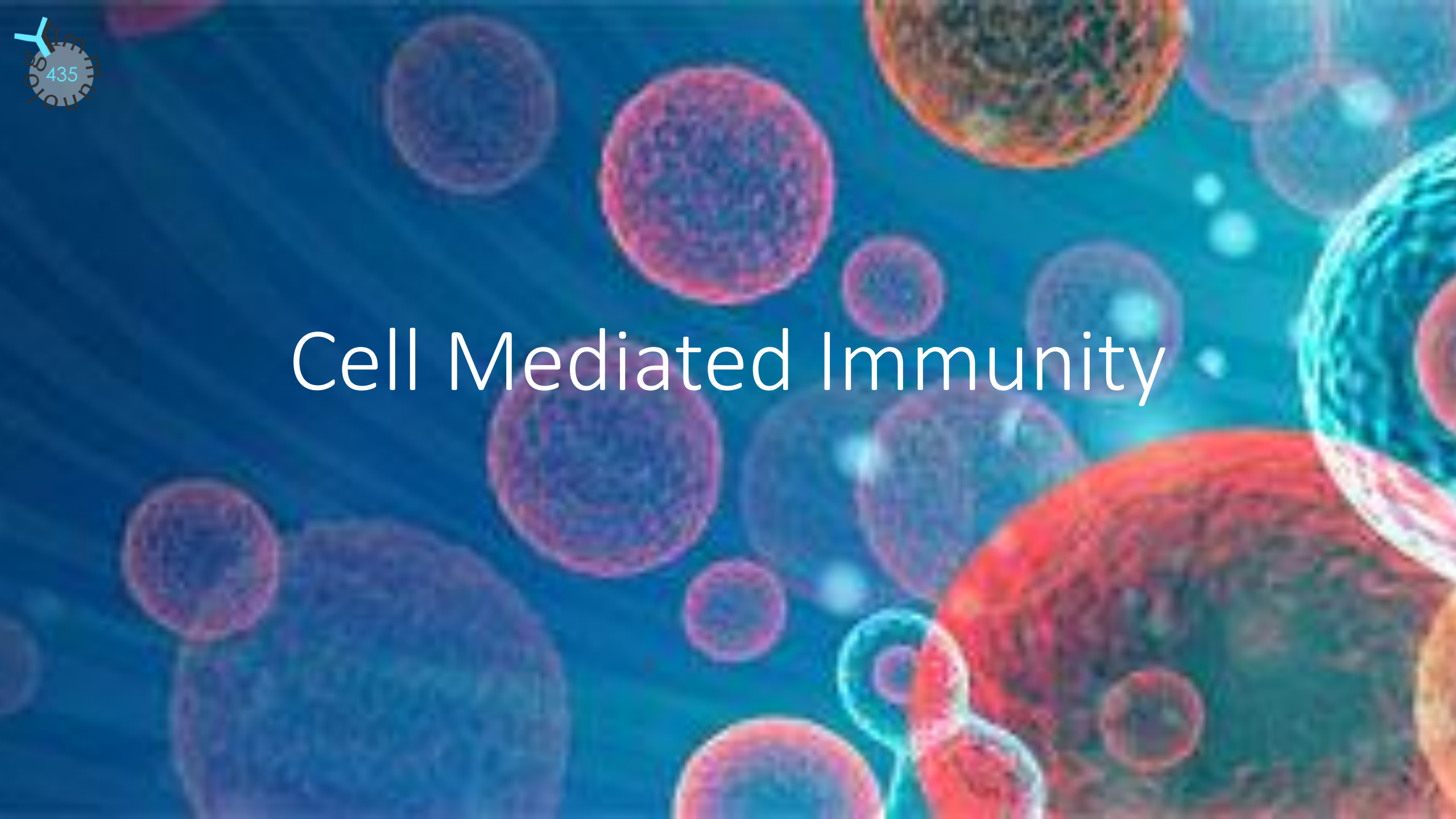
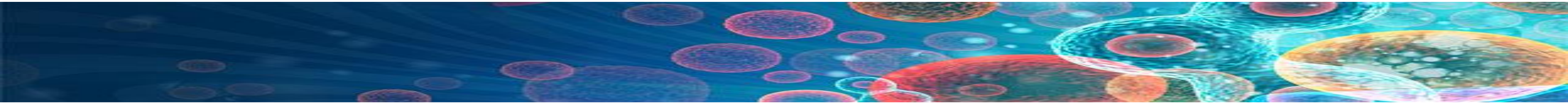


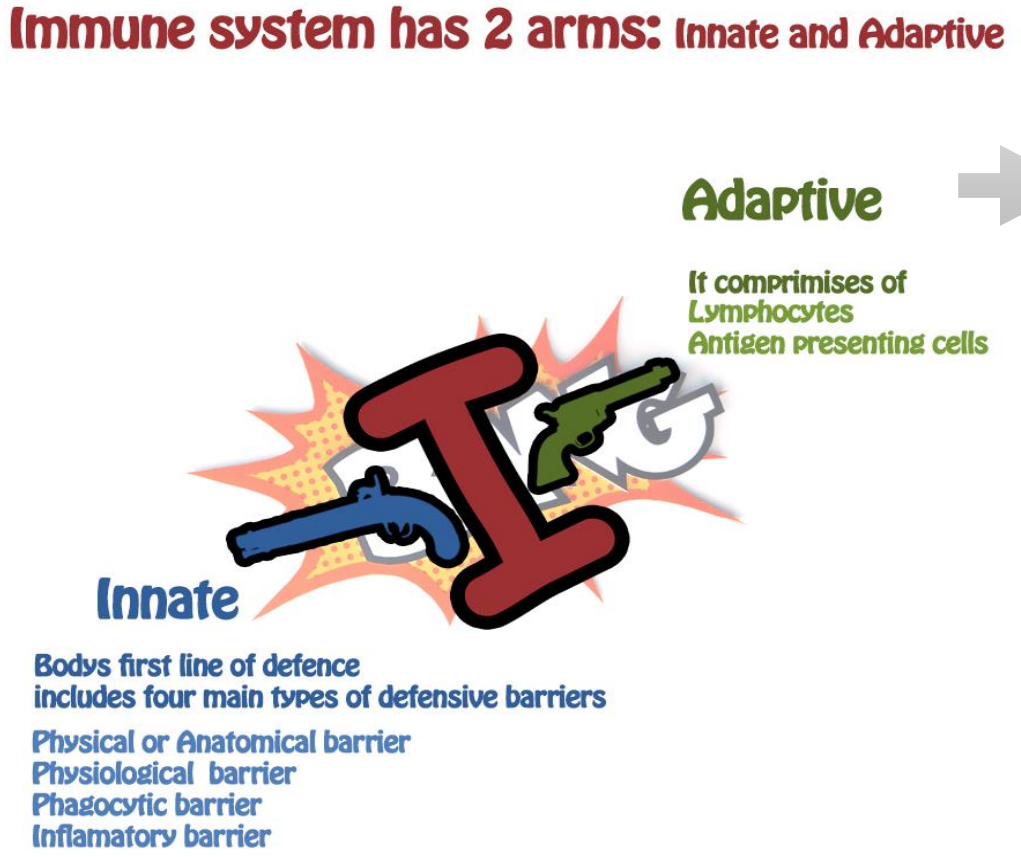
Cell Mediated Immunity

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)



