MED441
KING SAUD UNIVERSITY

Cell mediated immunity

Revised & Reviewed by: Abdulaziz & Bahammam
Faye Wael Sendi

Colour index:
Main text
IMPORTANT
Drs 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)

Quick introduction

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

Helpful video

- Types of Immunity
  - Innate (Natural) Immunity
  - Adaptive (Acquired) Immunity
    - Humoral immunity (AbMI)
    - Cell Mediated Immunity (CMI) — This lecture now

Immune response in which antigen specific **T cells** dominate.
"**Cell-mediated**" refers to the fact that the response is carried out by **cytotoxic** cells and will occur **inside** the cell.

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**

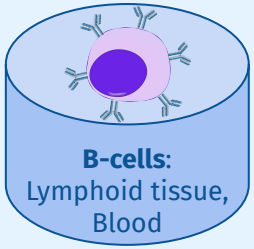
MHC: Processes **Antigen**, prepares it and **cuts** it into small fragments (peptides) and displays them on the **APC's** surface for **recognition** by the appropriate **T cells**

Antigen + MHC (Major Histocompatibility Complex) → T-Lymphocytes → Immune response

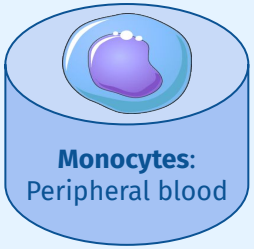
Everything will be explained in detail later

Antigen Presenting Cells (APC)

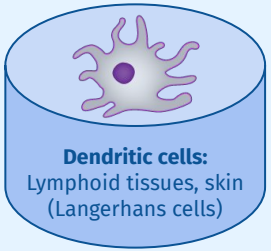
What are APCs? Antigen presenting cells are immune cells that specialize in presenting an antigen to a T-cell. A professional APC takes up an antigen, processes it, and returns part of it to its surface, along with a major histocompatibility complex (MHC). The T-cell is activated when it interacts with the formed complex.



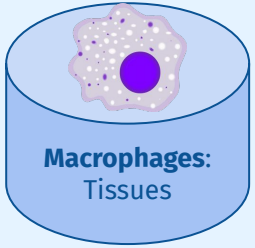
B-cells:
Lymphoid tissue, Blood



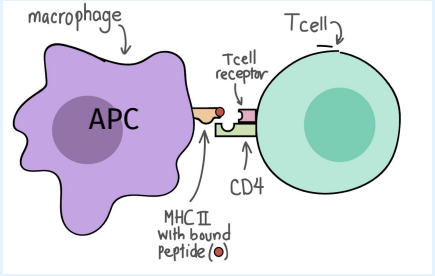
Monocytes:
Peripheral blood



Dendritic cells:
Lymphoid tissues, skin (Langerhans cells)

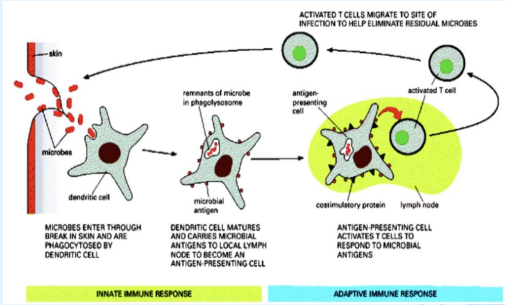


Macrophages:
Tissues



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

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



Major Histocompatibility Complex (MHC)

Helpful video

Definition

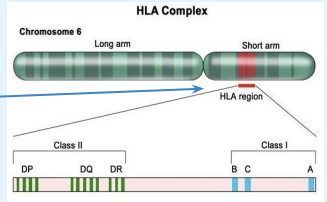
- MHC are membrane-bound surface receptors (protein molecules) on antigen-presenting cells موجودة على سطحها
- CD4 and CD8 play a role in T cell recognition and activation by binding to either MHC I or MHC II (in next slide)
- These proteins were discovered for the first time when tissue transplantation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

