

Namaste مرحبا **Willkommen** Bem Vindo Selamat Datang
Bienvenidos Namaste Bienvenue Croeso Welcome Bienvenidos أهلا وسهلا
Benvenuti Welkom Bienvenue **Welcome** **مرحبا** Croeso Namaste
Welkom Bienvenue **مرحبا** Welcome Welkom أهلا وسهلا
Bienvenidos **Bienvenue** **مرحبا** Croeso Namaste
Selamat Datang **Willkommen** **مرحبا** أهلا وسهلا Bem Vindo
Welcome **Bienvenue** **مرحبا** أهلا وسهلا Bem Vindo
Willkommen **Benvenuti** **مرحبا** Selamat Datang Croeso
доброе дошъл **Benvenuti** **مرحبا** Selamat Datang Croeso
καλώς ήλθατε **Benvenuti** **مرحبا** Selamat Datang Croeso

Let's start at the beginning





Jules Bordet

Jules Bordet **(1870-1961)**

**Belgian
microbiologist/
immunologist**

Nobel prize 1919

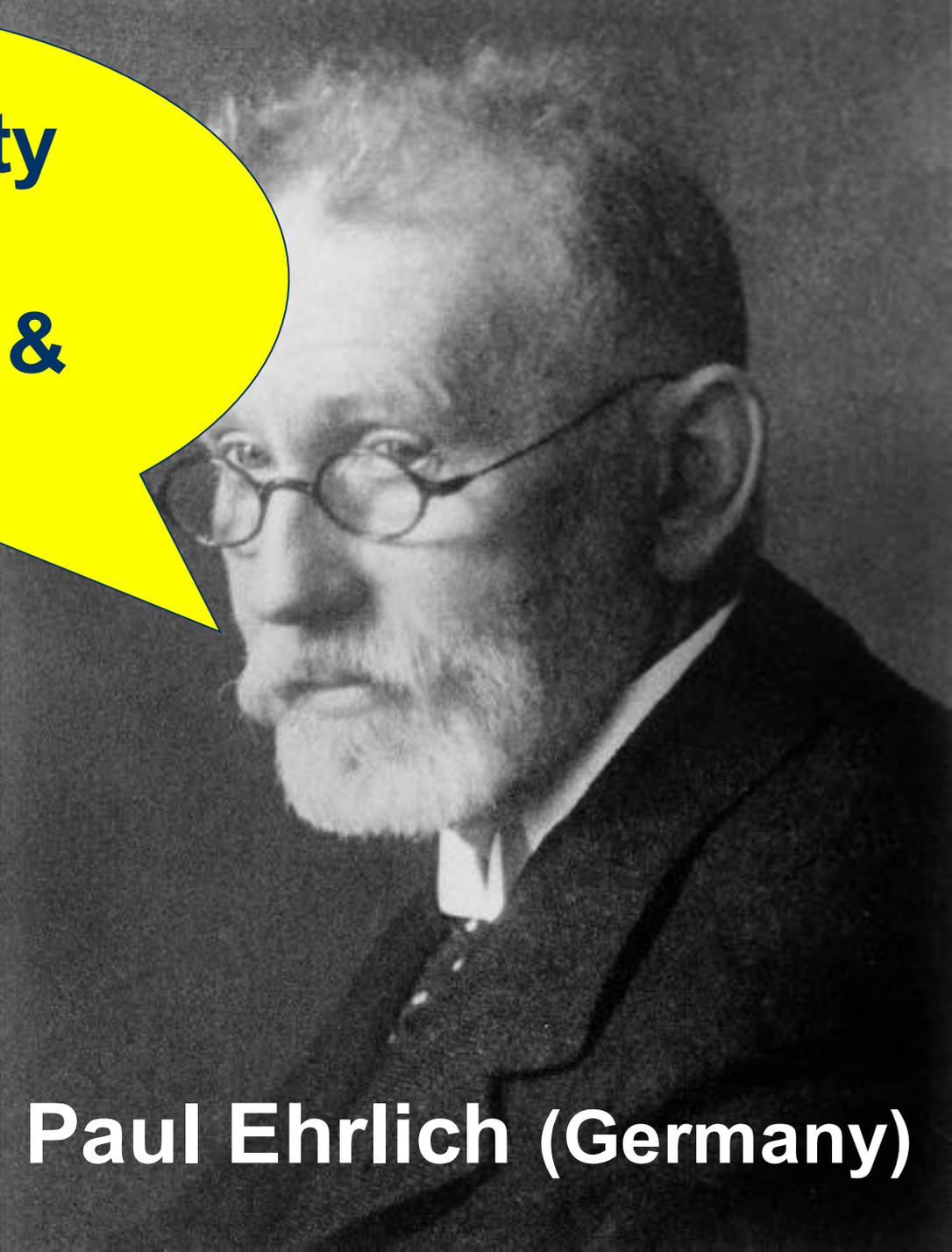
**“discoveries
relating to
immunity”**

Named Alexin: aids Abs to kill bacteria

1890s:

- ***While antibodies were heat stable, fresh serum contains a heat labile component that, when combined with Abs, killed bacteria***

