MEDICINE
KING SAUD UNIVERSITY

Foundation Block

Lecture Three

Cell mediated Immunity

IMMUNOLOGY

436's TEAMWORK

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 presenting to T cells.
- To describe the induction of cell mediated immunity (Chronic Inflammation).

- **Important.**
- Extra notes.
- **Females notes**
- **Males notes.**

Immune system:

Adaptive:

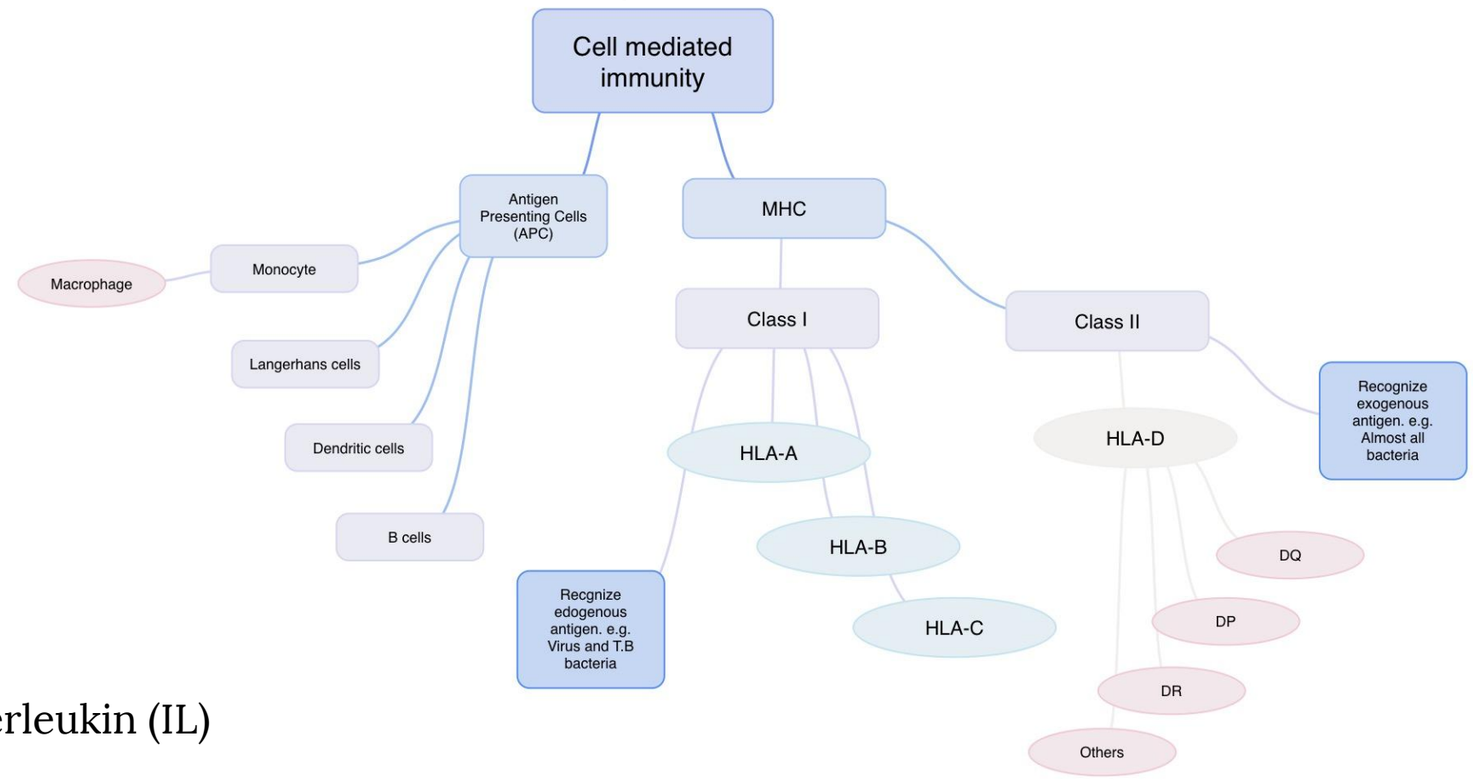
1- Humoral Immunity:
B lymphocyte

2- Cellular Immunity:
T lymphocyte:
- Th (helper)
- Tc (cytotoxic)

1- What the lecture is going to talk about about

2- summary of the lecture.