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

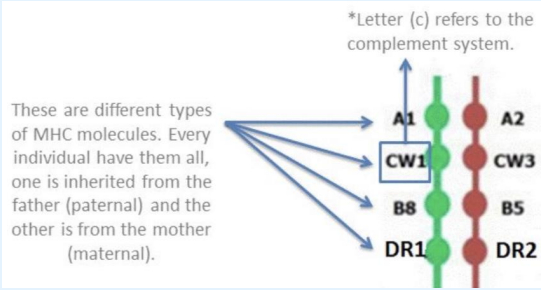
The success of tissue and organ transplantation depends upon the match of donor's and recipient's "human leukocyte antigens" (HLA) encoded by HLA genes

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

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



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)

Thanks to Team439

Helpful video

Helpful video

	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	

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

Endogenous and Exogenous Presenting Pathways

Helpful video

زبدة الكلام عشان يتحقق عندنا المبتغى الأساسي للمناعة الspecific ونكوّن memory cells لازم الدخيل على الخلية antigen يصير له processing و presentation للخلايا المناعية T. هذا الpresentation المسؤول عنه الMHC

There are two pathways in which an MHC molecule presents the Ag (antigen) to the T cells based on whether it is an endogenous or exogenous (as mentioned in previous slide)

Endogenous

Dissociation

Viral proteins are taken to the Proteasome inside the cell (where they are digested to peptide fragments) {after infection}

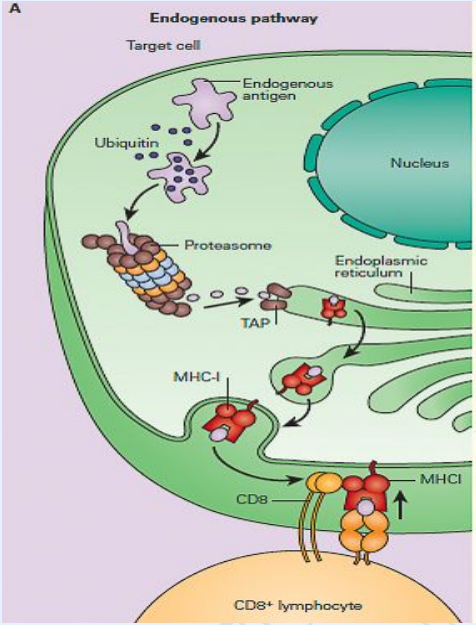
The virus can't produce its own protein, so the cell will act as if the protein is its own

MHC I Binding

The fragments are transported by TAP (Transporters associated with Antigen Processing) to the Rough ER where they bind with MHC Class I molecules.

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

An **AWESOME** summary by one of the students! Click here!

Exogenous

Interalization

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

Dissociation

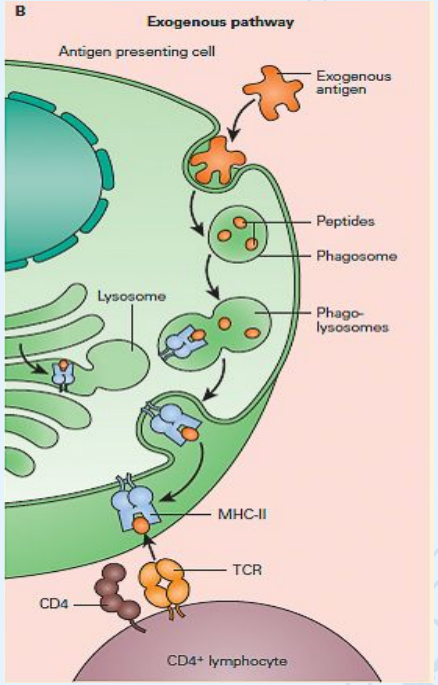
The endosome fuses with lysosomes to form endolysosome, where the antigen is digested to peptide fragments

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

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

T-Cell activation

★Thanks to Teams 438 + 439

☆Helpful video

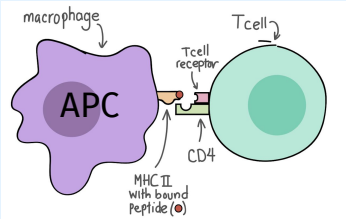
First signal:-

Class I - endogenous
Class II - exogenous

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)

