



Immunology

Title : Tolerance and Autoimmunity

Lec no : 12

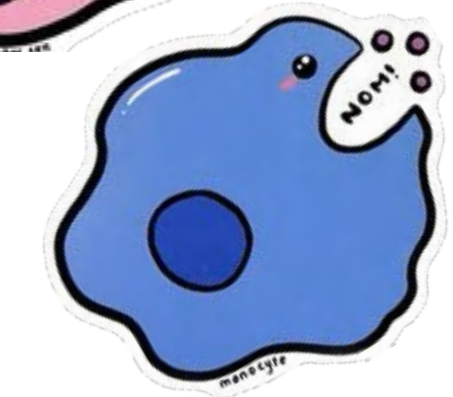
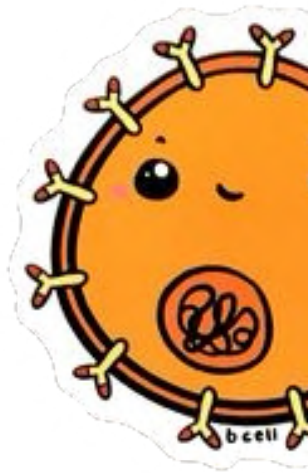
Done By : Tariq al-sboul + Omer Al-shanaq + Johainah taha

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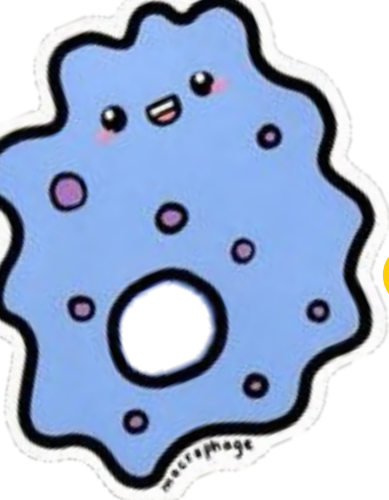


سلام سلام ❤️
عدنا لكم بتفاريغ محاضرات دكتور حافظ
اللون الاسود السلايدات و الاحمر هي النوتات
اي شي بحكي عنه الدكتور مهم بكون عليه نجمة و المو مهم حيكون
جنبه ملاحظة
بعد كل موضوع حاترك الكم فيديو قصير لو حابين تتوسعوا بالمادة
❤️ و موفقين ❤️

ملخص الفترة الحالية :
لقد انطلقت الصافرة، و لم يعد في وسعنا إلا أن نركض



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Immune tolerance, or immunological tolerance

- The process by which immune cells are made unresponsive to self-antigens to prevent damage to healthy tissues.

The ability of our tissue to recognize the self antigen and not product any response against itself.

- It prevents an immune response to antigens produced by the body itself
- Tolerance is built by the body's ability to determine self vs. non-self cells

unresponsiveness to self antigens

When lymphocytes exposed to an antigen:

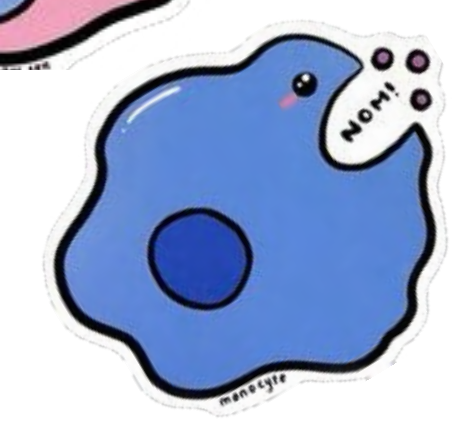
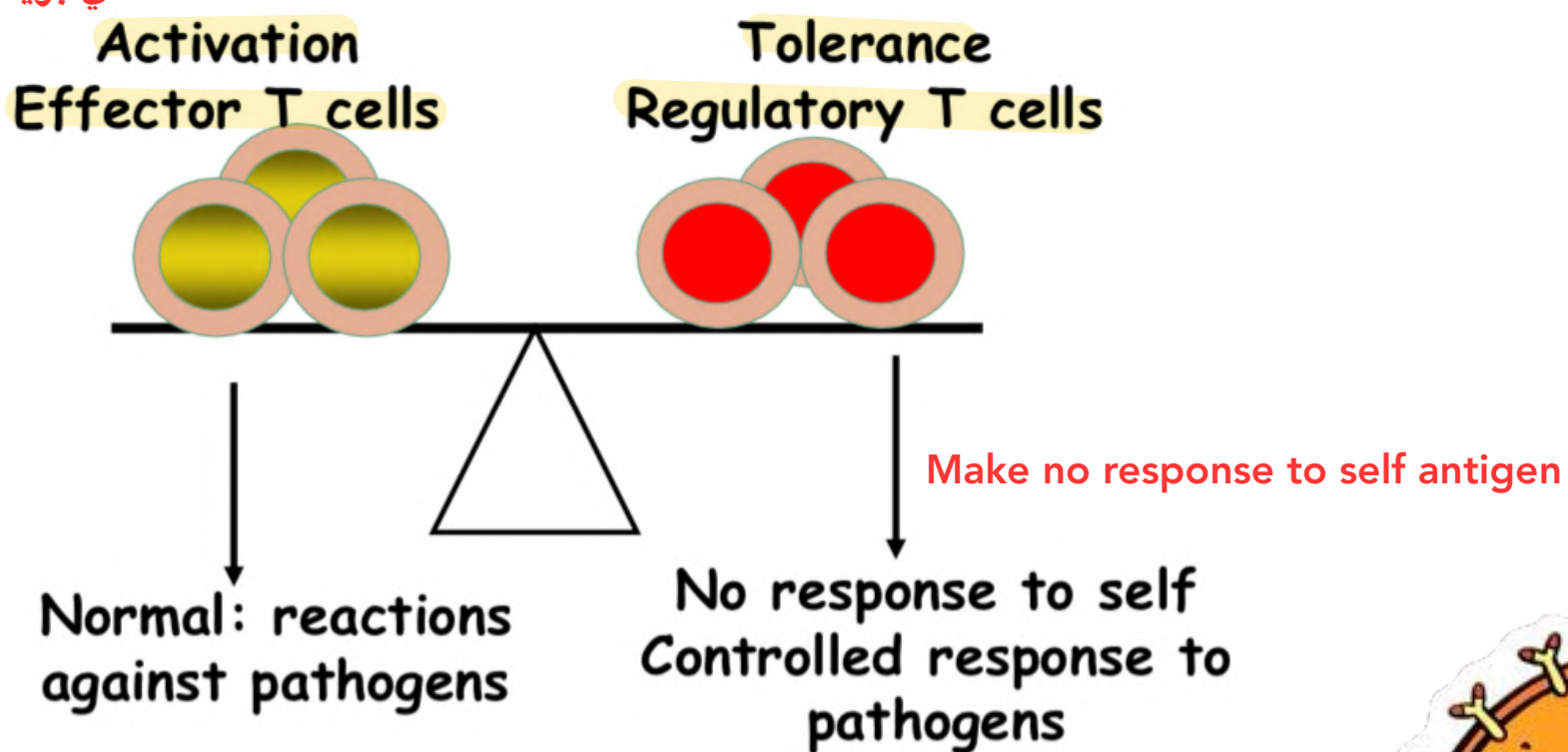
- The lymphocytes may be activated to proliferate and to differentiate into effector cells, leading to a productive immune response;
 - antigens that elicit such a response are said to be immunogenic
- The lymphocytes may be functionally inactivated or killed, resulting in tolerance;
 - antigens that induce tolerance are said to be tolerogenic.

-If itself--->not product an immune responses --> and if the cell that product immune responses for itself --> detect and kill it.

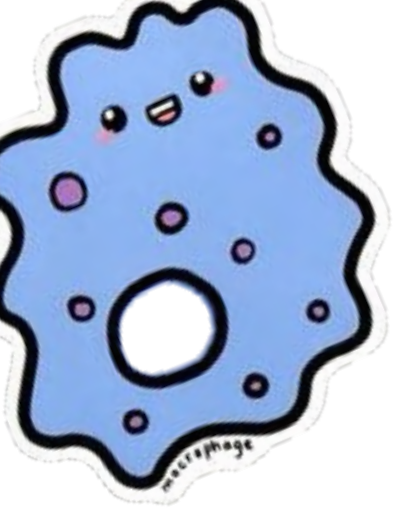
-If forigen body antigen: activation --> proliferation--> differentiation

Balancing lymphocyte activation and control

اللي بزييد عن حده بنقلب ضده



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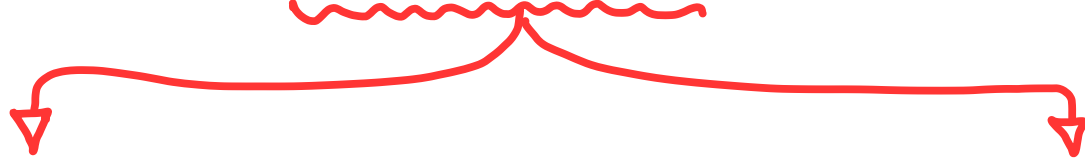


Immunological tolerance to different self antigens may be induced when developing lymphocytes encounter these antigens in the generative (central) lymphoid organs, called **central tolerance** (Bone marrow or thymus),

or when mature lymphocytes encounter self antigens in peripheral tissues, called **peripheral tolerance**

ال tolerance هي عملية التحكم في ال Lymphocyte حتى ما يكون active على نفسه

-There are two type of tolerance:



1) Central (in central or primary lymph organ) --> tolerance --> while lymphocytes is developing.