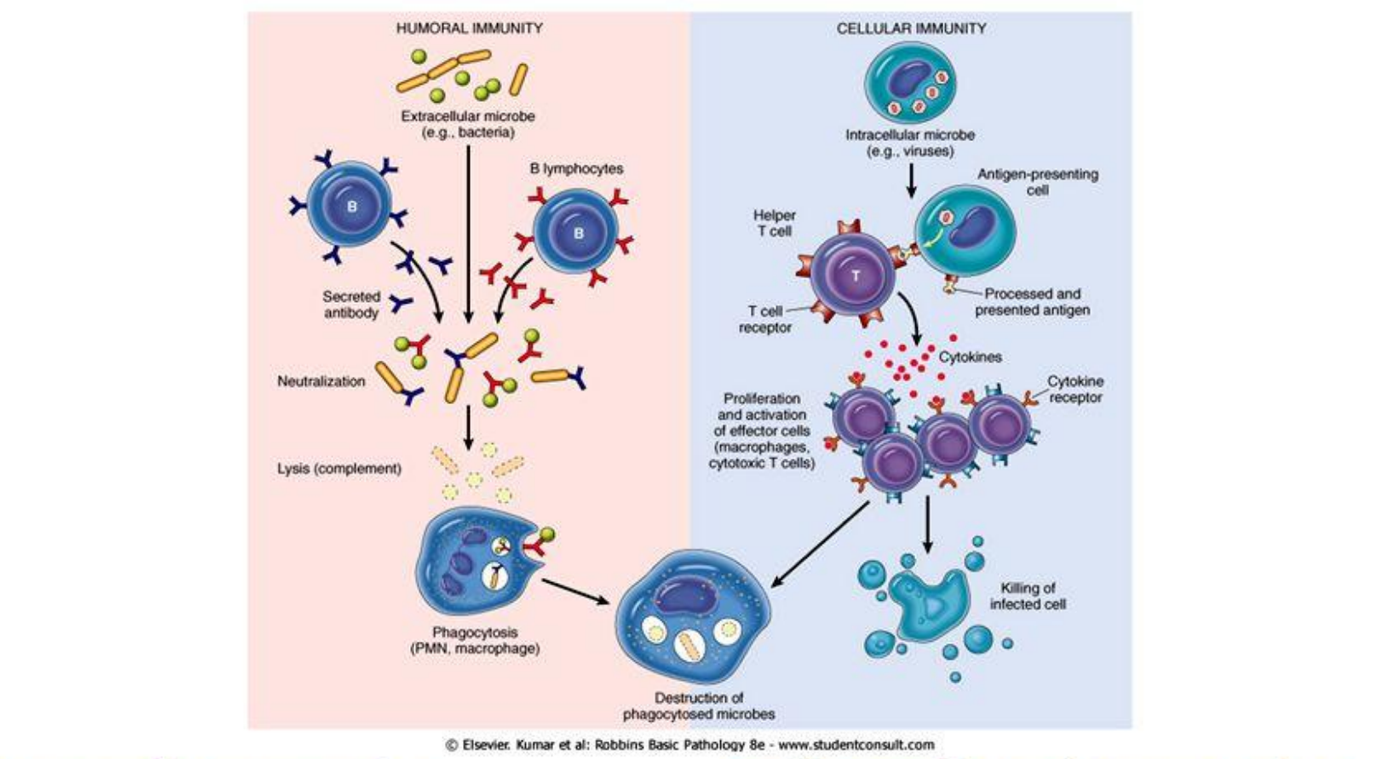
Characteristics of Adaptive Immunity:
- Antigenic specificity.
- Diversity, can recognize billion different antigens.
- Immunological memory
- Self vs non-self recognition



Innate:

Body's first line of defence.

