Immunology

Title : Adaptive Immunity
(cellular Immunity)

Lec no : 8

Done By : Johainah Taha

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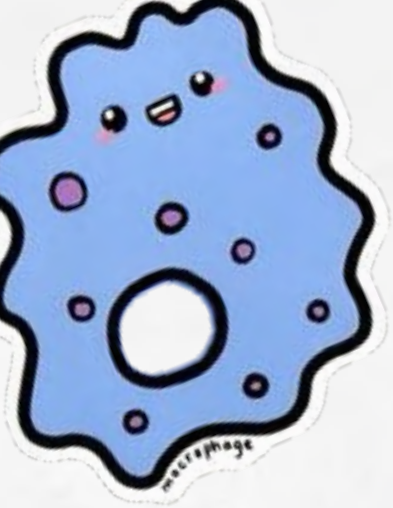

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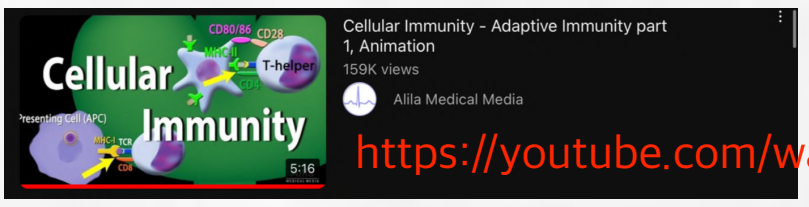
1. 

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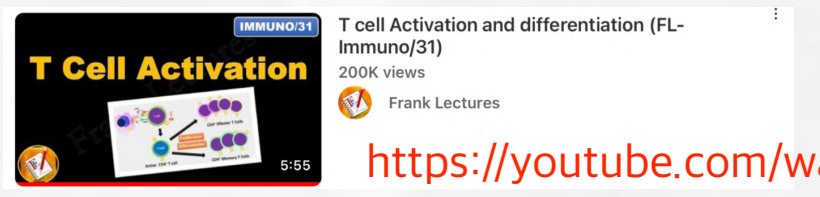
2. 

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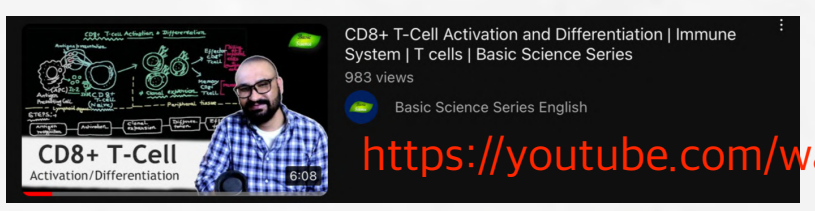
3. 

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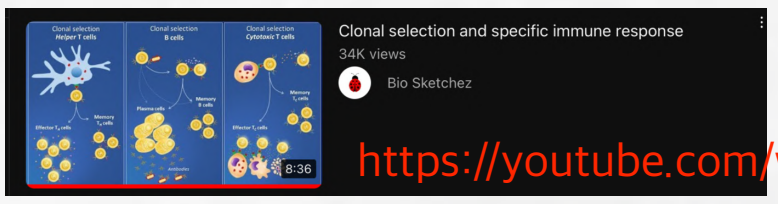
4. 

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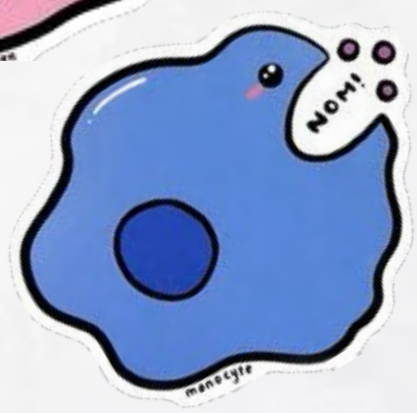
عادي.. مو لازم
كل شي يكون بيرفكت!



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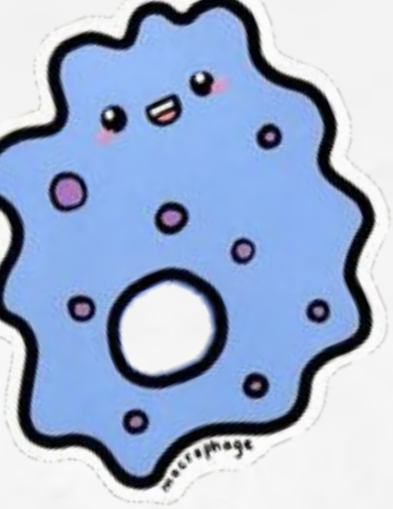


Adaptive Immunity

Adaptive immunity :

-Induced resistance to a specific pathogen

في الinnate immunity كانت non-specific، فكان عنا immune response بهاجم الpathogen بنفس الطريقة بغض النظر عن الtype او الnumber of exposures

-Learnt by experience

The more the immune system is exposed to this antigen the more immunity is going to develop.

-Confers pathogen-specific immunity

-Enhanced by second exposure

-Has memory

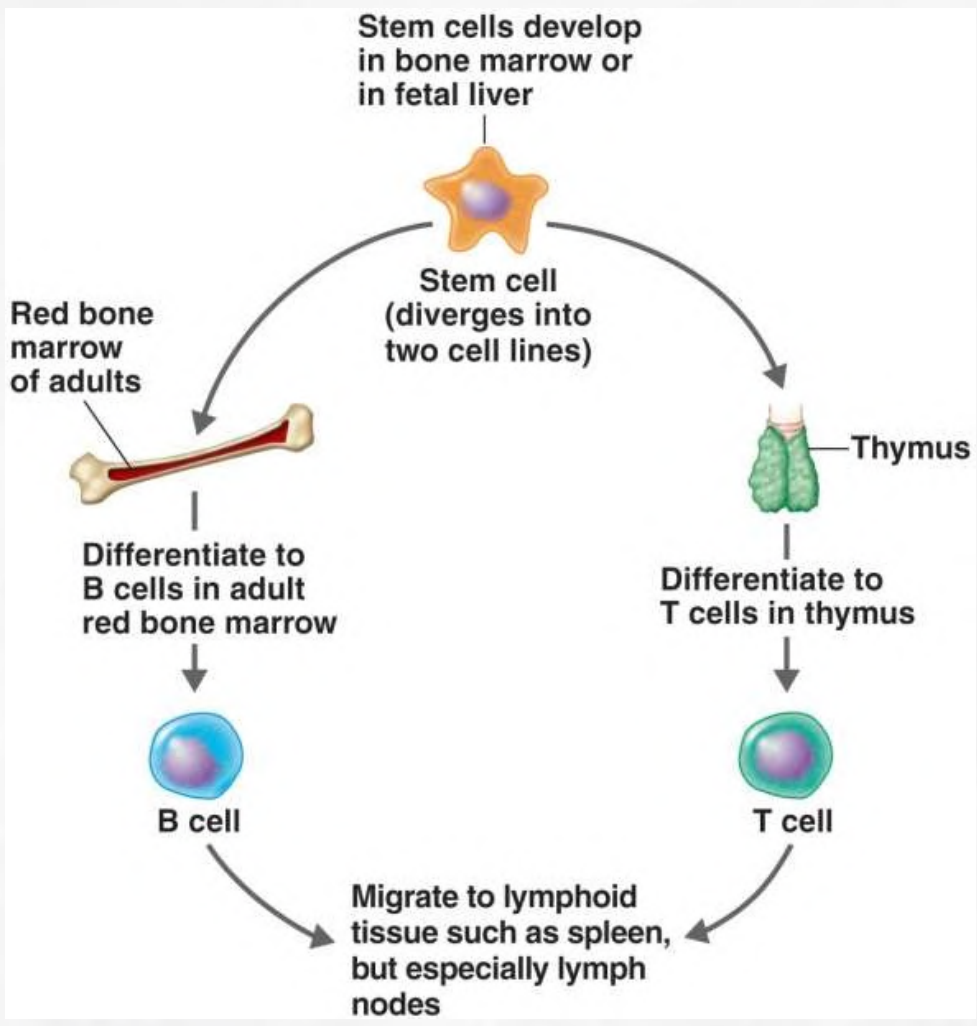
-Is poorly effective without innate immunity

-Adaptive immunity is devided into :

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

خلاصة هاد السلايد أنه ال adaptive immunity عكس ال innate immunity وأهم ما يميزها أنها تقدر تكون memory , بحيث أنها تتعامل مع ال foreign Ag للمرة الثانية بشكل أقوى وأسرع مو مثل ال innate يلي كانت تتعامل معه سواء دخل لأول مرة أو للمرة الألف بنفس الطريقة .

Dual Nature of Adaptive Immunity



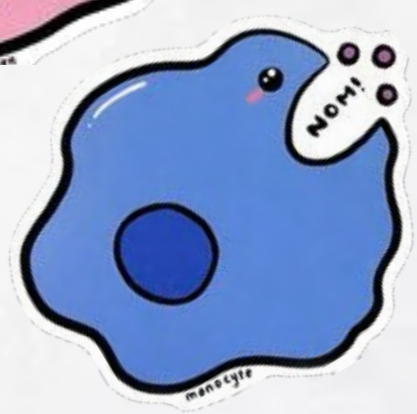
-The B and T cells are produced in the bone marrow -> T cells develop in Thymus

-> B cells develop in Bone marrow

-Both of them circulate in lymphoid organs

-Once T cells recognise the antigen, they become activated, then they go to the site of the infection .