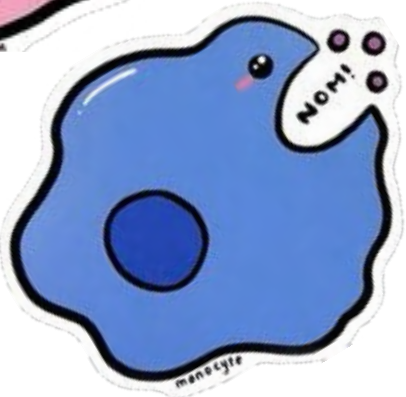
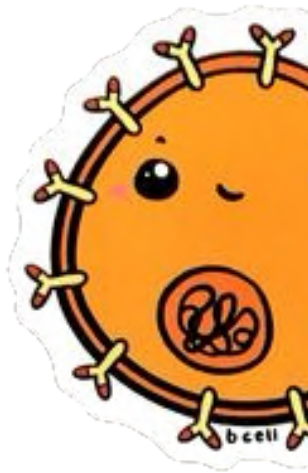
2) Peripheral (in secondary lymph organ) --> while lymphocytes is mature.

• **Immunological tolerance**: specific unresponsiveness to an antigen that is induced by exposure of lymphocytes to that antigen (tolerogen vs immunogen)

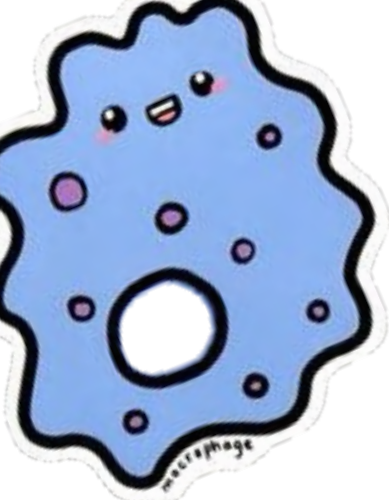
• **Autoimmunity**: immune response against self (auto-) antigen, by implication pathologic

– Disorders are often classified under “immune- mediated inflammatory diseases”

هي عبارة عن immune response against self antigen



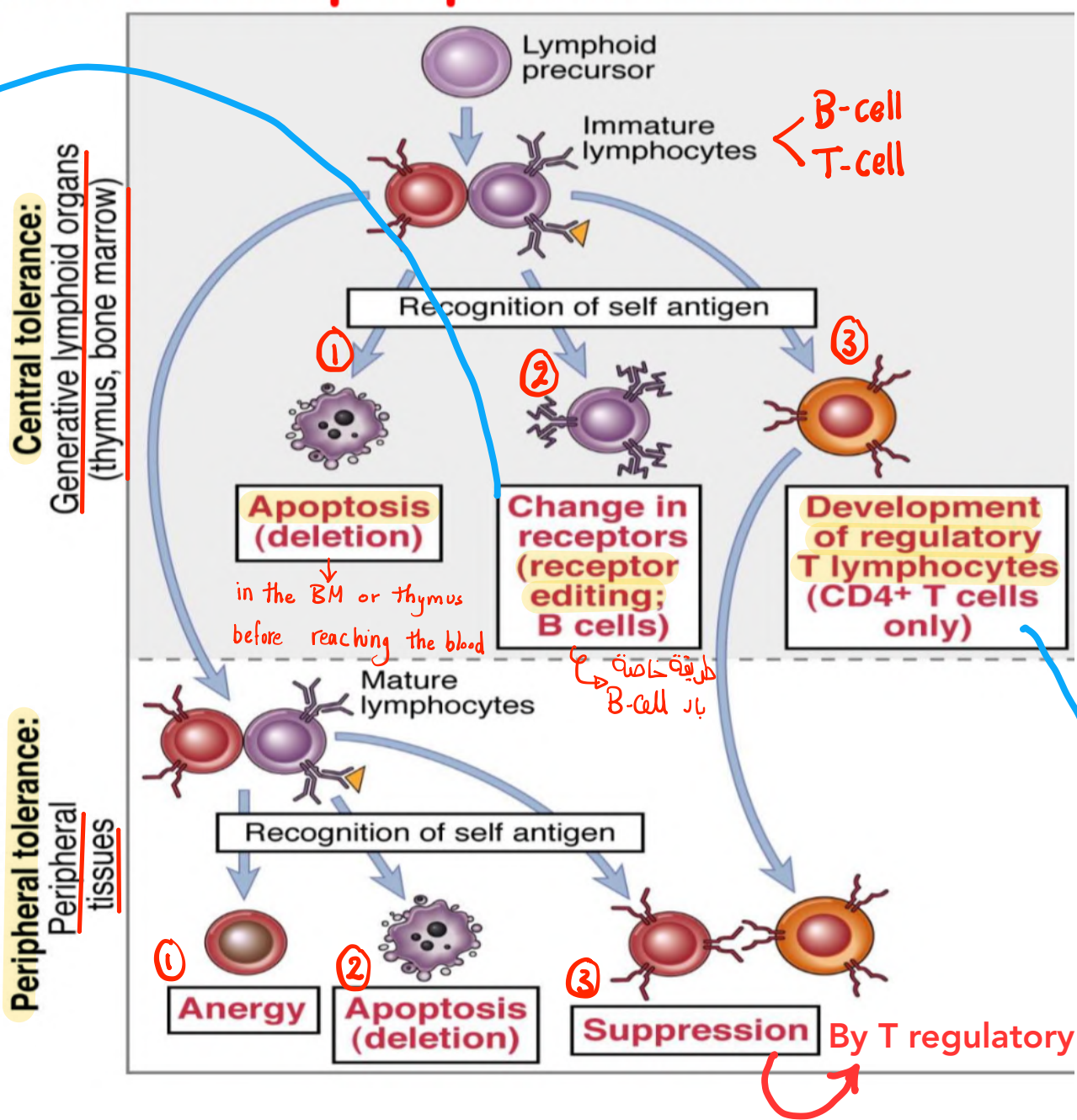
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الموت المبرمج

Central and peripheral tolerance

Receptor editing is the process that replaces the heavy chain or light chain variable region genes in a B-cell immunoglobulin receptor that is already productively rearranged. It is a major mechanism in the bone marrow for maintaining B-cell tolerance to autoantigens



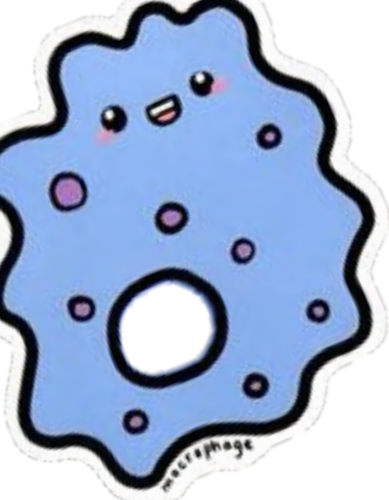
From the book : Some immature CD4+ T cells that recognize self antigens in the thymus with high affinity do not die but develop into regulatory T cells and enter peripheral tissues. What determines whether a thymic CD4+ T cell that recognizes a self antigen will die or become a regulatory T cell is also not established.

Mechanism of Central tolerance

- The principal fate of lymphocytes that recognize self antigens in the generative organs is death (deletion)
- Some B cells may change their specificity (called "receptor editing")
- Some CD4 T cells may differentiate into regulatory (suppressive) T lymphocytes (Just CD4)

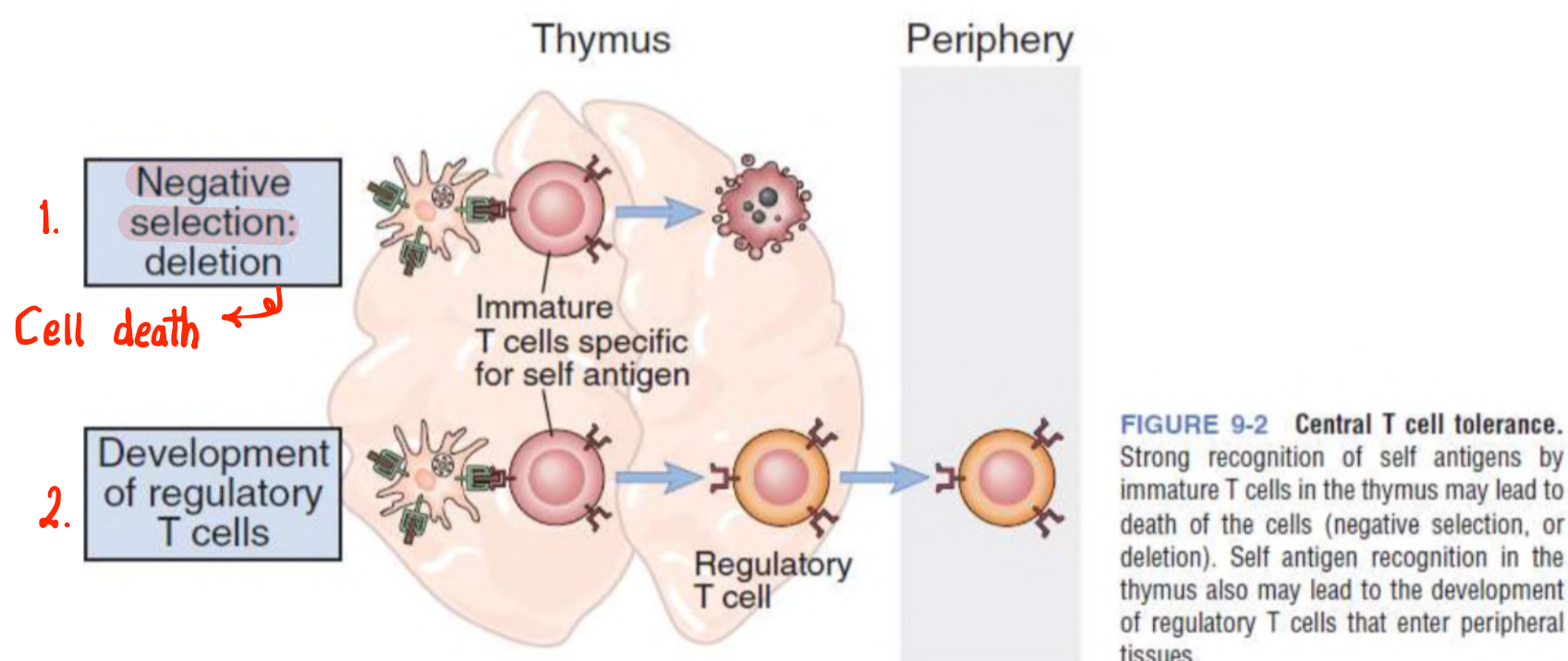


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The principal mechanisms of central tolerance in T cells are:

- Cell death (negative selection)
- The generation of regulatory T cells

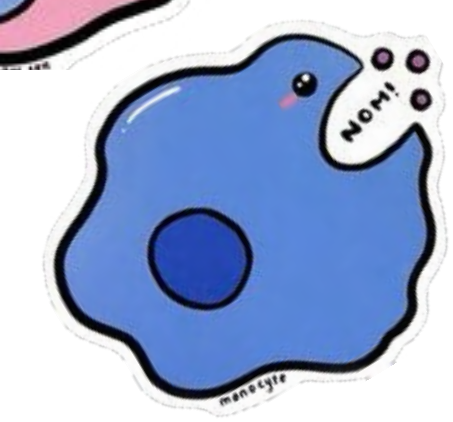
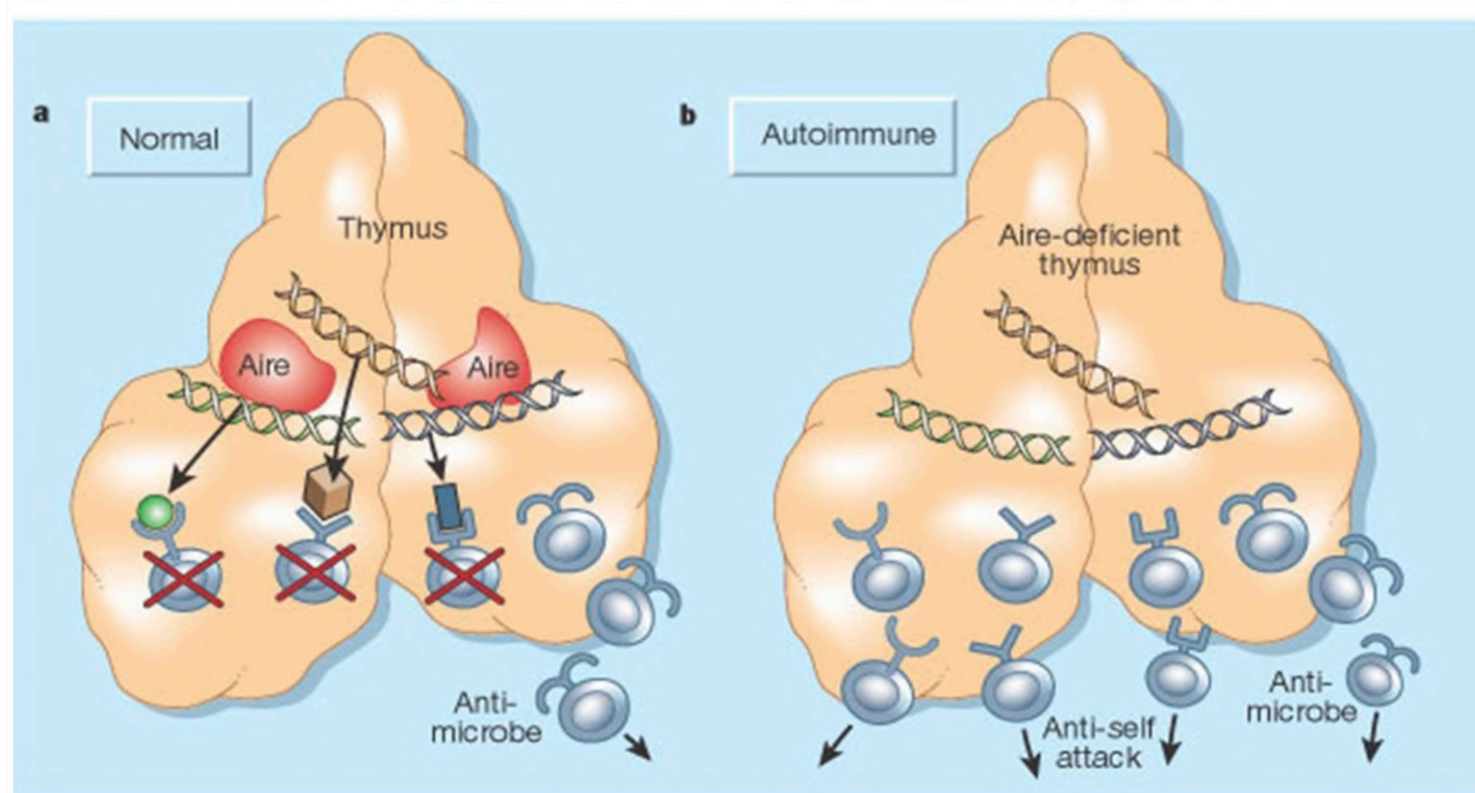


T cell Central tolerance : Cell death

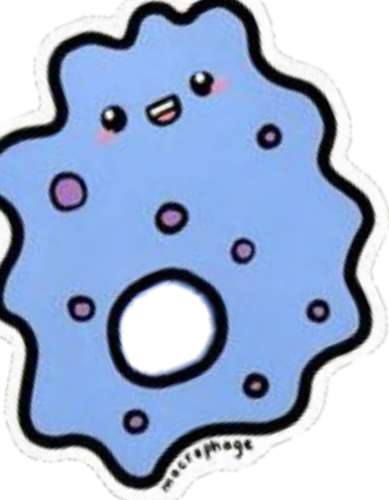
(negative selection) → for T-cells

- The autoimmune regulator (AIRE) is a protein that in humans is encoded by the AIRE gene. AIRE is a transcription factor expressed in the medulla (inner part) of the thymus and controls a mechanism that prevents the immune system from attacking the body.

Autoimmune Regulator (AIRE)



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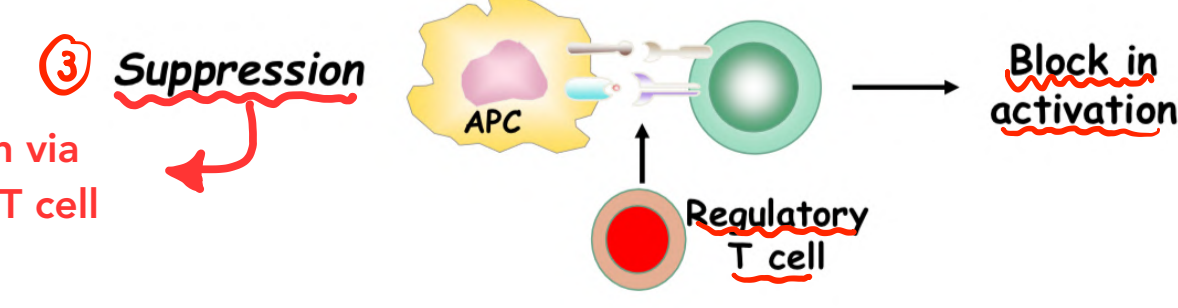
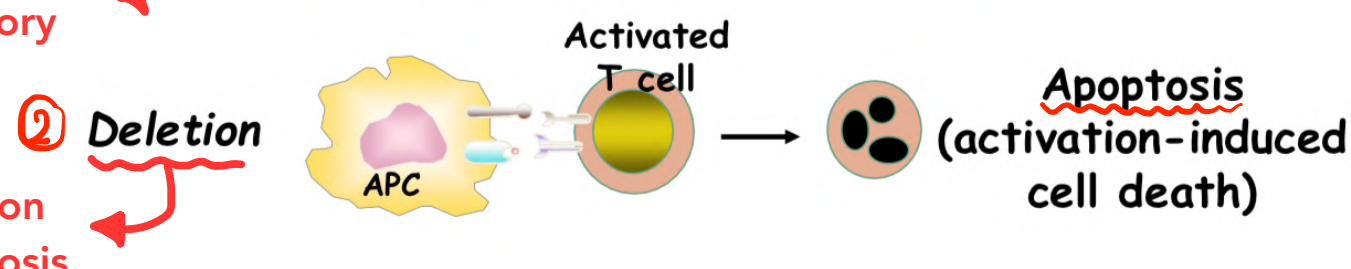
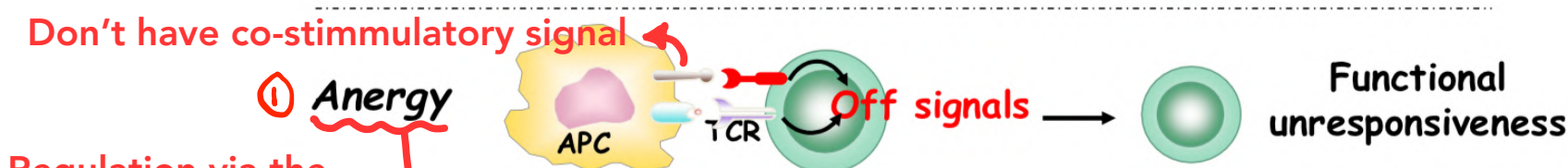
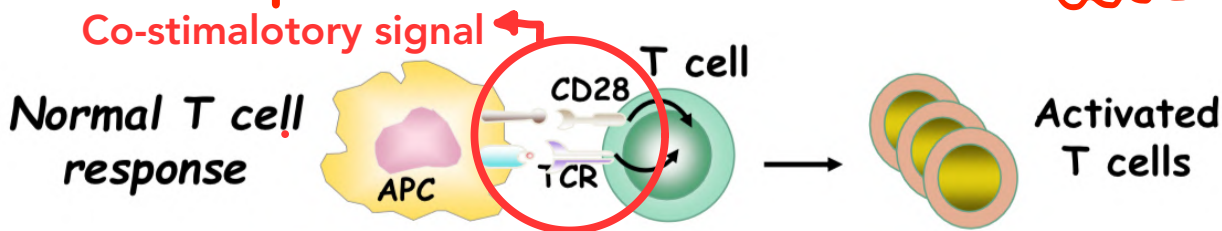
Thymic ("natural") regulatory T cells (Treg)

