



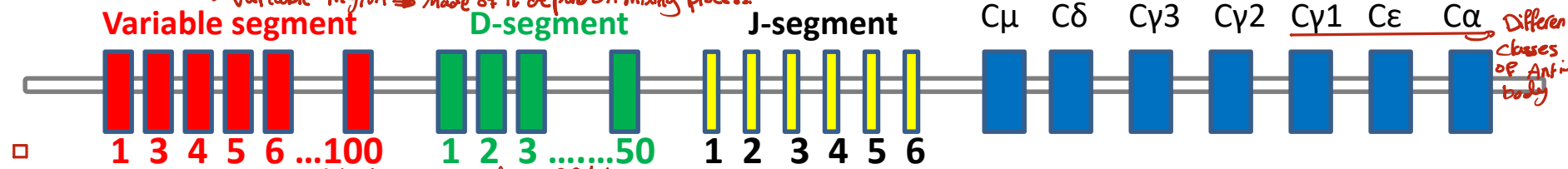
Immunology
Adaptive Immunity and Complement System
Lecture 6
2024-2025

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Faculty of Medicine, Mutah University

Why do we have millions of different versions of Fab?

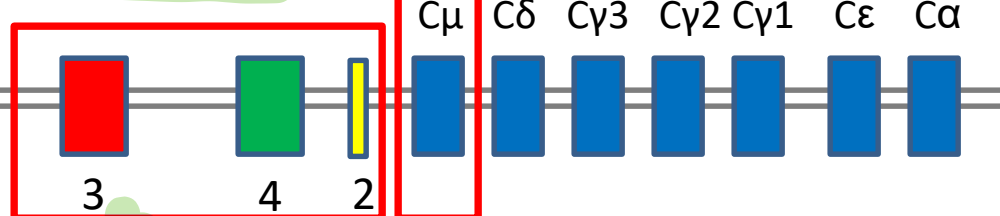
DNA consist of
 Constant Region
 Variable Region
 Made of it depend on mixing process.

Variable segment = 100 Allele.
 D seg. = 60, J-seg = 6
Chromosome 14

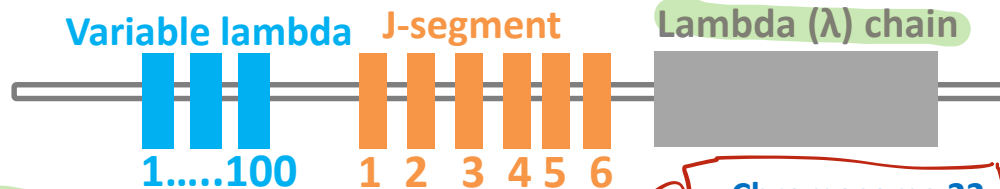
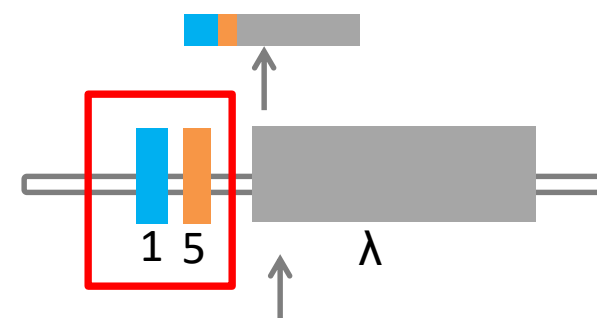
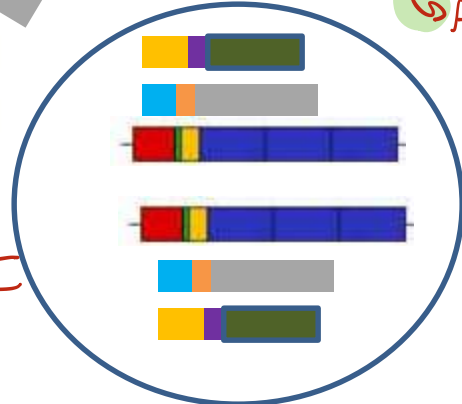
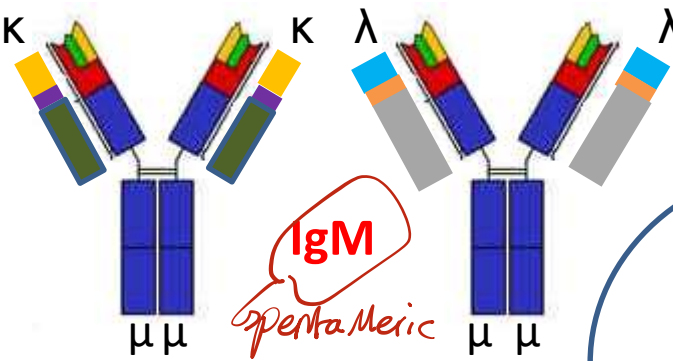


Allele = gen, produce proteins

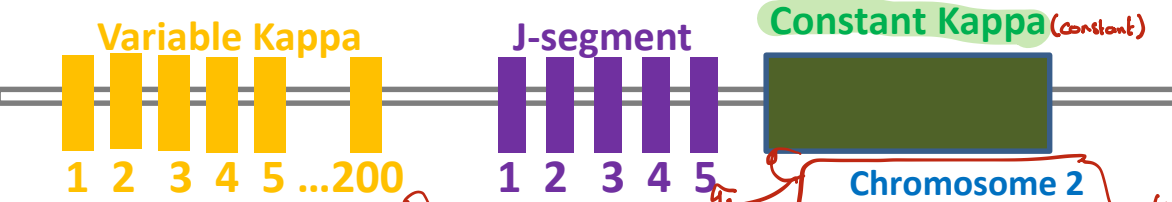
Recombinases \Rightarrow Do the Mixing



Alleles



Chromosome 22



Chromosome 2

Light chain

Light chains

Objectives

You should know the followings:

The **definition** of complement system

The **different pathways** associated with complement activation

Why dose complement system is activated?

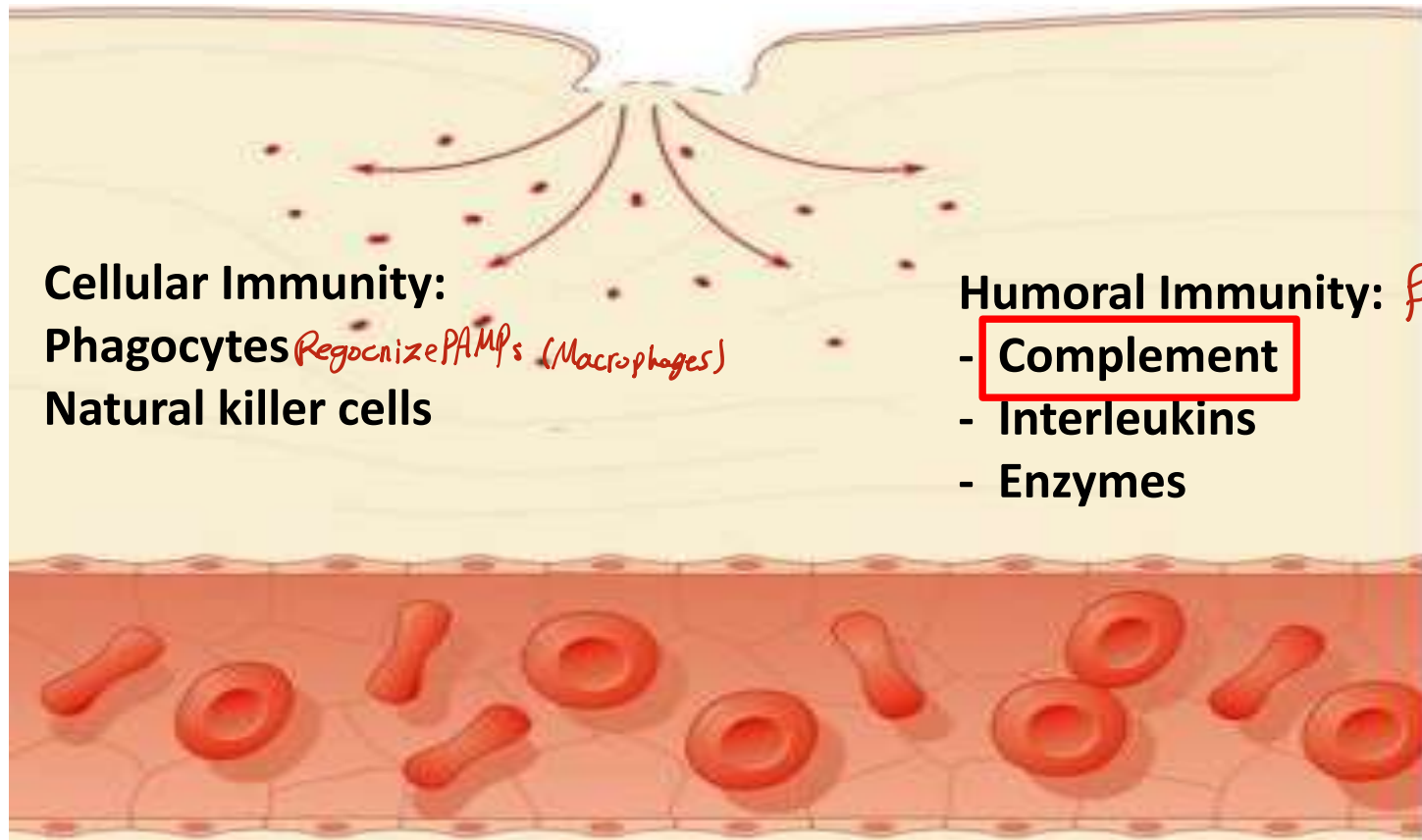
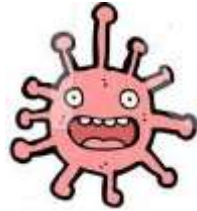
How dose complement system activate inflammatory response, lyses of foreign cells, and phagocytosis?

The **disorders** associated complement system

Innate immunity = Non-specific

↳ work in groups Not only Bacteria itself

Second line defense of the innate immune system



Cellular Immunity:

Phagocytes *Recognize PAMPs (Macrophages)*

Natural killer cells

Humoral Immunity: *Fluid (b)*

- **Complement**

- Interleukins

- Enzymes

Innate immunity



**Third line defense
Adaptive Immunity**

Activate of
B+T cells
to produce
Antibodies

3- Classical complement pathway

Humoral
cellular
**Second line defense
Innate Immunity**

1- Alternative complement pathway

2- Mannan binding lectin (MBL)

First line defense (skin, mucous)

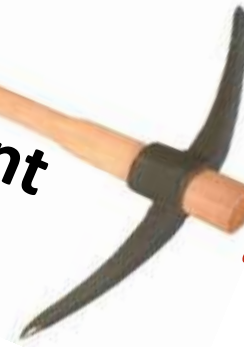
Innate = cuz it isn't specific



work in the
absence of
Antibodies.

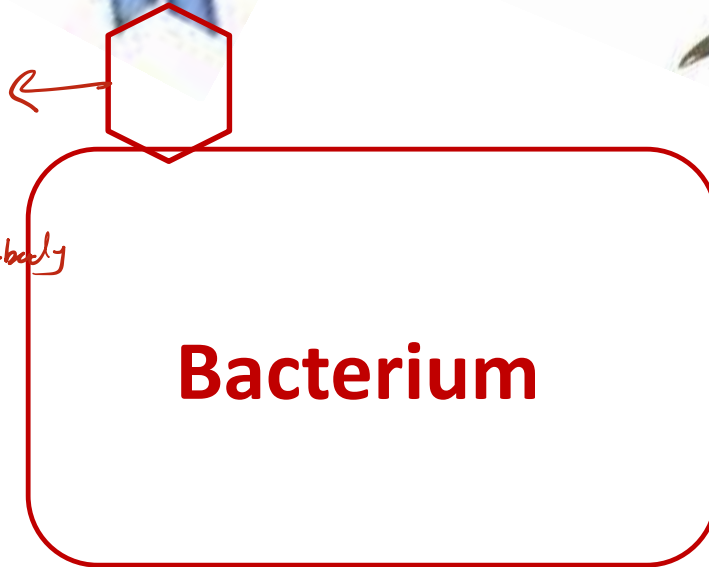


Complement
Proteins



⇒ destroy the surface
and release out the contents
so, the bacteria die.

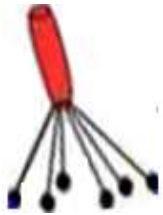
Epitope
↳ partial Antigen
which bind to the Anti-body



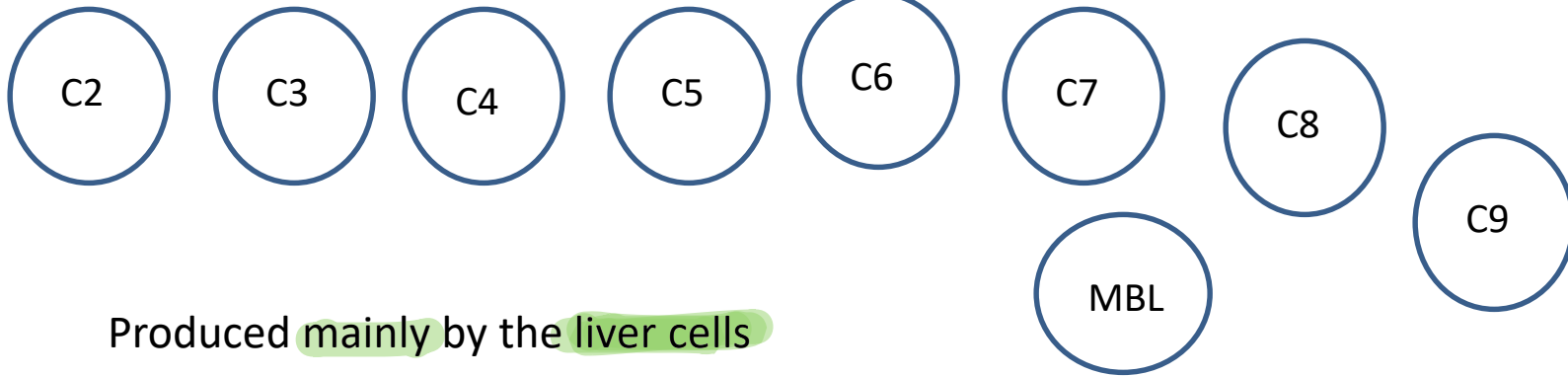
Bacterium

The definition of complement system?

