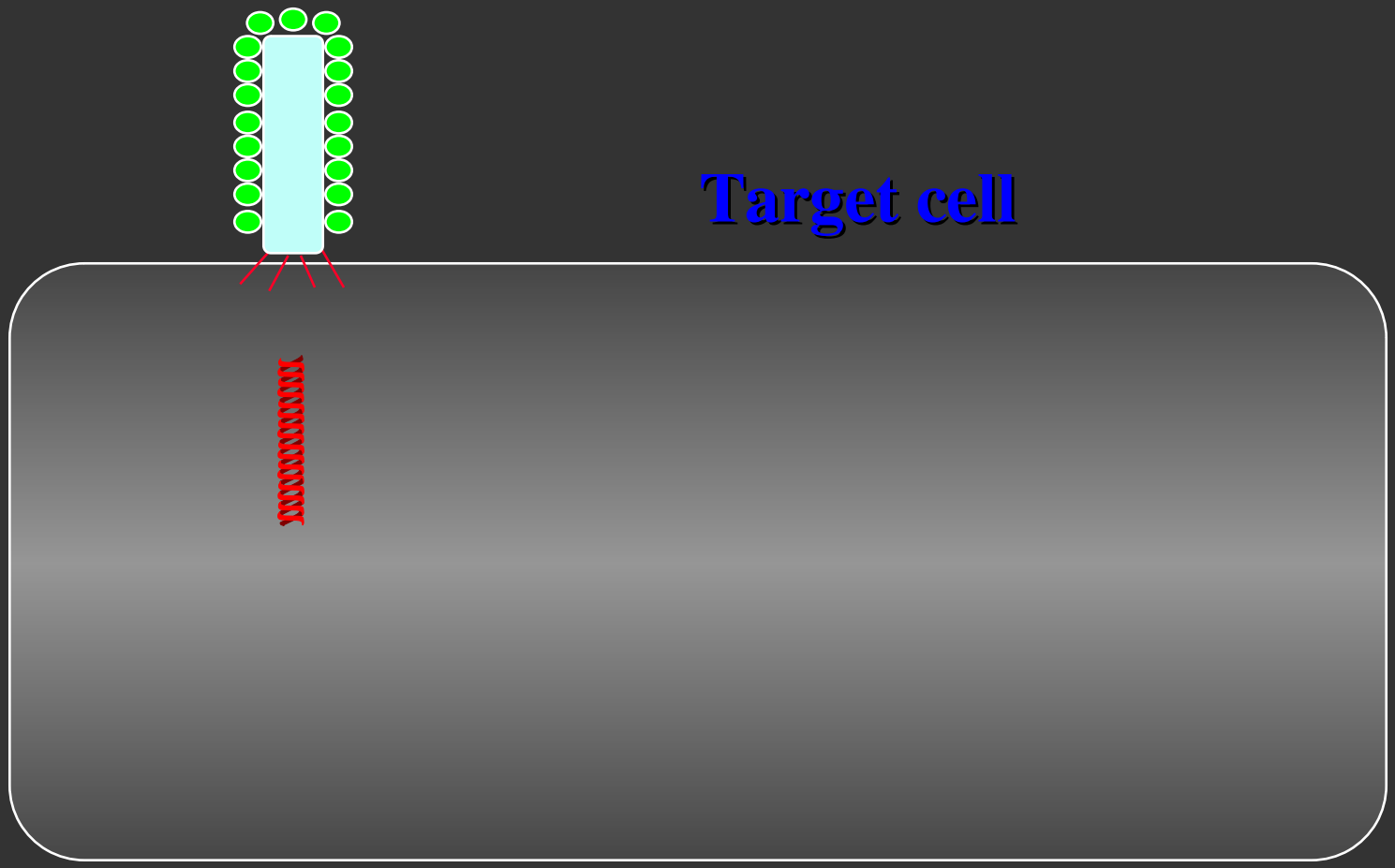
2. Exogenous antigen

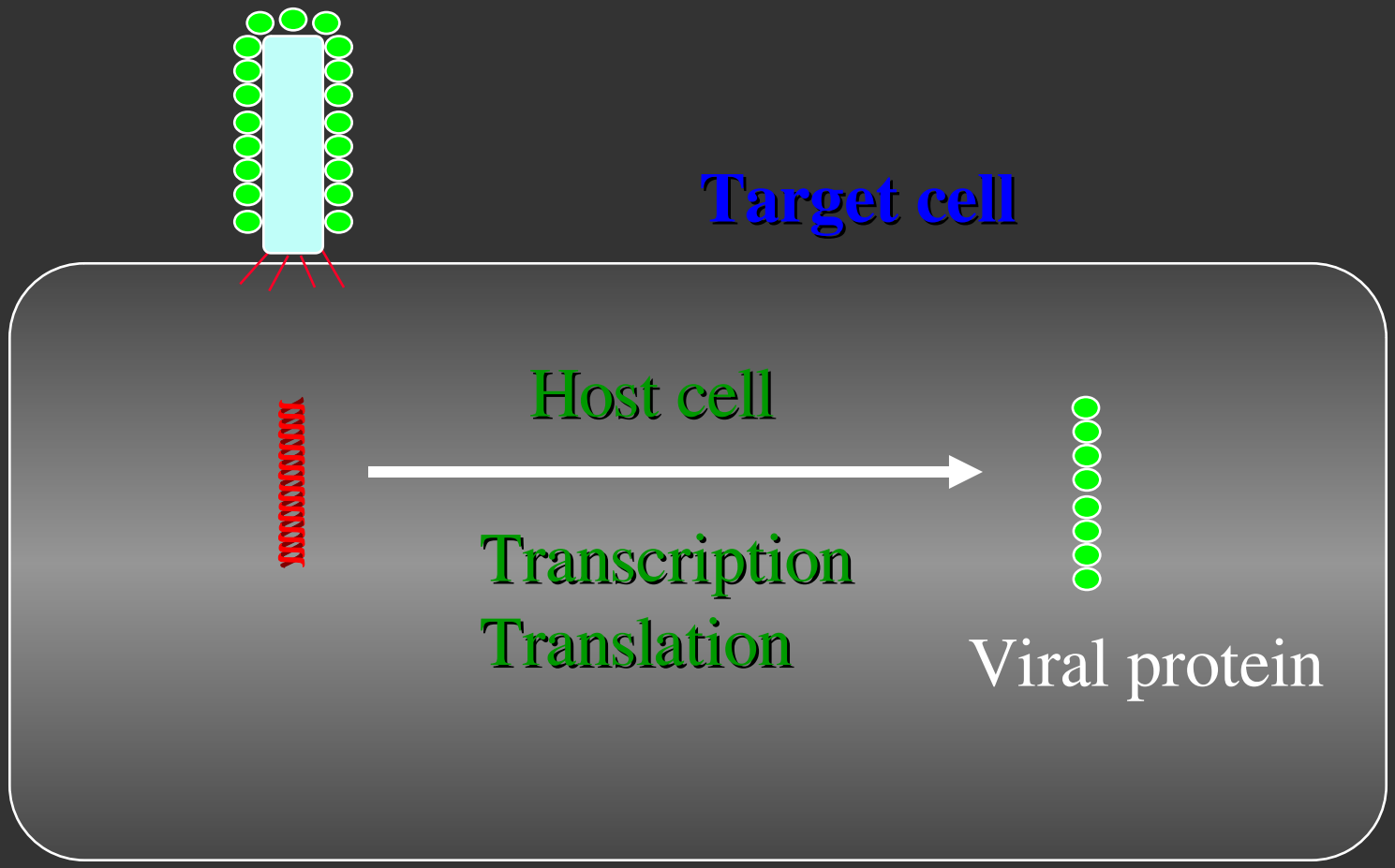


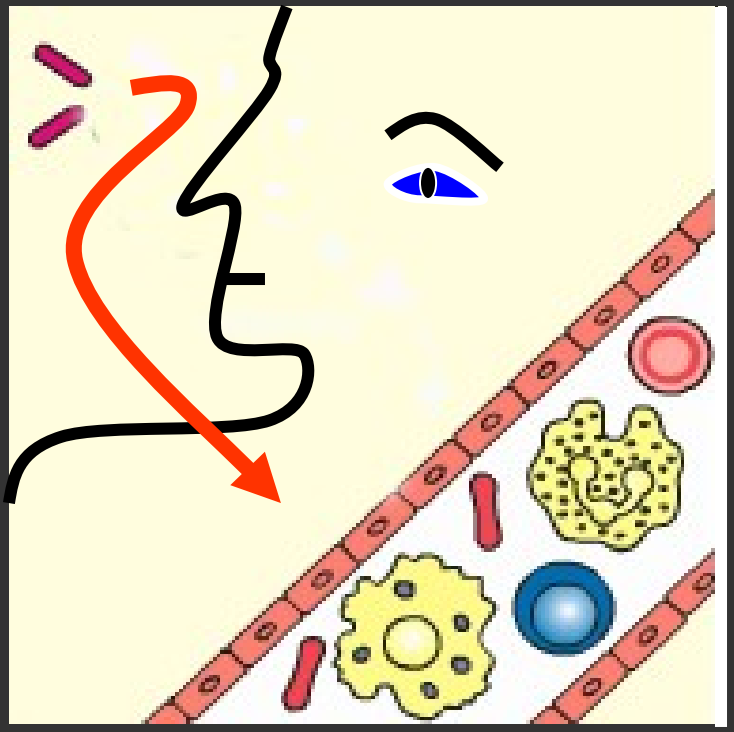
Virus