- Development requires recognition of self antigen during T cell maturation
- Reside in peripheral tissues to prevent harmful reactions against self

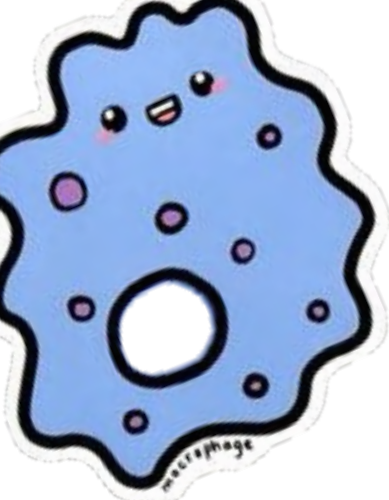
اول اشبي هي عملية تحويل ال Tcell من حالة

- Effector ---> Regulatory
هاي العملية حصراً لل CD4+
- CD8+ ---> Deletion only

Peripheral tolerance of T cell ^{*} 3 mechanisms

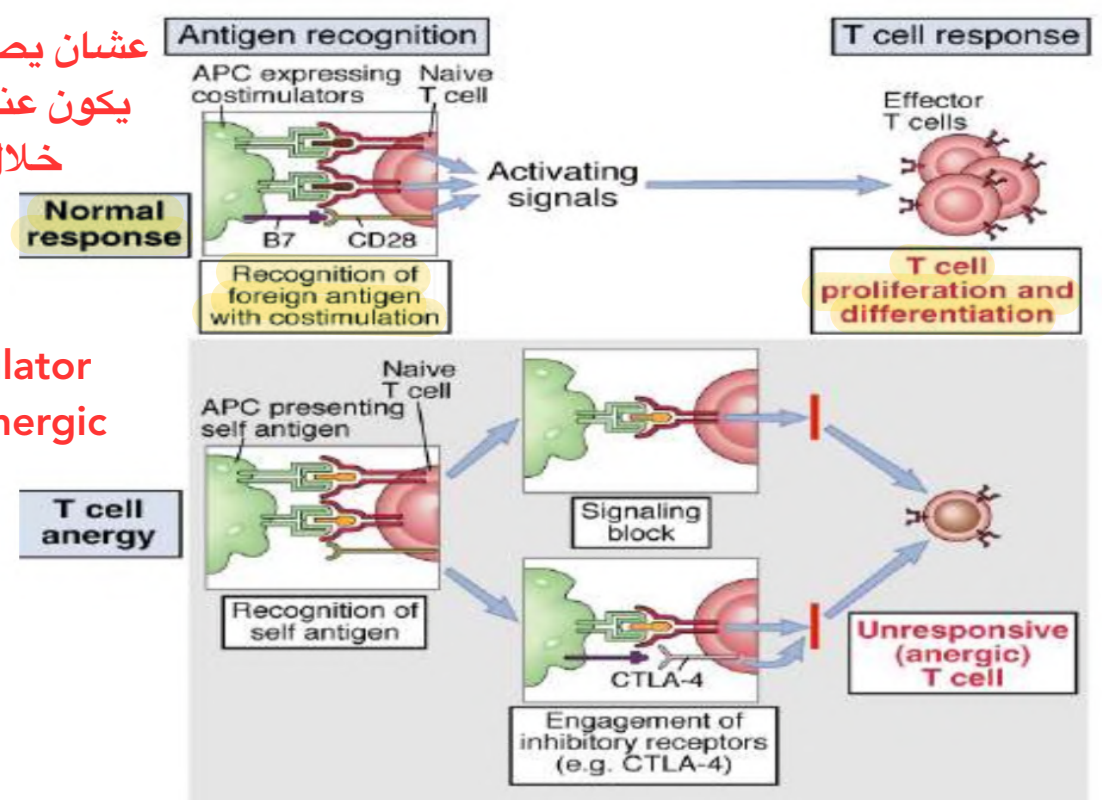


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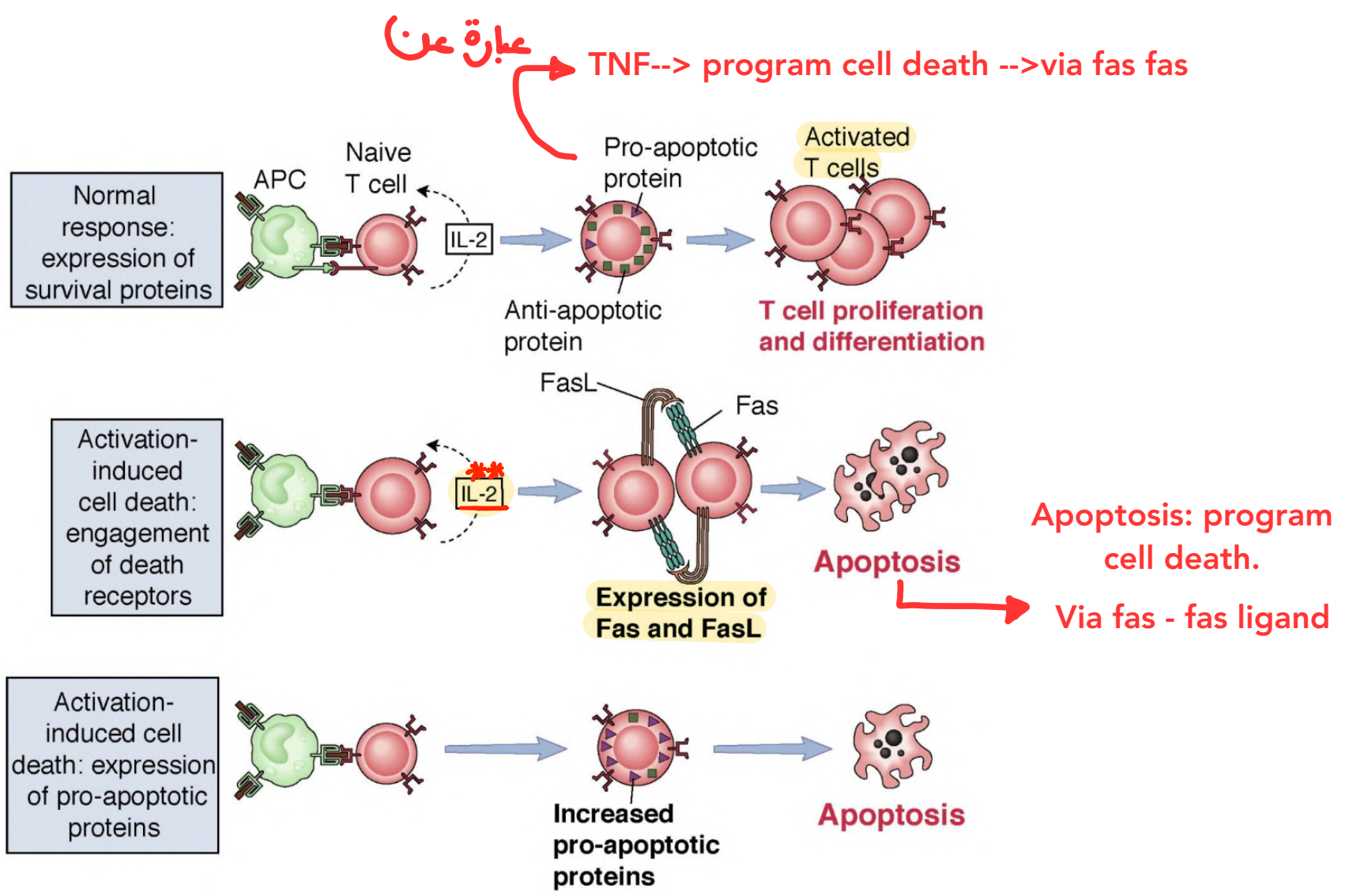
1. T cell anergy

عشان يصير عنا activation لازم
 يكون عنا co-stimulation من
 خلال B7 with CD28
 A lack in co-stimulator
 signal means an anergic
 response

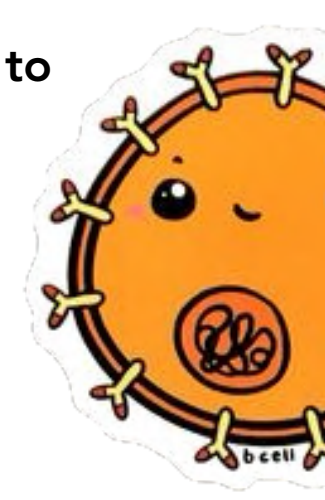


Anergy is the functional inactivation of T lymphocytes that occurs when these cells recognize antigens without adequate levels of the costimulators (second signals) that are needed for full T cell activation