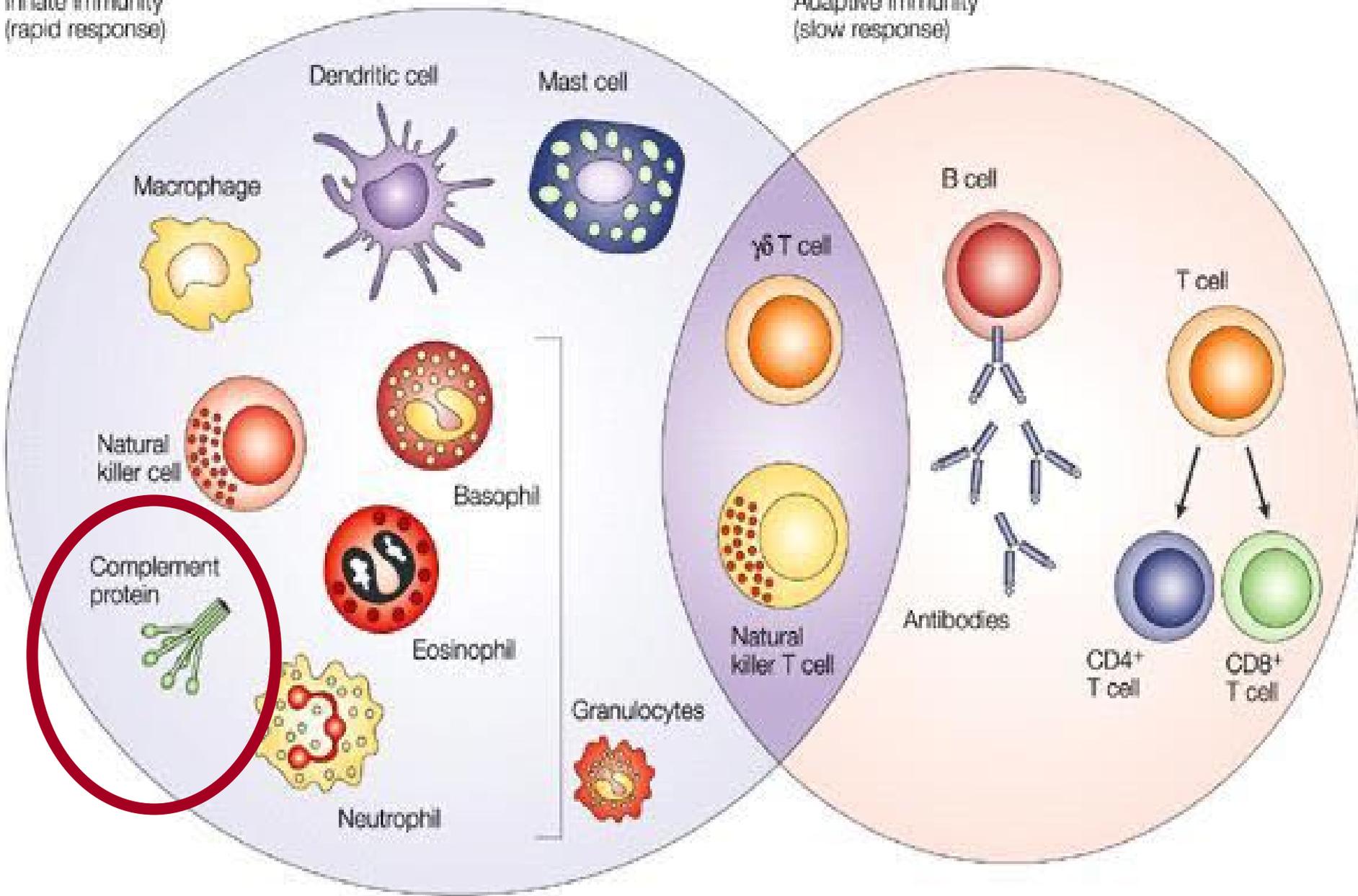
**Autoimmunity
would be
catastrophic &
CANNOT
OCCUR**

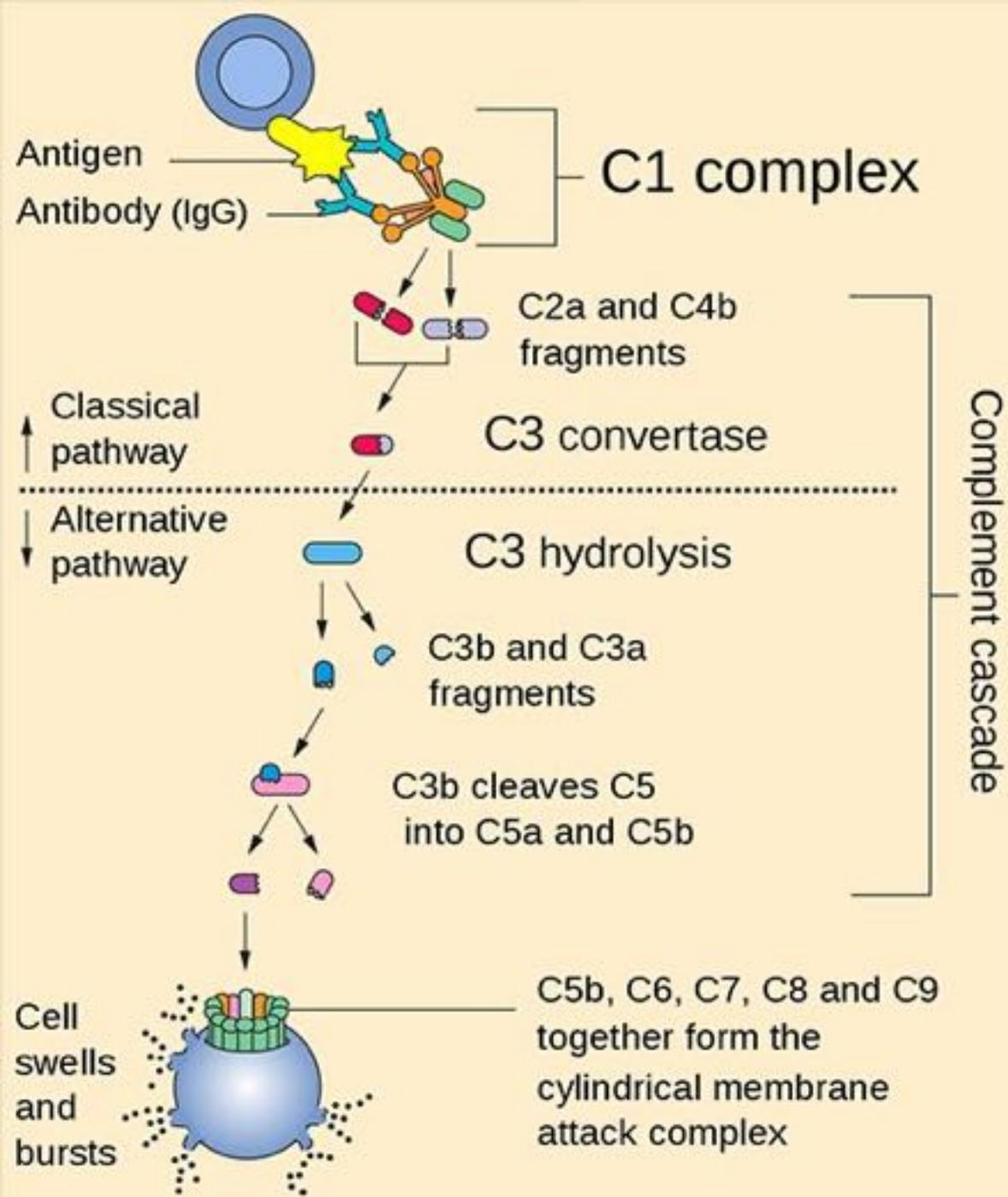
A black and white portrait of Paul Ehrlich, a German physician and immunologist. He is shown from the chest up, wearing a dark suit jacket, a white shirt, and a dark tie. He has a full white beard and mustache and is wearing round-rimmed glasses. He is looking slightly to the left of the camera.

