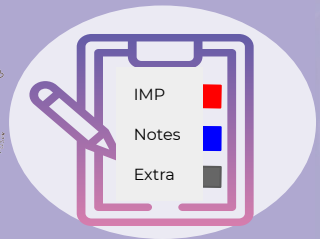
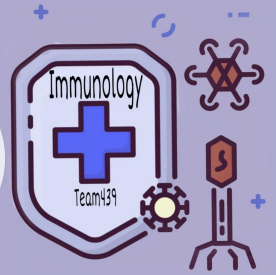
Cell Mediated Immunity





Objectives

01

To describe antigen recognition by T cells

02

To describe the pathways involved in processing endogenous and exogenous antigens

03

To discuss self MHC restriction in Ag (antigen) presentation to T cells

04

To describe the induction of cell mediated immunity (Chronic Inflammation)

Antigen processing: is an immunological process that prepares antigens for presentation to special cells of the immune system called T lymphocytes.

Adaptive Immunity

Antibody Mediated Cell (Humoral)

Cell Mediated Immunity (CMI)

The antigen has to be processed

without it, T-cell can't recognize the antigen

Antigen + MHC (Major Histocompatibility Complex)

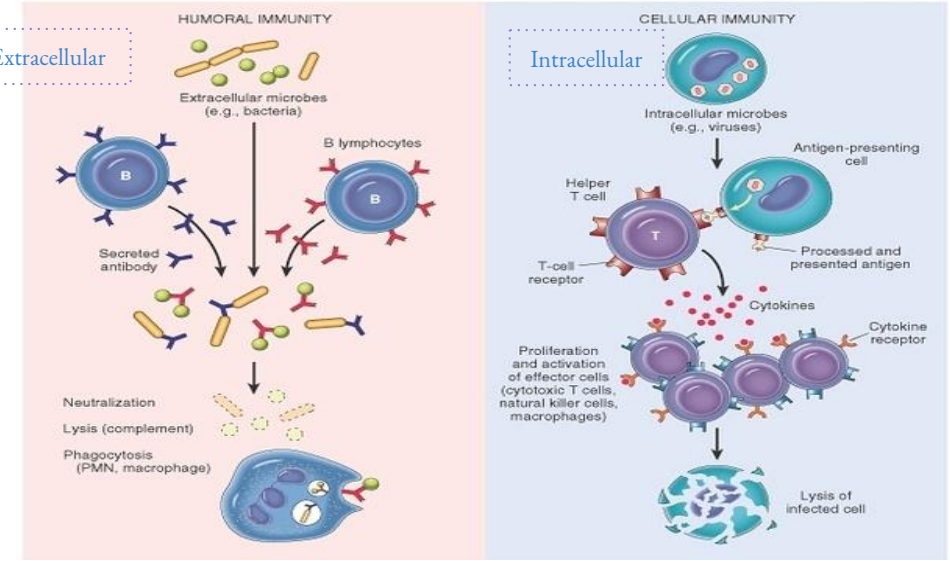
↓

T-Lymphocytes

↓

Immune Response

Activated



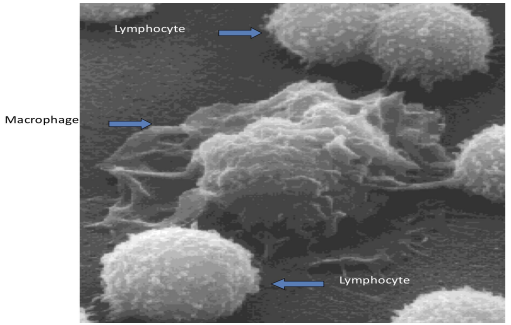
Antigen Presenting Cells (APCs)

1. **Monocytes**
   Peripheral blood

2. **Macrophages**
   Tissues

3. **Dendritic cells**
   Lymphoid tissues,
   skin (Langerhans cells)
   Dendritic cells found in Skin are called (langerhans cells)

