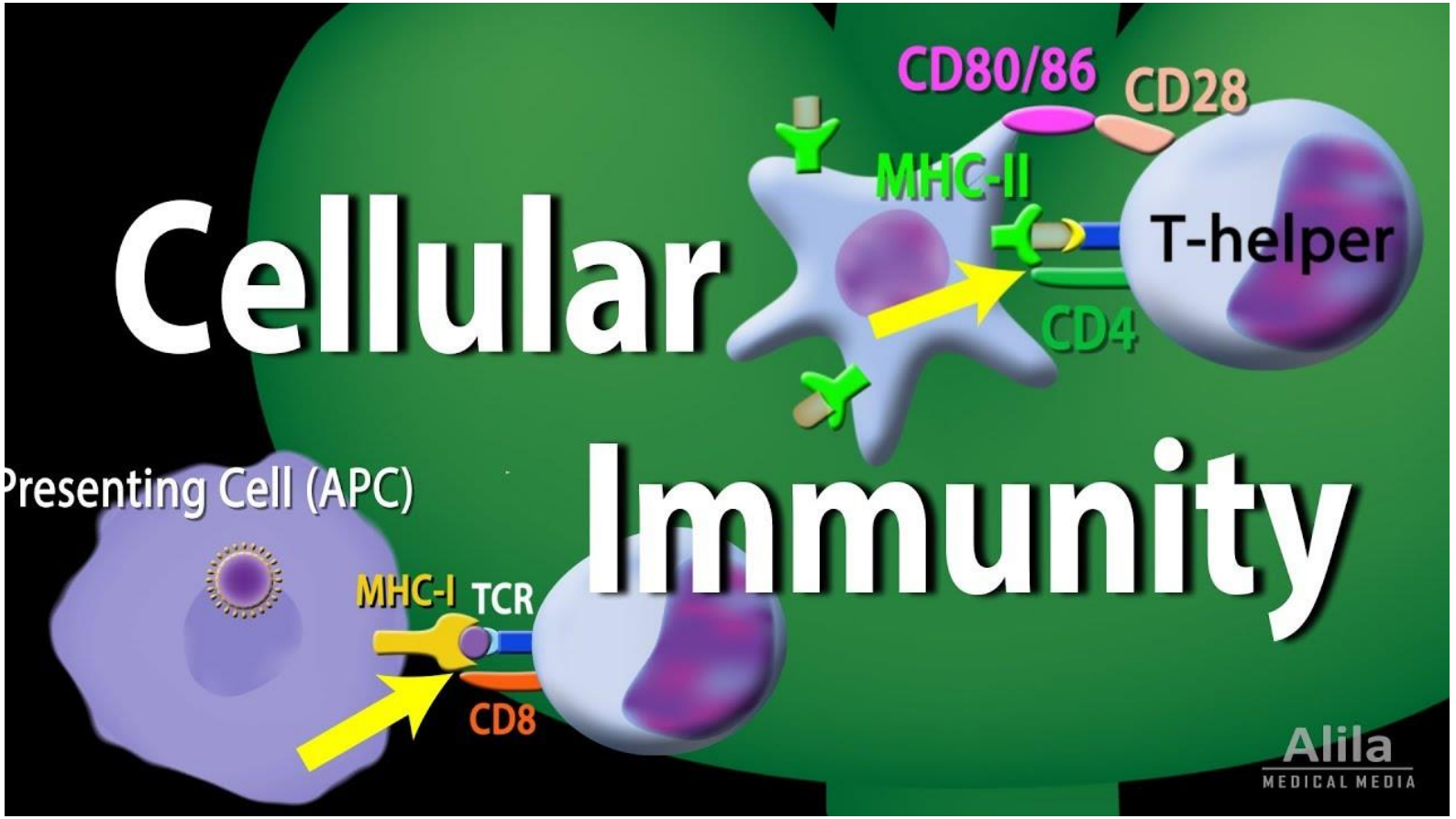
MIRACLE
Academy

قال تعالى (يَرْفَعِ اللَّهَ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)

