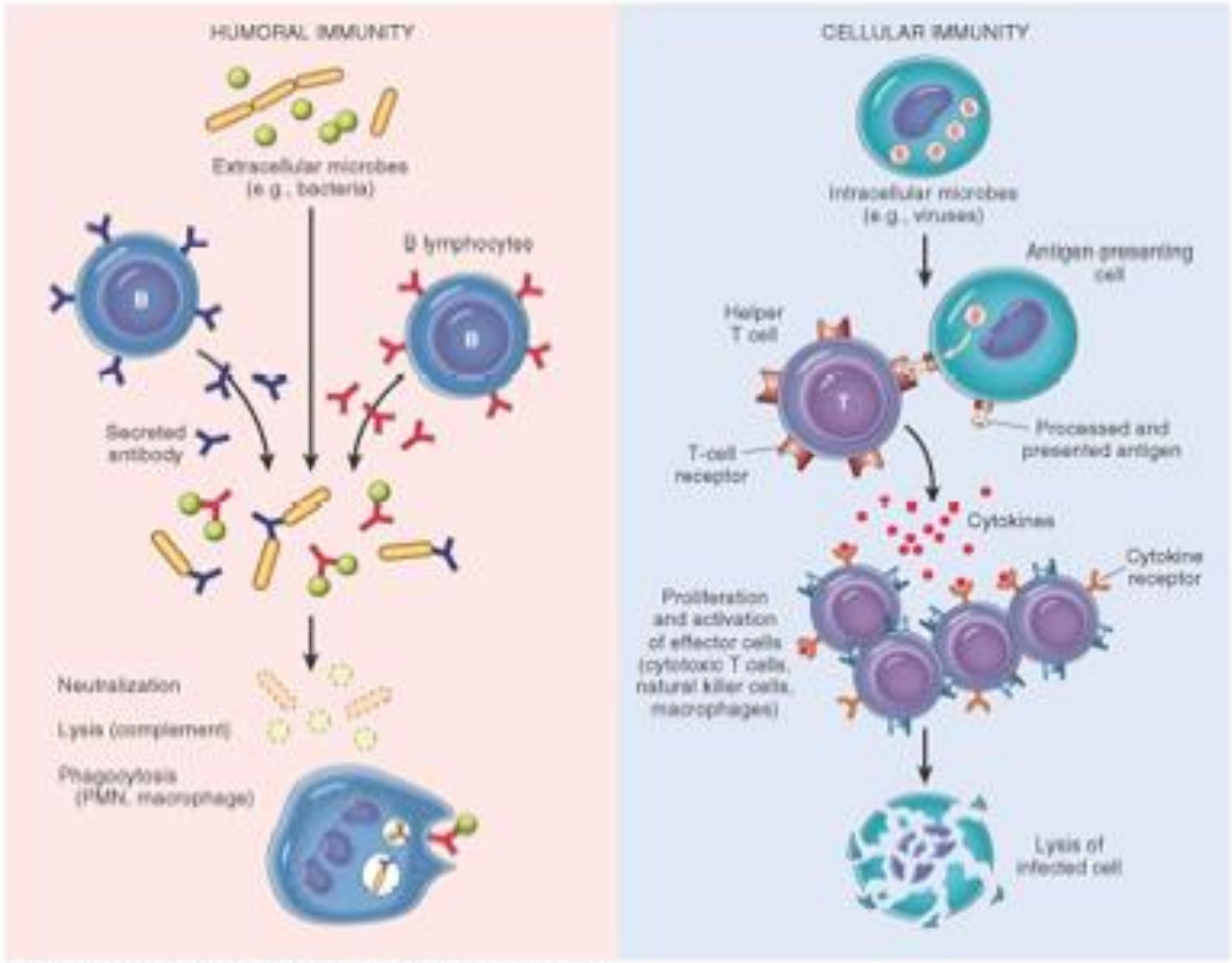
Cell Mediated Immunity

Immunology Unit
Department of Pathology
College of Medicine
KSU

Lecture # 3/6
Foundation block

Teaching objectives

- To describe antigen recognition by T cells
- To describe the pathways involved in processing endogenous and exogenous antigens
- To discuss self MHC restriction in Ag presentation to T cells
- To describe the induction of cell meditated immunity (Chronic Inflammation)



Other cells

Cell Mediated Immunity (CMI)

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

- Mononuclear cell inflammatory process usually associated with chronic inflammations

