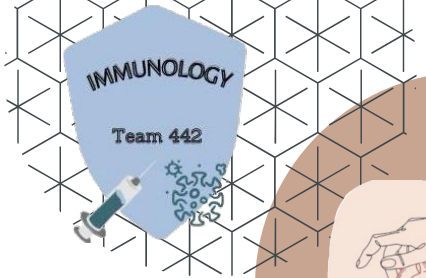
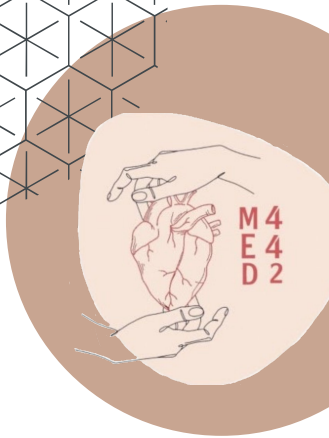
Foundation block

KSU





Cell Mediated Immunity

W6
L3

Color index :

- Main text
- Important
- Dr notes
- Females slides
- Male slides
- Extra

Editing File

Objectives:

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

Introduction:

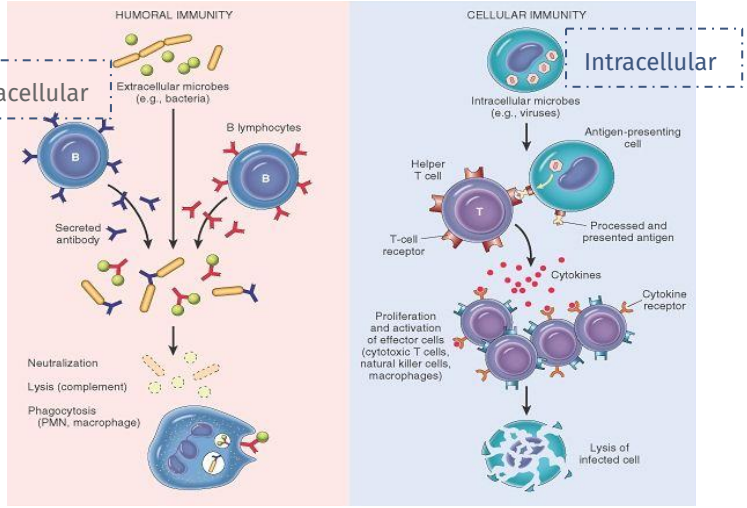
Adaptive Immunity

APC = Antigen Presenting Cell (slide 4)
MHC = Major Histocompatibility Complex (slide 5)

Helpful video

Humoral Immunity (abMI)

Cell Mediated Immunity (CMI)



Antigen + MHC (Major Histocompatibility Complex

↓

T-Lymphocytes

↓

Immune Response

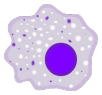
MHC: Processes **Antigen**, prepares it and **cuts** it into small fragments (peptides) and displays them on the **APC's** surface for **recognition** by the appropriate **T cells**

T cell (lymphocyte) via its receptors bind to the surface of the other cell (**APC**) and recognizes the **antigen** on **APC** surface which is held by the **MHC**

Mononuclear cells
One round nucleus (lymphocytes and monocytes)

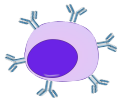
Mononuclear cell
inflammatory process usually associated with **chronic** inflammations

Antigen Presenting Cells (APCs)



Macrophages

Tissues



B-Cells

Lymphoid tissue, Blood

Monocytes

Peripheral blood

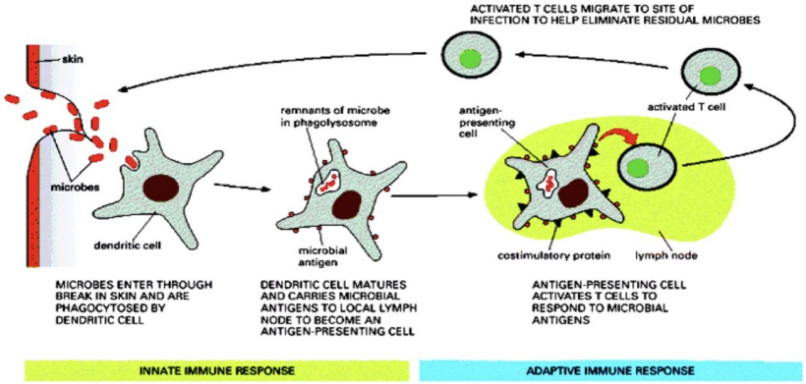
Dendritic cells

Lymphoid tissue,
Skin (Langerhans Cells)