Immune System



Phagocytes
- Neutrophils
- Monocytes/Macrophage
- Natural Killer

Interferon

Chemokine

Tumor Necrosis Factors(TNF)

Interleukin (IL)

Complement System

Humoral Immunity:

B lymphocyte

Cellular Immunity:

T lymphocyte:
- Th (helper)
- Tc (cytotoxic)

Characteristics of Adaptive Immunity:

- Antigenic specificity.
- Diversity, can recognize billion different antigens.
- Immunological memory
- Self vs non-self recognition

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.

- Mononuclear cell inflammatory process usually associated with chronic inflammations.

APC	Location
Monocyte	Peripheral Blood
Macrophage	Tissues
Dendritic cells	Lymphoid tissue
Langerhans cells	Epidermis
B cells	Lymphoid tissue, Blood

Major Histocompatibility Complex (MHC)

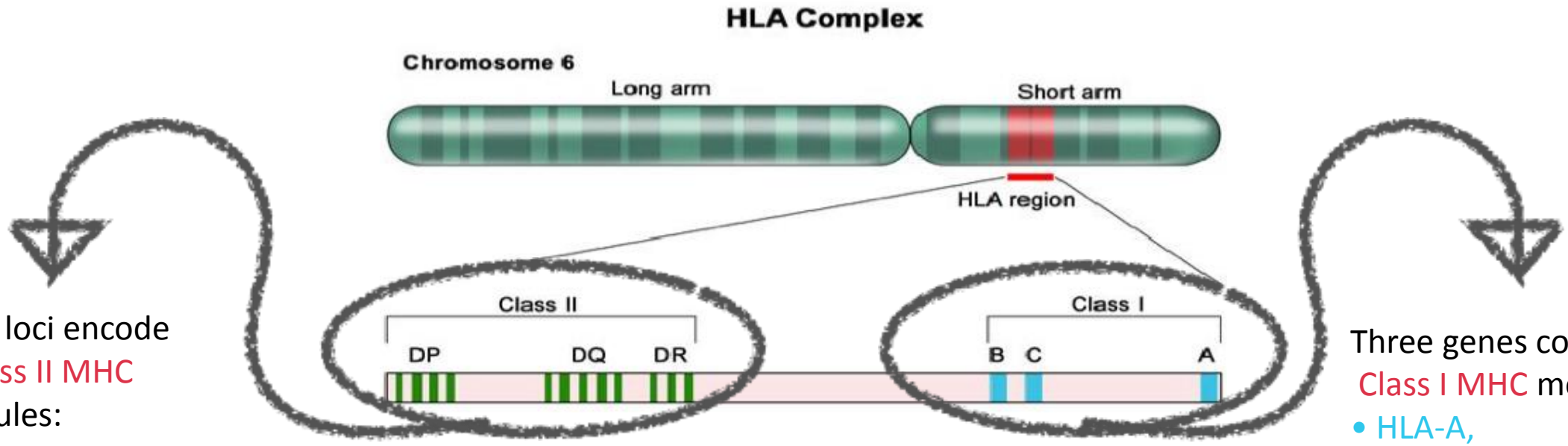
- (MHC) proteins were discovered for the first time with when tissue transplantation started.
- The success of tissue and organ transplantation depends upon the match of donor's and recipient's **"human leukocyte antigens" (HLA)** encoded by HLA genes.
- Each group of MHC consists of several glycoproteins

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,
Langerhans cells of skin,
B cells.

MHC - HLA Complex



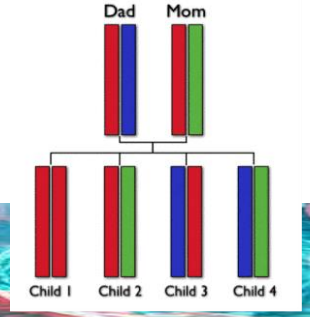
HLA-D loci encode for Class II MHC molecules:

- DP
- DQ
- DR

Three genes code for Class I MHC molecules:

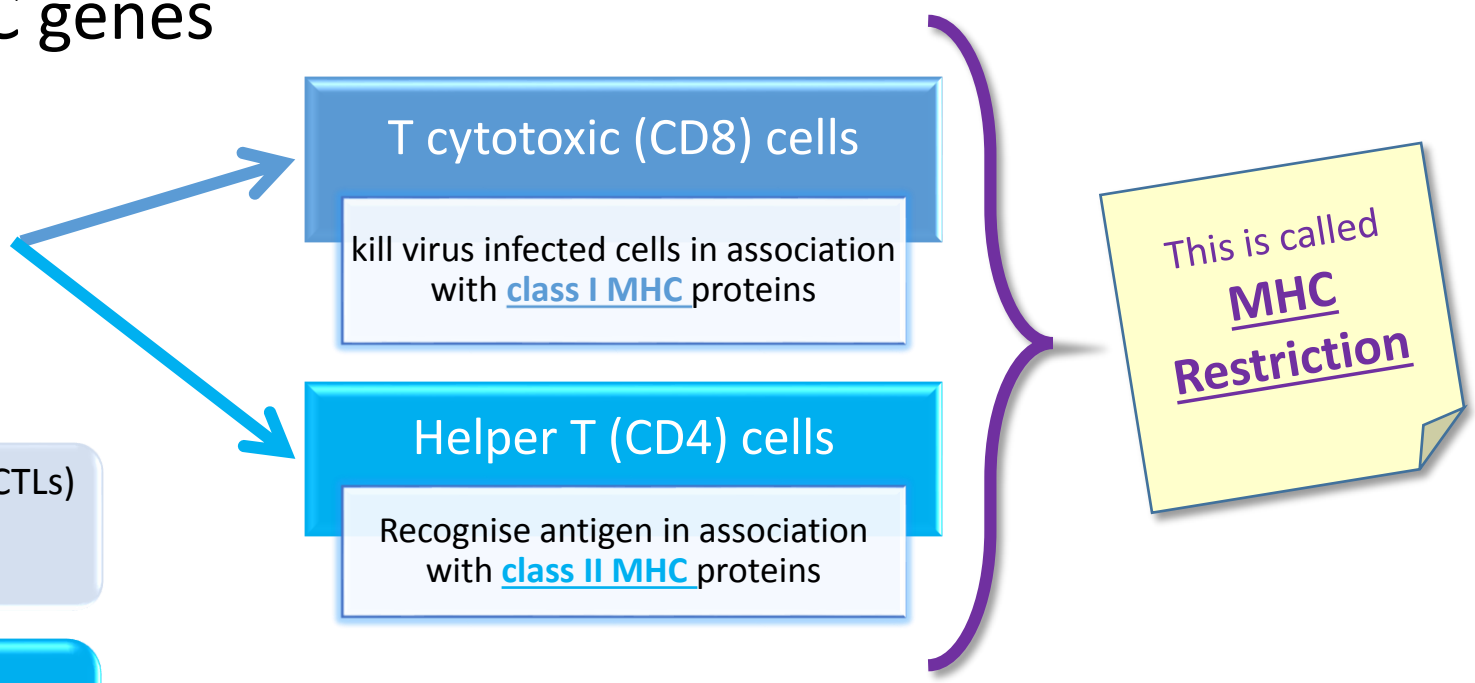
- HLA-A,
- HLA-B
- HLA-C

- Genes for HLA proteins are clustered in the MHC complex located on the short arm of chromosome 6.
- Each individual has two "***Haplotypes***", two sets of these genes one paternal and one maternal



Biologic Importance of MHC

- Transplantation: Success of an organ transplant is determined by compatibility of the MHC genes
- Antigen Recognition



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

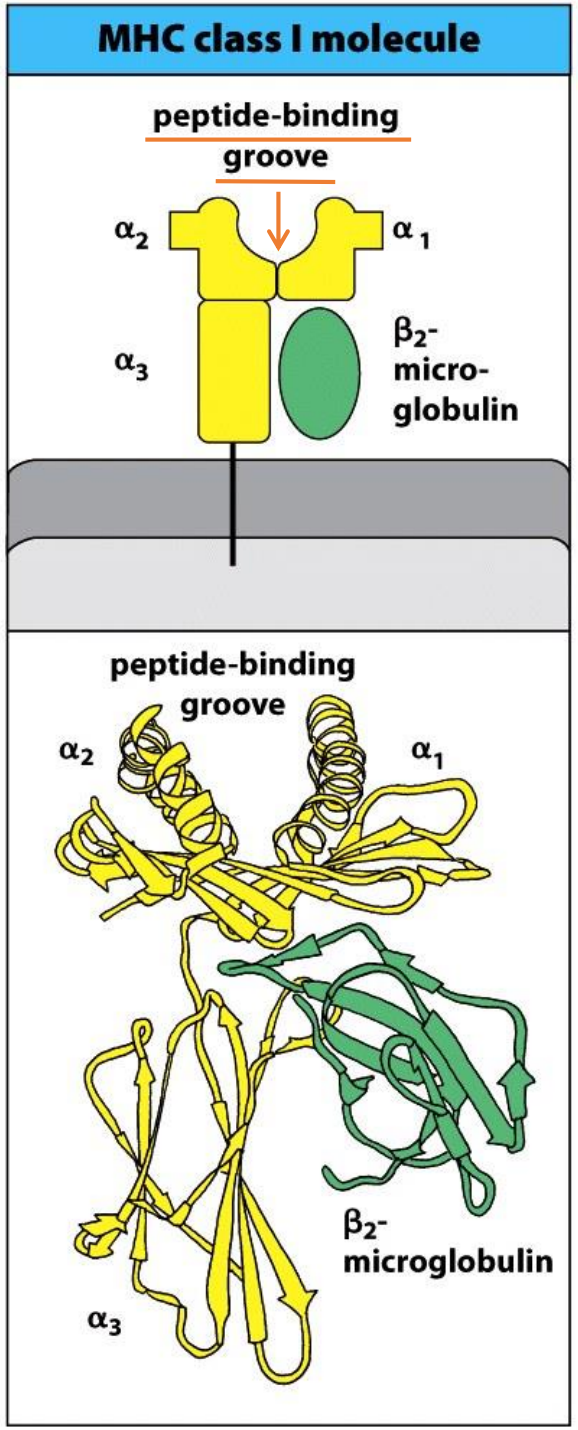
What is the function of MHC I?

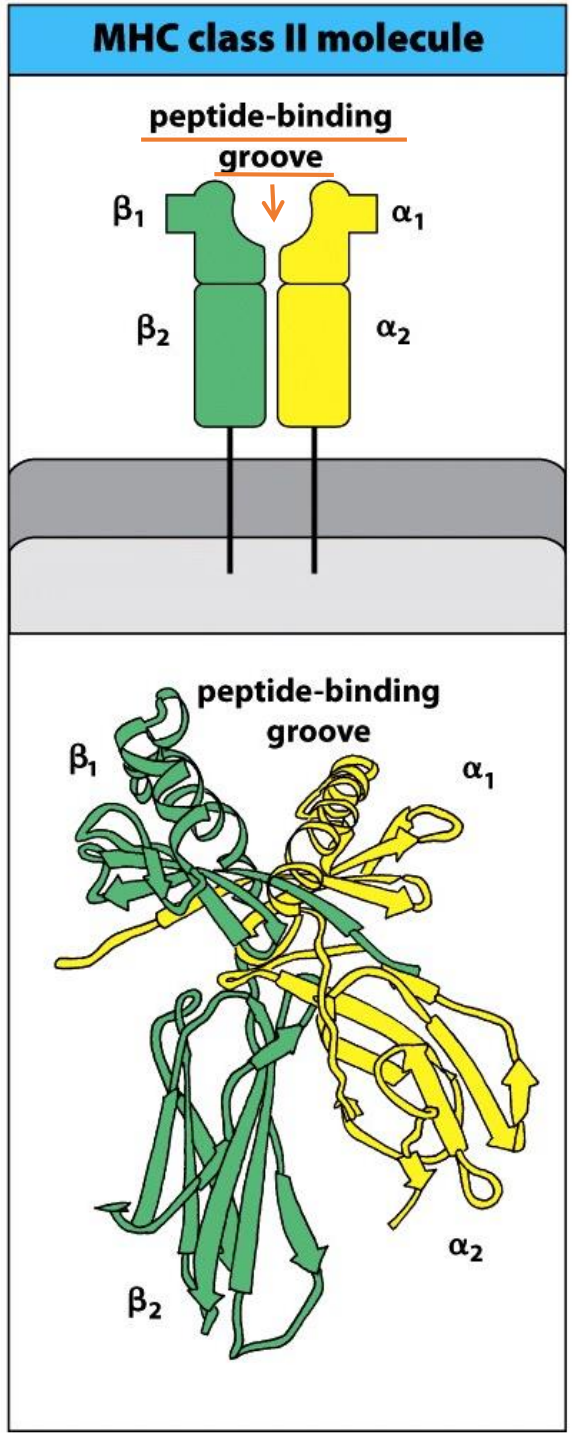
presenting antigens **processed in cytosol** to cell surface to **CD8 T-cells** (Tc-cells)