Antigen Presenting cells

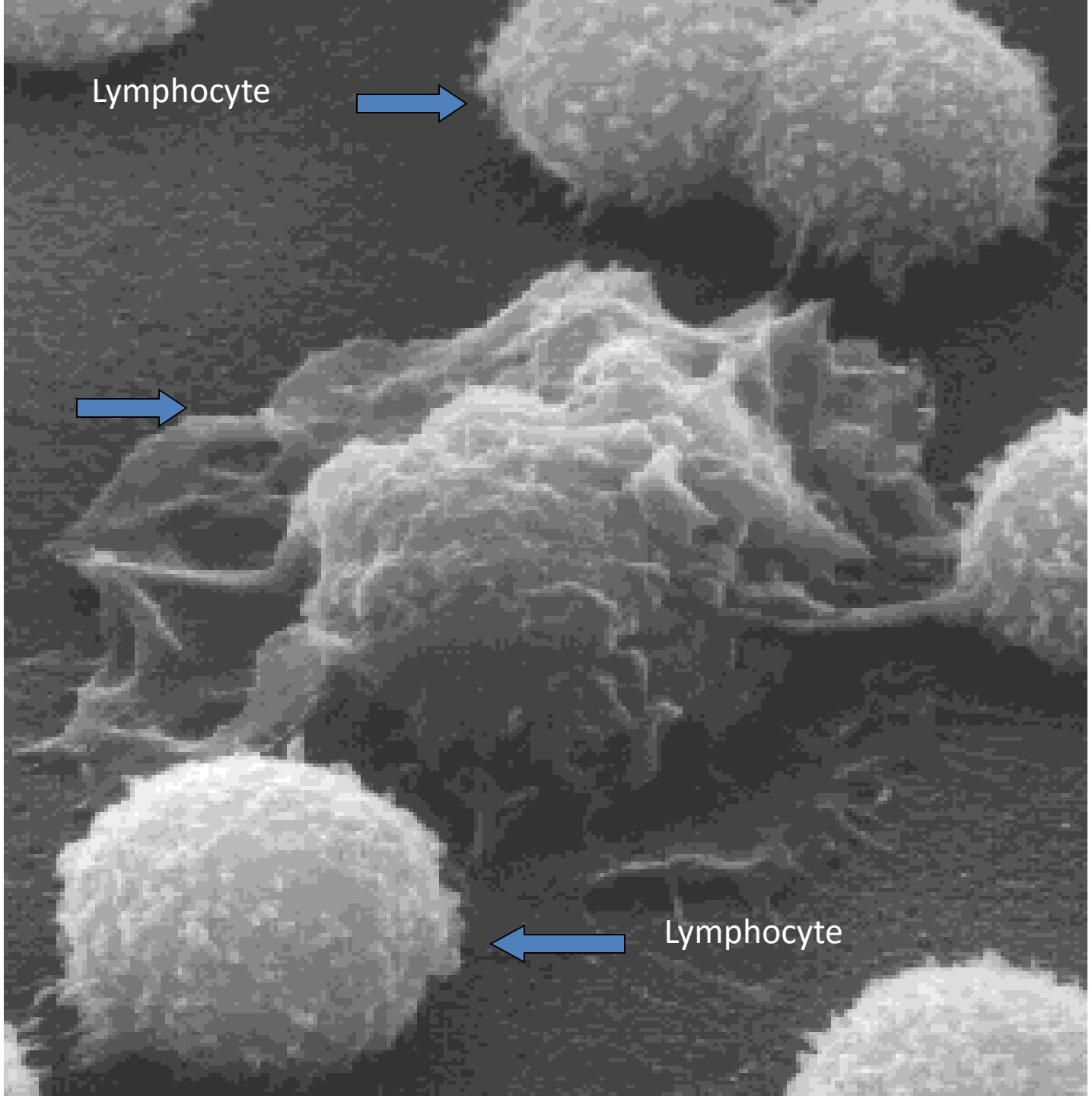
Monocytes : Peripheral blood

Macrophages : Tissues

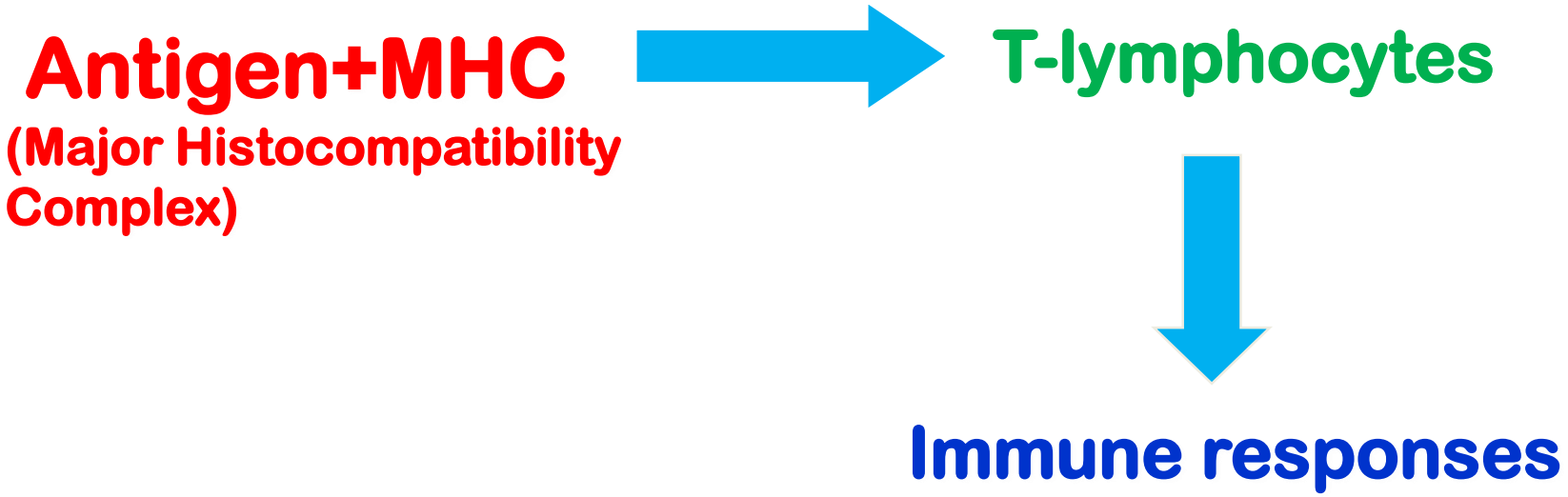
Dendritic cells : Lymphoid tissues

Langerhans cells : Epidermis

B-cells : Lymphoid tissue, Blood


Lymphocyte
Macrophage
Lymphocyte

Cell-Mediated Immunity (CMI)



Major Histocompatibility Complex (MHC)

- Major histocompatibility complex (MHC) proteins were discovered for the first time when tissue transplantation started

- The success of tissue and organ transplantation depends upon the match of donor's and recipient's "***human leukocyte antigens***" (HLA) encoded by HLA genes

- Genes for HLA proteins are clustered in the MHC complex located on the short arm of chromosome 6

MHC

- Three genes code for Class I MHC molecules
  - HLA-A,
  - HLA-B
  - HLA-C
- HLA-D loci encode for Class II MHC molecules ie,
  - DP
  - DQ
  - DR
- Eeach group of MHC consists of several glycoproteins

MHC

- Each individual has two "***haplotypes***" ie, two sets of these genes one paternal and one maternal
- MHC Class I molecules are found on the surface of virtually all nucleated cells
- MHC Class II molecules are normally present of the surface of antigen presenting cells such as:
  - Marophages,
  - Dendritic cells
  - Langerhans cells of skin
  - B cells

Biologic Importance of MHC

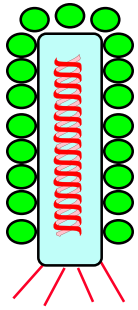
- Antigen recognition
  - T cytotoxic (CD8) cells kill virus infected cells in association with class I MHC proteins
  - T helper (CD4) cells recognize antigen in association with class II MHC proteins

This is called MHC restriction

- Transplantation
  - Success of organ transplant is determined by compatibility of the MHC genes