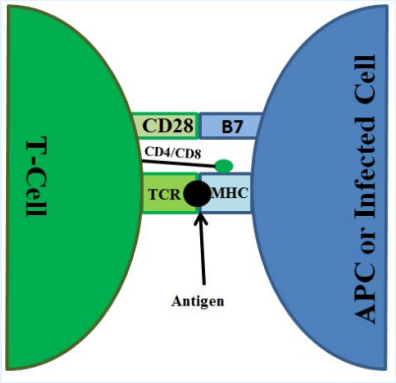
Without IL-1, LFA-1 and ICAM, the **first** signal is **impaired** ضعف which causes a **dysfunction** in T helper cells, leading to intracellular **infections**



Second signal:-

Also known as Costimulatory signal

Most important costimulators in this process are **B7**(CD80/86) (on APC) that binds with **CD28** (on T helper lymphocyte)



Outcome of T helper cell activation

Production of IL-2 and its receptor (CD25)

- ★ 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** cytotoxic cells

Memory T cells

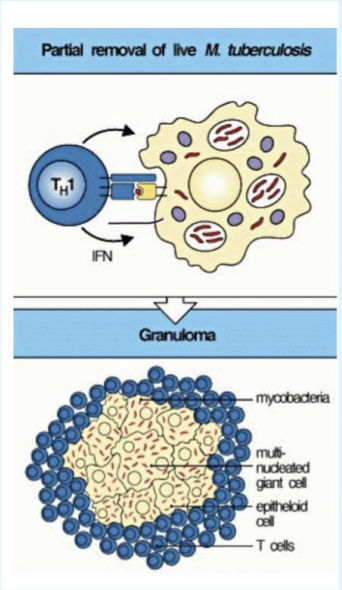
- ★ Respond rapidly for many years after **initial** exposure to antigen
- ★ A large number of memory cells are produced so that the **secondary** response is greater than the **primary**
- ★ Memory cells live for many years and have the capacity to multiply
- ★ They are activated by smaller amount of antigen
- ★ They produce greater amounts of interleukins