Target cell


Target cell


Target cell

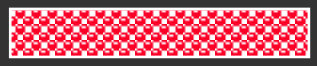

Target cell
Host cell
Transcription
Translation
Viral protein



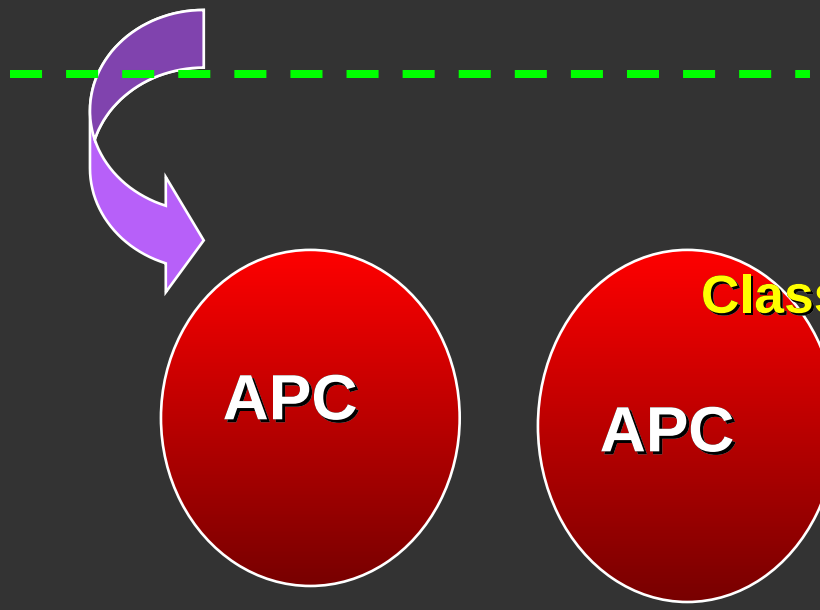
Exogenous antigen

- Microbes
- Proteins

Cell-mediated immun



Exogenous antigen



CD4+ T-lymphocytes (CD4+ cells)

