

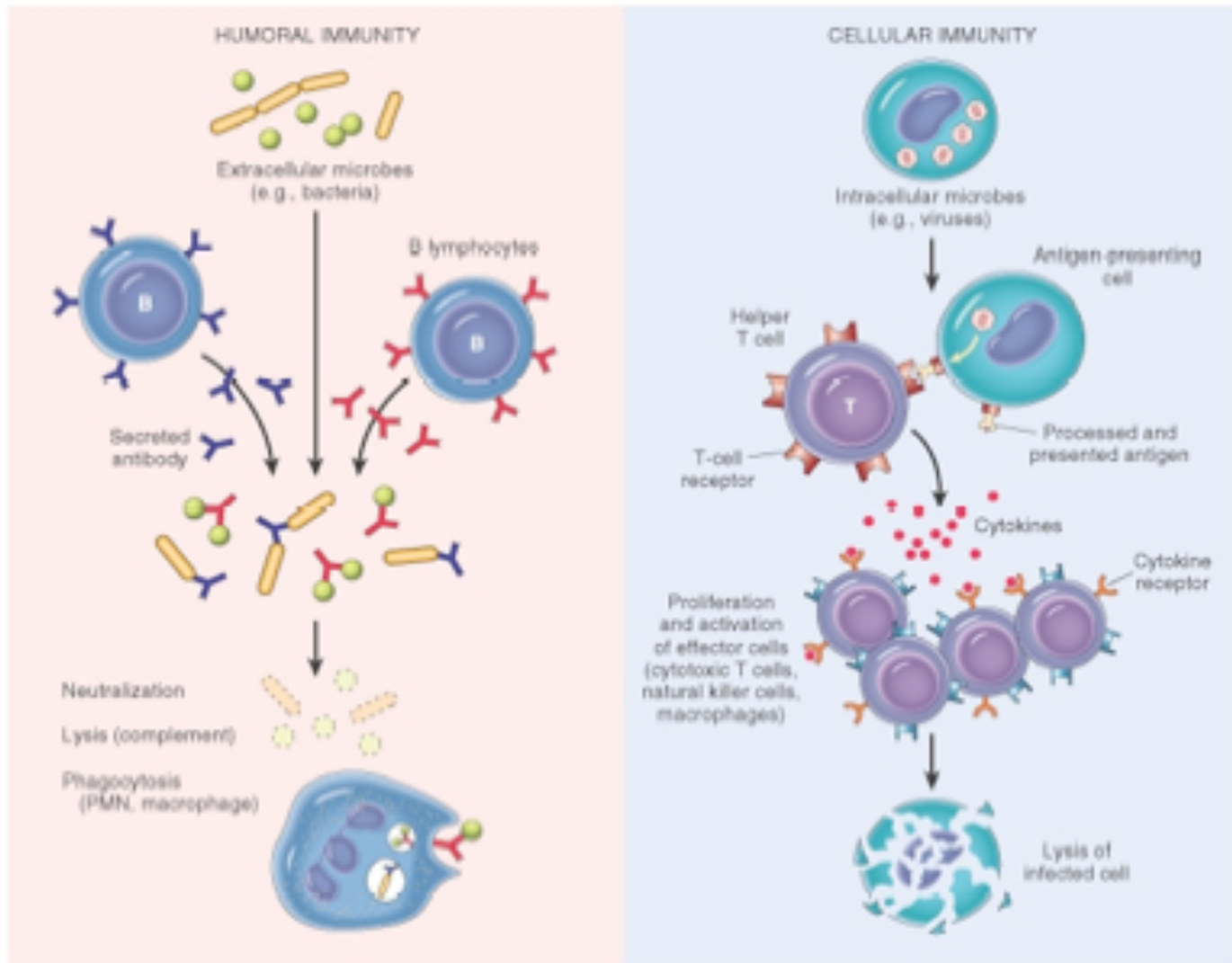
Cell Mediated Immunity

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Reference
Kuby Immunology 8th Edition
Chapter 8
Chapter 11

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 mediated immunity (Chronic Inflammation)



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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