all nucleated cells present MHC I

أي بعدما يدخل الباثوجين للخلية ويُطلق antigens، يرتبط الـ antigens للـ peptide-binding groove وينتقلون إلى سطح الخلية ليرتبط مع الـ CD8 T-cells المسمى أيضاً بـ T-cytotoxic cell ليقتل الخلية التي تحمل الباثوجين

Click that to → Watch the MHC Class I journey.





What is the function of MHC II?

presenting antigens **processed in endocytic vesicles** to cell surface to **CD4 T-cells** (Th-cells)

professional APCs present MHC II (macrophages, dendritic cells, B-cells)

أي بعدما يدخل الباثوجين للخلية عن طريق phagocytosis/endocytic vesicles، يتحول إلى antigens ويرتبط للـ peptide-binding groove وينتقل إلى سطح الخلية ليرتبط مع الـ Naïve CD4 T-cells ليُفعِّله إلى Activated T-helper cells

ومن ثم:

The body's immune response is activated.

← Click this to Watch the MHC class II journey.

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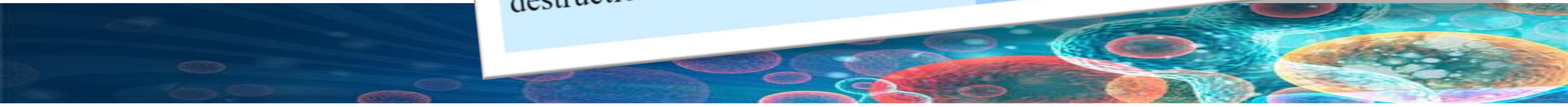
Major Differences between MHC classes I and II

MHC class I	MHC class II
Comprised of an MHC-encoded α chain and a β2-microglobulin chain	Comprised of MHC-encoded α and β chains
Present on most cells	Present only on antigen-presenting cells
Bind endogenous antigens synthesized in a cell	Binds exogenous antigens
Present antigen to cytotoxic T cell lymphocytes	Present antigen to helper T cell lymphocytes
Bind CD8 adhesion molecules on cytotoxic T cells	Bind CD4 adhesion molecules on helper T cells
Presence of foreign or over-abundant antigens targets cell for destruction	Presence of foreign antigens induces antibody production, and attracts immune cells to area of infection



Antigen Presentation

Associated with MHC class I

Internal Source i.e. within the body

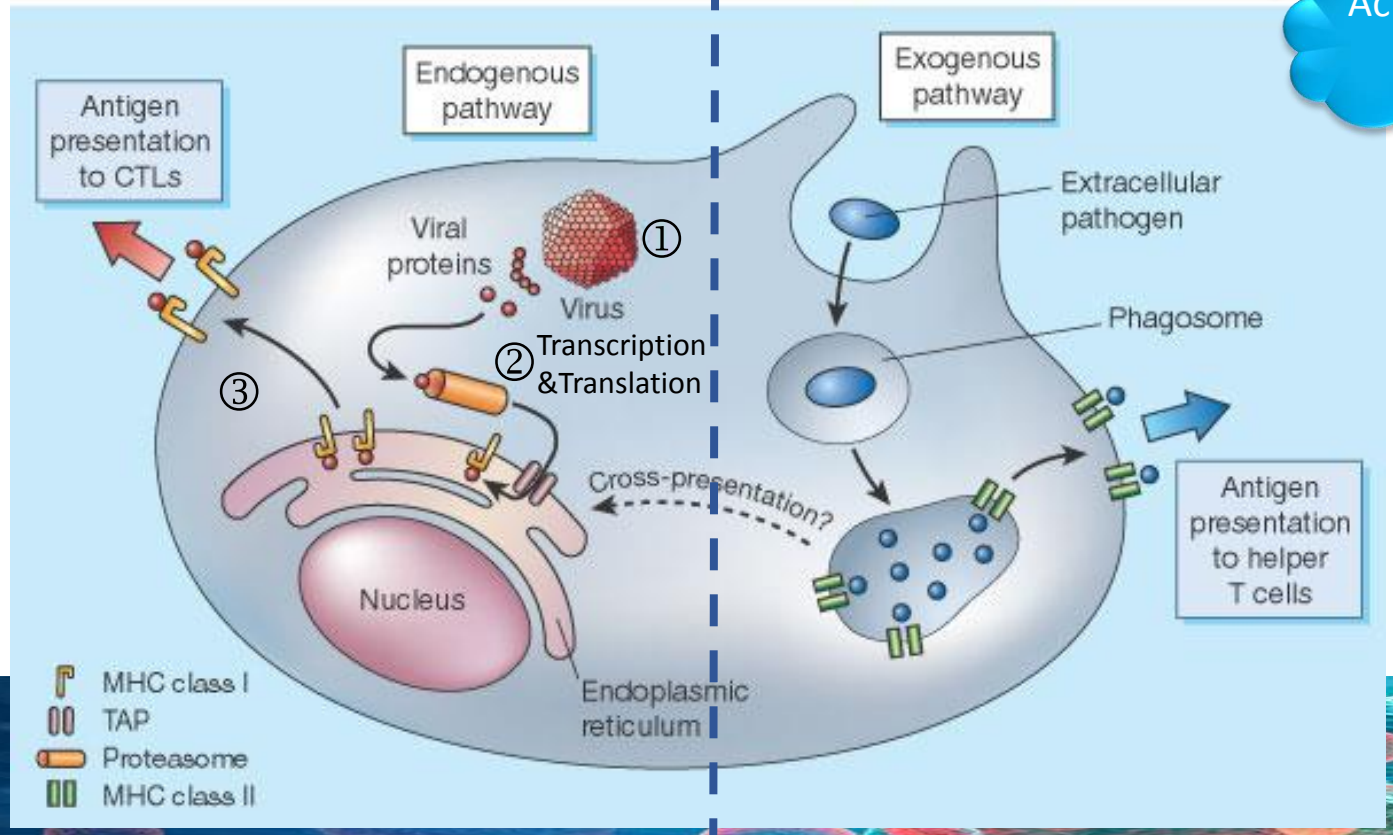
Endogenous antigen (Cytoplasm)