2. Apoptosis "Activation-induced cell death"

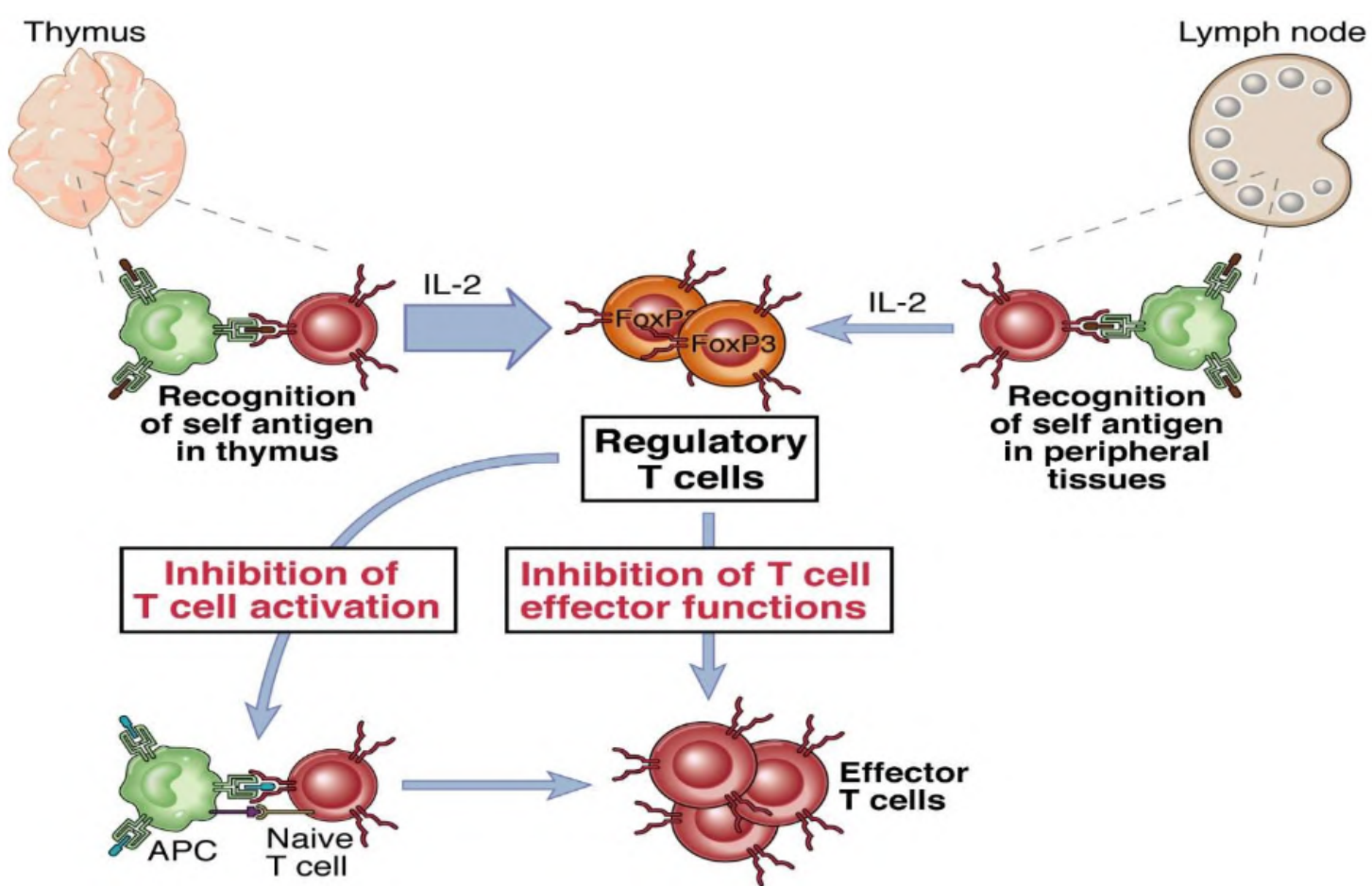


Fas ligand (FasL or CD95L) is a type-II transmembrane protein that belongs to the tumor necrosis factor (TNF) family. Its binding with its receptor induces apoptosis



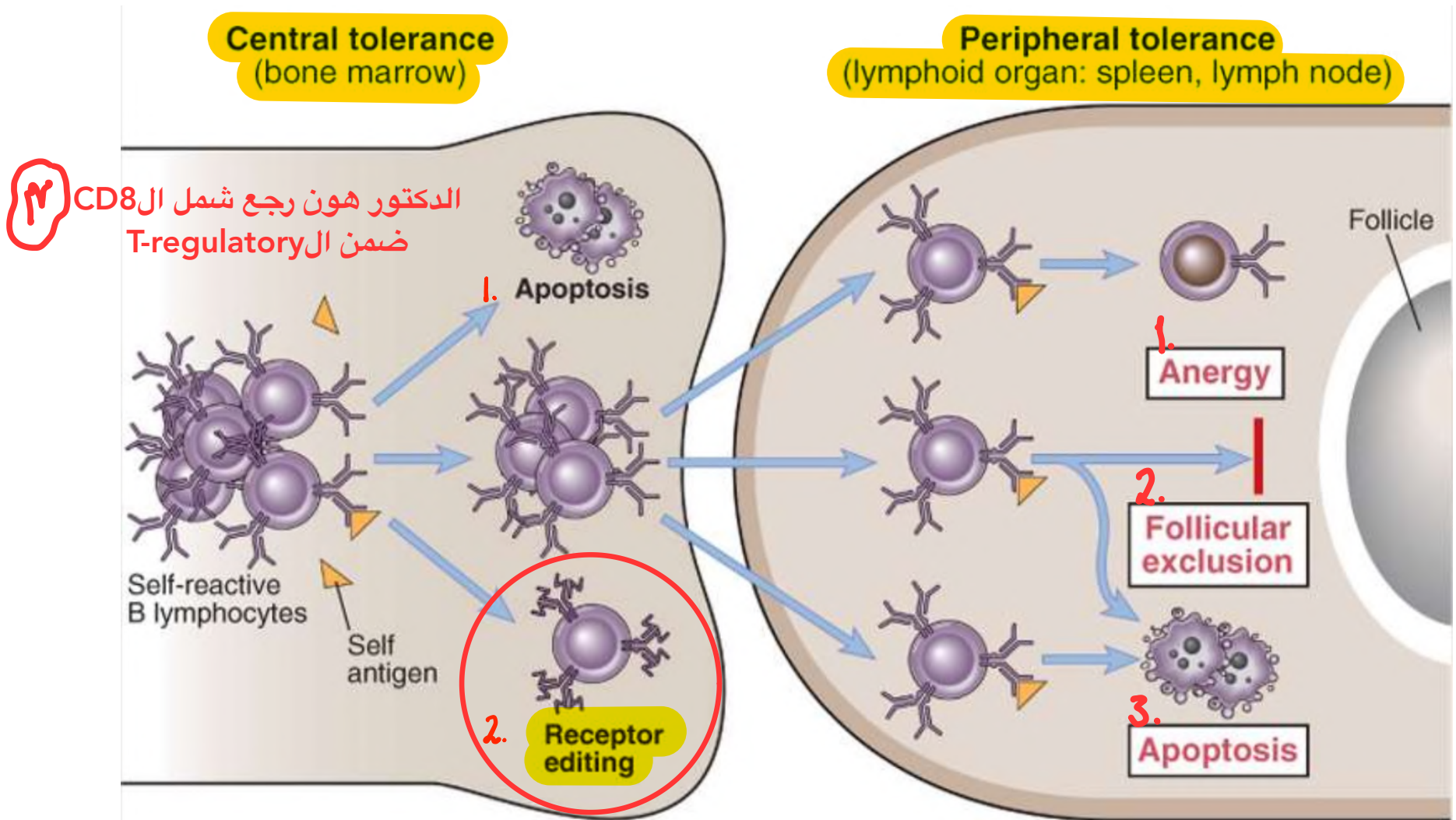
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3. Regulatory T cells



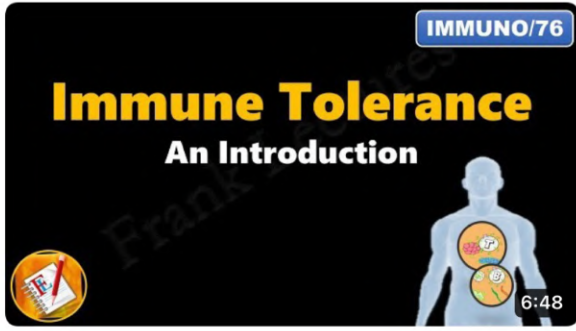
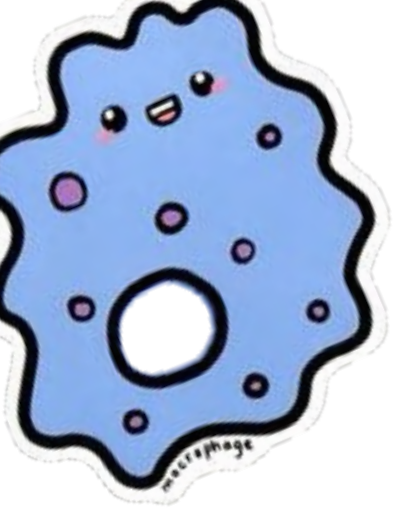
Regulatory T cells develop in the thymus or peripheral tissues on recognition of and block the activation of potentially harmful lymphocytes specific for these self antigens

Central and peripheral Tolerance in B cells



***Apoptosis is done by :
 1) Autoimmune regulatory
 2) CD95L

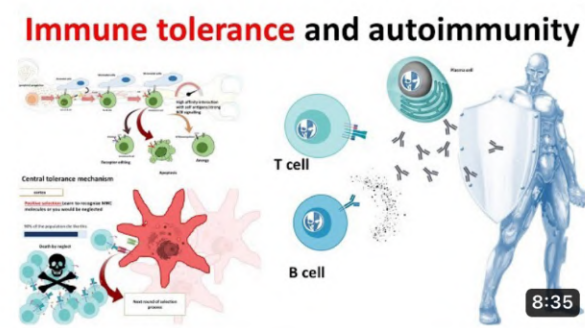
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Immune tolerance - An introduction (FL-Immuno/76)
175K views · 5 years ago