B cells do not go to the site of infection, they produce antibodies that circulate in the blood to reach the site of the infection



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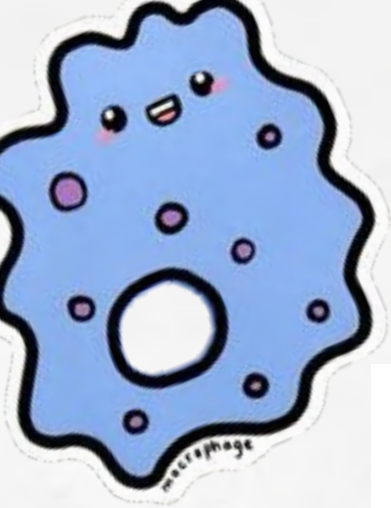


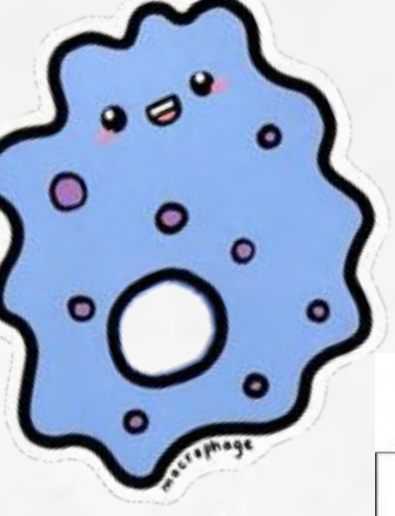
Types of Adaptive Immunity

	Humoral immunity	Cell-mediated immunity	
Microbe	Extracellular microbes	Phagocytosed microbes in macrophage	Intracellular microbes (e.g., viruses) replicating within infected cell
Responding lymphocytes	B lymphocyte	Helper T lymphocyte	Cytotoxic T lymphocyte
Effector mechanism	Secreted antibody		
Functions	Block infections and eliminate extracellular microbes	Activate macrophages to kill phagocytosed microbes	Kill infected cells and eliminate reservoirs of infection

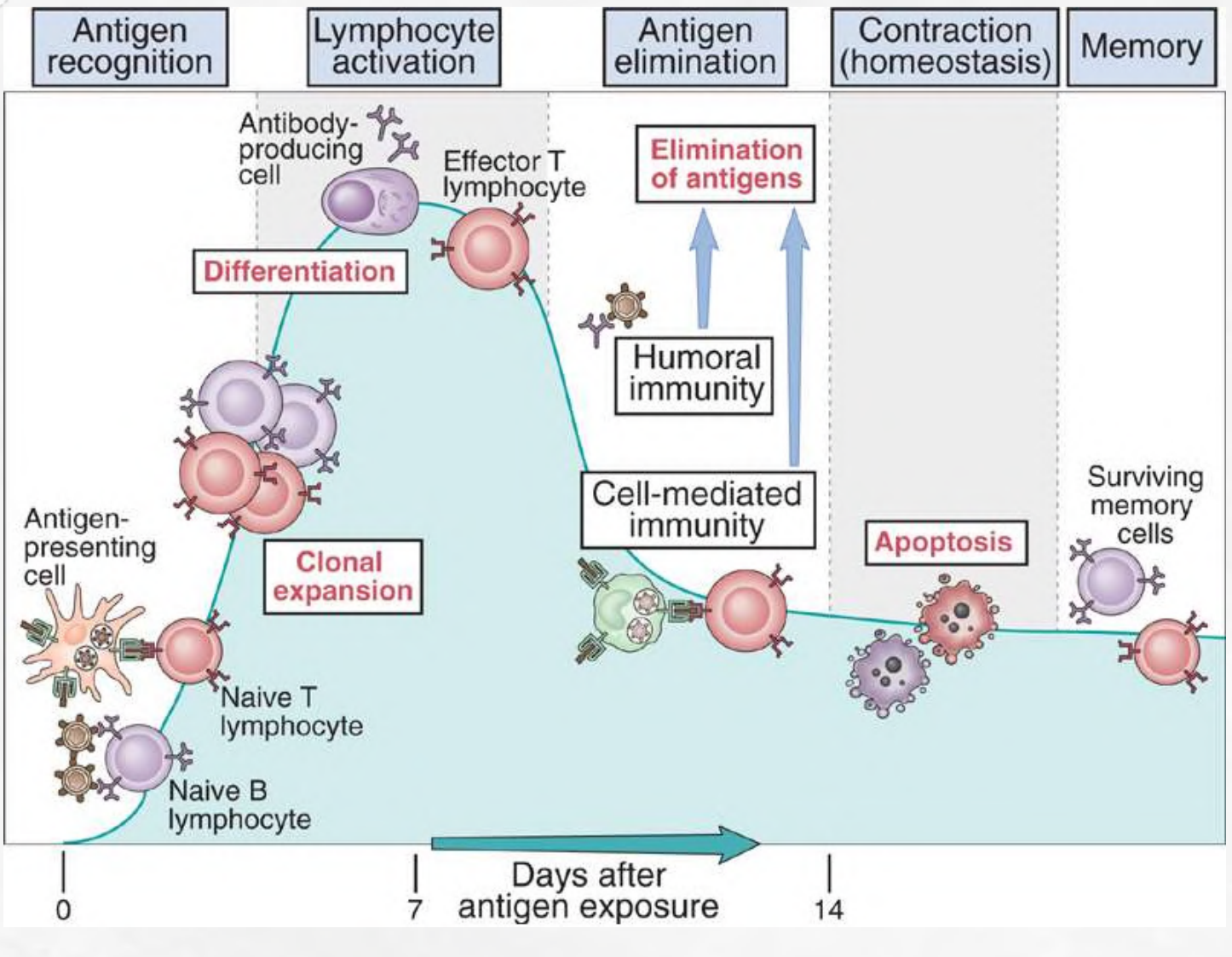
In the cellular immunity, antigens are going to be recognized by the T helper lymphocyte which will give us multiple T helper cells (T helper 1, Th2 ,Th17, Tf helper) + cytotoxic T lymphocyte

ستمُر بإذن الله وكأنها لم تكُن

وقل رب زدني علماً



Phases of Adaptive Immune Responses



The foreign antigen enters the body, then it is going to be captured by antigen presenting cells and presented to the T cells or antigen binding on the B cell
After that the clonal expansion occure either on the B cell or T cell

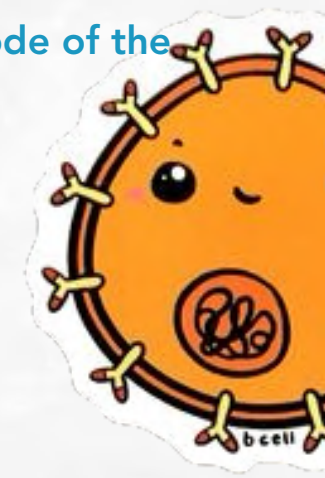
الدكتور بعدين سأل شو يعني clone ؟
هو ال B cell او ال T cell الي بكونوا specefic ل certain antigen
يعني ال antigen فلنفرض انه HIV Virus، اذاً الT cell او B cell الي بتكون specific لل Gp41 من الHIV virus
هاي الspecifity بنسميها clone .

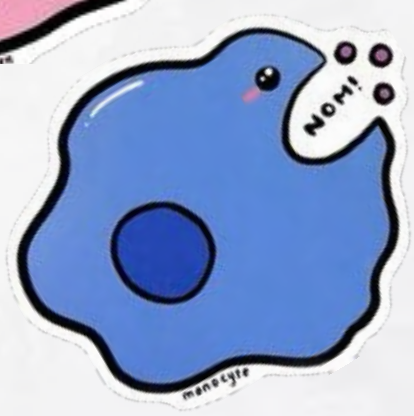
ال clonal expansion يعني زيادة ملحوظة و كبيرة في عدد الT cells او الB cells الي بتكون specific الagainst antigen بعدين بصير في عنا differentiation لل B cells ليعطونا antibodies و الeffector T cells حيعطونا الخلايا الي حكينا عنهم زي (Th1-Th2-T cytotoxic)

وبعدين حيصير عنا humoral immunity بحيث الantibody is produced against this antigen او بصير عنا cell mediated immuntity
بعدين بصير عنا apoptosis لهاي الخلايا و elimitaion لل eradicating antigen
و حتبدأ ال immune responses تعمل subside يعني كل الsignals زي الcytokines حتخف بالتدريج
لما تخف ال T cells و B cells الي شاركوا بالimmune response حيصير الها apoptosis and death و بالتالي حيضل منهم الmemory cells، و هدول survive لسنوات و السبب انه فينا عنا cytokines مثل IL7 و IL15 الي بخلوا الmemory cells تضل عايشة لفترات طويلة و ببطؤوا الmetabolic activity

Each naïve B & T cells can recognize single Ag , once it exposed to these Ag , clonal expansion will occur -> differintiation of Naïve cells to effector B & T cells -> humoral & celluler immunity -> death of the effected cell -> formation of memmory against this Ag .

* clonal expansion : increase in the number of the activated T or B cell the that carries the code of the antigen encountered.





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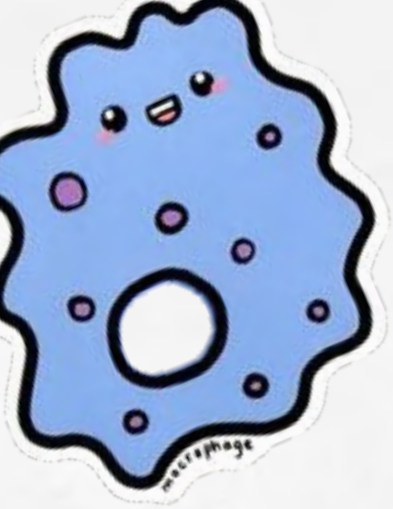

now, we're going to talle about cellular immunity

T Cells and Cellular Immunity

الصنحة مهمة جدًا جدًا

- This type of immunity is performed by T cells to combat 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

حكينا الفيروس أول ما يدخل عالجسم وقبل ما يربط عال receptor on the target cell يعتبر exogenous أما لو ارتبط عال receptor و عمل fussion و دخل جوا الخلية بصير endogenous

- 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

شرح تفصيلي هام جدًا

- In the intracellular infections (cells infected with viruses or bacteria which replicate intracellularly) , the cell mediated immunity will be activated to give us a cytotoxic T cells (CD8+) in order to target these infected cells and kill them .