Associated with MHC class II

External source i.e. from outside the body

Exogenous antigen (Membrane Bound)

Activates CMI



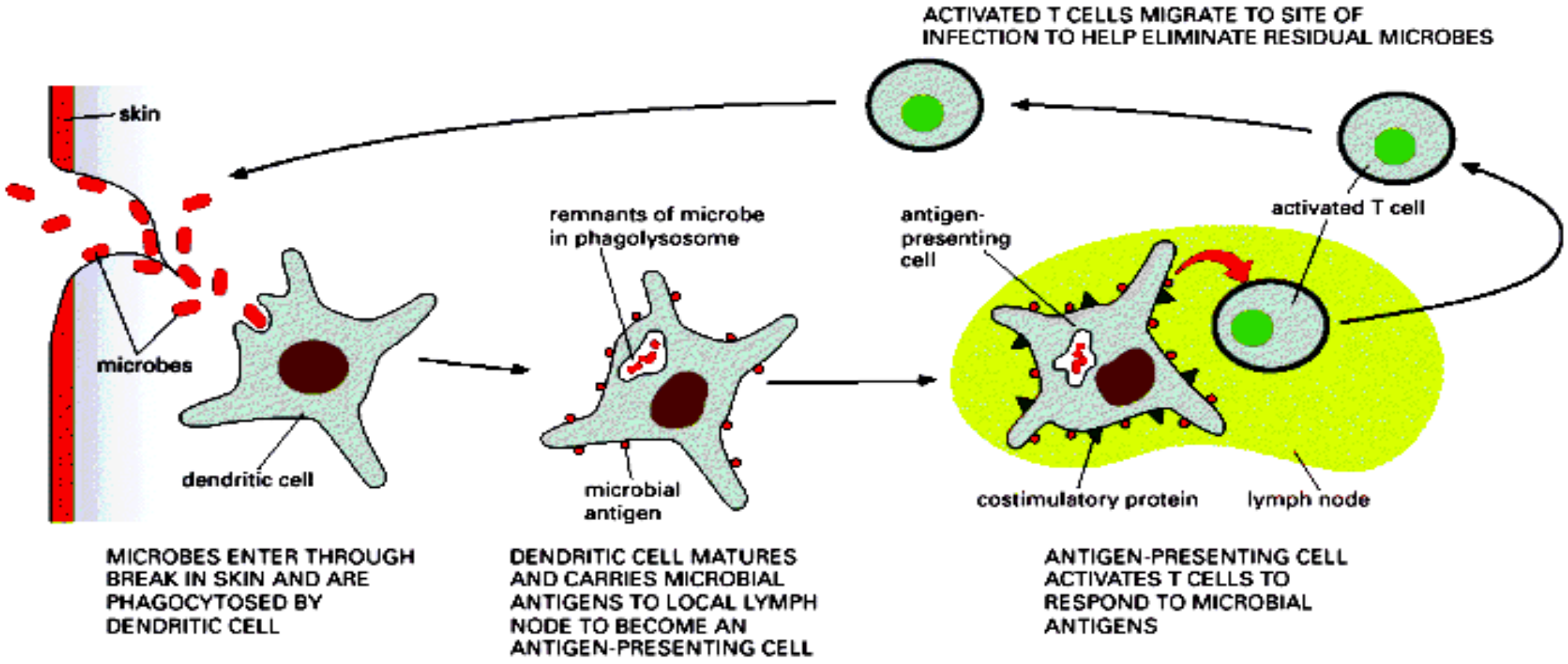
من داخل الجسم مثل:
Viral Infection
Or
Cancer Cells

مثال :أثناء عملية لزراعة الكلية، خرج من الكلية antigens وبما أنه كلية جديدة خارجية، فإنه يعتبر exogenous antigen

فيدخل عن طريق phagocytosis لخلية APC ليكوّن MHC II ليرتبط مع T h-cells

Antigen Presenting Cell APC

- **<u>Dendritic cells</u>** and **<u>macrophages</u>** digest invading microbe and then present the antigen of the microbe **<u>to lymphocytes in lymphoid organs</u>**



