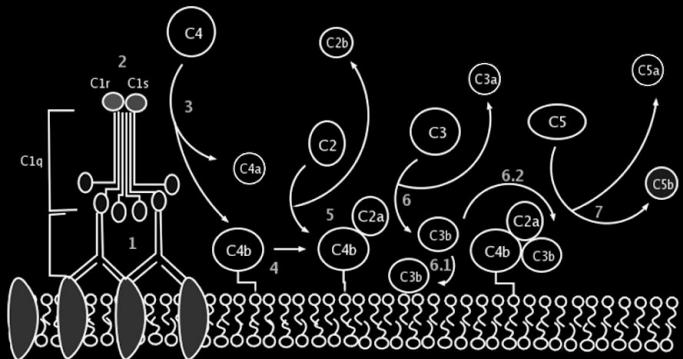


The **COMPLEMENT SYSTEM**

Immune



Rafael Nozal Cañadas

HDL Seminar 2020.11.16



PEDRITO: glóbulo blanco héroe de la policía del cuerpo humano.

METRO: líder de los cuerpos paracaidistas siempre contento con su trabajo.

KIRA: la simpática lugarteniente de Pedro, ágil descubridora de virus.



TIÑOSO: un microbio grande enemigo sádico del bueno de Gordito.



GORDITO: glóbulo blanco pionero siempre dispuesto a combatir los us y microbios comilabot y Tiñoso



NABOT: te presentamos a un virus y jefe de virus, individuo muy poco recomendable.

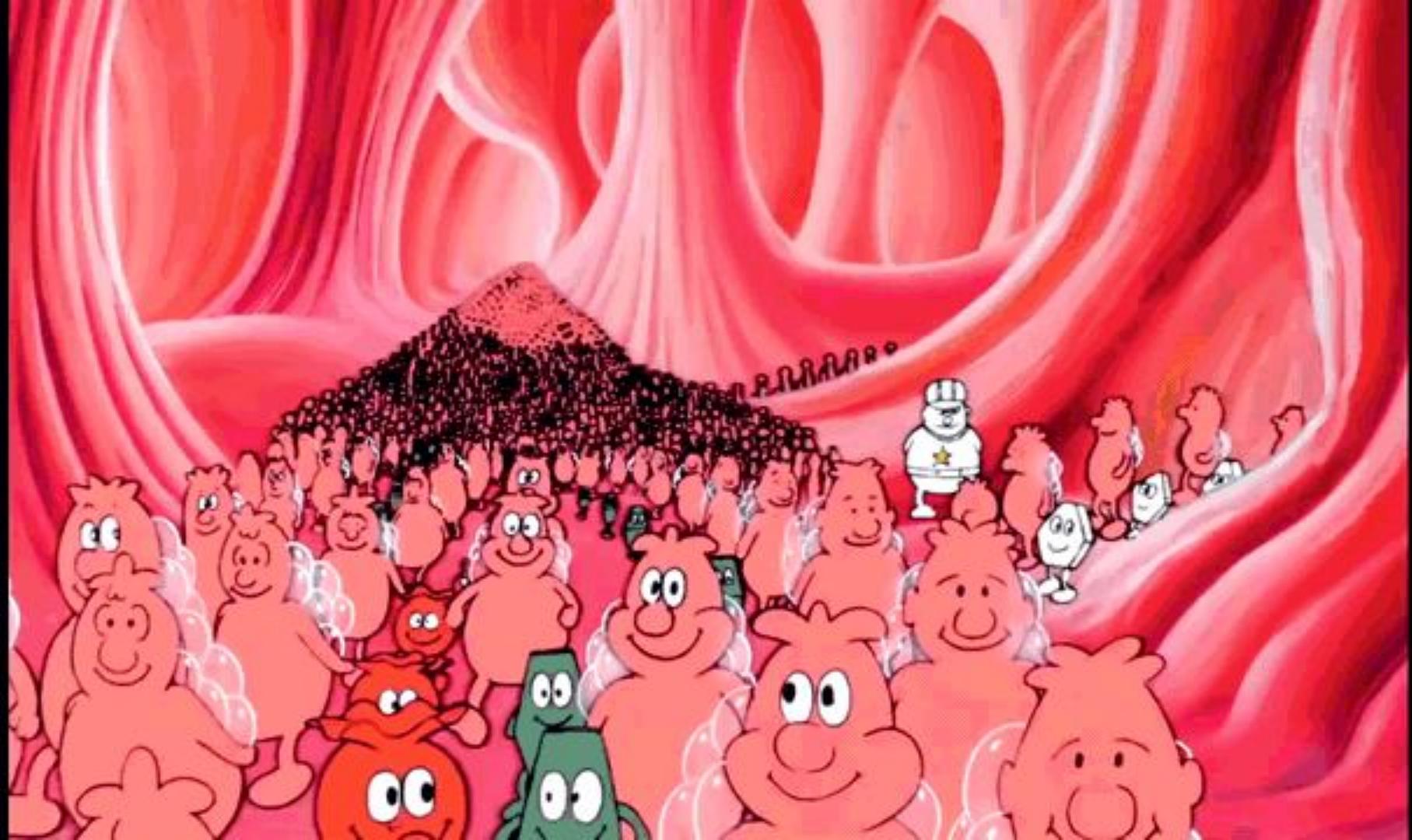


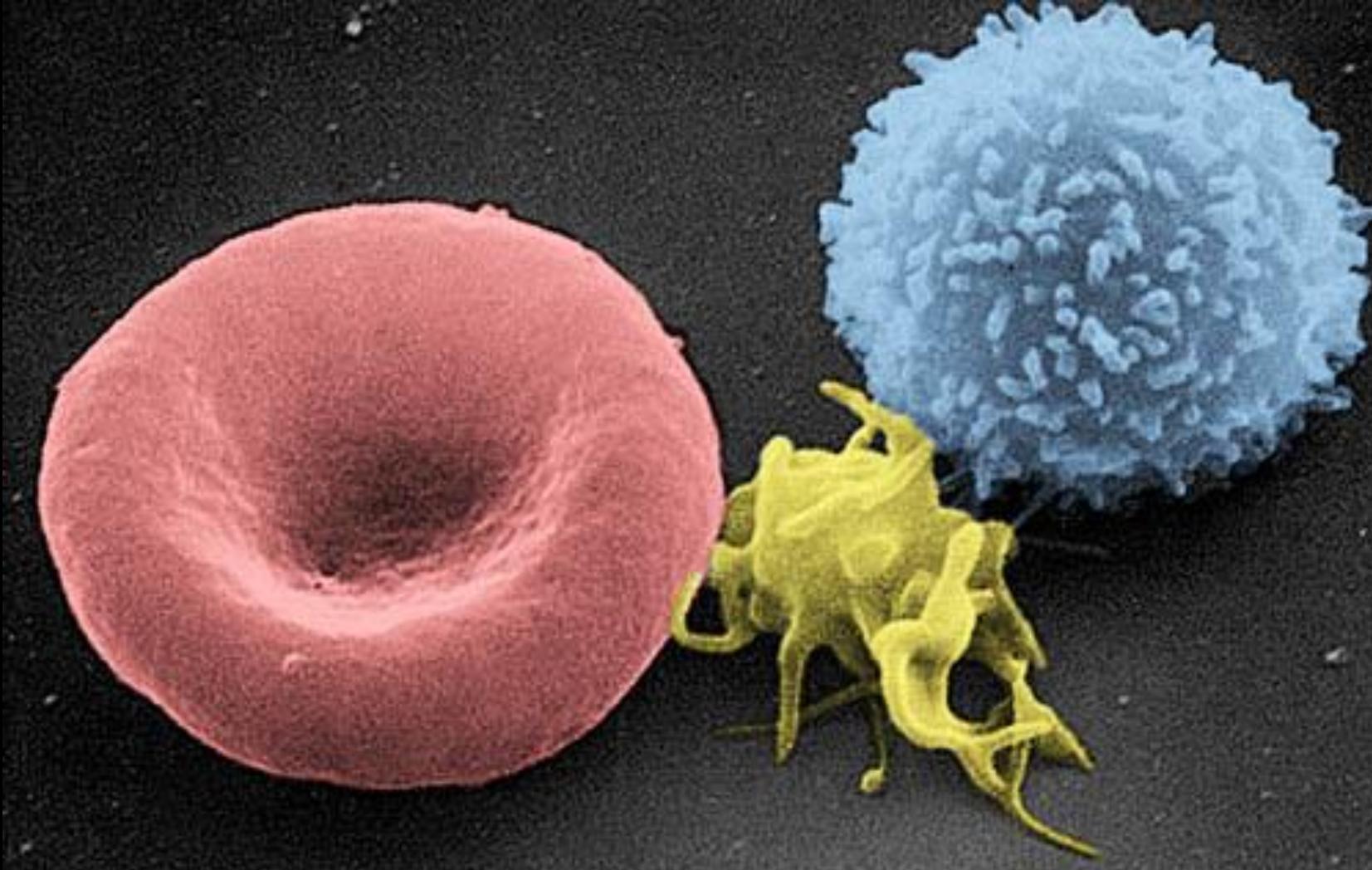
GLOBUS: viejo y sabio glóbulo rojo, mentor de los jóvenes Hemo y Globina, a los que enseña los misterios del cuerpo humano.

HEMO: glóbulo rojo siempre cargado de oxígeno. Tierno y bonachón, se dice que abusan de él.

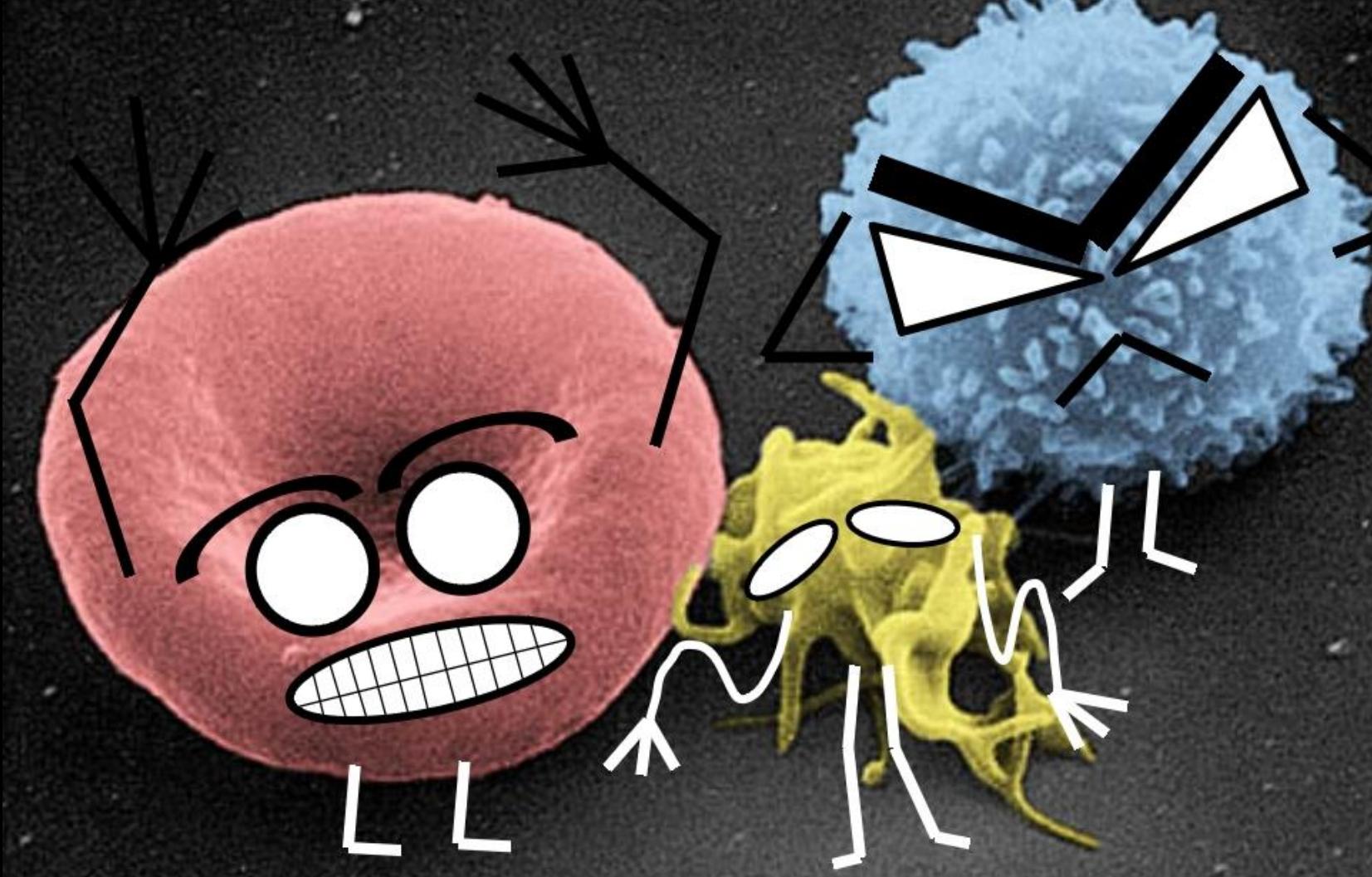
GLOBINA: la pequeña Globina amiga de Globus, lista como un centella.