- If the bacteria or virus is engulfed by the macrophages or dendritic cells , these pathogen still can survive and evade (for example they can move from the phagosome into the cytoplasm of the antigen prersenting cells)

- Example of MO that can survive and evade from cell mediated immunity:

Bacteria -> Mycobacterium, listeria, TB, legionella
Fungi -> Creptococcus neoformans
Protozoa -> Leishmania, Trypanosoma
Viruses -> herpes simplex virus, cytomegalovirus , Epstein barr virus, Pox virus

- Let talk about viruses in more details...

When the virus enters the cell it should be displayed on MHC 1
Some viruses can evade this whole mechanism of presentation
كلهم بيعملوا inhibition لل antigen presentation ولكن ب mechanism مختلفة

Herpes simplex = interfere with transport of antigen
ال transport of antigen هي مثل القناة الي بمر منها الفايروس بعد ما تكسر من الproteosomes ليوصل لل ER و يتصنع ال MHC1 و يرتبط فيه و بعدها يصير اله presentation
هسا الherpes شو بيعمل ؟؟ بينتج peptides بتوقف عملية ال transporting لل ER

CMV = inhibit the proteosomal activity
يعني طريقته مختلفة عن الherpes , هاد الفايروس بمنع عملية تكسير الantigen و تصنيع الMHC في الER

EBV = proteosomal activity + it produces IL10 (cytokine) to inibit macrophage + dedritic cell activation

Pox Virus = inhibit effector T cells activation
IL1 and IF gamma induce the activation of T cells, this virus produces a soluble IL1 and IF gamma receptors
بدل ما ترتبط هاي الcytokines مع الreceptors على الeffector T cells بتروح ترتبط مع الsoluble receptors الي انتجهم الpox
هاي الreceptors و كأنها عم تعمل neutralization للcytokines

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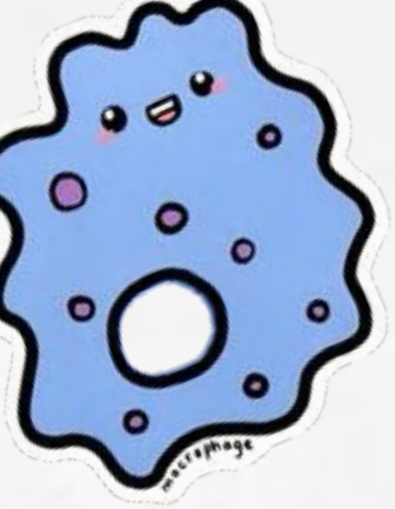

Stages of Cellular Immunity

يمكان شوي حنفصلهم ...

1. Antigen processing and presentations (APC's and MHC's)

   This step happen through antigen presenting cells.
   In cellular immunity -> dendritic cells

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

1. Antigen Processing and Presentation

- Naïve T cells can not recognize antigens directly before processing

لازم يصير عنا presentation قبل و بالغالب طالما بنحكي عن T cell الpresentation حيصير عبر dendritic cells

Superantigen can interact with T cells in different ways (how?) (homework)

- 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

EFFECT OF SUPERANTIGENS ON T CELLS

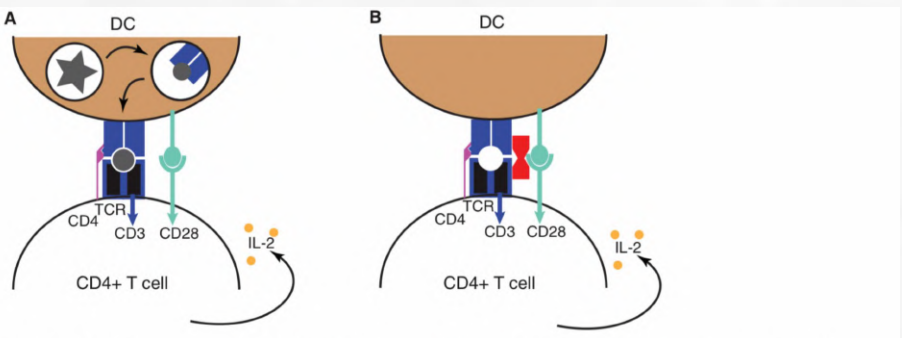

FIGURE 60–8 Activation of helper T cells by superantigen. **A: Activation by an Antigen that is not a Superantigen**. An antigen (gray star) is processed by a dendritic cell (DC) and presented to a CD4-positive T cell in association with a class II major histocompatibility complex (MHC) protein along with co-stimulation. (Note that additional cell–cell adhesion proteins are not shown.) Only the T cells with T-cell receptors (TCRs) specific for that antigen will be activated. **B: Activation by a Superantigen.** The CD4-positive T cell is activated by the binding of *unprocessed* superantigen (red dumbbell) to the Vβ portion of the TCR *outside* of its antigen-specific site. Because it bypasses the antigen-binding site, superantigen can activate many more helper T cells. Note that the activation signal "per cell" is the same, represented in this case by the cells producing the same amount of interleukin (IL)-2.

Superantigens bind to the MHC proteins and the TCRs (T cell receptors) on the surfaces of adjacent APCs (antigen presenting cells) and T cells, forcing the signaling molecules together. As a result, the T cell receives a strong TCR signal regardless of the peptide that is displayed in complex with the MHC molecule. Superantigens are "super" not because they activate each individual T cell more strongly, but rather because they activate a vastly larger number of the available T cells, in many cases bypassing the need for co-stimulation.

For example, staphylococcal toxic shock syndrome toxin-1 (TSST-1) binds class II MHC proteins directly to the variable portion of the β chain of the TCR, specifically Vβ2. This causes unrestrained activation of any CD4-positive T cells that use this Vβ in their TCR, regardless of that TCR's antigen specificity and regardless of the peptide complexed with the MHC protein.Because a large percentage of human T cells use Vβ2 (up to 30%), if all of these T cells are activated, it causes massive amounts of IL-2 released from the T cells and IL-1 and TNF from macrophages. These cytokines account for many of the findings seen in toxin-mediated staphylococcal diseases, such as toxic shock syndrome.

Certain viral proteins (e.g., those of mouse mammary tumor virus [a retrovirus]) also possess superantigen activity. (Although not all superantigens bind Vβ2, they all cause pathology by activating an excessive number of T cells irrespective of those cells' TCR specificities.)

لو في اي اضافات او تعديلات

Comments بابعتكم بال

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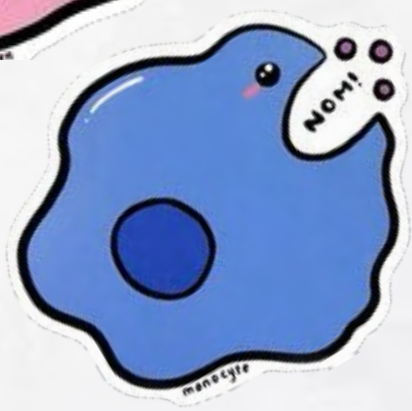
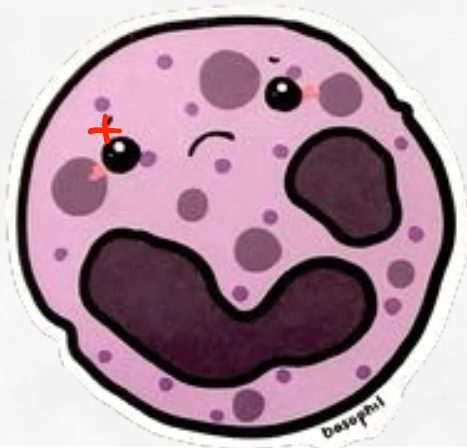
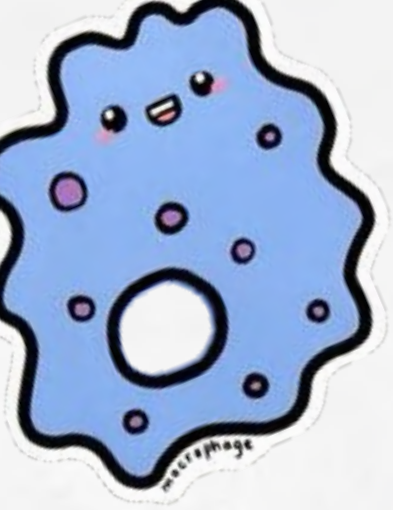