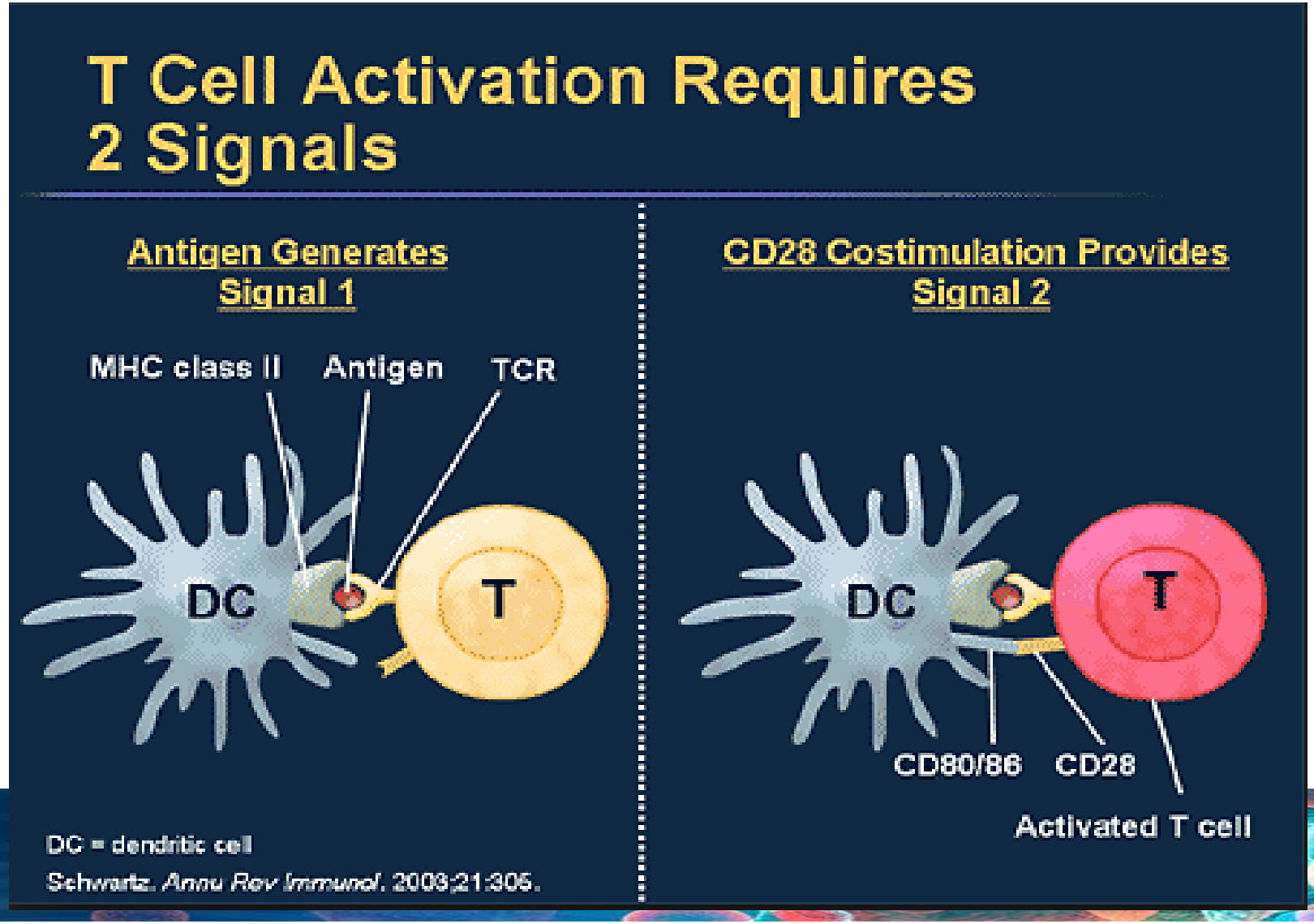
First Signal:

- MHC class II + antigen ***binds to*** TCR (T-cell receptor)
- IL-1, LFA-1 with ICAM

T-cell activation requires 2 signals

Second Signal (Costimulatory):

- B7 on APC ***interacts with*** CD28 on lymphocyte



Extra info:
ICAM: (Intercellular Adhesion Molecule)

IL-1: is a group of 11 cytokines, which plays a central role in the regulation of immune and inflammatory responses

LFA-1: is involved in recruitment to the site of infection.

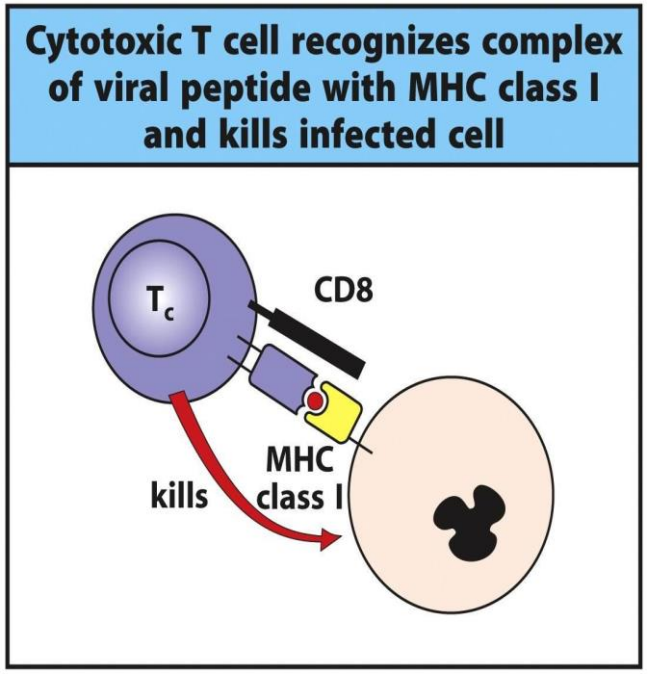
Cytokines: loose category of small proteins that are important in cell signalling.

Extra info:
B7: is a type of peripheral membrane protein

There are two major types of B7 proteins: B7-1 or CD80, and B7-2 or CD86.

Role of TCR

The TCR on CD8 + T cells interact with the MHC class I molecule & Ag.



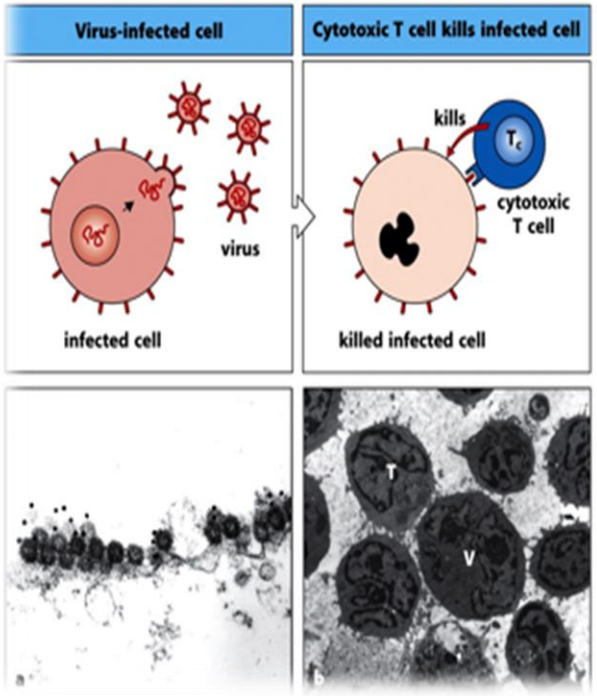
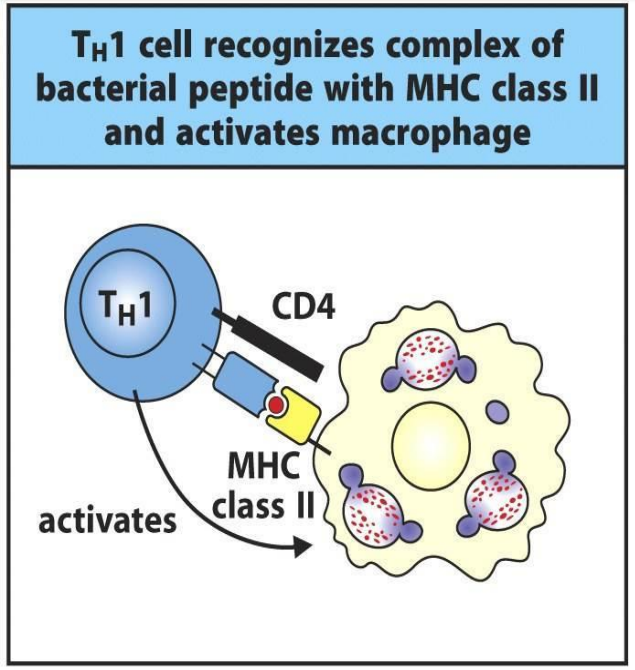