Paul Ehrlich (Germany)

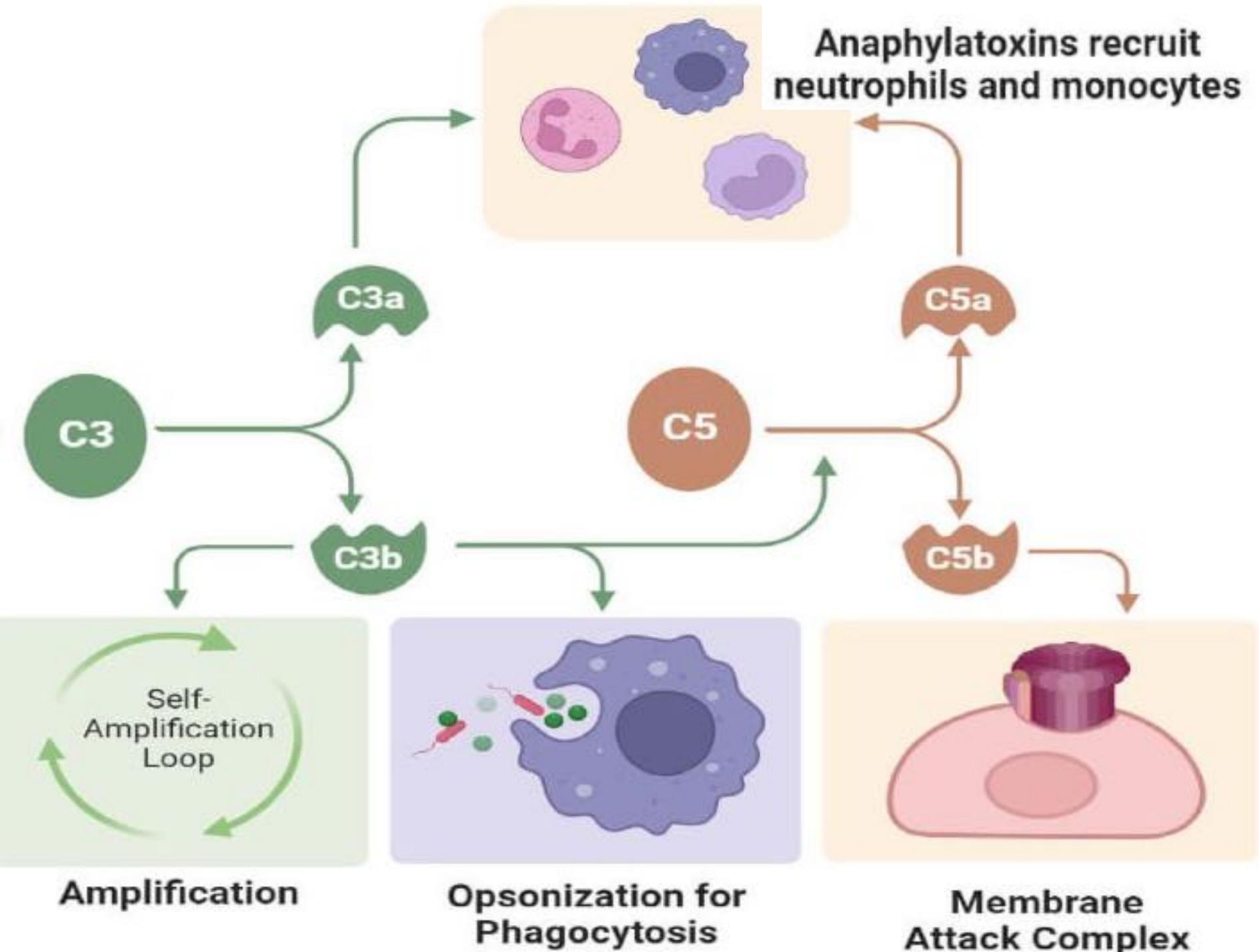
Innate immunity
(rapid response)

Adaptive immunity
(slow response)





First..





First

Then

Classical pathway	Lectin pathway	Alternative pathway	Extrinsic pathway
Ag-Ab complexes Apoptotic cells/DNA C reactive protein (CRP) β -amyloid	High-density arrays of mannose, fucose and N-acetylated sugars on cell surfaces	Unknown molecules on pathogen surfaces C3-tick over	Tissue factor