439: **Monocytes** are in blood, but when there is tissue damage or infection they **leave** the bloodstream and transform to **macrophages**

Denetric cells found in skin are called (Langerhans Cells), which plays a major role in induction of adaptive immune response against allergens

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



Innate and adaptive immunity work together

Major Histocompatibility Complex (MHC)

Helpful video

Definition:

Glycoproteins

- MHC are membrane-bound surface receptors (protein molecules) on antigen-presenting cells
- CD4 and CD8 play a role in T cell recognition and activation by binding to either MHC I or MHC II
- These proteins were discovered for the first time when tissue transplantation started

باختصار هو عبارة عن بروتين ينتج من الرايبوسوم (آلة تصنيع البروتين) يطلع على سطح الخلية زي ال **receptor** لما يدخل بانوجين للخلية
يطلع عشان تتعرف عليه **T helper + T cytotoxic** عن طريق ال**TCR** وتعرف ان الخلية مصابة ببانوجين.(436)

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

Same as MHC

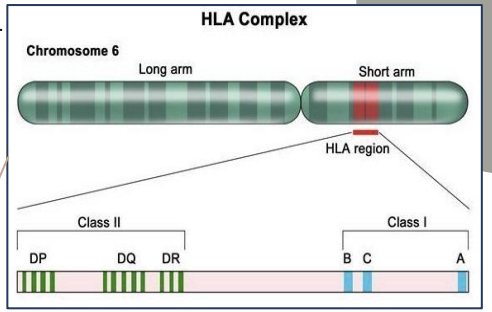
Genes for HLA proteins are clustered in the MHC complex located on the short arm of chromosome 6

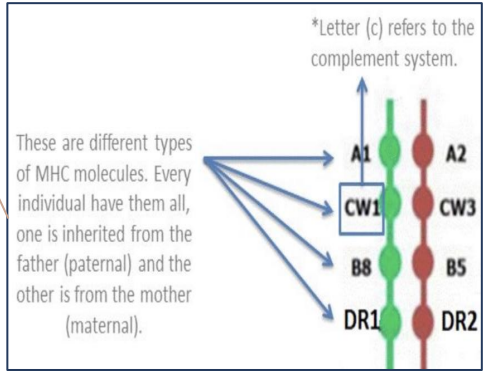
Each individual has two " haplotypes" ie, two sets of these genes one paternal and one maternal

Note 437: haplotype A (haploid genotype) is a group of genes in an organism that are inherited together from a single parent

Mononuclear cell inflammatory process usually associated with chronic inflammation

Note 438: Lymphocytes **T-B-NK** 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)

Helpful video

Thanks to Team439

	MHC I	MHC II
Location	Surface of all nucleated cells **Except RBCs**	Surface of Antigen presenting cells (APCs)
Association	**Endo**genous (reproduce in cytoplasm) (Intracellularly)	**Exo**genous (reproduce outside cell) (Extracellularly)
Antigen recognition (MHC restricted)	T cytotoxic (CD8) cells kill virus-infected cells and tumor cells	T helper (CD4) cells enhance CMI and production of antibodies by **B** cells
Transplantation	Organ transplant success is determined by the compatibility of MHC genes	

Have class I and II because they are both nucleated and have antigen.

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

Endogenous and Exogenous Presenting Pathways

Helpful video

Endogenous:

1 Infection

Pathogen (eg, virus) infect the cell with its own protein.