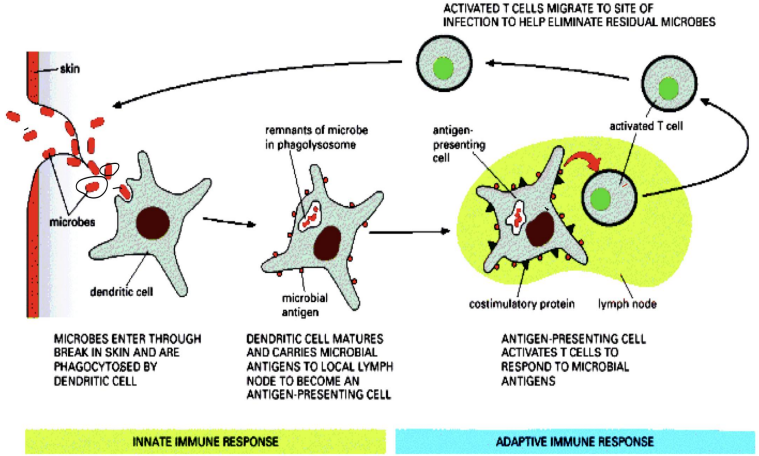
4. **B-cells**
   Lymphoid tissue, Blood



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

Antigen Presenting Cell

T-cells go back to the site of infection

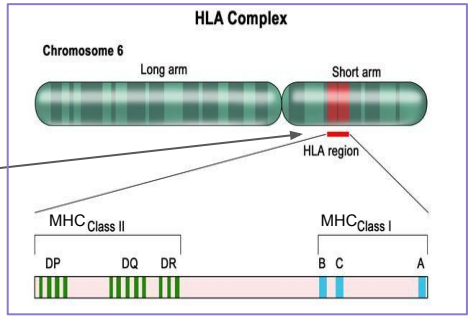


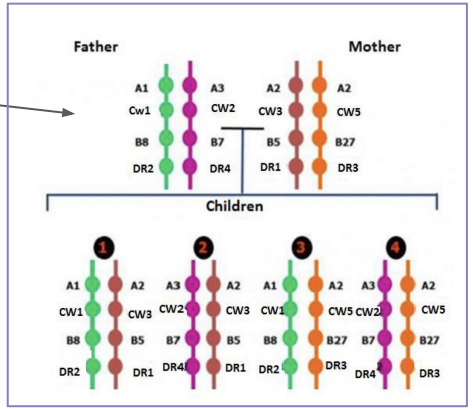
Major Histocompatibility Complex (MHC)

Definition

(MHC)'s are proteins that were found on cell surface required for recognition of foreign substances. It was 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 *HLA and MHC are the same
- Genes for HLA proteins are clustered in the MHC complex located on the short arm of chromosome 6
- 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
- Each individual has two "haplotypes" ie, two sets of these genes one paternal and one maternal
- Mononuclear cell inflammatory process usually associated with chronic inflammations





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Lymphocytes (T,B and NK cells) and Monocytes are called mononuclear cells (consist of one round nucleus), and they are associated with inflammation (body's internal fire alarm).

Major Histocompatibility Complex (MHC)

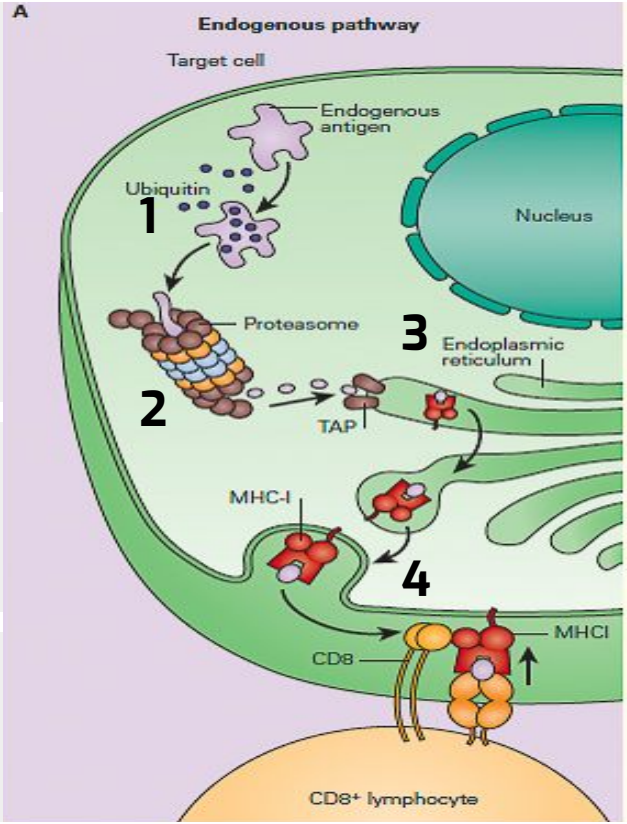
	MHC I	MHC II
Location	Surface of all nucleated cells except RBCs	Surface of Antigen presenting cells (APCs)
Association	endogenous(reproduce in cytoplasm)	exogenous(reproduce in cell)
Antigen recognition (MHC restriction)	T cytotoxic (CD8) cells kill virus-infected cells and tumor cells	T helper (CD4) cells enhance CMI and production of antibodies by B cells. it helps in activation of cytotoxic T cells
Transplantation	Organ transplant success is determined by the compatibility of MHC genes	