A set of over 20 different protein molecules always found in the blood



C1



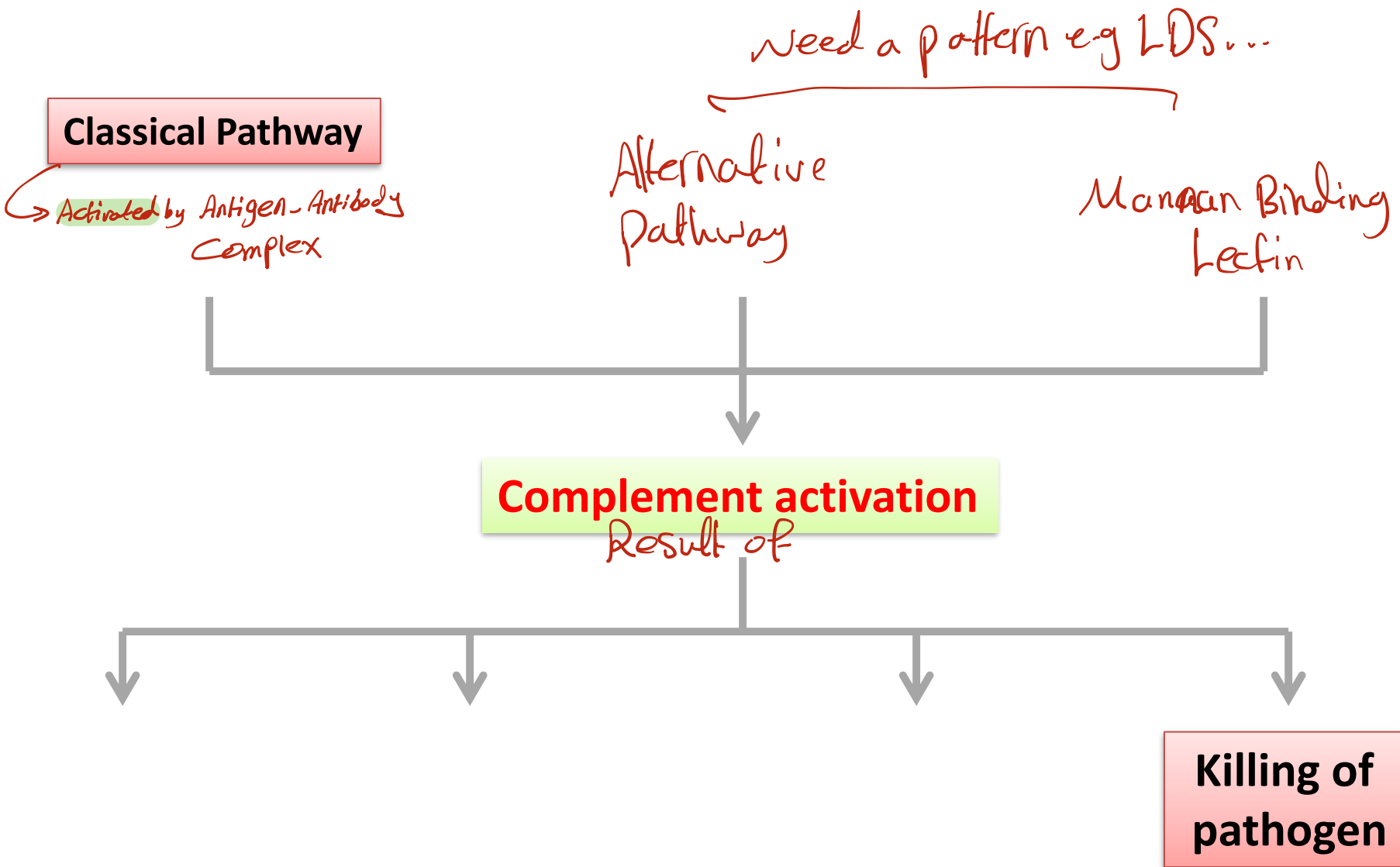
Produced mainly by the liver cells

Present in the blood as inactive enzymes called proenzymes

When occur a damage in tissue they become Active.

There are no cells in the system

Complement pathways activation



Complement pathways activation

2

3

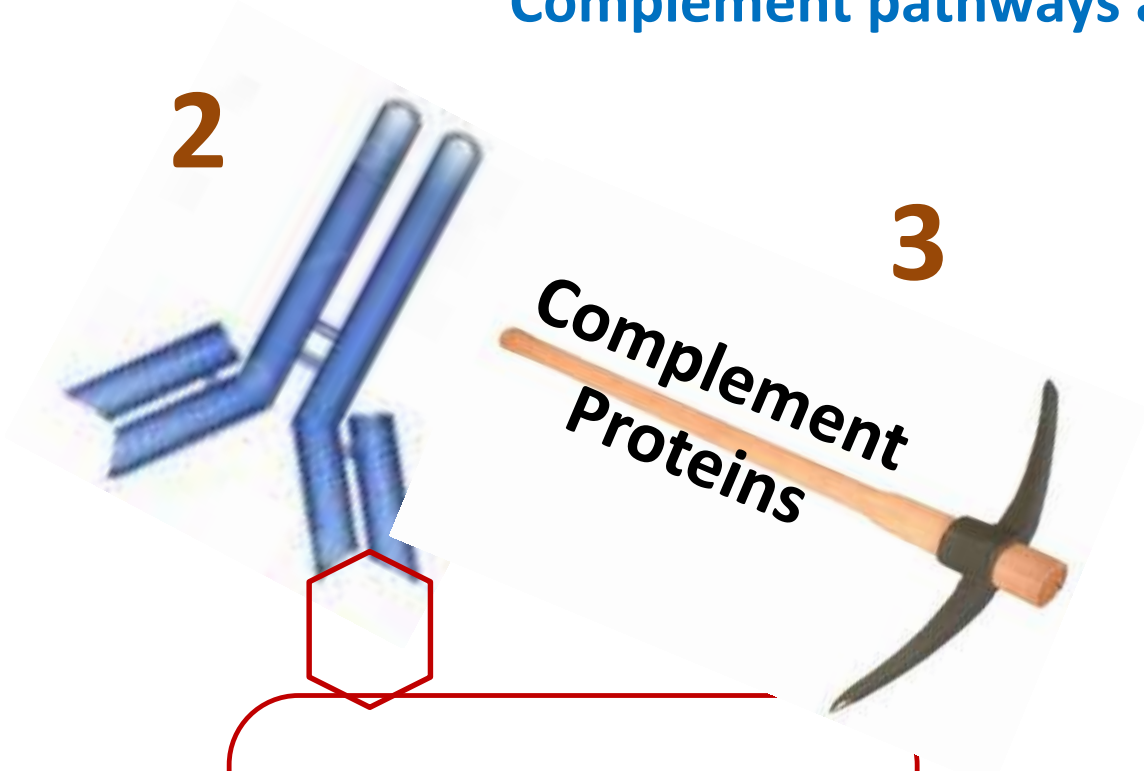
Complement
Proteins

1

Bacterium

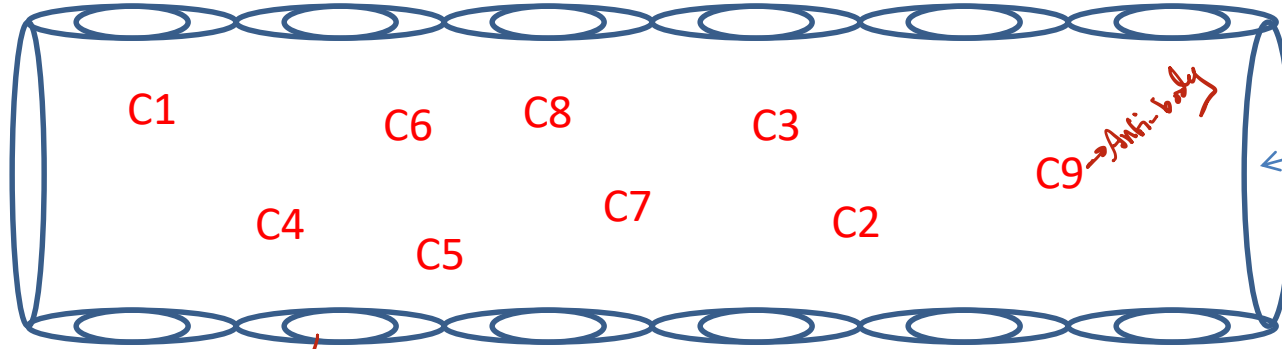
= Classical Complement Pathway

↳ we need antibody + Anti-gen



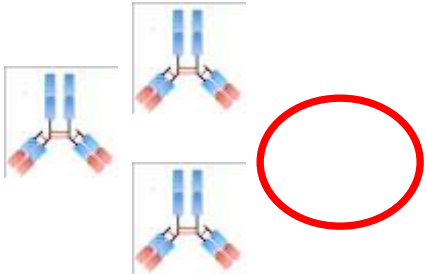
Classical Complement Pathway

↳ Complement + Antibody + Antigen



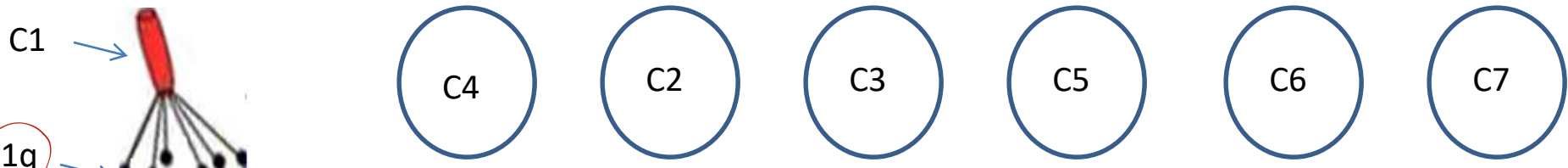
Blood vessel
↳ contain proenzymes

↳ proteins go to the site of Infection



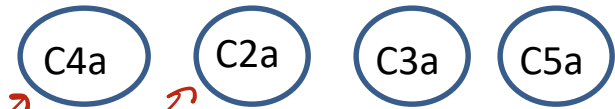
Infection



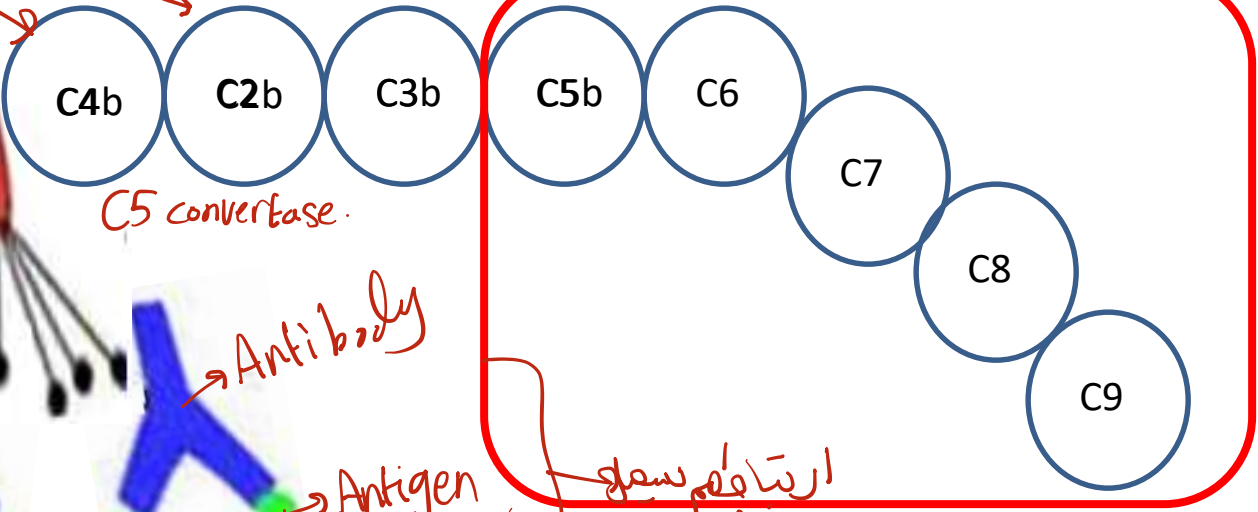


Make conformational change in C1 so C4 bind with C1

enzyme cut



Separation



C5 convertase

Antibody

Antigen

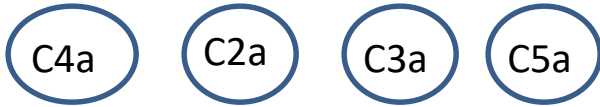
*ارتباط مع مستضاد
bind C1 with Antigen*

Membrane Attack Complex (MAC)

