Microbiology

Subject :

Lec no : 29

Done By : Tabark Aldaboubi , Dana khalaf

وقل رب زدني علماً

Immunology of viral infections

Virology Lecture 4

Ashraf Khasawneh
Faculty of Medicine
The Hashemite University

بتحطين plasma لـ وهاي (specific immunity) plasma cell بتحطين Activation عبارة عن ← B cell
Antibody or immune globin

Body Defense Mechanisms

B cell exposure to Antigen going to reduce specific plasma cell against Antigen

Humoral (antibody) response:

Like other infectious agents, viruses induce production of antibodies in the blood. Antibodies are:

1) Immunoglobulins- proteins which react specifically with antigens- which are also usually proteins and of which the most important in protective immunity are those on the surface of virus particles.
(glycoprotein or spike)

2) Plasma cells- formed when B-lymphocytes are activated by encounter with antigen. B-lymphocytes have immunoglobulin on their surface, which acts as receptors for virus antigen. Helper T cells contribute to the differentiation of B- cells into plasma cells.
مهمة
!! B cell لـ Activation or Production في دور الها T-cell هيل

* interaction between innate and Adaptive
* " " Adaptive it self
* B cell have aT-cell لوالعكس !!
T cell have aB cell

بالفيروسات الـ antigen بكون بروتين
بالبكتيريا الـ (other than protein) antigen
مثل Polysaccharide ، Lipid ، Pili
Capsule

(Activation of B cell) T- independant في عنا اشي اسمه

only recognize protein Antigen (Activation of T cell) T- dependant

These release the type of Antigen. : independant and dependent ترتيبي ✱

اذا كان

dependent

protein
then the T-cell
going to recognize

اذا ما كان
بروتين
independant
اذا كان غير عن البروتين (ما) بصيرلها
recognize by T cell
B cell وانما

✱ T cell only recognize
Protein Antigen

!! independent or dependent بين احسن

✱ الفيروس بنحكي عن glycoprotein and spike

protein هذول

T-cell dependent بالتالي بحكي عن (dependent)
↳ activation by T-cell

✱ الـ capsule and polysacchrid ← independent
recognize Antigen with out the بيقي لحالها Bcell
the T-cell going to for Antibody

✱ what is the character the Antibodies
for the B-cell alone: (independent)
specifity اقل , duration اقل
protection at small age is non protective (توضيح هاي النقطة تحت)

** جابوا Polysccharide تاعت streptopnomonia واعطوها

Vaccine لحالها

بدي اضع Vaccine شوالفكرة !!

تعمل ← exposure of immune system to Specific Antigen

(اجيب جزء من البروتين تاع الفيروس ، جزء من البروتين تبع البكتيريا، جزء من Polysccharide تاع البكتيريا واعمله ingected على ال human body ←

as a result going to mount of immune system charactries by immunoglubain and memory and cell mediated immunity)

عملوا هيك واعطوه للأطفال على عمر months

What they found given polysccharide didn't protective response of these children !! independent or dependent وجدوا انه في اسئلة اسمها

immune respons which protein antigen through the T-cell activation → stronger

(conjucated Vaccine) Polysccharide and protein بين compind !! ايش فكروا يعملوا

T-cell الي فرق انه هون صار يحفز ال

going to Amount of immunity ← هداي الشغلة حققوا

حكا الدكتور اقرأوا عنها

* ليش T-cell independent they don't confirm enough immunity for a children !!

اللهم اني احاول فأعني .

Pentamer
IGM → Y 5 مع بعض بواسطة s-s bond)
وبالاخر بمسكهم الـ J chain

* خلل بالـ J-chain بعمل مشاكل بـ IGA IGM

IGG, IGE, IGD ← monomer بين من هدول

2 Y بشبكوا ببعض dimer (Secration)
بواسطة (s-s bond) + J Chain

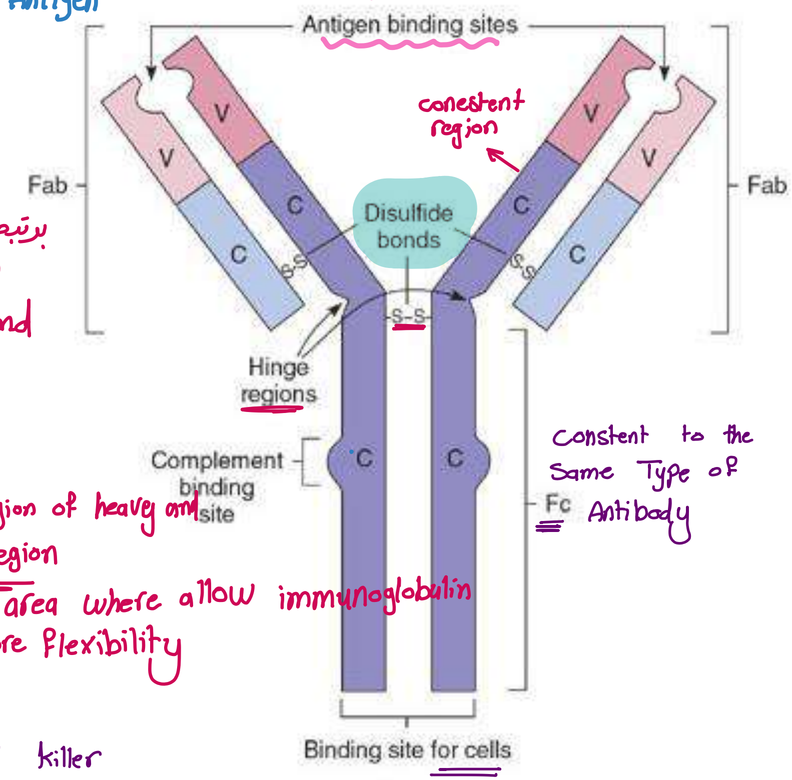
ما mono IGA, IGM, IGD, IGE, IGE اشكال

Antibodies

- **Immunoglobulin** (Ig)
- A large Y-shaped protein
- Consists of 4 polypeptide chains
  - 2 Light chain — الي على الجنب
  - 2 hevey chain — الي بالوسط
  - برتبطوا ببعض بـ (s-s bond) disulfid bond
- Contains 2 identical fragments (Fab) with ends that bind to specific antigen
  → Varible region + Fronstent region of heavy and light chain لحالها الـ
  Hinge region → area where allow immunoglobulin more Flexibility
- Fc binds to Fc receptor on B lymphocytes, DC, NK, macrophages, neutrophils, eosinophils, basophils, platelets, and mast cells.
  - Fc: ثابت constent
  - opsonization ← برتبط فيهم ← وبصير phagocytosis for all thing
  - DC: dentritic cell
  - NK = Natural killer

(V) Veriable region this is accomote the diffrent type of Antigen

** How many Antigen binding site in any Y shape !! (2)



(a)

Epetope → unit of Antigen
Specific Antibody بتعرف Antigen or epetope

Body Defense Mechanisms

* اذا بدي اشوف resint infection ولا لا !! بدور بالاول عال IgM

Humoral (antibody) response:

Three immunoglobulins are mainly responsible for humoral immunity in virus infections:

Pentomer 5 Y

←**1) IgM-** the earliest antibody produced: appears at a variable interval after exposure, depending on the virus, incubation period, dose and route of transmission; persists for about 4-6 weeks, sometimes longer; a pentamer of five IgG molecules.

mono

←**2) IgG-** formed later than IgM but persists long term, often for years: responsible for immunity to reinfection.

