Immunology

Title : Innate immunity

Lec no : 7

Done By : Khalid Awadallah

وَقُل رَّبِّ زِدْنِي عِلْمًا

Innate Immunity

Immunology Lecture 7

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Objectives

- Discuss the concept of innate immunity - features, importance.
- Explain how the innate immune system recognizes foreign antigens in general.
- Outline the components of the innate immune system.
- Discuss how these components combat various foreign antigens. MOA

يعطيكم العافية...
هسا عشان نكون متفقين ، اي اشي بالاسود او الاحمر او الكحلي مطلوب فهم وحفظ ، اي لون ثاني بكون عشان اربط النقاط ببعض ولكم الحرية تقرؤه او تسيبوه

Introduction

- protection against infections that relies on the mechanisms that exist before infection and are capable of rapid response to pathogens
- Innate immunity is the first line of defence against infection
- Characteristics:
  - set up at birth
  - non –specific*
  - hereditable
  - no immune memory
  - Little individual difference

Explanation :
The characteristics of the innate immunity are :
Its set up at birth => it existed before the infection ∴ capable of rapid response against pathogens in general.
Its non specific => covers a wide spectrum of pathogens
It has no immune memory => 2nd and 3rd exposure to the pathogen wont increase the rapidity of the response like the adaptive immunity

Lines the body from the inside and outside

Innate (Nonspecific) Immunity	Circulation related
First line of defense	**Second line of defense**
• Intact skin • Mucous membranes and their secretions • Normal microbiota	• Natural killer cells and phagocytic white blood cells • Inflammation • Fever • Antimicrobial substances

Innate Host Defense Mechanisms

Contains components as well

- Physical factors
- Biochemical factors
- Microbiological factors
- Fever
- Innate Immune cells
- Cytokines
- Complement system
- Inflammation

When we mention innate immunity put in mind the end result of it
1) recruitment of the inflammatory cells => inflammation => elimination of the microorganisms
2) Antiviral activity => interferons

Both mechanisms will be further discussed in the lecture

1. Physical Factors

1. Skin: microbes sloughed off along with skin cells, Microbes must penetrate several layers
   - Stratified and cornified epithelium provides a mechanical barrier
   - Indigenous microbial flora competes with pathogens
   - Acid pH inhibits growth of disease producing bacteria
   - Bactericidal long chain fatty acids in sebaceous gland secretions
2. Mucous Membranes: produce mucus to trap microbes, Most lined with cilia

Skin => 4 components :

1) Epithelial cells : mechanical barrier
2) Normal flora : competition with pathogens
3) Acidic pH : bacterial growth inhibition
4) Sebaceous gland : bactericidal long FA chains in secretions

Mucous membrane => 2 mechanisms

1) Microbial trapping : Mucus
2) Cilia movement : gets rid of microbes

*Low pH inhibits bacterial growth

2. Biochemical Factors

1. Low pH in vaginal and urinary tracts, and stomach
2. Defensins*: short antimicrobial peptides, insert into bacterial membranes and form pores
3. Lysozyme: degrades peptidoglycan
   - Tears contain a high concentration of lysozymes (effective against gram positive microorganisms)
4. Interferon: are cytokines that trigger:
   - macrophage activation
   - production of substances to interfere with RNA viral reproduction

Short summary : biochemical factors consists of 4 : 1) low pH in vagina , UT and stomach (not skin otherwise its physical). 2) defensins : discussed later. 3) lysozymes : peptidoglycan degradation (found in bacterial and viral membranes). 4) interferons : 2 functions => A) Macrophage activation. B) interfering من اسمها with RNA viral reproduction (innate immunity end results slide of mechanisms)

Defensins: short antimicrobial peptides that form pores into bacterial membranes ∴ increasing the cell permeability leading it to death by lysis

Antimicrobial Peptides/Defensins

- Originally isolated from frog skin based on their ability to kill bacteria
- Four hundred peptides described to date
- Defensins (four families in eukaryotes) (only 2 found in humans)
  - α-defensins (neutrophils and intestinal Paneth cells)
  - β-defensins (epithelial cells)
  - Insect defensins
  - Plant defensins

Found in 3 places :
1) PMNs (neutrophils)
2) Paneth cells (intestine)
3) Epithelial cells

- Defensins appear to act by binding to outer membrane of bacteria, resulting in increased membrane permeability MOA
- Classified based on their secondary structural features.
  - Cathelicidins (**CAT**ionic **HELI**cal bacteri**CID**al prote**IN**) are α-helical peptides
    - Human cathelicidin LL37 is highly expressed by PMNs and numerous mucosal and epithelial cell types.
  - Defensins are β-strand peptides connected by disulfide bonds
- Most are short peptides (<100 amino acids) and carry a positive charge
  - AKA – "cationic antimicrobial peptides"
- Interact with microbial cell membrane components to increase cellular permeability resulting in cell death. They also act to modulate the inflammatory response and wound repair.

Functions

3. Microbiological Barriers

- Normal Flora: **not part of immune system**, but are part of first line of defense
- Protection they provide is considerable
  - Competitive exclusion of invading microbes
  - Produce compounds that are toxic to other bacteria
  - Stimulates immune system, providing a moderate amount of "exercise" to system, thereby enhancing it's function

Functions of normal flora that contribute to immunity :

1) Competitive exclusion of pathogens
2) Toxic compounds production against other bacteria
3) Immune system STIMULATION => providing exercise to the system ∴ enhances the function

Note: its stimulation not activation
It doesn't activate the immune system since it recognizes the normal flora as non pathogenic
Stimulating the immune system keeps it alerted and ready for any pathogenic stimulant

4. Fever

- Mechanism of fever:
  - Results from
    - release of pyrogens such as interleukin 1, interferons
    - toxins from infectious agents, drug reactions toxins, brain tumors
  - **Pyrogens** released and circulate through the body
    - target hypothalamus and cause release of prostaglandin E_2
    - raises temperature set point of hypothalamus

- **Benefits of fever**
  - Inhibits reproduction of bacteria and viruses (Like low pH as well)
  - ↑ interferon activity (positive feedback and other IFN functions increased)
  - ↑ activity of adaptive immunity*
  - Accelerates tissue repair
  - Increases CAMs on endothelium of capillaries in lymph nodes
    - additional immune cells migrating out of blood => inflammation
- **Recommended to leave a low fever untreated******
- **Risks of a high fever** significant above 100 degrees F (37.7 C)
  - High fevers potentially dangerous above 103^0 in children (39.4 C)
  - Changes in metabolic pathways and denaturation of proteins
  - Possible seizures, irreversible brain damage at greater than 106^0, death above 109^0 (41.1 C) (42.7 C)

2 causes of fever :
1) Pyrogens release
2) Toxins and brain tumors

MOA of pyrogens (IL-1 and IFN):
Pyrogens released in circulation as a response => targets the hypothalamus => release of PGE2 => ↑ temp. set point of hypothalamus => fever

Febrile convulsion :
Sudden increase in temp. in children > 5 y/o
Caused by an underlying infection
Symptoms : Foaming at the mouth , rolled up eyes , spasm and twitching limbs
The temp. isn't a serious problem depending on how frequent=> once or twice within 7 days u can reassure parents , more than that => refer pediatrician.
Treatment for the fever : antipyretic drugs rectally, Revanin and Paracetamol. **U don't give them Voltaren**
No hospital admission needed, unless its pneumonia related .