- Phagocytes
  - Neutrophils
  - Monocytes/Macrophage
  - Natural Killer
- Interferon
- Chemokine
- Tumor Necrosis Factors (TNF) Interleukin (IL)
- Complement System



Humoral Immunity

Involves B-cell production of antibodies that bind antigens resulting in either:
1. Neutralization
2. lysis (by the complement system), or
3. phagocytosis and destruction

Cell-mediated Immunity

Involves T-cell recognition of abnormal antigens on the surface of host cells (indicating viral infection or tumorigenic change) and the killing of infected cells.

Humoral vs. 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.

*Only T and B lymphocytes are able to recognize the antigens, because they have specialized receptors.

• Mononuclear cell inflammatory process usually associated with chronic inflammations

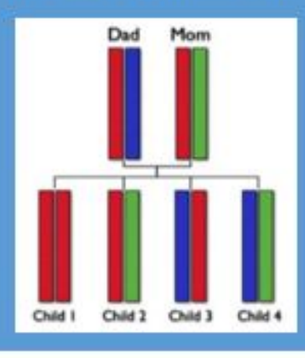
Antigen Presenting cells	
monocytes	Peripheral blood
macrophage	tissue
Dendritic cells	Lymphoid tissue
B-cells	Lymphoid tissue, Blood
Langerhans cells	Epidermis

*HLA: Refers to the same MHC molecules.

Major Histocompatibility Complex (MHC)

عبارة عن بروتين ينتج من الرايبوزوم (آلة تصنيع البروتين) يطلع على سطح الخلية زي الريسبتر لما يدخل باثوجين للخلية. يطلع عشان تتعرف عليه تي هيلبر + سايتوتوكسك وتعرف ان الخلية مصابة بباثوجين

- (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
- 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



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.

MHC I Processing VIDEO ***MHC II Processing VIDEO***

فديوز مهمة للتوضيح!

Peptide (antigen) will be in the middle of the MHC to be recognized by T-Lymphocytes

Antigen + MHC → **T-Lymphocytes** → **Immune Response**

*The antigen presenting cells will phagocytose the microorganism and will process it as antigen (which is a peptide).

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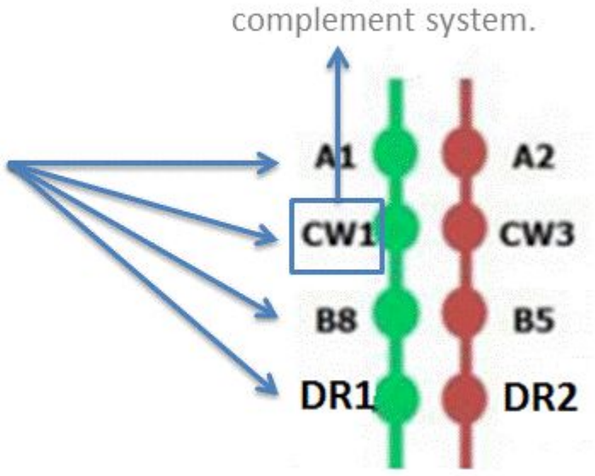
*Letter (c) refers to the complement system.

These are different types of MHC molecules. Every individual have them all, one is inherited from the father (paternal) and the other is from the mother (maternal).