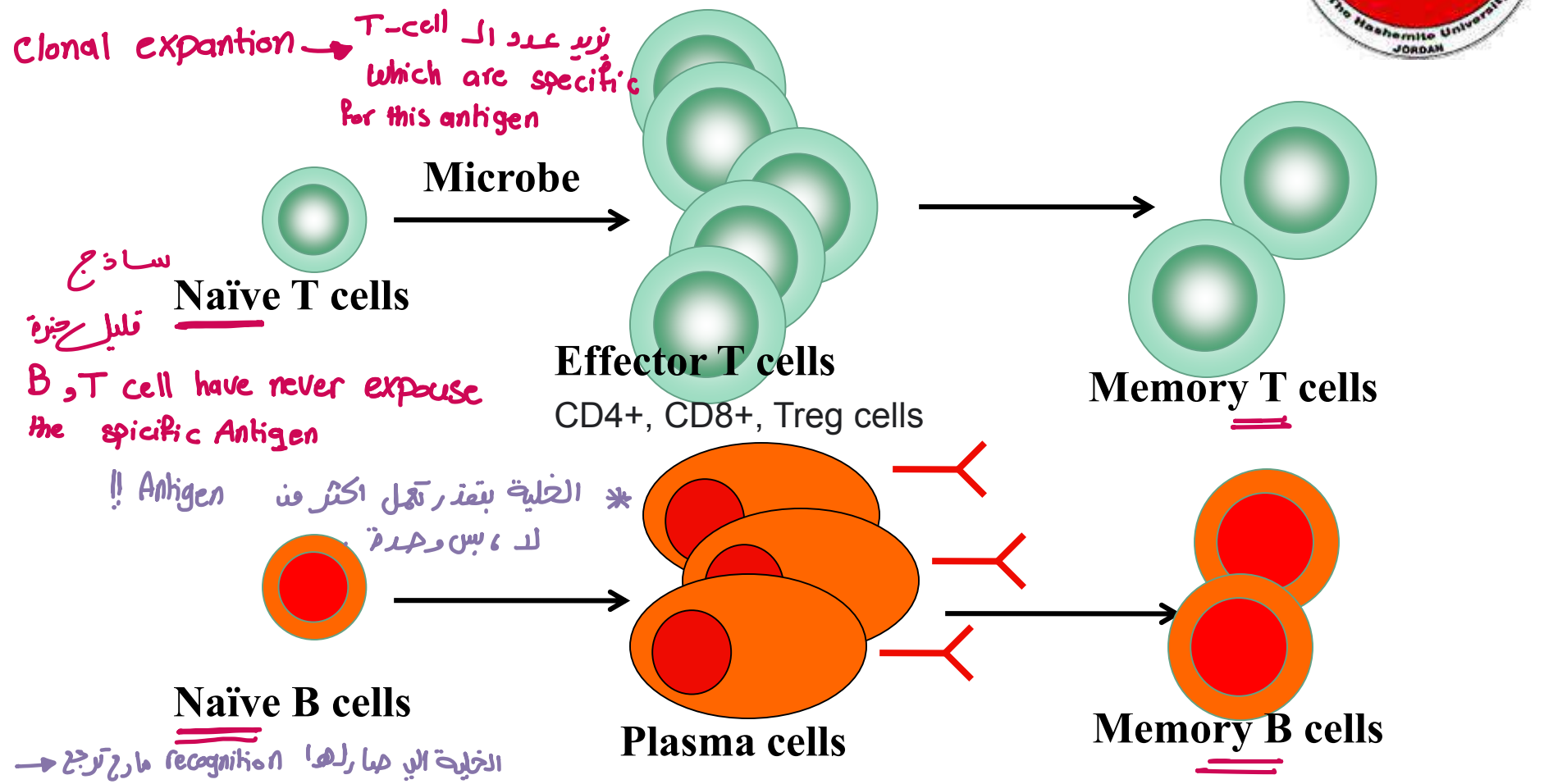
dimer or mono

←**3) IgA-** a dimeric molecule, found in body secretions (as well as blood), i.e., saliva, respiratory secretions, tears and intestinal contents; the main antibody involved in immunity to respiratory viruses and in gut immunity associated with enteric virus infection; secretory IgA acquires a carbohydrate 'transport piece" in extracellular fluids that is absent from serum IgA.

* ليش في مصطلح !! booster doeses زي وطعوم فايزر اللي اعطوه بكورونا اكثر من مرة

Protective level لتوصل لل increase in IgG ←

Phases of immune responses



Rapid protection **Long-lived protection**

* مجموعة من الجينات V, D, G على ال heavy و Light اللي بيصيرلهم Arrangment كاحتمالات
ممكن يتعرفوا ع 10,11 (different Antigen).

من تفاريغ برجس

Humoral (antibody) response:

Three immunoglobulins are mainly responsible for humoral immunity in virus infections:

انواع ال immunoglobins اللي بنعرفهم همه ال IgA /IgG/IgM/IgE/IgD
لما يدخل الفيروس على الجسم اول واحد من هذول ال Ig هو ال IgM و اللي بتزيد نسبته بعد ل ايام
و برجع يقل بعد اسابيع شكله بكون pentamer يعني بكون عبارة عن 5 Y shaped و برتبطوا ببعض عن طريق disulfide bond
و ال J chains

1) IgM- the earliest antibody produced: appears at a variable interval after exposure, depending on the virus, incubation period, dose and route of transmission; persists for about 4-6 weeks, sometimes longer; a pentamer of five IgG molecules.

هسه IgM بشتغل وقت ال acute infection
و لما تتعرض لل infection لاول مرة ال IgM بتوصل ال peak ابطئ من لما يصيرلك reinfection
فيعني لو قعدت اسبوع باول مرة راح تقعد يومين تلاث بال reinfection
و بعدها بتكون عندي ال IgG اللي بتحمي جسمك من الفيروس لسنوات و هاي فكرة المطاعيم

2) IgG- formed later than IgM but persists long term, often for years: responsible for immunity to reinfection.

ثاني respond هو ال IgG و اللي هو السبب لل humoral immunity و اللي بتسبب long term protection against viruses
and it is the component that we look for if we want to see if the patient has been infected with this virus previously
لانه لو كان عنده IgG للفيروس يعني انصاب في قبل هالمرة و راح يعطي نتيجة ايجابية
and we look for it after vaccination to see if the patient has developed protective level of immunity
نفس الاشي بس اعطي المرض مطعوم لازم يتكون عنده IgG للفيروس
مثلا عندك الكورونا عنا two doses لو اخذت الاول اليوم الثاني بتوخذه بعد اسبوعين او تلات
protective level of IgG = 100 لو كان ال
و اعطيته او جرعة وصل 70 هيك ال مريض لسا من immunized لانه لازم تكون فوق ال 100 فلما تعطيه الجرعة الثانية بوصل 120

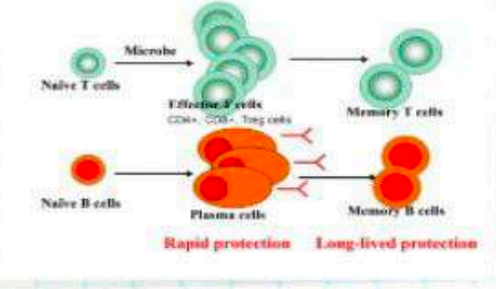
3) IgA- a dimeric molecule, found in body secretions (as well as blood), i.e., saliva, respiratory secretions, tears and intestinal contents; the main antibody involved in immunity to respiratory viruses and in gut immunity associated with enteric virus infection; secretory IgA acquires a carbohydrate 'transport piece" in extracellular fluids that is absent from serum IgA.

3) IgA- a dimeric molecule, found in body secretions (as well as blood), i.e., saliva, respiratory secretions, tears and intestinal contents; the main antibody involved in immunity to respiratory viruses and in gut immunity associated with enteric virus infection; secretory IgA acquires a carbohydrate 'transport piece" in extracellular fluids that is absent from serum IgA.

بتكون موجودة بال secretions تبعت الجسم و بتكون بصورة dimeric اللي همه نتين monomers شابكين ببعض

Phases of immune responses

عنا هون مصطلح ال naive cell و الي معناه الحرفي الخلية الساذجة
يعني الخلية مكونة بس مش عارفة شو بدها
هسه بس تتعرض هاي الخلية لل microbe بتتمايز
اذا كانت t cell و اتعرضت ل antigen راح تتحول ل effector T cell
و اللي راح بنتجوا ال cd4 , cd8 , Treg cells
cd8 هي خلايا T الفاتلة cytotoxic T cells
cd4 هي خلايا T المساعدة اللي بتحفز ال TH1 , TH2
Treg اول ما ال infection بصير ال Treg راح تقلل عدد ال cd4 , cd8
و بتعمل regulate للمناعة
و بعد كل هالحكي بتنتج عنا ال T memory cells اللي بتكون مسؤول عن الاستجابة تكون اسرع في الاصابة الثانية و الثالثة



بالنسبة لل B cell اول ما تتعرض لل antigen برضو بتكون ال plasma cell و بعدها ال memory B cells

Body Defense Mechanisms

Cell-mediated immunity: T cell

Cellular immunity plays an important part in the response of the body to viruses.