اه درجات الحرارة وشو بتسوي كل درجة مطلوبة حفظ ☺
مش فهرنهايت

5. Innate Immune Cells

Cell type	Pricipal function(s)
Monocytes/Macrophages	Phagocytosis, inflammation, T-cell activation, tissue repair
Neutrophils	Phagocytosis, inflammation
NK cells	Killing of infected or tumor cells
Dendritic cells	Phagocytosis, activation of naive T-cells
Mast cells	Inflammation
Eosinophils	Defense against parasites

بصراحة شايف الجدول الماضي احسن اذا كان التركيز عال function مش عال cell type بس انا ححط الثنين

Innate Immunity Cells

Function	Cell types
Phagocytosis	Macrophages, Dendritic cells, Neutrophils
Inflammation	Macrophages, Neutrophils, Mast cells
T-cell activation	Macrophages, Dendritic cells (naïve T-cells)
Infected or tumor cell killing	NK
Tissue repair	Macrophages
Defense against parasites	Eosinophils (IgE)

Dendritic cell is an antigen presenting cell (MHC II)

ADCC (Antibody-dependent cell-mediated cytotoxicity) : the killing of a target cell which is coated with antibodies by an effector cell of the immune system.
ADCC cells : macrophages, NK cells, neutrophils, and eosinophils.

Innate immunity activates the adaptive immunity when 2 signals are present :

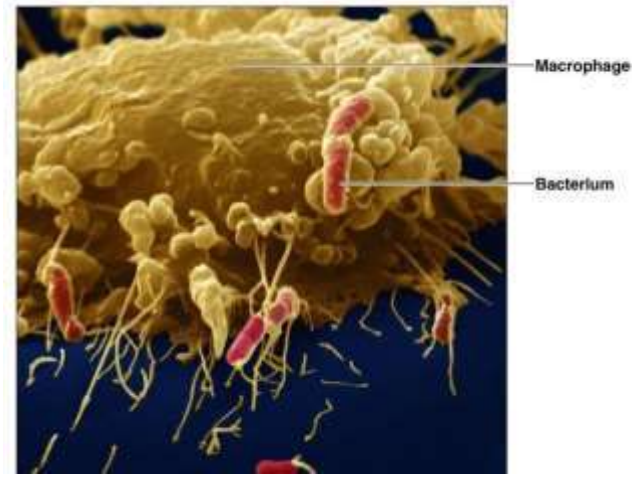
1) The Antigen itself
2) Co stimulatory proteins produced by Dendritic cells.

The 2 signals bind to the T cell activating the adaptive immunity

2 types of Cytokines so far :
INF : macrophage activation / interfere RNA viral production
Chemokines : Chemoattractant

Phagocytes

- Performed by Neutrophils and Macrophages and Dendritic
  1. Phagocytosis is the capture and digestion of foreign particles
  2. Chemokines are cytokines that attract macrophages and neutrophils to infected tissues (Chemoattractant)
  3. Opsonins attach to microbes to increase the ability of phagocytes to adhere (opsonization)



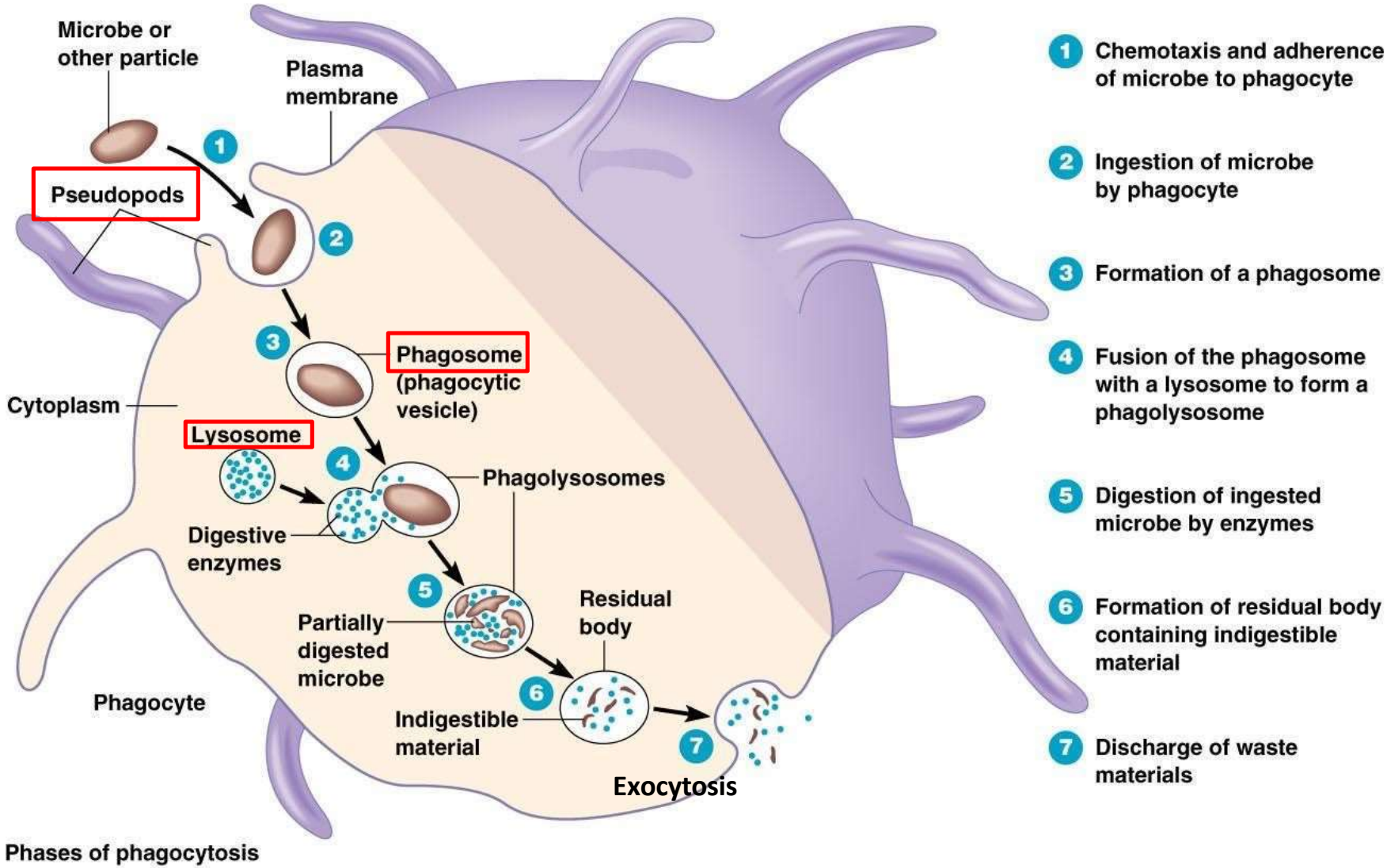
Opsonins (such as C3B and IgG) are molecules that tag (label) the microbes so they become recognizable by the immune cells. They usually attach to the microbes containing CHO in their membranes.