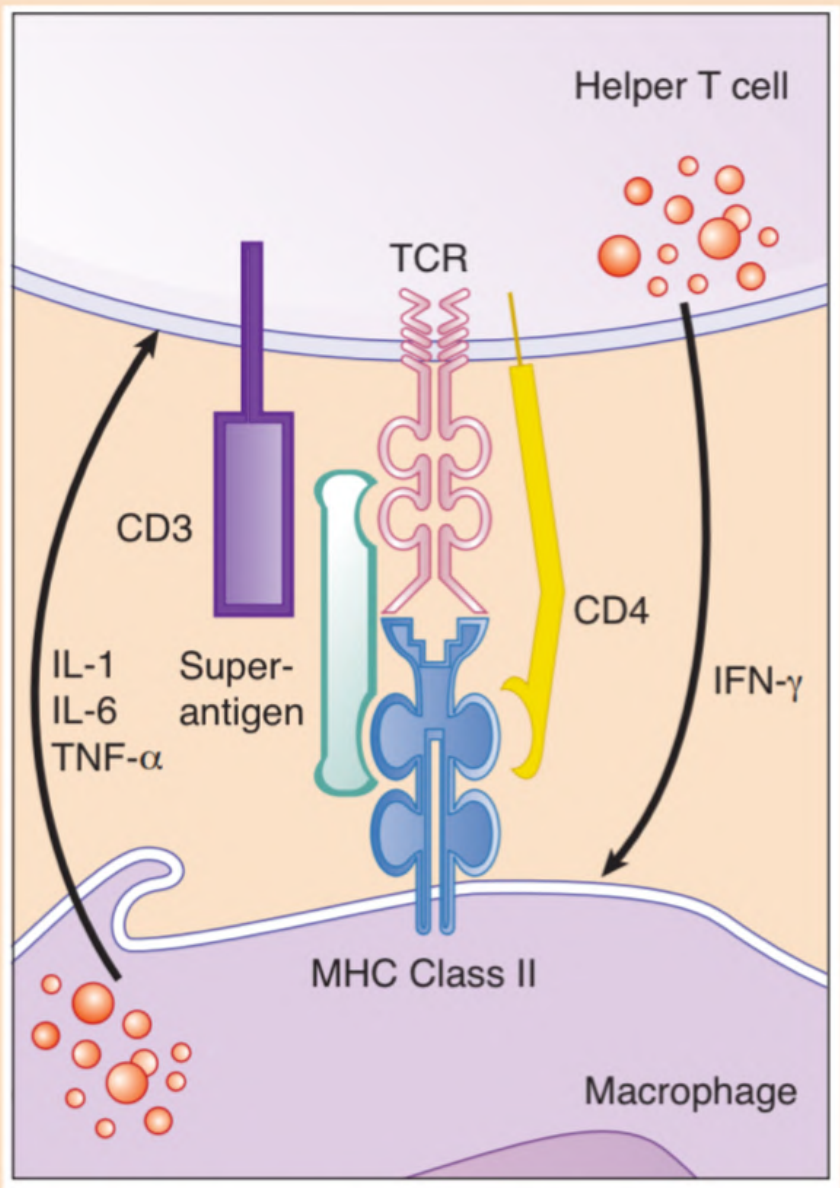




Clinical Correlate

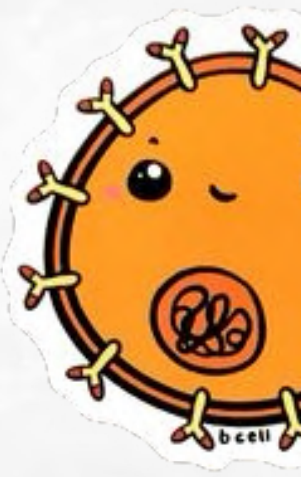
Superantigens are viral and bacterial proteins that cross-link the variable β domain of a T-cell receptor to an α chain of a class II MHC molecule outside the normal peptide-binding groove. This cross-linkage provides an activating signal that induces T-cell activation and proliferation, in the absence of antigen-specific recognition of peptides in the MHC class II groove.

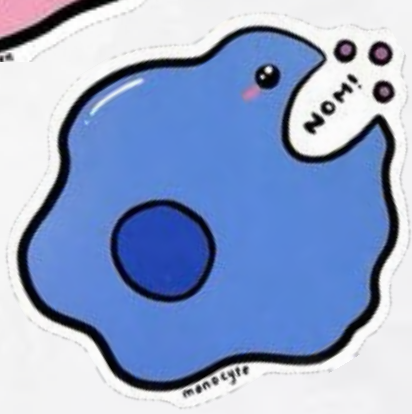
Because superantigens bind outside of the antigen-binding cleft, they activate any clones of T cells expressing a particular variable β sequence and thus cause polyclonal activation of T cells, resulting in the over-production of IFN-γ. This, in turn, activates macrophages, resulting in overexpression of proinflammatory cytokines (IL-1, IL-6 and TNF-α). Excess amounts of these cytokines induce systemic toxicity. Molecules produced during infectious processes and known to act as superantigens include staphylococcal enterotoxins, toxic-shock syndrome toxin-1 (TSST-1), and streptococcal pyrogenic exotoxins.



Superantigen Activation

Note that there is no complementarity between the TCR and MHC/peptide complex.





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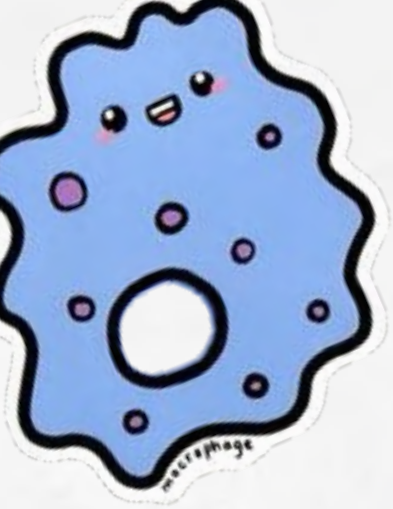
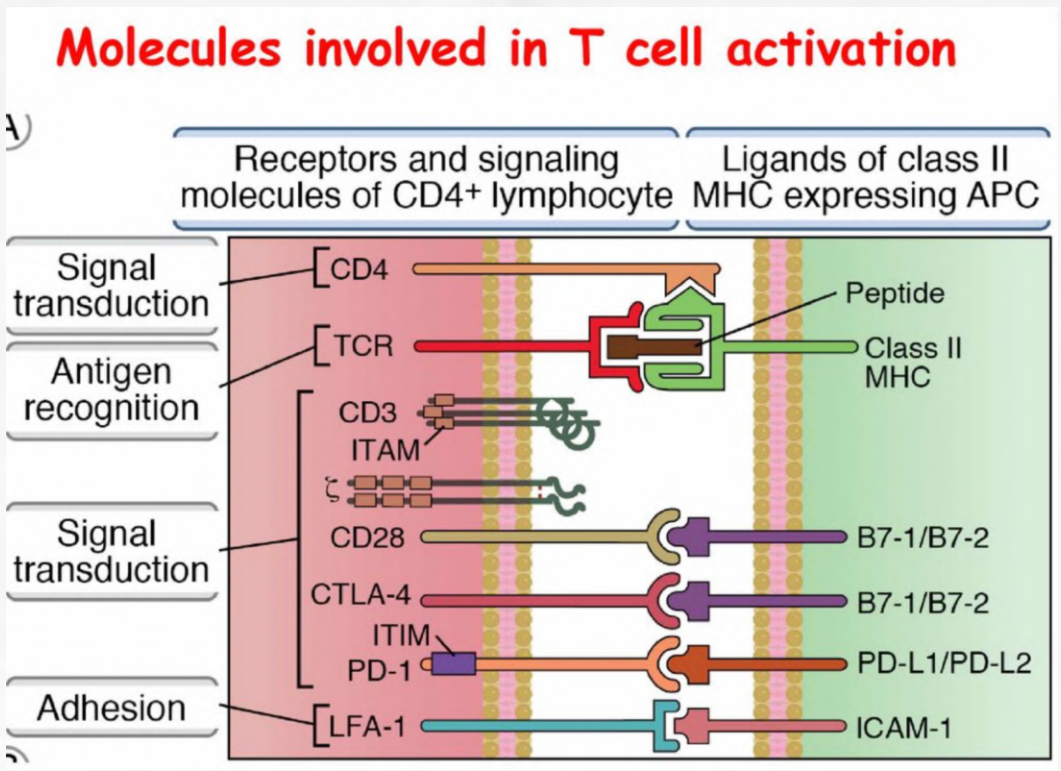
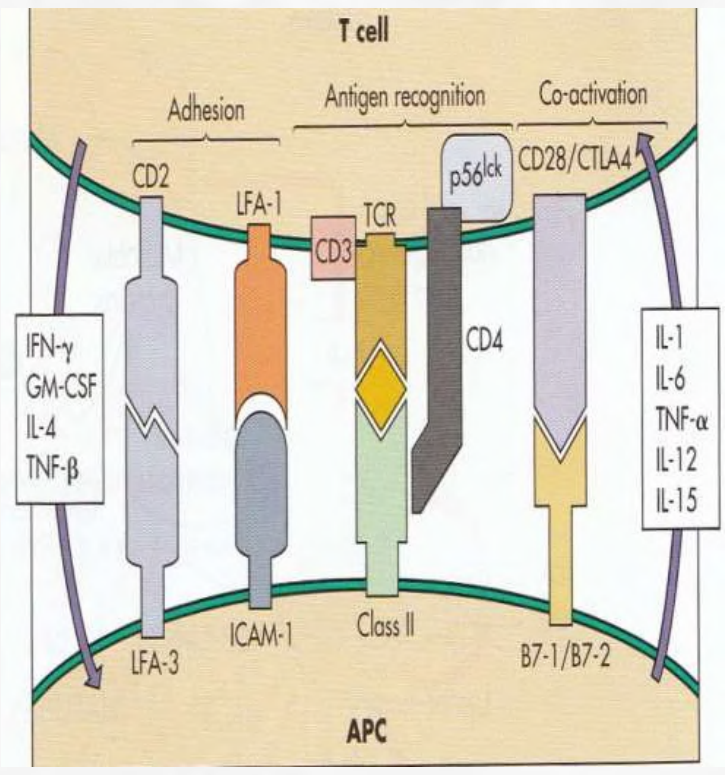


2. Recognition and Binding

- Naive T cells circulate through peripheral lymphoid organs
- T cells possess specific receptors that bind antigen ligands on APCs these receptors called TCR
  ↳ T-Cell Receptor
- TCRs bind epitopes associated with an MHC protein

– Adhesion molecules strengthen the binding of T cells to APCs through integrins (1), selctins (2), LFA (3) (leukocyte function-associated antigen)-1, CD2 (4) adhesion molecules





Molecules involved in T cell activation :

1- TCR (T cell receptor) bind to the peptide of MHC II receptor

2- Adhesion molecules (LFA-1) binds to ICAM-1 to allow enough time for the interaction between T cell and the dendretic cells to have an effector T cells (بتعطيني وقت زيادة لأكمل كل الخطوات)

3- The coreceptor (CD4 or CD8) binds to the ligand of MHC (I or II) presented on the antigen presenting cell

لو كانت T cell مع antigen presenting cell = حيكون عنا CD4 مع MHC II

لو كانت خلية عادية مع T cell = حيكون عنا CD8 مع MHC I

4- the signal transductor molecule -> (3 molecules of CD3 + zeta chain)

هدول الثنتين ما الهم علاقة بالantigen presenting cell بل عملهم هو signaling inside T cell بعد ما صارت الproccess تبعت الantigen presentation