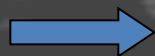
Monocytes : Peripheral blood

Macrophages : Tissues

**Dendritic cells : Lymphoid tissues, skin
(Langerhans cells)**

B-cells : Lymphoid tissue, Blood

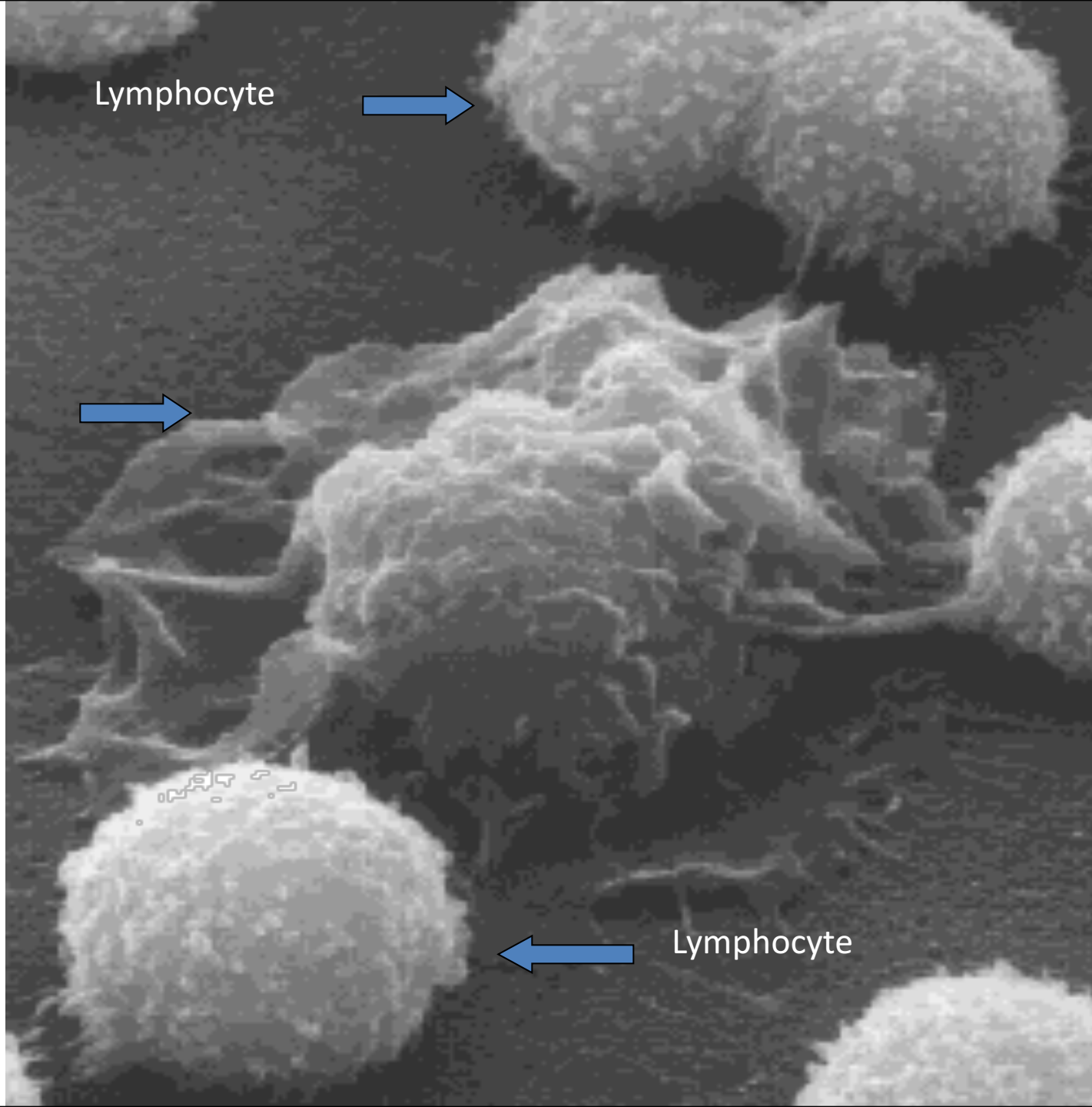
Lymphocyte



Macrophage



Lymphocyte



Cell-Mediated Immunity (CMI)

Antigen+MHC
(Major Histocompatibility
Complex)



T-lymphocytes



Immune responses

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

- 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 on the surface of antigen presenting cells such as:
 - Macrophages,
 - Dendritic cells
 - B cells

Biologic Importance of MHC

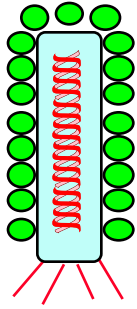
- Antigen recognition
 - T cytotoxic (CD8) cells kill virus infected cells in association with class I MHC proteins
 - T helper (CD4) cells recognize antigen in association with class II MHC proteins

This is called MHC restriction

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

**1. Endogenous antigen
(Cytoplasm)**

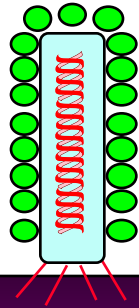
**2. Exogenous antigen
(Membrane Bound)**