تفريغ المناعة
زميلتكم جنين الخطيب

لجان الرُّفعات

Adaptive Immunity
Cellular Immunity



Objectives

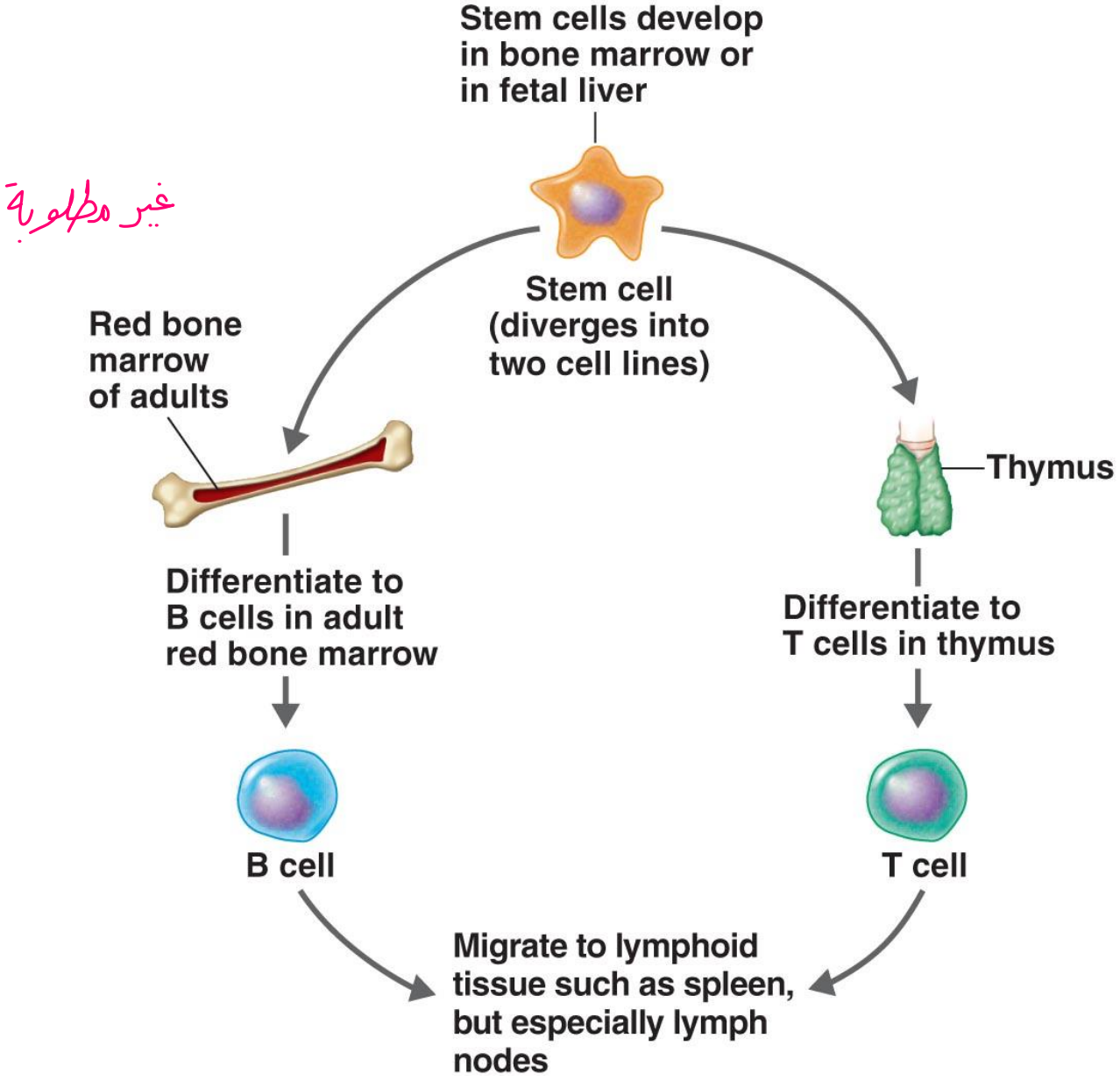
- Explain the principles of adaptive immunity
- Introduce the immune cells that mediate adaptive immunity and their specific roles
- Discuss the differences between cell-mediate immunity and humoral immunity
- Explain what interactions are required for activation of T cells and B cells
- Discuss the stages of cellular and humoral immunity
- Discuss immunological memory and outline the differences between primary and secondary responses
- Compare and contrast the innate and adaptive immune response

Adaptive Immunity

- **Adaptive immunity:**
  - Induced resistance to a specific pathogen
  - Learnt by experience أول مرة تكون استجابة بطيئة بعدين بتصير أسرع
  - Confers pathogen-specific immunity
  - Enhanced by second exposure
  - Has memory
  - Is poorly effective without innate immunity

1. **Humoral immunity:** B cells and antibodies
2. **Cellular immunity:** Due to T cells and cytokines