From C5b to C9 that make holes in Membrane

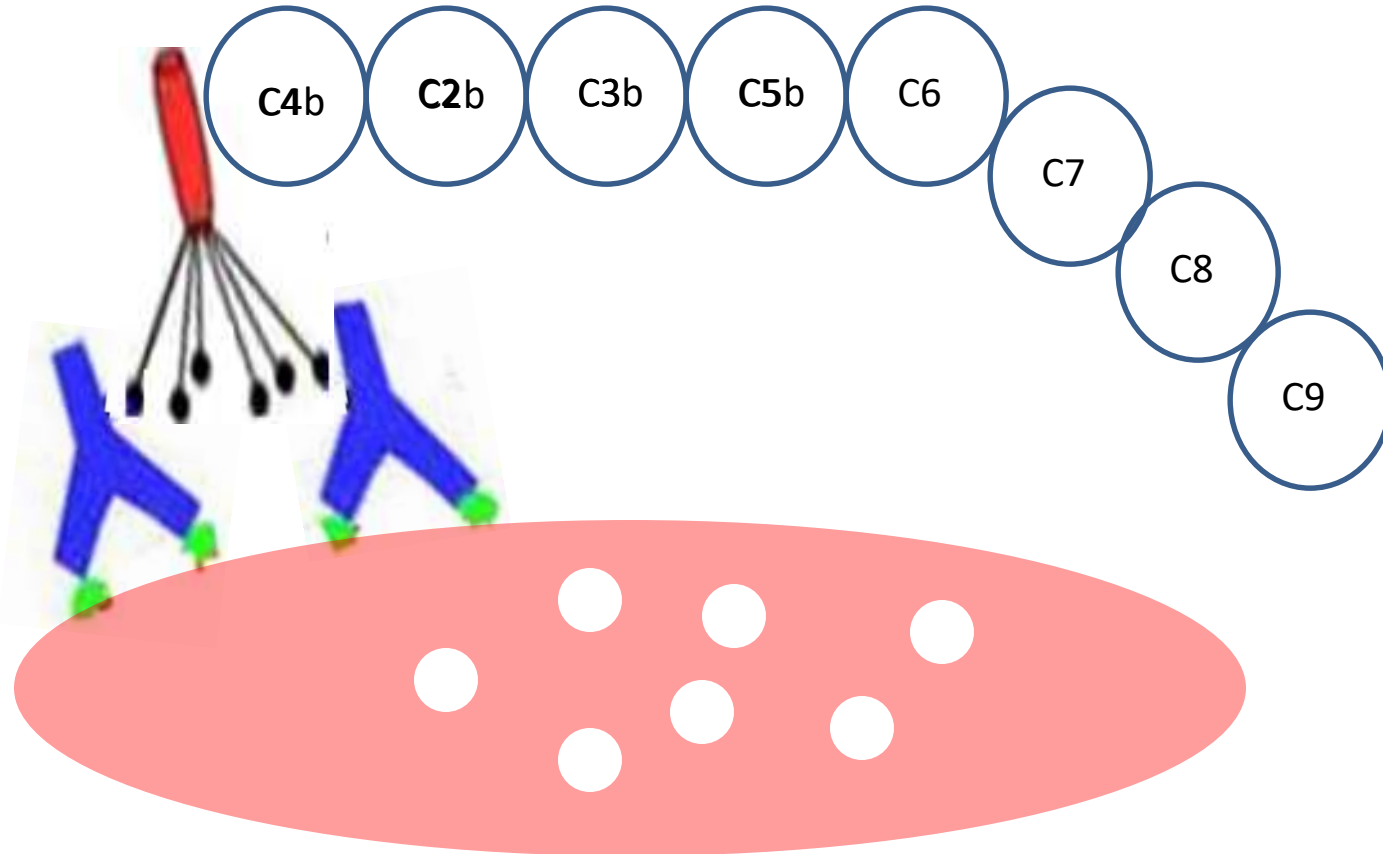
Bacteria

Classical Complement Pathway



C5 convertase

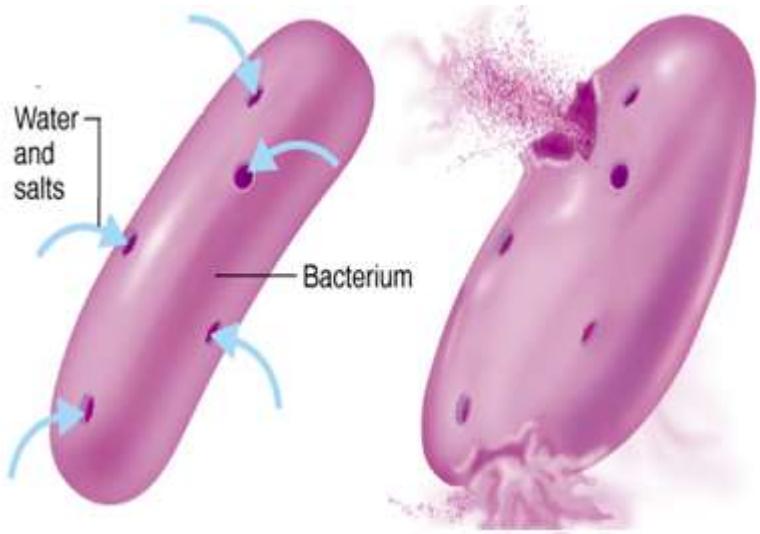
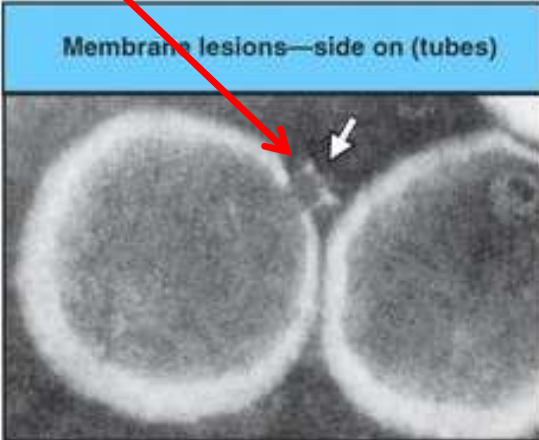
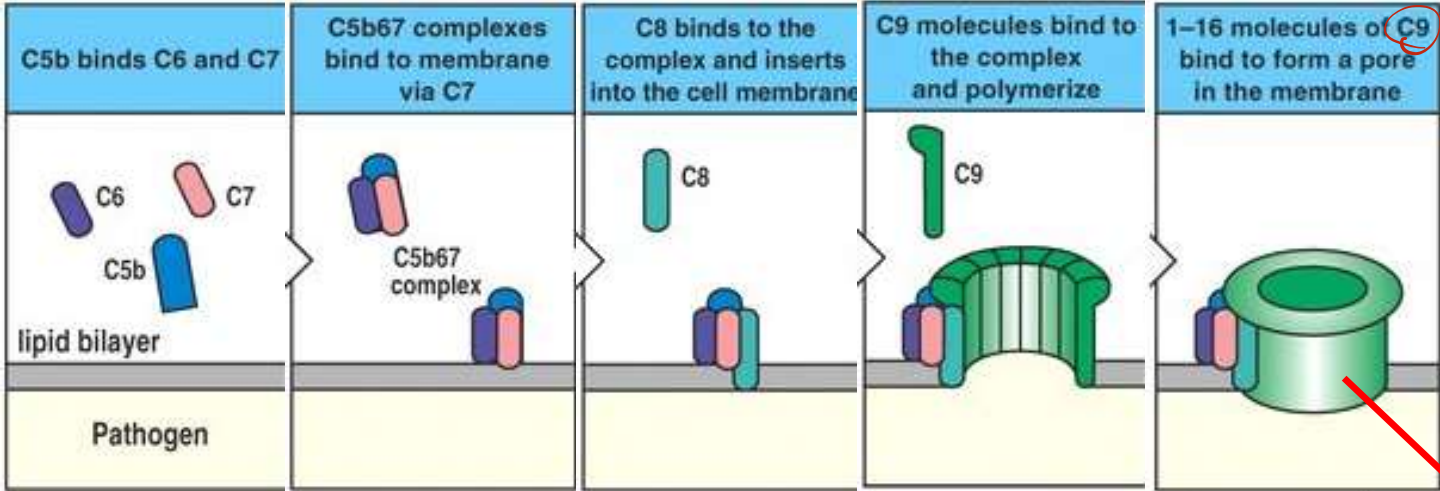
C3 convertase



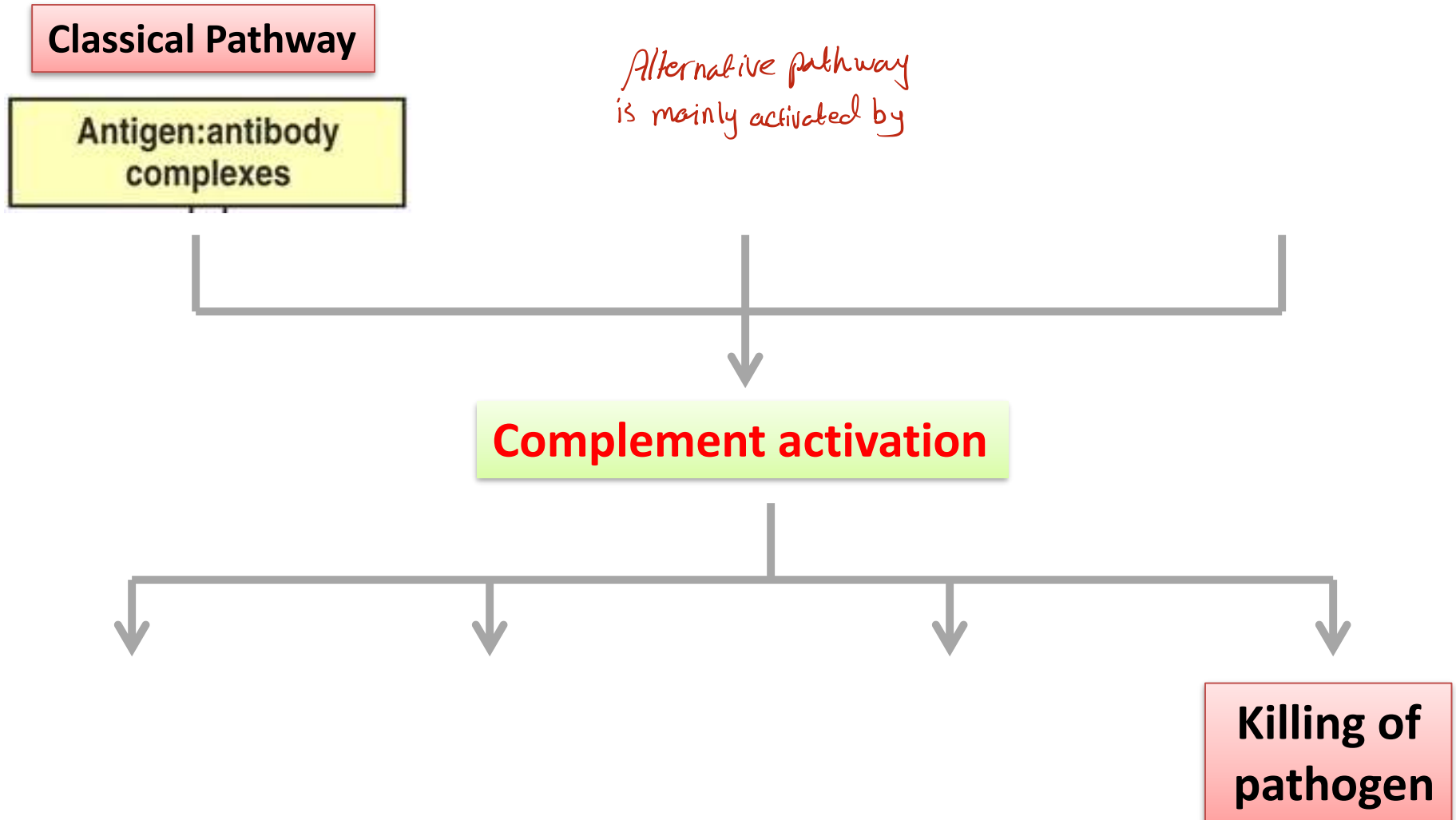
**Classical
Complement
Pathway**

Classical Complement Pathway

who make holes



Complement pathways activation



Complement pathways activation

Infection



5-7 days

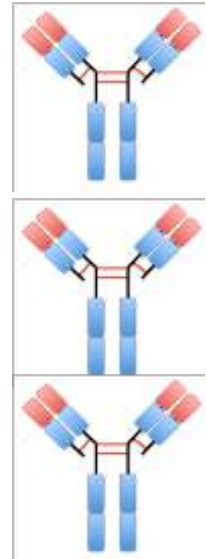
*To make Anti-bodies, we can't wait a week
to occur an Immune Response, so we turn on
the Alternative Complement pathway.*



?