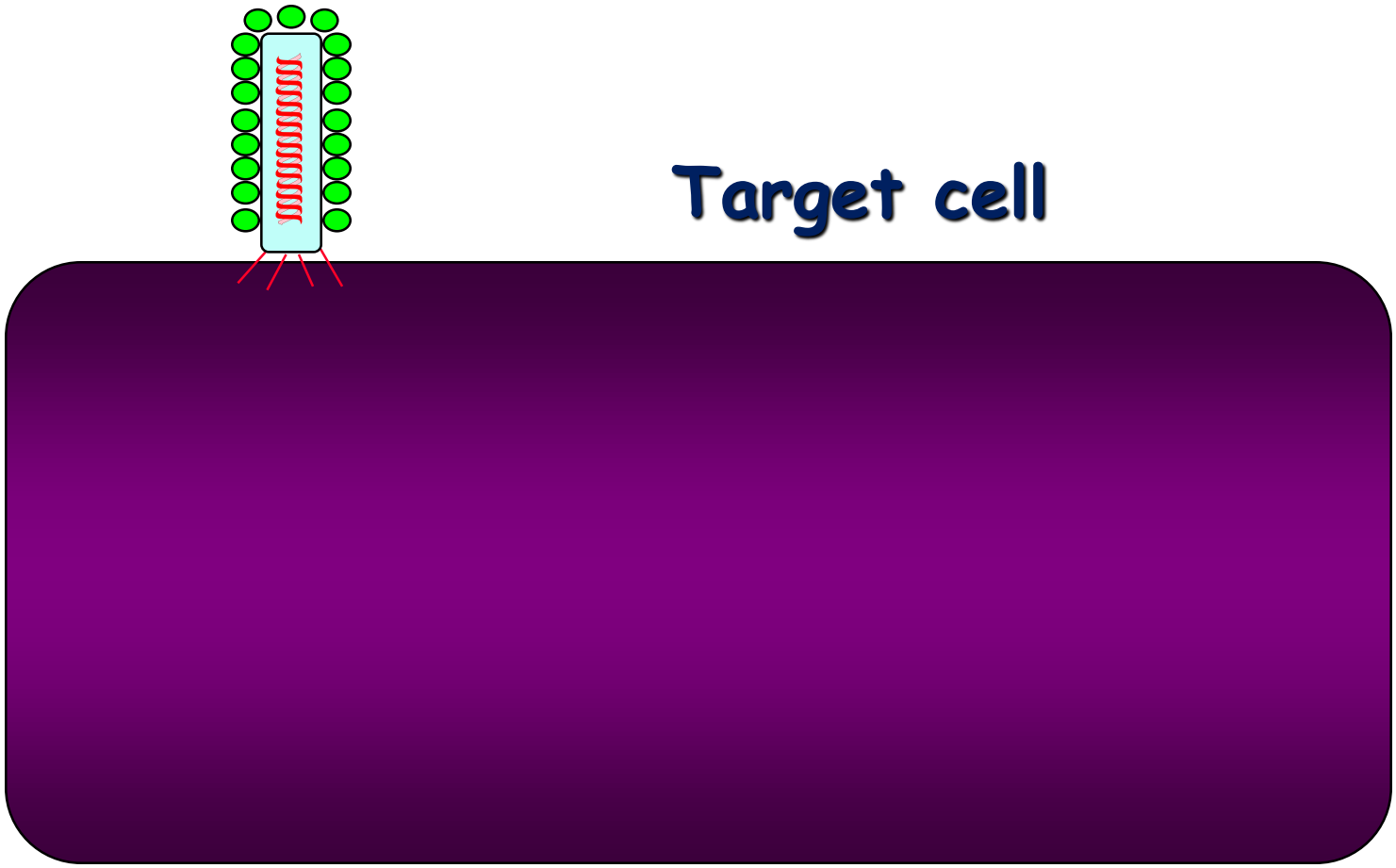
1. Endogenous antigen (Cytoplasm)

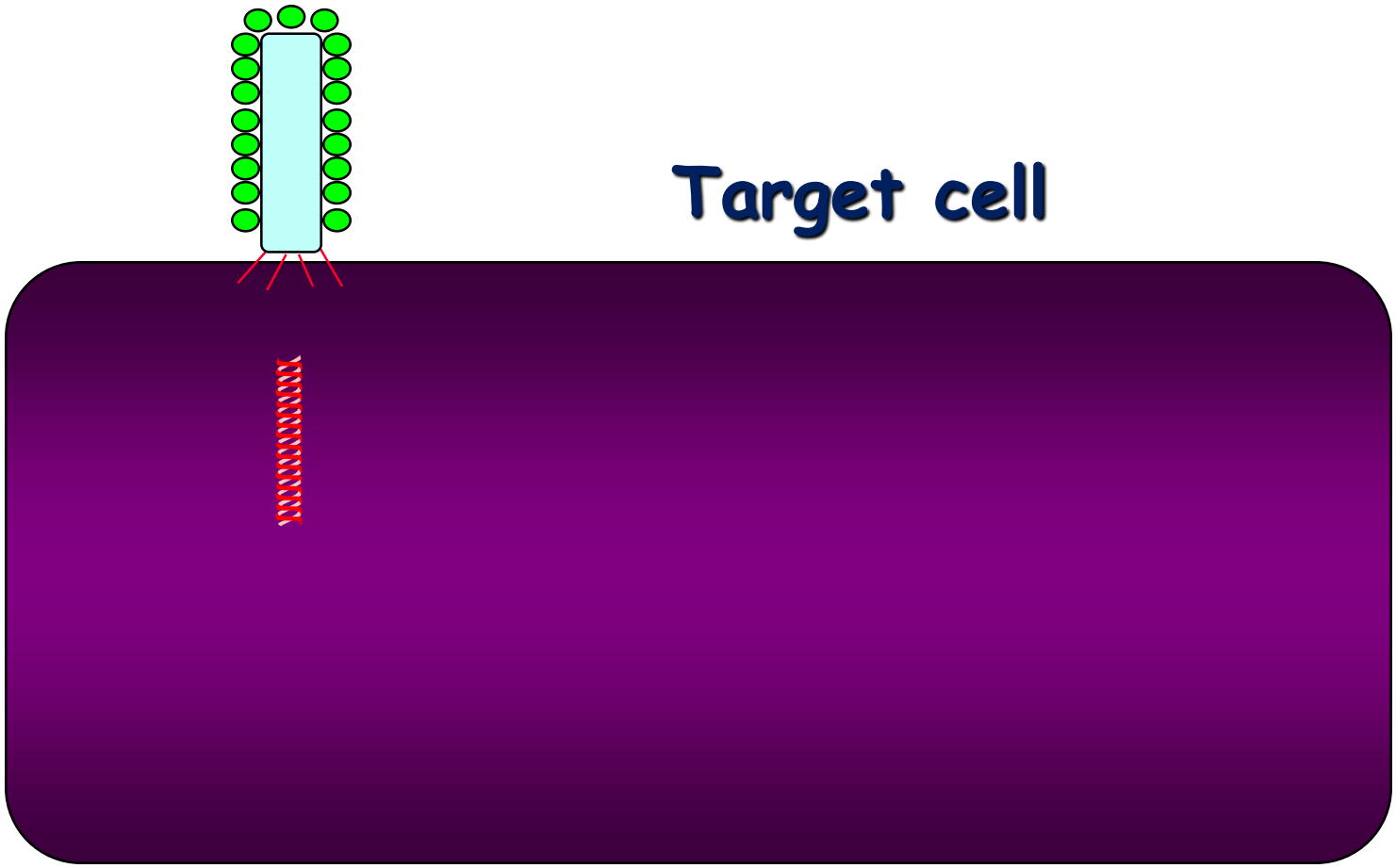
2. Exogenous antigen (Membrane Bound)