Frank Lectures

<https://youtube.com/watch?v=rHx30H3dUKQ&si=cuW322pMB2NgAih0>



Immune Tolerance and autoimmunity (overview)
121K views · 3 years ago

Animated biology With arpan

https://youtube.com/watch?v=vDwNpDT-8L0&si=pt18JqWPDq_woHVu

Autoimmune Diseases

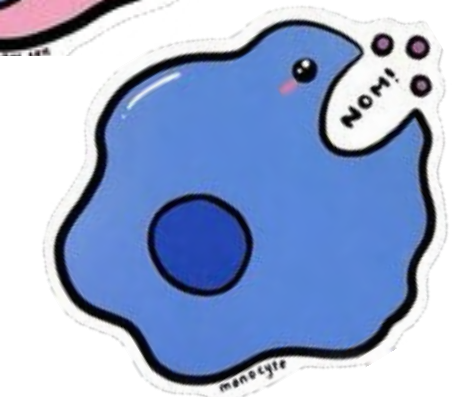
- *Chronic progress disease
- *Cause a morbidity and mortality
- *Some of them look dangerous as cancer

Introduction

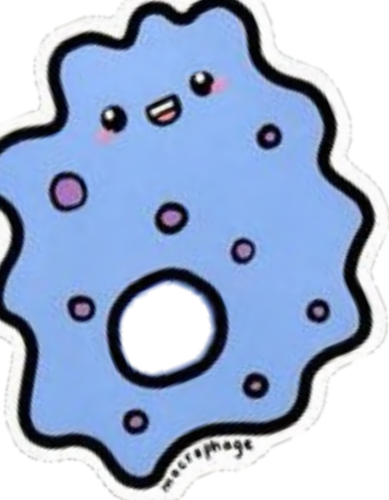
- Autoimmunity is defined as an immune response against self (autologous) antigens.

تحدث بسبب خلل في tolerance mechanisms

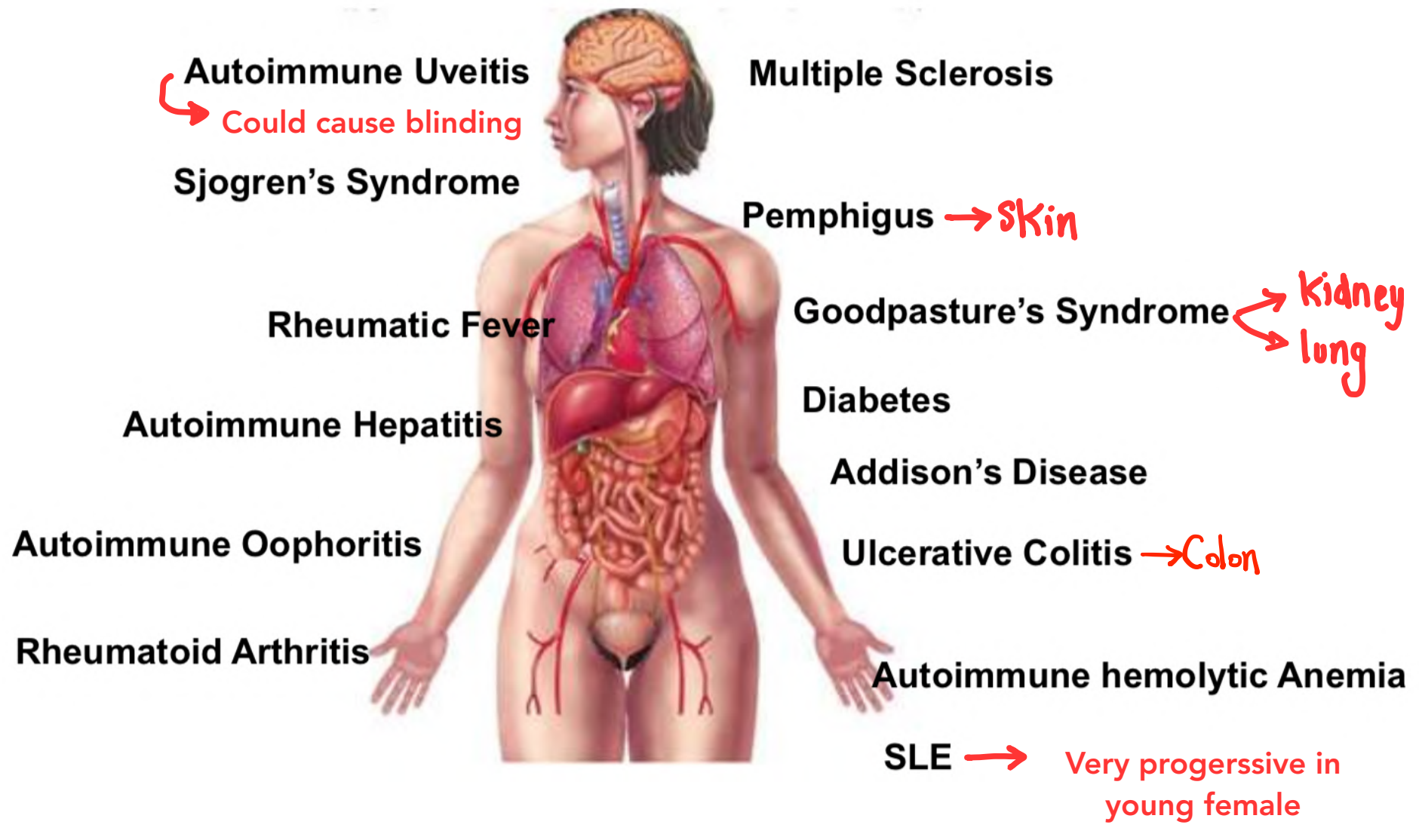
- It is an important cause of disease, estimated to affect at least 1% to 2% of persons in developed countries, and with an apparently increasing prevalence.
- Result from immune responses against self antigens (autoimmunity)
- May be caused by T cells and/or antibodies
- May be systemic or organ-specific
- These diseases often become chronic and self-perpetuating



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Examples of Autoimmune diseases



Classification of Autoimmune diseases

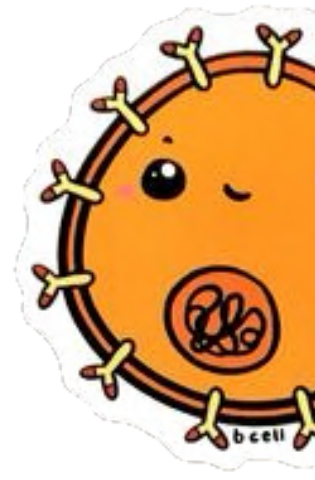
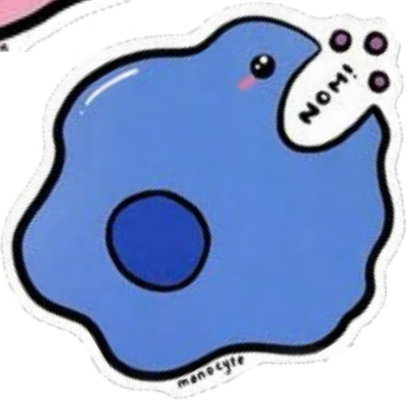
Can be classified into clusters that are either **organ-specific** or **systemic**

affect one organ

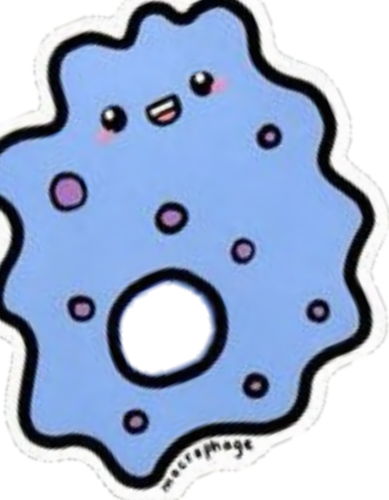
Organ-specific autoimmune diseases
1. Type I diabetes mellitus → ^{بصبيب} young
2. Goodpasture's syndrome
3. Multiple sclerosis
4. Graves' disease
5. Hashimoto's thyroiditis
6. Autoimmune pernicious anemia
7. Autoimmune Addison's disease
8. Vitiligo
9. Myasthenia gravis

affect more than one organ.

Systemic autoimmune diseases
1. Rheumatoid arthritis
2. Scleroderma
3. Systemic lupus erythematosus
4. Primary Sjögren's syndrome
5. Polymyositis



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Examples of organ specific

Hashimoto's disease (thyroiditis)



Leading to reduction of thyroid hormone (T3+T4)