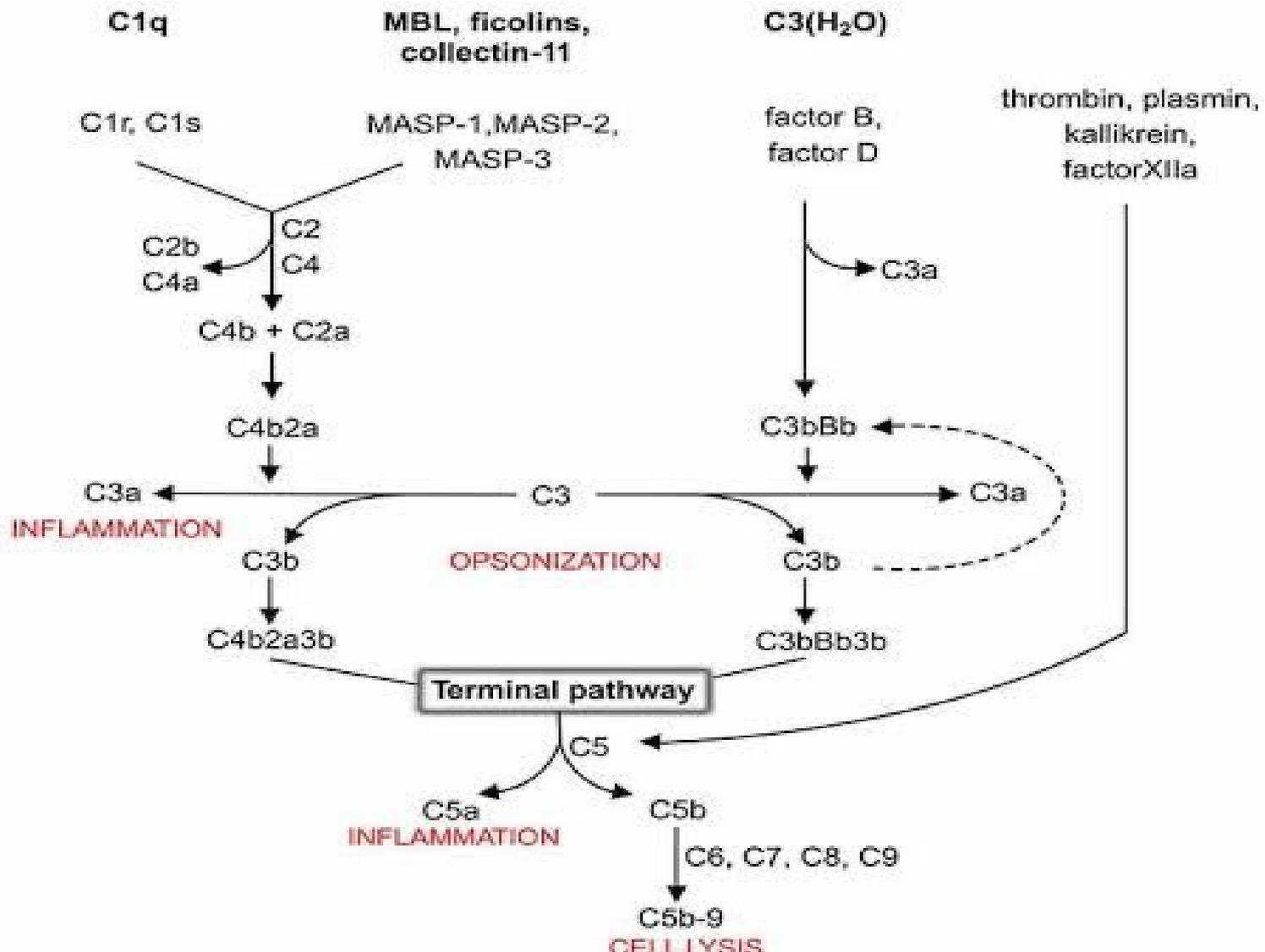
PAMPs and DAMPs

Initiator Molecules

Proteases

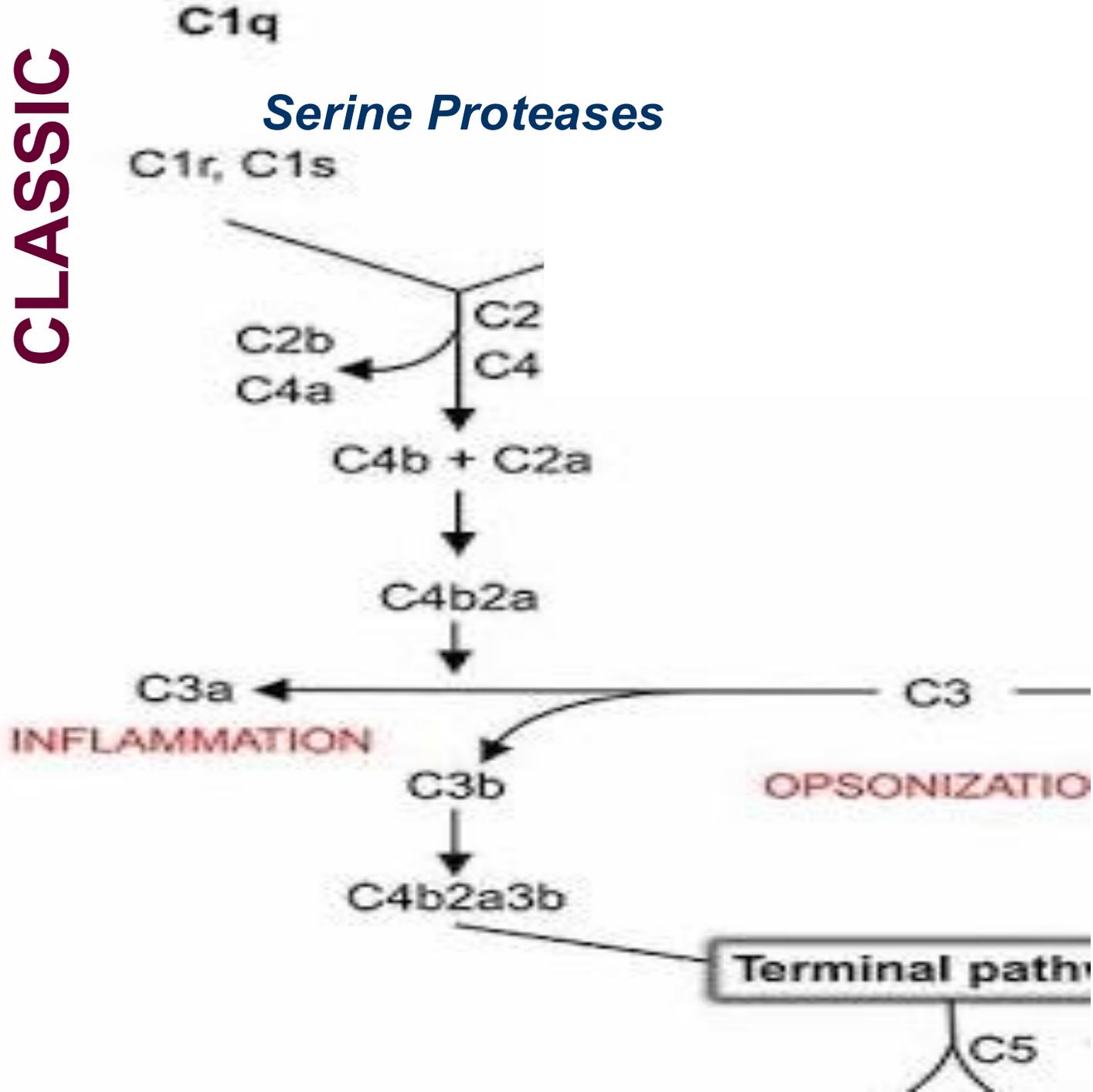
C3 convertase

C5 convertase



CLASSIC

Serine Proteases

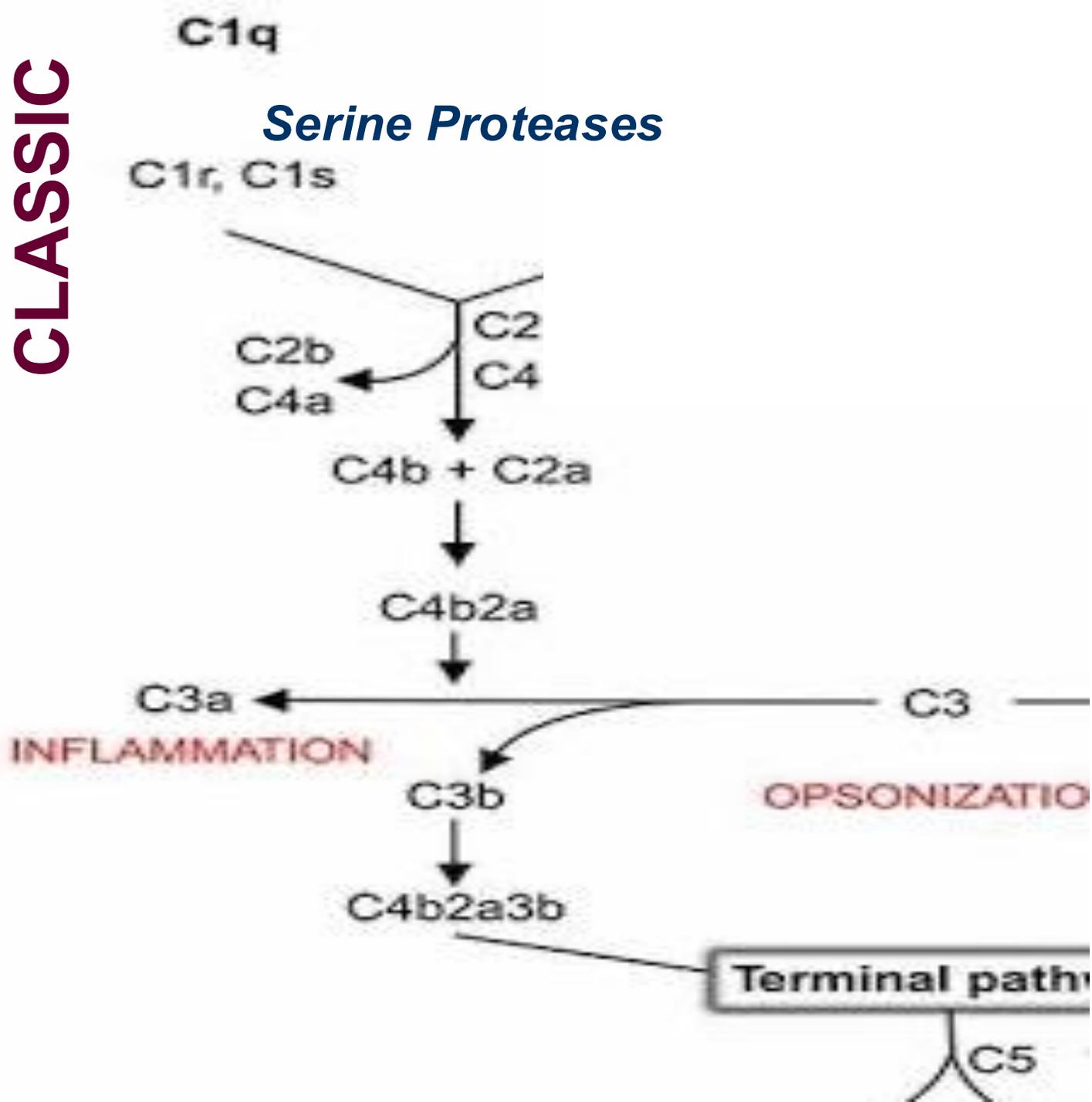


Classical pathway

- **Ag- Ab (IgG/IgM) complex**
- **Ab Fc binds C1q**
- **Activate C1r, C1s → C4 & C2
Cleavage → C3 convertase**
- **Enhances AB effectiveness**
 - **Lysis (MAC)**
 - **Infl. & Opsonin**

CLASSIC

Serine Proteases



Lectin pathway

- **Mannose-binding lectin binds microbial C/h (innate)**
- **Associated serine proteases
MASPs cleave C4, C2 → C3
convertase**

C4b2a3b

C3bBb3b

Terminal pathway

C5

C5a

INFLAMMATION

C5b

C6, C7, C8, C9

C5b-9

CELL LYSIS



ALTERNATIVE

Surveillance

Low-level activation

C3(H₂O)

EXTRINSIC
(Tissue factor)