MAESTRO: sabio y más de de cícula que imaginar, dispuesto a enseñanzas y





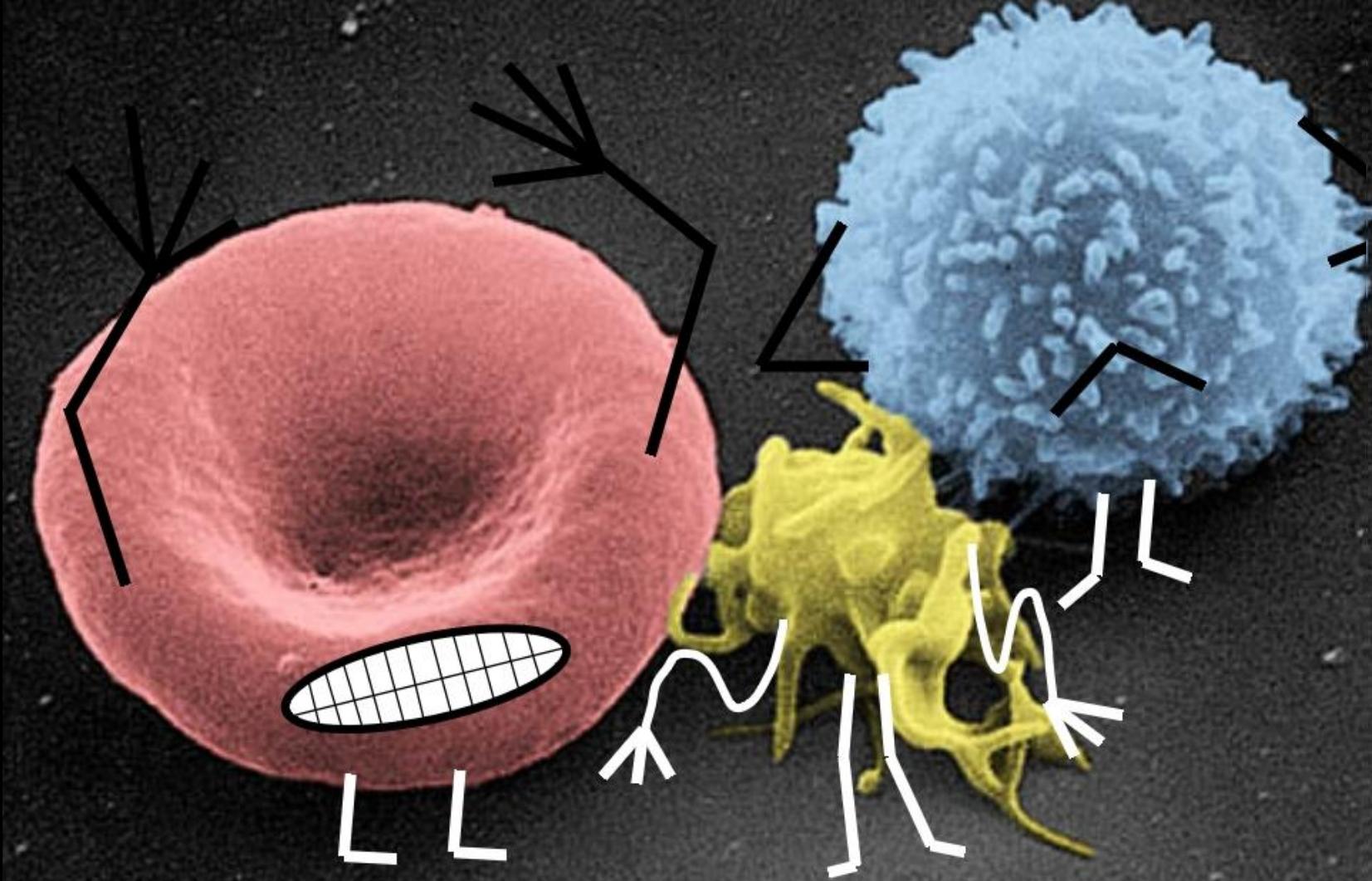
Test 0: Fully human





Test 0: Fully human

Test 1: Same vision range



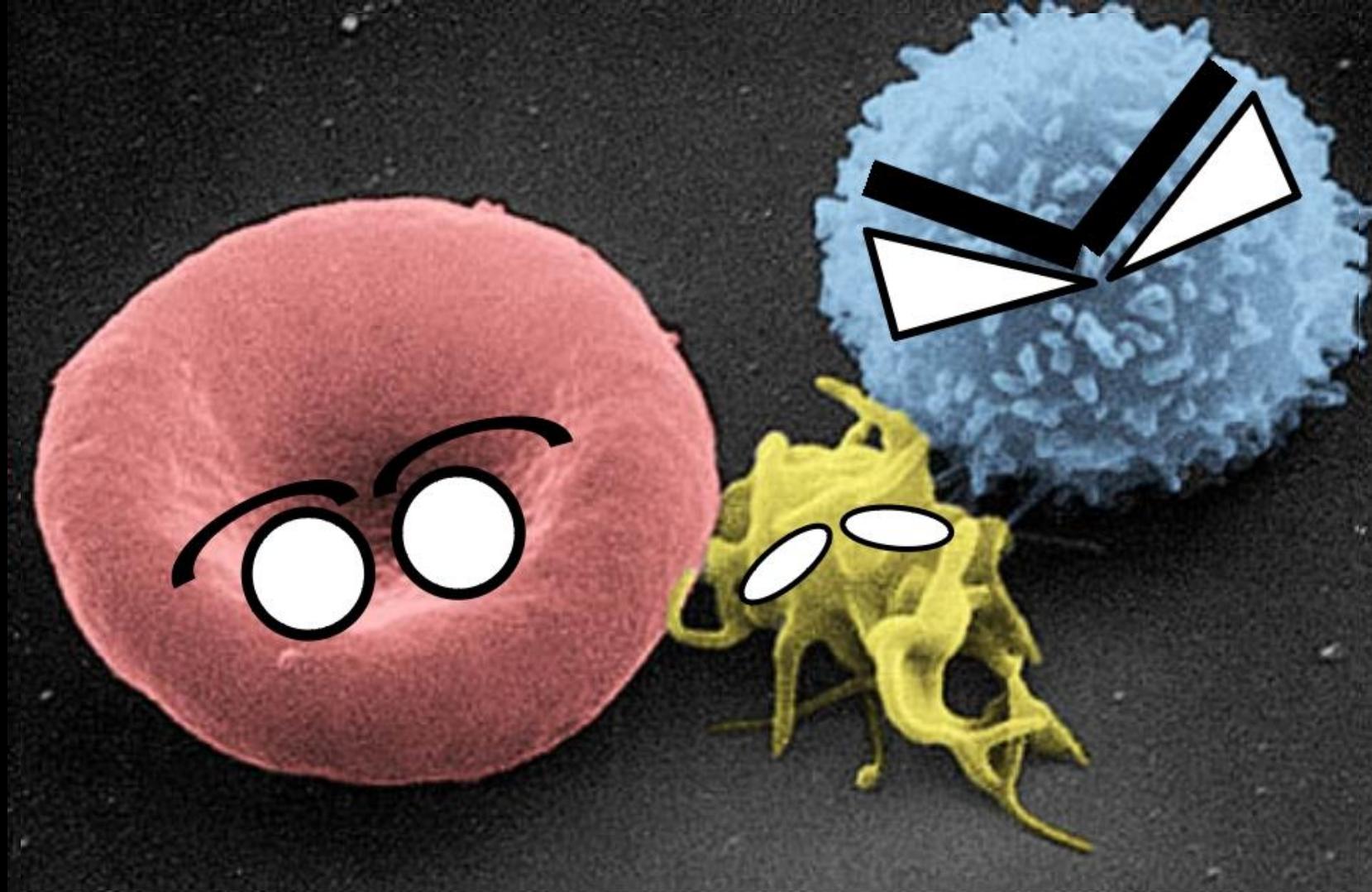


Test 0: Fully human



Test 1: Same vision range

Test 2: Same dexterity

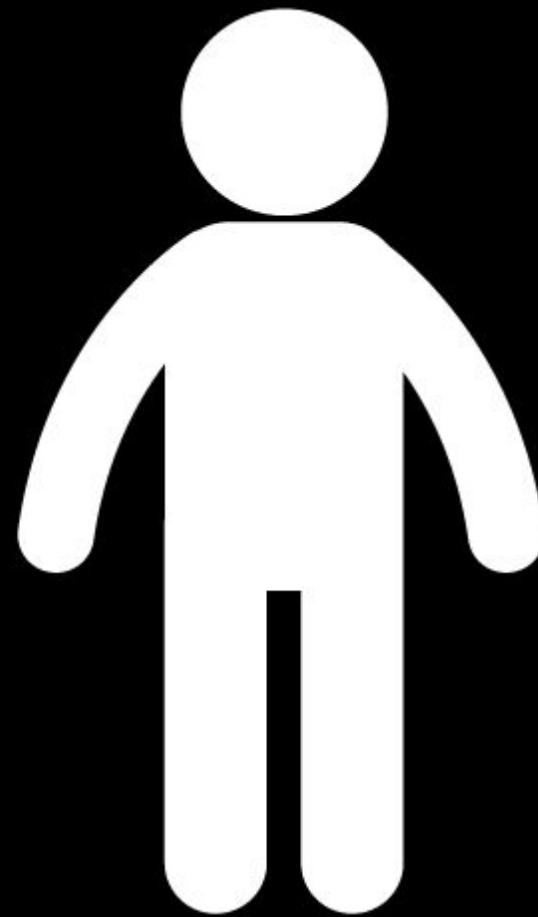
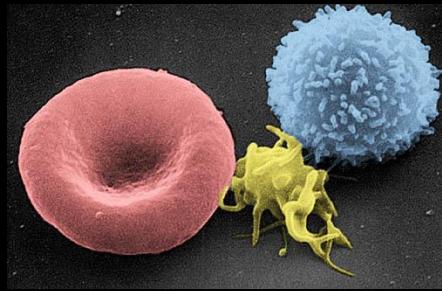


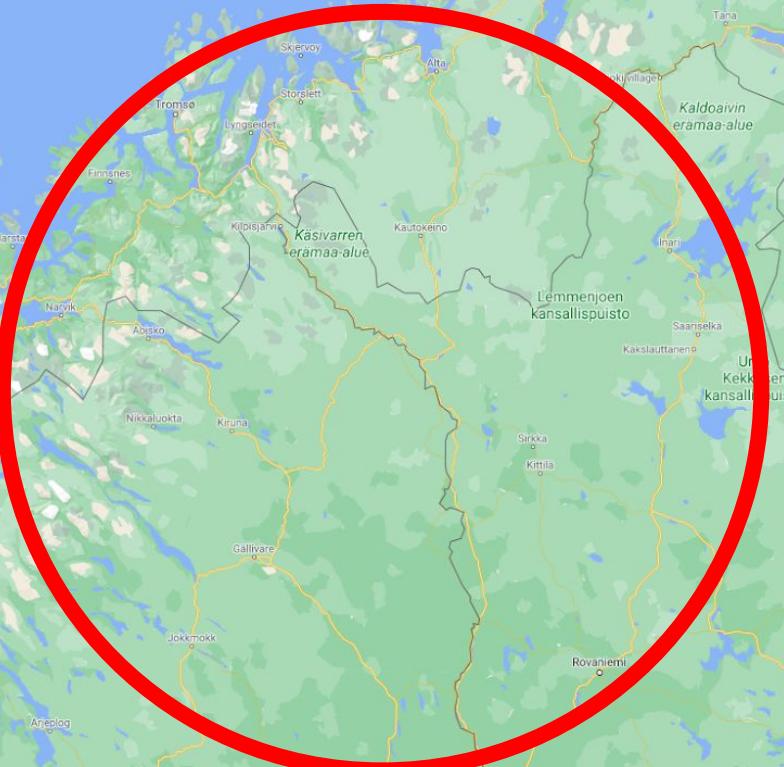
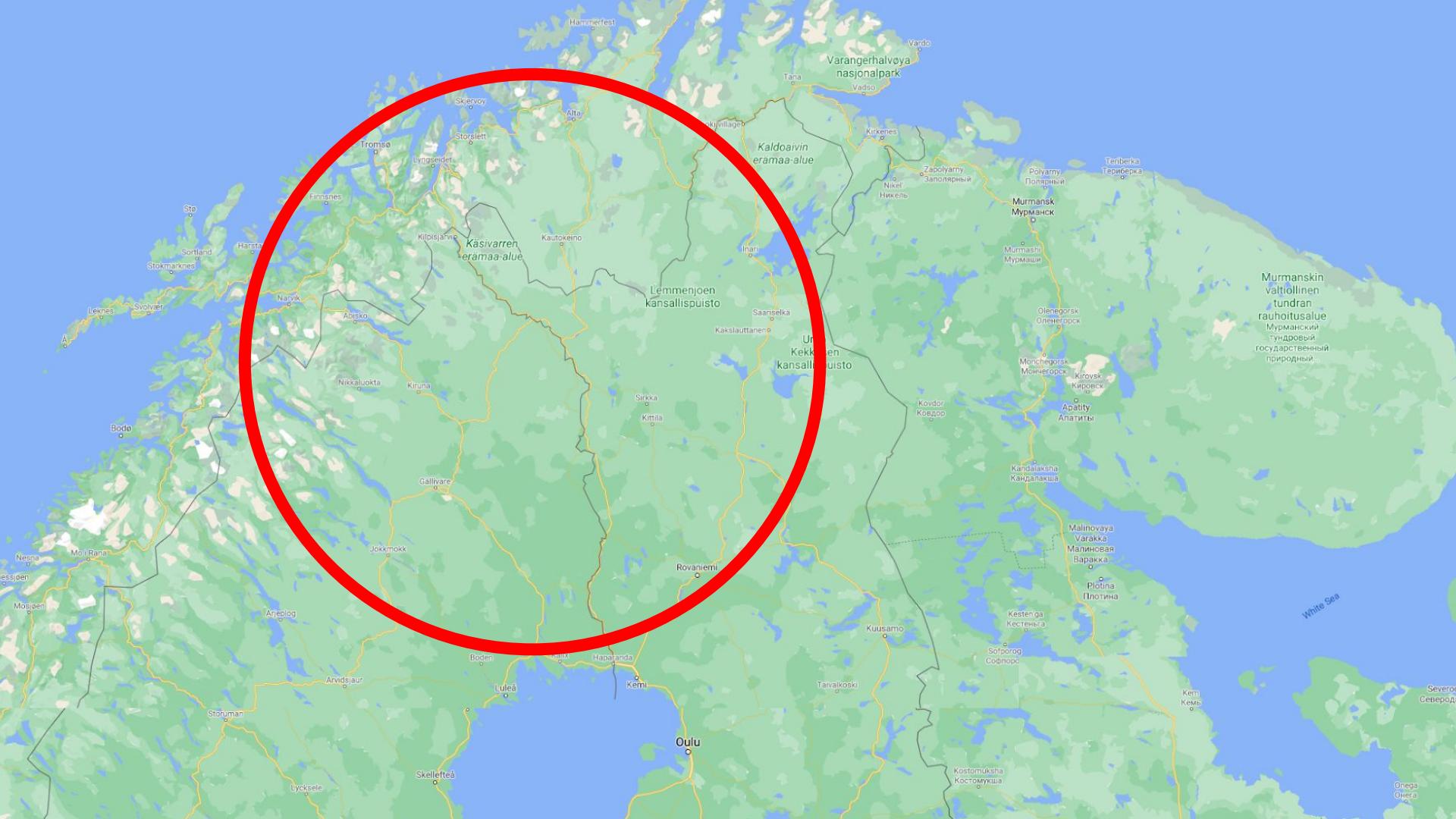
✓ Test 0: Fully human