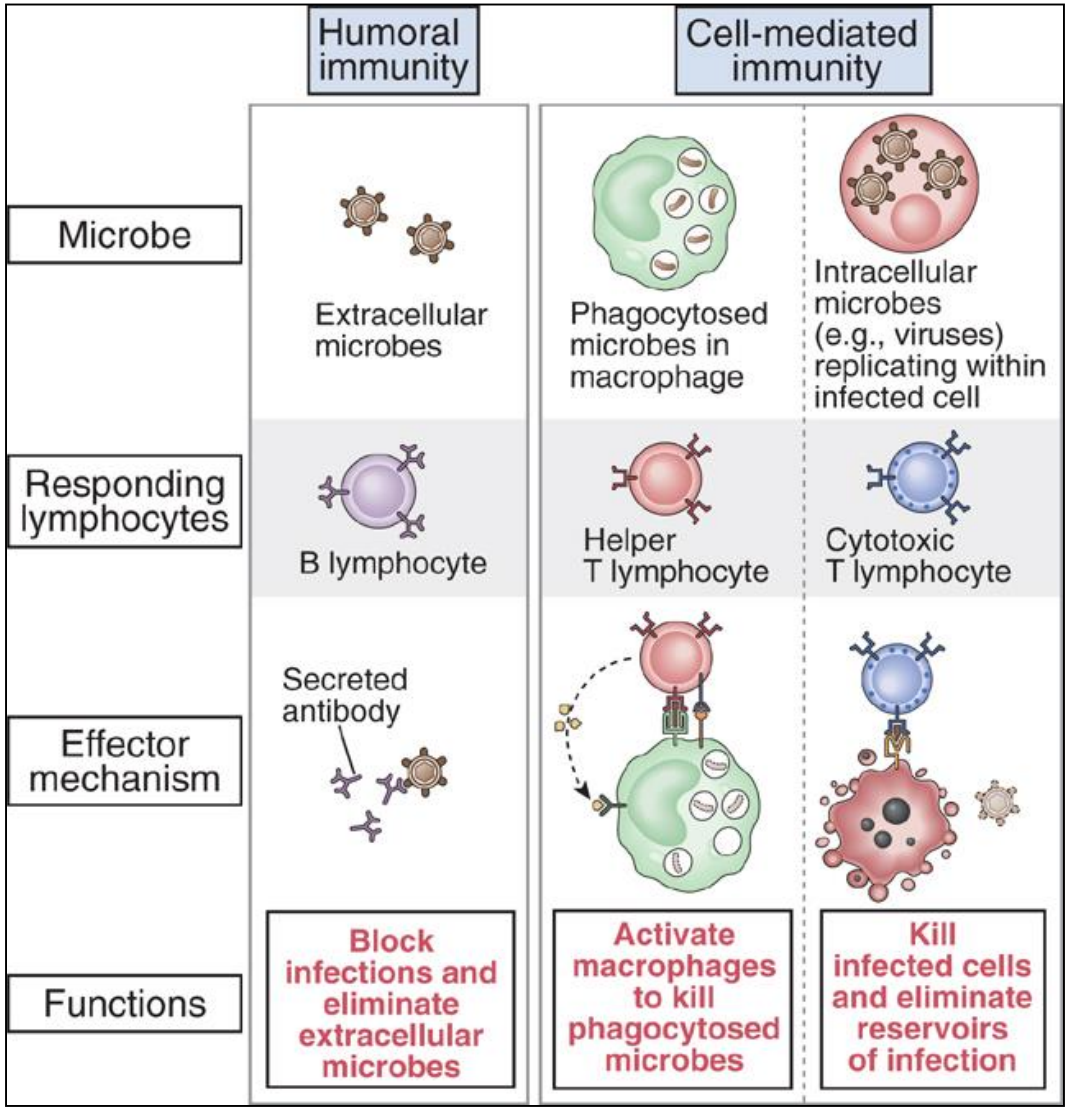
Dual Nature of Adaptive Immunity



Types of Adaptive Immunity

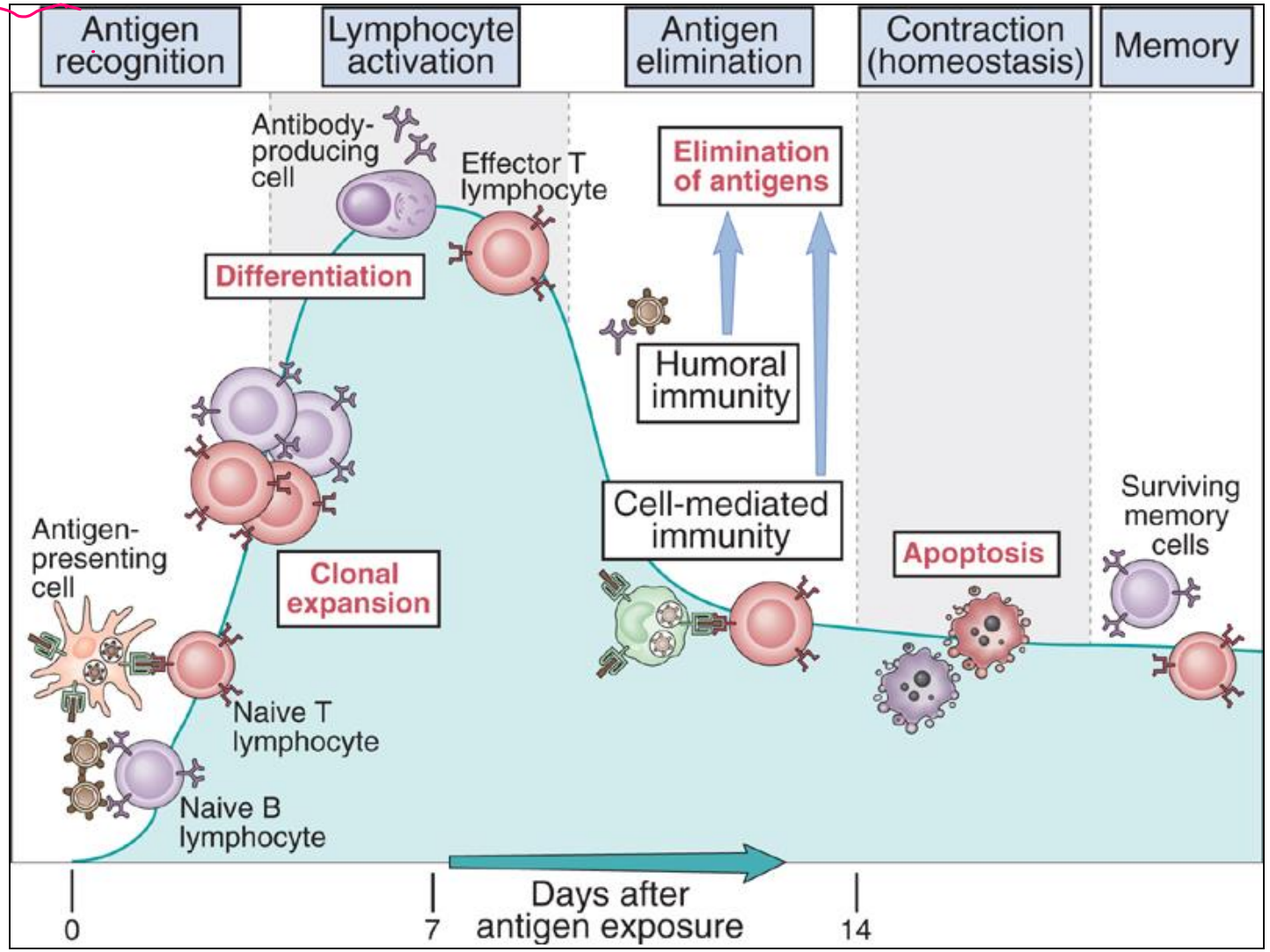
مطلوبة

Comparassion between Humoral and Cell mediated immunity.



Phases of Adaptive Immune Responses

غير مطلوبة



Cellular Immunity

T Cells and Cellular Immunity

- This type of immunity is performed by T cells to compate infection by intracellular microbes
- Intracellular infections include:
  - Microbes ingested by macrophage that resist microbicidal activity of macrophage
  - Viruses that binds to cells receptors and replicate in the cytoplasm of these cells
- T cells help B cells to produce antibodies
- T cells interact with other cells of the immune system
- Types of T cells:
  1. Helper T cells
  2. Cytotoxic T cells
  3. Regulatory T cells

ما بيشتغلو بمعزل عن بعض، التنين بيشتغلو مع بعض وبيعتمدوا على بعض cell mediated والـ humoral

Stages of Cellular Immunity

1. Antigen processing and presentations (APC's and MHC's)
2. T cells recognize and bind to Ag by T-cell receptors **(TCRs)**
3. Activation and signaling
