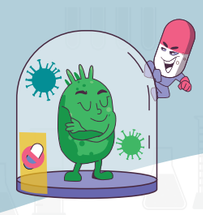
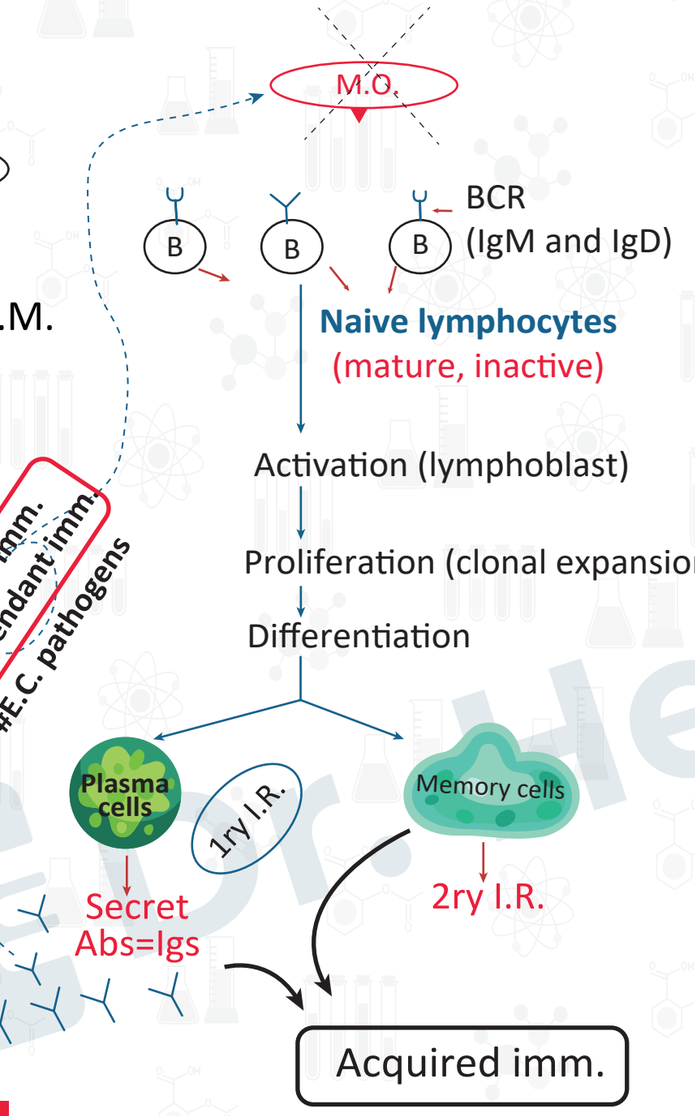


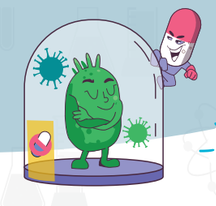
Chapter 4: T-cell mediated imm.

1 B-cells

10% of PBLs

- **Origin :** B.M.
- **Maturation:** B.M.