✓ Test 1: Same vision range

✗ Test 2: Same dexterity

Test 3: Same range





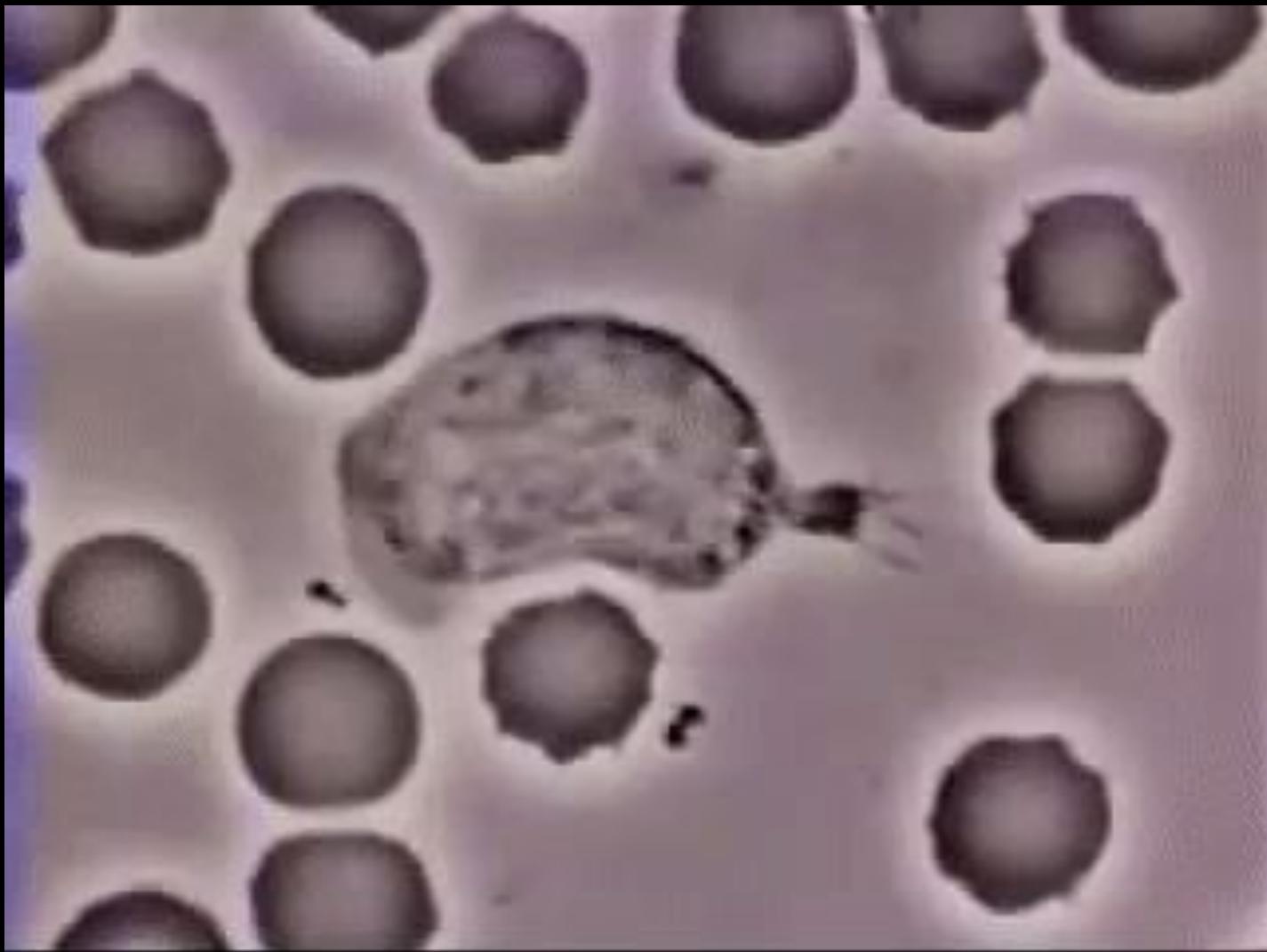
✓ Test 0: Fully human

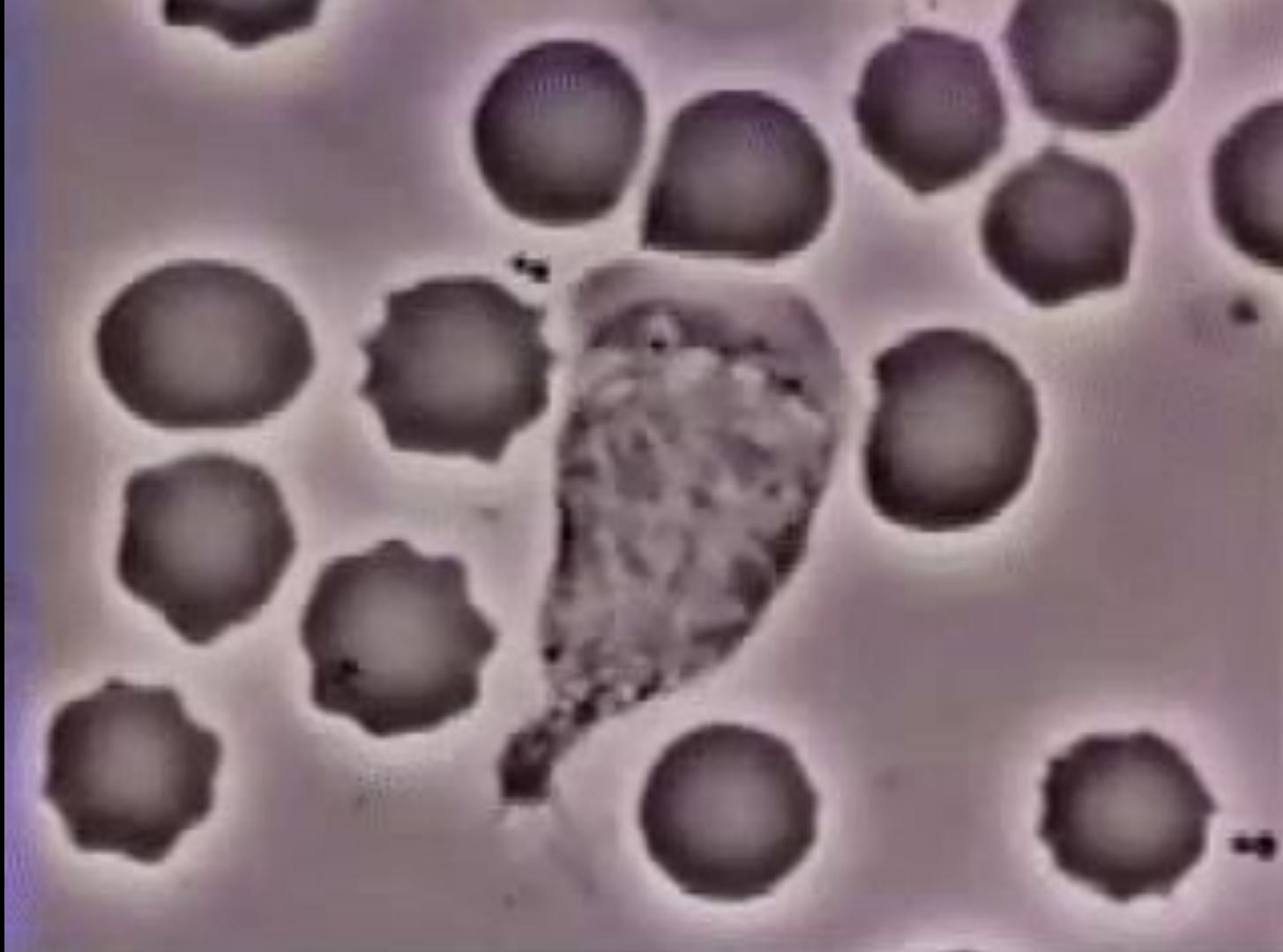
✓ Test 1: Same vision range

✗ Test 2: Same dexterity

✗ Test 3: Same range

How does a, **brainless**,
unicellular organism performs in
comparison with _____ ?





...FIND?

...SEE?

How do they...

...GRAB?

...KILL?

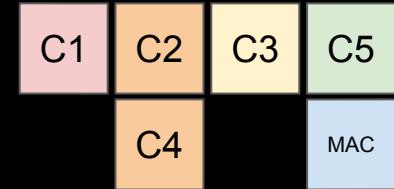
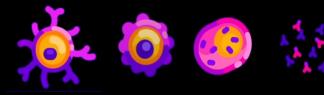
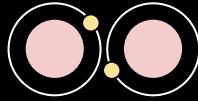
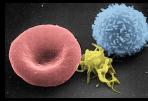
SEMINAR

Intro

Summary

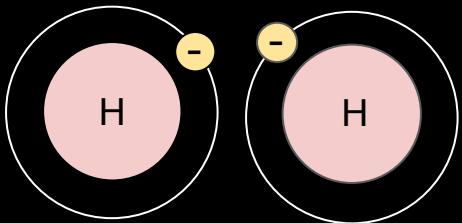
Pre-initiation

Complement System

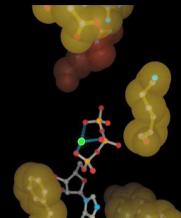


You are here!

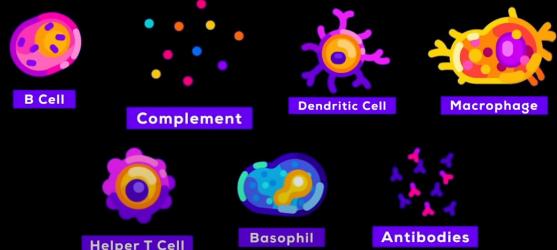
SUMMARY



Chemical bonds



Confirmational
changes



Immunity Simplified

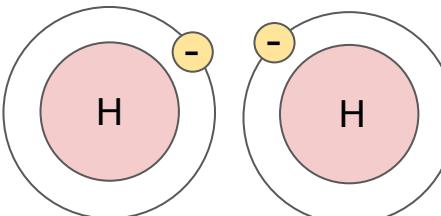
What is a covalent bond?

Non-metal Bond

Covalent

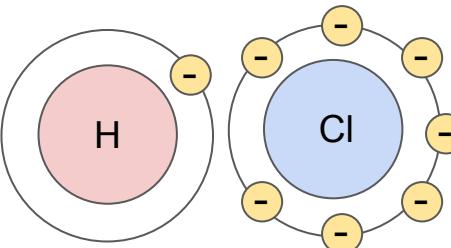
Non polar:

Δ Electronegativity < 0.5
Sharing electrons



Polar:

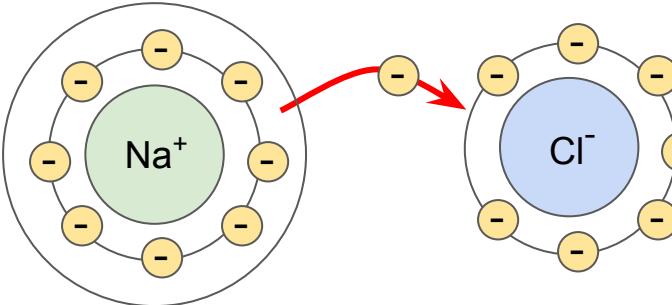
Δ Electronegativity > 0.5
Hoarding electrons



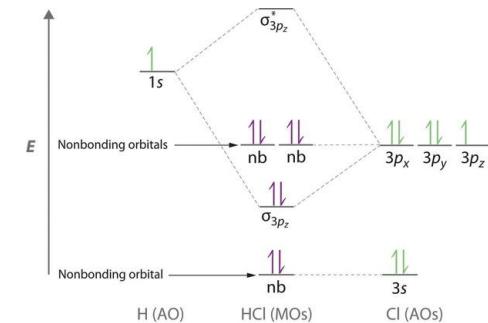
Ionic

Covalent:

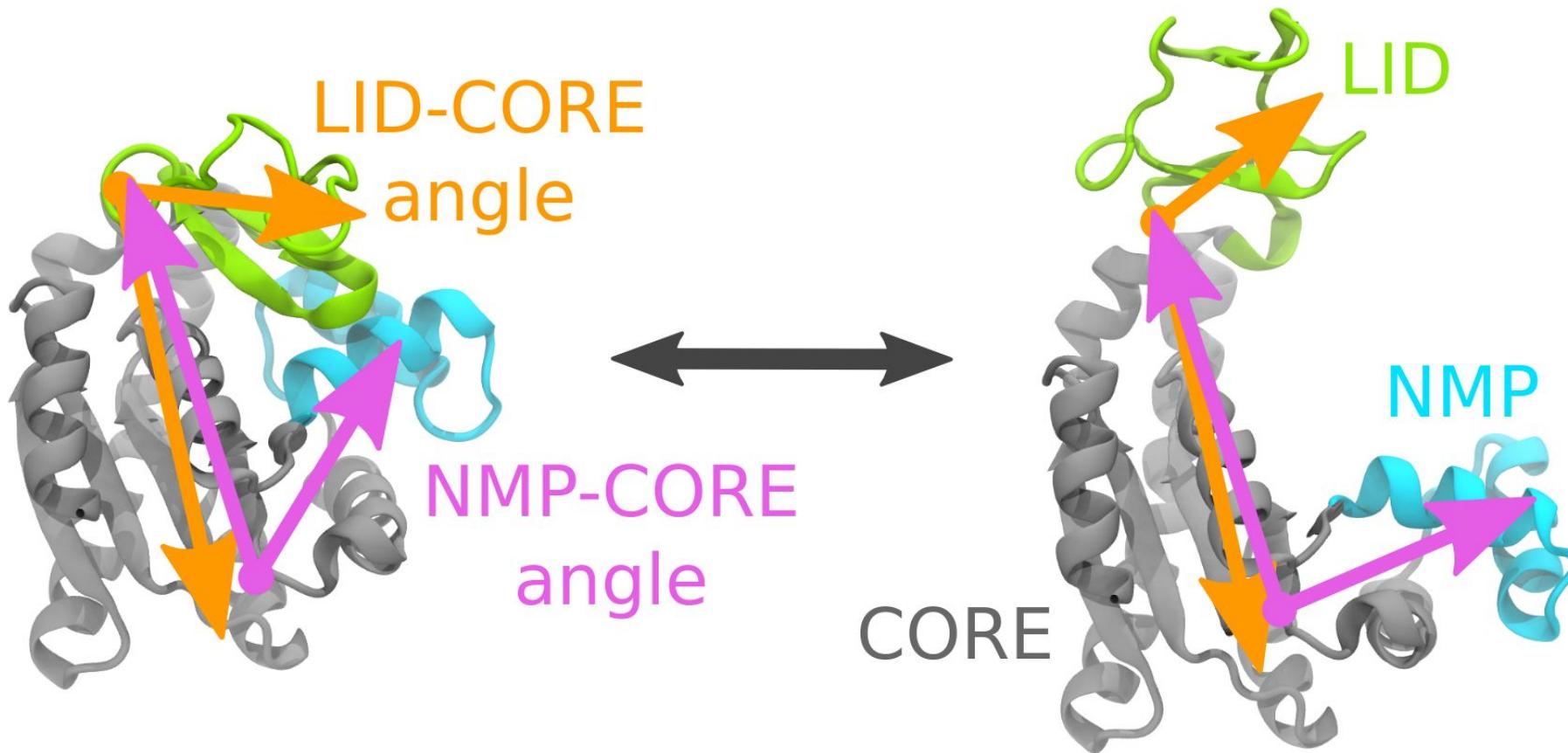
Δ Electronegativity > 2.0
Steal electrons

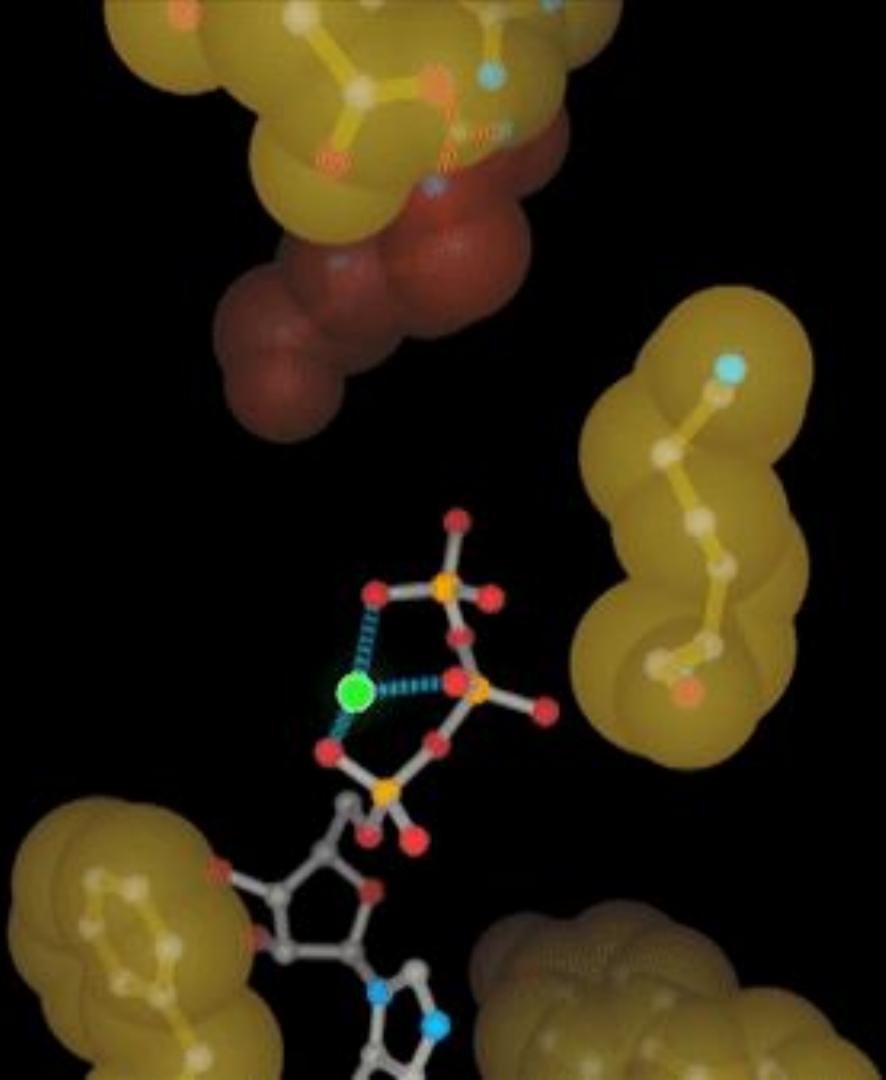


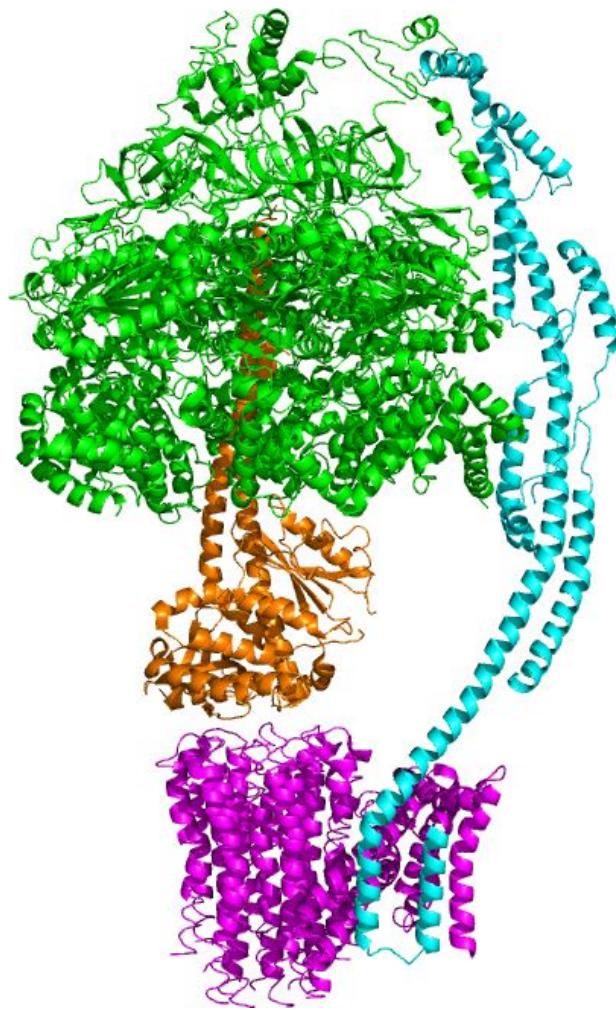
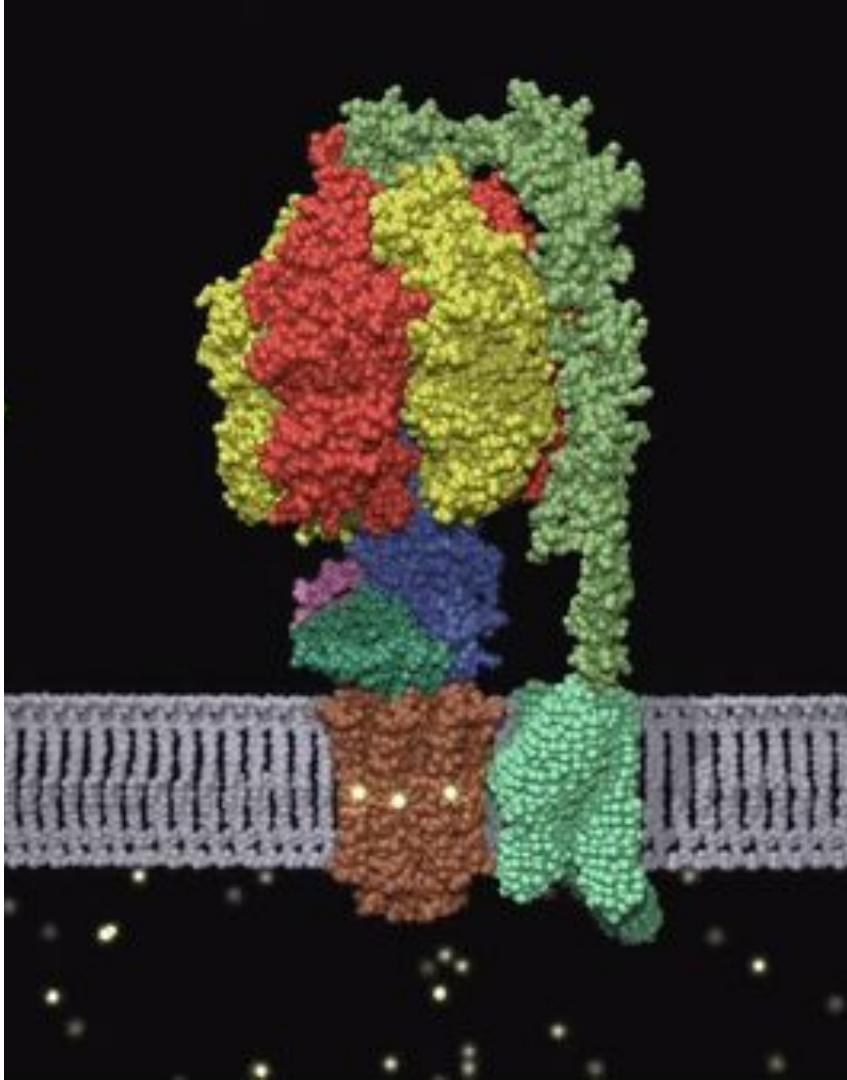
$$\vec{F} = q_a \left(\frac{k_e q_b}{\vec{r}^2} \right) + q_a \vec{v} \times \vec{B}$$

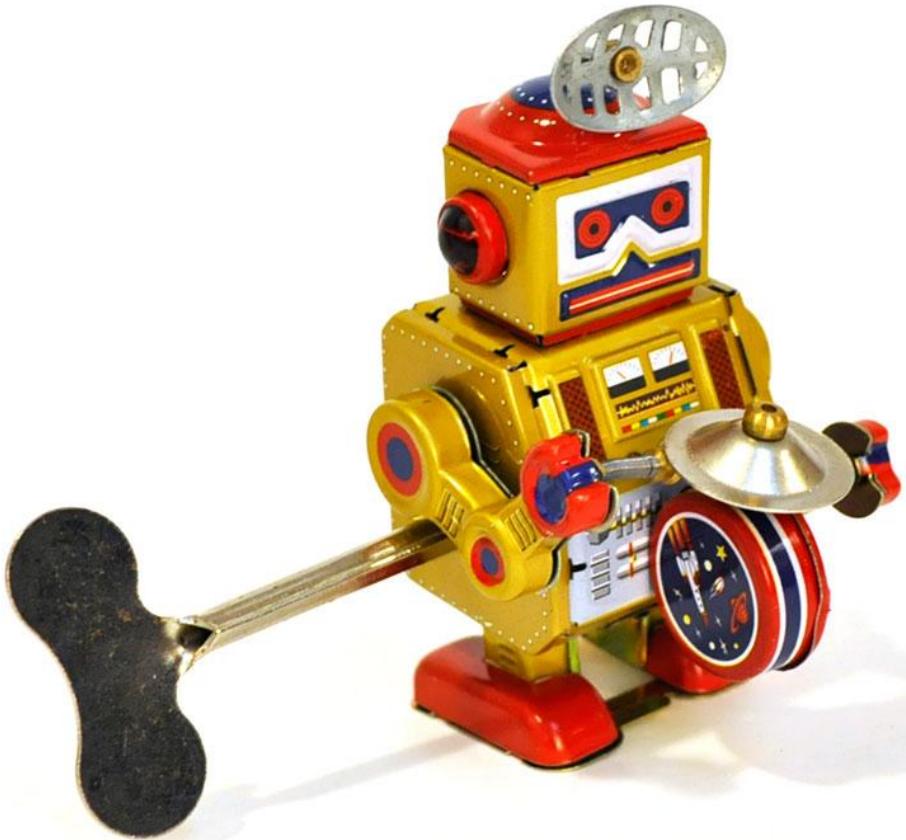


What is confirmational changes?









What is the immune system?