4. Clonal expansion and differentiation of T cells
5. Effector functions
6. Shut down of immune response and formation of T memory cells

هاد أخدناه بمادة الفيرست بالتفصيل ودرسنا انه الـ antigen لحتى يصير اله recognition عن طريق الـ T cells لازم يصير اله presentation بالأول وأخدنا كيف .

1. Antigen Processing and Presentation

- Naïve T cells can not recognize antigens directly before processing
- The antigens need to be processed and displayed by MHC molecules on professional antigen presenting cells
- For details see lecture on antigen presentation and processing

2. Recognition and Binding

- Naive T cells circulate through peripheral lymphoid organs
- T cells posses specific receptors that bind antigen ligands on APCs these receptors called TCR

Antigen presenting cells.

Antigen + MHC (APCs) – Adhesion molecule – T cell

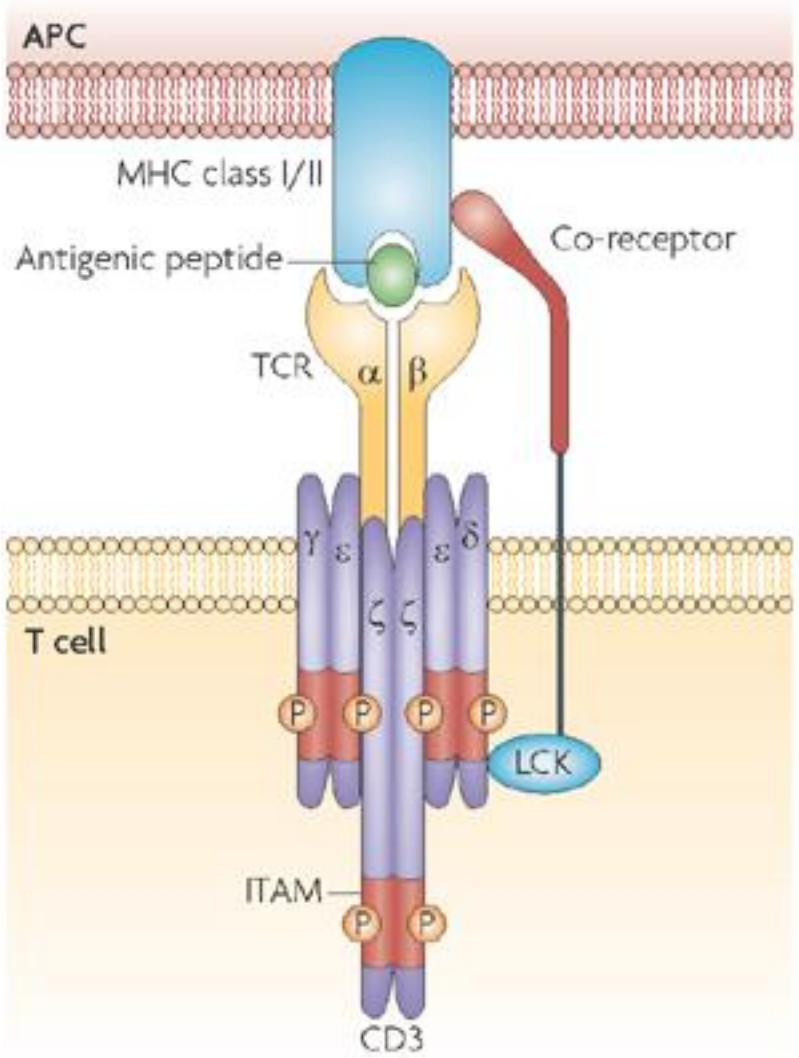
- TCRs bind epitopes associated with a MHC protein
- Adhesion molecules strengthen the binding of T cells to APCs through integrin, selectins, LFA (leukocyte function-associated antigen)-1, CD2 adhesion molecules