CMI

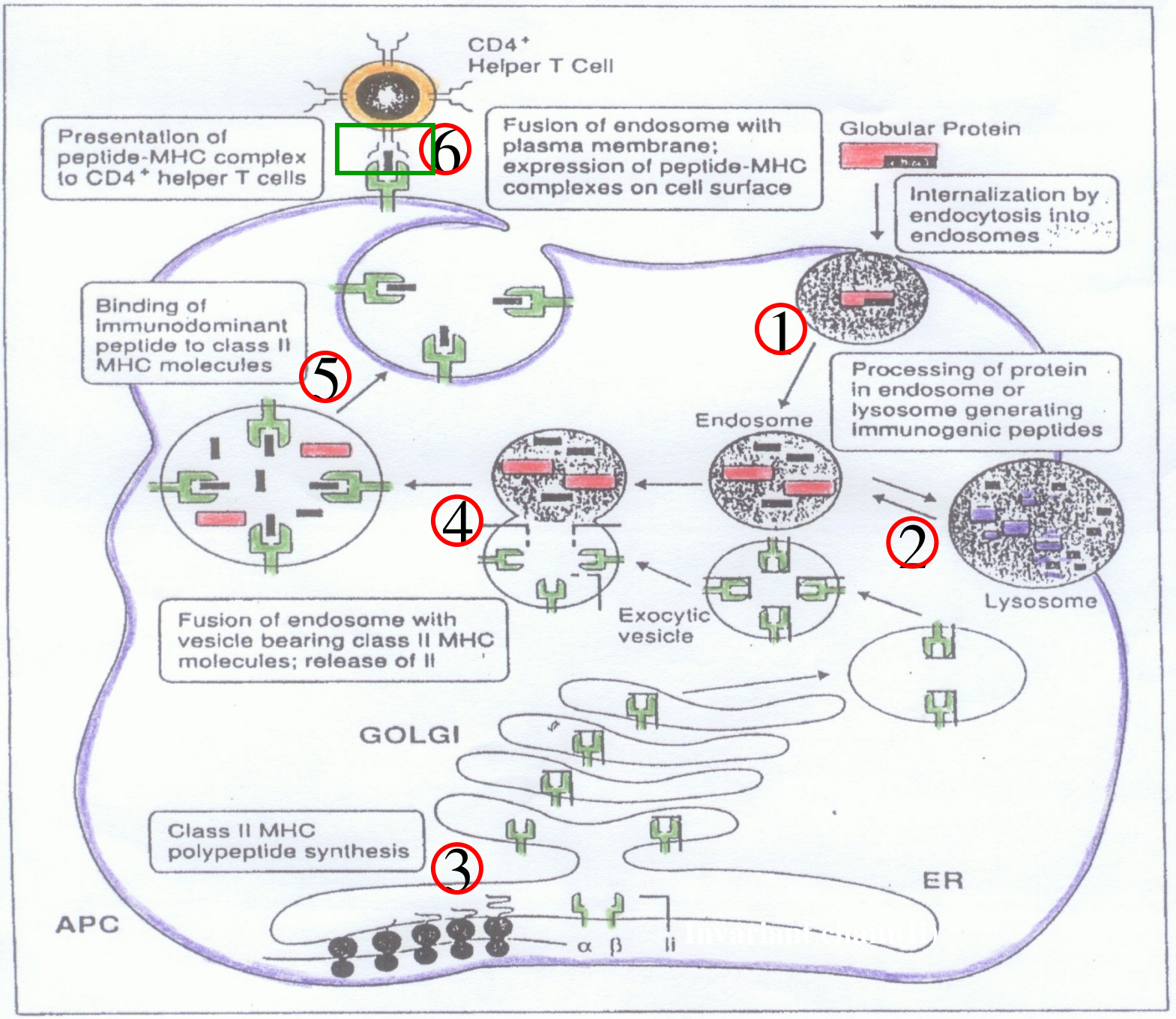
Antigen presenting cells

Monocytes/Macrophages

Dendritic cells

Langerhans cells

B-cells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