Virus

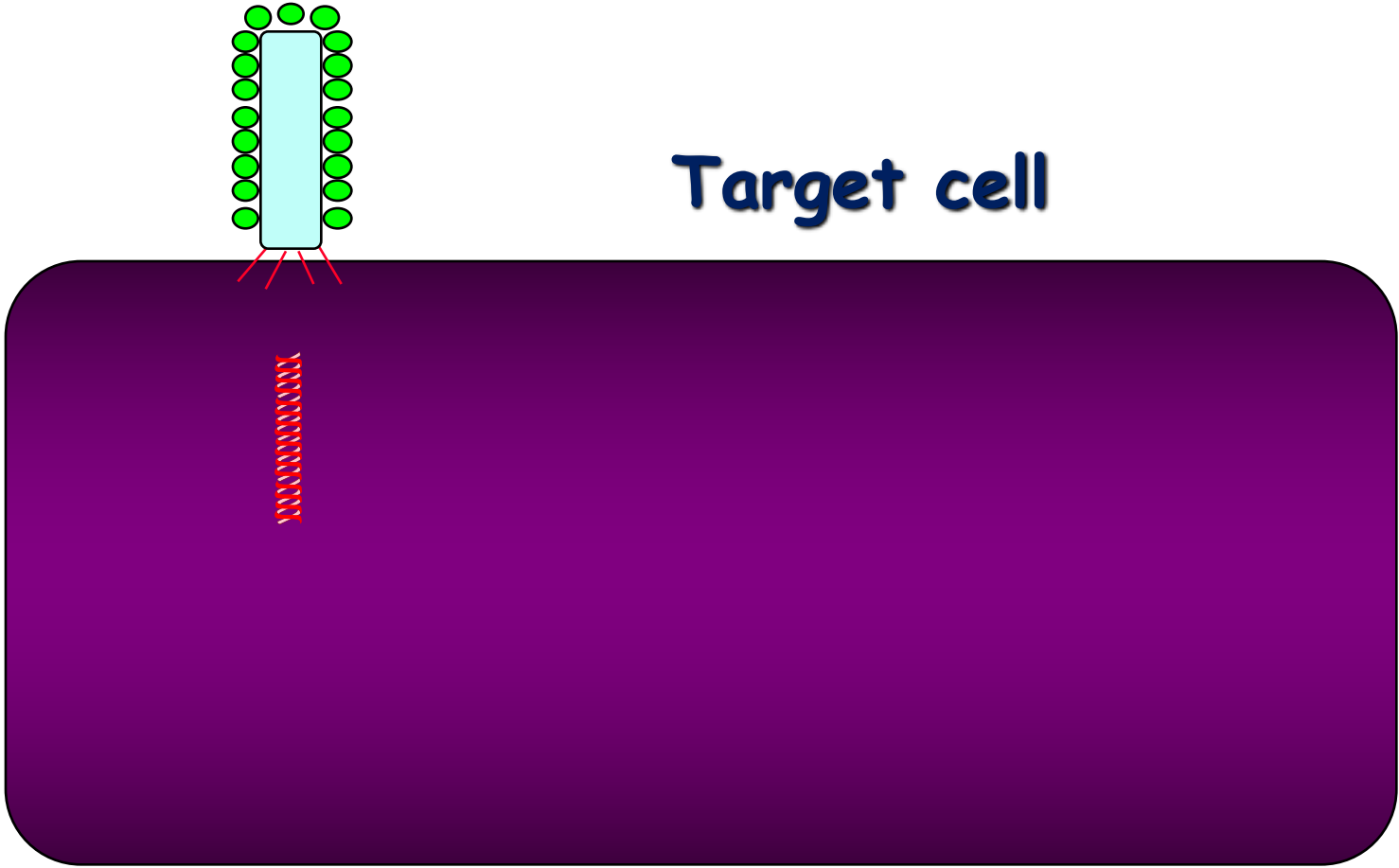
Target cell

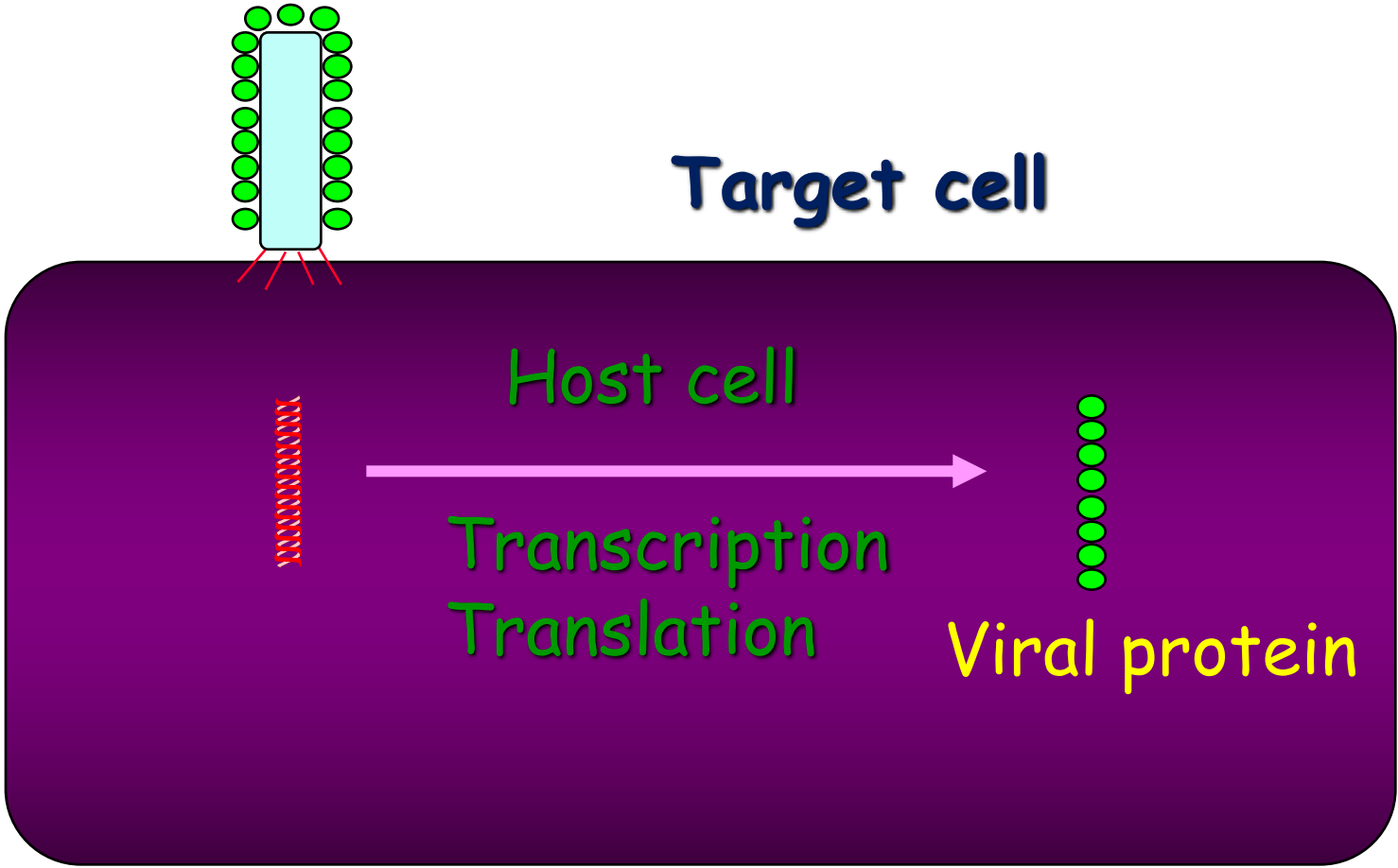


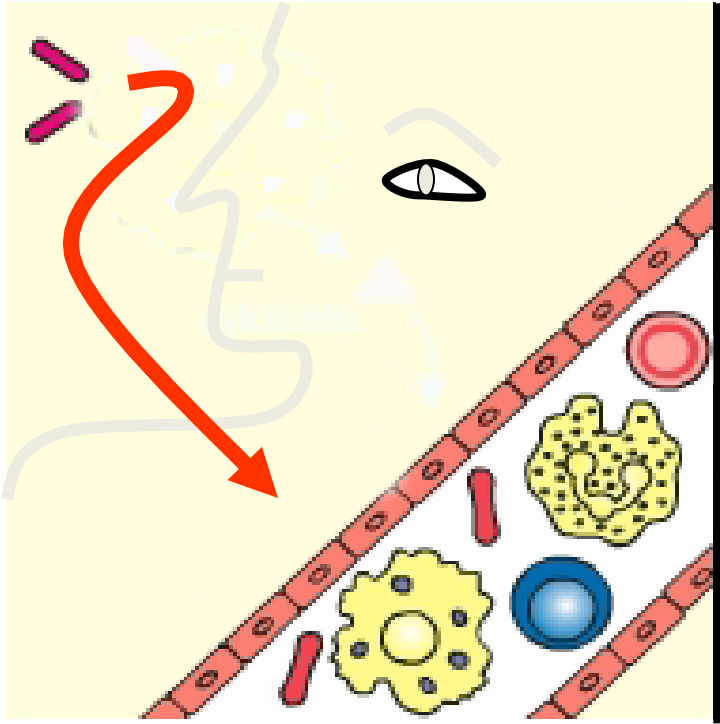


Target cell

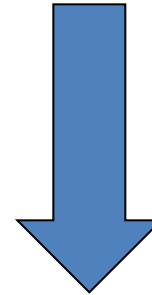
Target cell







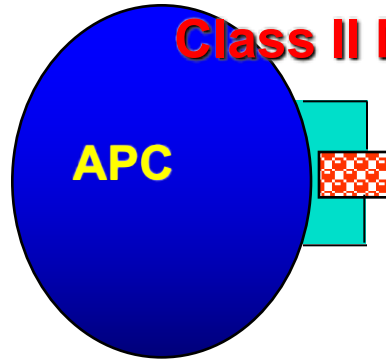
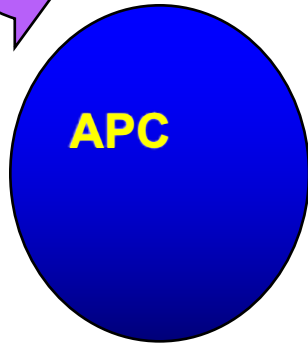
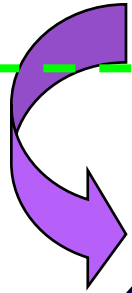
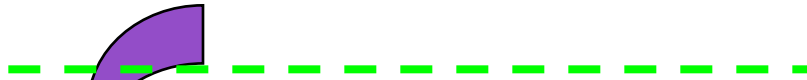
Exogenous antigen



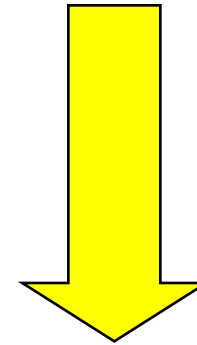
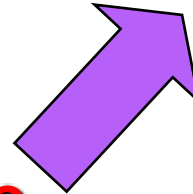
Cell-mediated immunity



Exogenous antigen



**CD4+ T-lymphocytes
(CD4+ cells)**



CMI

(Cell Mediated Immunity)