Children with congenital deficiency of cellular immunity are abnormally susceptible to virus infection and often (although not always) develop unusually severe disease: those with humoral immune deficiency, on the other hand, respond normally to virus infections.

Cell-mediated immunity is the mechanism for the elimination of virus-infected cells- and therefore virus- from the body.

لو هو موجودة رح يصير في نقص بـ B cells

T- or thymus-dependent lymphocytes are the principal cells involved in this.

T cell بتيجي من bone اما برضو فيه، maturation وبصيرلها bone marrow تبعها origin ال B cell ال

There are two main types: marrow وبصيرلها maturation ب thymus

1) **CD4-positive helper T-cells**
2) **CD8-positive cytotoxic T-cells**

Body Defense Mechanisms

هسه راح نحكي عن ثاني نوع من الspesific response ال cellular immunity و بدنا نسأل مين اهم هي ولا ال humoral ؟؟
الثنين مهمين و بشتغلوا مع بعض بس اذا اضطرينا نختار فال cellular immunity اهم لانه حتى مع وجود ال humoral بعض
الفيروسات ممكن تقدر تهرب منه و تفوت جوا الخلايا

Cell-mediated immunity: بس اذا عنا strong cellular immunity راح نقتل الخلايا
اللي انصابت و نمنع انتشار الفيروس

Cellular immunity plays an important part in the response of the body to viruses.

Children with congenital deficiency of cellular immunity are abnormally susceptible to virus infection and often (although not always) develop unusually severe disease: those with humoral immune deficiency, on the other hand, respond normally to virus infections.

الاطفال اللي عندهم نقص في ال cellular راح يعانوا من مشاكل لانه ما في اي طريقة تطلع الفيروس لبرا
اذا قدر يعدي من ال humoral
لكن اذا كان عنده مشكلة بال humoral ممكن يكون عنده respond طبيعي للفيروسات لانه لسا عنده خط دفاعي بحمي
خلاياه اللي هو ال cellular

Antigen processing and presentation

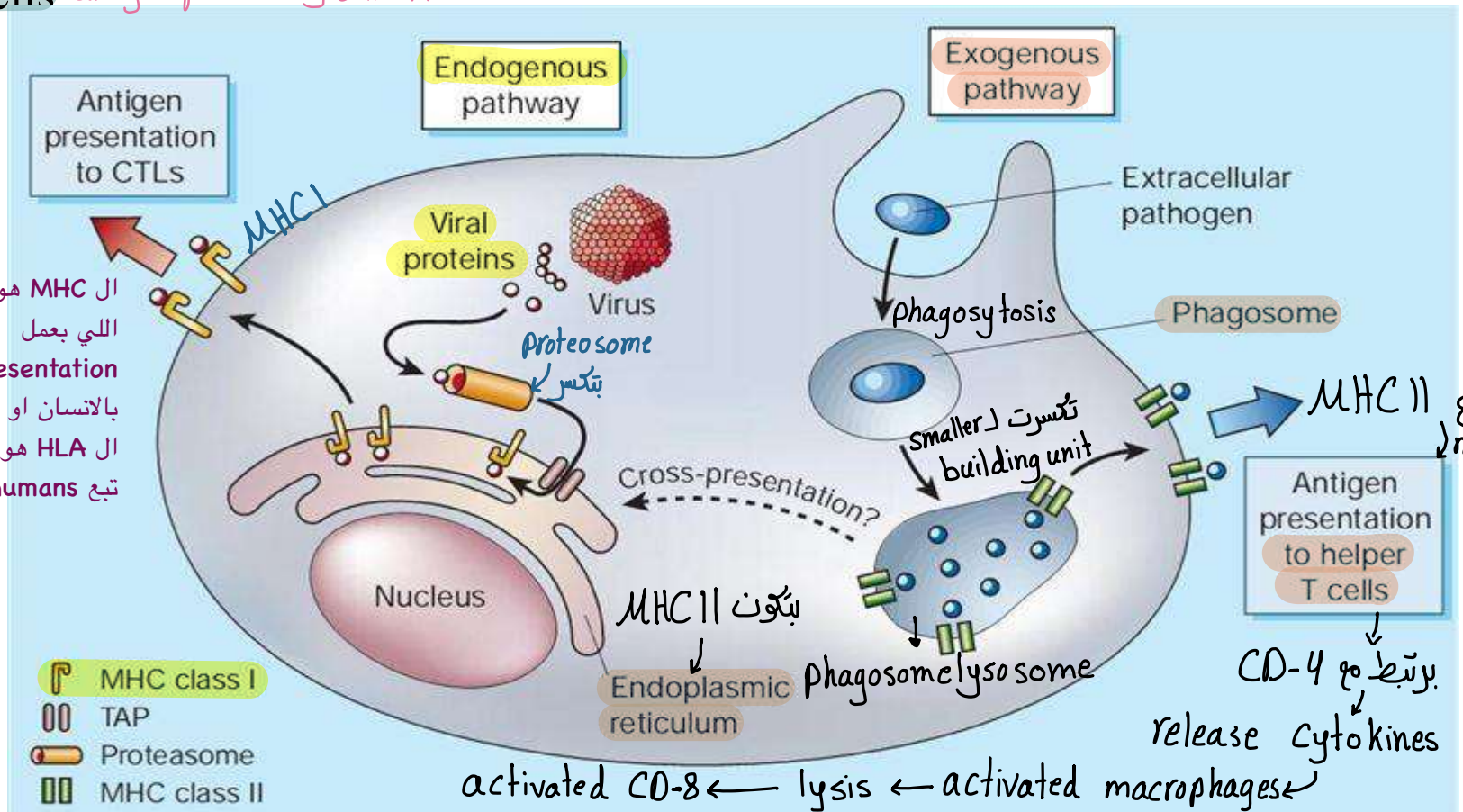
جهاز المناعة مو بس بقرأ antigen تبعت MHC لا كمان بقرأ MHC itself وبحكيلي اذا هو self ولا nonself بمعنى لو واحد عمل kidney transplant ال MHC اللي كان self رح يصيرله recognise nonself ل ،، طبعا لو ما تصنع MHC جهاز المناعة ما رح يقدر يتعرف ع antigen

Epitope ✓

MHC Distinguish between self and nonself

MHC I all cells

MHCII Macrophages, dendritic cells, some T and B cells antigen presenting cells ⇒ MHC 1/2



ال MHC هو النظام اللي بعمل presentation بالانسان او بالحيوان.. ال HLA هو MHC تبع humans

Antigen processing and presentation

ال antigen بتكون من protein او glycoprotein

هسه ال antigen بتكون من multiple arms كل arm منهم الها شكل اما دائرة او مثلث

كل هذول الarms او ال shapes بعلموا ال antigen

لكن الshape الواحد منهم بعمل epitope

Epitope

MHC Distinguish between self and nonself

ال Major histocompatibility complex بكزن موجود ع ال surface تاع الخلية

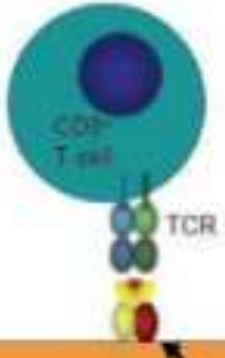
بفرق بين ال antigen تبع خلايا الجسم و ال antigen تبع الاجسام الغريبة

عندك نوعين منه MHC I الموجود بكل الخلايا ما عدا ال RBCs

MHC I all cells

MHCII Macrophages, dendritic cells, some T and B cells

و ال MHC II و اللي بكون موجود بال Macrophages, dendritic cells, some T and B cells



اذا ال antigen دخل عالخلية

ال proteasome راح تكسره لقطع صغيرة بعدها راح تروح القطع على ال MHC الموجود على ال ER

و اللي بغير شكل ال MHC تبع الخلية لواحد جديد و غريب عن الجسم اللي راح يتعرف عليه هو ال cd8

واللي راح تقتل الخلية

هذا الحكي لو كان ال antigen جوا الخلية

طيب اذا كان برا الخلية

راح تبتلعه ال Macrophage و اللي راح تدمره و تنقله ع ال MCH component اللي في ال ER