Steps of Phagocytosis

عن طريق ال PAMPs رح نحكي عنهم لقدام وعنا بكون نوعين من
ال responses يا اما phagocytic دغري او signaling عن طريق ال
chemokines (الطريقة الثانية عشان اذا كان عدد الAg كثير كبير)

- Recognition
- Ingestion- pseudopods* engulf microbe through endocytosis
- Vacuole Formation- vacuole contains microbe Phagosome
- Digestion- vacuole merges with enzymes to destroy microbes Phagolysosome
- Exocytosis- microbial debris is released

الخطوات هون اوضح ف الصورة حفظ اكيد



Phases of phagocytosis

ال recognition كثير مهم

Innate Immune Recognition

- All multi-cellular organisms are able to recognize and eliminate pathogens
- Despite their extreme heterogeneity, pathogens share highly conserved molecules, called “pathogen-associated molecular patterns” (PAMPs)

Means variousity

Which is unique and **cant be found** in healthy bodies ∴ recognized by the immune system

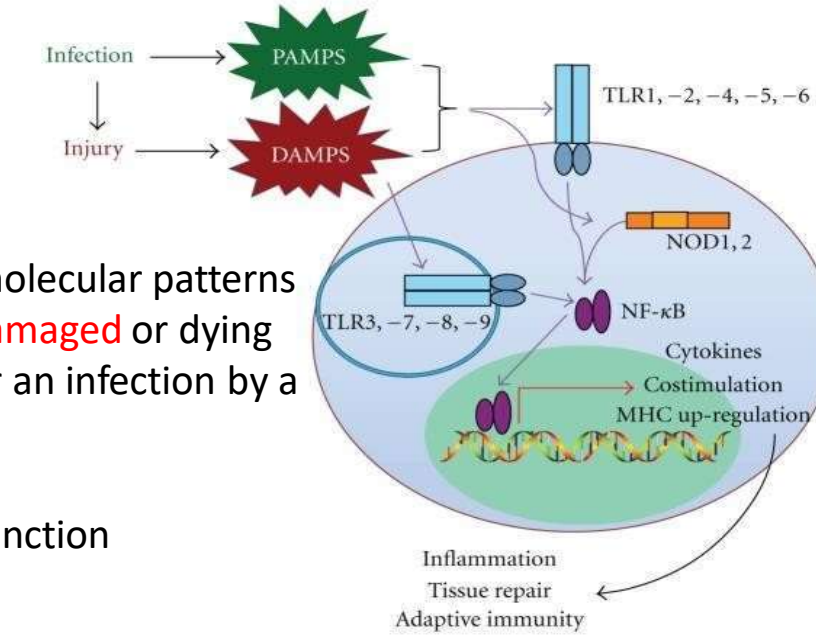
- *Host cells do not share PAMPs with pathogens
- PAMPs are recognized by innate immune recognition receptors called pattern-recognition molecules/receptors (PRMs/PRRs)

الملخص للسلايد اللي كله اقواس :

الpathogens بتحتوي كلها على molecules بتكون مش موجودة ابدا بالخلايا تبعتنا PAMPs => ف خلايا الجهاز المناعي عليها مستقبلات PRRs وظيفتها ترتبط بالPAMPs اللي بالPathogens => وبصير عنا activation اما انو مباشرة بنبدا Phagocytosis أو بنعمل chemokines production و chemotaxis عشان نكمل phagocytosis.

DAMPs اللي هو ال PAMPs عنا اشي كمان زي ال

Typical PAMPs



- Typical PAMPs:
  - Lipopolysaccharides
  - Peptidoglycans
  - Certain nucleotide sequences unique to bacteria
  - Other bacterial components
- Binding of Innate immune receptors and PAMPs:
  - Mediate inflammatory cytokines
  - Antigen-presenting cells recognize PAMPs

Damage-associated molecular patterns (DAMP) : found in damaged or dying cells due to trauma or an infection by a pathogen.
Tumor related
Similar to PAMPs in function

Unmethylated cytosine–guanine dinucleotide (CpG) motifs

DSRNA found only in pathogens

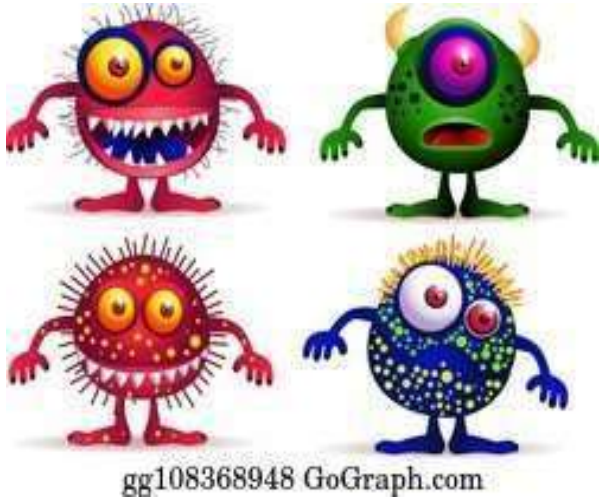
When PRRs bind with PAMPs:
Mediate cytokines
The antigen presenting cells recognize PAMPs

Innate Receptors

Done by : dr.malak issa “Hussein Abu-Awwad”

هاي هون مراجعة بسيطة من زميلتنا حنكمل التفريغ من عند ال receptors

Pathogen pathway



When the pathogen enter , what is the innate host defense mechanism?