2 Dissociation

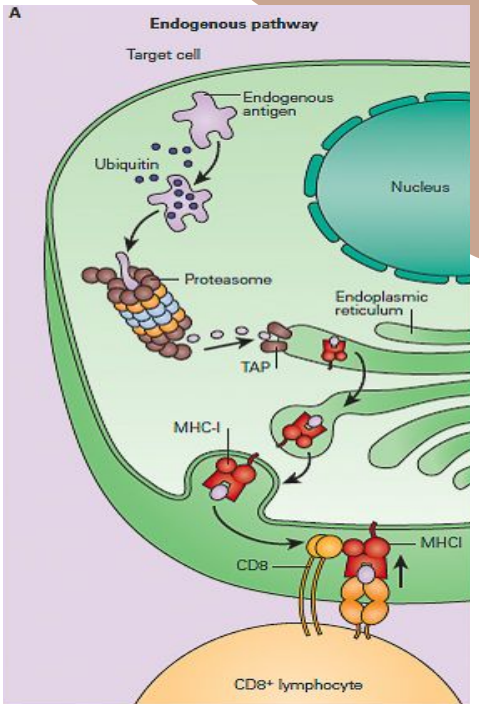
Viral proteins are taken to the Proteasome (where they are digested to peptide fragments).

3 MHC I Binding

The small fragments are transported by peptide transporter **TAP** (Transport associated with Antigen Processing) to rER where they bind with MHC I molecules.

4 Surface display

The MHC I-peptide complex is then transported to the Golgi Apparatus, where it secretes it to the surface of the cell. There it interacts with the receptor of a Cytotoxic CD8 cell.



Endogenous and Exogenous Presenting Pathways

Helpful video Helpful video

Exogenous

1 Interalization

The extracellular antigen (e.g. bacteria) is engulfed by an APC and surrounded by an intracellular vesicle known as a Phagosome (endosome)

2 Dissociation

The endosome fuses with lysosomes to form endolysosome, where the antigen is digested to peptide fragments

3 MHC II binding

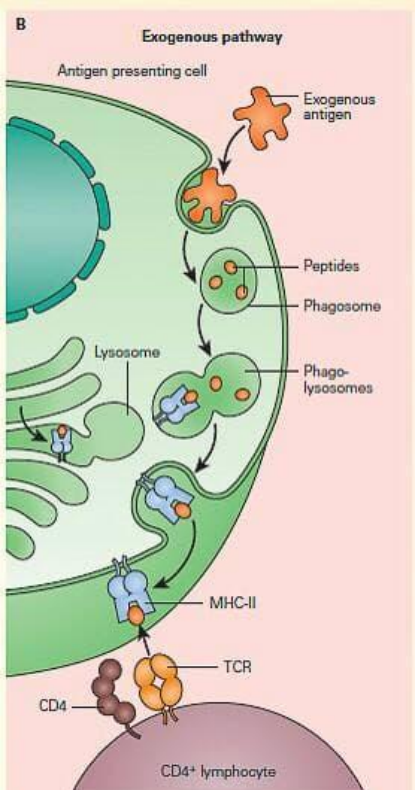
MHC Class II molecules are synthesized in the Rough ER. They are transported to the Golgi Apparatus, and then put inside a vesicle. This vesicle will bind with the endolysosome, where the antigen binds to the MHC class II molecule

4 Surface display

The MHC II-peptide complex is displayed on the surface of the cell, where it will interact with TCR* of a T helper (CD4) cell

*TCR: T Cell Receptor

Presented by class II



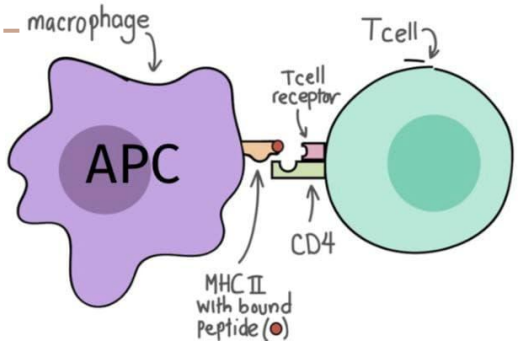
T lymphocytes

Supsets 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 cell
- NKT cells, and NK cells can also eliminate infected cells and abnormal tumor cells