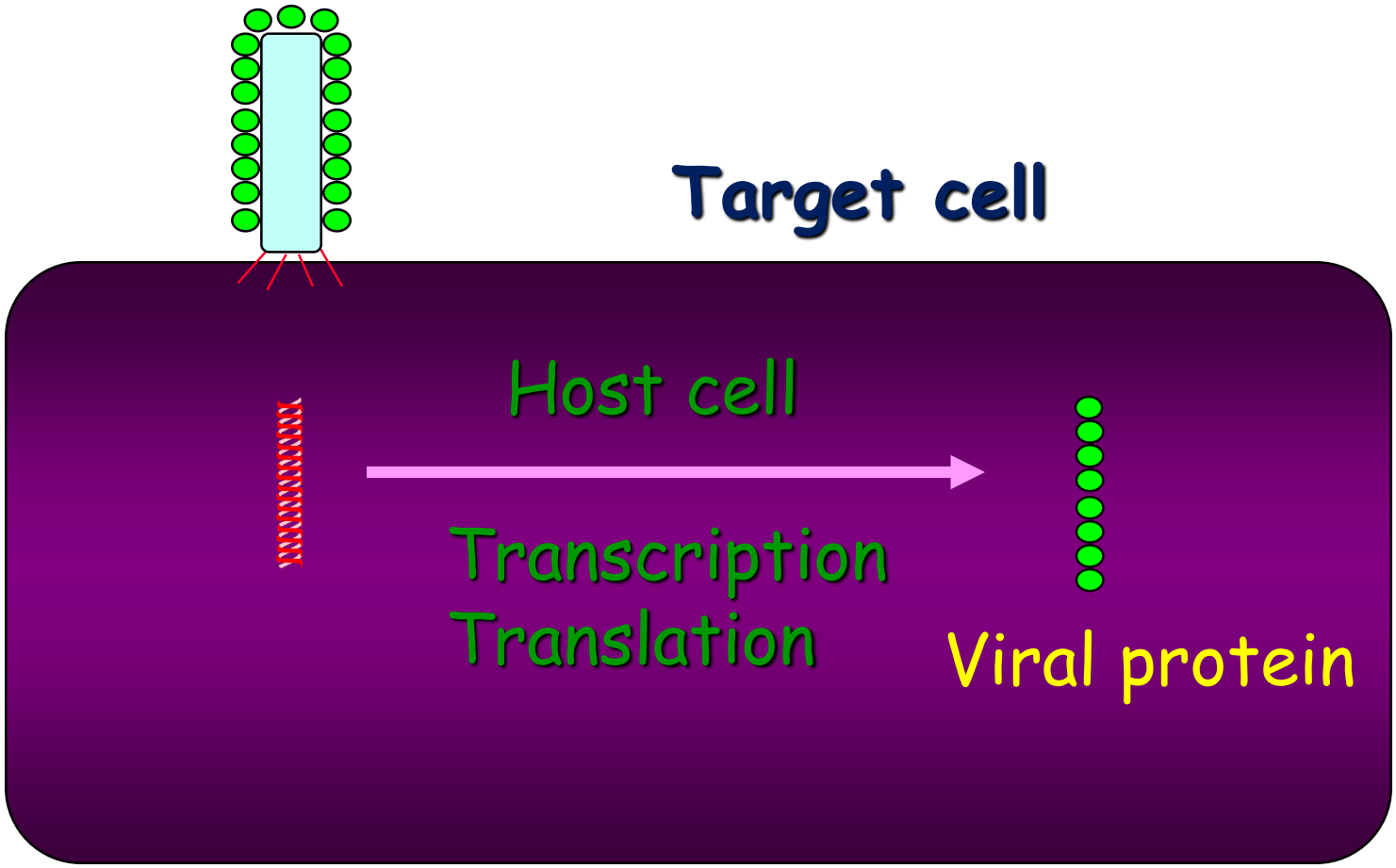


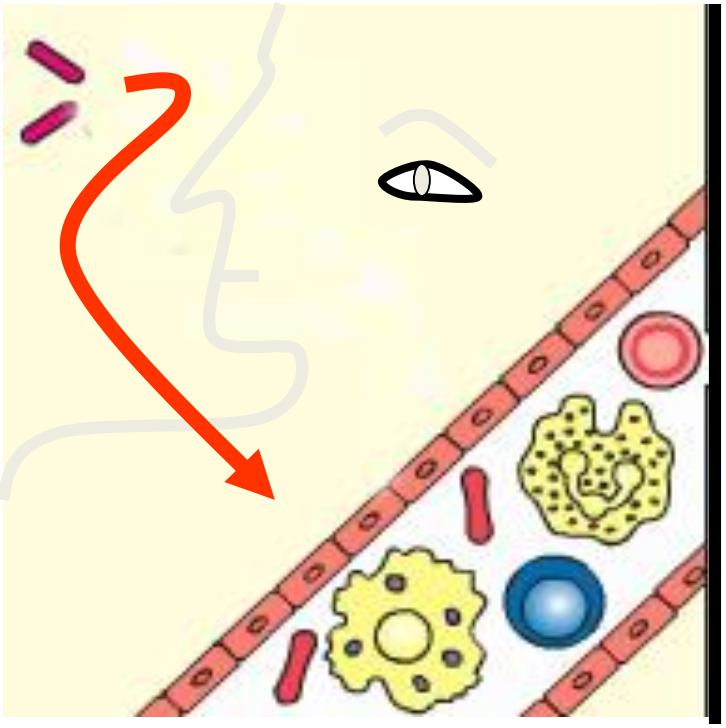
Virus

Target cell


Target cell


Target cell

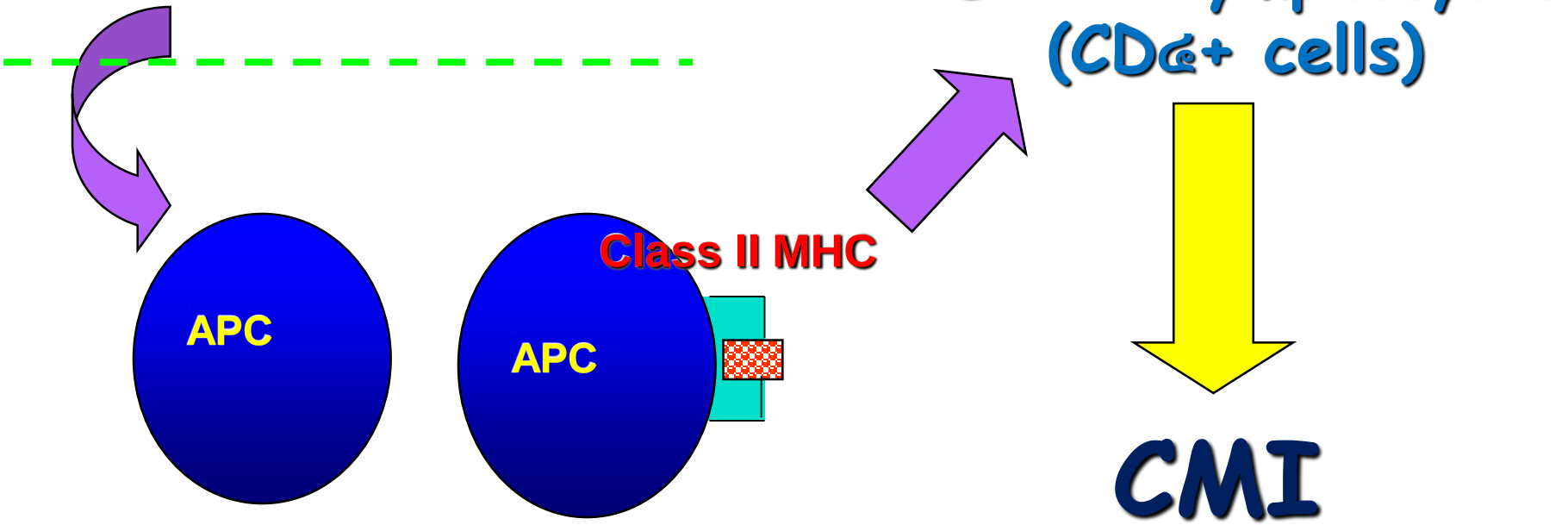

Target cell
Host cell
Transcription
Translation
Viral protein



Exogenous antigen

Cell-mediated immunity

Exogenous antigen



Antigen presenting cells