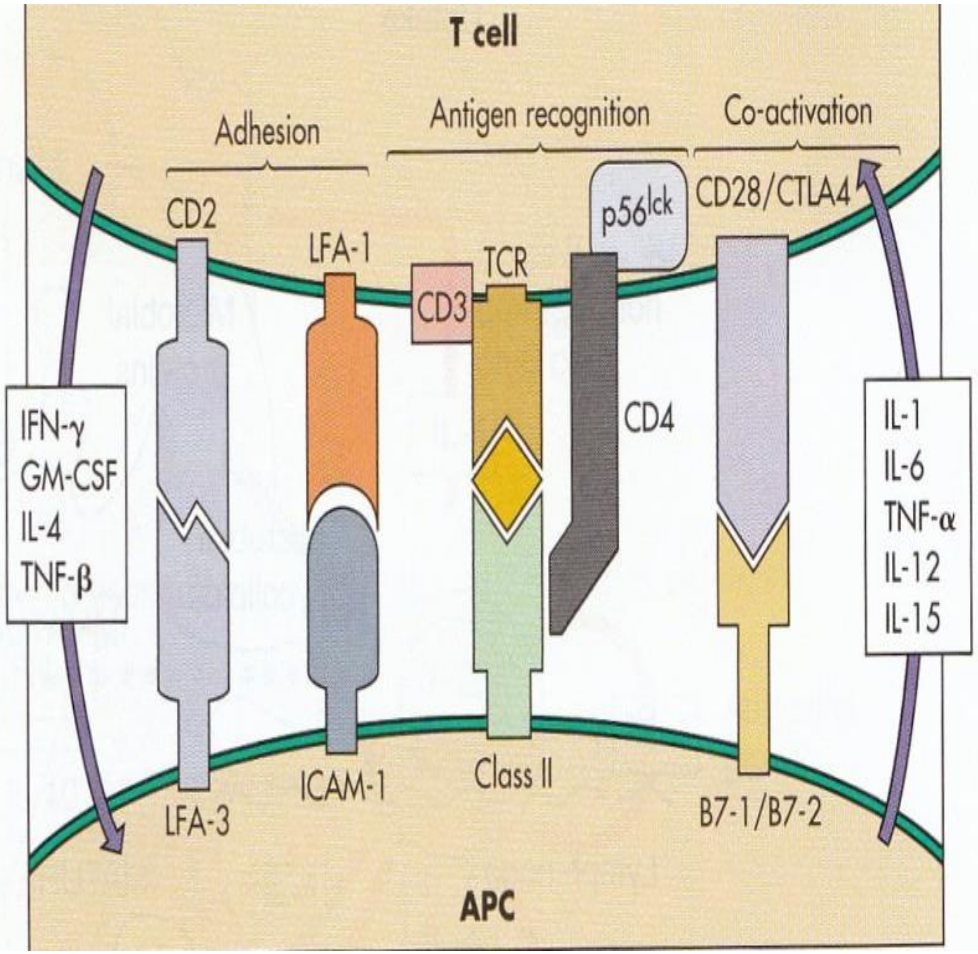
Examples on adhesion molecules.

① ② ③ ④

طبعًا أنا ليس بيهمني انه يكون الارتباط قوي، لحتى أقدر بعدين أنتقل للخطوة اللي بعدها ويعمل Signaling ويعمل Activation

غير مطلوبة


APC
MHC class I/II
Antigenic peptide
Co-receptor
TCR
α
β
γ
ε
ε
δ
ζ
ζ
T cell
P
P
P
P
LCK
ITAM
P
P
CD3


T cell
Adhesion
Antigen recognition
Co-activation
CD2
LFA-1
TCR
CD3
p56lck
CD28/CTLA4
CD4
IFN-γ
GM-CSF
IL-4
TNF-β
IL-1
IL-6
TNF-α
IL-12
IL-15
LFA-3
ICAM-1
Class II
B7-1/B7-2
APC