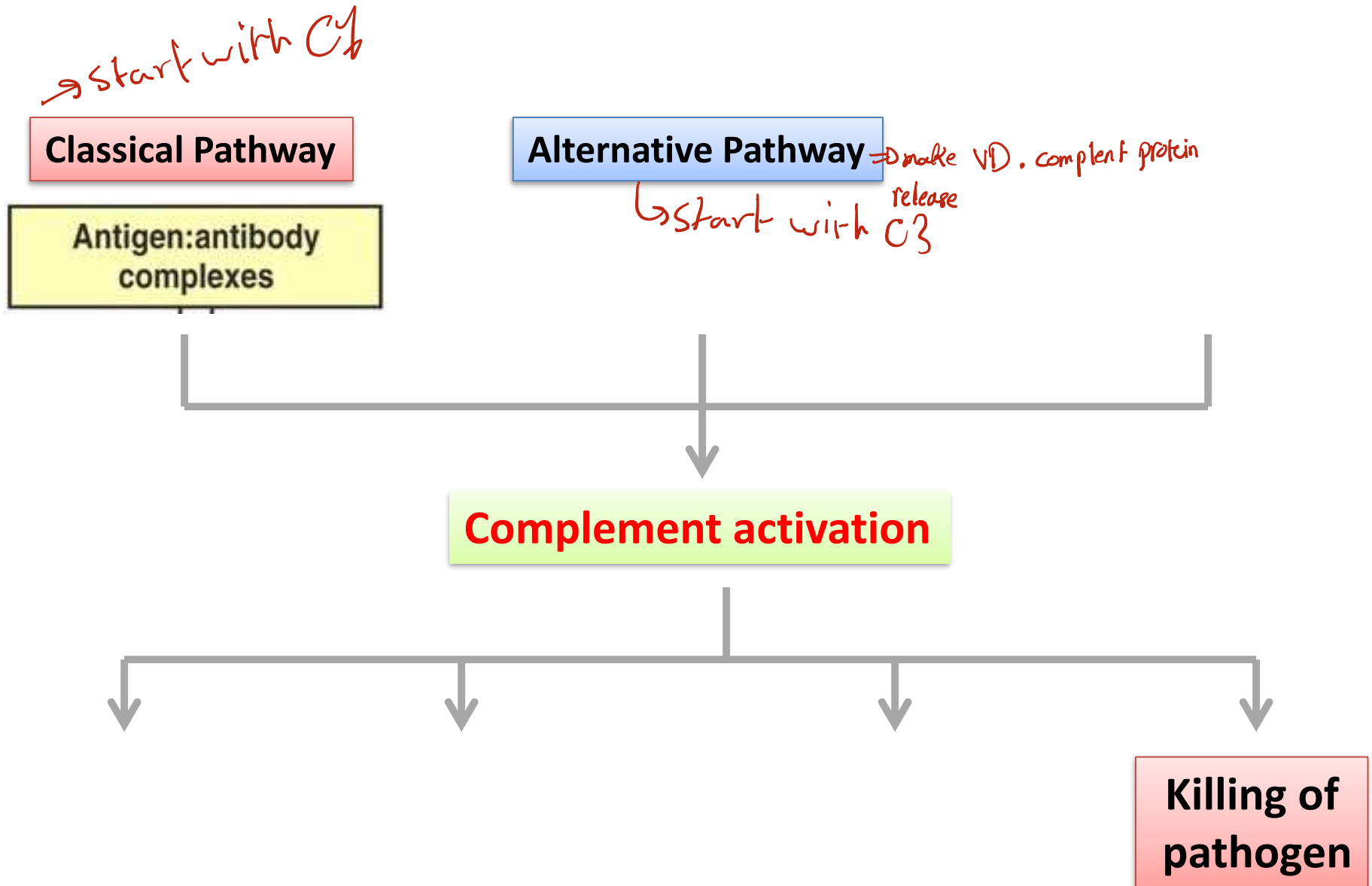
Alternative Pathways

Mannan Binding Lectin Pathway

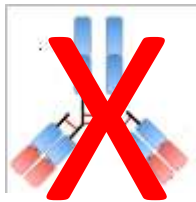
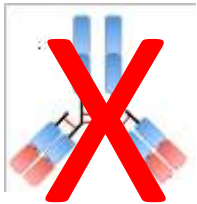
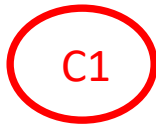
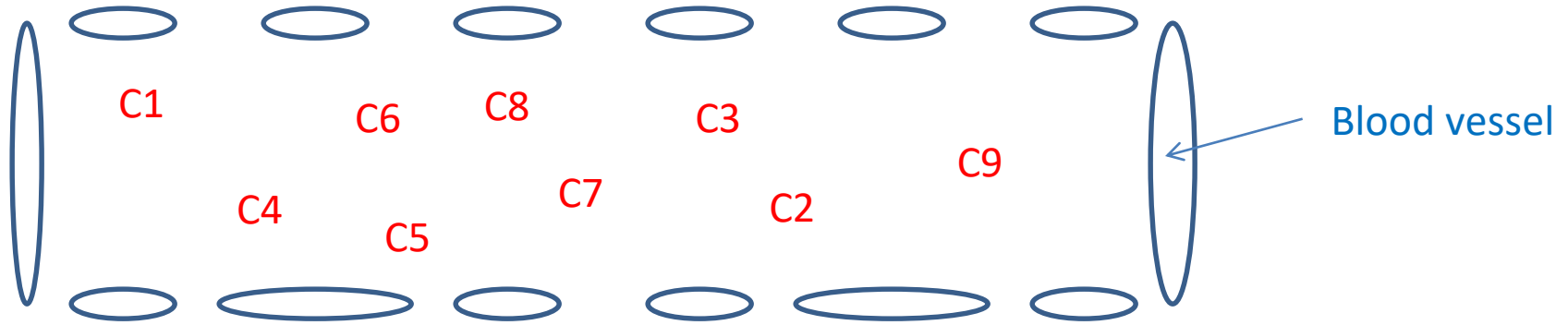