Biologic Importance of MHC

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

called MHC restriction

(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

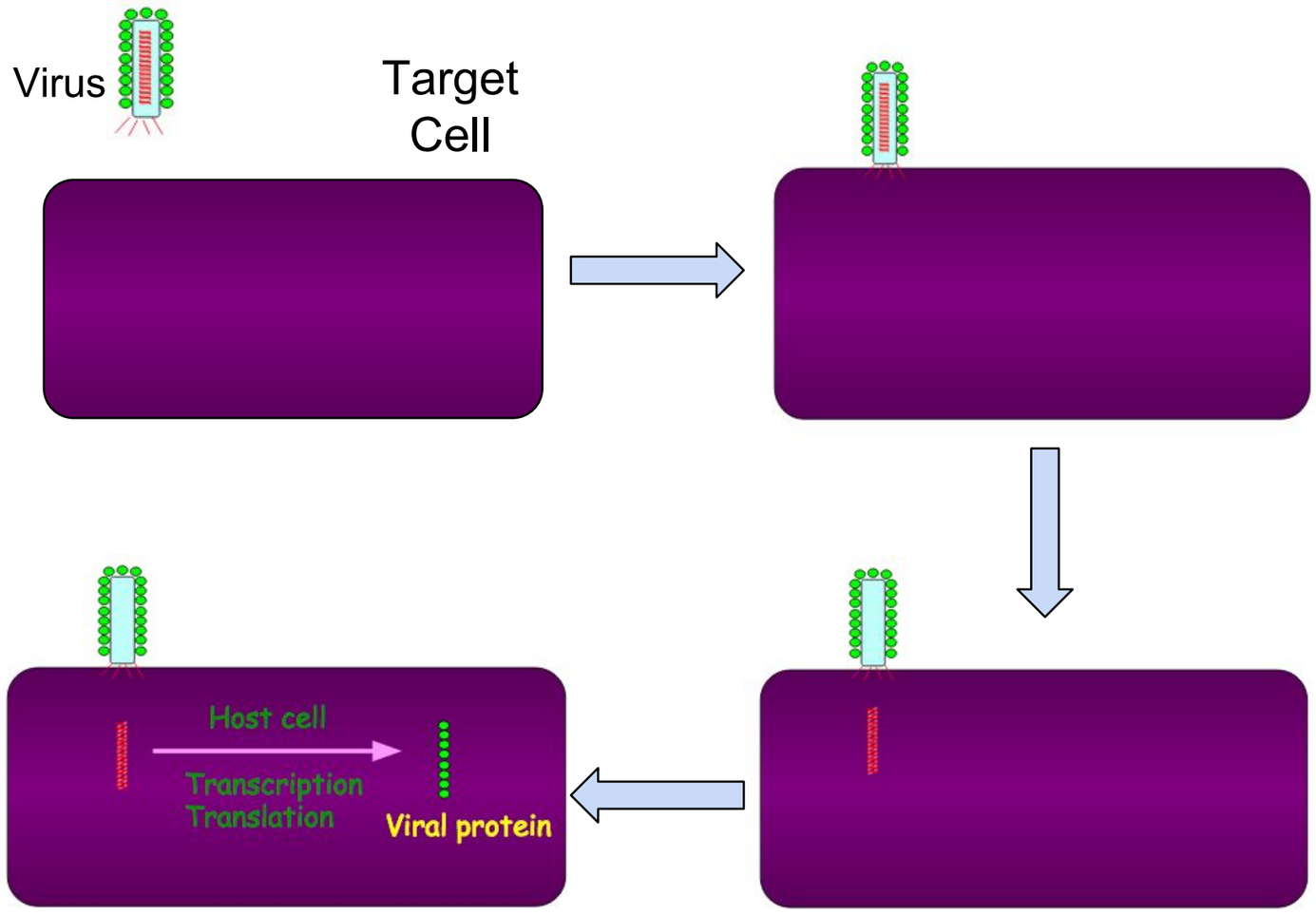
1-Endogenous antigen (Cytoplasm):

1-internal virus or intracellular bacteria -processed Ag combine with **class I MHC** molecule in RER.

2- they go to Golgi then to secretory vesicle and then they are pushed to the surface.