- Natural killer T cell
- Natural killer cells

T-Cell activation



1. **First signal:**

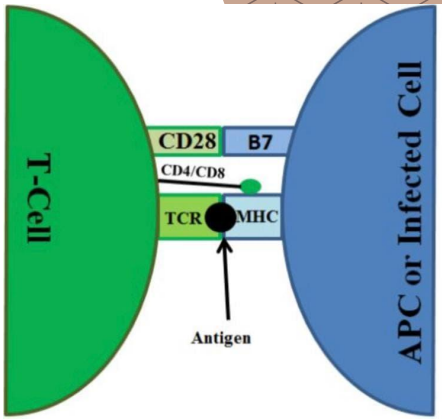
   Recognition and binding of MHC II (located on the surface of an APC) to TCR (T-cell receptor) and CD4 (T-cell Co-receptor) which leads to the production of:

- IL-1 (interleukin 1)
- LFA-1 (Lymphocyte Function-associated Antigen) with its ligand
- ICAM-1 (InterCellular Adhesion Molecule)

Helpful video

2. **Second signal:**

   Also known as Costimulatory signal Most important costimulators in this process are B7 (on APC) that binds with CD28 (on T helper lymphocyte)



first signal is not enough so we need second signal

Production of IL-2 and its receptor

- IL-2 is also known as T cell growth factor
- Proliferation تزايد of antigen specific T cells
- Effector and regulatory cells are produced along with "memory" cells
- **IL-2** also stimulates **CD8** cells

Outcome of T helper cell activation

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

Examples of Cell Mediated Immunity

- **Delayed type of hypersensitivity (DTH) reaction:** tuberculin test - Mediated by CD4+ T cells and takes about 72 hours to develop

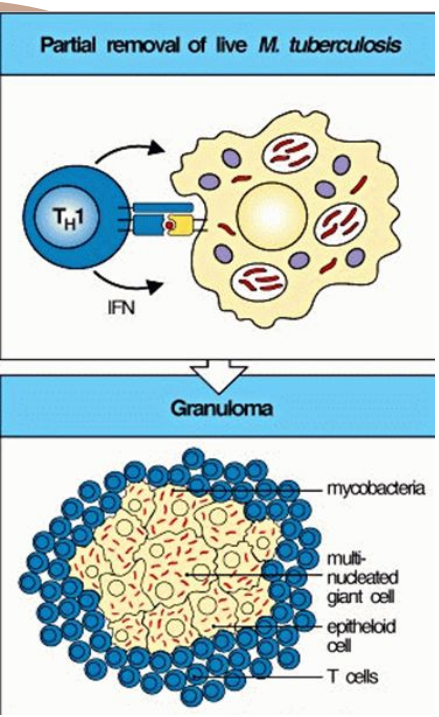
- **Contact hypersensitivity**
  Many people develop rashes on their skin following contact with certain chemicals such as nickel, certain dyes, and poison ivy plant. The response takes some 24 hours to occur and like DTH, is triggered by CD4+ T cells