Classical pathway

Complement pathways activation



Alternative Complement Pathway

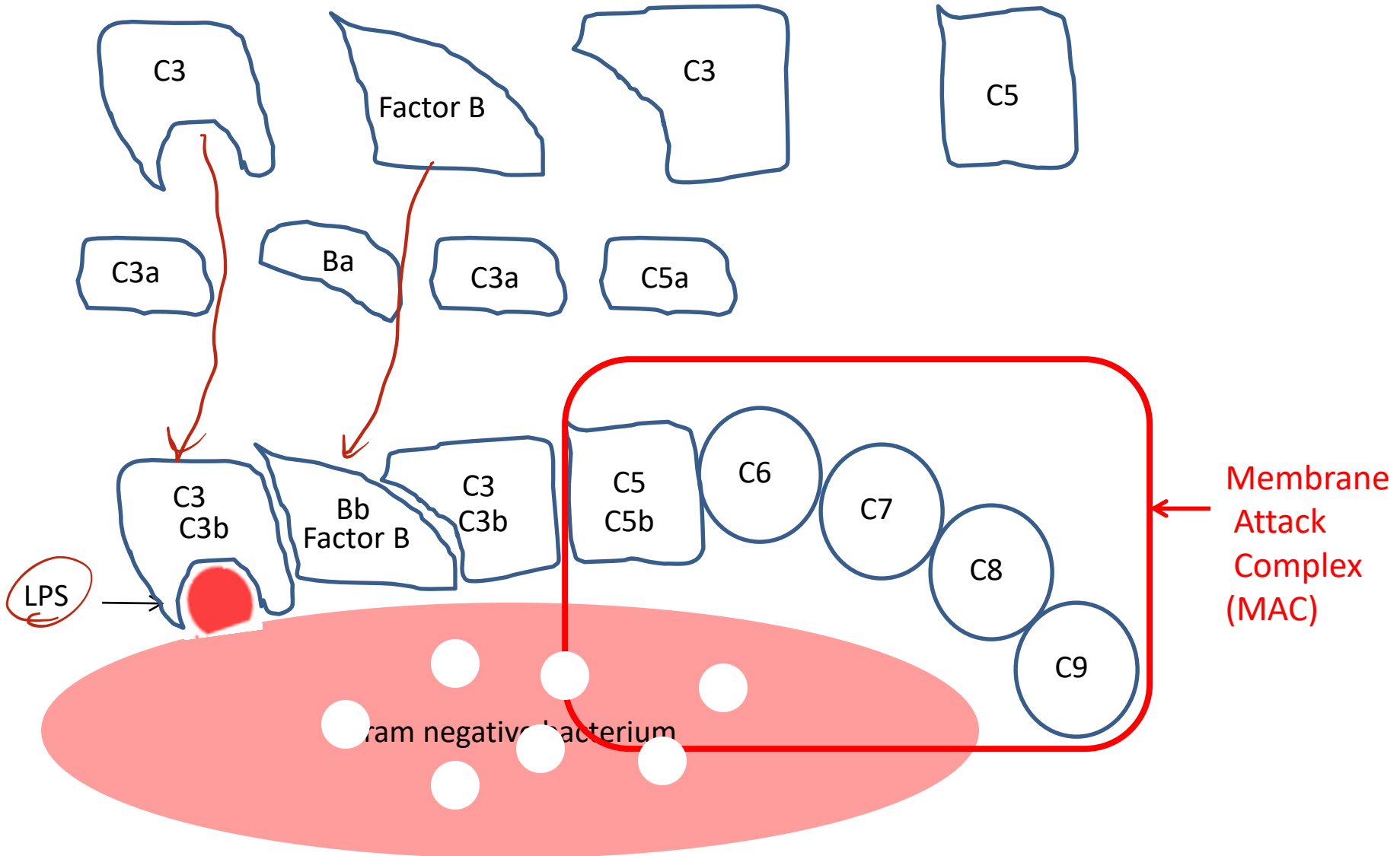


C6 C8 C3 C9
C4 C5 C7 C2

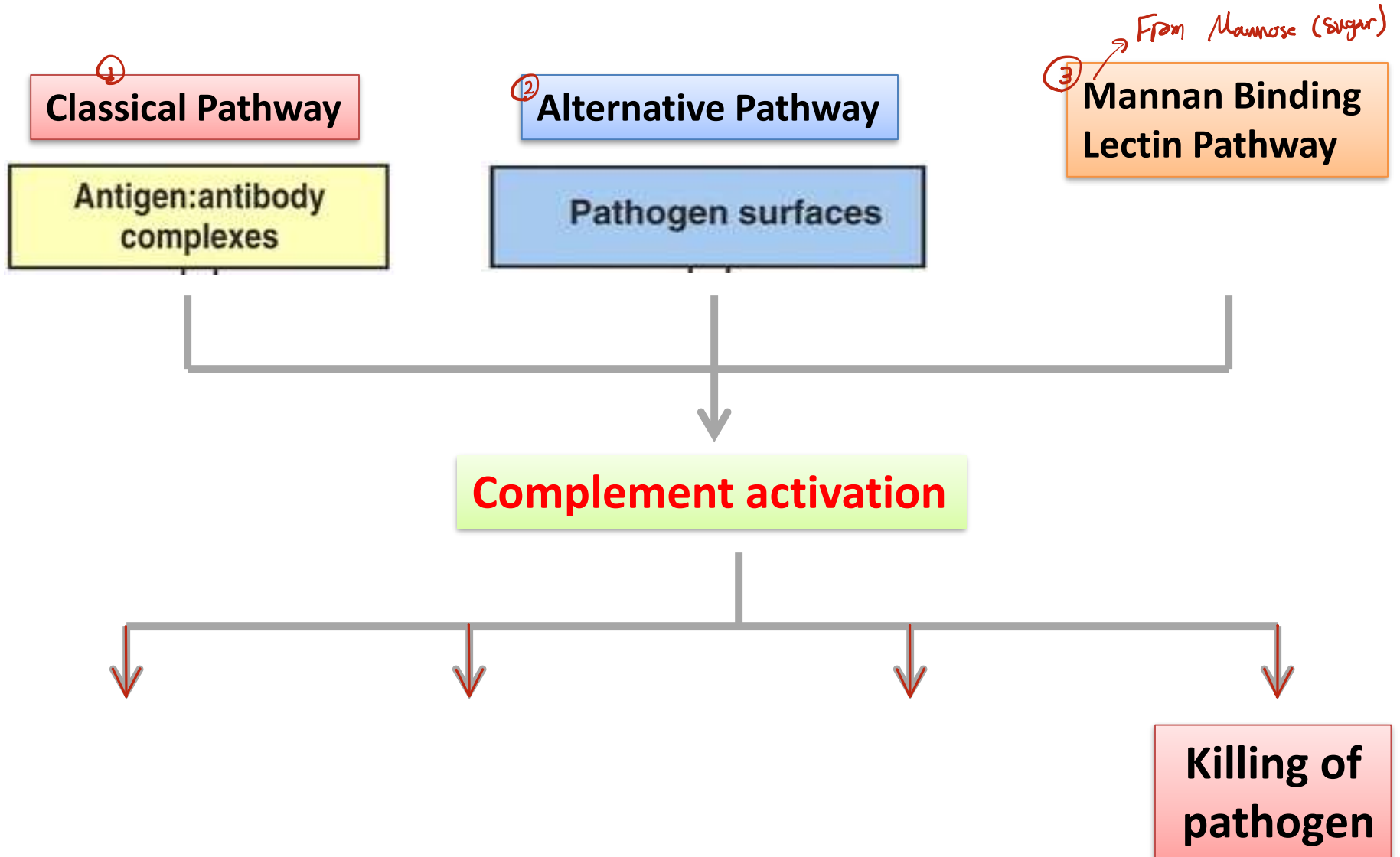
Inflammation



Alternative Complement Pathway



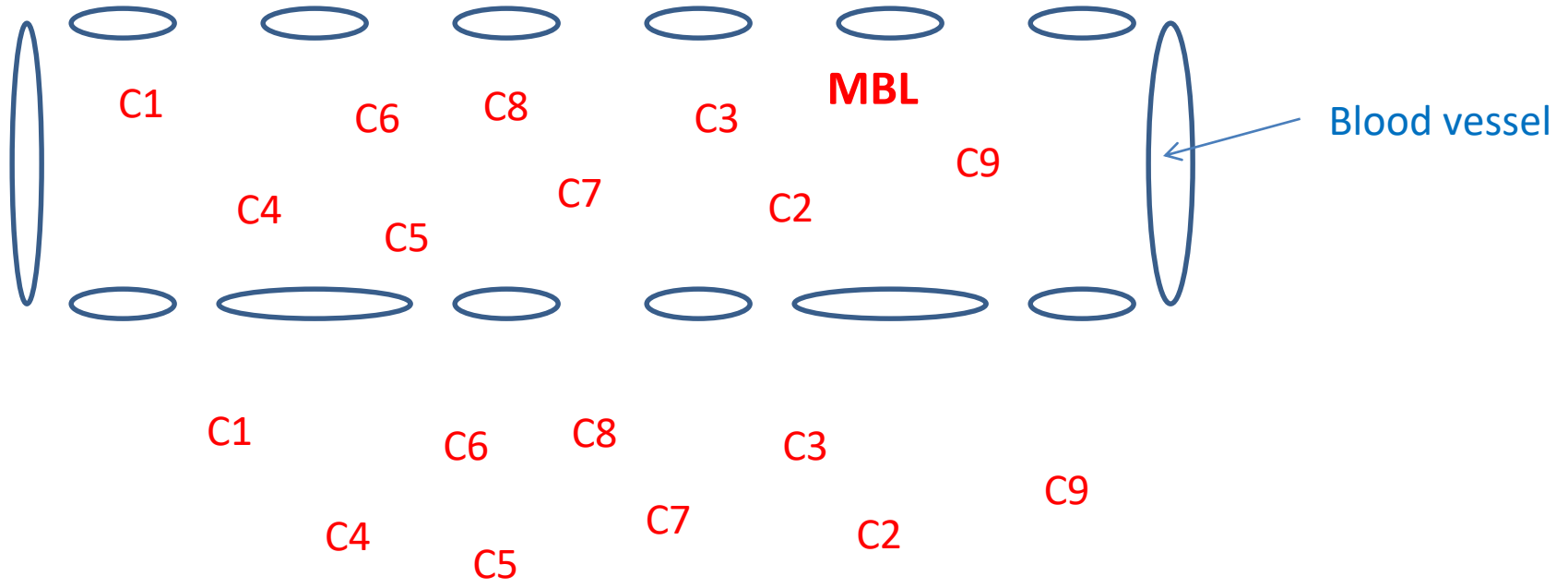
Complement pathways activation



Mannan Binding Lectin Pathway



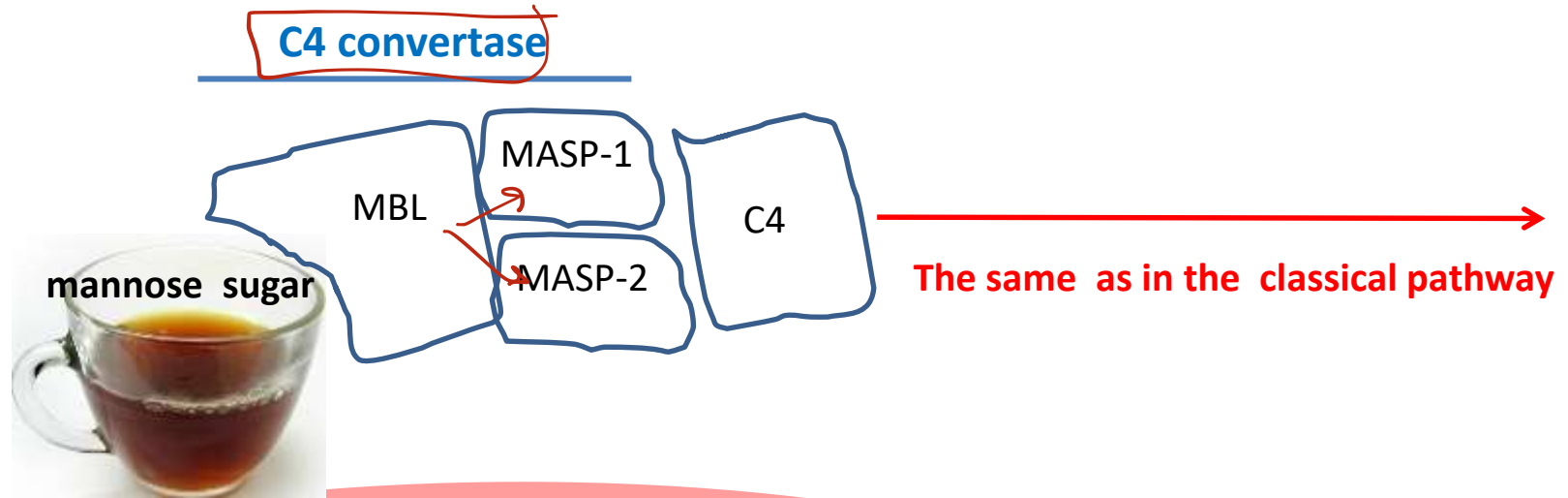
Mannan Binding Lectin Pathway



Inflammation



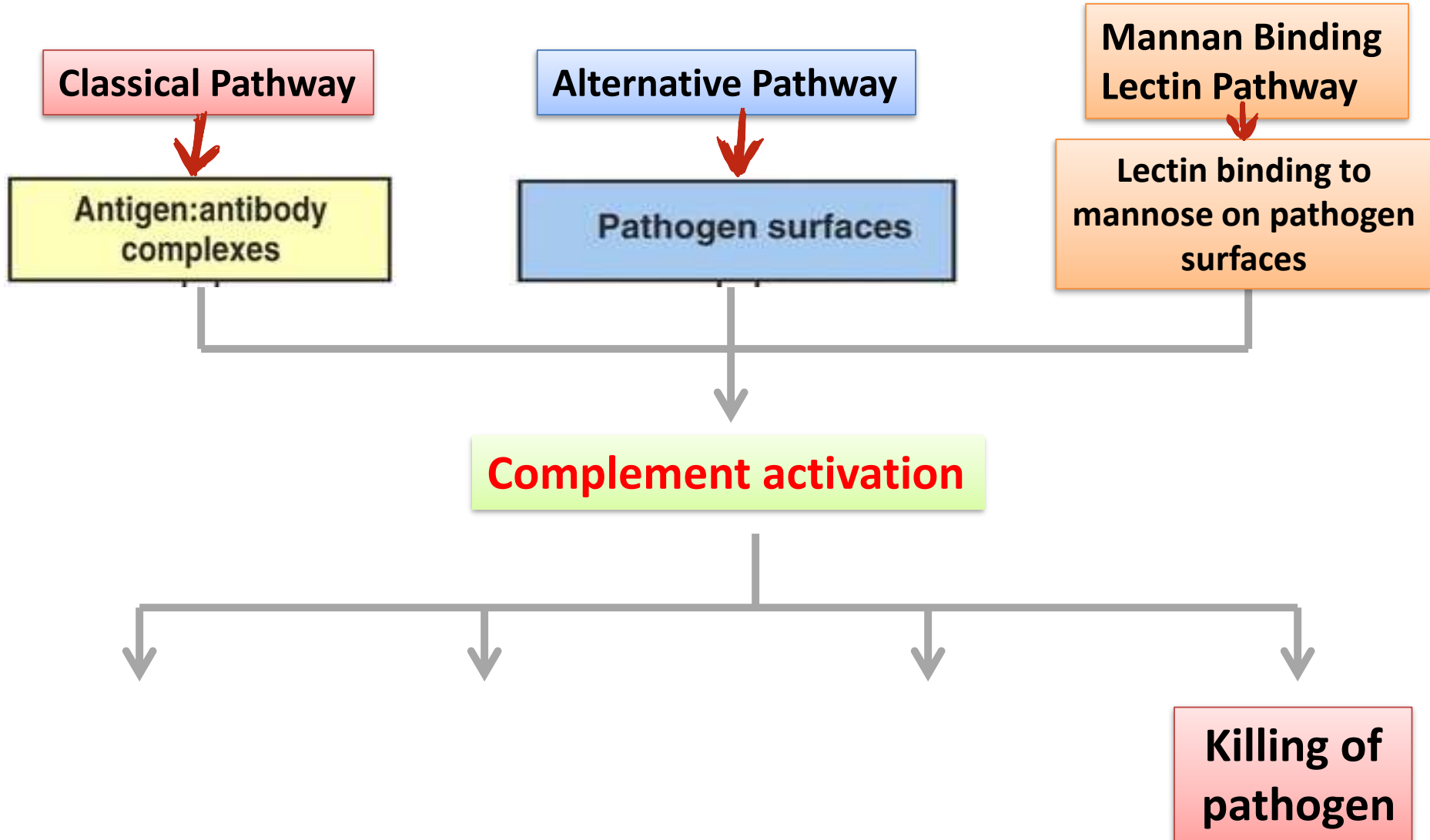
Mannan Binding Lectin Pathway



mannose residues on the surface of a large number of pathogens including bacteria, viruses, protozoa and fungi.

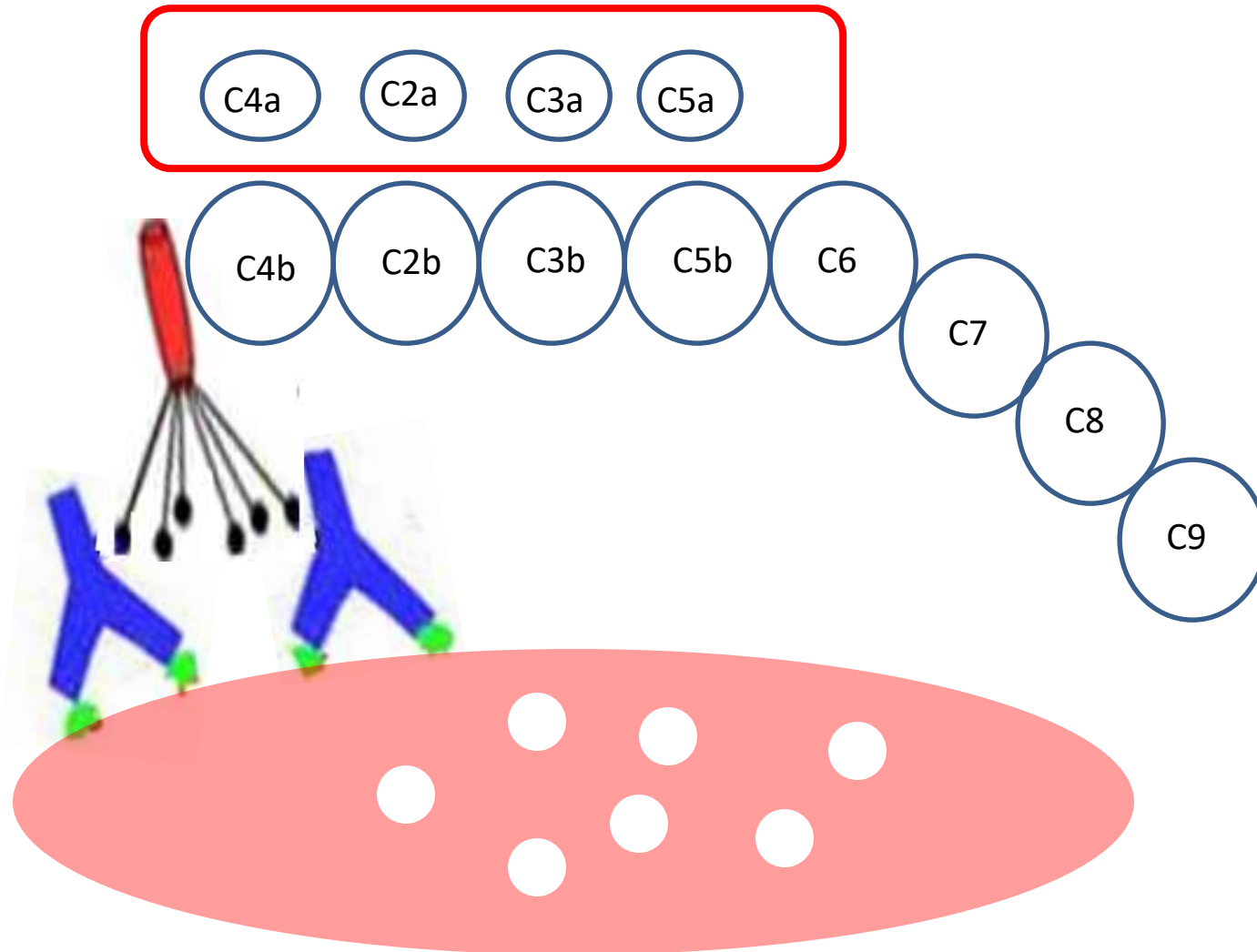
MASP: Mannan-binding lectin-associated **serine** protease