Antigen presenting cells

Monocytes/Macrophages

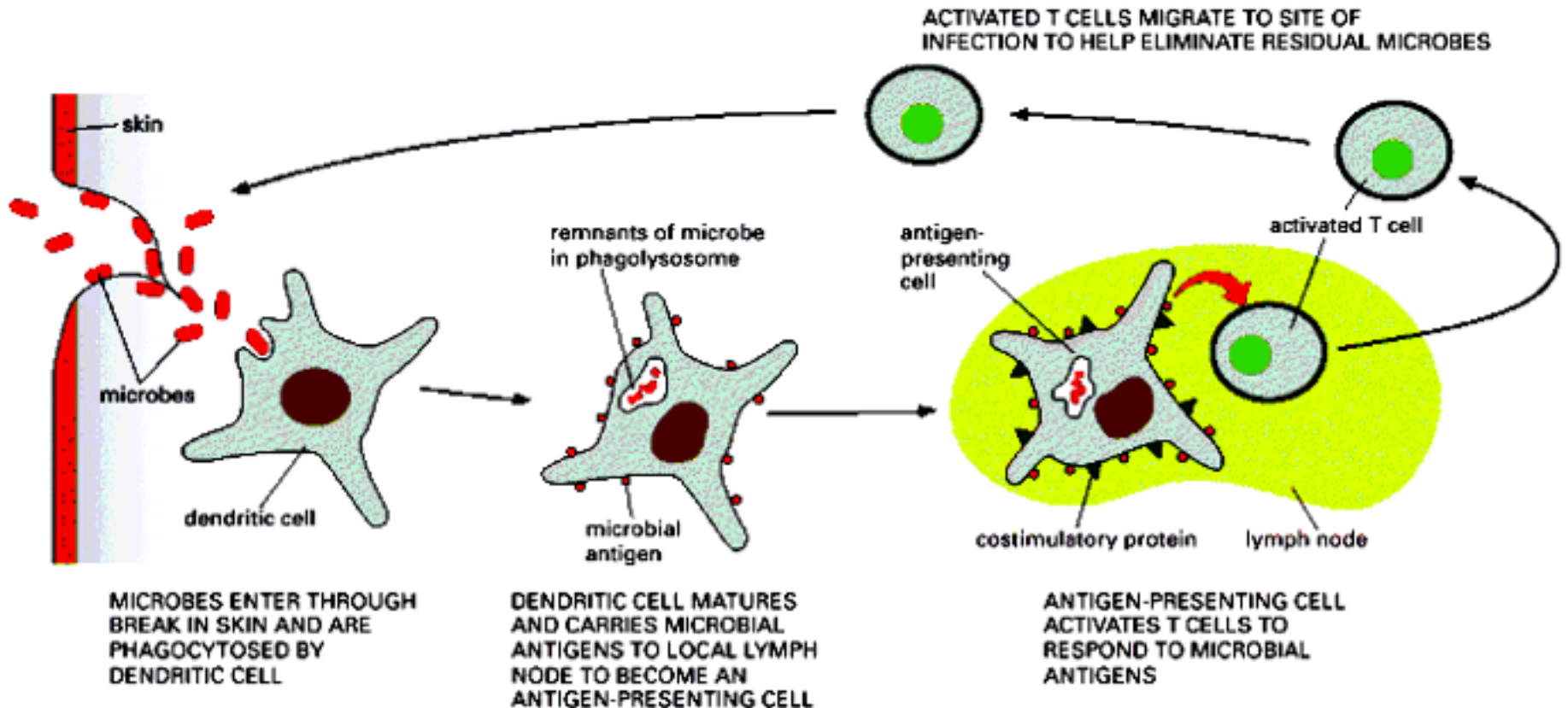
Dendritic cells

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.