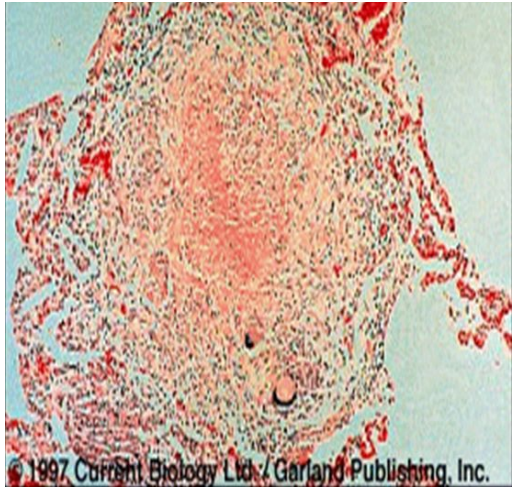
Contact Dermatitis

Necklace Rash

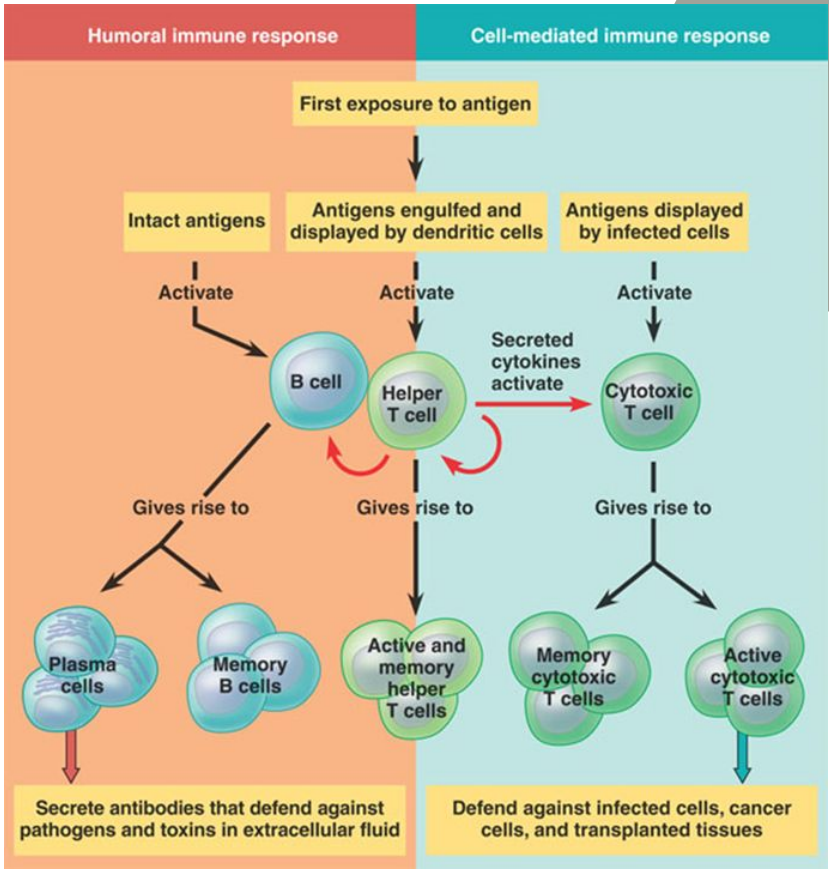
Granuloma
(Chronic Inflammation, e.g., TB)

Helpful video





Picture showing the overall process of Humoral and Adaptive immunity



Take home massages

1

Cell mediated adaptive immune response is specific and develops after exposure to a pathogen (antigen)

2

Initial antigen exposure results in generation of memory cells for a stronger & a quicker response against future exposures to the same pathogen

3

It is usually associated with chronic infections

4

Antibodies are not involved

MCQs

Q1-which of the following is an example of APC?			
A) monocytes	B)B-cells	C) langerhans cells	D) all of them
Q2-Antigen recognition is also called?			
A)Reproduction	B) Restrictivation	C) Restriction	D) None of the above
Q3- Which of the following is the location of the HLA?			
A)Long arm of chromosome 6	B)Short arm of chromosome 9	C)Short arm of chromosome 6	D)Long arm of chromosome 9
Q4- the cytotoxic T cells are associated with which class of MHC?			
A)class II	B) class I	C)class III	D)not associated

1:D
2:C
3:C
4:B

MCQs

Q5- Which of the following cells digest invading microbe?			
A) Denetric cells	B)Microphages	C) B-Cells	D)A&B
Q6-Endogenous will be treated by any cell?			
A)CD28	B) CD8	C) CD3	D) CD4
Q7- The response of hypersensitivity is triggered by?			
A)APCs	B)CD4+T cells	C)CD4+APCs	D)Antigens

3:B
2:B
1:D

Special thanks to
Immunology Team 441

Team Leaders:

Reema Mohammed - Mohammed ibn Saqyan

Team members:

- Mayssam Aljaloud
- Raneem Alwatban
- **Maha bakheet**
- Raghad Bander
- Reema Alhussien
- Walaa AlMutawa
- Shahad Aljeri
- Mohammed AL-Zeer
- Rayan Bosaid
- **Mohammed Alhussini**
- Ahmad almarshed
- Qusai alsultan
- Faisal Alkhunein
- Abdullah Alshamrani

immunologymed442@gmail.com