• V • T • E		Cell signaling / Signal transduction	
Signaling pathways		• GPCR • Wnt • RTK • TGF beta • MAPK/ERK) • Notch • JAK-STAT • Akt/PKB • Fas apoptosis • Hippo • PI3K/AKT/mTOR pathway • Integrin receptors	
Agents	Receptor ligands	• Hormones • Neurotransmitters/Neuropeptides/Neurohormones • Cytokines • Growth factors • Signaling molecules	
	Receptors	• Cell surface • Intracellular • Co-receptor	
	Second messenger	• cAMP-dependent pathway • Ca ²⁺ signaling • Lipid signaling	
	Assistants:	• Signal transducing adaptor protein • Scaffold protein	
	Transcription factors	• General • Transcription preinitiation complex • TFIID • TFIIFH	
By distance		• Juxtacrine • Autocrine / Paracrine • Endocrine	
Other concepts		• Intracrine action • Neurocrine signaling • Synaptic transmission • Chemical synapse) • Neuroendocrine signaling • Exocrine signalling • Pheromones) • Mechanotransduction • Phototransduction • Ion channel gating • Gap junction	

• V • T • E		Immunology: lymphocytic adaptive immune system and complement	
Lymphoid	Antigens	• Antigen • Superantigen • Allergen) • Hapten • Epitope • Linear • Conformational) • Mimotope • Antigen presentation/Professional APCs: Dendritic cell • Macrophage • B cell • Immunogen	
	Antibodies	• Antibody • Monoclonal antibodies • Polyclonal antibodies • Autoantibody • Microantibody) • Polyclonal B cell response • Allotype • Isotype • Idiotype • Immune complex • Paratope	
	Immunity vs. tolerance	• action: Immunity • Autoimmunity • Alloimmunity • Allergy • Hypersensitivity • Inflammation • Cross-reactivity • inaction: Tolerance • Central • Peripheral • Clonal anergy • Clonal deletion • Tolerance in pregnancy) • Immunodeficiency	
	Immunogenetics	• Affinity maturation • Somatic hypermutation • Clonal selection) • V(D)J recombination • Junctional diversity • Immunoglobulin class switching • MHC/HLA	
Lymphocytes		• Cellular • T cell) • Humoral • B cell) • NK cell	
Substances		• Cytokines • Opsonin • Cytolysin	

• V • T • E		Cell signaling: cytokines	
By family	Chemokine	CCL	• CCL1 • CCL2/MCP1 • CCL3/MIP1 α • CCL4/MIP1 β • CCL5/RANTES • CCL6 • CCL7 • CCL8 • CCL9 • CCL11 • CCL12 • CCL13 • CCL14 • CCL15 • CCL16 • CCL17 • CCL18/PARC/DCCK1/AMAC1/MIP4 • CCL19 • CCL20 • CCL21 • CCL22 • CCL23 • CCL24 • CCL25 • CCL26 • CCL27 • CCL28
		CXCL	• CXCL1/KC • CXCL2 • CXCL3 • CXCL4 • CXCL5 • CXCL6 • CXCL7 • CXCL8/IL8 • CXCL9 • CXCL10 • CXCL11 • CXCL12 • CXCL13 • CXCL14 • CXCL15 • CXCL16 • CXCL17
		CX3CL	• CX3CL1
		XCL	• XCL1 • XCL2
		TNF	• TNFA • Lymphotoxin • TNFB/LTA • TNFC/LTB) • TNFSF4 • TNFSF5/CD40LG • TNFSF6 • TNFSF7 • TNFSF8 • TNFSF9 • TNFSF10 • TNFSF11 • TNFSF13 • TNFSF13B • EDA
	Interleukin	Type I (grouped by receptor subunit)	γ chain • IL2/IL15 • IL4/IL13 • IL7 • IL9 • IL21
			β chain • IL3 • IL5 • GMCSF
			IL6 like/gp130 • IL6 • IL11 • IL27 • IL30 • IL31 • +non IL OSM • LIF • CNTF • CTF1)
			IL12 family/IL12RB1 • IL12 • IL23 • IL27 • IL35
		Type II	Other • IL14 • IL16 • IL32 • IL34
			IL10 family • IL10/IL22 • IL19 • IL20 • IL24 • IL26 • Interferon type III • IL28/IFNL2+3 • IL29/IFNL1)
			Interferon I • IFNA1 • IFNA2 • IFNA4 • IFNA5 • IFNA6 • IFNA7 • IFNA8 • IFNA10 • IFNA13 • IFNA14 • IFNA16 • IFNA17 • IFNA21 • IFNB1 II • IFNK • IFNW1
	Ig superfamily		• IL1 family: IL1A/IL1F1 • IL1B/IL1F2 • 1Ra/IL1F3 • IL1F5 • IL1F6 • IL1F7 • IL1F8 • IL1F9 • IL1F10 • 33/IL1F11 • 18/IL1G
	IL17 family		• IL17/IL25 (IL17A)
	Other		• Hematopoietic • KITLG • Colony-stimulating factor) • SPP1 • MIF
By function/ cell		proinflammatory cytokine • IL1 • TNFA) Monokine • Lymphokine • Th1 • IFNγ • TNFβ) • Th2 • IL4 • IL5 • IL6 • IL10 • IL13))	

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• V • T • E		Cell signaling: cytokines																		
By function/ cell		Chemokine • CCL1 • CCL2/MCP1 • CCL3/MIP1 α • CCL4/MIP1 β • CCL5/RANTES • CCL6 • CCL7 • CCL8 • CCL9 • CCL11 • CCL12 • CCL13 • CCL14 • CCL15 • CCL16 • CCL17 • CCL18/PARC/DCCK1/AMAC1/MIP4 • CCL19 • CCL20 • CCL21 • CCL22 • CCL23 • CCL24 • CCL25 • CCL26 • CCL27 • CCL28 CXCL • CXCL1/KC • CXCL2 • CXCL3 • CXCL4 • CXCL5 • CXCL6 • CXCL7 • CXCL8/IL8 • CXCL9 • CXCL10 • CXCL11 • CXCL12 • CXCL13 • CXCL14 • CXCL15 • CXCL16 • CXCL17 CX3CL • CX3CL1 XCL • XCL1 • XCL2 TNF • TNFA • Lymphotxin • TNFB/LTA • TNFC/LTB) • TNFSF4 • TNFSF5/CD40LG • TNFSF6 • TNFSF7 • TNFSF8 • TNFSF9 • TNFSF10 • TNFSF11 • TNFSF13 • TNFSF13B • EDA																		
By family		Interleukin <table border="1"> <tr> <td rowspan="4" style="vertical-align: middle; text-align: center;"> Type I (grouped by receptor subunit) </td> <td>γ chain • IL2/IL15 • IL4/IL13 • IL7 • IL9 • IL21</td> </tr> <tr> <td>β chain • IL3 • IL5 • GMCSF</td> </tr> <tr> <td>IL6 like/gp130 • IL6 • IL11 • IL27 • IL30 • IL31 • non IL OSM • LIF • CNTF • CTF1)</td> </tr> <tr> <td>IL12 family/IL12RB1 • IL12 • IL23 • IL27 • IL35</td> </tr> <tr> <td>Other • IL14 • IL16 • IL32 • IL34</td> </tr> <tr> <td rowspan="3" style="vertical-align: middle; text-align: center;"> Type II </td> <td>IL10 family • IL10/IL22 • IL19 • IL20 • IL24 • IL26 • Interferon type III • IL28/IFNL2+3 • IL29/IFNL1)</td> </tr> <tr> <td>Interferon <table border="1"> <tr> <td>I</td> <td>• IFNA1 • IFNA2 • IFNA4 • IFNA5 • IFNA6 • IFNA7 • IFNA8 • IFNA10 • IFNA13 • IFNA14 • IFNA16 • IFNA17 • IFNA21 • IFNB1</td> </tr> <tr> <td>II</td> <td>• IFNK • IFNW1</td> </tr> </table> </td> </tr> <tr> <td>IFNG</td> </tr> <tr> <td>Ig superfamily • IL1 family: IL1A/IL1F1 • IL1B/IL1F2 • 1Ra/IL1F3 • IL1F5 • IL1F6 • IL1F7 • IL1F8 • IL1F9 • IL1F10 • 33/IL1F11 • 18/IL1G</td> </tr> <tr> <td>IL17 family • IL17/IL25 (IL17A)</td> </tr> <tr> <td>Other • Hematopoietic • KITLG • Colony-stimulating factor) • SPP1 • MIF</td> </tr> </table>		Type I (grouped by receptor subunit)	γ chain • IL2/IL15 • IL4/IL13 • IL7 • IL9 • IL21	β chain • IL3 • IL5 • GMCSF	IL6 like/gp130 • IL6 • IL11 • IL27 • IL30 • IL31 • non IL OSM • LIF • CNTF • CTF1)	IL12 family/IL12RB1 • IL12 • IL23 • IL27 • IL35	Other • IL14 • IL16 • IL32 • IL34	Type II	IL10 family • IL10/IL22 • IL19 • IL20 • IL24 • IL26 • Interferon type III • IL28/IFNL2+3 • IL29/IFNL1)	Interferon <table border="1"> <tr> <td>I</td> <td>• IFNA1 • IFNA2 • IFNA4 • IFNA5 • IFNA6 • IFNA7 • IFNA8 • IFNA10 • IFNA13 • IFNA14 • IFNA16 • IFNA17 • IFNA21 • IFNB1</td> </tr> <tr> <td>II</td> <td>• IFNK • IFNW1</td> </tr> </table>	I	• IFNA1 • IFNA2 • IFNA4 • IFNA5 • IFNA6 • IFNA7 • IFNA8 • IFNA10 • IFNA13 • IFNA14 • IFNA16 • IFNA17 • IFNA21 • IFNB1	II	• IFNK • IFNW1	IFNG	Ig superfamily • IL1 family: IL1A/IL1F1 • IL1B/IL1F2 • 1Ra/IL1F3 • IL1F5 • IL1F6 • IL1F7 • IL1F8 • IL1F9 • IL1F10 • 33/IL1F11 • 18/IL1G	IL17 family • IL17/IL25 (IL17A)	Other • Hematopoietic • KITLG • Colony-stimulating factor) • SPP1 • MIF
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By function/ cell		• proinflammatory cytokine • IL1 • TNFA) • Monokine • Lymphokine • Th1 • IFN γ • TNF β) • Th2 • IL4 • IL5 • IL6 • IL10 • IL13))																		



Macrophage



Dendritic Cell



Helper T Cell



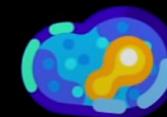
B Cell



Antibodies



Complement



Basophil



Dendritic Cell



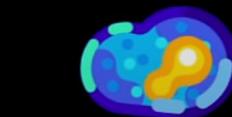
Helper T Cell



B Cell



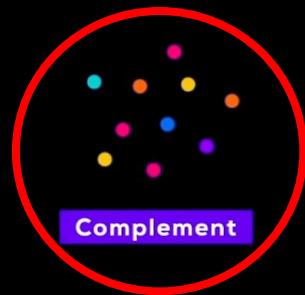
Antibodies



Basophil



Macrophage



Complement



Dendritic Cell



Helper T Cell



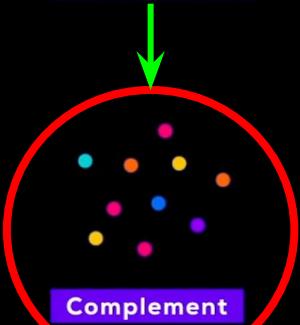
B Cell



Antibodies



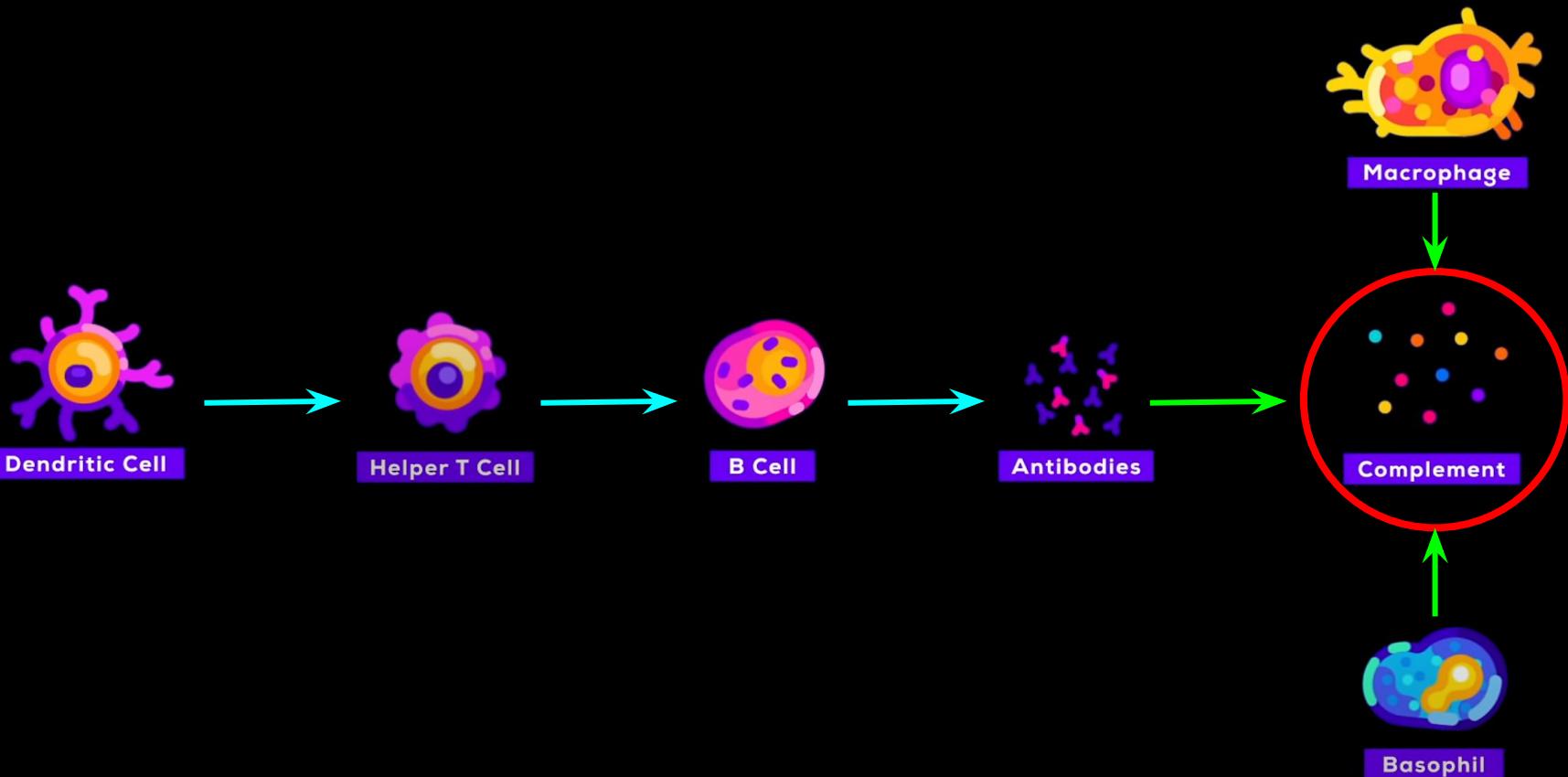
Macrophage



Complement



Basophil



What is the complement system?