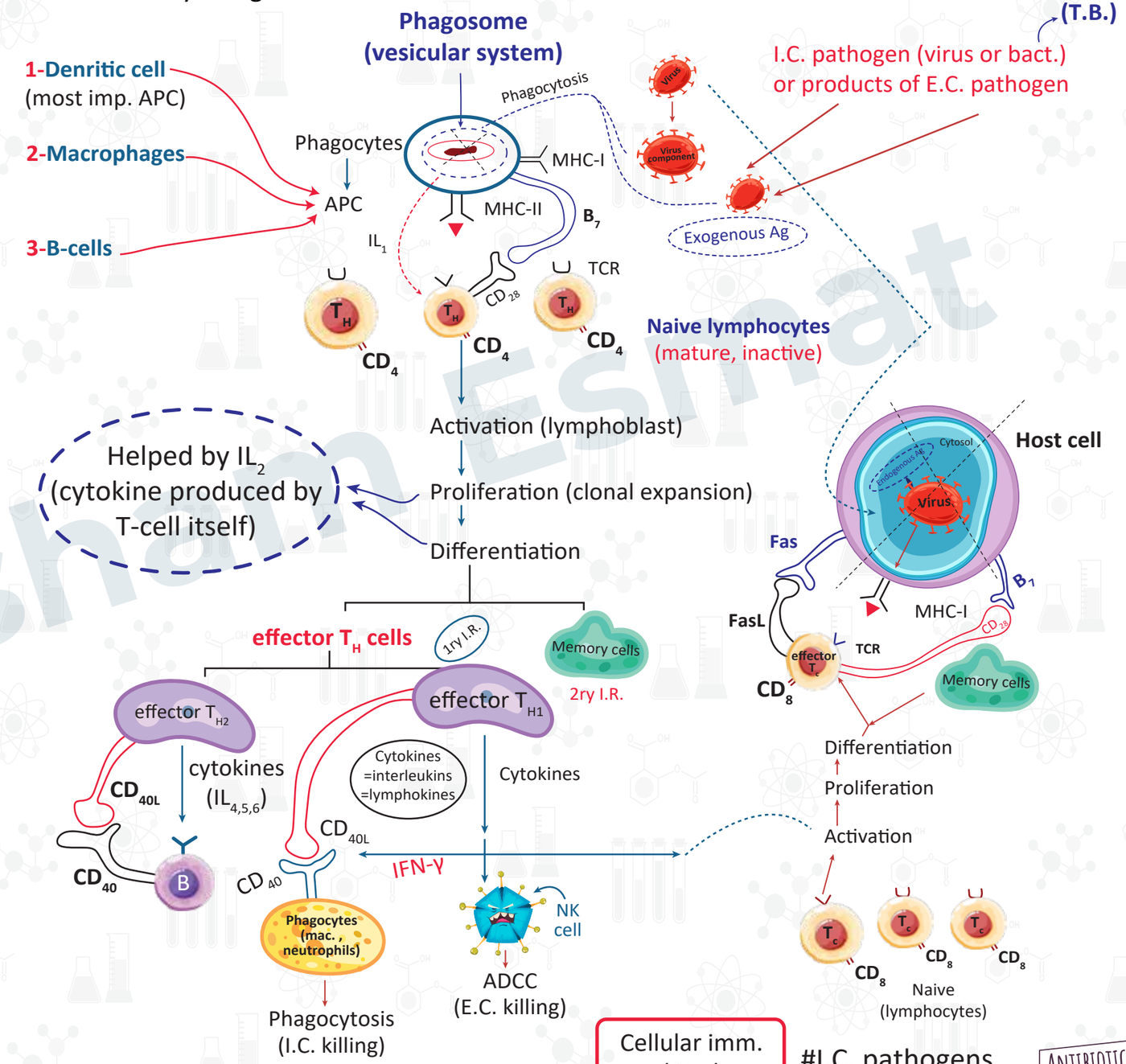


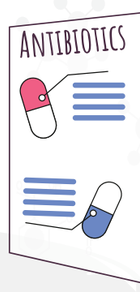


2 T-cells

75% pf PBLs

- **Origin :** B.M.
- **Maturation:** Thymus gland





Immunity (4)

Professional APC

Only cells capable of activating Naive T-cells

- Present in L.Ns → trap Ag and present it to recirculating T-cells

1 Dendritic cells

- The most imp. and most efficient Apc
- So called → have projections (Dendrites)
- Present in all tissues of the body

2 Macrophages

- Imp. phagocytic cell (innate I.R.)
- Their action as APC allow them to help acquired imm.

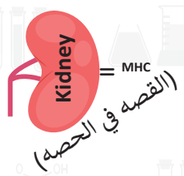
3 B-cells

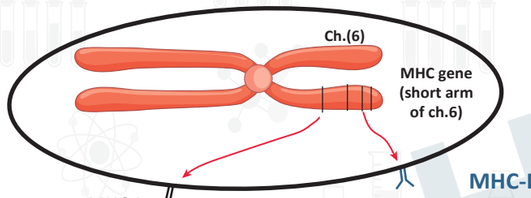
- Humoral imm. cell
- Also they act as APC

MHC = HLA

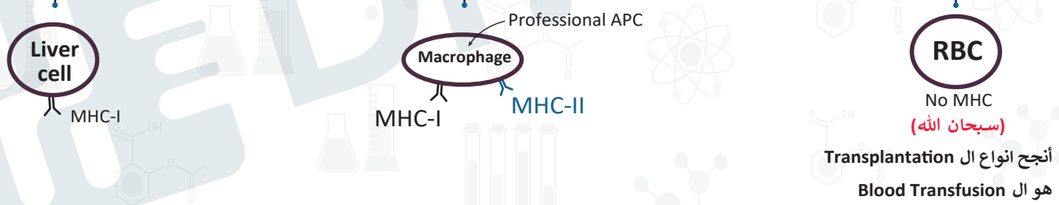
(Major Histo-comptability complex)
يحدد توافق الانسجه

(Human leucocyte Ag)
(1st Discovered on WBCs)