3. Signaling and Activation

ايش الأشياء اللي بتحفز انه يصير Signaling للـ Tcell ؟؟

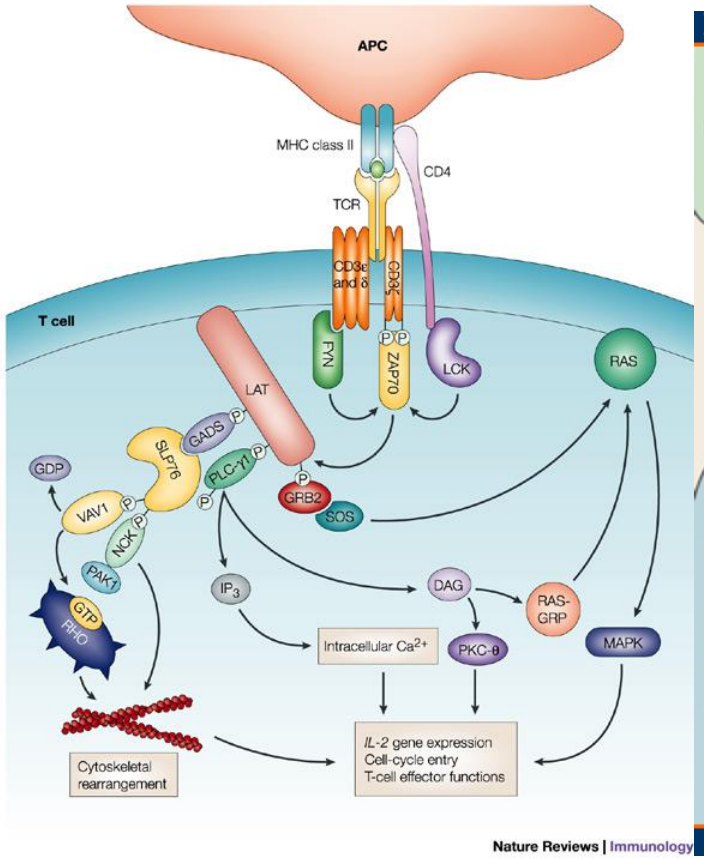
1. MHC + antigen – TCR binding and activation of CD3 and zeta chain do the function of signaling (**TCR complex**)
2. Co-receptors including CD4 and CD8 play role in signaling
3. Other accessory molecules including CD45 and CD2 participate in signaling
4. Co-stimulatory signal
   - B7 on APC interacts with CD28 on lymphocyte
   - Receptors for co-stimulation recognize second signal provided by APCs
   - Without co-stimulation T cells remain **not active** (anergy)

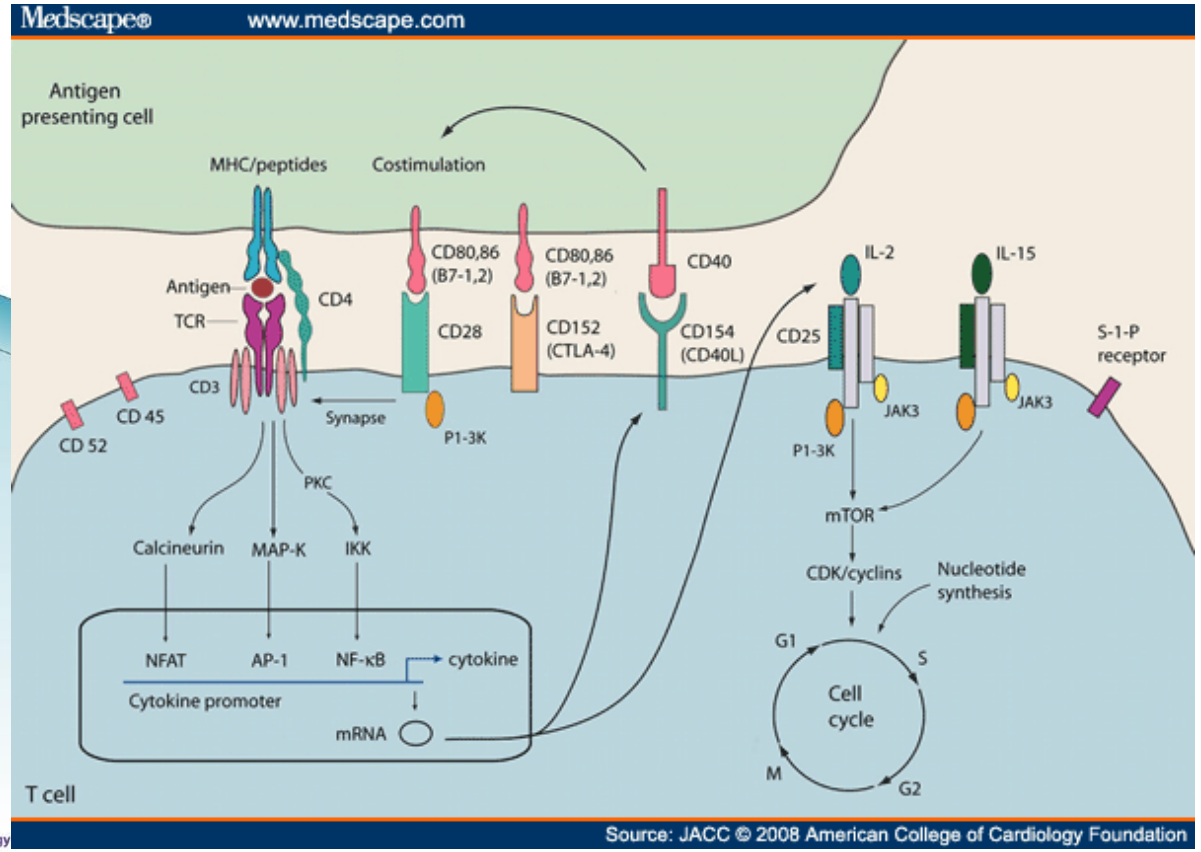
يعني انه الـ Co-stimulatory كمان مهم لحتى يصير Signaling and activation للـ T-cell بدونه رح تظل الـ Tcell ← not active (anergy)

T cell Activation

1. Antigen recognition, primary and secondary signaling leads to T cells activation
2. Release of biochemical mediator and active enzymes that end by activation of transcription factors
3. This results in influx of calcium into the cell
4. Calcium activates calcineurin
5. Calcineurin activates gene for IL-2 and its receptor necessary for T cells proliferation and differentiation and cytokine release