V T E

complement system

Pathways • C • L • A

Activators/enzymes

- Early
 - C: C1 • C1q • C1r • C1s) • C4 • C4a • C4b) • C2
 - L: MASP1/MASP2 • MBL
 - A: Factor B • Factor D • Factor P/Properdin
- Middle
 - C3 • C3a • C3b/iC3b) • C5 • C5a • C5b)
 - C3-convertase • C5-convertase
- Late
 - MAC • C5b • C6 • C7 • C8 • C9)

Inhibitors

- CLA: C1-inhibitor • Decay-accelerating factor/CD59 • Factor I
- CL: C4BP
- A: Factor H

Complement receptors

- CR1 • CR2 • CR3 • CR4 • CD11b/CD11c/CD18 • Anaphylatoxin • C3a • C5a)

Function

- Cytotoxicity(by MAC) • immune adherence • Inducing inflammation • Opsonization

V T E

complement system

Pathways • C • L • A

Activators/enzymes

- | | | |
|--------------------|--|---|
| Activators/enzymes | Early | • C (C1 • C1q • C1r • C1s) • C4 • C4a • C4b) • C2 |
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| | • C3-convertase • C5-convertase | |
| Late | • MAC • C5b • C6 • C7 • C8 • C9) | |

Inhibitors

• CLA: C1-inhibitor • Decay-accelerating factor/CD59 • Factor I

• CL: C4BP

• A: Factor H

Complement receptors

• CR1 • CR2 • CR3 • CR4 • CD11b/CD11c/CD18 • Anaphylatoxin • C3a • C5a)

Function

• Cytotoxicity(by MAC) • immune adherence • Inducing inflammation • Opsonization

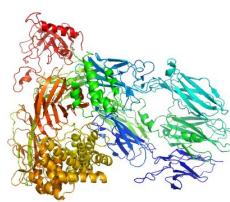
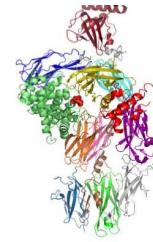
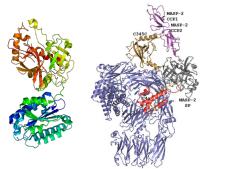
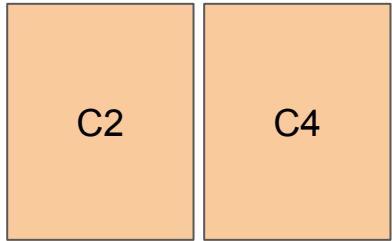
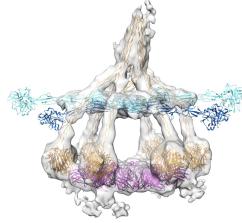
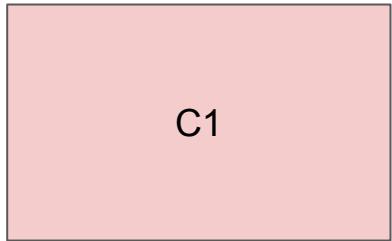
C1

C2

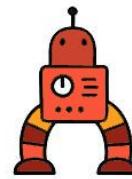
C4

C3

C5

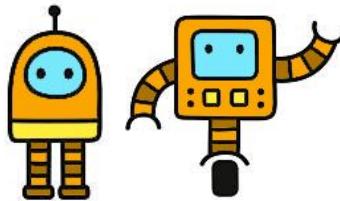


C1

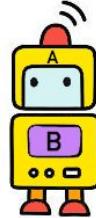


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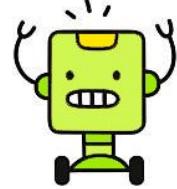
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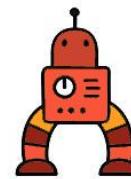
C3



C5

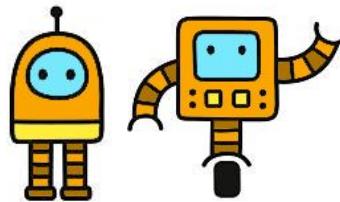


C1

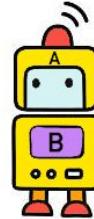


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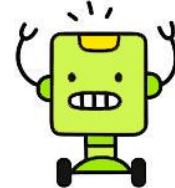
C4



C3



C5



Membrane Attack Complex (MAC)

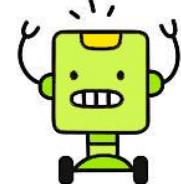
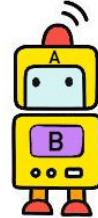
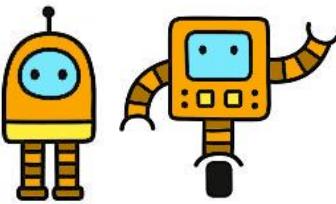
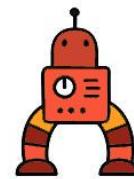
C1

C2

C4

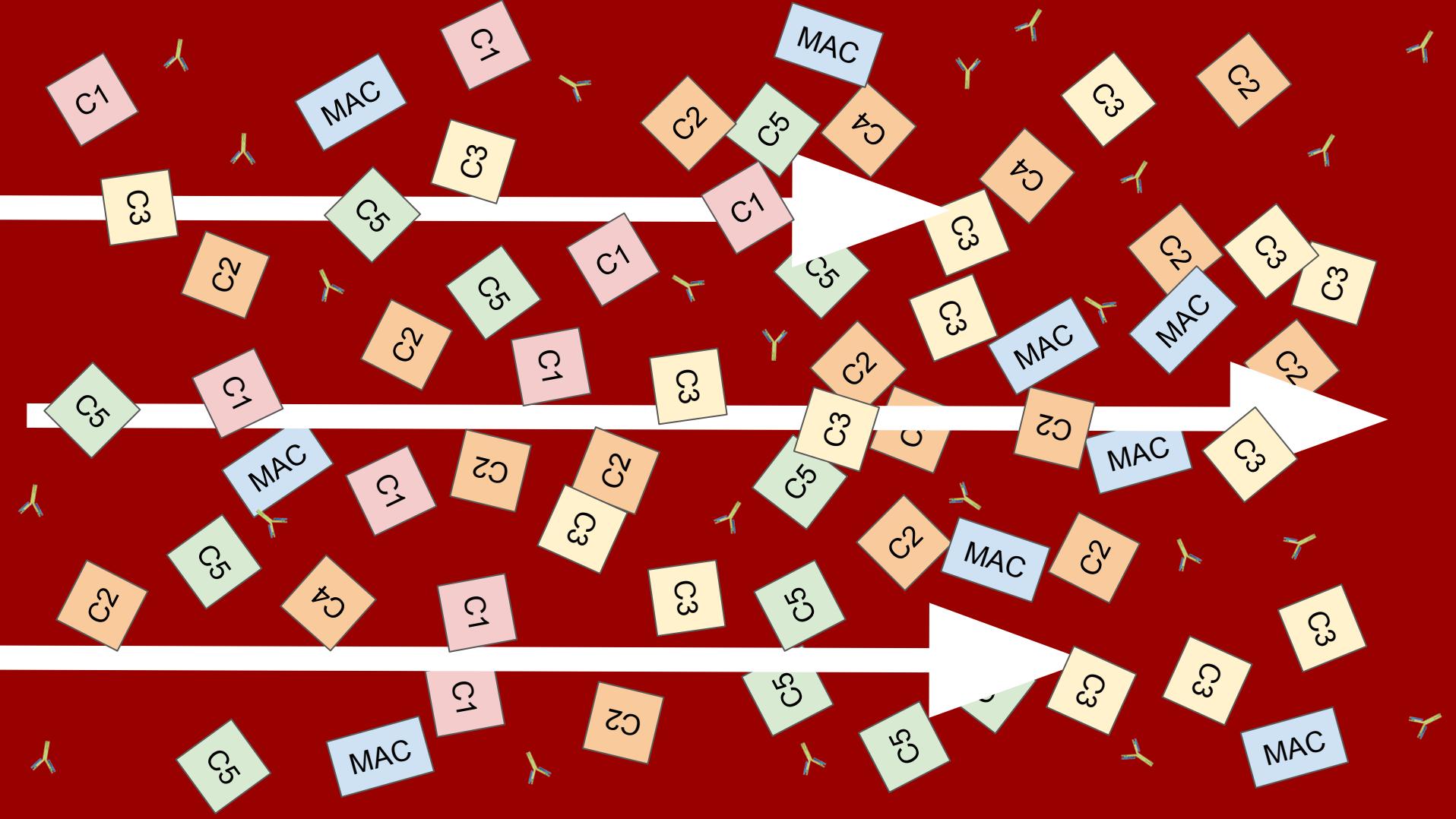
C3

C5



Membrane Attack Complex (MAC)





V T E

complement system

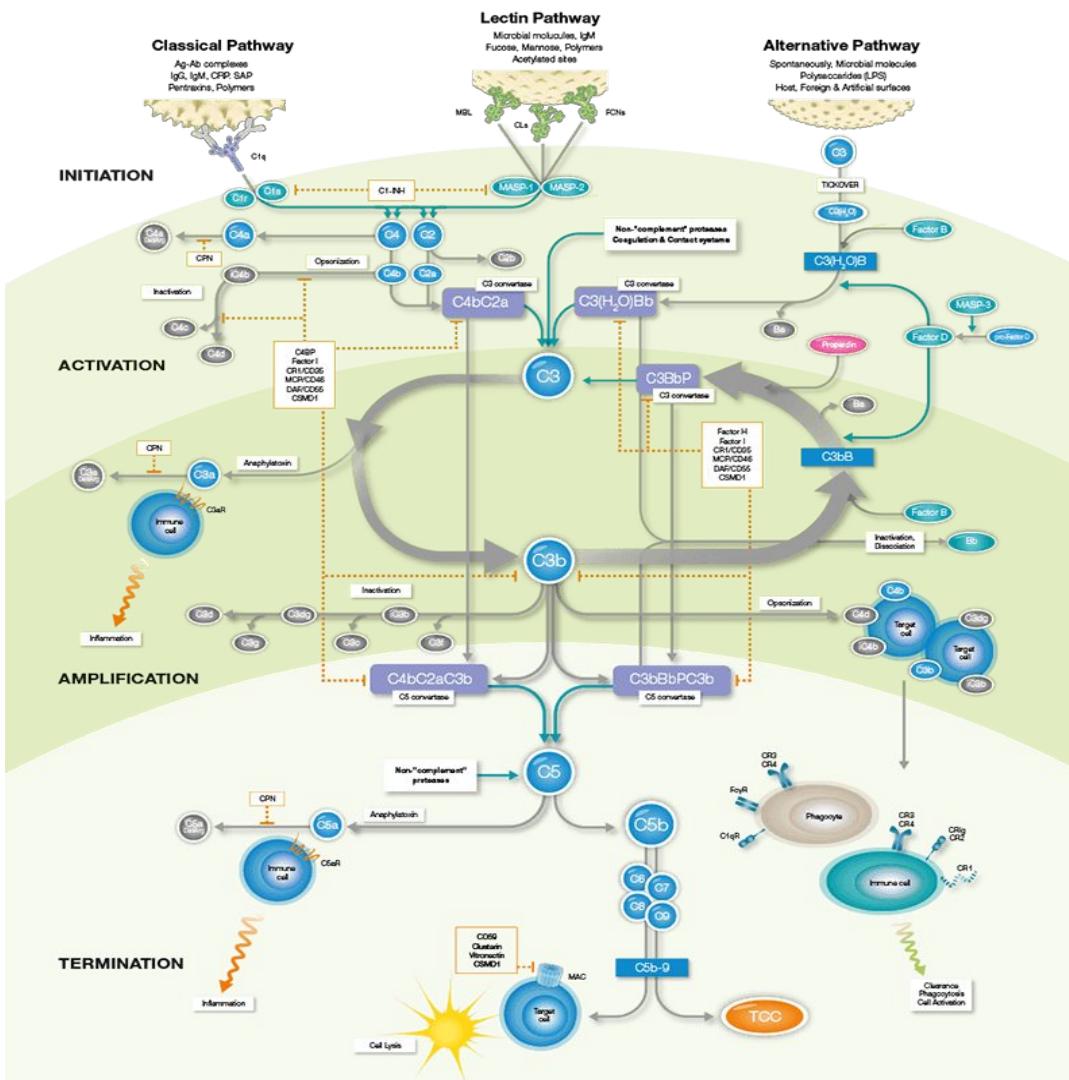
Pathways • C • L • A

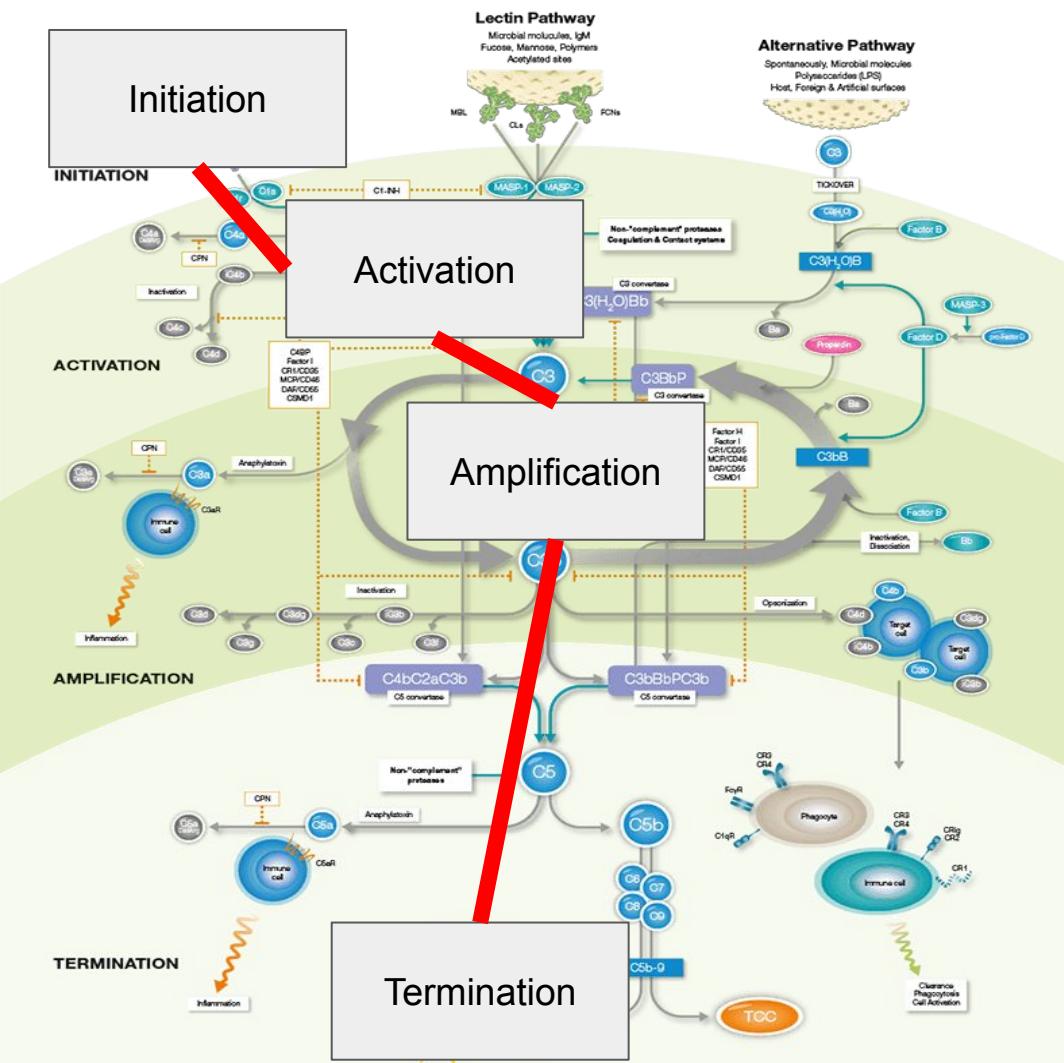
Activators/enzymes	Early	• C: C1 • C1q • C1r • C1s) • C4 • C4a • C4b) • C2 • L: MASP1/MASP2 • MBL • A: Factor B • Factor D • Factor P/Properdin
	Middle	• C3 • C3a • C3b/iC3b) • C5 • C5a • C5b) • C3-convertase • C5-convertase
	Late	• MAC • C5b • C6 • C7 • C8 • C9)