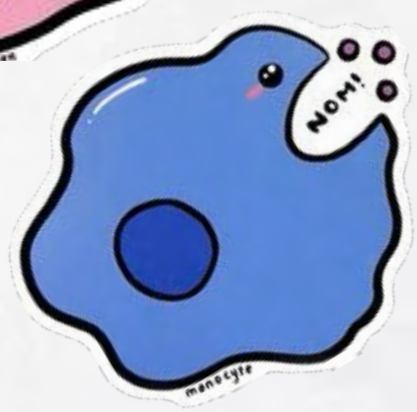
-> (CD 28) binds to B7-1/B7-2

CD28 is a costimulatory signal

-> (CTLA-4) that binds to B7-1/B7-2

-> (PD-1) that binds to PD-L1/PD-L2

CTLA-4 and PD-1 have an inhibatory effect so we can call them (coinhibitors)



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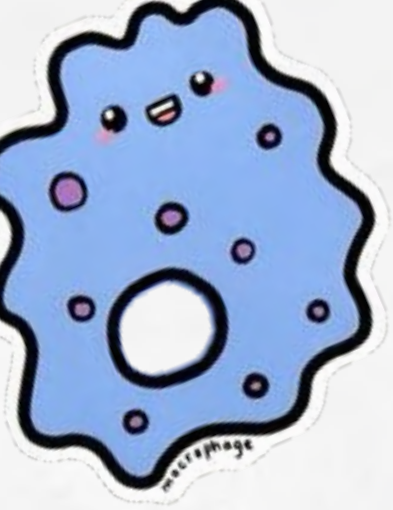
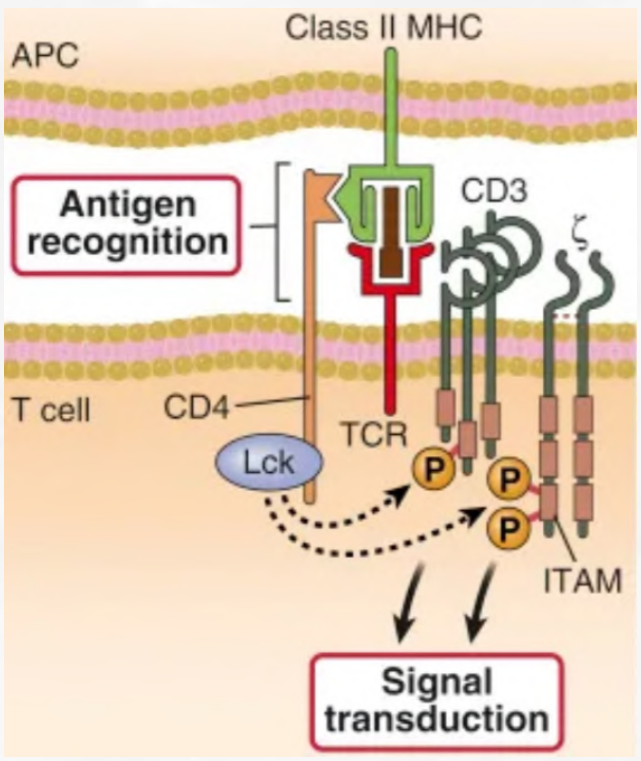
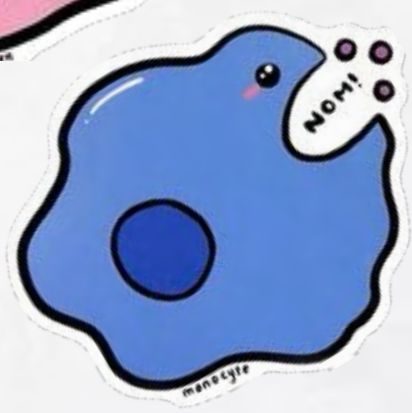


B

Surface molecules of T lymphocytes	Function	Ligand	
		Name	Expressed on
TCR	Antigen recognition	Peptide-MHC	All T cells
CD3		None	
ζ (Zeta Chain)	Signal transduction by TCR complex	None	
CD4	Signal transduction	Class II MHC	Antigen-presenting cells
CD8	Signal transduction	Class I MHC	All nucleated cells
CD28	Signal transduction (costimulation)	B7-1/B7-2	Antigen-presenting cells
CTLA-4	Negative regulation	B7-1/B7-2	Antigen-presenting cells
PD-1	Negative regulation	PD-L1/PD-L2	Antigen-presenting cells, tissue cells, tumor cells
LFA-1	Adhesion	ICAM-1	Antigen-presenting cells, endothelium



Antigen recognition and signal transduction during T cell activation.
Different T cell molecules recognize antigen and deliver biochemical signals to the interior of the cell as a result of antigen recognition. The CD3 and ζ proteins are noncovalently attached to the T cell receptor (TCR) α and β chains by interactions between charged amino acids in the transmembrane domains of these proteins (not shown). The figure illustrates a CD4 + T cell; the same interactions are involved in the activation of CD8 + T cells, except that the coreceptor is CD8 and the TCR recognizes a peptide–class I MHC complex. APC, Antigen-presenting cell; ITAM, immunoreceptor tyrosine-based activation motifs; MHC, major histocompatibility complex



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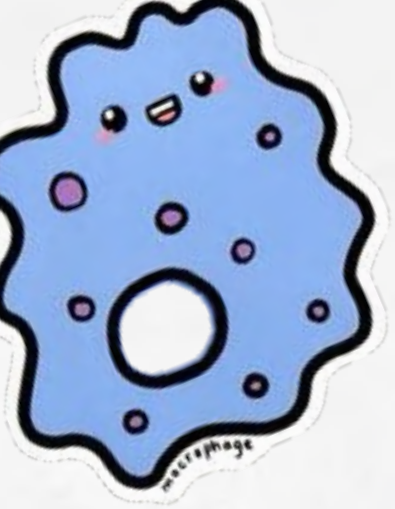


شرح اضافي خارجي ولكن مهم 🤭
لتفهموا تسلسل الأحداث للآن

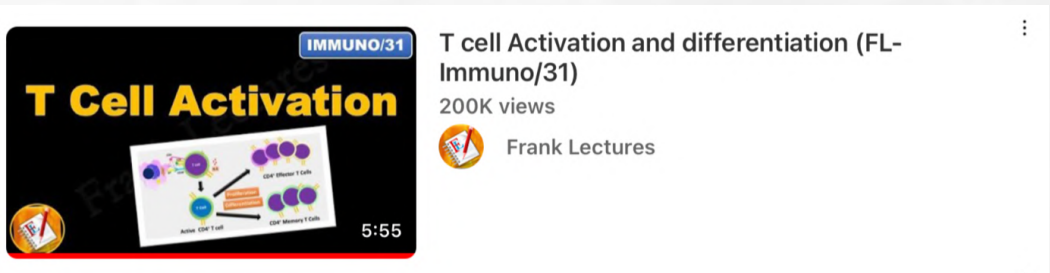
**We know that Mature T cells are 2 types :
1. CD4+ T cells
2. CD8+ T cells
These are naive T cells since they have not encountered any antigen

**APC digest the engulfed antigen into peptides fragments and display them on its plasma membrane.
Now peptide antigen is presented on the surface of the antigen presenting cell as MHC ll - peptide complex , this proccessis called Antigen proccessing and presentation
Now these cells migrate from the site of the infection to the lymph nodes where they present antigen to the recirculating naive T cells, these cells are CD4+ naive cells because they recognize MHC ll peptide complex displayed by antigen presenting cell

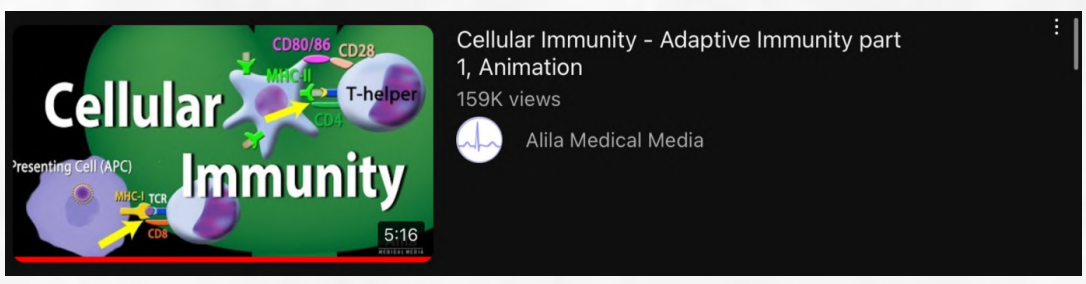
**The activation of this naive T cell requires 2 signals (So T cell activation is a two signal process)
1- First signal :
Recognition and binding by TCR and CD4 generates the first signal of T cell activation
2- Second signal :
It is known as costimulation, and without costimulation the T cells which have recognized the antigen remain in a prolonged state of inactivity which is known as Anergy
The costimulatoes include cytokines or pair of plasma membrane molecules
More than 20 costimulators are know, the most important pair is B7 (CD80) and CD28, other examples include CD 2, CD28 and CD45.