factor B,
factor D

C3a

Cleavage FB by FD

C3bBb

C3a

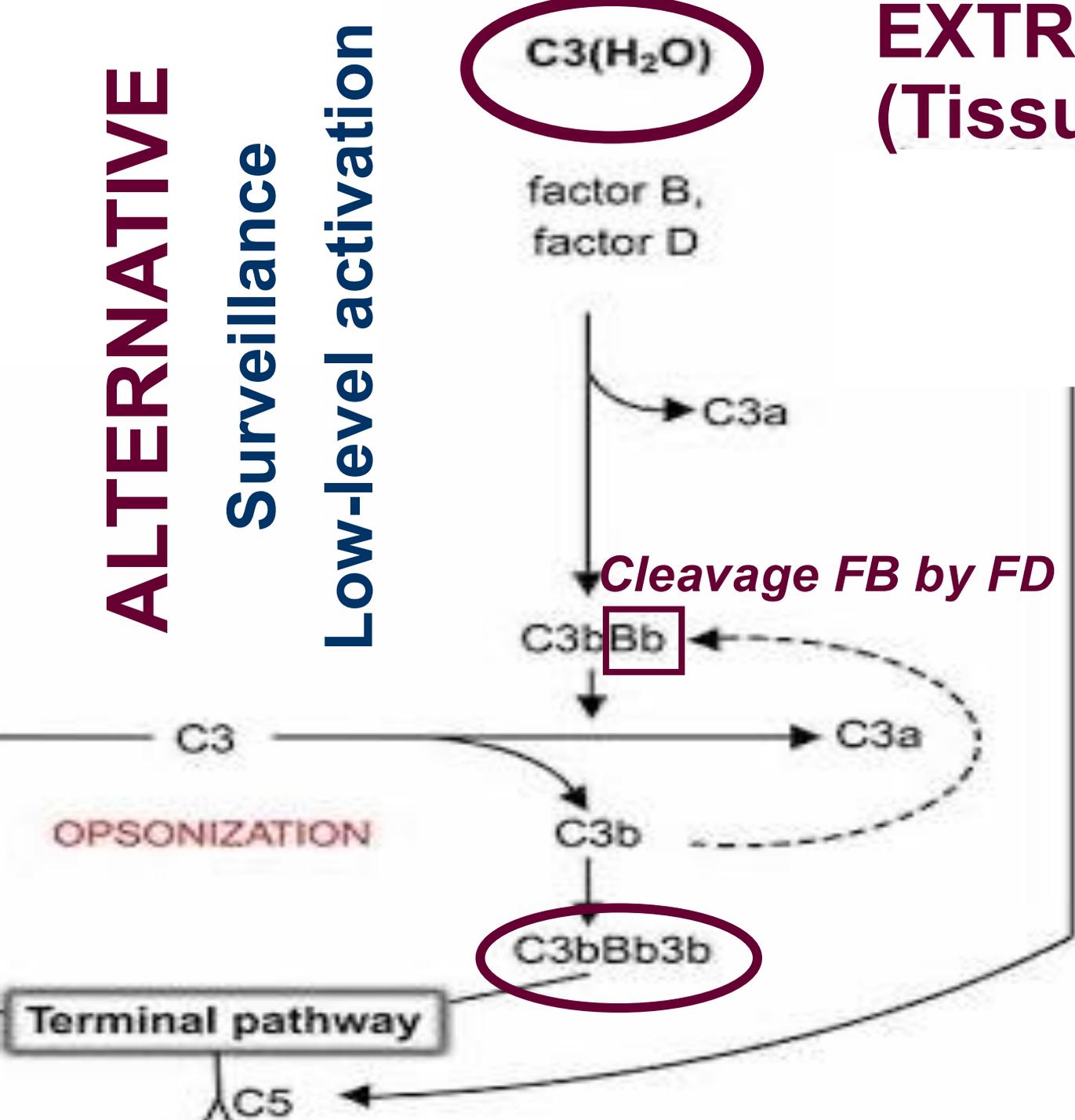
OPSONIZATION

C3b

C3bBb3b

Terminal pathway

C5



Alternative pathway

- **C3 hydrolysis on microbial surface (innate)**
- **Factor B, D, Properdin stabilize C3 convertase**
- **Innate amplification loop boosts C activation by any pathway**
- & including Ab bound pathogens (classic)**

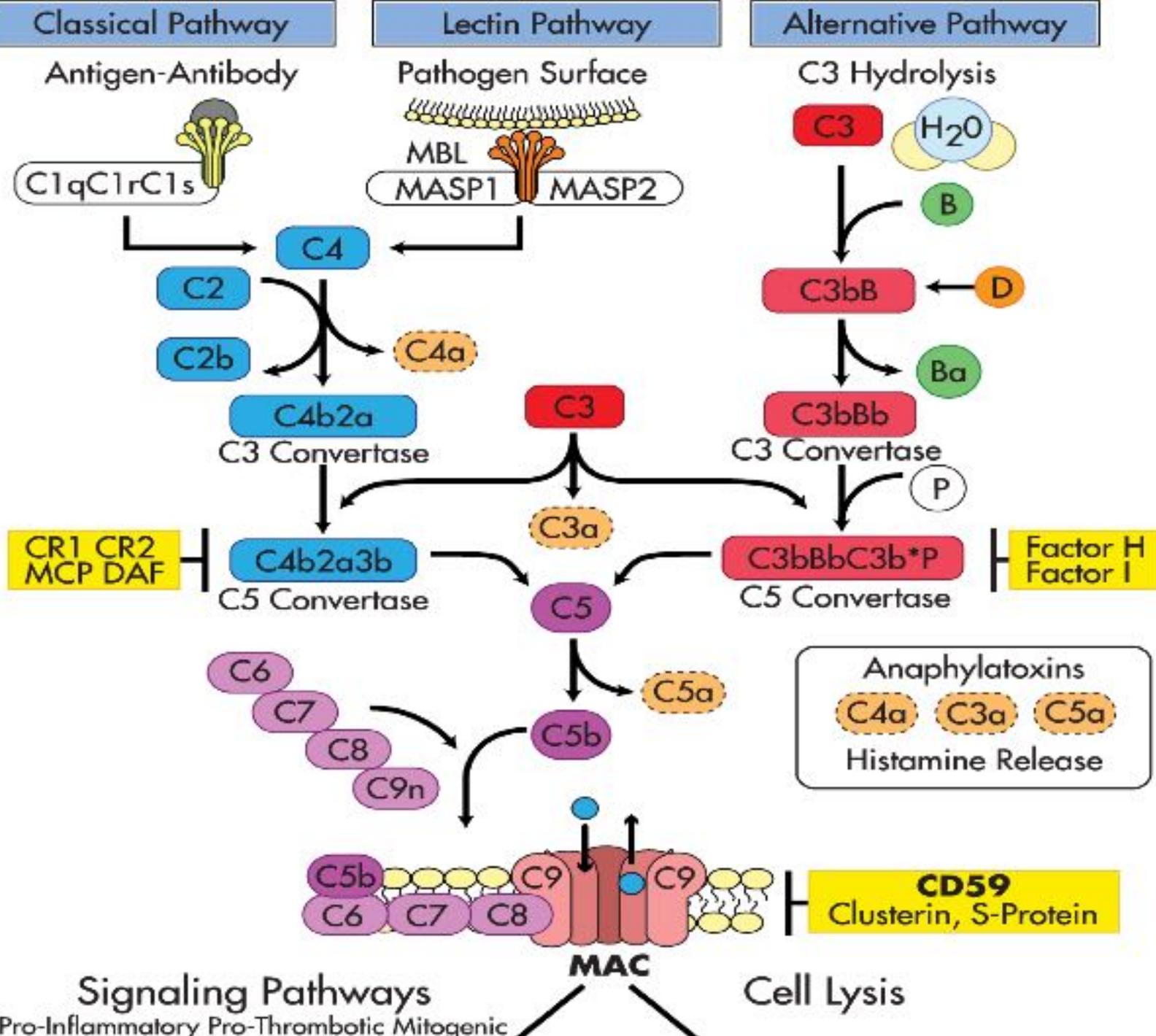
Classical → Pre—regulated

- **Specific Ag- Ab complex**

(May involve Non-immune ligands)

Non-classical →

- **Less specific initiators**
- **Only post-regulated**



1q32

Complement Regulatory Proteins

Factor H: C3b cleavage, Cofactor I

Factor I: C3b & C4b cleavage → Alt.

Reg.