غير مطلوبة

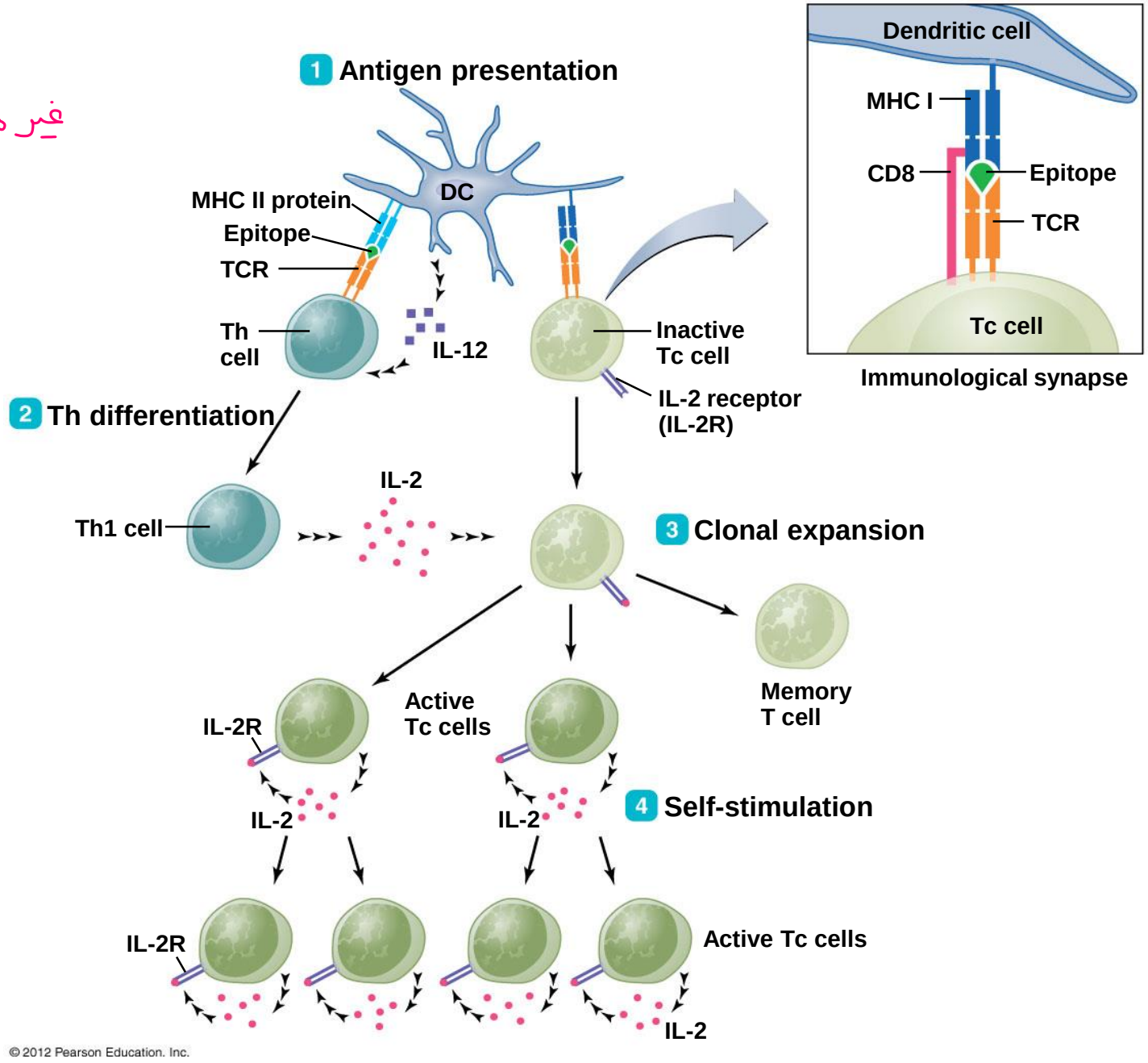

APC
MHC class II
CD4
TCR
CD3ε and δ
CD3ζ
T cell
FYN
ZAP70
LCK
RAS
LAT
GADS
SLP76
PLC-γ1
GRB2
SOS
GDP
VAV1
NCK
PAK1
GTP
RHO
IP3
DAG
RAS-GRP
Intracellular Ca2+
PKC-θ
MAPK
Cytoskeletal rearrangement
IL-2 gene expression
Cell-cycle entry
T-cell effector functions
Nature Reviews | Immunology


Medscape®
www.medscape.com
Antigen presenting cell
MHC/peptides
Costimulation
Antigen
TCR
CD4
CD3
CD80,86 (B7-1,2)
CD28
CD80,86 (B7-1,2)
CD152 (CTLA-4)
CD40
CD154 (CD40L)
CD 45
CD 52
Synapse
P1-3K
PKC
Calcineurin
MAP-K
IKK
NFAT
AP-1
NF-κB
cytokine
Cytokine promoter
mRNA
T cell
IL-2
IL-15
CD25
JAK3
JAK3
S-1-P receptor
P1-3K
mTOR
CDK/cyclins
Nucleotide synthesis
G1
S
Cell cycle
M
G2
Source: JACC © 2008 American College of Cardiology Foundation