Physical factors | **Biochemical factors** | **Microbiological factors** | **Fever** | **Innate Immune cells**

Such as :
1- skin
2-mucus membrane

Such as :
1- low PH
2- Interferon

Such as :
Normal Flora

Such as :
release of pyrogens that promote the interferon

Innate immunity cells

01

Monocytes/Macrophages

Phagocytosis, inflammation,
T-cell activation, tissue repair

02

Neutrophils

Phagocytosis, inflammation

03

NK cells

Killing of infected or tumor cells

04

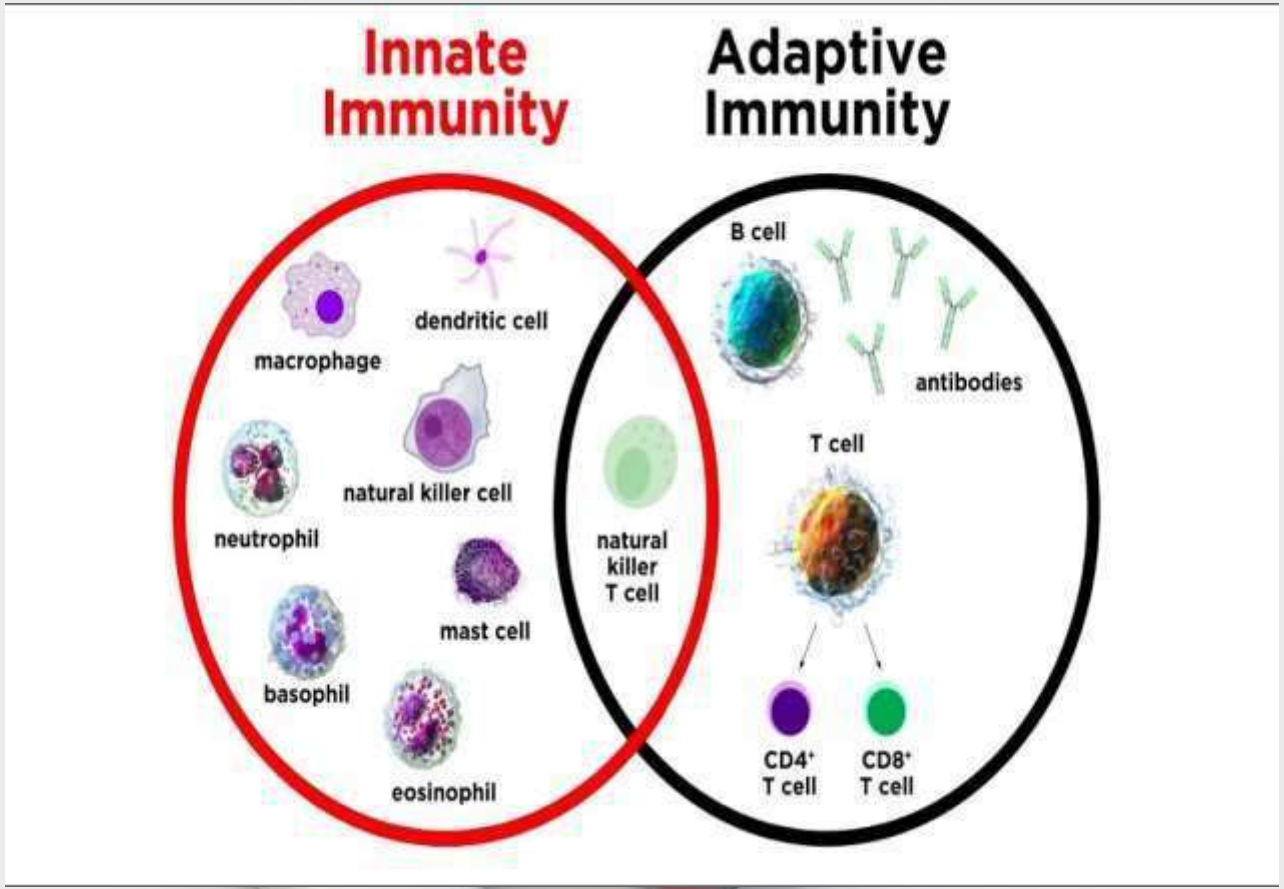
Dendritic cells

Phagocytosis, activation of naive T-cells, APC

05

Mast cells

You can simply impress your audience and add a unique
zing and appeal to your Presentations.
Inflammation, production of histamine

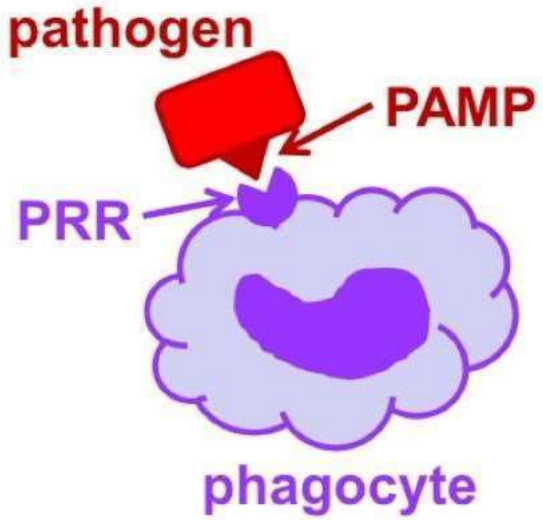


06

Eosinophils

Defense against parasites

PAMP : Pathogen Associated Molecular Pattern



** note : DAMP it's a part of damaged host cell that attract innate immune

•It's a specific part in the pathogen only and it could recognized by PRR

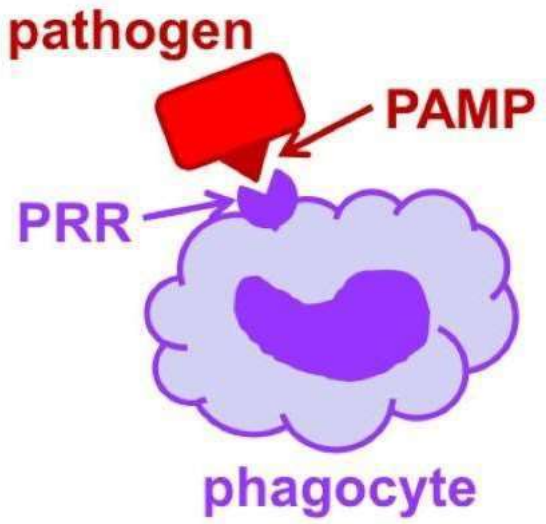
•Host cells do not share PAMPs with pathogens