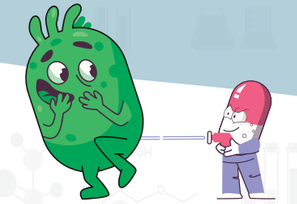


MHC: Cell surface glycoptns

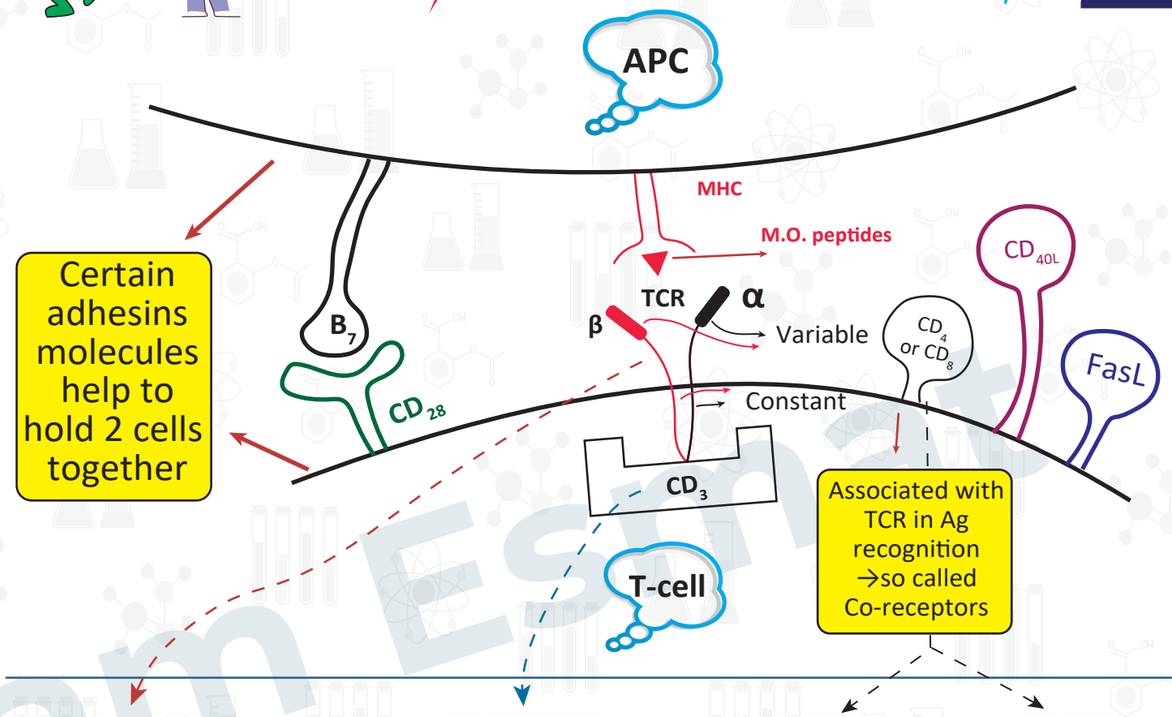


NK # Tc

- Innate imm. cell → imp. in early stages of inf.
- Not MHC restricted → recognize Ag without MHC
- Non specific
- Abs can help NK to recognize abnormal cell→ ADCC



T cell surface molecules



1 TCR

- 2 p.p. chains (α , β)
- **Both chains have:**
  1) Constant part (near cell memb.)
  2) peripheral Variable part
- Variable part → Detect Ag recognized
- All TCRs on single T-call are identical and recognize the Same Ag
- Small proportion of TCR → 2 different chains (δ,γ) → differ from other T-cell in recognition & effector mechanisms

2 CD_3 Rec.

- Close to TCR on all T-cells
- 1st signal for T-cell activation

3 CD_4 Or 4 CD_8

- On T_H cells → Secret cytokines (++ other Imm. Cells)
- Also on T_{reg} → Inhibit IR

- On T_c cells → Kill infected cells + tumor cells
- Also on T_S → Inhibit IR

5 CD_{40L}

- Present on activated T_H
- Activation of B-cells and mac. by T-cells

6 CD_{28}

- Present on all T-cells
- Binds to B_7 on APC→2nd signal for T-cell activation
- So, called→ Co-stimulatory molecule
- Without its binding to B_7 on APC → NO T-cell respone → Anergy

7 FasL

- On activated T_c
- Bind to fas (on diff. body cells)→ killing of target cells by T_c

Dr Reshan Essa

Ag presentation to T-cells

- For Ag to be presented to T-cells → must 1st enter APC → degradation (Ag processing)

Peptide → Carried inside cleft on MHC (on cell surface) → Ag Presentation to T-cells

on Type I or Type II → depends on the part of the cell in which the pathogen is present