**Then the activated T cells start to secretes cytokine IL-2 leading to proliferation and differentiation rapidly to generate a lot of CD4+ effector T cells and CD4+ Memory T cells . If it was CD8+ naive it will generate cytotoxic T cells and T memory cells.

watch these videos



T cell Activation and differentiation (FL-Immuno/31)
200K views
Frank Lectures



Cellular Immunity - Adaptive Immunity part 1, Animation
159K views
Alila Medical Media

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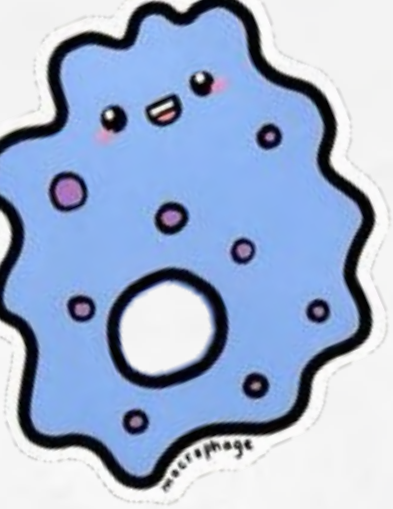


3.Signaling and Activation

1.MHC + antigen – TCR binding and activation of CD3 and ζ (zeta) do the function of signaling (TCR complex)

2.Coreceptors including CD4 and CD8 play role in signaling

3.Other accessory molecules including CD45 and CD2 participate in signaling

4.Costimulatory signal

- B7 on APC interacts with CD28 on lymphocyte
- Receptors for costimulation recognize second signal provided by APCs
- With out co-stimulation T cells remain not active (anergy)

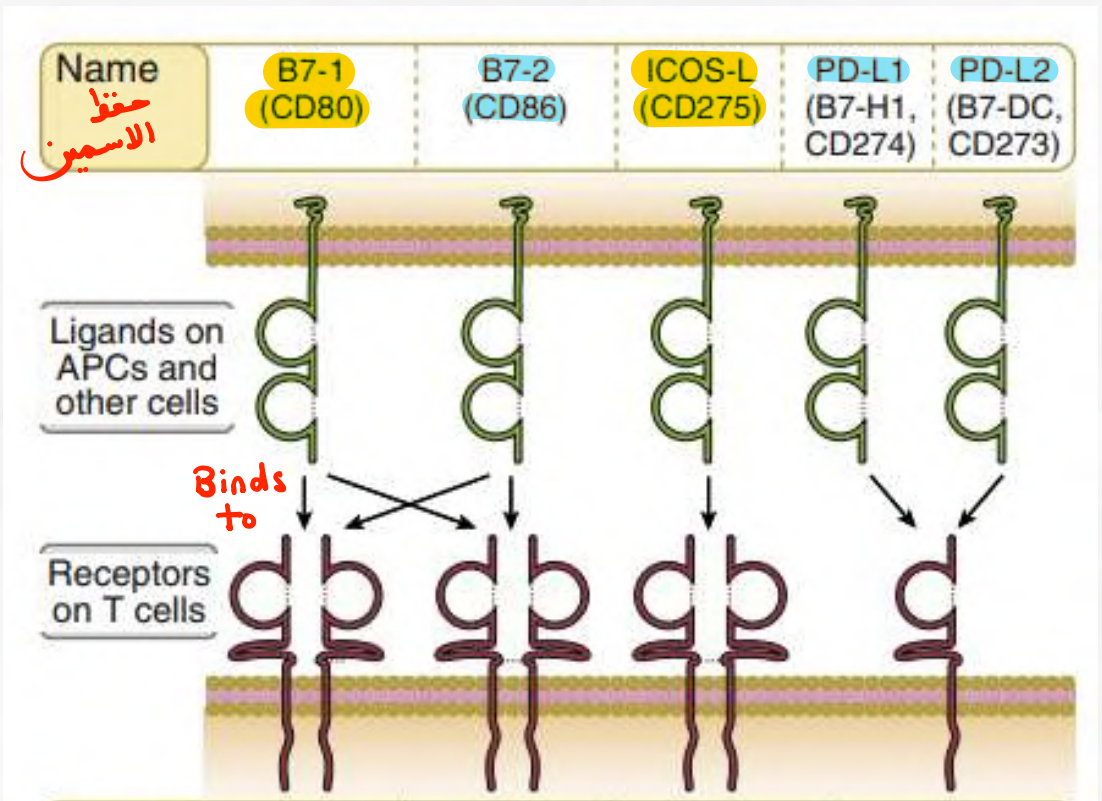
هاي الخطوة (4) كثير مهمة، و لو ما صارت ما حيصير عنا activation لل T cell و بهاي الحالة بنسميها Anergy و الدكتور سأل سؤال متى بصير عندي displaying لل B7 و متى ما بصير ؟

الها علاقة بطبيعة الantigen فلو كان self antigen ما بخلي الAPC تعمل Upregulation لل B7 بالتالي بصير عنا Anergy

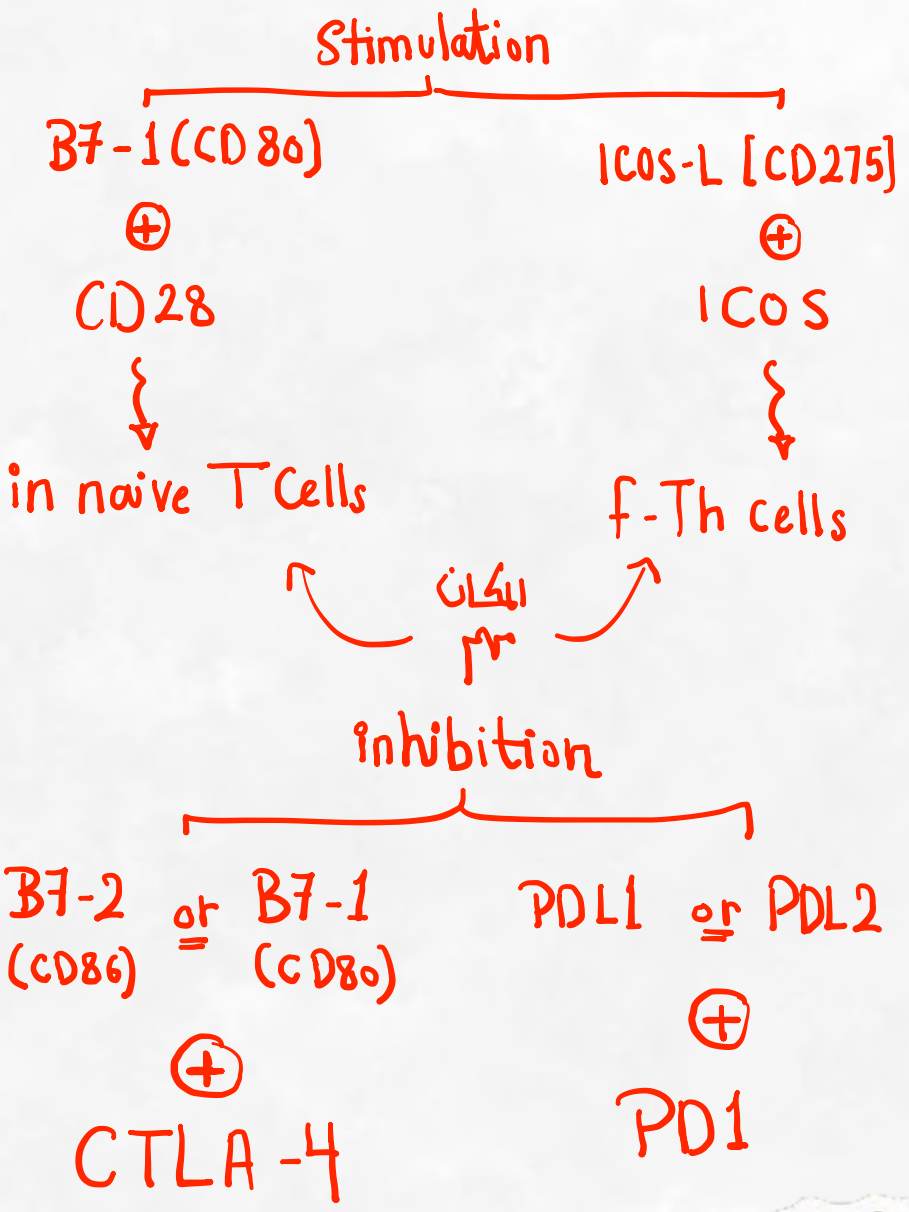
و لما نحكي عن الTolerance بالمحاضرات القادمة وحدة من ال mechanisims انه اصلا ما عنا B7 على الAPS للSelf antigen بالتالي ما بصير عنا stimulation

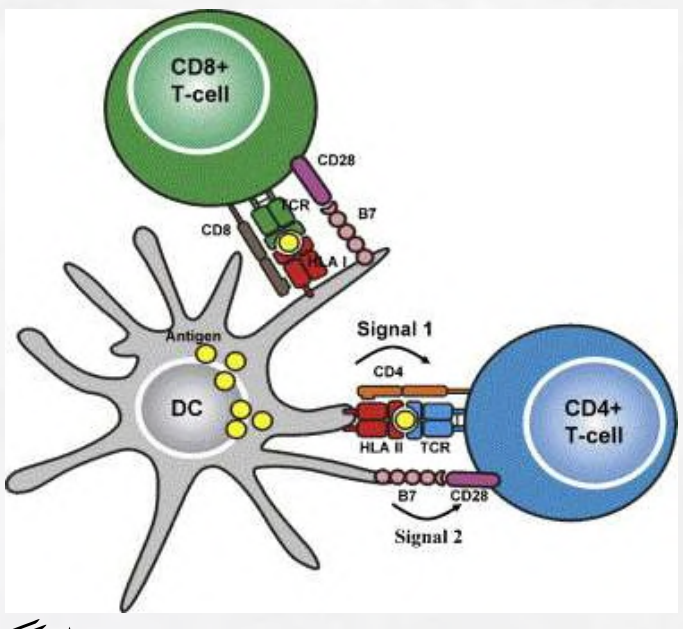
ايضا ال harmless antigen

Immunological tolerance is a complex series of mechanisms that impair the immune system to mount responses against self antigens. Central tolerance occurs when immature lymphocytes encounter self antigens in the primary lymphoid organs, and consequently they die or become unreactive.