•PAMPs are recognized by innate immune recognition
•receptors called pattern-recognition
•molecules/receptors (PRMs/PRRs)

•Typical PAMPs:
•- Lipopolysaccharides
•- Peptidoglycans
•- Certain nucleotide sequences unique to bacteria
•- Other bacterial components
**note they aren't found in our body

*Binding of Innate immune receptors and PAMPs:
- Mediate inflammatory cytokines
-Antigen-presenting cells recognize PAMPs (protein synthesis)

PRR: Pathogen Recognition Receptor



Function
هاي حنيجي عليها كيف لقدام

بعيدها كمان مرة :

PAMP binding to PRR will activate a chain reaction leading to the end result of the innate immunity :
1) Inflammation
2) Antiviral reaction
Both by IFN by NF-κB

- It's a non specific -innate- receptor that found on host cell membrane
- They play a vital role in recognizing conserved molecular patterns present in pathogens (PAMPs).
- PRRs initiate the immune response, leading to the elimination of pathogens and activation of the adaptive immune system.
- once PAMP is recognized it will bind with PRR
- we have a limited no. of receptors to a limited no. of pathogens cuz the cell has a limitation with its outer membrane and inner space
- They could be found :
  - intra cellular
  - Extracellular on surface
  - Secreted => Complementary system cascade

اماكن تواجد ال PRR بالخلية

Antigen Presenting Cells (APCs) only <=

1- extra cellular receptor

كلشي بحط عنده ! ركزولي عليه

1- Engulf the pathogen

Killing pathogen by lysosome and phagosome

Such as :

A- C-type Lectin Receptors (CLRs)

Type of PRR: Transmembrane or soluble receptor

!Cell Types: Expressed on dendritic cells and macrophages (APCs)

!Recognize: Carbohydrate structures on the surface of pathogens, such as mannose* and glucans.

!Pathogens Recognized: Fungal pathogens and bacterial pathogens

!Deficiency Impact: This can result in an increased risk of fungal and bacterial infections.

The deficiency impact is the same as the recognized pathogens => فهم احسن

ما ركز عليه كثير

B- Scavenger Receptors

Type of PRR: Transmembrane or soluble receptor

!Cell Types: Found on macrophages and dendritic cells.

!Recognize: oxidized low-density lipoproteins (LDL)

!Pathogens Recognized: Bacterial pathogens and cellular debris. (Only bacterial)

Deficiency Impact: Reduced ability to clear modified self-molecules and pathogens, leading to the accumulation of cellular debris and potentially contributing to chronic inflammatory conditions and atherosclerosis.

1- extra cellular receptor

2- signaling receptor (transcription)

Produce protein

Such as :

- Toll-like Receptors (TLRs)

Type of PRR: Transmembrane receptor

!Cell Types: Found on macrophages, dendritic cells (APCs)

!Recognize: Various (PAMPs), such as bacterial lipopolysaccharides (LPS), viral nucleic acids, and fungal cell wall components.

!Pathogens Recognized: Bacterial (Gram-positive and Gram-negative), viral, and fungal pathogens. (All)

!Deficiency Impact: increas susceptibility to certain bacterial, viral, and fungal infections.