و لتعوض النقص بتبدأ تكبر بحجمها

Vitiligo in melanin



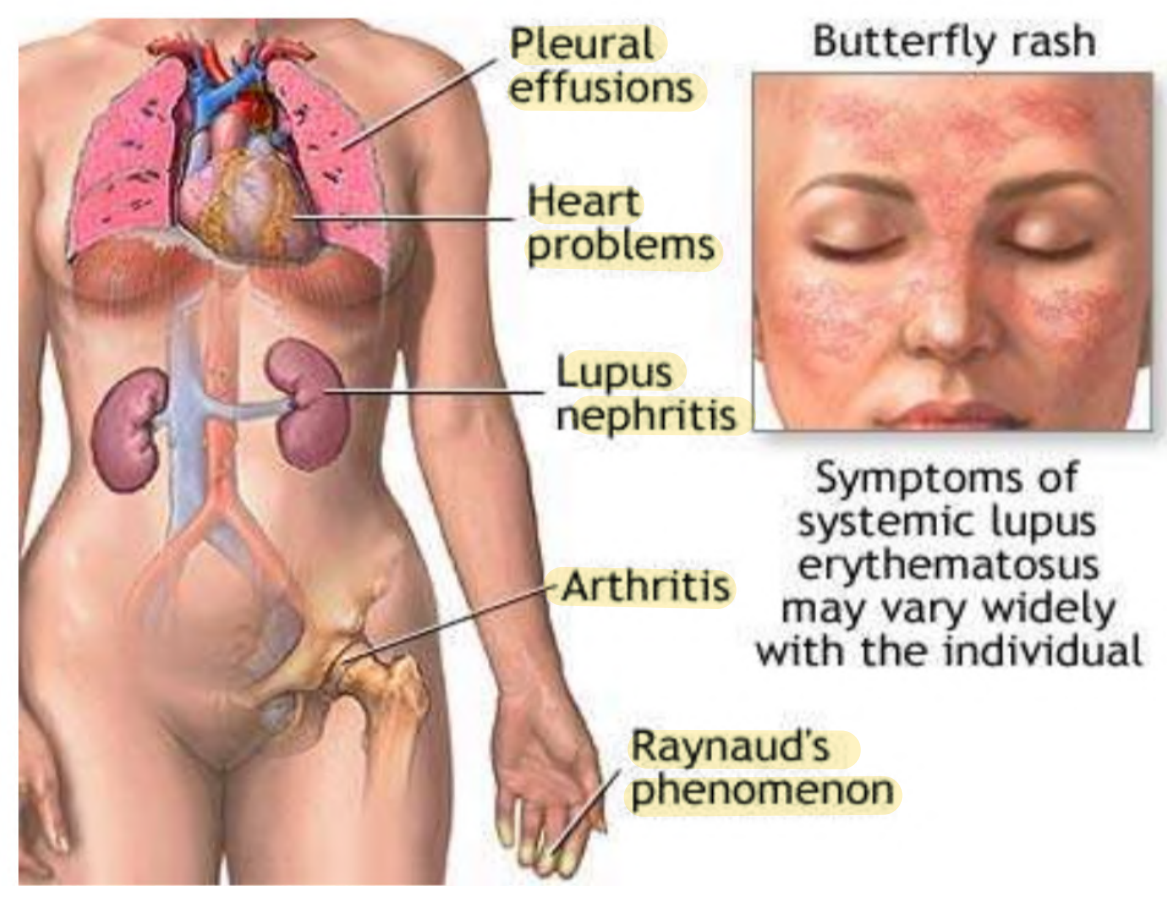
White color batches

Lungs of a patient with Goodpasture's



Example of systemic Autoimmunity

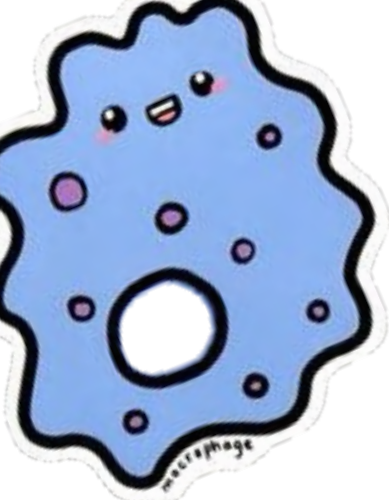
SLE (systemic Lupus Erythrematosus)



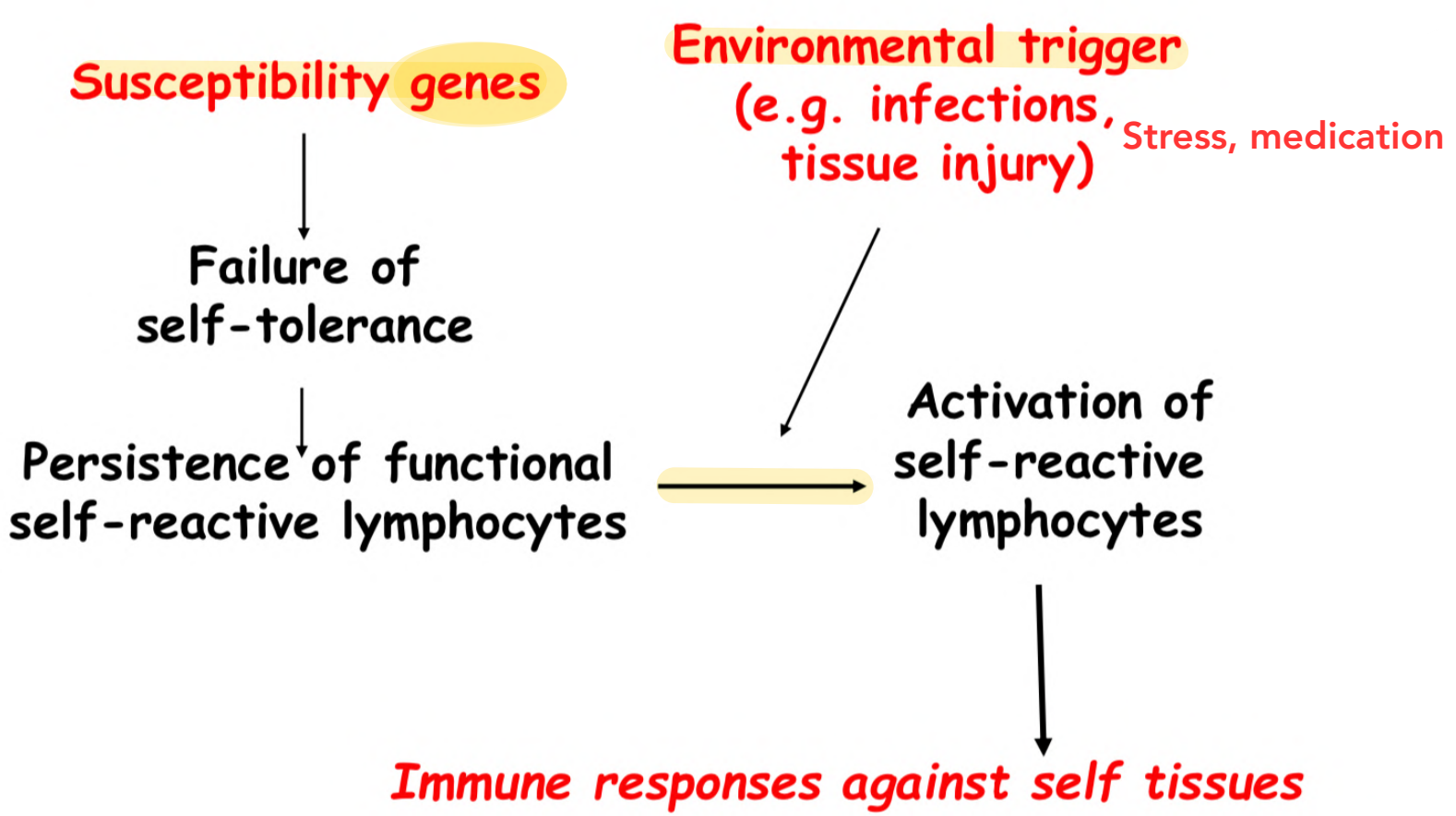
Symptoms of systemic lupus erythematosus may vary widely with the individual



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Pathogenesis of autoimmunity



1. Genetics of autoimmunity

هون بنحكي انه autoimmune disease الها ارتباط اكثر بال gene

- Human autoimmune diseases are complex polygenic traits
- Some polymorphisms are associated with multiple diseases. Other genetic associations are disease-specific

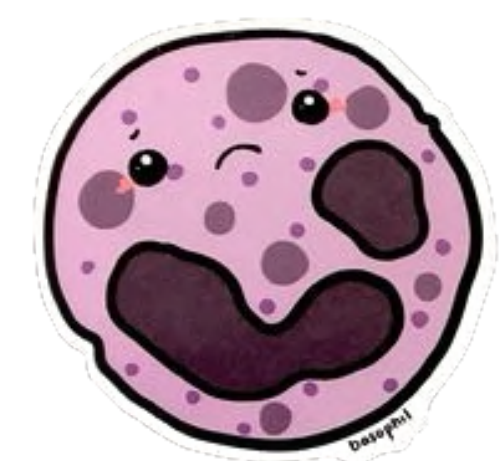
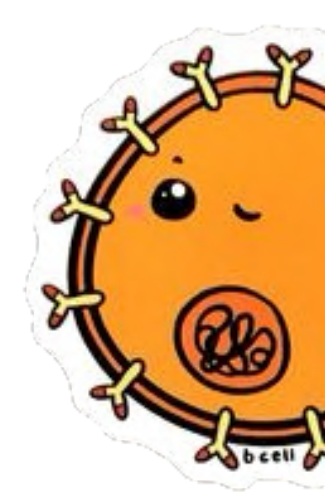
2. Environment Ex : viral pathogen

- Pathogens, drugs, hormones, and toxins are just a few ways that the environment can trigger autoimmunity
- 1. Drugs: Drug induced lupus
- 2. Toxins
- 3. Hormones: **Females are much more likely to develop autoimmune illness**
- Hypothesis: estrogen response elements (EREs) in several genes

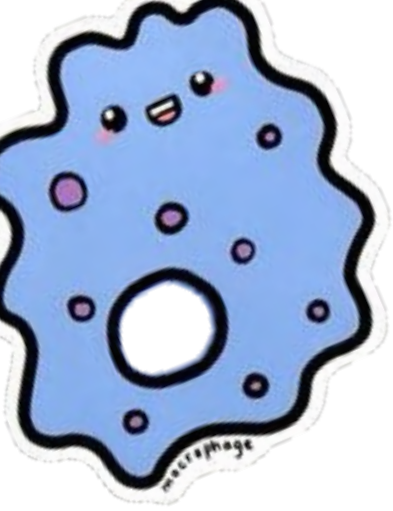
3. Infections and autoimmunity

Ex ; Corona

- Infections trigger autoimmune reactions
- Autoimmunity develops after infection is eradicated (i.e. the autoimmune disease is precipitated by infection but is not directly caused by the infection)