Monocytes/Macrophages

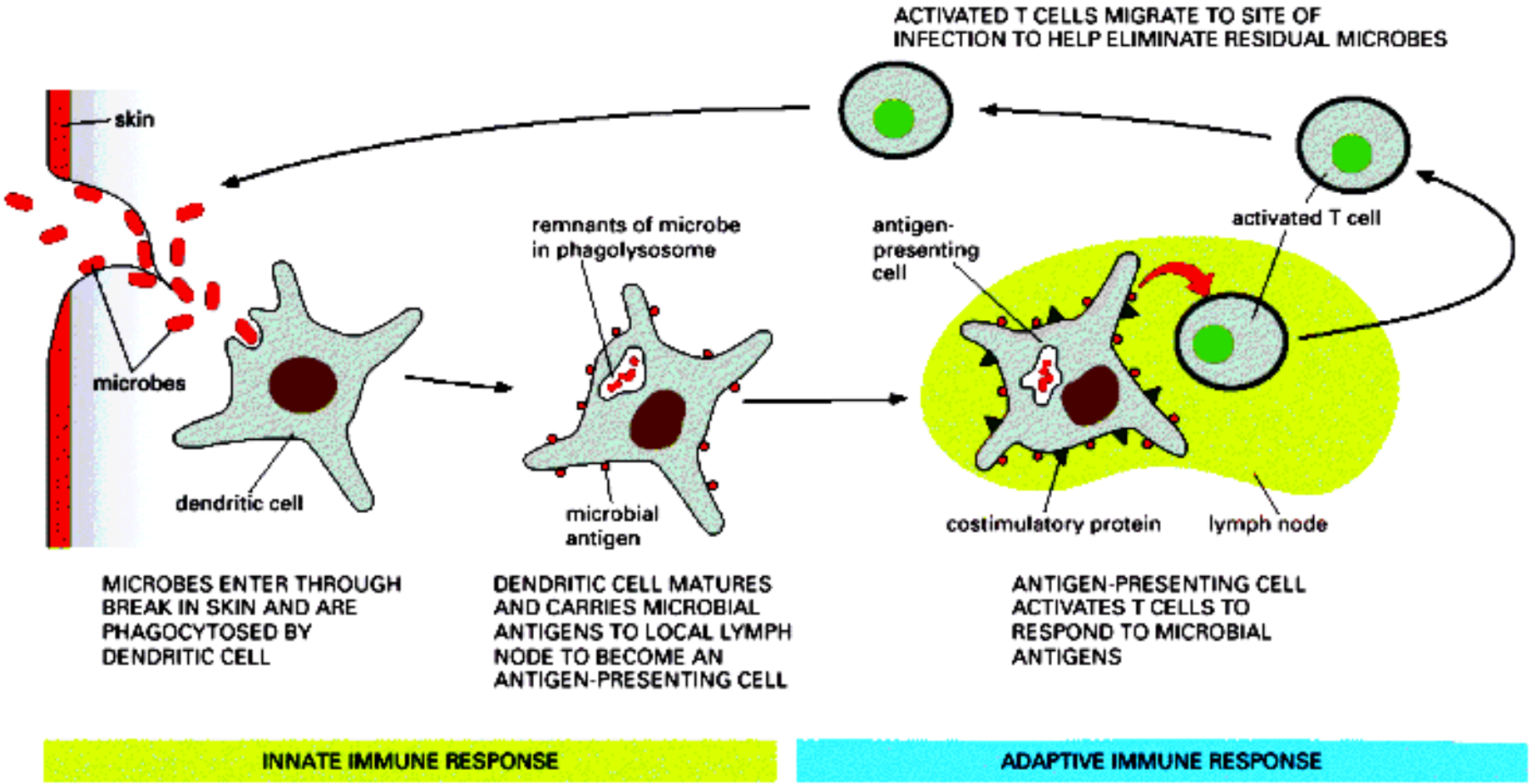
Dendritic cells

Langerhans cells

B-cells

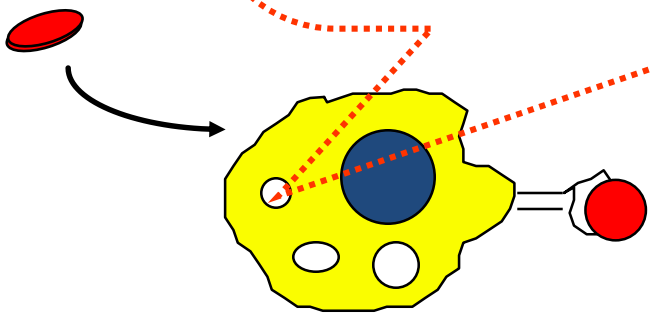
Antigen Presenting Cells

•Dendritic cells and macrophages digest invading microbe and then present the antigen of the microbe to lymphocytes in lymphoid organs.