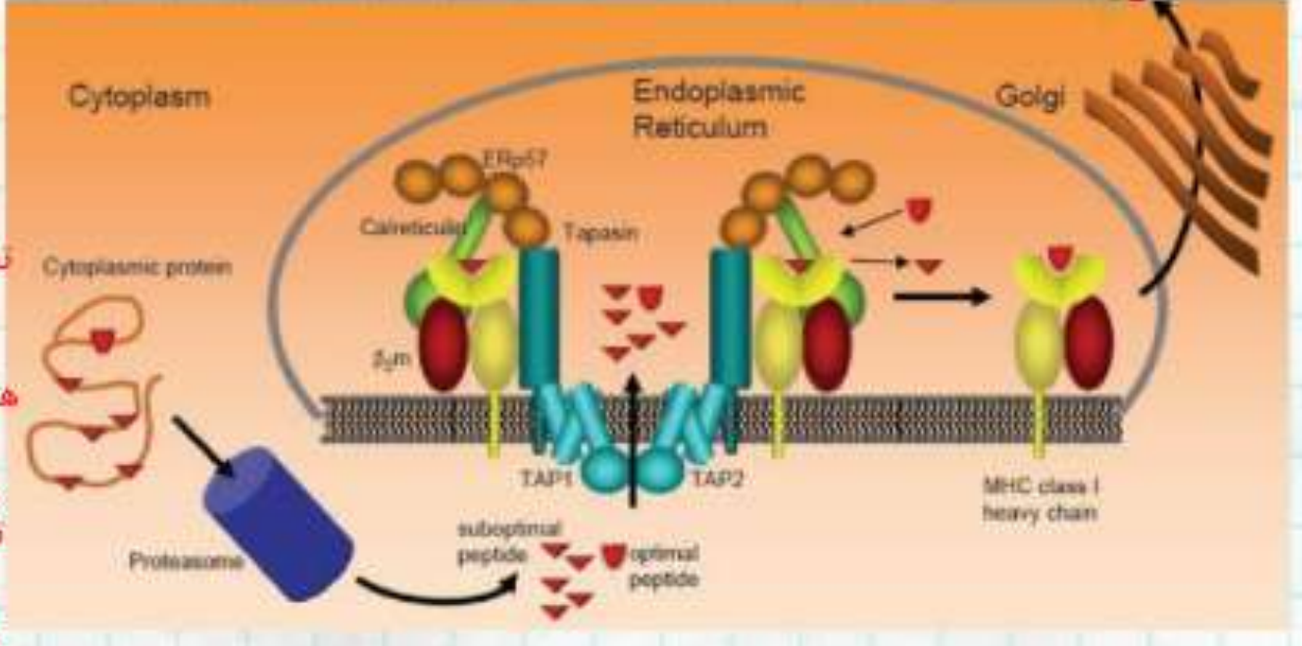
و ترتبط ع ال MHC II على ال surface

المهم هون ال cd4 هون هي اللي بتشتغل

و اللي بتفعل ال TH1 , TH2

TH1 بعمل cellular immunity

TH2 بعمل humoral immunity



ال natural killer cells او لقو خلية ما عليها MHC بتفترض ال killer جدلا انو هاي الخلية فيها فايروس
مانع انو يصير لMHC ف بتقتلها،، لانو بالوضع الطبيعي الخلية اللي مو infected بكون عليها MHC

Body Defense Mechanisms

Cell-mediated immunity:(continue)

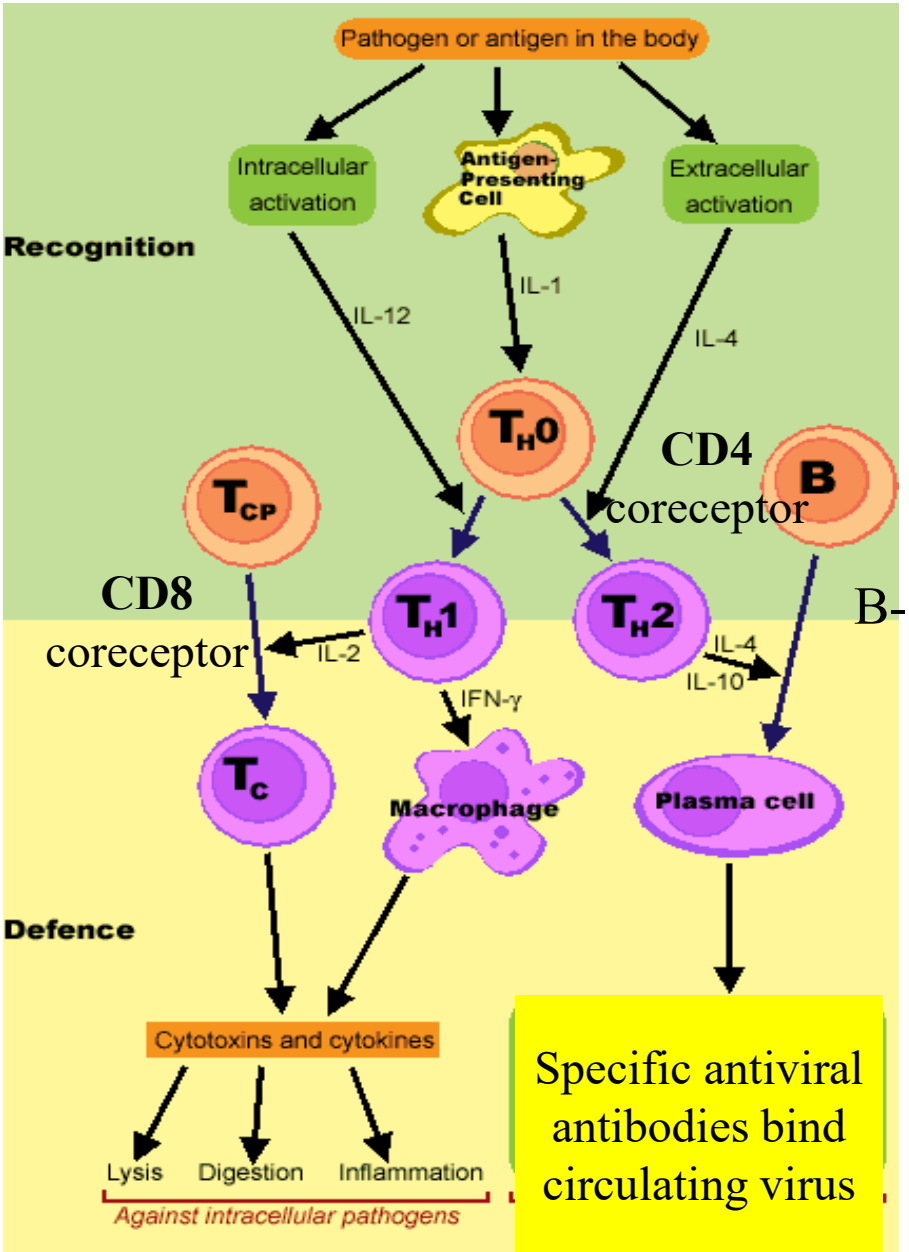
1) **CD4-positive helper T-cells-** **carry CD4 receptors as markers on the their surface. The most important cells in the cellular response, they liberate *cytokines* that activate and modulate cellular immune responses. They require MHC (Major Histocompatibility Complex) class II antigens to be presented in association with the target antigen for their activation. They also interact with B-lymphocytes for antibody production.**

2) **CD8-positive cytotoxic T-cells- carry the marker CD8 receptor on their surface and are MHC Class I antigen-restricted. They lyse target cells such as virus-infected cells and tumour cells; the main mechanism for elimination of virus-infected cells from the body; also release cytokines.**

Suppressor function: note that both CD4 and CD8 cells can suppress as well as activate the cellular response. بدخل influenza virus شغل جهاز المناعة، رفع الطاقة الانتاجية للخلايا لحتى يخلص من foreign antigen„ هون بصير start having inhibitors signals لانو بدي اكسر هاي الخلايا وخلص،، مين بعمل هيك ؟ T regulatory with cytokines

Virus is recognized as antigen by helper T-cells when presented by a macrophage or dendritic cell (found in lymph nodes and skin) acting as an antigen-presenting cell: recognition is dependent on MHC Class II antigens.