4. Proliferation and Differentiation

- As a result of T cells activation and Interleukins secretion T cells start to proliferate resulting in expansion of antigen specific cells or clones (1-2 days)
- after 4-5 days T cells differentiate and expand to yield enough numbers of functional T cells (effectors cells)
- These cells leave the peripheral lymphoid tissue and migrate to site of infection → to kill the microbes.
- A small subset of T cells will differentiate into memory T cells

غير مطلوبة



5. Effector Mechanisms

- Effector mechanisms are responsible of the final killing of microbes
- The main effector function of T cells include:

1. Activation of macrophage → to go to site of infection, and phagocyte and digest the microb.
2. Activation of cytotoxic T cells → to kill the microbes by different mechanisms.
3. Activation of B cells and humoral response → this is the link between cellular and humoral immunity.
   ↓ to produce the antibodies

T Helper Cells

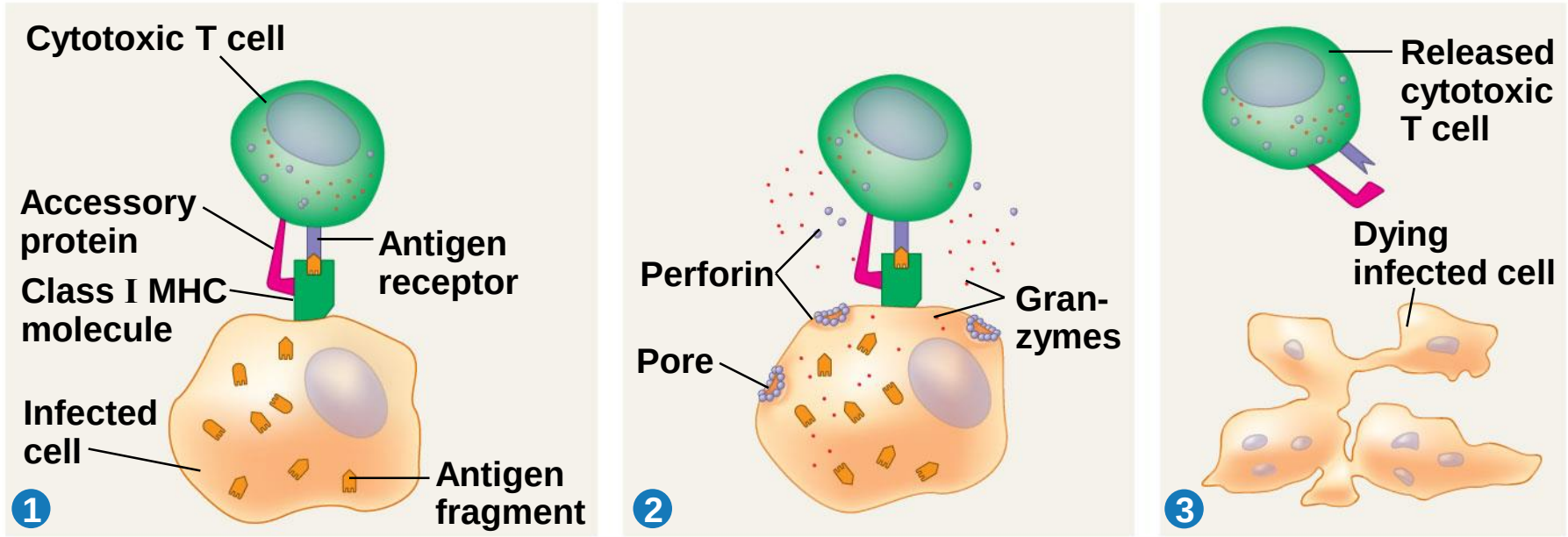
- **$CD4^+$ or T_H cells**
  - T_H cells produce cytokines and differentiate into
    - T_H1
    - T_H2
    - T_H17
    - Memory cells
- TH1 produces IFN-gamma which activates cells related to cell-mediated immunity, macrophages, and Abs
- TH2 activate eosinophils and B cells to produce IgE

as we studied before, this Ig is important for allergy.

T Cytotoxic Cells

- **$CD8^+$** or **T_C** cells
- Target cells are self carrying **endogenous antigens**
- Activated into **cytotoxic T lymphocytes (CTLs)**
  - CTLs recognize Ag + MHC I
  - Induce **apoptosis** in target cell
- Cytotoxic T cells kills microorganism by:
  - Perforins → بتعمل فتحات بالـ microb
  - Granzymes – degrading enzymes
  - Fas-Fas Ligand interaction - apoptosis
  - Antibody dependent cellular cytotoxicity مثل ما عرفنا انها بتحفز زيادة تصنيع الـ antibodies

هي نفس الحكي اللي فوق بس اللي بيجب يشوف صور



طبيعًا بعد ما تم القضاء على الـmicrob لازم يصير inactivation لـimmune system وهاد الشي بيصير عن طريق الـ Tregulatory cells .

6. Shut down of Immune Response and Formation of T Memory Cells

- T_{reg} cells (have CD4 and CD25 on surface): Suppress T cells and shut down the T cells immune response after the microbe is eradicated
- As the infection is cleared proliferated immune cells are deprived of survival factors and the cells die by programmed cells death (apoptosis)
- A fraction of antigen-activated T cells differentiate into long lived memory T cells
- Memory T cells do not produce any cytokines and they do not kill microorganism, they recognize the same antigen if it enters the body again and activate the immune response faster in the second attack of microorganism