MICROBES ENTER THROUGH BREAK IN SKIN AND ARE PHAGOCYTOSED BY DENDRITIC CELL

DENDRITIC CELL MATURES AND CARRIES MICROBIAL ANTIGENS TO LOCAL LYMPH NODE TO BECOME AN ANTIGEN-PRESENTING CELL

ANTIGEN-PRESENTING CELL ACTIVATES T CELLS TO RESPOND TO MICROBIAL ANTIGENS

INNATE IMMUNE RESPONSE

ADAPTIVE IMMUNE RESPONSE



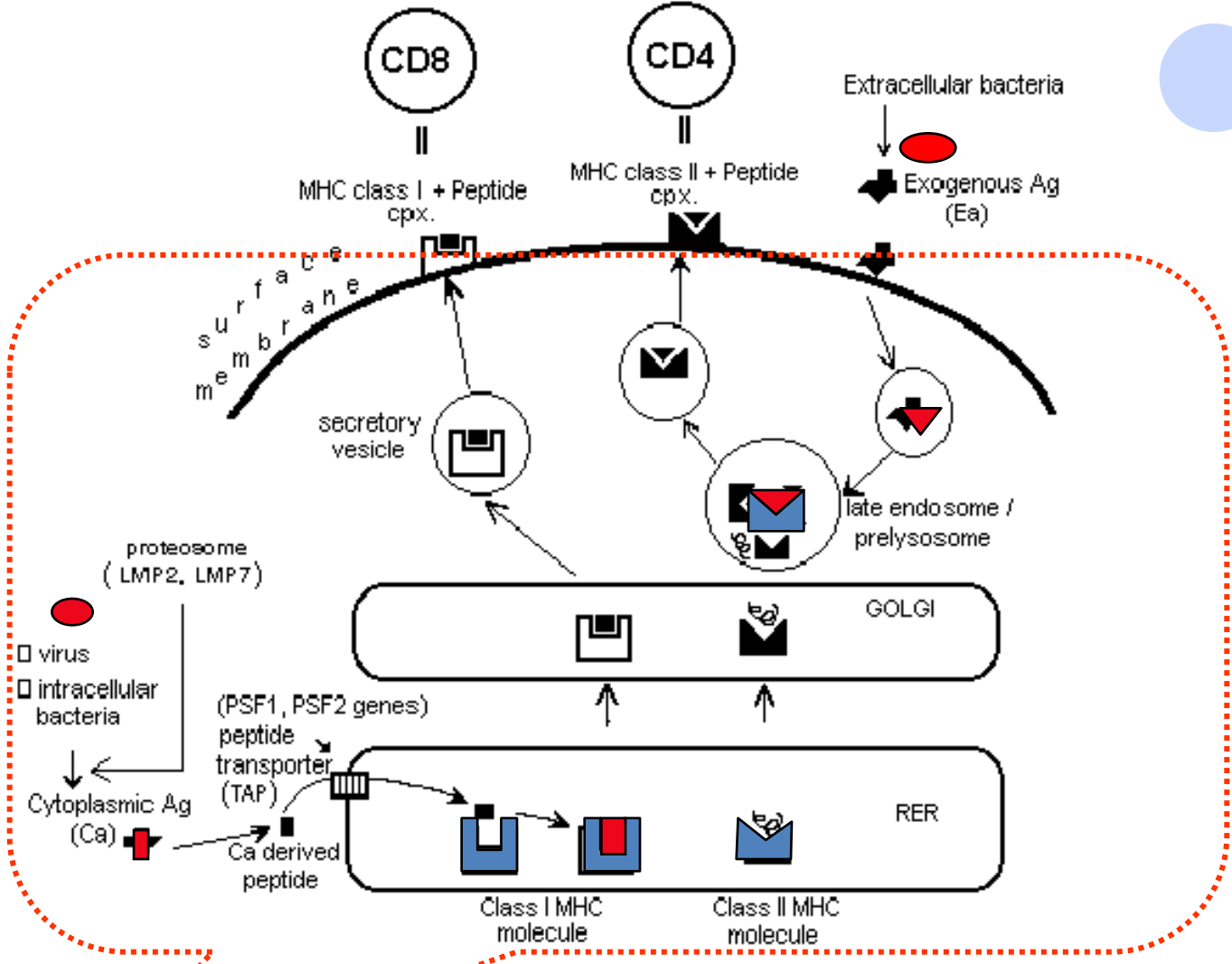
endogenous

Antigen

exogenous

Antigen processing

Antigen Presenting Cell



Two signals are required of activation of T cells

- Two signals are required to activate T cells

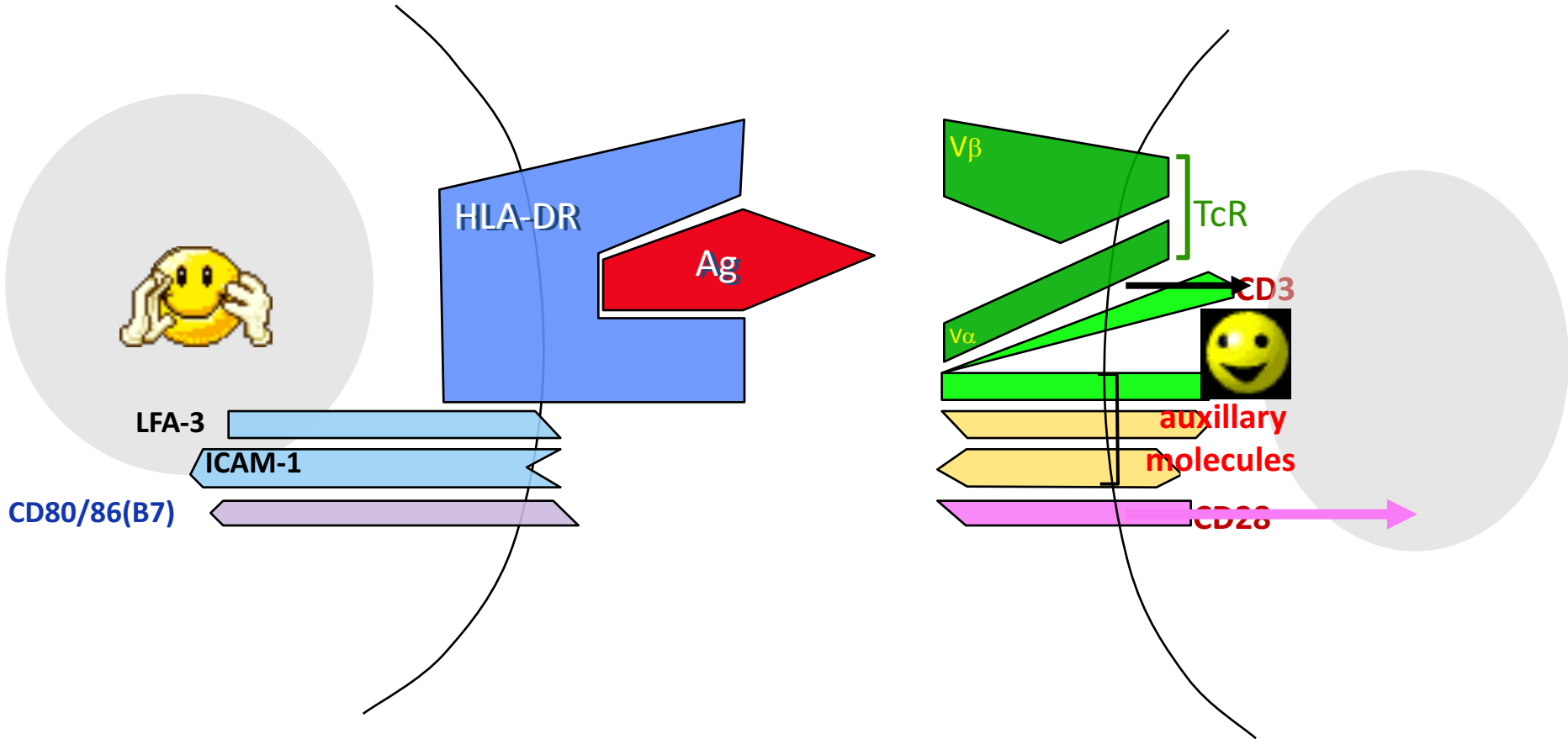
- First signal

Class II MHC + antigen – TCR

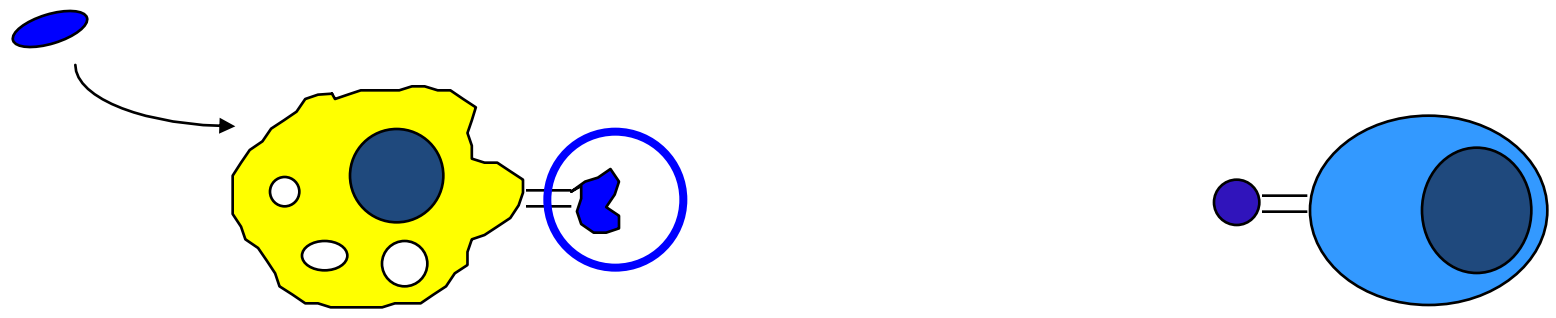
IL-1, LFA-1 with ICAM