Figure 1.30 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

The TCR on the CD4 + T cell engages the MHC class II molecule on APC.



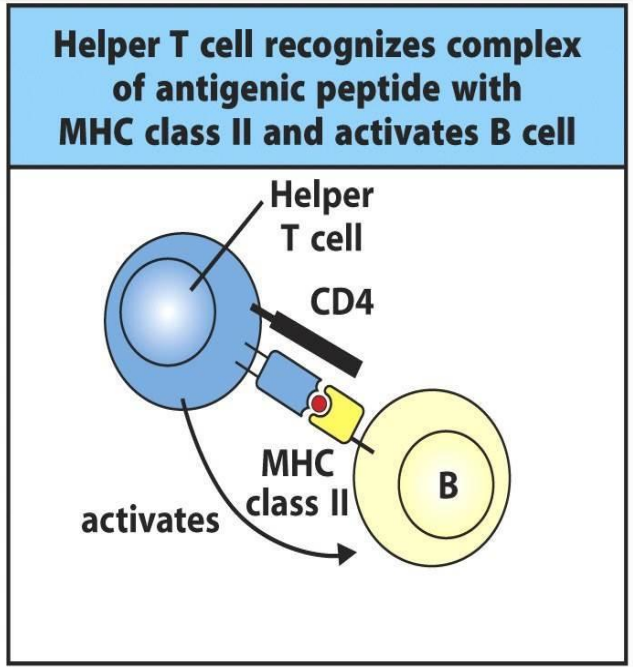


Figure 1.31 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Check :)