Complement pathways activation

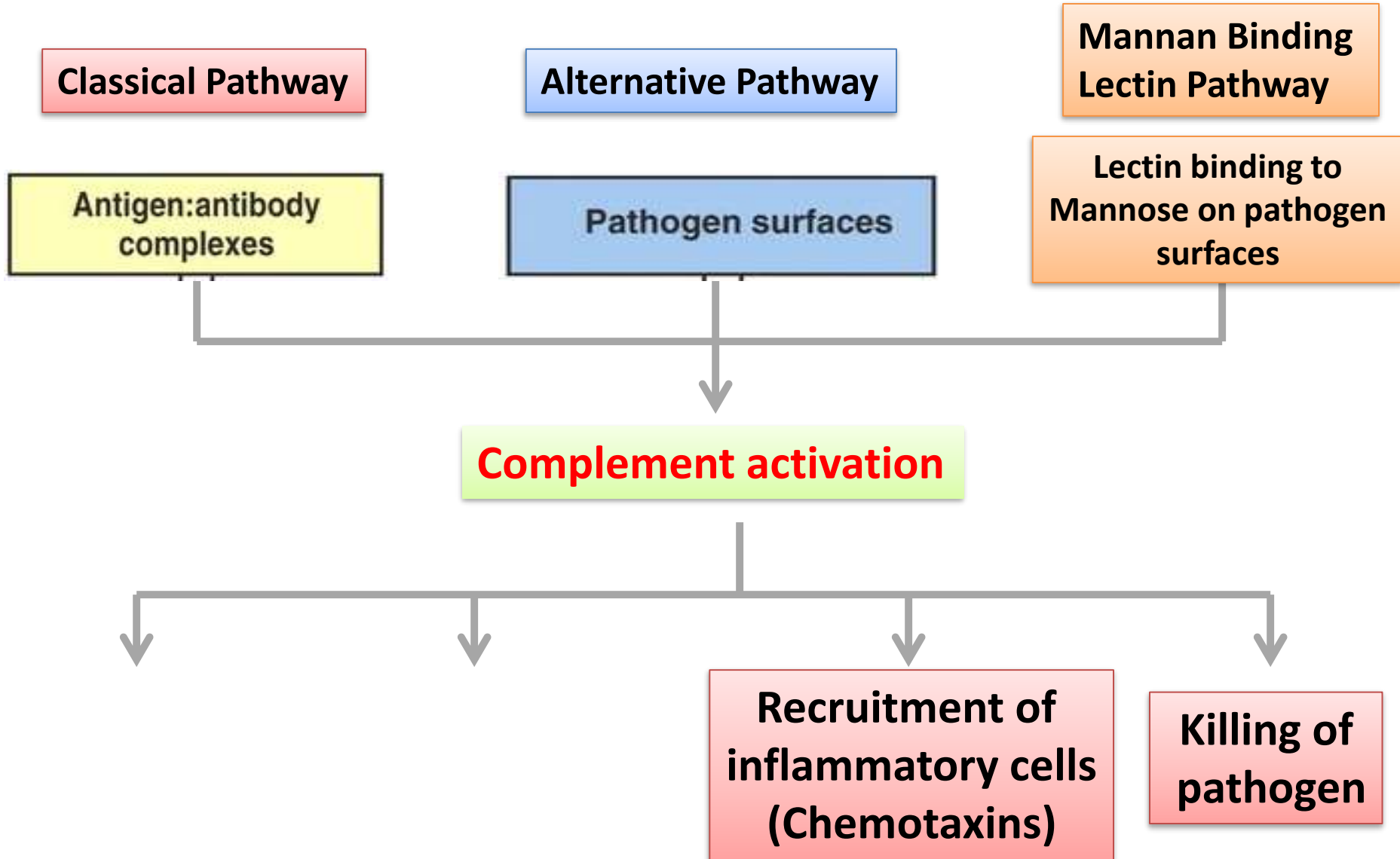


Biological activities of complement components

Biological activities of complement components



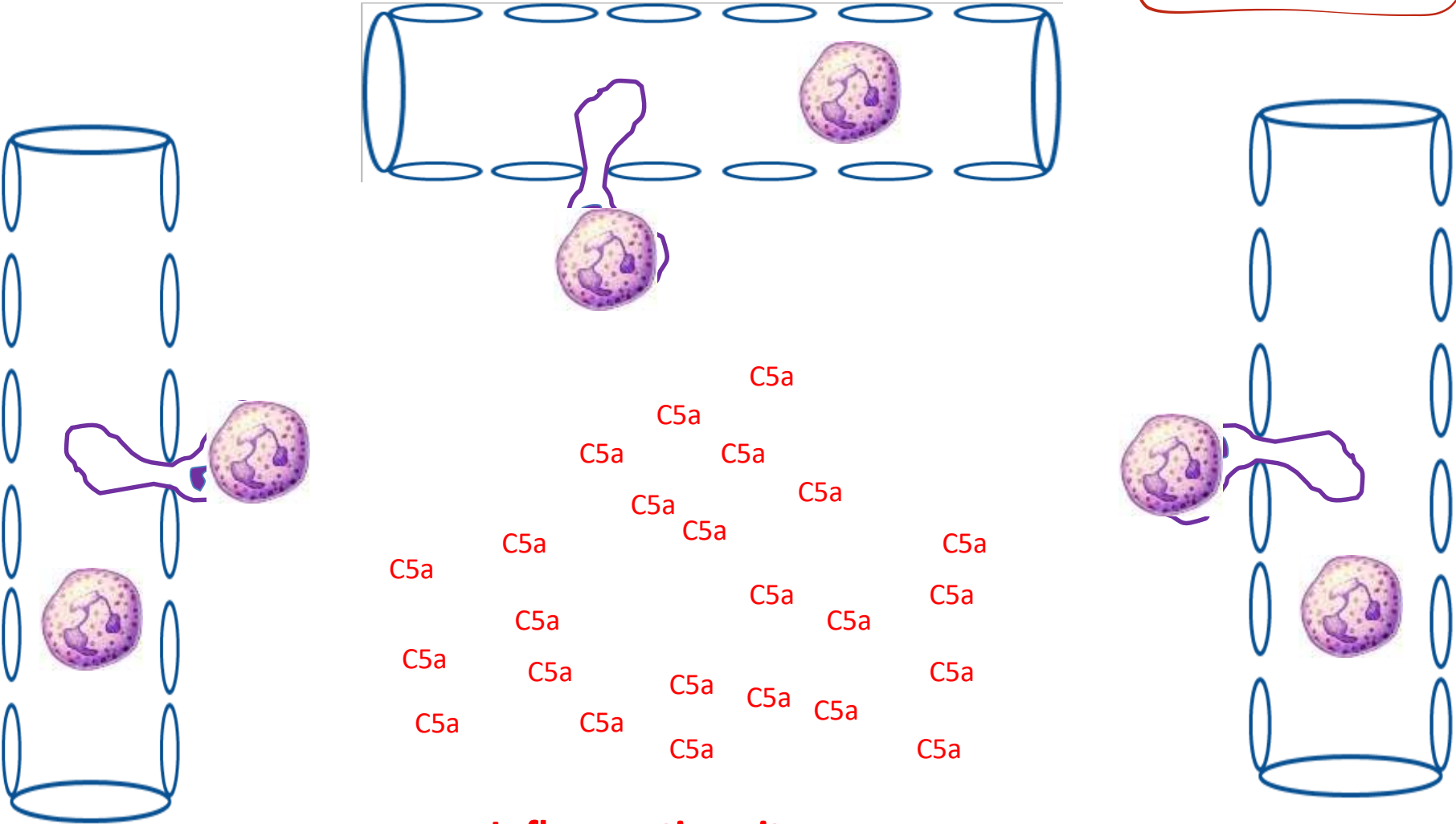
Complement pathways activation



Biological activities of complement components

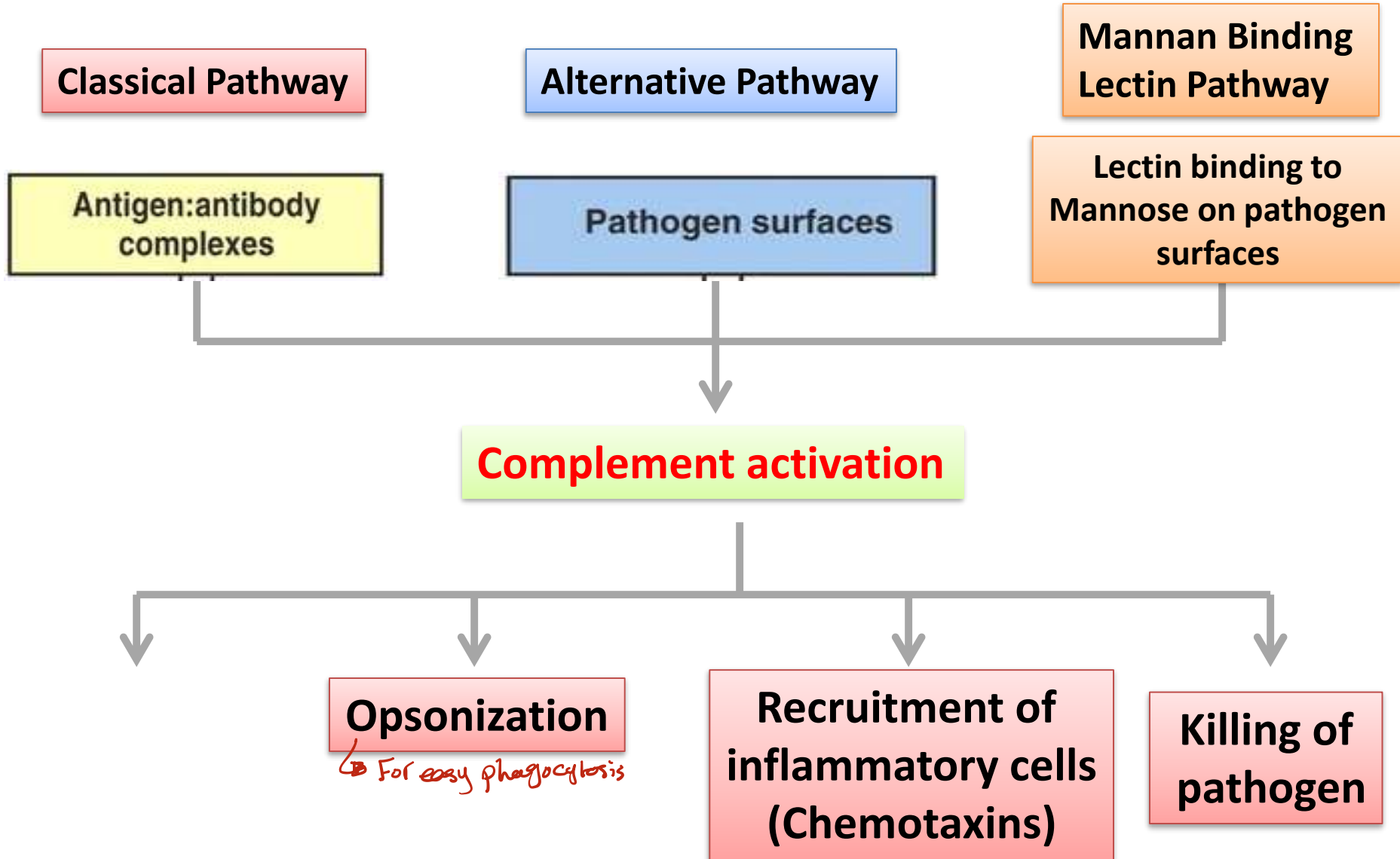
Recruitment of Inflammatory cells → Chemotaxis

act as
C3a, C5a



Inflammation site

Complement pathways activation

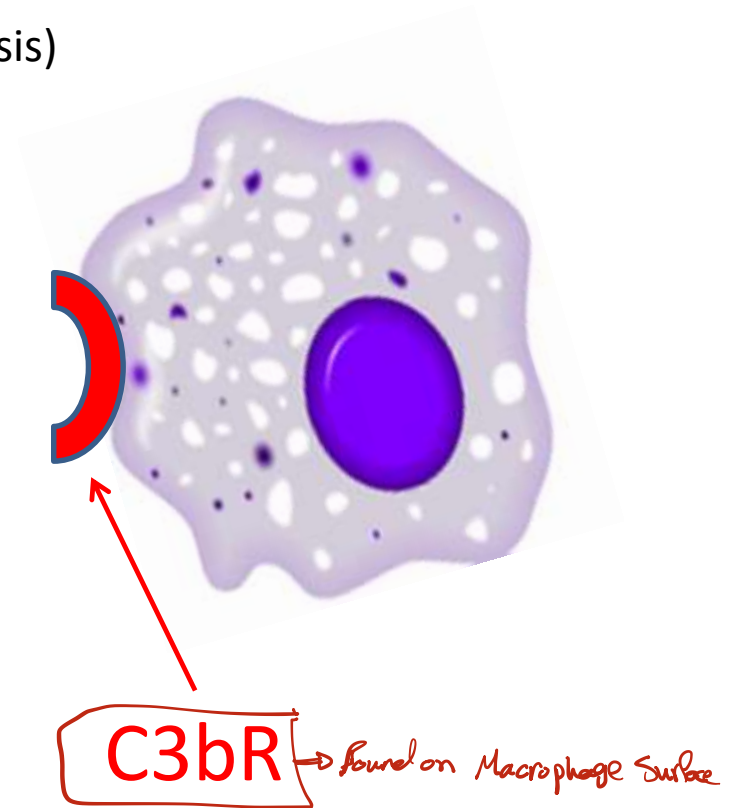
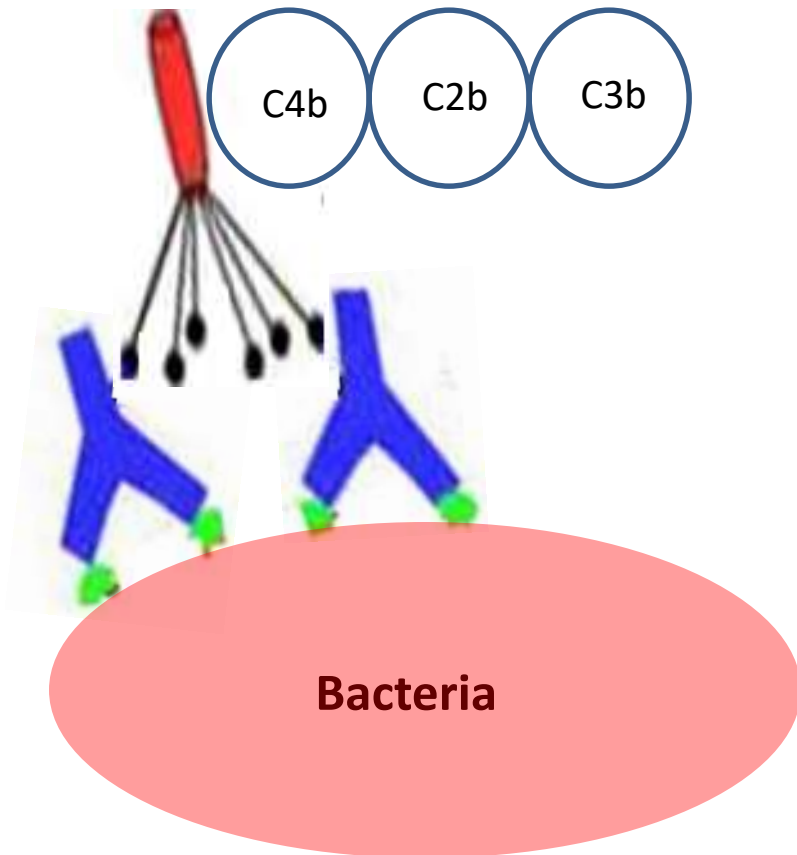