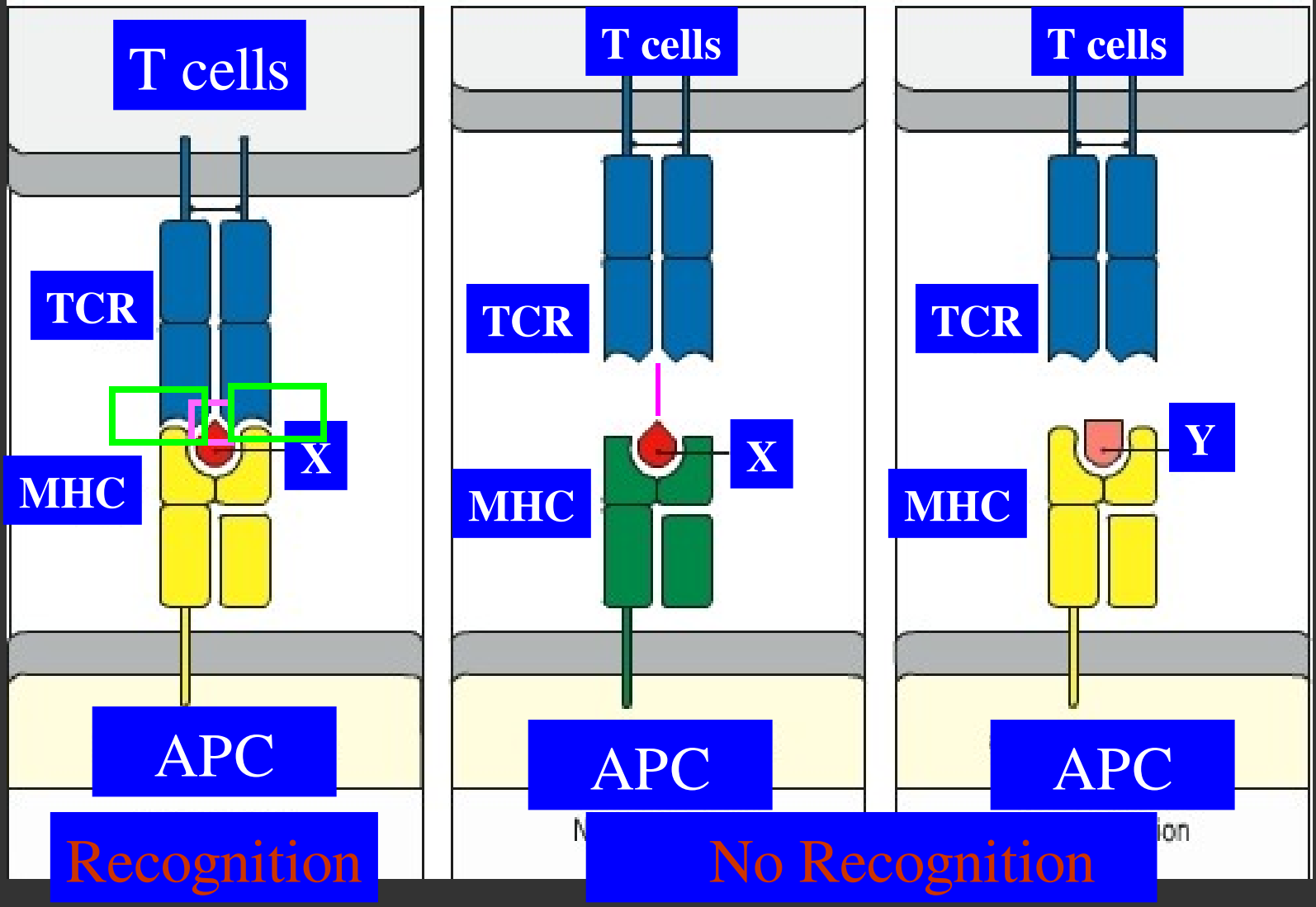
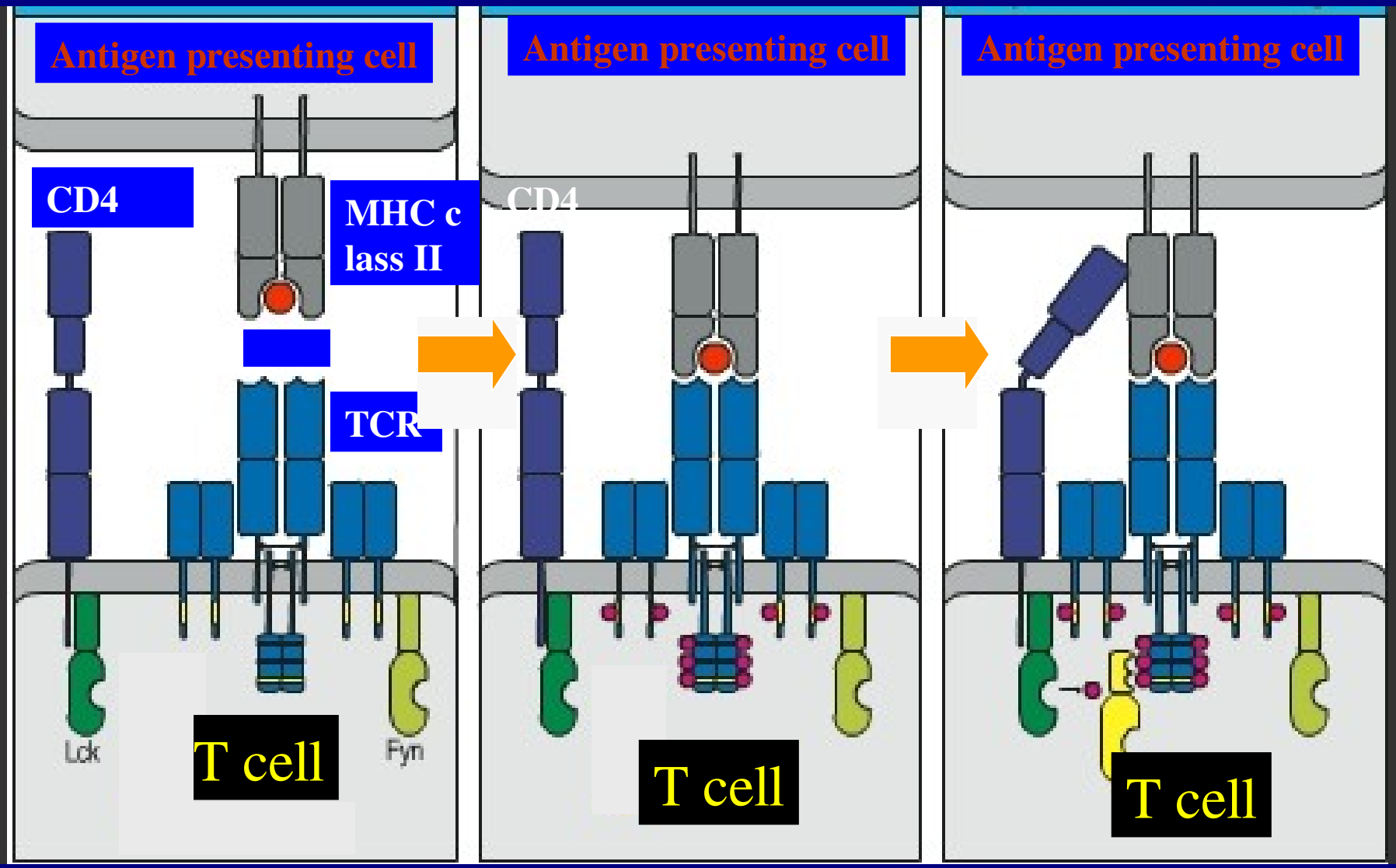
Processing of protein in endosome or lysosome generating immunogenic peptides
Endosome
4
2
Lysosome
Exocytic vesicle
Fusion of endosome with vesicle bearing class II MHC molecules; release of Ii
GOLGI
Class II MHC polypeptide synthesis
3
ER
APC
α β Ii