C4b binding protein:

inactivates C4b2a

C1 inhibitor: C1r,s & MASPs

**Vitronectin (S protein) prevent MAC
insertion to membranes**

Complement Regulatory Proteins

MEMBRANE BOUND

- **CD59** (protectin) bind C8,9 preventing MAC assembly
- **CD55** Decay accelerating F (C3 & C5 convertases)
- **CD46 (MCP):** cofactor I (C3b, C4b)
- **CR1&2:** C3b, C4b



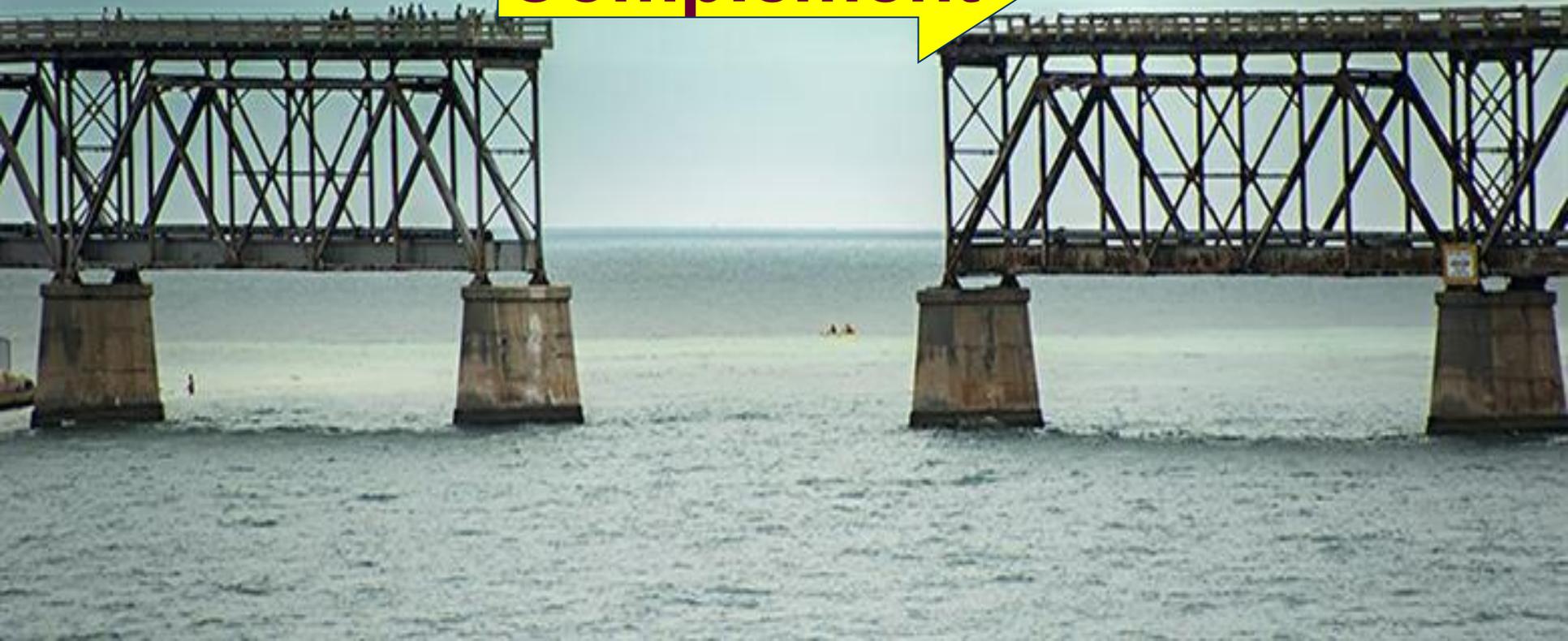
Abs

Adaptive immune response

Innate effector mechanisms

**Infl., chemotaxis,
Cell lysis**

Complement



**Ag
presentation**

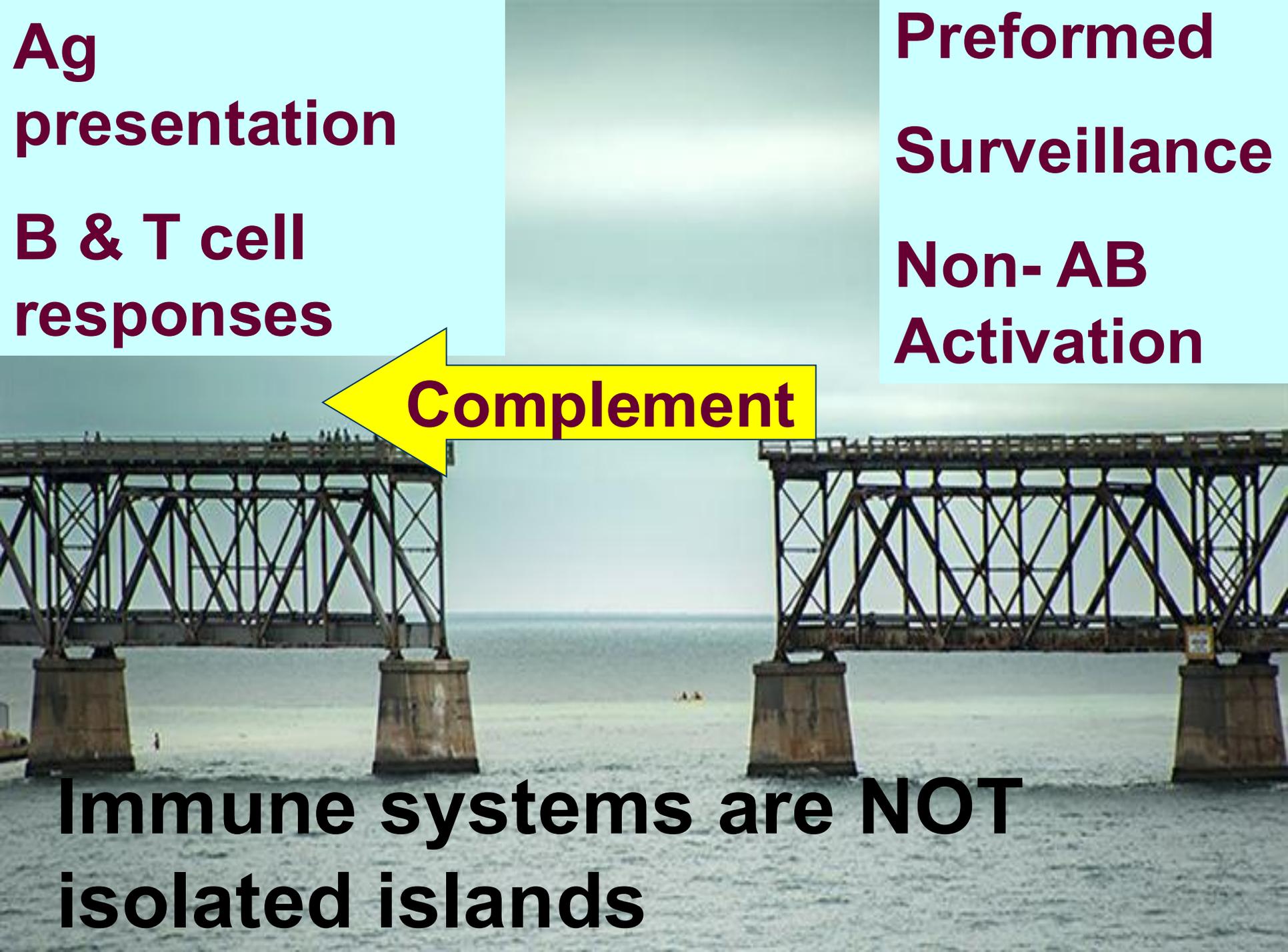
**B & T cell
responses**

**Preformed
Surveillance**

**Non- AB
Activation**

← Complement

**Immune systems are NOT
isolated islands**



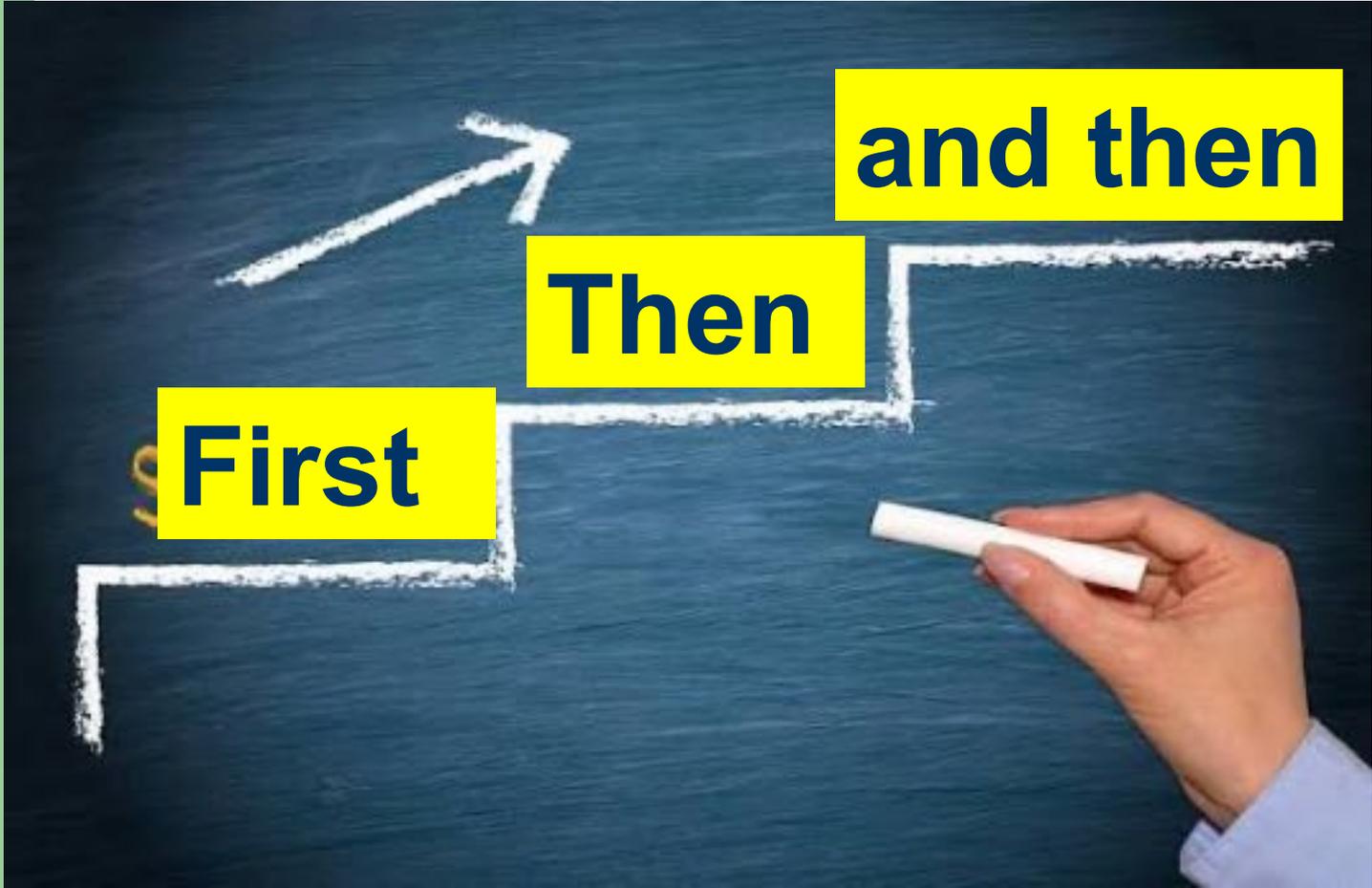
Complement supports adaptive immunity

Ag presentation	C3b, C3d tag antigens Tagged Ag bind CR1,2 on B cells & dendritic cells
B cell response (AB)	BCR binds Ag C3d binds B cell CR2 (CD21) ↓ activation threshold
T cell response	C3a, C5a recruit APCs & ↑ cytokine prod



Complement

Complement



First

Then

and then

Complement

**Surveillance: sensing pattern
recognition receptor PRR**

- **Opsonisation**
- **Chemotaxis & permeability**
- **Membrane attack**

Complement

- **AB trafficking & elimination (macrophages & podocytes)**
- **Coagulation**
- **Intracellular complexosome**
- **Immuno-metabolism & survival/ death balance**

Complement

- **Lysosomes, mTOR, mitochondria, transporters**
- **Self tolerance autophagy**
- **Synaptic pruning (modulation both dev & adult) & astrocyte interaction**

Conclusion

What started as a mechanism to support Ab effects in host protection

- **Widely distributed & intracellular**
- **Multiple pathways & regulators**
- **Wide array of functions**

Conclusion

What started as a mechanism to support Ab effects in host protection

- **Potential as a dse mechanism**
- **Therapeutic target**



Thank you