Biological activities of complement components

Opsonization

C3b

Opsonin: to prepare for eating (facilitate phagocytosis)



C3b act as opsonin which makes phagocytosis easier and faster

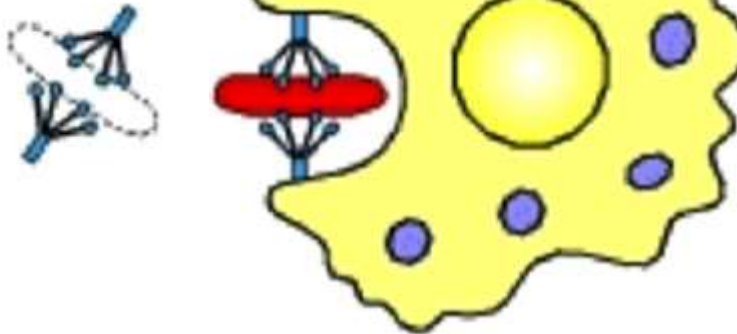
Biological activities of complement components

Opsonization

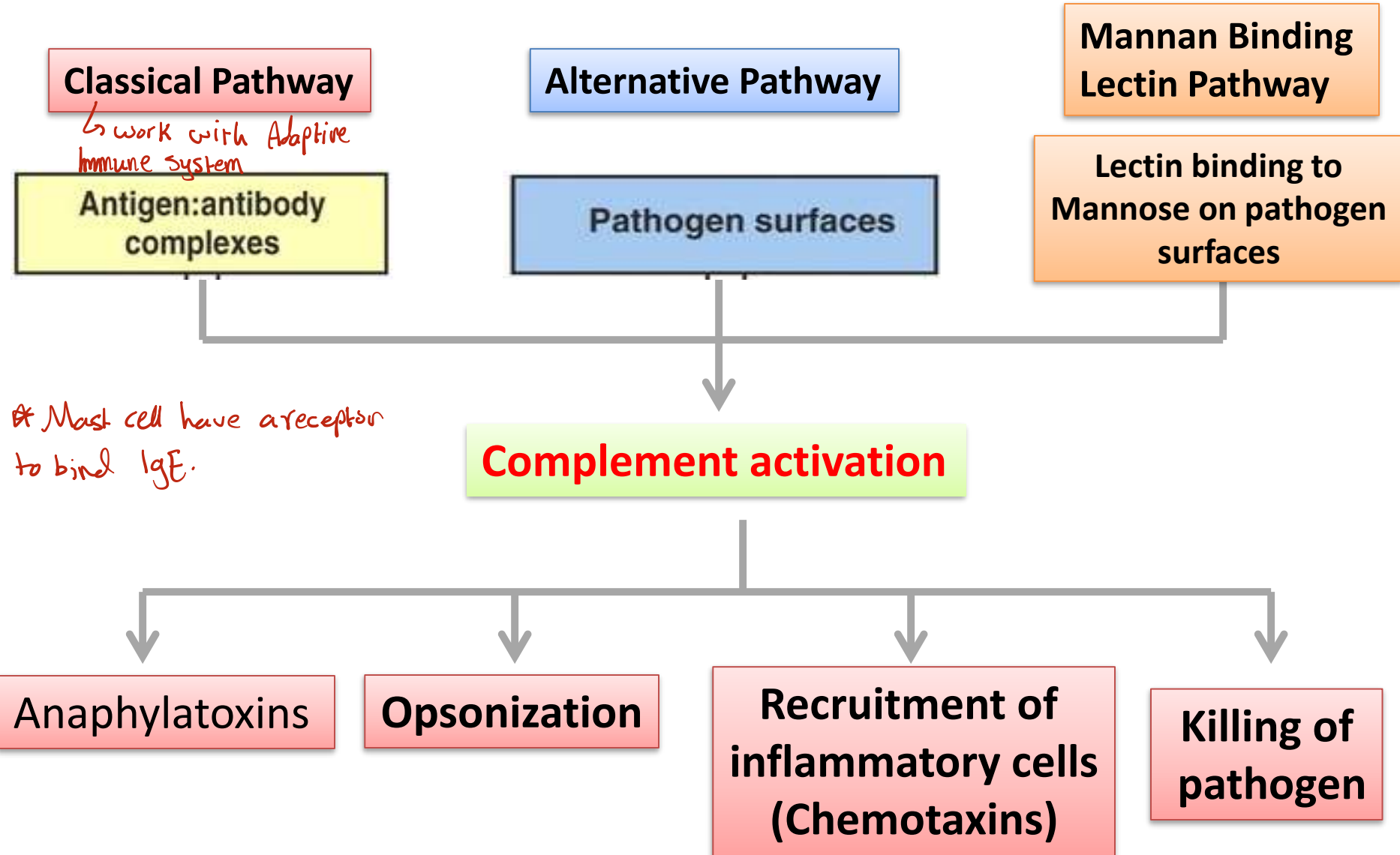
MBL

** Lectin have a receptor on the surface of Macrophage*

MBL act as opsonin



Complement pathways activation



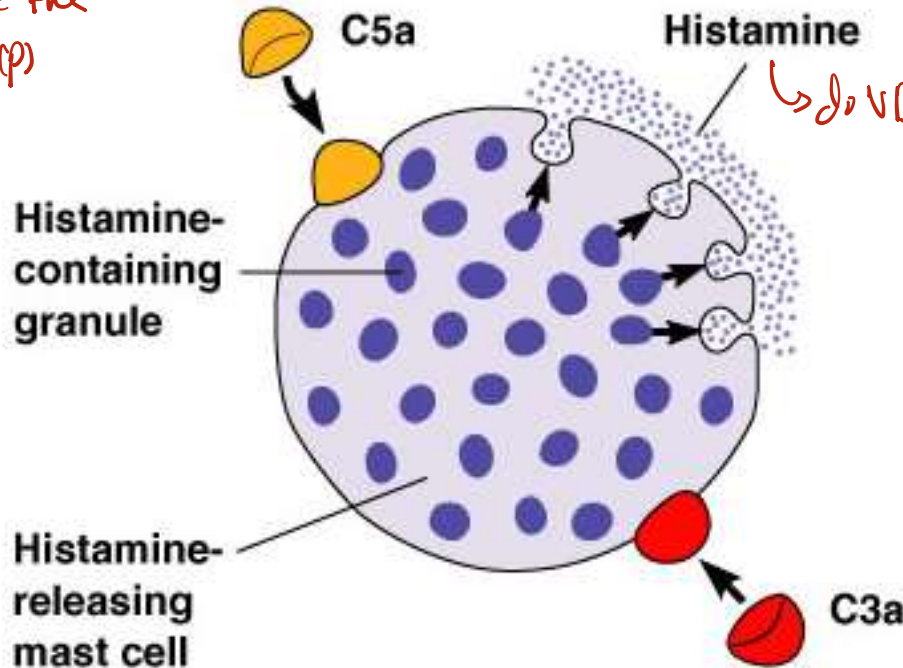
Biological activities of complement components

Anaphylatoxins

Release of Histamine outside the cell increase the Amount of complement (p)

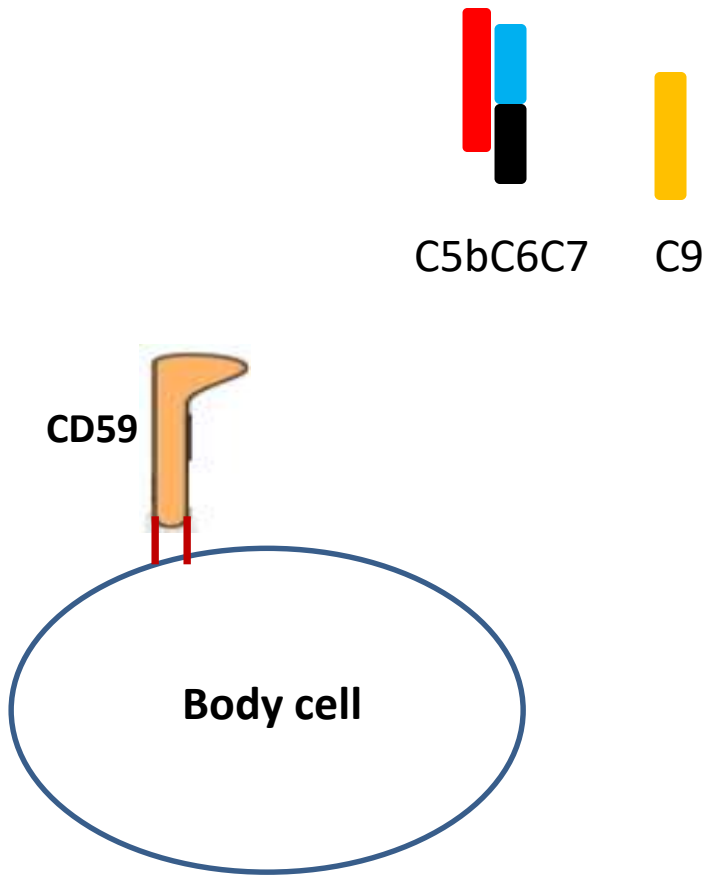
C3a, C4a, C5a

↳ have receptors on surface of Mast cells



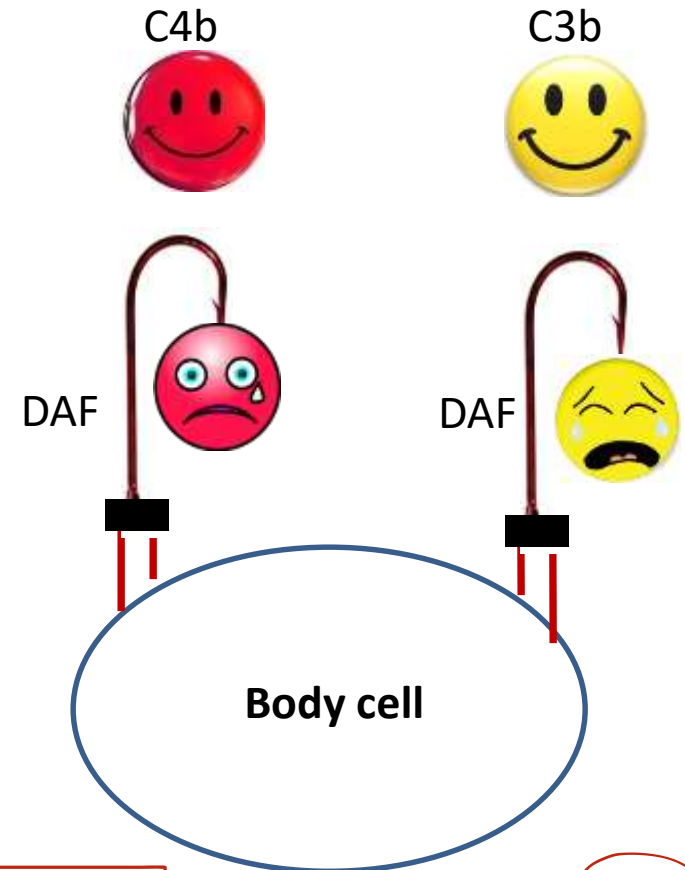
What protect our cells from complement system?