- 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

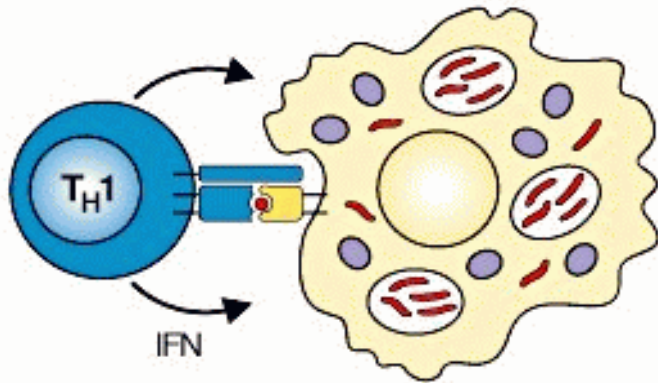
NKT cells, and NK cells can also eliminate infected cells and abnormal tumor cells

Out come of T helper cell activation

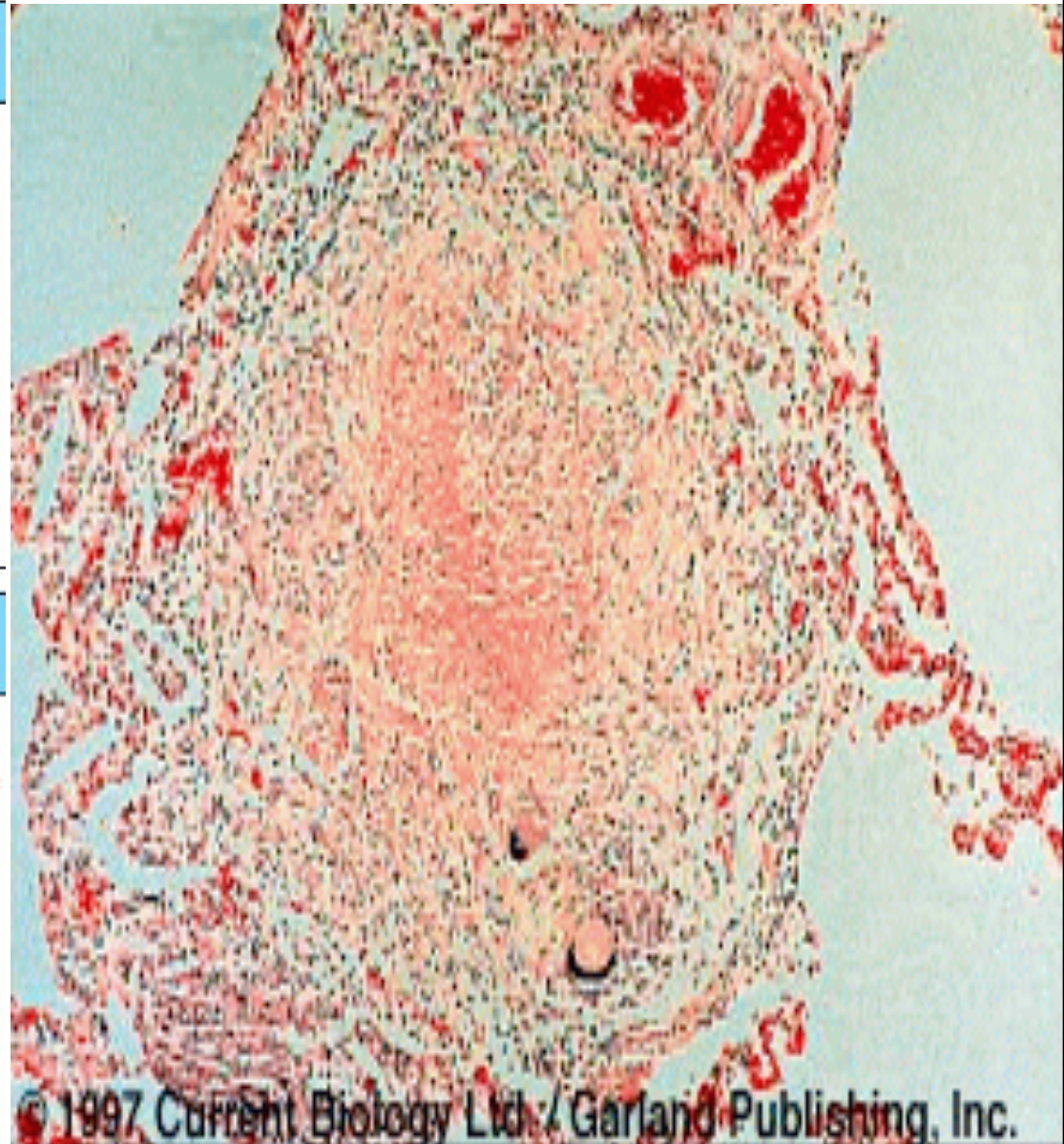
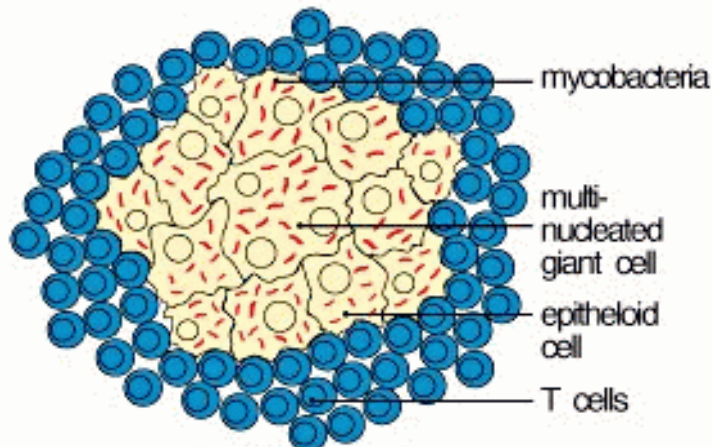
- **Production of IL-2 and its receptor**
 - IL-2 is also know as T cell growth factor
 - Proliferation of antigen specific T cells
 - Effector and regulatory cells are produced along with *“memory”* cells
 - IL-2 also stimulates CD8 cytotoxic cells
- **Production of Interferons**
 - Enhances anti-microbial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