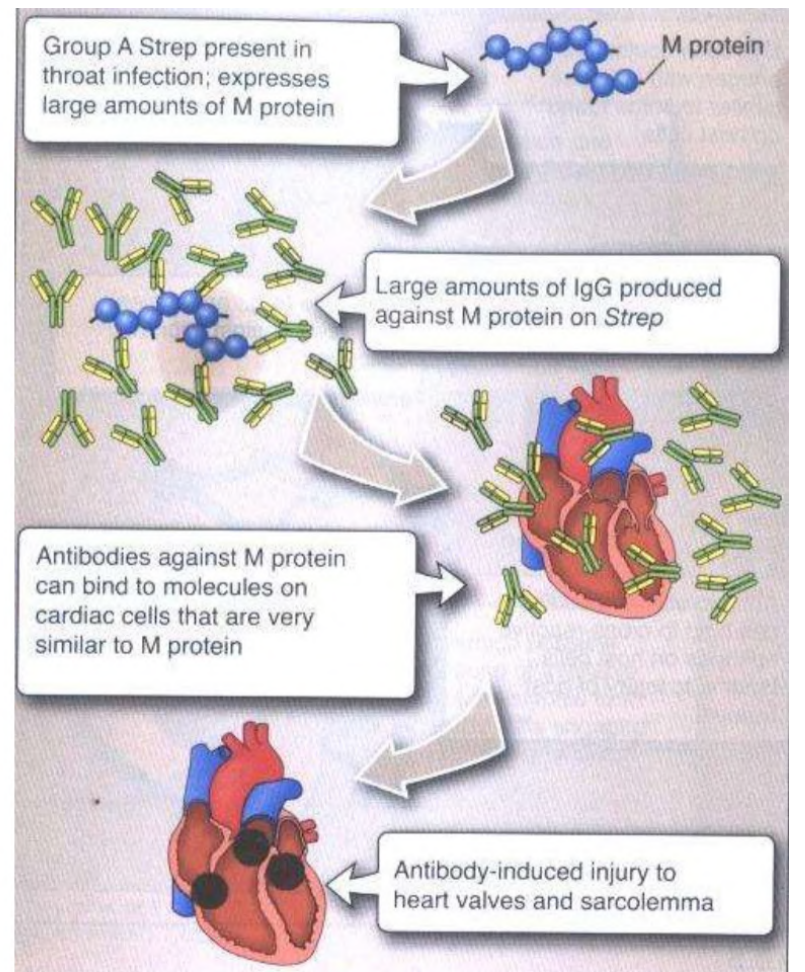
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Rheumatic fever is a classic example of molecular mimicry

مثال كيف ال infection ممكن يحفز ال genes و يطلع ال rheumatic fever

فلما ننصاب ب group A من ال Staphylococcus و بصير عنا sore throat و الجسم بصير يعمل antibody لهاي البكتيريا و لكن لان هذه البكتيريا عليها m protein بشبه تبع heart valve ، بتروح هاي ال antibody و بتعمل لنا damage بال heart valve ممكن اعطي Antibiotic لو عملت diagnose بكير، و لكن لو ما كشفته بكير بتكون ال antibody و بعد سنين بصير مع المريض heart valve بال destruction

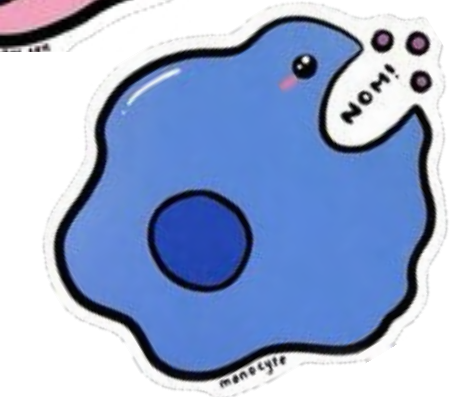
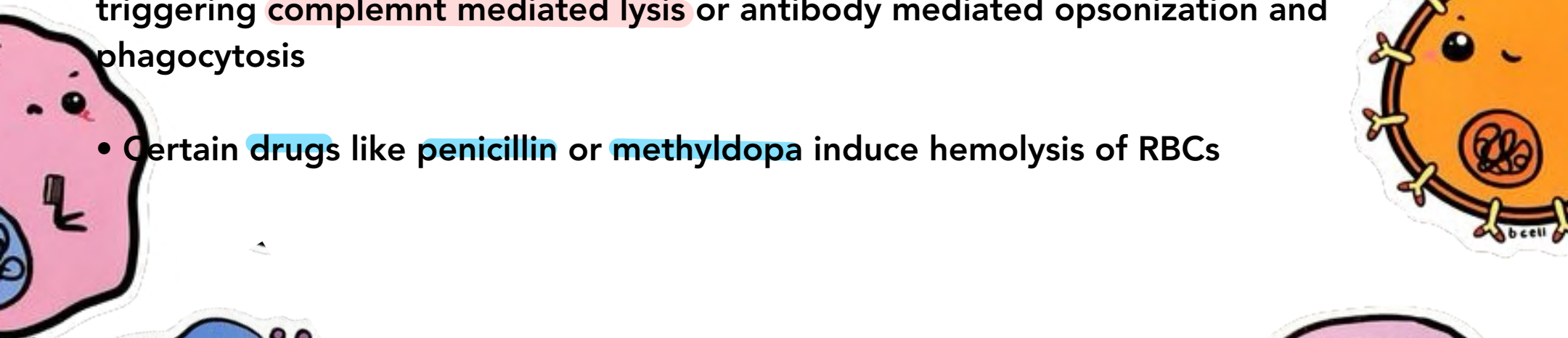


1. Hashemot's thyroiditis

- Individual produce autoantibodies and sensitize Th1 cells specific for thyroid antigen
- Antibodies are formed against thyroid proteins including thyroglobulin and thyroid peroxidase.
- Binding of these antibodies to these proteins interferes with iodine uptake leading to hypothyroidism
- Intense infiltration of thyroid gland with lymphocytes, macrophages, and plasma cells
- Inflammatory response leads to goiter and hypothyroidism

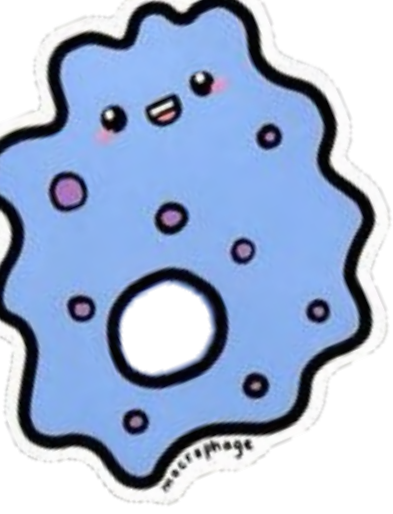
2. Autoimmune anemias

- It includes pernicious anemia, autoimmune hemolytic anemia and drug induced hemolytic anemia
- Pernicious anemia is caused by antibodies to intrinsic factors on gastric parietal cells which blocks vit B12 absorption necessary for haematopoiesis.
- Autoimmune hemolytic anemia results from autoantibodies to RBCs antigens triggering complement mediated lysis or antibody mediated opsonization and phagocytosis
- Certain drugs like penicillin or methyldopa induce hemolysis of RBCs



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3. Goodpasture's syndrome

- Autoantibodies specific for basement membrane antigens of kidney glomeruli and alevoli
- Complement activation and inflammatory response induce cellular damage leading to progressive kidney damage and lung hemorrhage

ممکن يكون ال presentation تبعتها عبارة عن hmoptysis

** 4. IDDM AS: DM Type

الدكتور وضح النقطة انه ال DM Type 2 غير مرتبط بامراض المناعة وانه ال type2 مرتبط يال lifestyle

- Immune response against beta cells of lanchans islets in pancreas
- The autoimmune attack induce damage of beta cells with decrease production of insulin which leads to increased levels of blood glucose

5. Graves' disease

No Destruction --> stimulation

- In Graves' disease autoantibodies binds receptors for TSH and mimic the normal action of TSH resulting in the production of thyroid hormones

TSH = Thyroid stimulating hormons
حكى الدكتور بزيد عنه T4,T3 وبدخل فى hyperthroidism

6. Myasthenia gravis

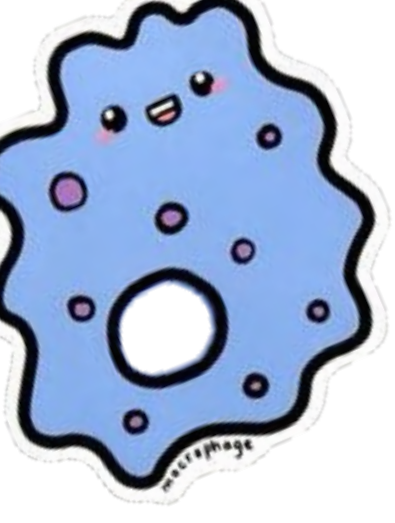
- Autoantibodies that bind the acetylcholine receptors on the motor end of muscles blocking the normal binding of acetylcholine and induce compliment mediated lysis of cells
- This results of progressive weakness of the muscles

بتزيد خطورة ال myasthenia gravis لما تكون في Diaphragm لانها بتعمل عنا Respiratory arrest

وبخربوا الدنيا acetylcholine تبع ال receptor بربطوا على ال Igm,IgG



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7. SLE

- Autoantibodies against DNA, histones, RBCs, WBCs, platelets manifested mainly by systemic vasculitis and glomerulonephritis

8. Rheumatoid arthritis

- Autoantibodies called rheumatic factor of IgM class react with determinants on the FC portion of IgG. IgM/ IgG complex deposited on joint surface leading to arthritis

ال IgM يرتبط بال Fc تبع ال IgG و يعمل complex بيتربسب في ال Joints

باخر المحاضرة حكي الدكتور مهم تعرف العضو المرتبط بالمرض وتعرف كيف يكون ال Damage و تم بحمد الله ❤️

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