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

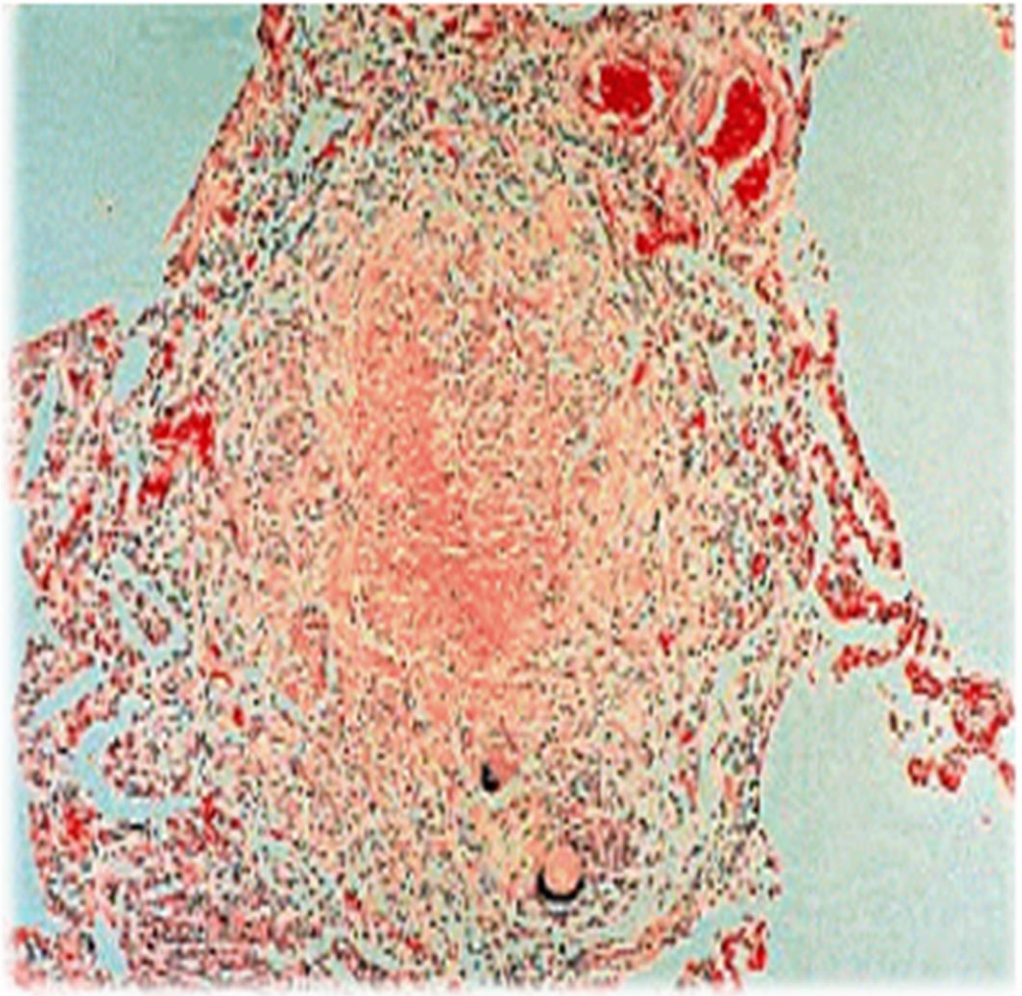
Production of Interferons

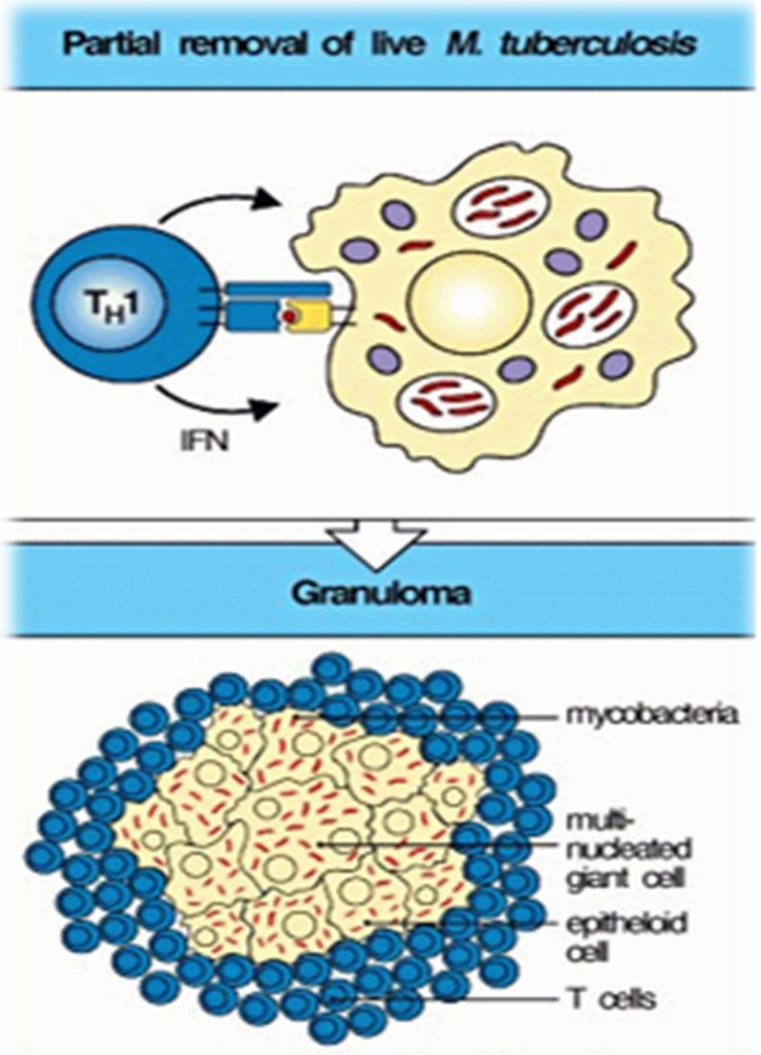
- Enhances anti-microbial activity of macrophages

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

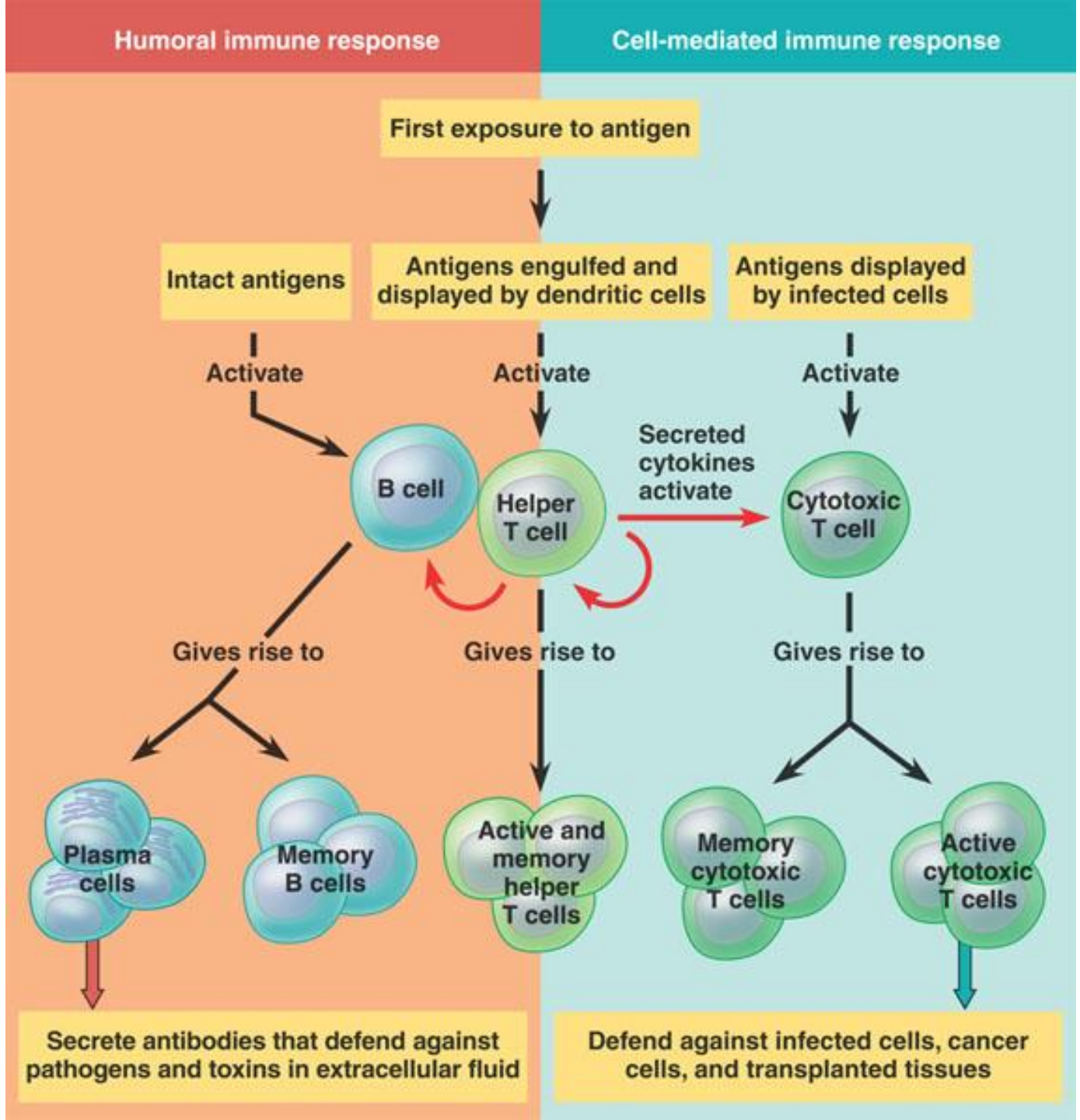
An example of immune system response **is : Granuloma Formation**
(Chronic Inflammation, e.g. TB)





Explanation :

- **T helper** activates both B cells and T cytotoxic lymphocyte.
- **T helper cell** is the linkage between two response (Humoral immune and Cell mediated immune)



Examples of Cell Mediated Immunity

Delayed type of hypersensitivity (DTH) reaction:

The tuberculin test

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

Contact Sensitivity:

- 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, it is triggered by CD4+ T cells

Summary

- 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

Thank you!

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