T-cell response

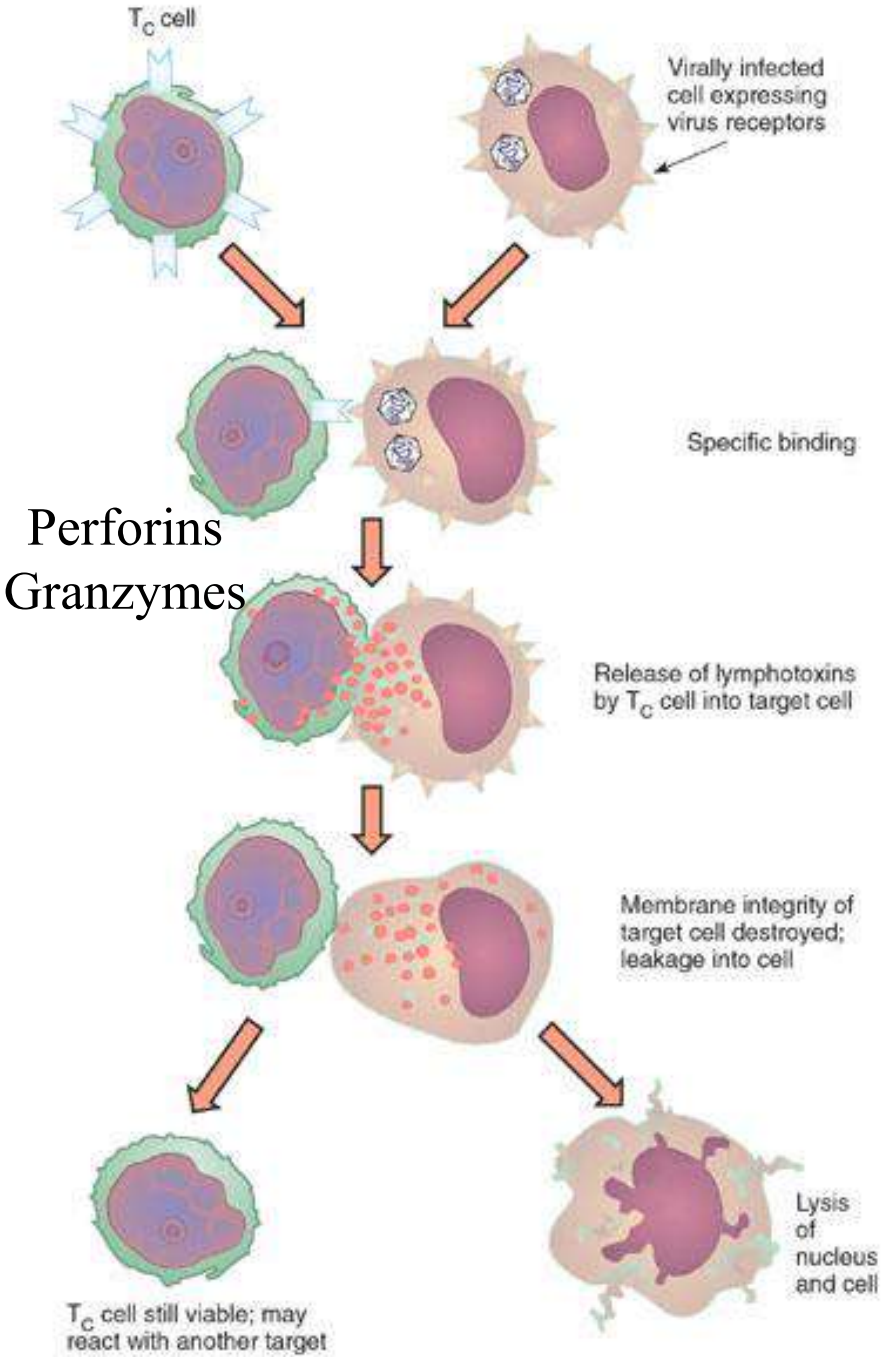


antibody production: T_H2

T dependant activation B cell: T_H2

B-cell proliferation and differentiation

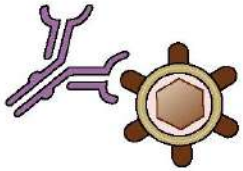
Cytotoxic T cells



Principal mechanisms of defense against microbes

Antibodies

Antibodies block infectivity of microbes



Best way of preventing infection before it takes hold (goal of vaccination)

All microbes

Phagocytes

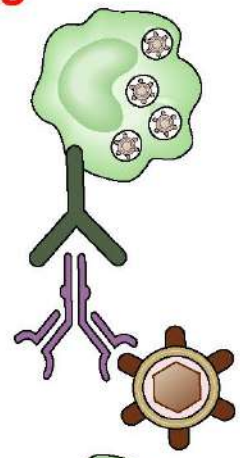
opsonisation

TH1

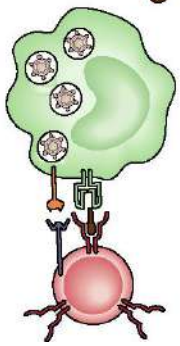
(may work with antibodies, T cells)

Phagocytosis and intracellular killing of microbes

Antibodies (and complement proteins) coat microbes and promote phagocytosis and intracellular killing



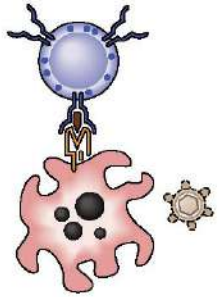
T lymphocytes recognize antigens of ingested microbes and activate phagocytes to become better killers



All microbes

T cells (CTLs)

T lymphocytes kill infected cells



When infection cannot be blocked, or cleared by phagocytes

Intracellular microbes, esp. viruses

Properties and roles of memory cells

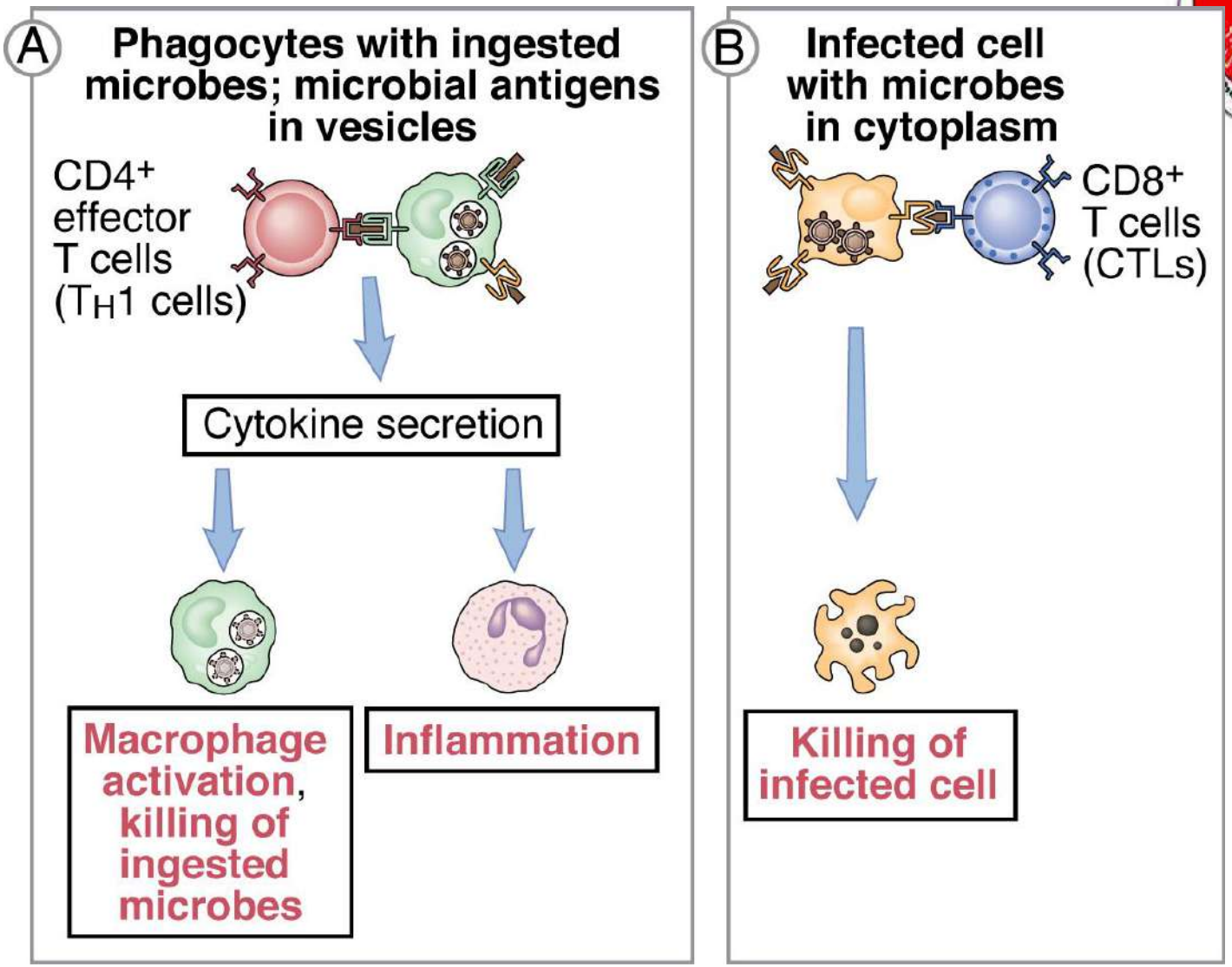
- Survive even after infection is cleared
- Numbers more than naïve cells
- Respond to antigen challenge (recall) more rapidly than do naïve cells
- Memory T cells: migrate to tissues, some live-in mucosal tissues and skin
- Memory B cells: produce high affinity antibodies
- Provide rapid protection against recurrent or persistent infections
- Goal of vaccination is to induce effective memory