Inhibitors	• CLA: C1-inhibitor • Decay-accelerating factor/CD59 • Factor I • CL: C4BP • A: Factor H
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Complement receptors	• CR1 • CR2 • CR3 • CR4 • CD11b/CD11c/CD18 • Anaphylatoxin • C3a • C5a)
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Function	• Cytotoxicity(by MAC) • immune adherence • Inducing inflammation • Opsonization
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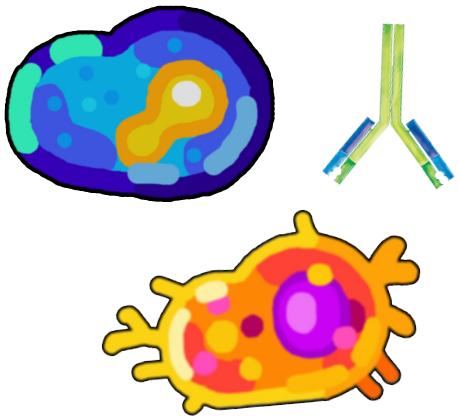


Initiation

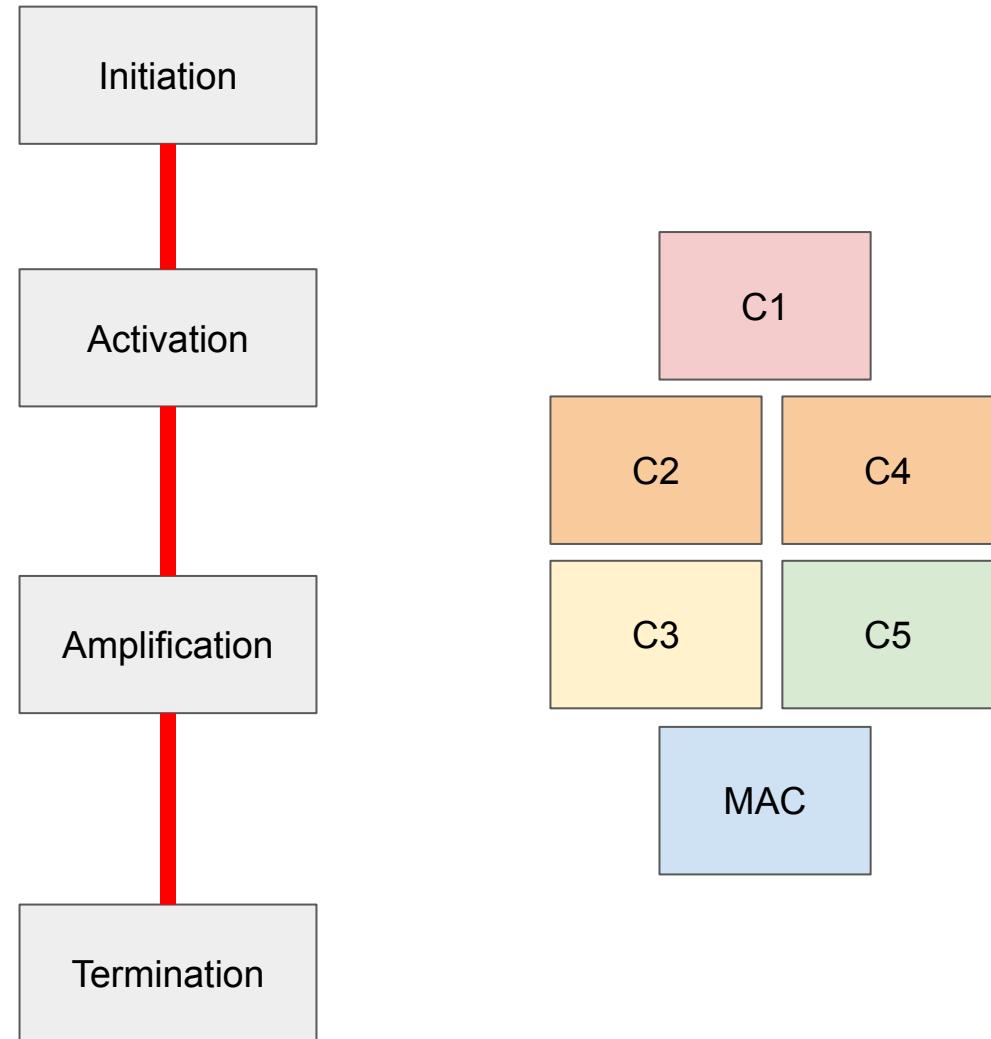
Activation

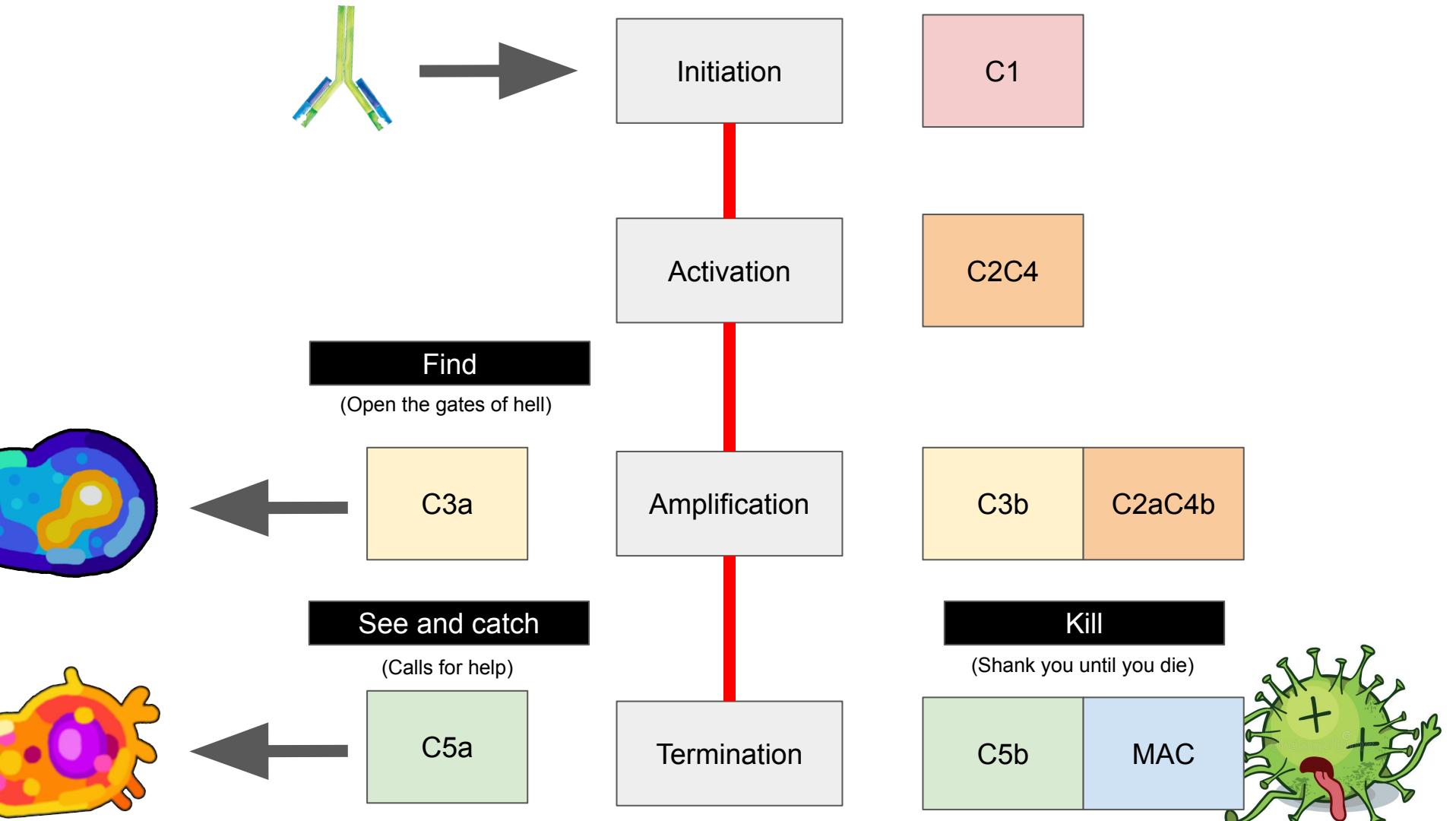
Amplification

Termination

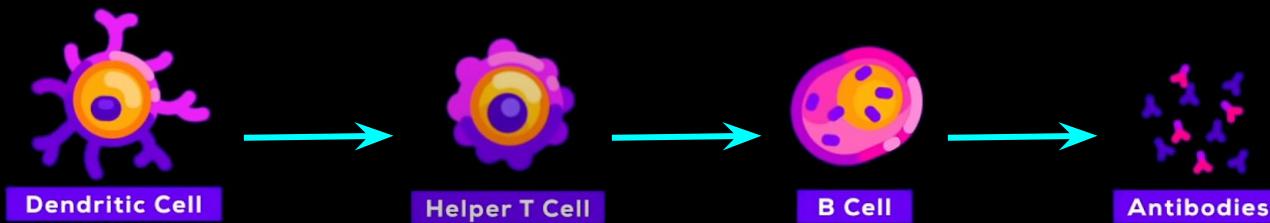


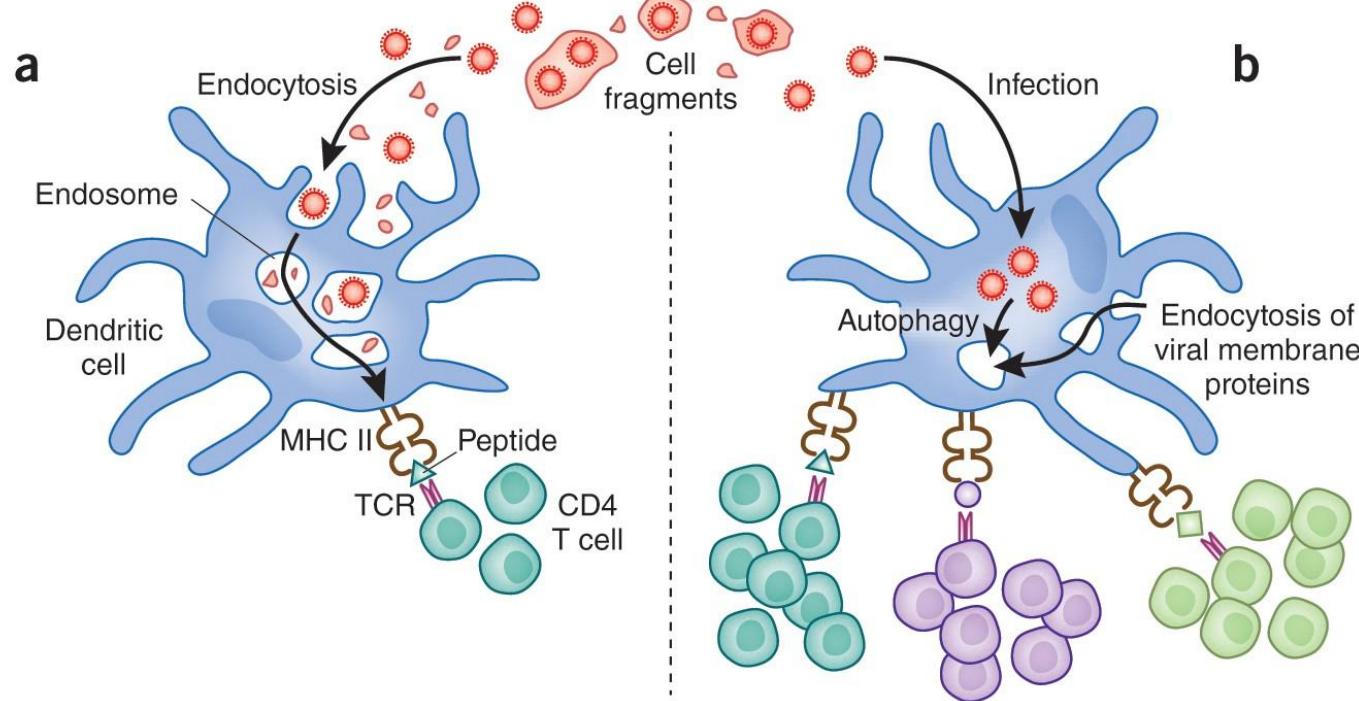
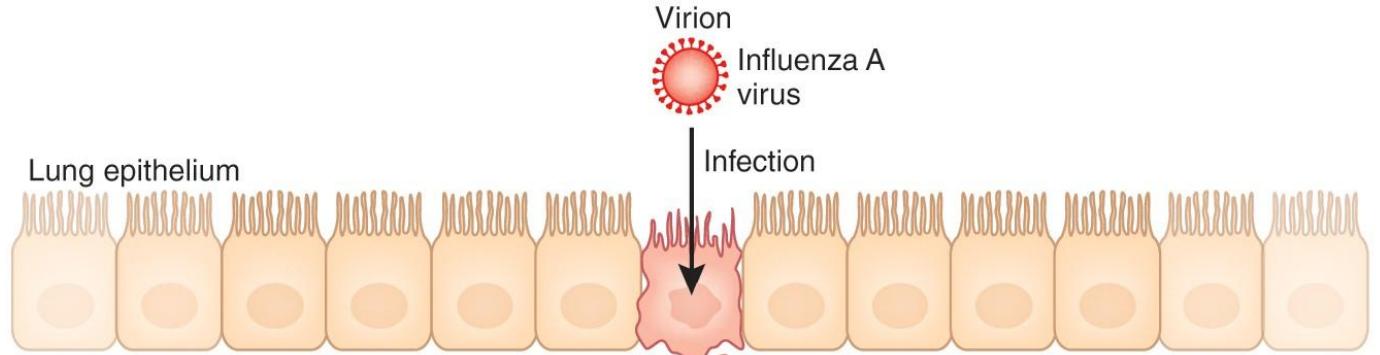
Find
See and catch
Kill