TCR-MHC interaction



CD4-MHC class II interaction



Cell-Mediated Immunity

- **Lymphocytes: (B & T lymphocytes)**

- **B lymphocytes** ("B cells"): These are responsible for making antibodies (humoral immunity)

- **T lymphocytes** ("T cells"): CMI
- Subsets include:
  - **CD8+ cytotoxic T lymphocytes** (CTLs) that kill virus-infected and tumor cells
  - **CD4+ helper T cells** enhance CMI and production of antibodies by B cells

Cell-Mediated Immunity

- **Examples of Cell-Mediated Immunity**
- **Delayed-Type Hypersensitivity (DTH): the tuberculin test (or Mantoux test)**
- Tuberculosis: a chronic disease, caused by **Mycobacterium tuberculosis**
- The response to tuberculin is called "delayed" because of the time it takes to occur (in contrast to the "immediate" responses characteristic of many antibody-mediated sensitivities like an allergic response to a bee sting).

Cell Mediated Immunity

- DTH is a cell-mediated response
- Anti-tuberculin antibodies are rarely found in tuberculin-positive people
- The T cells responsible for DTH are members of the CD4+ subset

Cell-Mediated Immunity

- **Contact Sensitivity**
- Many people develop rashes on their skin following contact with certain chemicals such as nickel, certain dyes, and the active ingredient of the poison ivy plant
- The response takes some 24 hours to occur, and like DTH, is triggered by CD4+ T cells
- The actual antigen is probably created by the binding of the chemical to proteins in the skin
- The fragments of antigen are then presented to CD4+ T cells by phagocytic cells in the skin by antigen presentation

Activation of helper T cells

- Requires recognition of antigen complex on the surface of antigen-presenting cells eg, macrophages consisting of both antigen and class II MHC proteins
- Viral antigens are recognized in association with class I MHC proteins
- This is called MHC restriction

Cellular Basis of Immune Response

- Two signals are required to activate T cells
- First signal
- Class II MHC + antigen – TCR
  - IL-1, LFA-1 with ICAM
- Second signal (Costimulatory signal)
  - B7 on APC interacts with CD28 on lymphocyte

T cell Activation

- In the absence of co-stimulatory signal state of unresponsiveness called ***"anergy"*** develops
- Production of co-stimulatory protein depends on activation of the toll like receptor on antigen presenting cell
- Foreign antigens such as bacterial proteins induce B7 protein where as self proteins do not

T cell Activation

- Consequent to antigen recognition by TCR, signal is transmitted through CD3 molecule
- This results in influx of calcium into the cell
- Calcium activates calcineurin
- Calcineurin activates gene for IL-2 and its receptor

Out come of T helper cell activation

- Production of IL-2 and its receptor
  - IL-2 is also know as T cell growth factor
  - Proliferation of antigen specific T cells
  - Effector and regulatory cells are produced along with ***“memory”*** cells
  - IL-2 also stimulates CD8 cytotoxic cells

Out come of T helper cell activation

- Production of Gamma Interferon (IFγ)
  - It increases expression of Class II MHC proteins
  - It enhances the ability of APC to present antigen to T cells
  - It enhances the microbicidal activity of macrophages
  - Enhances immune response

Out come of T helper cell activation

- Memory T cells
- Respond rapidly for many years after initial exposure to antigen
- A large number of memory cells are produced so that the secondary response is greater than the primary
- Memory cells live for many years and have the capacity to multiply
- They are activated by smaller amount of antigen
- They produce greater amounts of interleukins