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

Partial removal of live *M. tuberculosis*



Granuloma



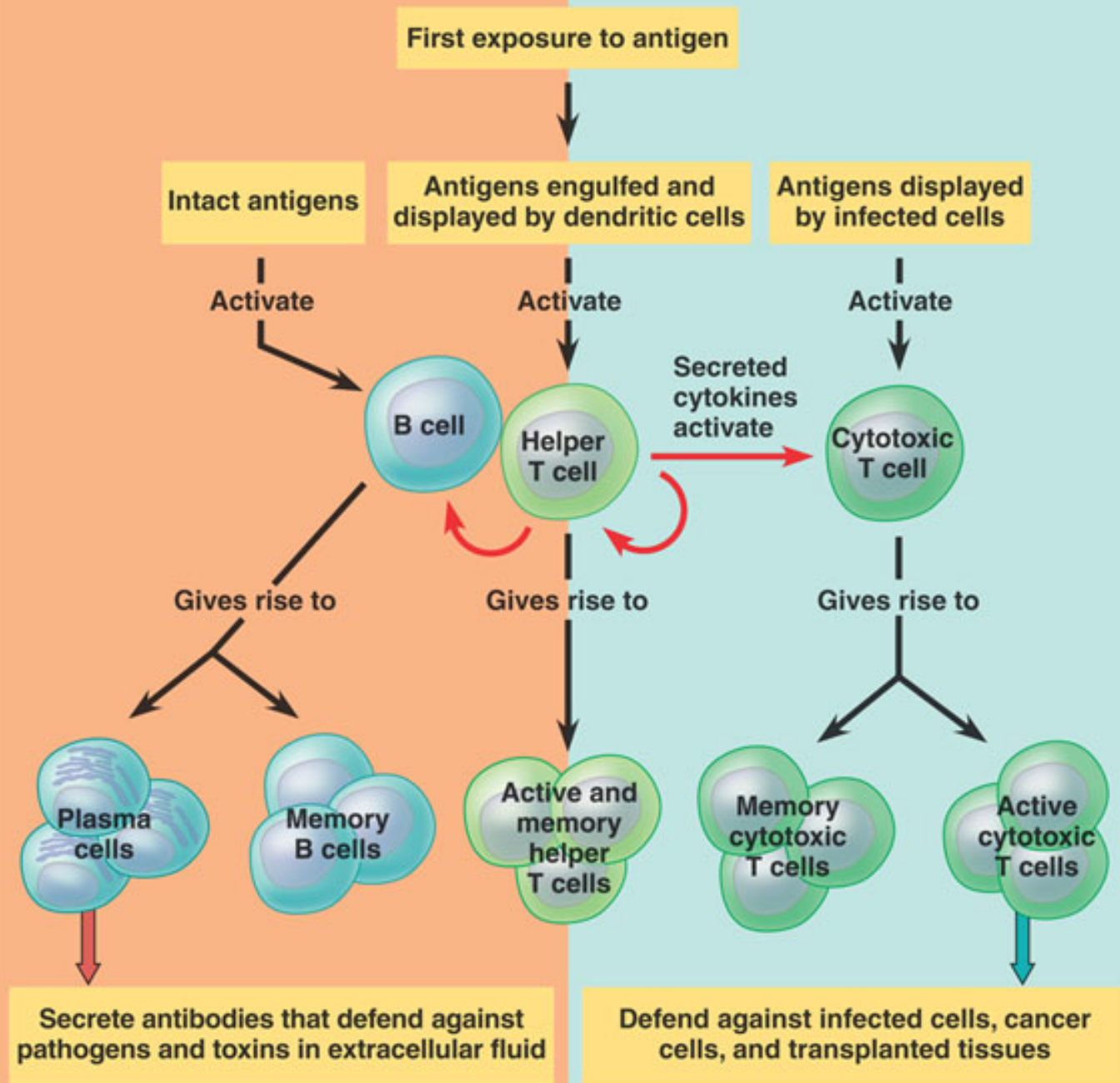
Out come of T helper cell activation

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



- **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 hypersensitivity

- 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

Necklace Rash



Contact Dermatitis



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