3 – MHC class I + peptide complex activates **CD8 T cytotoxic**

*الڤديوز في سلايد ٣ توضح الية الطريقتين جيداً

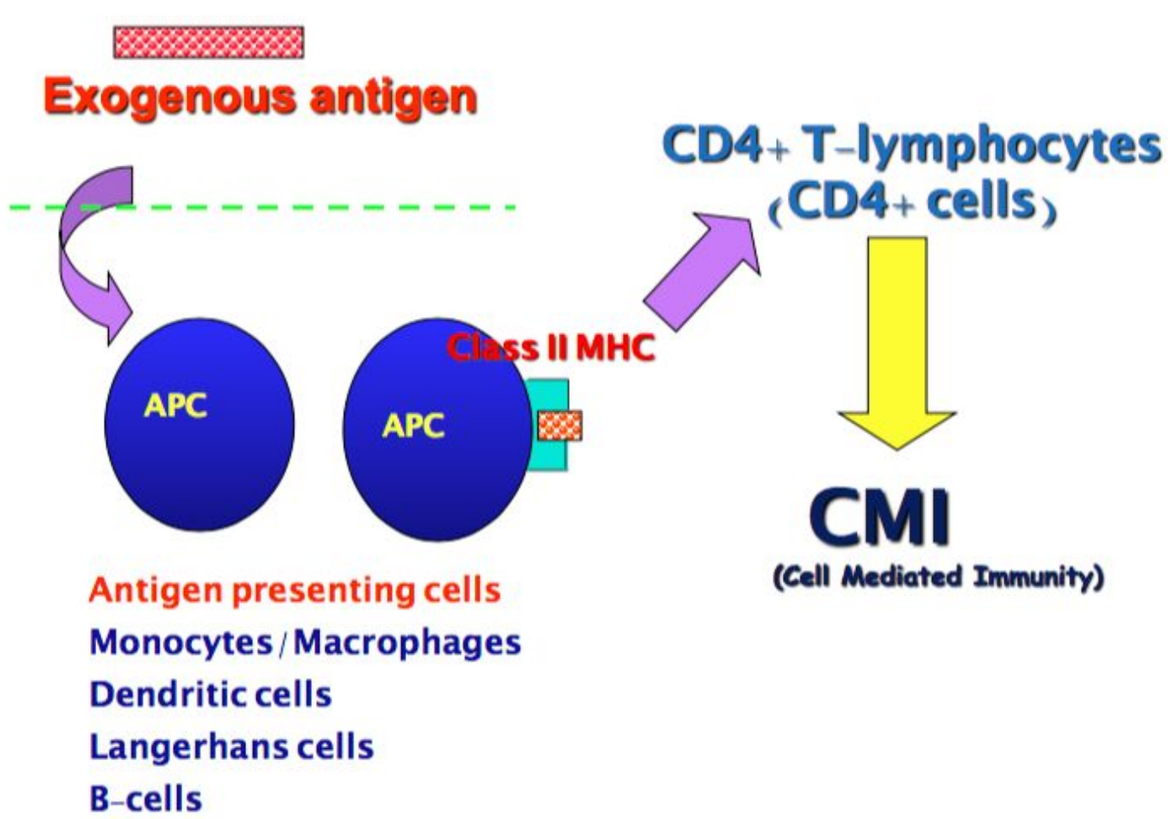


2-Exogenous antigen (Membrane bound)

1-Extracellular bacteria.