CMI: cell mediated immunity

Helpful Video

Endogenous pathway

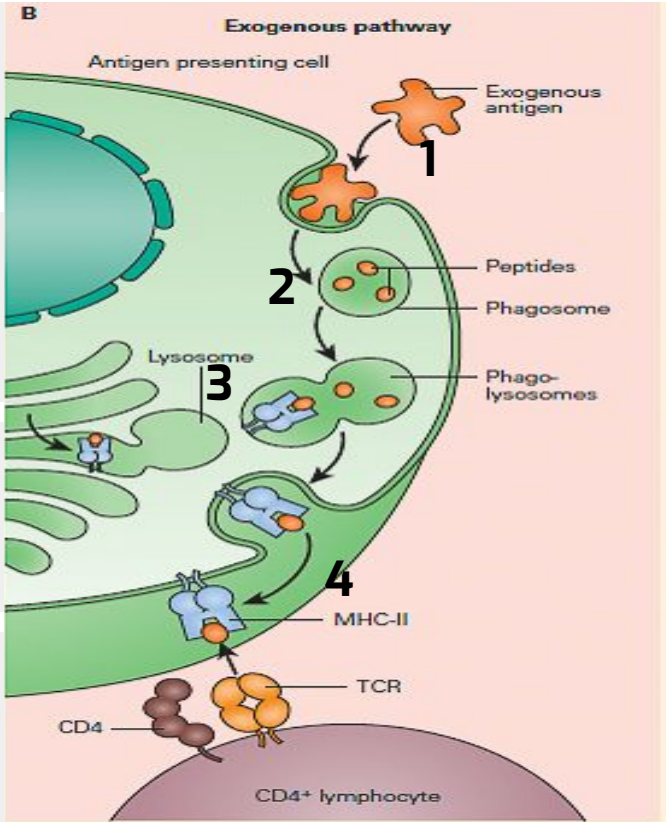
1. Pathogen(eg, virus) infect the cell with its own protein
2. Virus protein (cytosolic protein) is degraded inside **proteasome** (LMP2,LMP7) into small fragments
3. The small fragments will enter rough endoplasmic reticulum (rER) through peptide transporter **(TAP)** and bind with class I MHC
4. The MHC I peptide complex will be modified in Golgi apparatus and sent as secretory vesicle to the surface of the cell and interact with T cytotoxic receptor (CD8)



Helpful Video

Exogenous pathway

1. The antigen presenting cell engulfs a pathogen(eg, bacteria) by phagocytosis to form phagosome
2. The antigen presenting cell binds the phagosome with lysosome and form Phago-lysosome
3. The MHC II formed in rER. It is modified in Golgi apparatus and leave as endosome to bind with phago-lysosome
4. The MHC II-peptide complex is expressed on cell surface and interact with T cell receptor (TCR) of T helper cell (CD4)



Activation of T cells

Two signals are required to activate T cell :

1 First signal

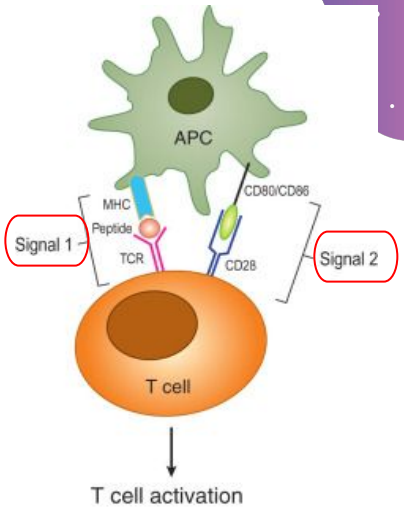
Binding of MHC class II located on the surface of an APC to TCR (T- cell receptor) **which lead to the production of:**