endogenous

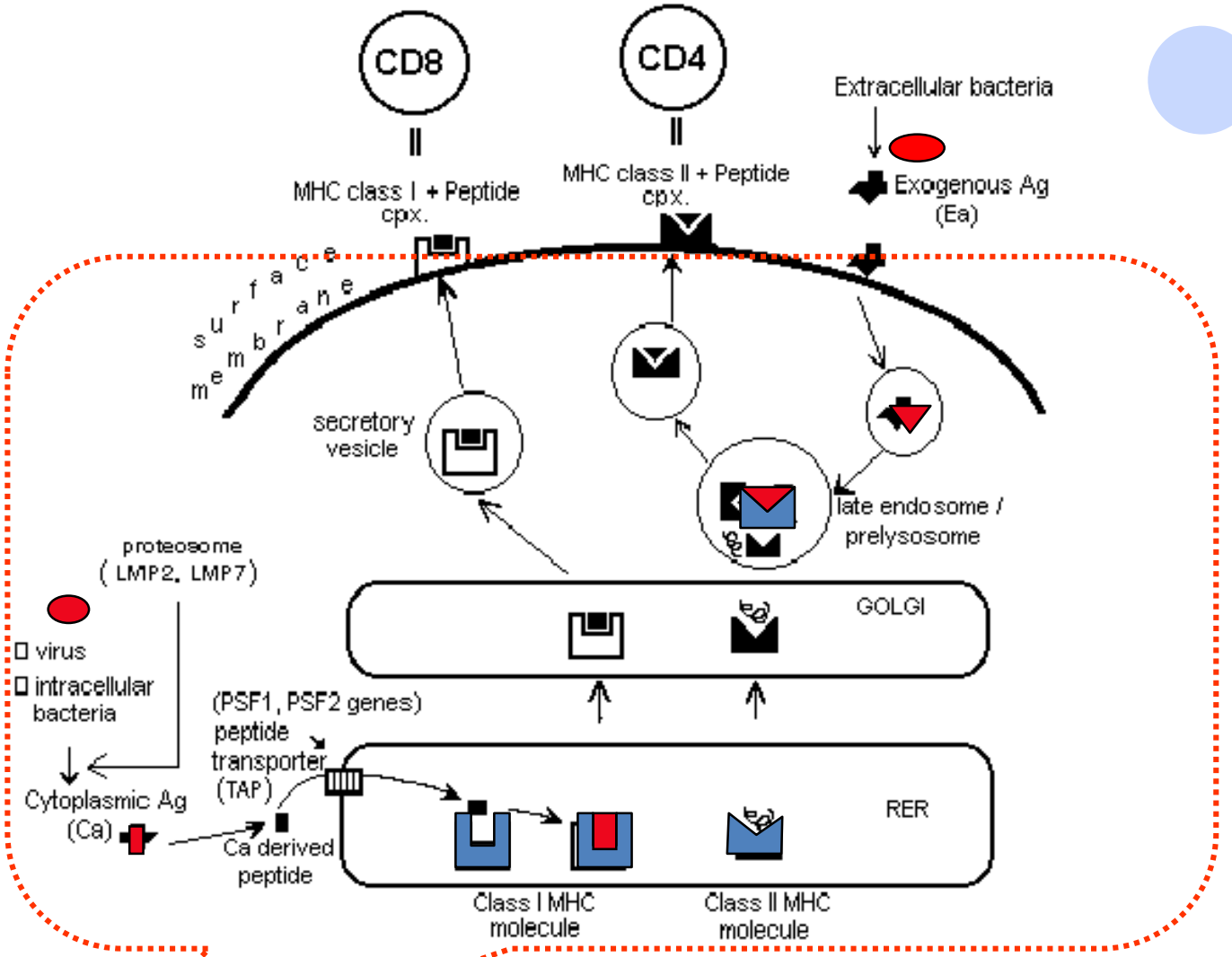
Antigen



exogenous

Antigen processing

Antigen Presenting Cell



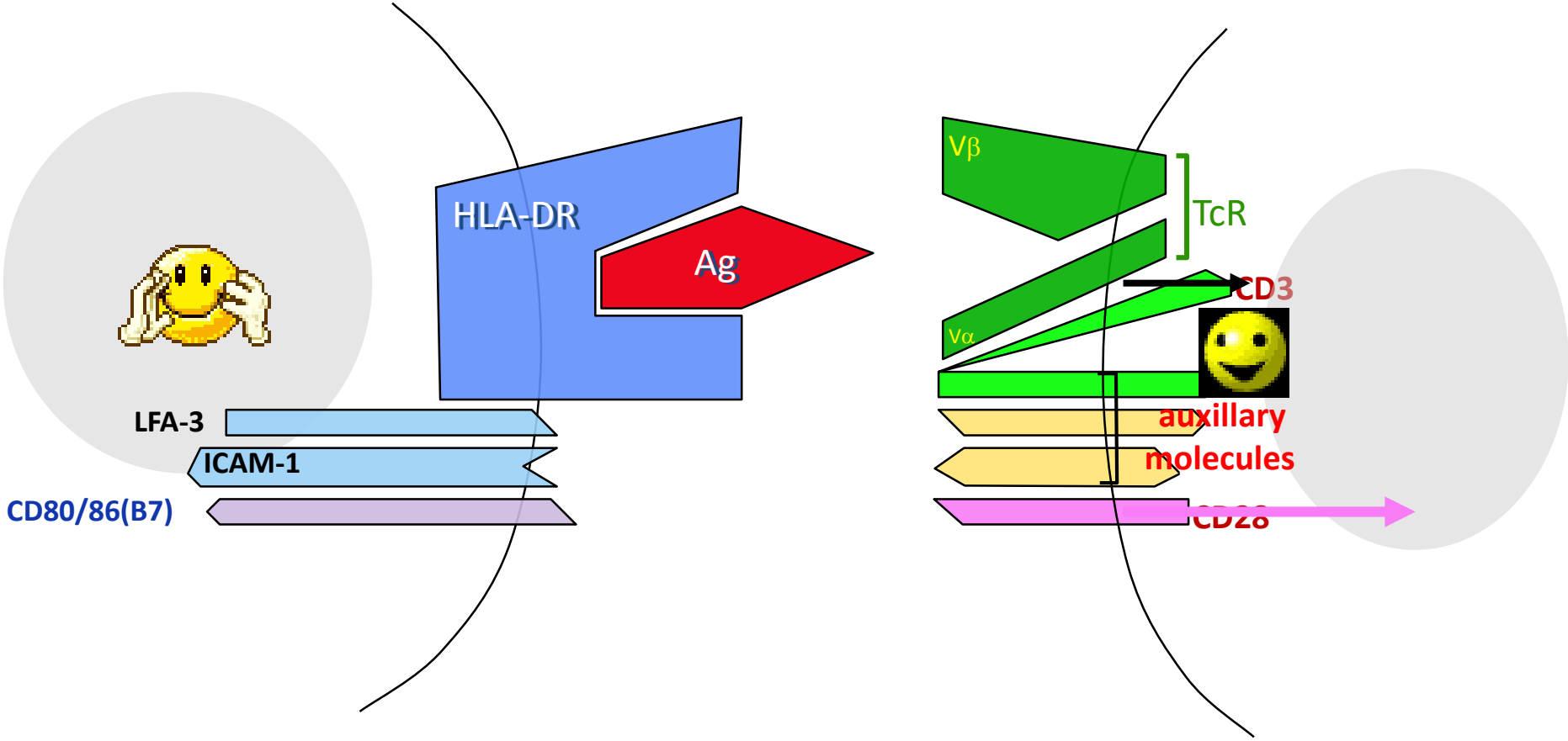
Two signals are required of activation of T cells