Specialization of immune responses to microbes

Type of microbe	Adaptive immune response	Effector mechanism
Extracellular microbe (bacteria, viruses)	Endocytosed antigen stimulates CD4+ helper T cells (T_H1, T_H17) --> antibody, inflammation	Neutralization, phagocytosis
Intracellular microbe in phagocytes	Antigen in vesicles or cytosol --> CD4+, CD8+ T cells	IFN-g activates phagocytes; killing of infected cells
Intracellular microbe in non-phagocytic cell (virus)	Antigen in cytosol --> CD8+ CTLs	Killing of infected cells

السلايدات اللي مرينا عنهم،، احنا اصلا حكيناهم ...😢👀

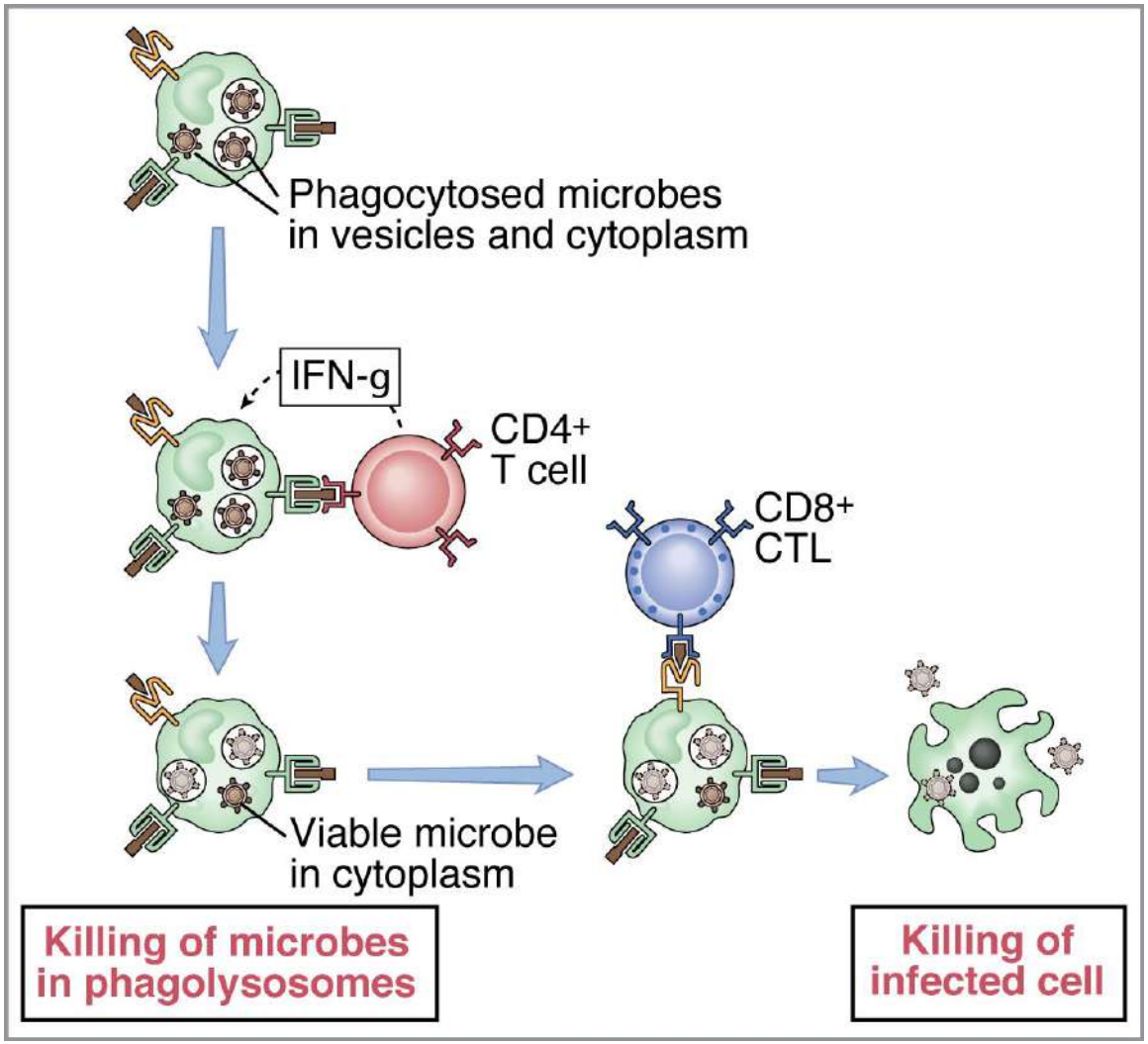
Cell-mediated immunity against intracellular microbes



CD4+ T cells: make phagocytes better killers of microbes

CTLs: eliminate the reservoir of infection

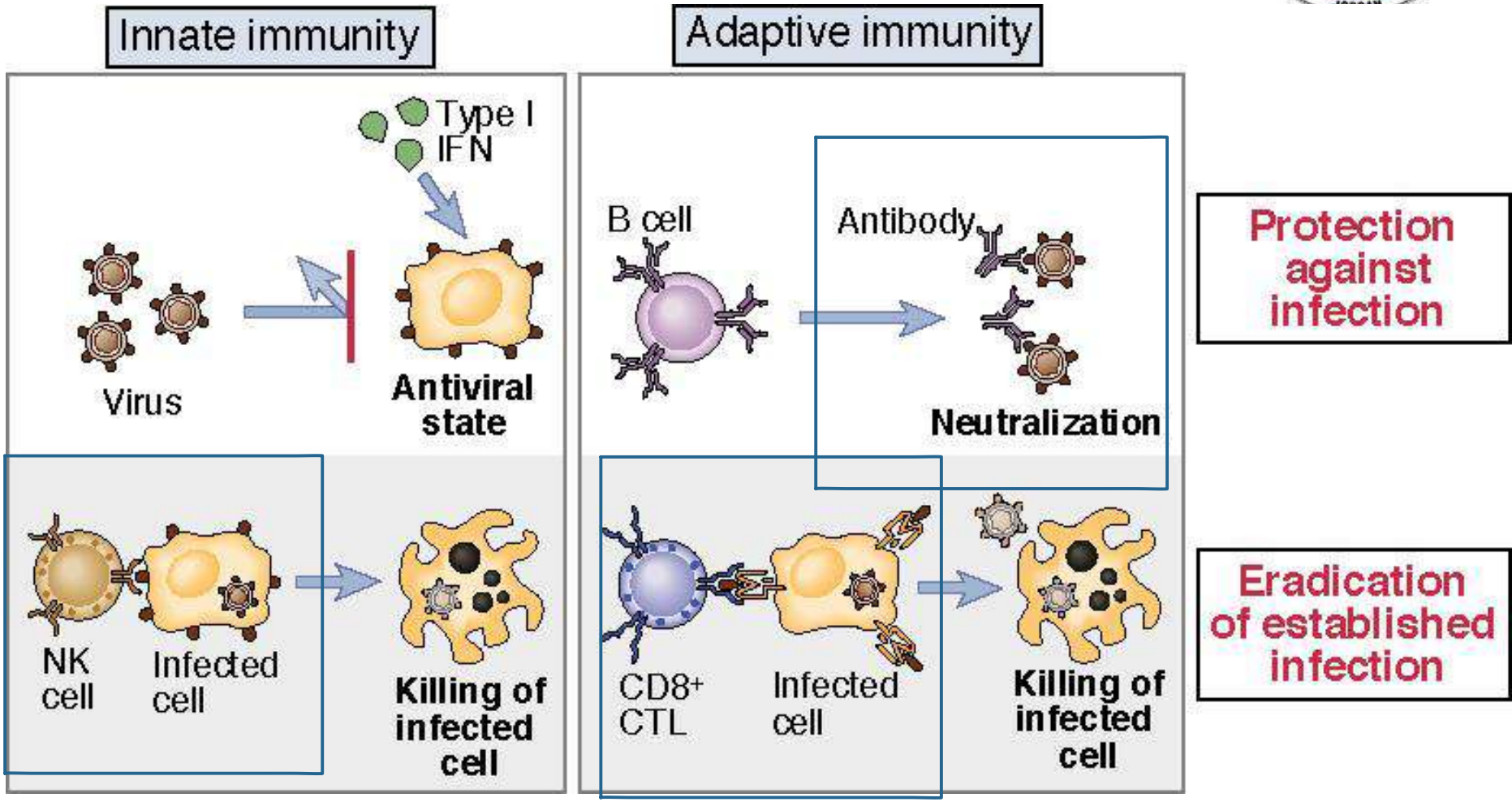
CD4+ and CD8+ T cells cooperate in cell-mediated immunity against intracellular microbes