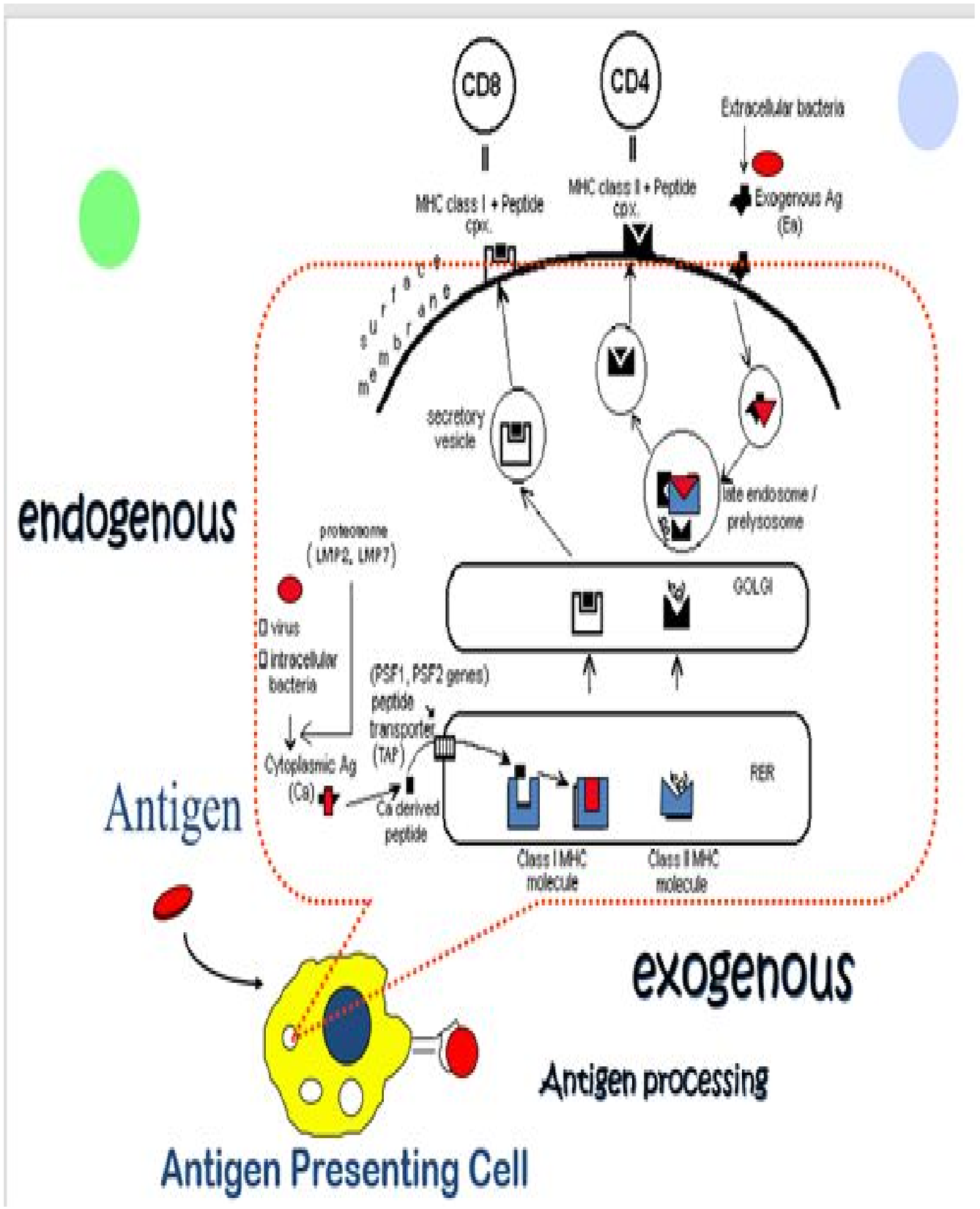
2-**class II MHC** molecules synthesized in RER then goes to Golgi apparatus

3- processed Ag combine with class II molecule (in prelysosome) then they are pushed to the surface, so the MHC class II + peptide complex (antigen) be presented to **CD4 T helper cell**