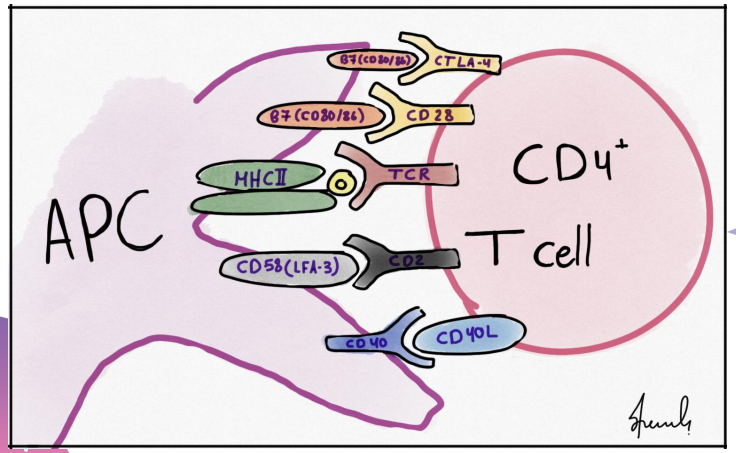
- IL-1(interleukin 1)
- LFA-1(Lymphocyte function associated antigen) with ICAM (intercellular adhesion molecule)

2 Second signal

(Costimulatory signal) also knowing as positive signal

Binding of B7 (CD 80) located on APC with CD28 on T- cell





1- B7 (CD80/86) with CTLA-4 " ↓Activation"
2- B7 (CD80/86) with CD 28 " ↑Activation"
3- MHC-II with TCR "Recognition"
4- CD 58 (LFA-3) with CD2 "Adhesion"
5- CD 40 with CD 40L " ↑ Activation"

Production of IL-2 and its receptor (CD25)

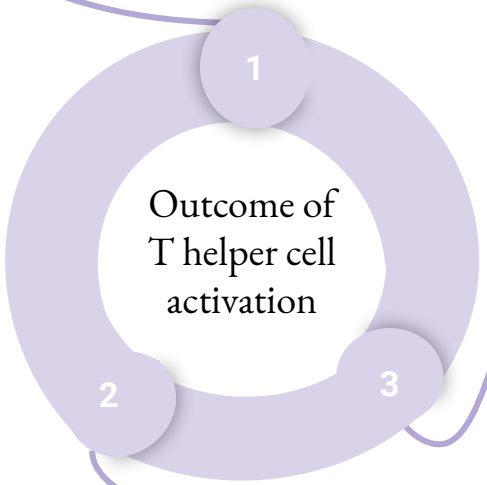
1- IL-2 is also know as T cell growth factor

2- Proliferation (division) of antigen specific T cells

3- Effector and regulatory cells are produced along with “memory” cells

4- IL-2 also stimulates CD8 cytotoxic cells

Extra:
IL-2 promotes differentiation when the initial T cell is stimulated by an antigen thus releasing effector cells that will induce the function of that cell (T helper cells , cytotoxic cd8 cells).
IL-2 promotes the differentiation of regulatory T-cells that recognize self and nonself cells.
*preventing autoimmune diseases
*Location in thymus.



Production of Interferons

Enhances anti-microbial activity of macrophages

Memory T cells

Also called antigen experienced T cell

1- Respond **rapidly** for many years after initial exposure to antigen

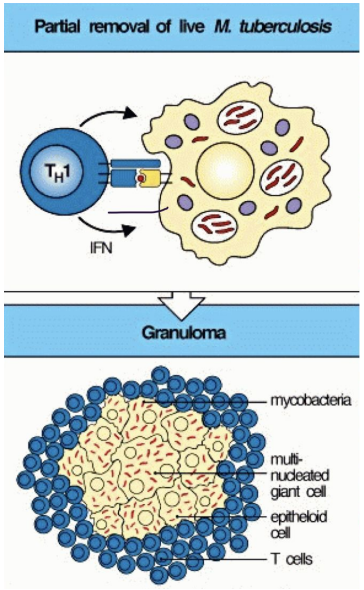
2- A large number of memory cells are produced so that the **secondary response** is greater than the primary

3- Memory cells **live for many years** and have the capacity to multiply

4- They are activated by **smaller amount of antigen**

5- They produce greater amounts of interleukins

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

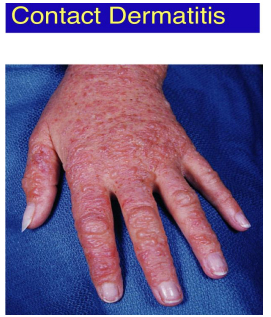


When T cell recognize the antigen of TB it will be come T helper and release interferon gamma (cytokines).