Name	CD28	CTLA-4	ICOS	PD-1
Major function	**Activation** (naive T cells)	**Inhibition** (mediates suppressive function of regulatory T cells)	**Activation** (follicular helper T cells in antibody responses)	**Inhibition**





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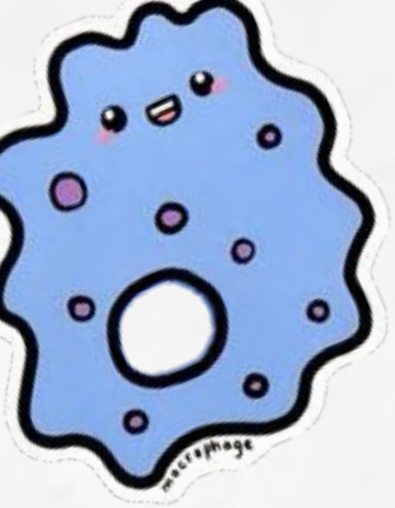
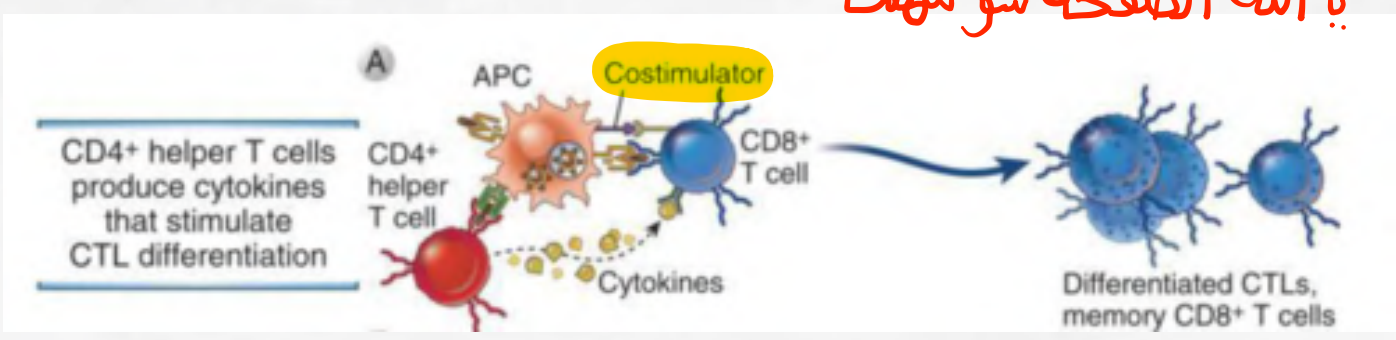


يا الله الصفحة شو مهمة ت



كل الي شرحناه للآن فهو عن CD4+ T cell ، هاي الرسمة عن CD8
ال antigen presenting cell عملت engulfment لل virus مثلا، حيروح الفايروس عالphagosome و يصير fusion بين (الفايروس و phagosome و الlysosomes) ليصير عنا destruction، و بعدها presentation للفايروس ، و ايضا exocytosis للwastes تبعت الphagosomes lysosomes
حلو لهسا ؟
في فيروسات بتعمل escaping من phagosome الى السيتوبلازم بهاي الحالة ما بعتبر الخلية antigen presenting cell انما بعتبرها خلية عادية و بالتالي بتعمل presentation على MHC I و بالتالي حيتعرف عليها +CD8

تخيلوا انه ممكن الخلية الوحدة تعمل presentation على MHC I او MHC II بنفس الوقت و هاد طبعا شي كويس و هاي العملية كلها بسميها cross presentation او cross priming

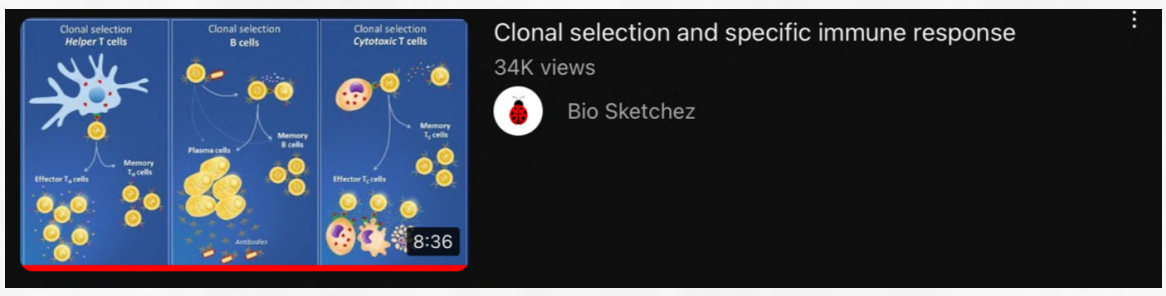
Cross-presentation is the ability of certain professional antigen-presenting cells (mostly dendritic cells) to take up, process and present extracellular antigens with MHC class I molecules to CD8 T cells (cytotoxic T cells).

بنلاحظ انه في عنا كمان costimulator عليها هايلايت من cd4 , طيب هاي شو بنستفيد منها ؟
بتسرع الprocess لل cd8+ cytotoxic T cell فمجرد ما صار عنا cross priming
حتتحول ال naive Cd8 T cell الى cytotoxic effector T cell بسرعة و حتصير مش بحاجة انها تروح للخلية الثانية و ترتبط مع الMHC بكفيها بس ترتبط مع MHC I تبع APC و تبلش عملية ال lysis و الdestruction و الcytotoxic t cell وظيفتها قتل الخلية فلو عملت الها activation بمرحلة البداية عند antigen presenting cell سواء ل tumor or virslly infected cell انت حفزتها و سرعت عملها

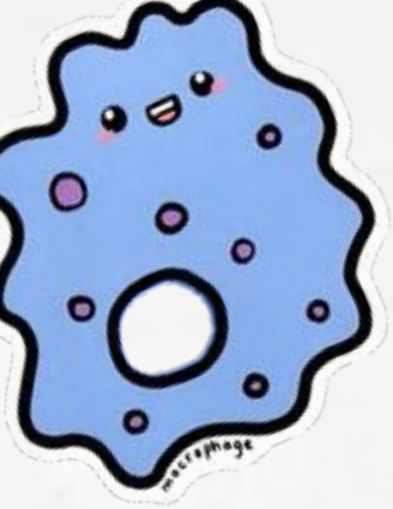
<u>في عنا شغلة مهمة جدا جدا !!!!</u>
<u>قبل ما تقرأوا الي بدي اكتبه احضروا الفيديو الي تحت لتفهموا شو يعني clone</u>
ال cytotoxic T cells مجرد ما يصير الها activation ممكن يزيد عددها عشر الاف مرة عن العدد الي كانت عليه ك naive T cell، بينما لما نحكي عن cd4 عم نحكي عن مئة لألف مرة زيادة في العدد فقط
طيب ليش؟
ال cytotoxic تستهدف tumor cells و viral cells لتعمل الهم killing و بالتالي لازم كل cytotoxic cell ترتبط مع كله خلية مصابة و بالتالي حنحتاج عدد اكبر من الcytotoxic cells لنقدر نحوي كل العدد الكبير من الخلايا المصابة
بينما cd4 differentiation اله علاقة بانتاج cytokines فما بنحتاج هالعدد الكبير من cd4 cells

المختصر : عندك منطقة مصابة لازم كل خلية يرتبط معها عالاقل cytotoxic t cell و بالتالي انت بتحتاج لعدد اكبر
حاولت اوضحها بقدر الامكان

What does it mean if your CD8 is high?
What does it mean if your Absolute CD8+ Cells result is too high? If your CD8 count is high, it means your viral load is low. Your CD4 count is likely to return to normal levels. CD8 cells are important in the body's defense against HIV, and high CD8 count means that your body is effectively controlling the infection.



وقل رب زدني علماً



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

Transcription factors like CD3 and zeta chains

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 releas

immune response مهم لاستمرار الIL2 استمرار افراز

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
- A small subset of T cells will differentiate into memory T cells

5. Effector Mechanisms

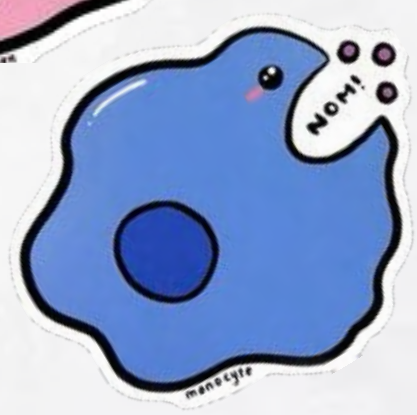
- Effector mechanisms are responsible of the final killing of microbes
- The main effector function of T cells include:

1. Activation of macrophage
2. Activation of cytotoxic T cells
3. Activation of B cells and humoral response

Effector T cells	Defining cytokines	Principal target cells	Major immune reactions	Host defense	Role in disease
Th1	IFN-γ	Macrophages	Macrophage activation	Intracellular pathogens	Autoimmunity; chronic inflammation
Th2	IL-4 IL-5 IL-13	Eosinophils	Eosinophil and mast cell activation; alternative macrophage activation	Helminths	Allergy
Th17	IL-17 IL-22	Neutrophils	Neutrophil recruitment and activation	Extracellular bacteria and fungi	Autoimmunity; inflammation
Tfh	IL-21 (and IFN-γ or IL-4)	B cells	Antibody production	Extracellular pathogens	Autoimmunity (autoantibodies)

example TB

الدكتور شرح هاي السلايد قبل موعدها
عملية الdifferentiation او effector T cells شو الي بقرر انها تروح ل Tfh - TH17 - TH2 - TH1
الجواب انه حسب الcytokines مثل ما هو موجود بالجدول المهم جداً
كل الجدول مطلوب بكل حرف فيه