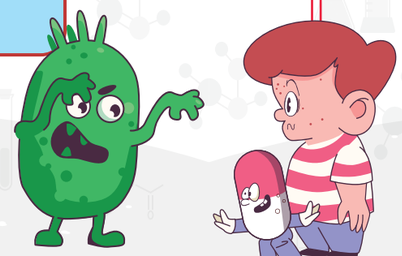
	Cytosolic (endogenous) Ags	Vesicular (exogenous) Ags
Exampe	**1-** All Viruses **2-** Some bact. → (I.C. bact.) → (as T.B.)	**1-** I.C. bact. (T.B.) **2-** Viral components **3-** E.C. bact. & their products(Toxins)
Degraded in	Cytoplasm	Vesicles
Peptides bind to	MHC-I	MHC-II
Presented to	CD_8 T_c cells	CD_4 T_H cells
Results	Cytotoxic killing of presenting cell by CD_8 T_c cell	Secretion of cytokines by CD_4 T_H cell → help all other imm. cells

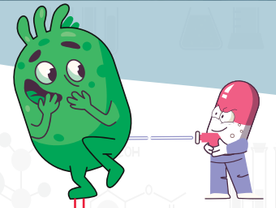
Sequence of events of activation of Naive T-cells

See Papers (page 81, 82)
مراجعة الكلام

N.B

- Effector T-cell differ from naive T-cell in:
  - **1)** Ready to start their function
  - **2)** Act as soon as their TCRs bind their specific MHC-peptide complex **(signal 1)** → without need for Co-stimulation **(signal 2)**





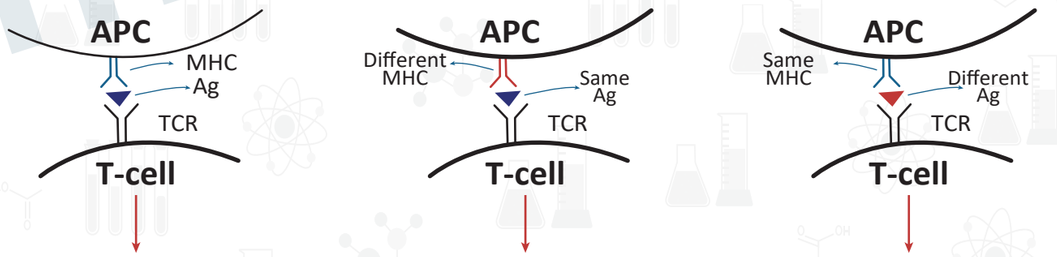
MHC Restriction

(Ag recognition by T-cells is restricted by MHC)

- **CD_8 T_c cells** → MHC-I resricted
- **CD_4 T_H cells** → MHC-II resricted
- **MHC polymorphism**
  - 1 cell may have many different MHC-I & MHC-II
  - Differences between MHC on cells of different people

TCR is specific to whole MHC-peptide complex (Not peptide alone)

T-cell can recognize certain peptide only bound to certain MHC and will not recognize the Same peptide bound to different MHC



Significant points related to functions of T-cells

See Papers (page 85, 86)
مراجعة الكلام

CMI

See Papers (page 87)

Functions of effector T-cells

1 Effect TH cell → Secret cytokines

1 Effector T_{H1}

Secret cytokines (most imp IFN-γ)

++ Macrophages

1- ++ Fusion of phagosome and lysomes

2- ++ Production of O_2 radicals and NO and anti-bact . Enz by mac

(Effective killing of I.C.bact.)

Can cause significant tissue damage

It's absence → Disseminated inf.
e.g. Seen in AIDs pt. with T.B. inf.
(since number of T_H cells is very low)

2 Effector T_{H2}

Secret cytokines IL 4,5,6

++ B cells

- Humoral imm.

2 Effector T_c Cells

- Eliminate virus infected cells or tumor cells by lethal hit

1 Induction of apoptosis (suicide of largest cells)

(main mechanism)
(faster)

1- Release of cytoplasmic granules

- T_c release two granules

Perfornis

- Causes holes (perforations) in the cell memb. of target cells

granzymes

- Enter target cell → ++ Enz in the target cell → DNA degradation

2- Interaction of cell surface molecules

- Fas (on mamy cells) → bind to FasL (on T_c cells) → Signal for apoptosis in target cell

2 Osmotic lysis

- Pores produced in target cells by perforins → fluid entry into the cell → Death by osmotic lysis

Apoptosis

- Clean cell death → Cell destroys itself (the enz. activated to destroy cellular DNA and can also degrade N.acids of I.C. pathogens → -- spread of inf.)

	Ordinary Ag	Super Ag
Processing inside APC	Yes	No
Presentation by MHC	Yes	No
Site of binding to MHC	Peptide binding cleft	Outside peptide binding cleft
Binding to TCR	Variable part of α and β -chains	Variable part of β-chains → Clamp between TCR and variable part of β-chains
Specificity of TCR to it	Very specific	Not very specific →Large number of T_H cells are activated → release of huge amounts of cytokines
Acquired IR	++	--
Development of memory	Yes	No
Result of T-cell stimulation	Beneficial to host	Harmful to host (systemic toxicity)
E.g.		1- Staphylococcal enterotoxin 2- Staphylococcal TSST