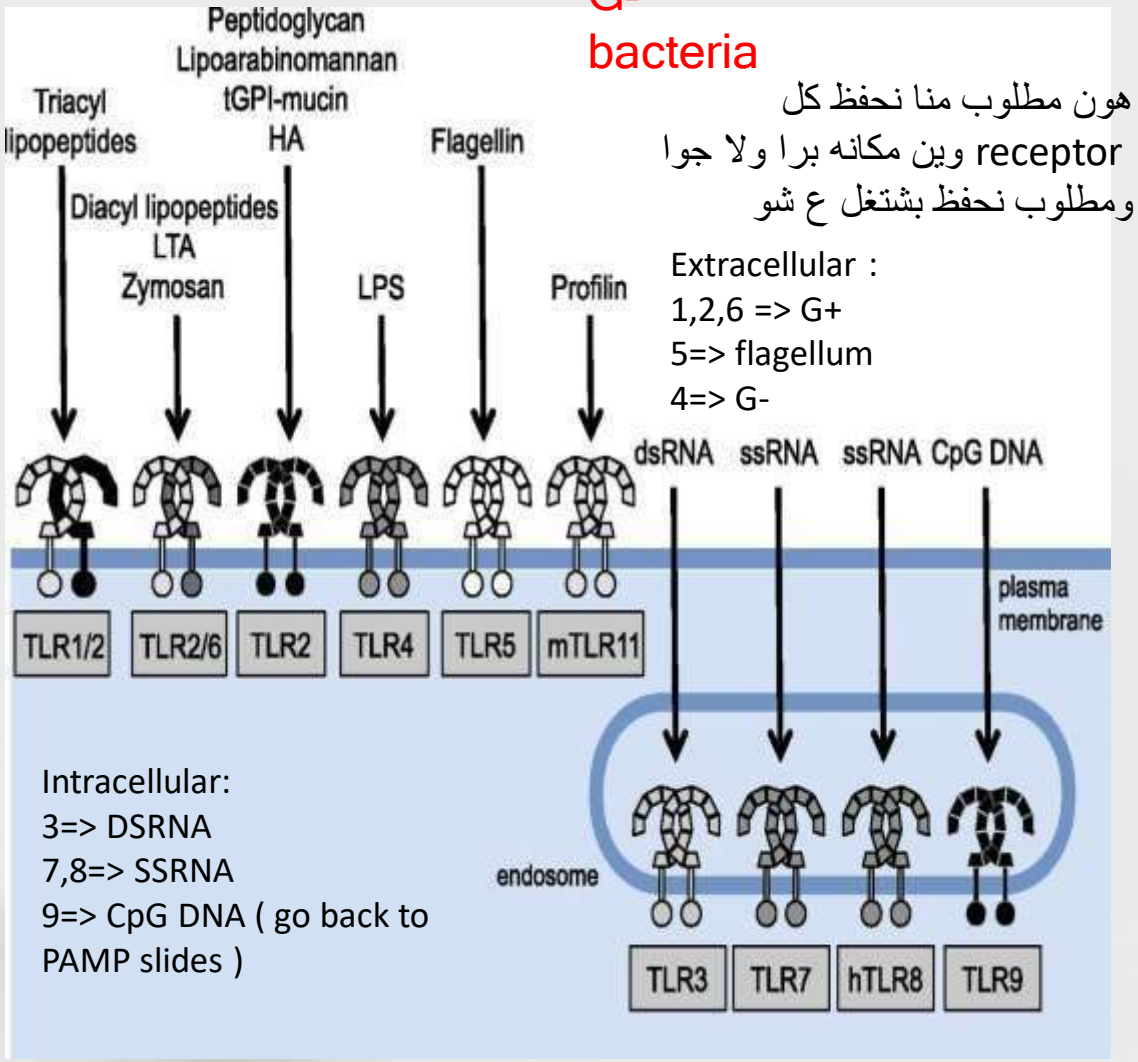
***imp: deficiency 2 type

- !In tol 3 result in mutation in recognition of dsRNA so we will have a viral infection with Retro, herpes v (susceptible)

-! In myd88 result in bacterial pneumonia***

!Tol 4 is the onle G- bacteria

هون مطلوب منا نحفظ كل receptor وين مكانه برا ولا جوا ومطلوب نحفظ بشتغل ع شو



!TLR3 deficiency doesn't increase Rota Viridae susceptibility

NLR1&2 act on NF-κB => INF production

NLR1: More abundant/ NLR2: in Paneth cells

2- Intra cellular receptor

NLR2=> inflammatory bowel syndrome

**** the pathogen will be inside the cell so it may be infected , o it may relese a cytokine**
****but if it got infected it will die**

Such as :

A- NOD-like Receptors (NLRs)

Type of PRR: Intracellular receptor

!Cell Types: Present in the cytoplasm of macrophages and dendritic cells.

!Recognize: Bacterial peptidoglycans and other intracellular components.

!Pathogens Recognized: Bacterial pathogens, both Gram-positive and Gram-negative bacteria.

Deficiency Impact: difficulties in initiating appropriate immune responses against bacterial pathogens. This can result in chronic or recurrent infections.

B- RIG-I-like Receptors (RLRs)

Type of PRR: Intracellular receptor

!Cell Types: Found in the cytoplasm of various cell types*

!Recognize: Viral RNA molecules, indicating viral infection.

!Pathogens Recognized: Viral pathogens, including RNA viruses.

Deficiency Impact: Reduced the detection of viral infections, potentially leading to prolonged viral illnesses and to difficulties in control viral replication and spread.

2- Intra cellular receptor

c- Inflammasomes

-associated with cell injury, and proteolytically generate active forms of the inflammatory cytokines IL-1β and IL-18

-Composed of a sensor, caspase-1, and an adaptor that links the two

- After recognition of microbial, the NLR3 sensors oligomerize with an adaptor protein and an inactive (pro) form of the enzyme caspase-1 to form the inflammasome, resulting in generation of the active form of caspase-1

- what does the active caspase1 do ?

cleaves pro-inflammatory cytokines, such as pro-IL-1β and pro-IL-18, into their active forms (IL-1β and IL-18, respectively).

These active cytokines are potent mediators of inflammation, promoting immune responses

So it mediate the inflamation

تعالو افهمكم القصة
هسا الinflammasome بتكون من 3 اشياء : sensor , caspase 1 , adaptor هسا ال sensor هو NLR3 بشبك مع adaptor ومع pro caspase 1
كل هاد يؤدي ل activation of pro caspase 1 to caspase 1
شو بسوي ال caspase 1 طيب ؟ cleaves pro inflammatory cytokines to their active forms
Inflammatory mediator

Common pathway of all receptor

PAMP / DAMP bind to PRR

Then many reactions will happen the most important will be the activation of NF-KB then this will activate interferon

3- secreted

** it is secreted by the liver and by immune cells but after they screated the have a no relation to the system so they charged to a completely different system
Such as complement receptor in complement system

هدول رح نكملهم ع سلايدات لقدام

The End

ANY QUISTION ?

DONE BY :
Malak Issa “Hussein Abu-Awwad”

The End


When the same kind of bacteria enters my body to cause infection
My immune system:
You forgot we played this game already?


" يقوم الجهاز المناعي بحمايه الجسم من المرض والميكروبات "
* جهازي المناعي *
طب ما تجيبلنا جهاز من ده يسطا

Complement system

by: Tariq Alsboul

lecture objectives:

- the definition of the complement system
- the activation of the complement system
- the function of the complement system
- the regulation of the complement system
- diseases related to the complement system

The definition :

هاي بتختلف بحسب نوع ال cascade وهسا بنشرح عنها

- The complement system is a collection of circulating and membrane associated proteins that are important in defence against microbes

- -the complement system considers as a part of the innate immunity

- It is not adaptable system but it could be recruited and activated via the adaptive system** (IgG , IgM)

- The complement system is synthesized in the liver and then circulating in the blood circulation as precursor