Effector functions of T cells

1. Delayed type of hypersensitivity mediated by Th-1 type of CD4 positive cells

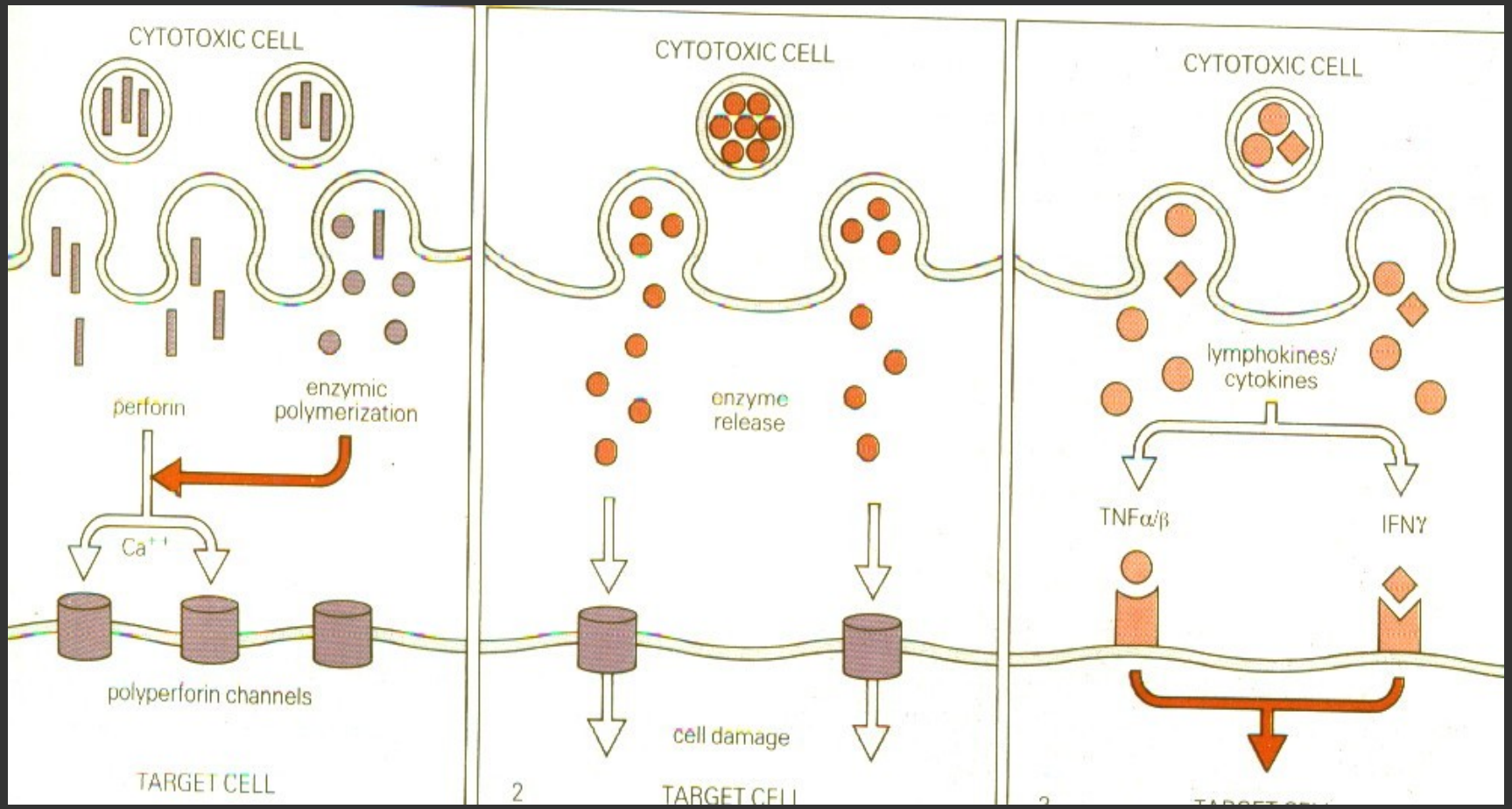
2. Cytotoxicity: mediated by CD8 +ve cells.

   Directed against virus infected cells, tumor cells and allografts

Killing by cytotoxic cells

- Perforins
- Granzymes – degrading enzymes
- Fas-Fas Ligand interaction - apoptosis
- Antibody dependent cellular cytotoxicity
- Immune surveillance
- Allograft rejection

Killing Mechanisms of Cytotoxic T cells



Activation of B cells

- B cell functions as APC
- Multivalent antigen binds to surface IgM
- Cross links adjacent Ig molecules
- Igs aggregate to form “patches” and migrate to one pole to form a cap
- Capped material is endocytosed
- Antigen is processed and epitopes appear on the cell surface in association with Class II MHC proteins