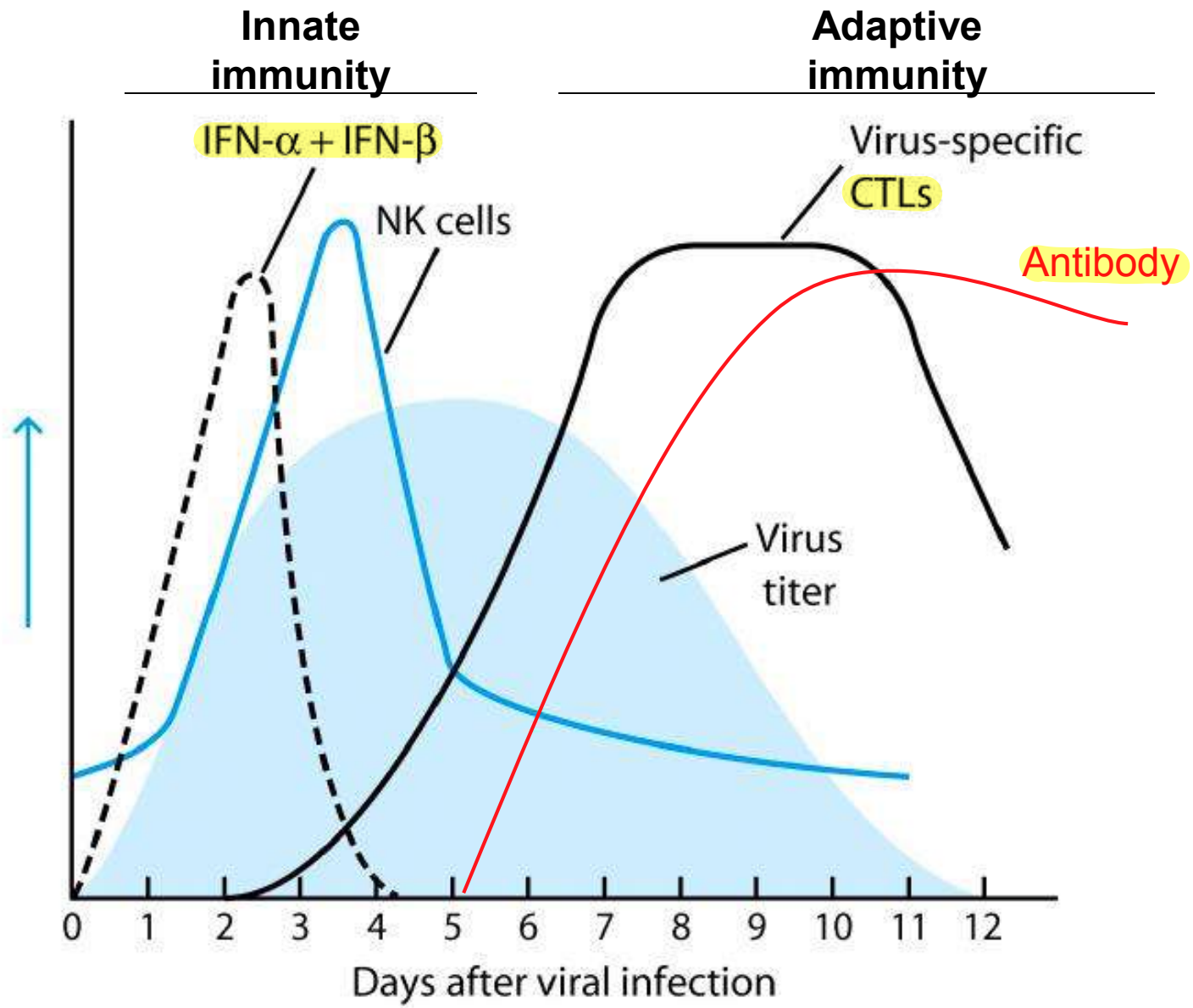
CD4+ T cells: help to kill microbes in vesicles of phagocytes