- It’s an proteolytic enzyme that need activation

The activation of the complement system

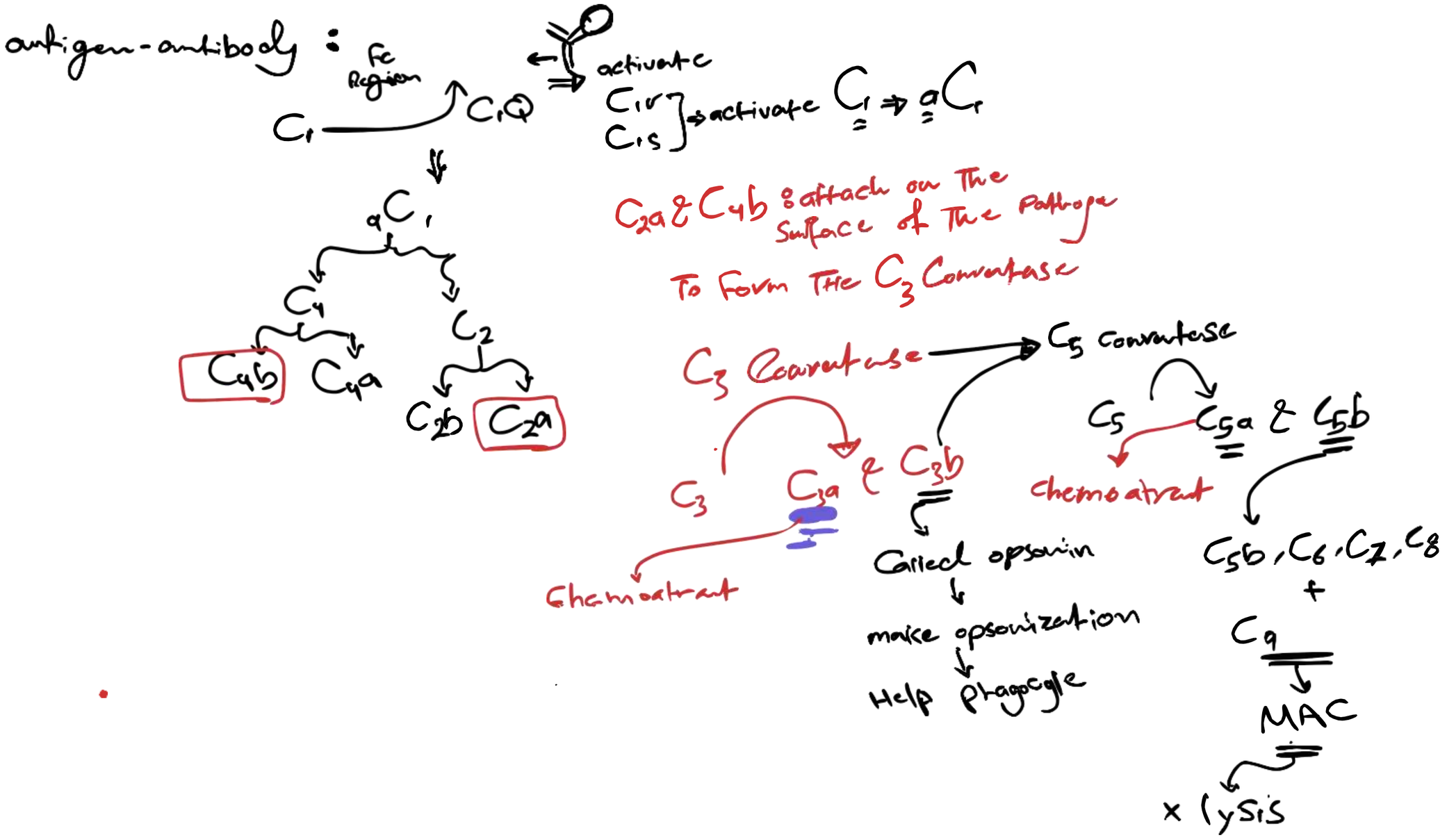
لحد هون كله حفظ فش شرح

- The activation of the complement system is multi-steps cascade

The complement system could be initiated by one of these three pathways

- The classical pathway: activated by antibody binding to antigen
- The alternative pathway :activated directly by the microbes
- Lectin pathway (MBL): binding to mannose containing carbohydrates

So : Classical

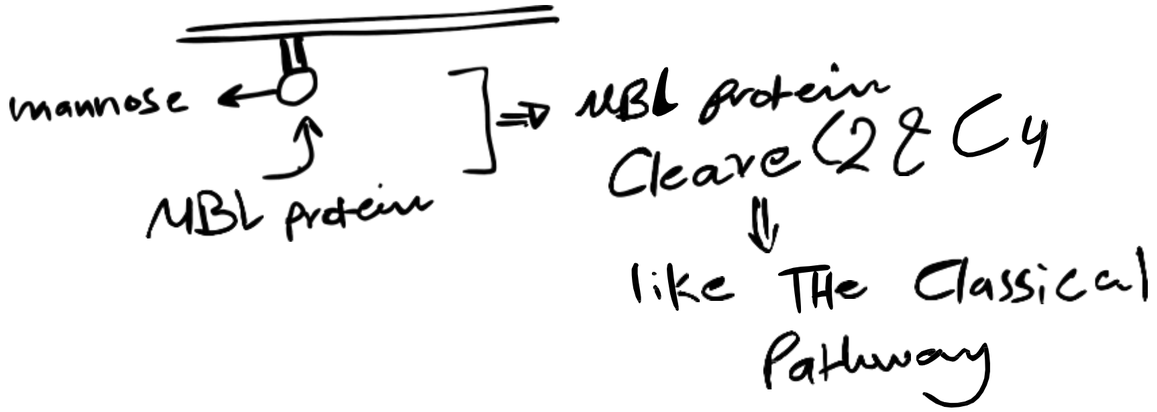


خلينا نشرح الشخابيط هون
هسا ال classical pathway بتكون من antigen-antibody complex
ال complex بتكون بداية من C1 الي بترتبط بال antibody
C1 is made of 3 subunits : C1q,r,s
The binding of C1q activates C1r=> C1r cleaves C1s => C1s also is a cleaving protein
هسا بس صلنا للC1s بروح بكمل باقي الcascade كالتالي:
C1s cleaves C2 and C4
هسا بس نقطع باقي ال complexes بطلع عنا 2 subunits من كل complex : a,b
Rule : a subunit is the smaller anaphylatoxin
B subunit is the larger binding portion
The smaller subunit is usually not important
Exception to the rule is only C2 => C2a is larger than C2b
So now we have C2a , C2b and C4a , C4b
The larger subunits form a complex : C2a-C4b complex , also named as C3 convertase
C3 convertase has 2 functions :
Function 1 : converting C3 to C3a and C3b by cleavage
C3a works as a chemoattractant
C3b works as an opsonin to help macrophages phagocyte CHO compounds (C3b Labels them)
Function2 : C3b gets added to the C3 convertase complex originally made by C2a and C4b forming the complex C5 convertase (made of C3b, C2a, C4b)
C5 convertase has similar functions to C3 convertase :
C5a is a chemoattractant like C3a
C5b contributes to a complex like C3b
C5b ,C6, C7, C8 is a complex
Then it adds to it C9 which activates MAC
Membrane Attacking Complex
Which leads to cell lysis and death