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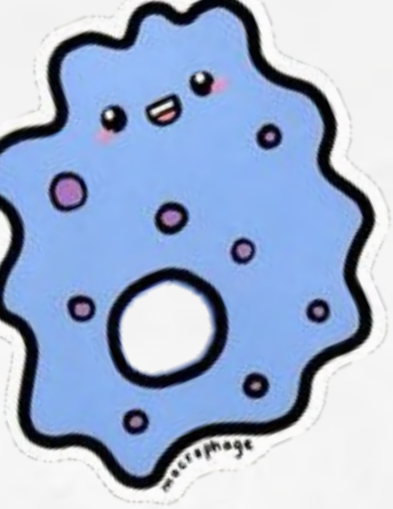
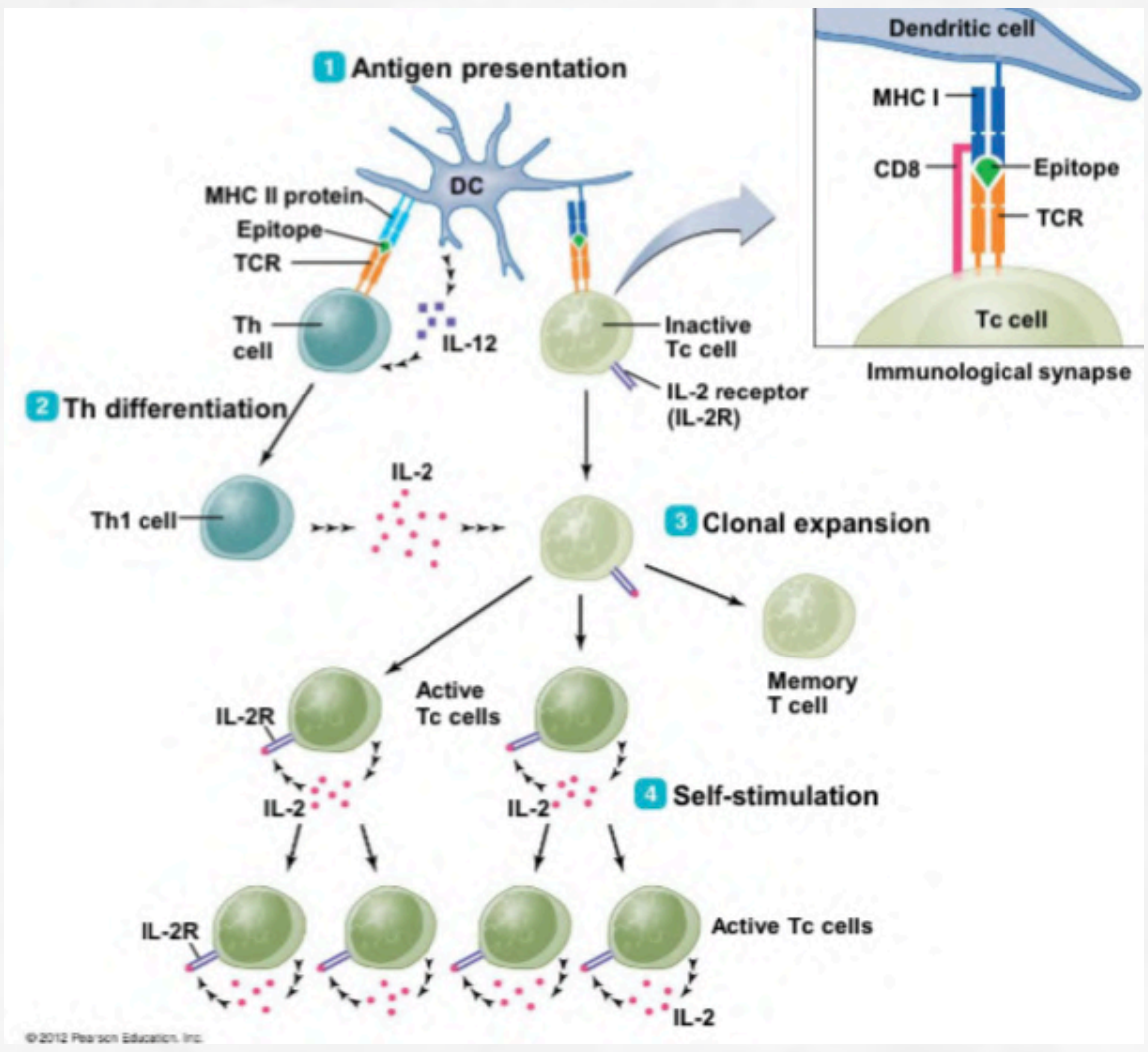




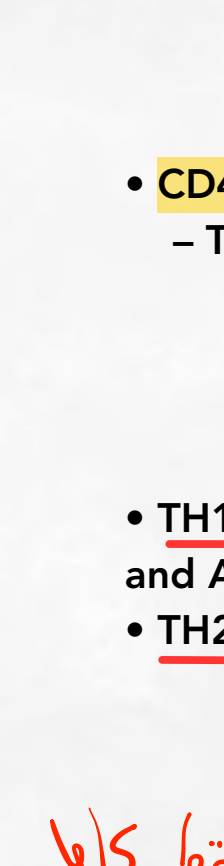
T Helper Cells

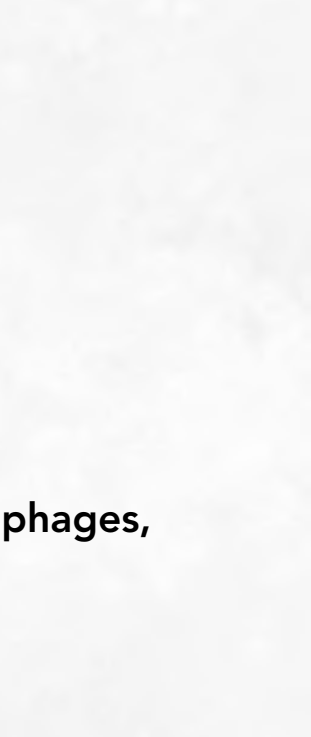
- CD4+ or TH cells
  - TH cells produce cytokines and differentiate into:
    - TH1
    - TH2
    - TH17
    - Memory cells
- TH1 produces IFN-gamma which activates cells related to cell-mediated immunity, macrophages, and Abs
- TH2 activate eosinophils and B cells to produce IgE

كمان حفظ كامل ..

B Biologic actions of selected T cell cytokines

Cytokine	Principal action	Cellular source(s)
IL-2	T cell proliferation; regulatory T cell survival	Activated T cells
Interferon-γ (IFN-γ)	Activation of macrophages (classical pathway)	$CD4^+$ Th1 and $CD8^+$ T cells, natural killer (NK) cells
IL-4	B cell switching to IgE; alternative macrophage activation	$CD4^+$ Th2 T cells, mast cells
IL-5	Activation of eosinophils	$CD4^+$ Th2 T cells, mast cells, innate lymphoid cells
IL-13	B cell switching to IgE; alternative macrophage activation	$CD4^+$ Th2 T cells, mast cells, innate lymphoid cells
IL-17	Stimulation of acute inflammation	$CD4^+$ Th17 T cells, other cells
IL-21	B cell activation; Tfh differentiation	$CD4^+$ Tfh T cells
IL-22	Maintenance of epithelial barrier function	$CD4^+$ Th17 T cells, NK cells, innate lymphoid cells





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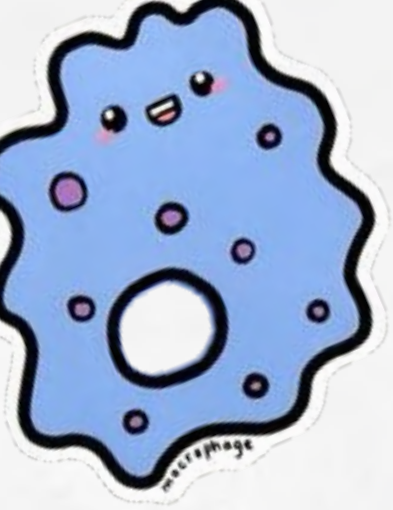
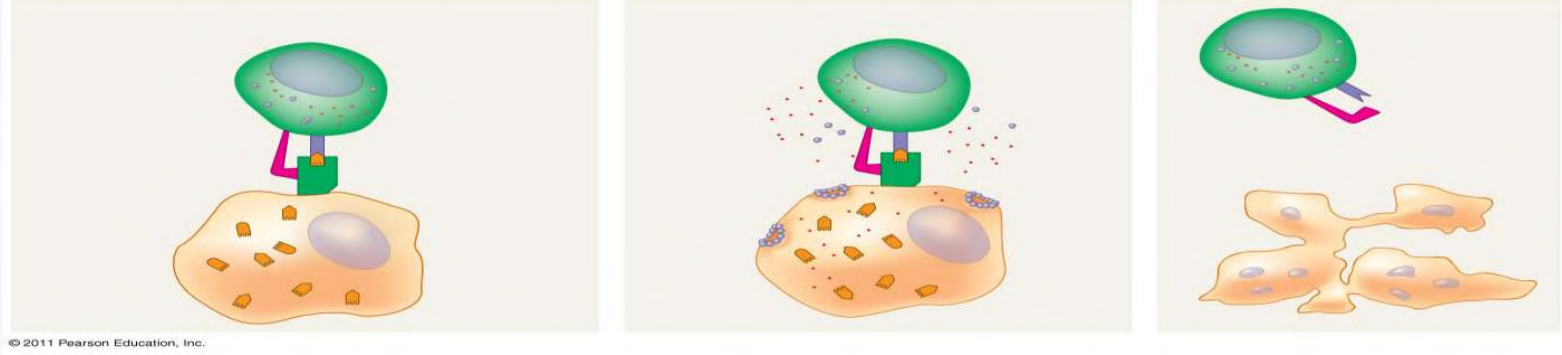


T Cytotoxic Cells

- CD8+ or TC 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
  - Granzymes – degrading enzymes
  - Fas-Fas Ligand interaction - apoptosis
  - Antibody dependent cellular cytotoxicity



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

مجرد ما صار عنا elimination و eradication لل pathogen رح يصير عنا shut down و inhibatory action
عبر regulatory cell

- T reg cells (have CD4 and CD25 on surface): Suppress T cells against self 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 cells can survies longer via cytokines (IL7+IL15) and theses cytokines will lead to long lived memory cells and their life cycle is going to be slower than other 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

<u>3 types of memory cells :</u>

1. effector memory (TEM) cells:

لما يتعرضوا للAg مرة اخرى بصير عنا rapid effectir function

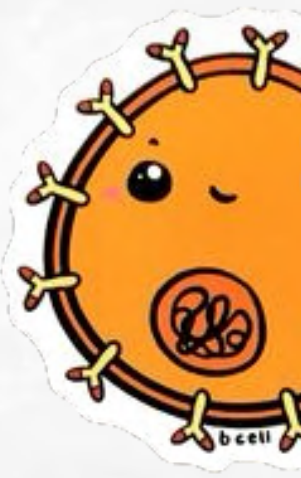
2. central memory (TCM) cells:

مجرد ما يتعرضوا للAg مرة اخرى بصير عنا rapid clonal expansion

3. tissue-resident memory (TRM) cells:

They are in tissues they do not circulte in the body.

مجرد ما يتعرضوا للAg مرة اخرى بصير عنا rapid effector function



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