- Two signals are required to activate T cells
- First signal

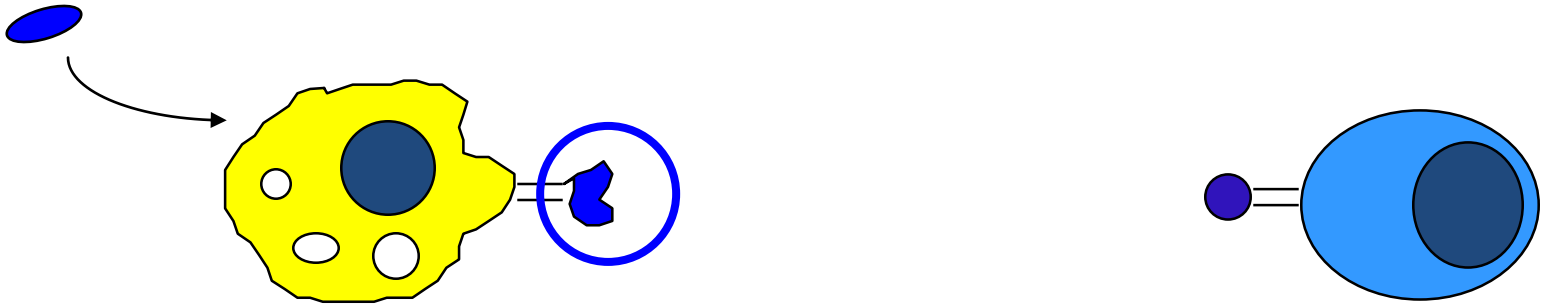
  Class II MHC + antigen – TCR

  IL-1, LFA-1 with ICAM
- Second signal (Costimulatory signal)

  B7 on APC interacts with CD28 on lymphocyte



Trimolecular complex



T lymphocytes ("T cells"): CMI

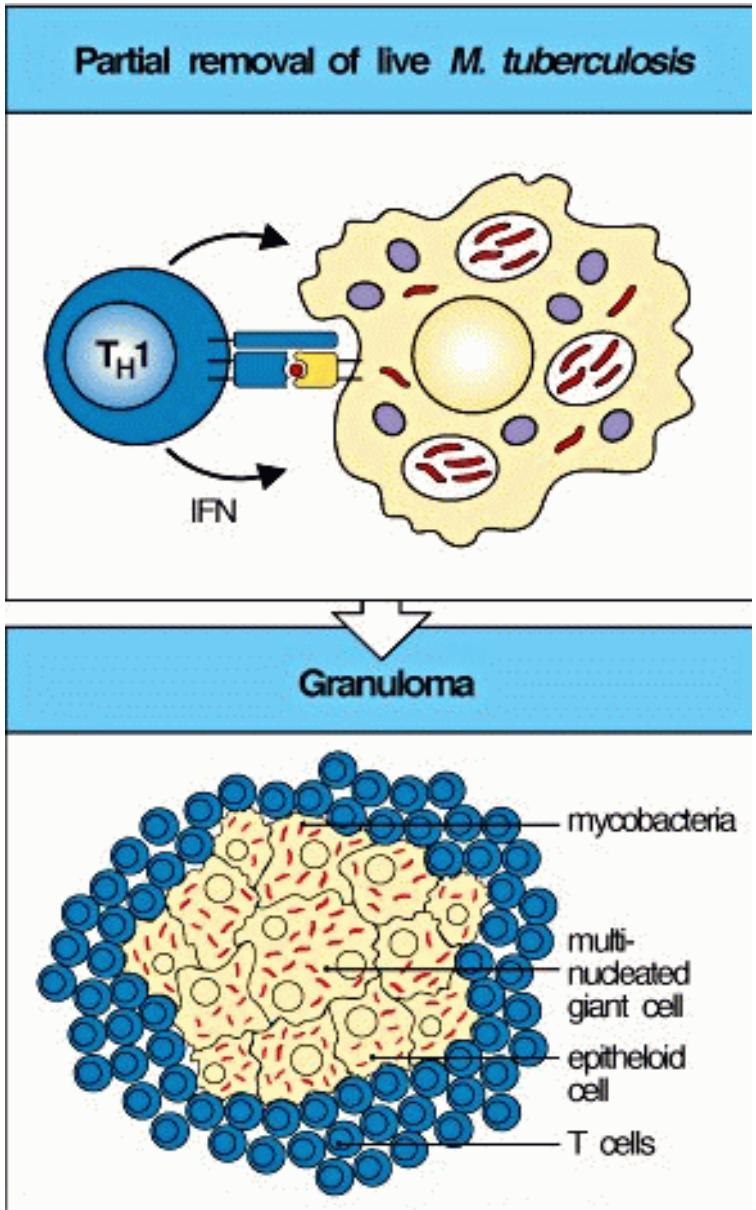
- **Subsets include:**
  - **CD4+ helper T cells** enhance CMI and production of antibodies by B cells
  - **CD8+ cytotoxic T lymphocytes** (CTLs) that kill virus-infected and tumor cells