1. MAC-inhibitory protein (CD59) *cluster of differentiation*



CD59 inhibits the recruitment of C9 which inhibits the formation of MAC

2. Decay-Accelerating Factor (DAF)

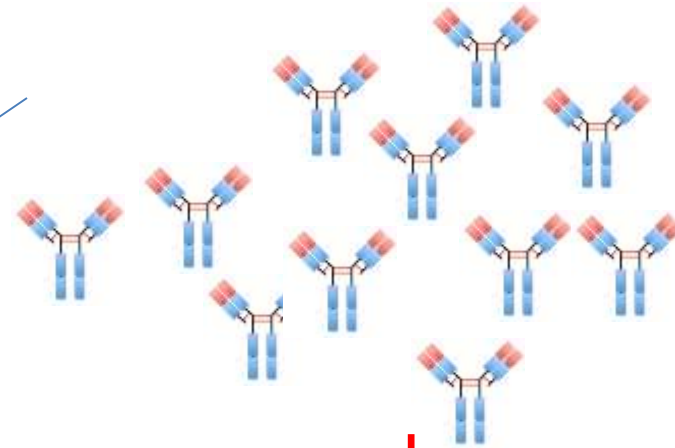
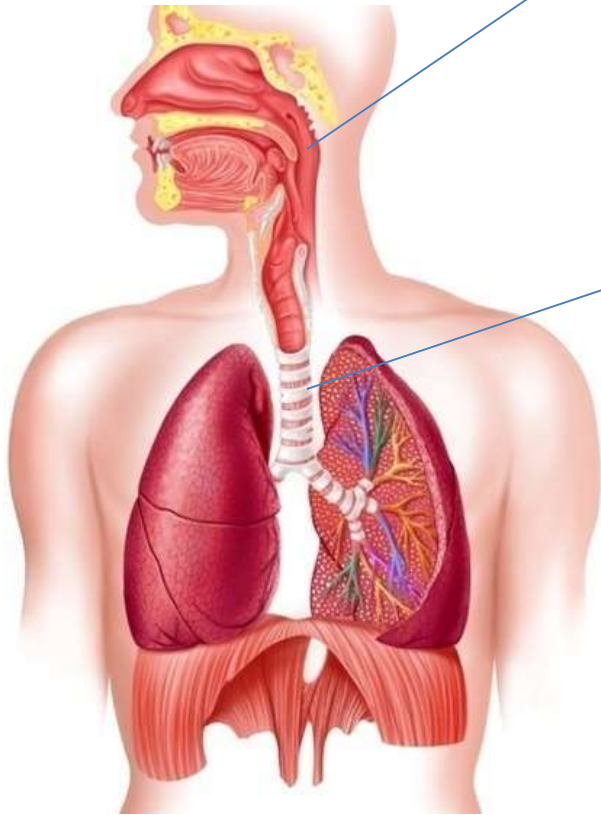


C4b and C3b interaction with DAF inhibits the stimulation of complement on the surface of body cells

Diseases associated with complement system

IgA nephropathy (Berger disease)

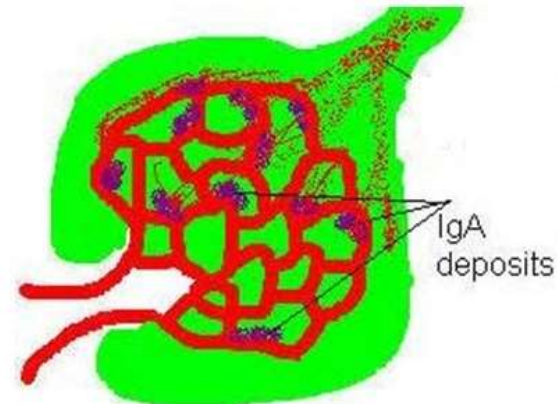
يُستعمل على حبة
مخاويين



Polymerization



Deposition in the glomerular mesangium



Patient with respiratory tract infection

Diseases associated with complement system

Henoch-Schönlein purpura (HSP) (IgA Vasculitis)

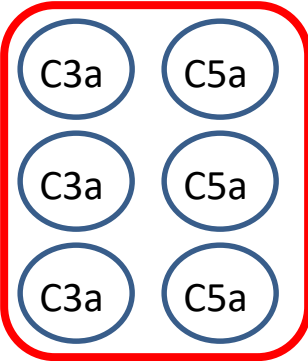
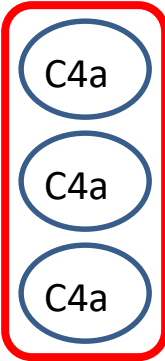
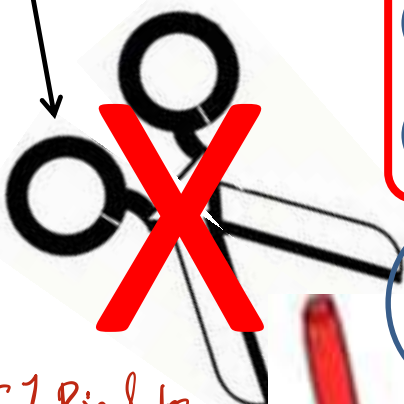


HSP is a small-vessel vasculitis in which complexes of IgA and complement component are deposited on arterioles, capillaries, and venules. HSP involves the skin and connective tissues, scrotum, joints, gastrointestinal tract and kidneys

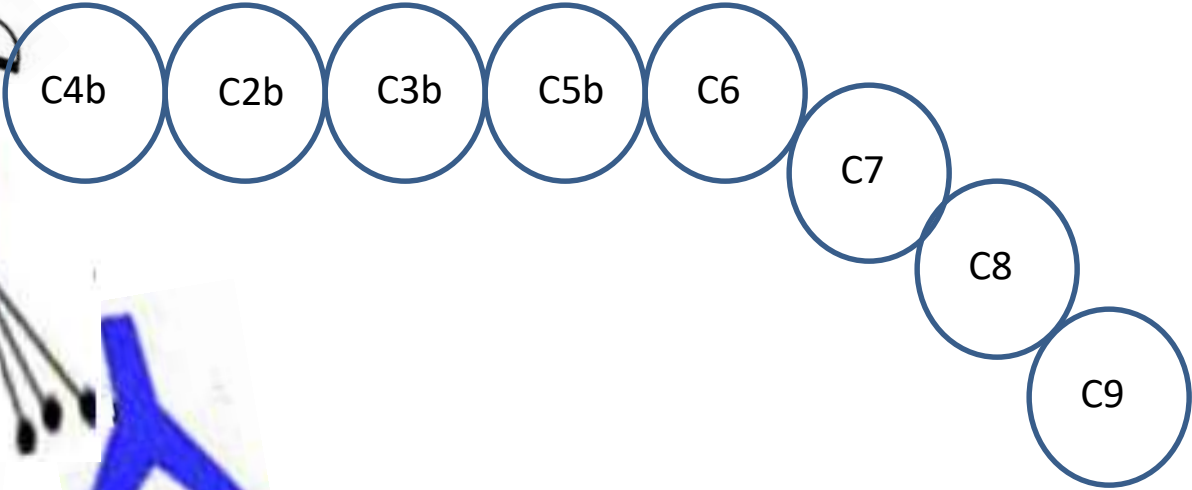
Diseases associated with complement system

Blood
Angioedema

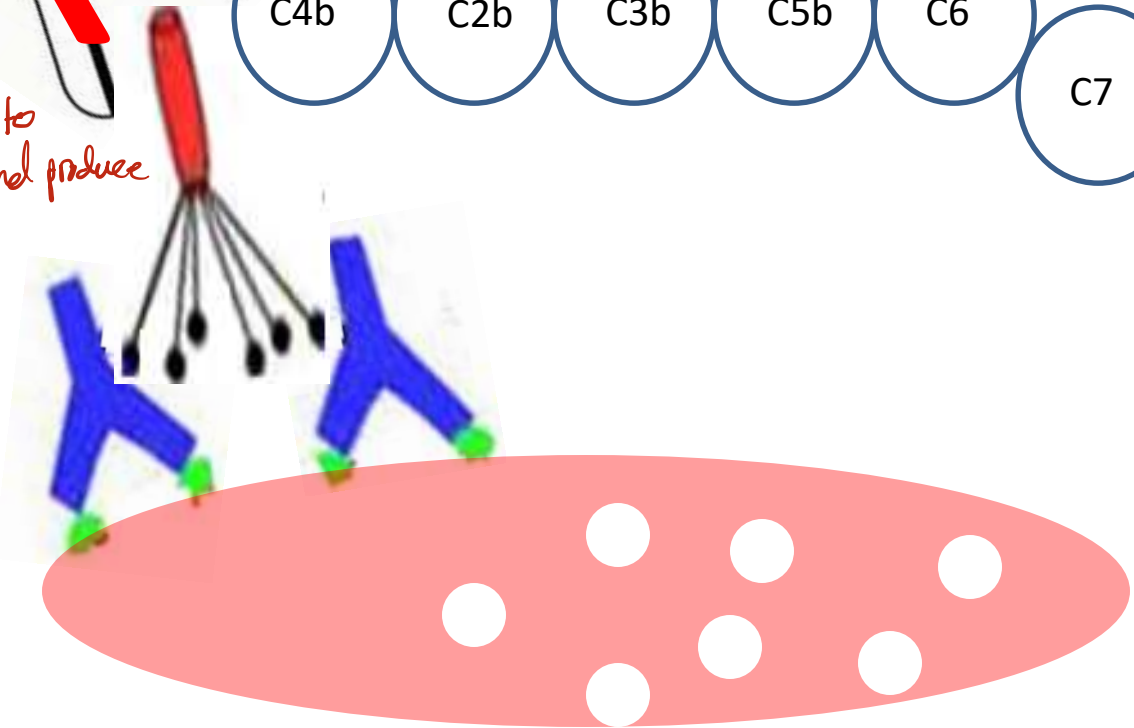
C1 esterase *cut C1*



Massive stimulation of mast cells and histamine releasing leading to generalized edema



*C1 Bind to Antibody and produce MAC



Diseases associated with complement system

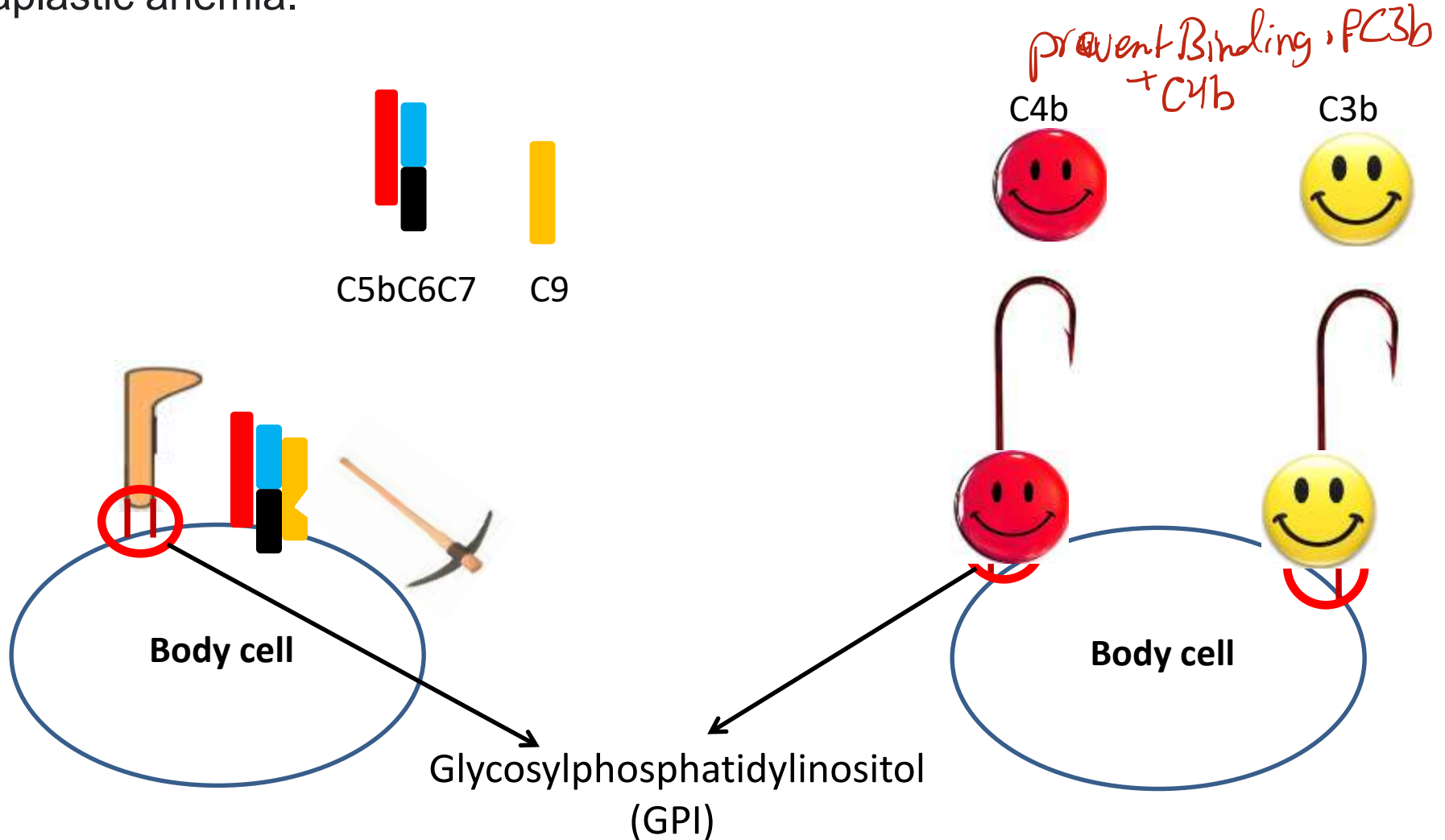
Angioedema *⇒ Thin skin*



Diseases associated with complement system

Paroxysmal Nocturnal Hemoglobinuria (PNH)

The disease is characterized by destruction of red blood cells, blood clots, and impaired bone marrow function. PNH is closely related to aplastic anemia.



* C3b \Rightarrow Opsonization

* C3a + C4a + C5a \Rightarrow act as anaphylatoxins

* C5b \Rightarrow Responsible of formation of MAC. + is a potent chemoattractant.

* CD59 \Rightarrow Inhibit Formating of MAC

* Decay Accelerating Factor (DAF) \Rightarrow primarily Inhibit the interaction between C4b + C3b.

* CD59 + DAF protect the body cells from complement system.

* C1 esterase deficient in heridity Angio edema, Mast cells resulting in edema.

* In PNH, the deficiency in (GPI) Glycophosphatidylinositol prevent binding of complement system to cell surface
 \hookrightarrow characterized by destruction of RBC's.

* Recruiting Inflammatory cells is the Main role of chemokines

* Berger disease \Rightarrow associated with the deposition of IgA + complement System. \boxtimes

* HSP disease \Rightarrow