CD8+ CTLs: kill microbes that have escaped into the cytoplasm

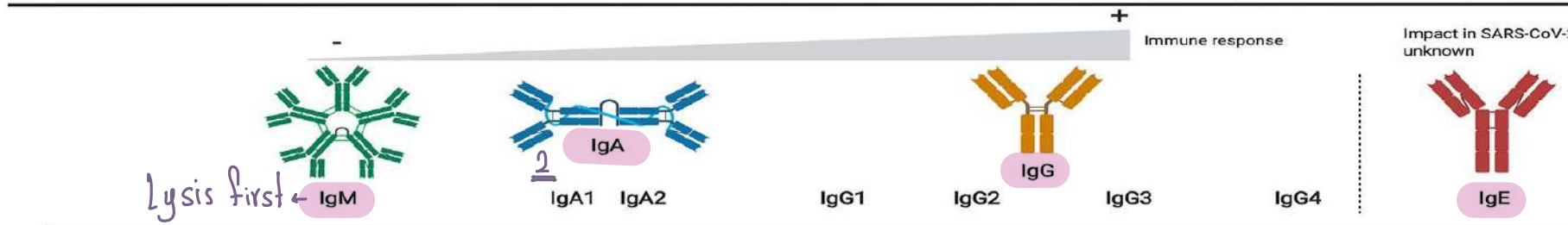
Innate and adaptive immunity to viruses



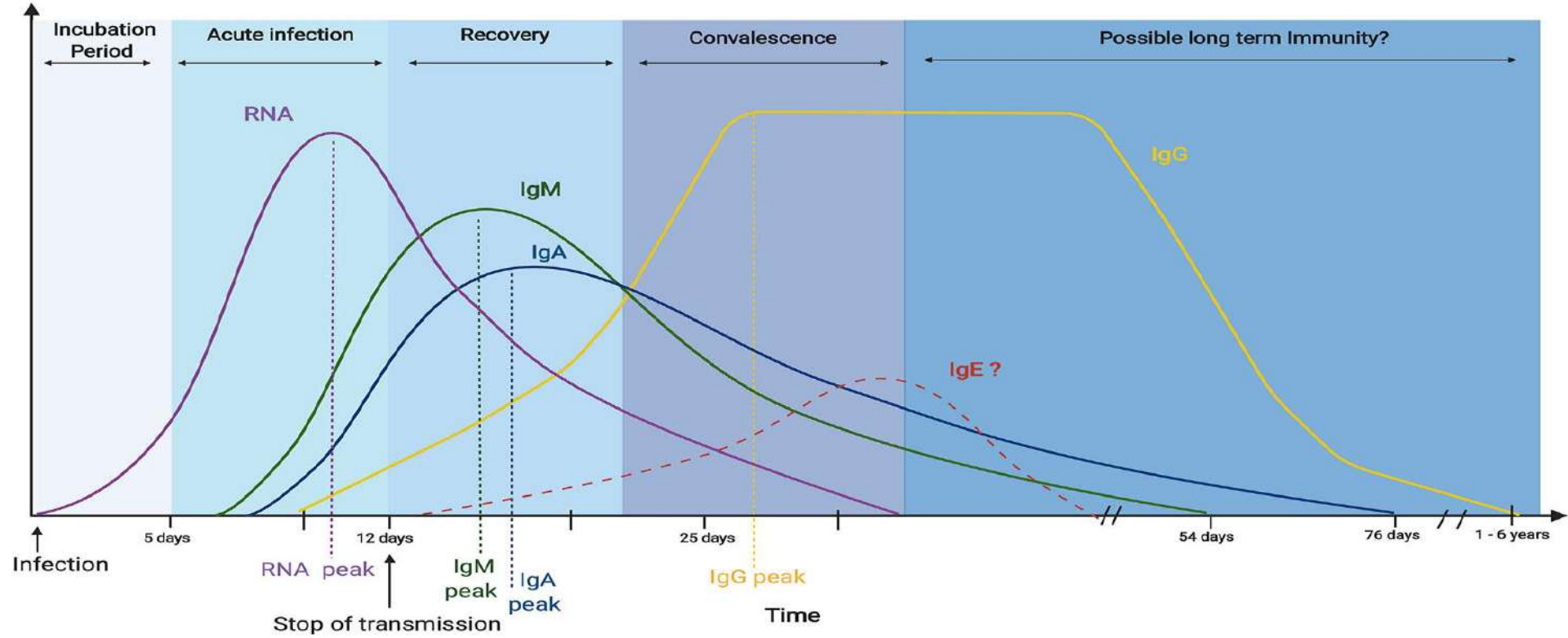
Innate and adaptive immune responses in viral infections



Antibody overview and timeline in Sars-CoV-2 infection



Form	Pentameric	Monomeric or Dimeric			Monomeric			Monomeric
Heavy chain	(μ) Mu	(α) Alpha			(γ) Gamma			(ε) Epsilon
Function	Humoral immunity Activates complement	Mucosal immunity, Neutralization Fc-mediated effector function			Humoral immunity , Neutralization Activates compliment, Binds C1q			Allergy & Parasite defense
Class switching cytokine	IL-4 ↓ IFN- γ ↓ TGF- β ↓	TGF-β ↑ IL-5 ↑ (increase production)	IFN- γ ↑ IL-10 ↑ IL-4 ↓	IFN- γ ↑ IL-4 ↑ TGF-β ↓	IFN- γ ↑ IL-10 ↑ TGF-β ↓ IL-4 ↓	IL-4 ↑		IL-4 ↑ IFN-γ ↓



Roles of antibodies and CTLs in adaptive immunity to viruses

- **Antibodies neutralize viruses and prevent infection**
  - **Block infectious virus early in course of infection (before entering cells) or after release from infected cells (prevents cell-to-cell spread)**
- **CTLs kill infected cells and eradicate reservoirs of established infection**
  - **In some latent viral infections (EBV, CMV), CTLs control but do not eradicate the infection; defective T cell immunity leads to reactivation of the virus (in HIV, immunosuppression caused by leukemias, treatment for graft rejection)**

Immune evasion by viruses

شو الطرق اللي بتخلي الفايروسات يتجاوزوا جهاز المناعة

- **Antigenic variation**
  - **Influenza, HIV, rhinovirus** RNA virus في ١٠٠ شكل مختلف لل glycoprotein تبعها
- **Inhibition of the class I MHC antigen processing pathway**
  - **Different viruses use different mechanisms**
  - **NK cells are the host adaptation for killing class I MHC-negative infected cells** الفايروس بمنع تصنيع MHC او بمنع ارتباط antigen معه، بنتغلب عليها عن طريق killer cells
- **Production of immune modulators**
  - **Soluble cytokine receptors may act as "decoys" and block actions of cytokines (poxviruses)** بصنع بروتينات بترتبط مع cytokines وبالتالي ما بتعمل لل activation لل immune system
  - **Immunosuppressive cytokines, e.g. IL-10 (EBV)** Suppression لل immunity
- **Infection of immune cells**
  - **HIV** infected CD-4

multiple antibodies

Efficacy of vaccines

- Vaccines have been useful for generating protective antibodies (أكثرشي), but so far, not for generating effective cell-mediated immunity

total radication of illness

- Vaccines work best against microbes that:
  - Do not vary their antigens كل ما يكون في إختلاف بدي اضل اعطي مطعوم جديد
  - Do not have animal reservoirs (ما بقدر اسيطر عليهم) → Human
  - Do not establish latent infection within host cells
  - Do not interfere with the host immune response

HIV زي

Roles of antibodies and CTLs in adaptive immunity to viruses

- **Antibodies neutralize viruses and prevent infection**

– **Block infectious virus early in course of infection (before entering cells) or after release from infected cells (prevents cell-to-cell spread)**

- **CTLs kill infected cells and eradicate reservoirs of established infection**

– **In some latent viral infections (EBV, CMV), CTLs control but do not eradicate the infection; defective T cell immunity leads to reactivation of the virus (in HIV, immunosuppression caused by leukemias, treatment for graft rejection)**

ال latent infection اللي حكينا انهم بتخبوا بال dorsal ganglia
هذول ما بتقدر ال CTLs انها تقتلهم كليا لكنها بتسيطر ع ال infection
تقص ال T cells راح يؤدي انه يرجع يصير عندك infection مرة ثانة

Immune evasion by viruses

هروب الفيروس من جهاز المناعة بيصير بكثير طرق
اولها ال antigenic variation الفكرة فيه انه هذول الفيروسات بتعمل الانزيمات تاعتها مشان هيك عندهم ضعف بال proofreading و اللي حيسبب mutation كل base pairs 10000-2000 هسه اذا صار ال mutation بال spike هذا راح يغير ال antigen و حتى لو كان مصاب فيه من قبل راح يتعامل معه الجسم كأنه اول مرة مثال عليه فيروس كورونا اللي كل فترة بنسمع ب new variant و اللي راح يقللوا كفائة المطاعيم مع كل mutation بتصير برضو عنا ال HIV اللي لهلحظة ما في اله vaccine بسبب التنوع الرهيب تبعه

- **Antigenic variation**
  - **Influenza, HIV, rhinovirus**
- **Inhibition of the class I MHC antigen processing pathway**
  - **Different viruses use different mechanisms**
  - **NK cells are the host adaptation for killing class I MHC-negative infected cells**

اذا ال MHC I انعطلت الجسم ما راح يميز اذا هذا ال antigen غريب اول لا و بالتالي ما بتموت الخلية المصابة

- **Production of immune modulators**
  - **Soluble cytokine receptors may act as "decoys" and block actions of cytokines (poxviruses)**
  - **Immunosuppressive cytokines, e.g. IL-10 (EBV)**
- **Infection of immune cells**
  - **HIV**

Efficacy of vaccines

- **Vaccines have been useful for generating protective antibodies, but so far, not for generating effective cell-mediated immunity**

بال vaccine احنا بنشتغل على انه نزيد عدد ال IgG و ما بنشتغل ع موضوع ال cellular response

- **Vaccines work best against microbes that:**
  - **Do not vary their antigens**
  - **Do not have animal reservoirs**
  - **Do not establish latent infection within host cells**
  - **Do not interfere with the host immune response**

طمأنينة

من الأقوال المطمئنة التي أستشعر بها لُطف الله عند أي مصيبة أو بلاء؛ قول النبي ﷺ "واعلم أنَّ ما أصابك لم يكن لِيُخْطِئَكَ، وما أخطأك لم يكن ليُصيبك، واعلم أنَّ النصر مع الصبر، وأنَّ الفرج مع الكرب، وأنَّ مع العسر يسرًا، واعلم أن الأُمَّة لو اجتمعت على أن ينفعوك بشيء لم ينفعوك إلا بشيء قد كتبه الله لك، وإن اجتمعوا على أن يضرُّوك بشيء لم يضروك إلا بشيء قد كتبه الله عليك، رُفِعَت الأقلام وجفَّت الصُّحف."

اذكروني بدعوة 🙏👈 ← وأنا معها 🥺💕🌸