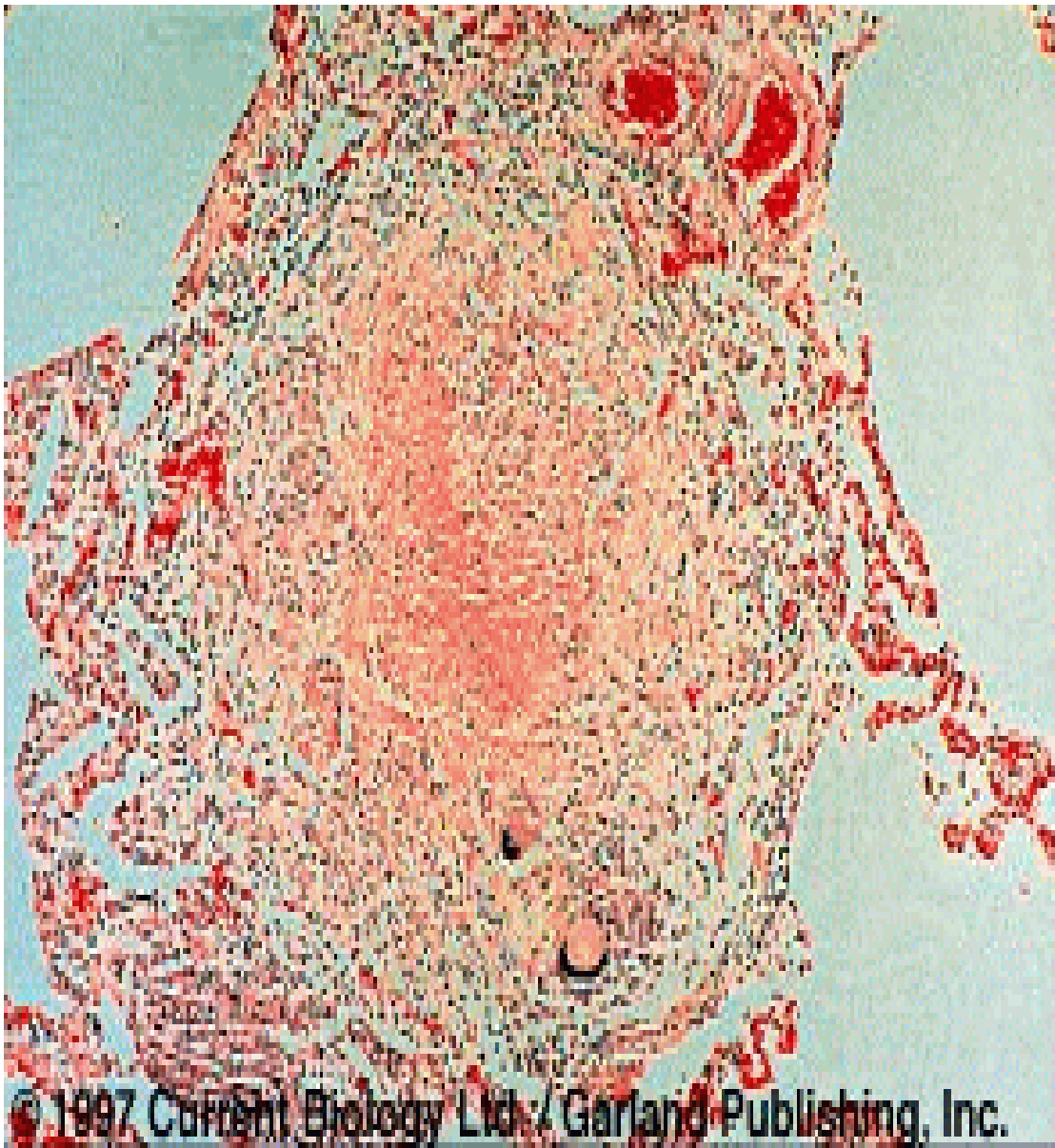
Out come of T helper cell activation

- **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

- **Production of Interferons**
  - Enhances anti-microbial activity of macrophages

Granuloma Formation
(Chronic Inflammation, e.g., TB)

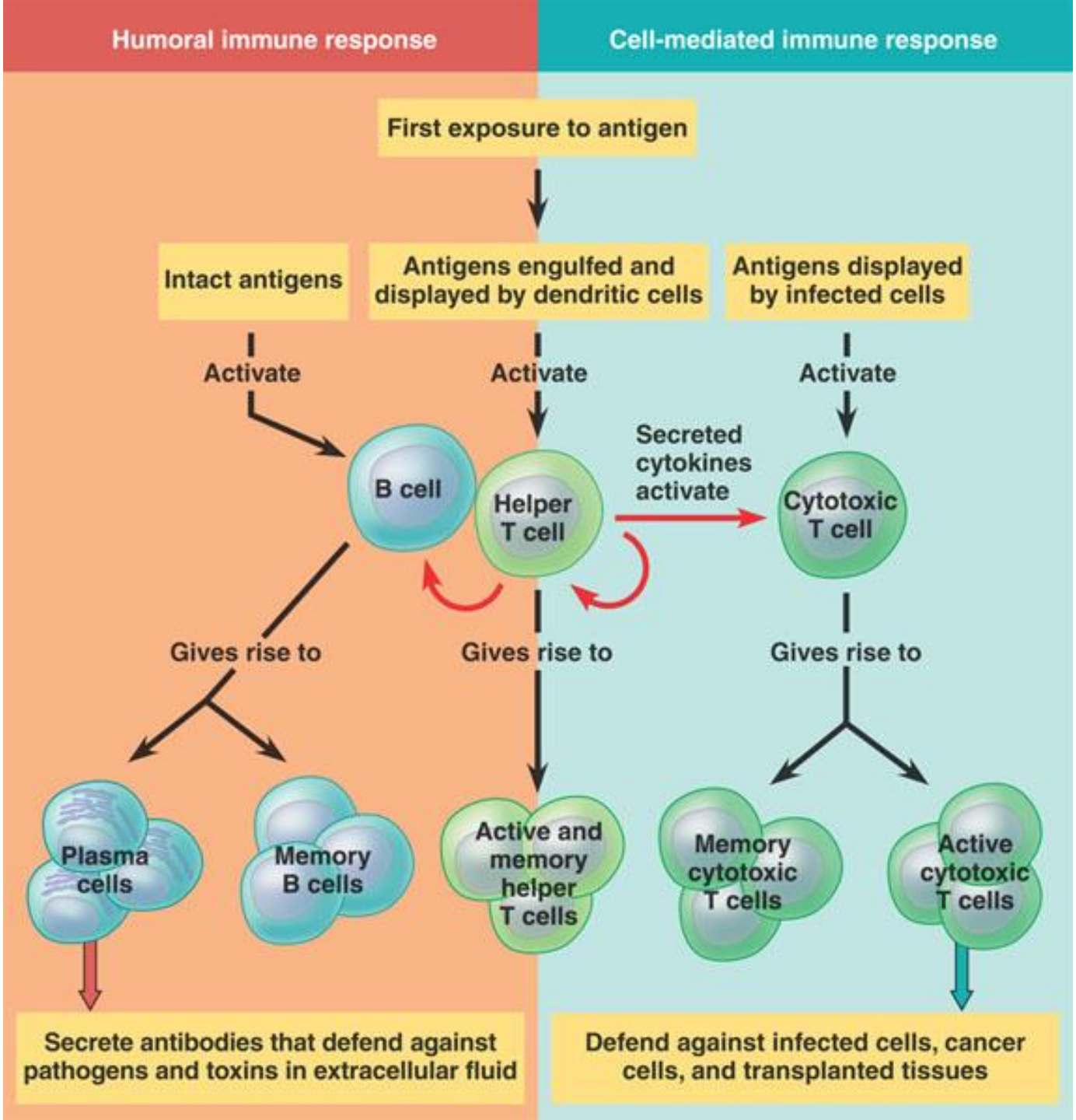




Out come of T helper cell activation

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


Humoral immune response
Cell-mediated immune response
First exposure to antigen
Intact antigens
Antigens engulfed and displayed by dendritic cells
Antigens displayed by infected cells
Activate
Activate
Activate
B cell
Helper T cell
Secreted cytokines activate
Cytotoxic T cell
Gives rise to
Gives rise to
Gives rise to
Plasma cells
Memory B cells
Active and memory helper T cells
Memory cytotoxic T cells
Active cytotoxic T cells
Secrete antibodies that defend against pathogens and toxins in extracellular fluid
Defend against infected cells, cancer cells, and transplanted tissues

- **Examples of Cell Mediated Immunity**

1. Delayed type of hypersensitivity (DTH) reaction:

   the tuberculin test

   – Mediated by CD4+ T cells and takes about 72 hours to develop

2. Contact hpersensitivity

   – Many people develop rashes on their skin following contact with certain chemicals such as nickel, certain dyes, and poison ivy plant

   – The response takes some 24 hours to occur and like DTH, is triggered by CD4+ T cells

Contact Dermatitis

Necklace Rash

Take Home Message

- Cell mediated adaptive immune response is specific and develops after exposure to a pathogen (antigen)
- Initial antigen exposure results in generation of memory cells for a stronger and a quicker response against future exposures to the same pathogen
- It is usually associated with chronic infections
- Antibodies are not involved