MBL

* When we are dealing with pathogen Contain mannose on his membrane

- MBL-protein

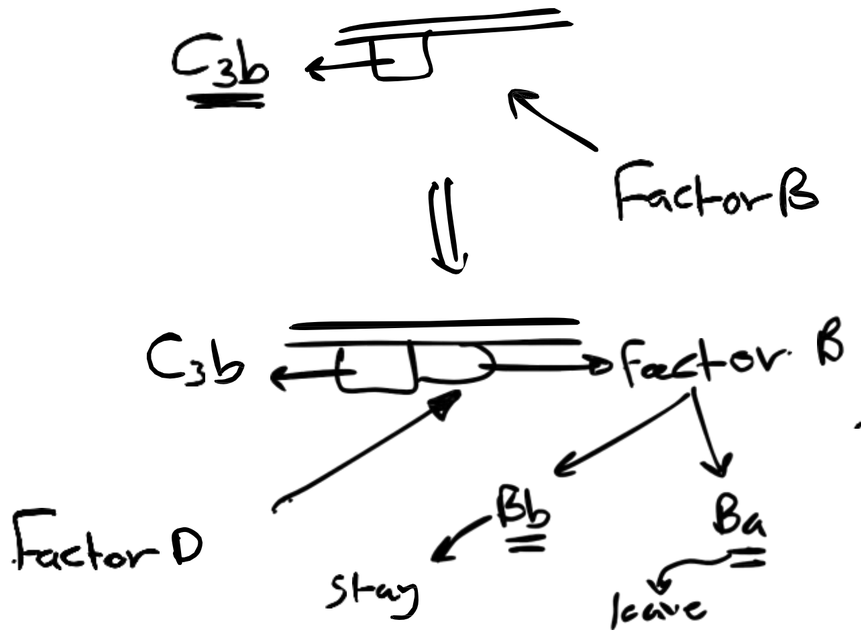


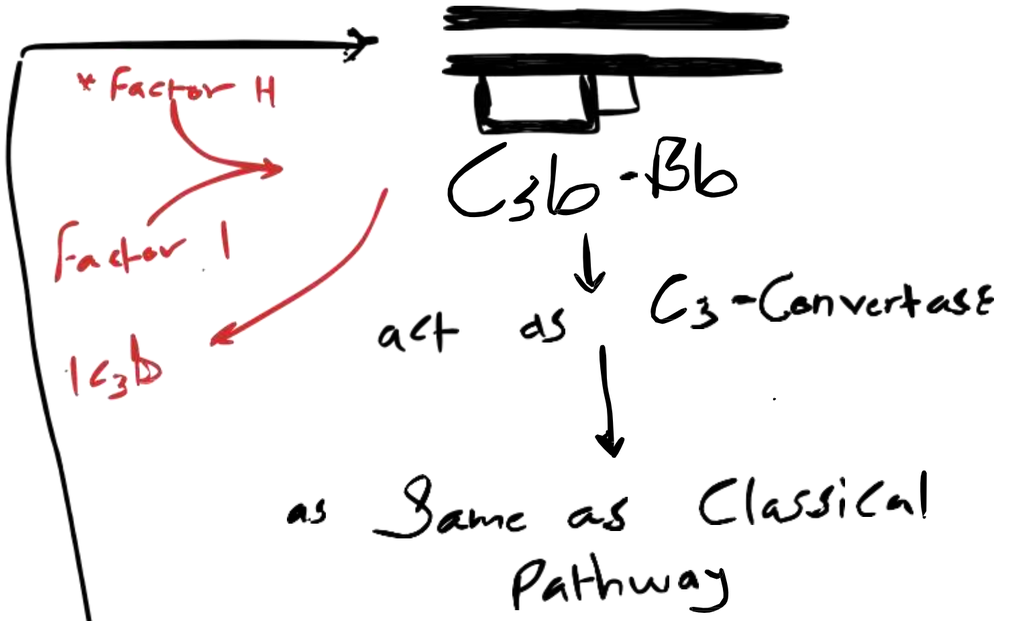
باقي الpathways سهلة وبتنبنى على الclassical
Mannose Binding Lectin pathway
Deals with pathogens who present mannose at their membrane
MBL-protein binds to the Mannose cleaving C2 and C4 (it plays the role of C1s)
Then continues like the classical pathway

alternative pathway :

C_3 → get cleave in the absence of Enzyme

C_{3b} → attach To The Bacteria





Alternative pathway starts from C3
C3 gets cleaved in circulation in the absence of the enzymes
C3b subunit attaches to the bacterial membrane
Sth called Factor B also attaches to the bacterial membrane next to the C3b subunit attached
Factor D comes to play cleaving Factor B into Ba and Bb subunits
Following the rule subunit Ba leaves and subunit Bb stays
C3b-Bb complex act as C3 convertase
And from here we go back to the same classical pathway

The function of the complement system

Opsonisation and phagocytosis : specially when we talk about the activity of the **c3b** that coat the antigen
so the phagocytic cells have the receptor to c3b so it will recognise the complement and ingest it with the antigen

Inflammation some proteolytic fragments of complementproteins especially **c5a & c3a** are chemoattractants for leukocyte (neutrophils & monocytes) and **c5a & c4a & c3a** they also activator to the mast cells and endothelial cells

Cell lysis complement activation will form **MAC**

Main function of complement system
MAC formation that causes cell lysis*

The regulation of the complement system

The complement system has the potential to be extremely damaging to host tissues, meaning its activation must be tightly regulated. The complement system is regulated by complement control proteins, which are present at blood plasma and host cell membrane

Some **complement control proteins** are present on the membranes of self-cells preventing them from being targeted by complement. One example is **CD59**, also known as **protectin**, which inhibits C9 polymerization during the formation of the membrane attack complex (MAC)

اهم اشي تعرفوه انه ال CD59 بعمل inhibition لل C9
polymerization ف بوقف ال MAC formation

The regulation of the complement system

The classical pathway is inhibited by C1-inhibitor, which binds to C1 to prevent its activation.

Factor H (FH), which has a key role in down-regulating the alternative pathway. Factor H, along with another protein called Factor I, inactivates C3b, the active form of C3. This process prevents the formation of C3 convertase and halts the progression of the complement cascade.

Factor H and Factor I both together inactivates C3b shutting down the whole complement cascade

Deficiency in the complement system

Deficiencies in the c1,c2,c3,c4 associated with

1. lupus like illness
2. chronic renal disease
3. repeated infections

هذول حفظ بصم
حيجي عليه سؤال
Cases
neiserria => c5 defeiciency
مثلا يعني

Deficiencies in the c5 ,c6,c7,c8 (MAC)

1. repeated neiserria infection
2. risk of gonorrhea or meningitis

Diagnostic tools to measure complement activity include the total complement activity test

اسم الفحص برضو احفظوه

Thank You