Note: also called Antigen experienced T cells

Production Of Interferons

- ★ Enhances anti-microbial activity of macrophages

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



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

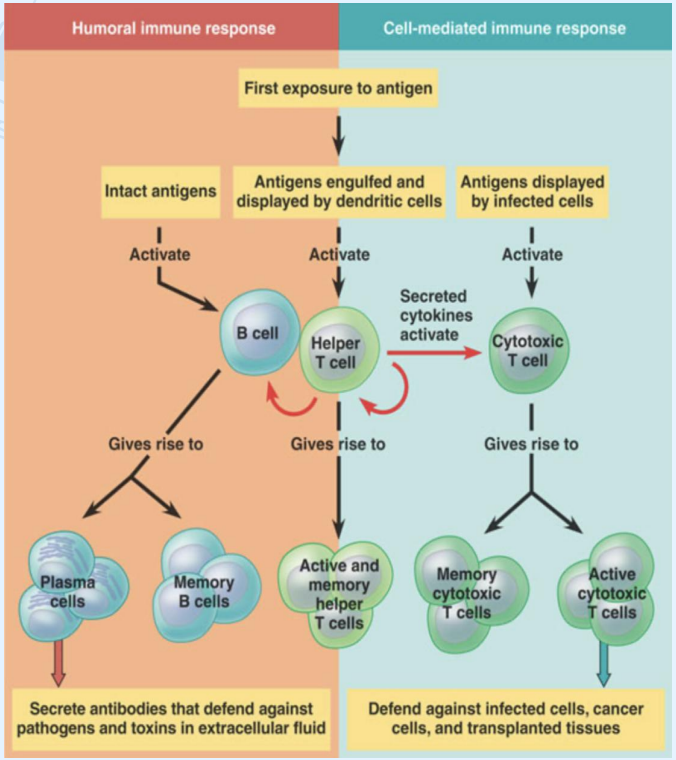
Necklace Rash

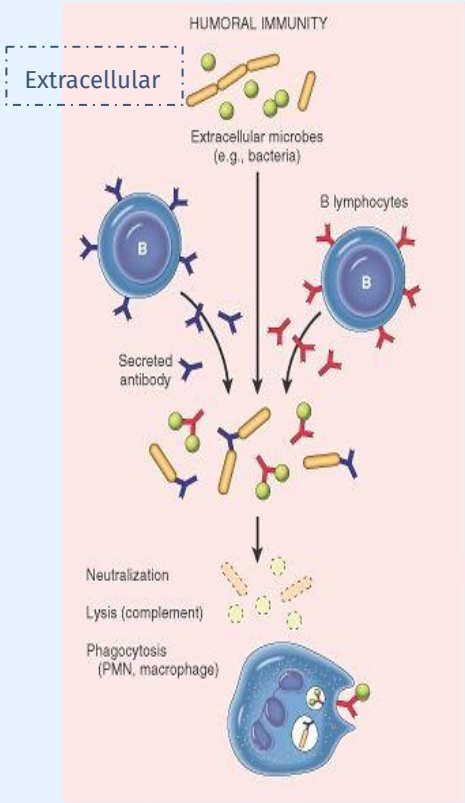
Contact Dermatitis

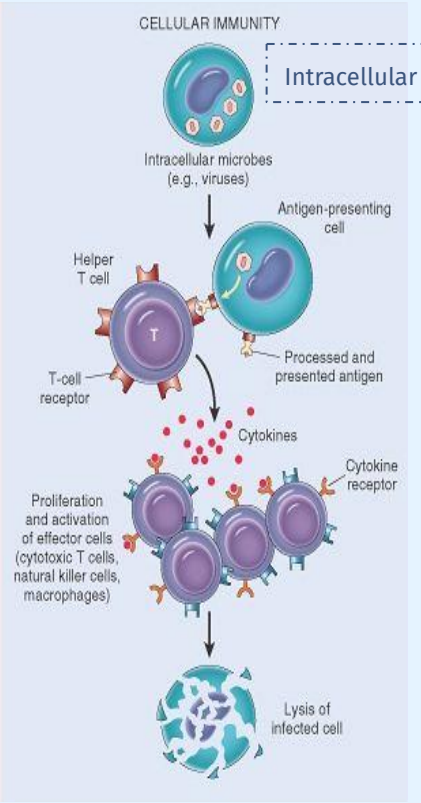
Pictures showing the overall process of Humoral and Adaptive immunity

(Humoral immunity will be discussed next lecture)

Summary video (recommended)







Take Home Messages

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:where can you find class I MHC?			
A- cytoplasm	B- surface of the cell	C- nucleus	D- in the plasma
Q3: CD4 cells are associated with which class of MHC?			
A- class I	B- class III	C- class II	D- not associated
Q4: exogenous antigen will be treated by any cell?			
A- CD4	B- CD8	C- CD3	D- CD28

Q1-D, Q2-B, Q3-C, Q4-A

MCQs

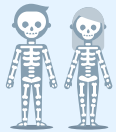
Q5: what does memory T cells do?			
A- decrease the response time than the initial exposure	B- help B cells	C- kill the infected cell	D- produce the NK cells
Q6: what is the result of activating T helper cell?			
A- production of IL-2	B- production of interferons	C- activate of T memory cells	D- all of them
Q7: the cytotoxic T cells are associated with which class of MHC?			
A- class II	B- class I	C- class III	D- not associated
Q8: endogenous antigen will be treated by any cell?			
A- CD28	B- CD3	C- CD8	D- CD4

Q5-A, Q6-D, Q7-B, Q8-C

Special thanks and gratitude to
Immunology Team (439)

Team leaders:

Yara Almufleh - Ibrahim Alahmadi



Team members:

- Sarah Alhamlan
- **Sahar Hakami**
- Maram Alenazi
- **Lama Bin Salamh**
- Rahaf Alrayes
- Areej Altamimi
- Leen alhadlaq
- Shaimaa Alqaoud
- Rahmah Alzahrani
- Aisha Alhamed
- Abdulaziz Annab
- Firas Alqahtani
- Mohammed Alfaris
- **Turki Alkhalifa**
- Abdulaziz Ayman

Immunology441@gmail.com