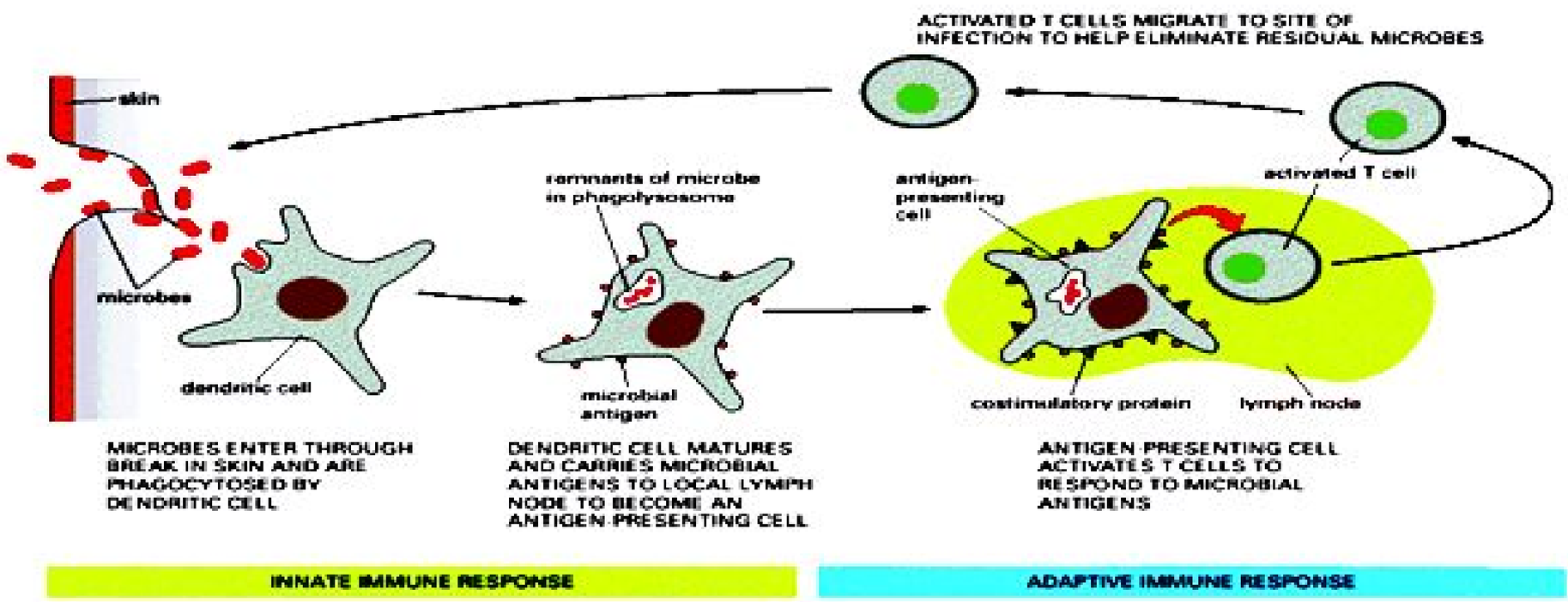
Video

*This picture is animated at Dr.' slides-power point.



Antigen Presenting Cells:

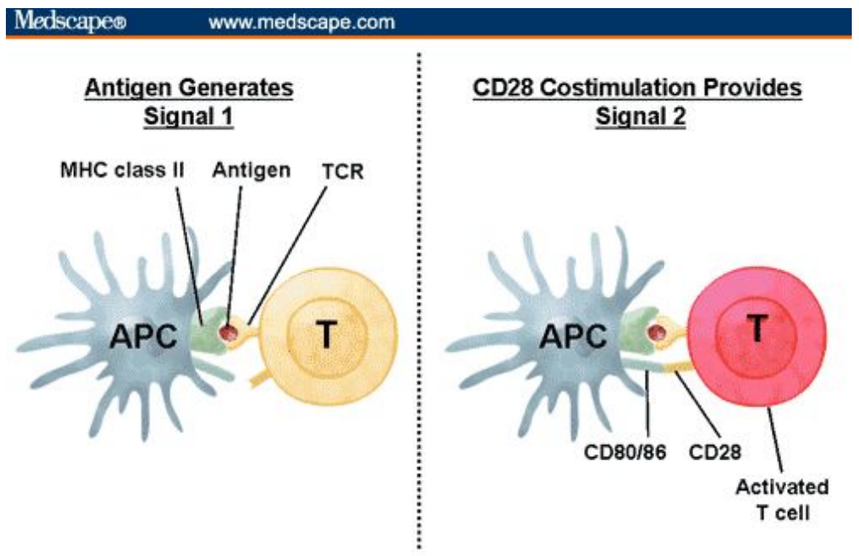
Dendritic cells and **macrophages** digest invading microbe and then present the antigen of the microbe to lymphocytes in lymphoid organs.



Activation of T cells:

T cell activation 1

T cell activation 2



Two cells are required to activate T cells:

First signal:

- Class II MHC + antigen binds to TCR
- IL-1, LFA-1 with ICAM

Second signal (Costimulatory signal):

- B7 on APC interacts with CD28 on lymphocyte.

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.