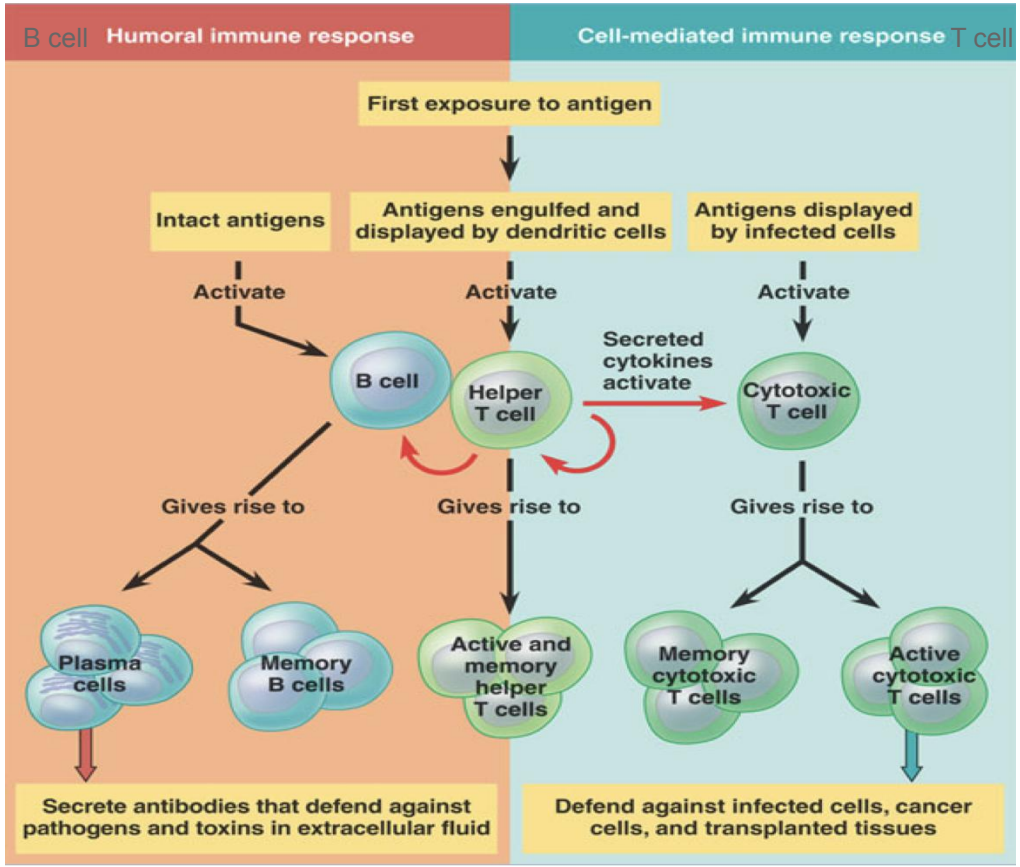
Examples of Cell Mediated Immunity

1. Delayed type of hypersensitivity (DTH) reaction (type IV):
the tuberculin test – Mediated by CD4+ T cells and takes about 72 hours to develop

2.Contact hypersensitivity (type 1)
– Many people develop rashes on their skin following contact with certain chemicals such as nickel, certain dyes, and poison ivy plant
– The response takes 24 hours to occur and like DTH, is triggered by CD4+ T cells



summary of humoral and adaptive responses



Take Home Messages:

- 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

Quiz

Question 1: MHC II molecules are found on the surface of			
A - all nucleated cells	B- APCs	C- RBCs	D- WBCs
Question 2: Antigen recognition is also called			
A - Reproduction	B- Restrictivation	C- Restriction	D- Non of the above
Question 3: The response of hypersensitivity is triggered by			
A - APCs	B- CD4+ T cells	C- CD4+ APCs	D- Antigens
Question 4: Initial antigen exposure results in generation of .... for a stronger and a quicker response against future exposures to the same pathogen			
A - Memory Cells	B- NK cells	C- WBCs	D- genetic cells

4: A
3: B
2: C
1: B

team leaders

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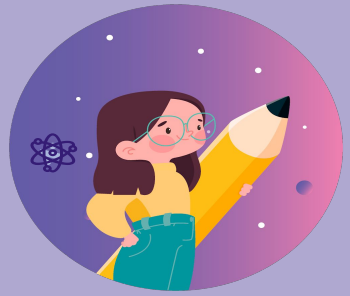

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