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.

T- lymphocytes CMI

Subunits 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.

Outcome of T helper cell activation:

1- Production of IL-2 and its receptor

- IL-2 is also known 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

2- Enhances anti-microbial activity of macrophages:

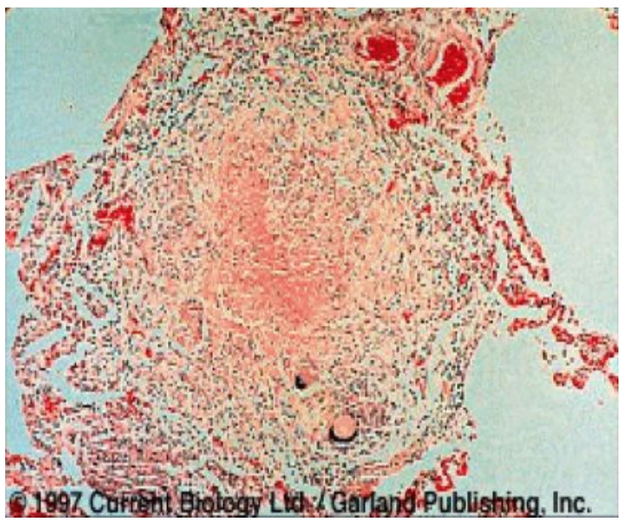
- Enhances anti-microbial activity of macrophages

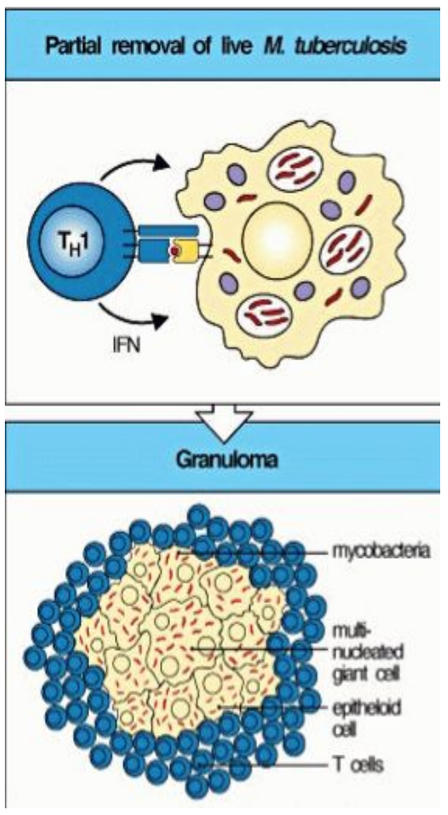
3- Memory T cells:

- 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:

Granuloma formation (chronic inflammation, e.g. Tuberculosis)





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.

MCQs

1- Antigen Presenting cells in the blood

A. Monocytes & Langerhans cells
B. B-cells & Monocytes
C. Dendritic cell

2- MHC class I molecules are NOT found on the surfaces of:

A. RBCs
B. B cells
C. Macrophages

3- the secondary response according to memory cells is:

A. Less than the primary response
B. More than the primary response
C. Equal to the primary response

4- the tuberculin test is mediated by:

A. CD4+
B. CD2+
C. CD28+

5- genes code for Class I MHC molecules

A. HLA-A
B. DR
C. DQ

6- when the antigen is a virus the recondition is through:

A. MHC class ll
B. MHC class l
C. IL1
D. CD 3

Answers
1. B
2. A
3. B
4. A
5. A
6. B

MEDICINE
KING SAUD UNIVERSITY

Contact us

Email: Immunology436@gmail.com

Twitter: Immunology436

IMMUNOLOGY
436's TEAMWORK

Team Leaders

Ghaida Alsaeed

Basel almeflh

Team members

Aroob Alhuthail

aldorah Alhamdi

Ghada Alskait

Hanin Bashaikh

Lara Alsaleem

Rawan Alwadee

Abdullah alharbi

Abdulmajeed almutairi

Abdulmajeed alammar

Basel alanazi

Moayed Ahmed

Mohammed alhammad