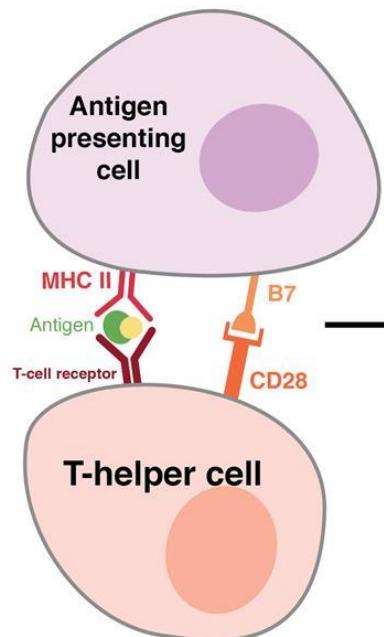
Pre-initiation process





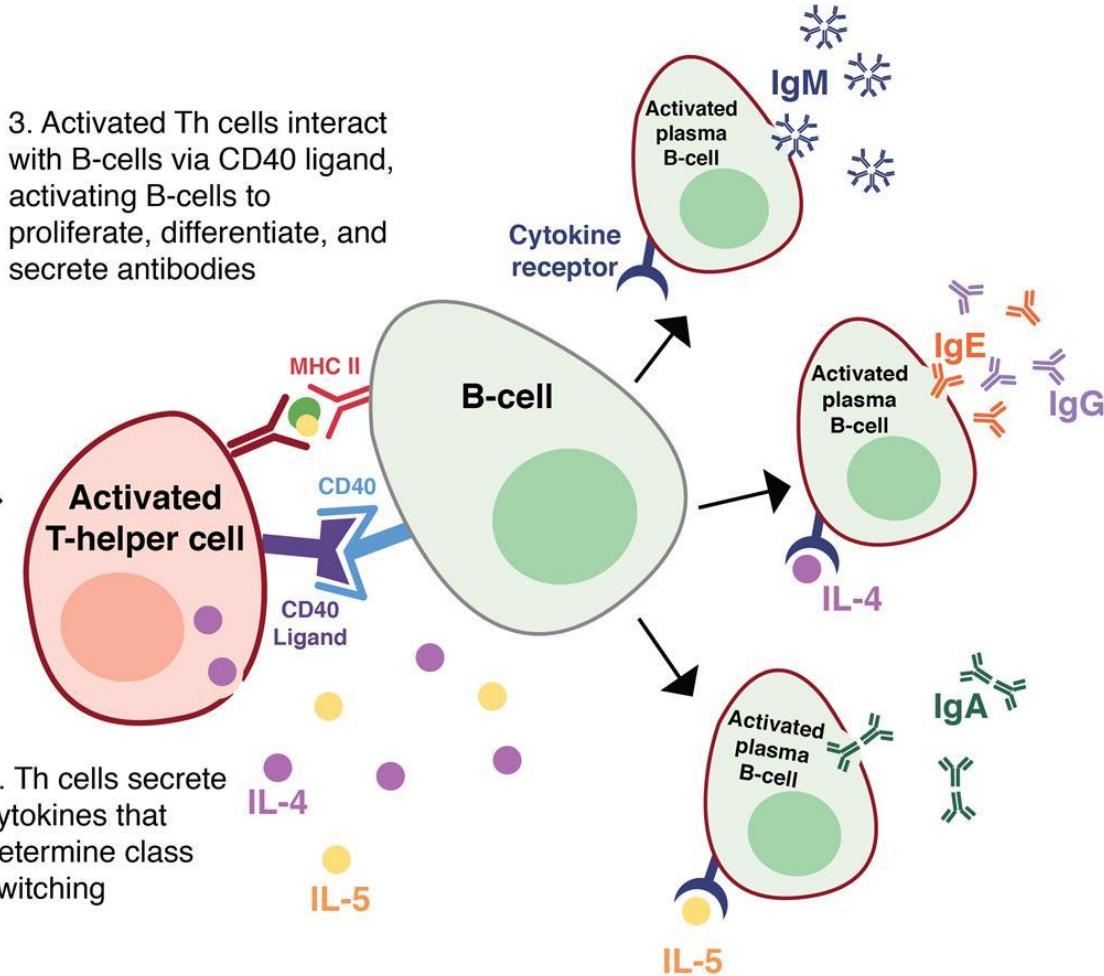
Activation and Class-switching of B-cells

1. APC presents antigen to T-helper cells

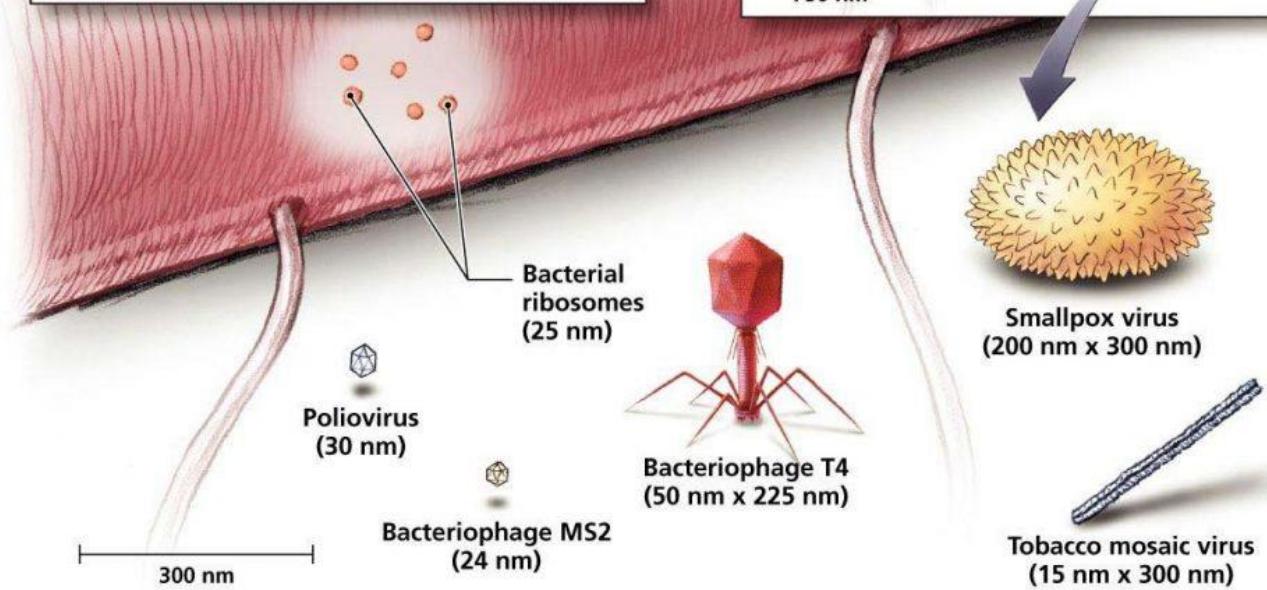
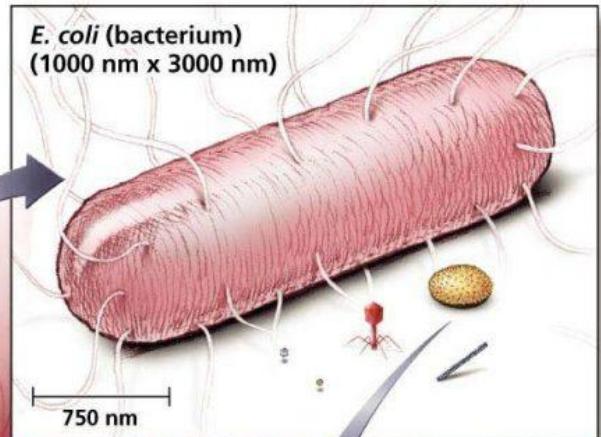
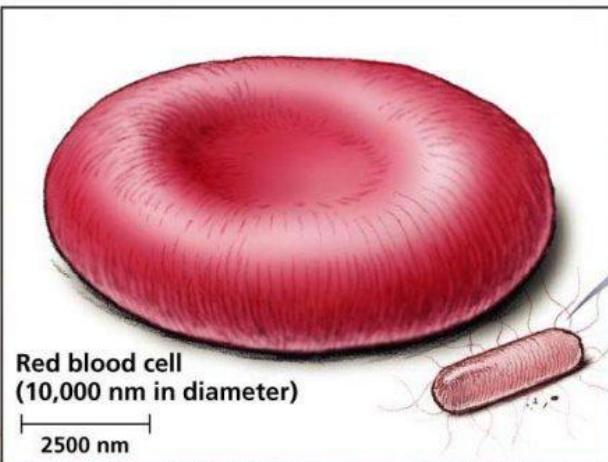


2. B7 is expressed and interacts with CD28, activating T-helper cells

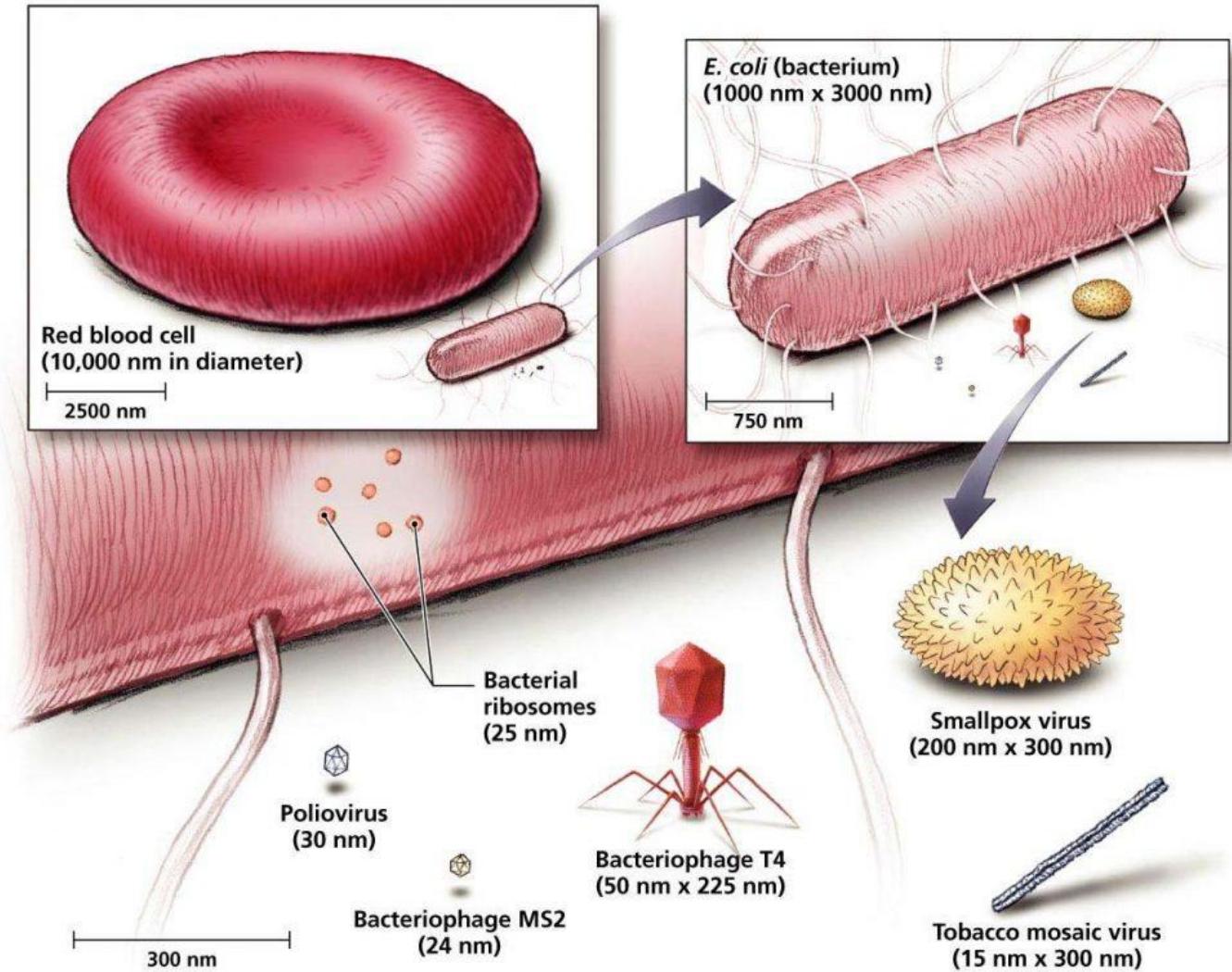
3. Activated Th cells interact with B-cells via CD40 ligand, activating B-cells to proliferate, differentiate, and secrete antibodies



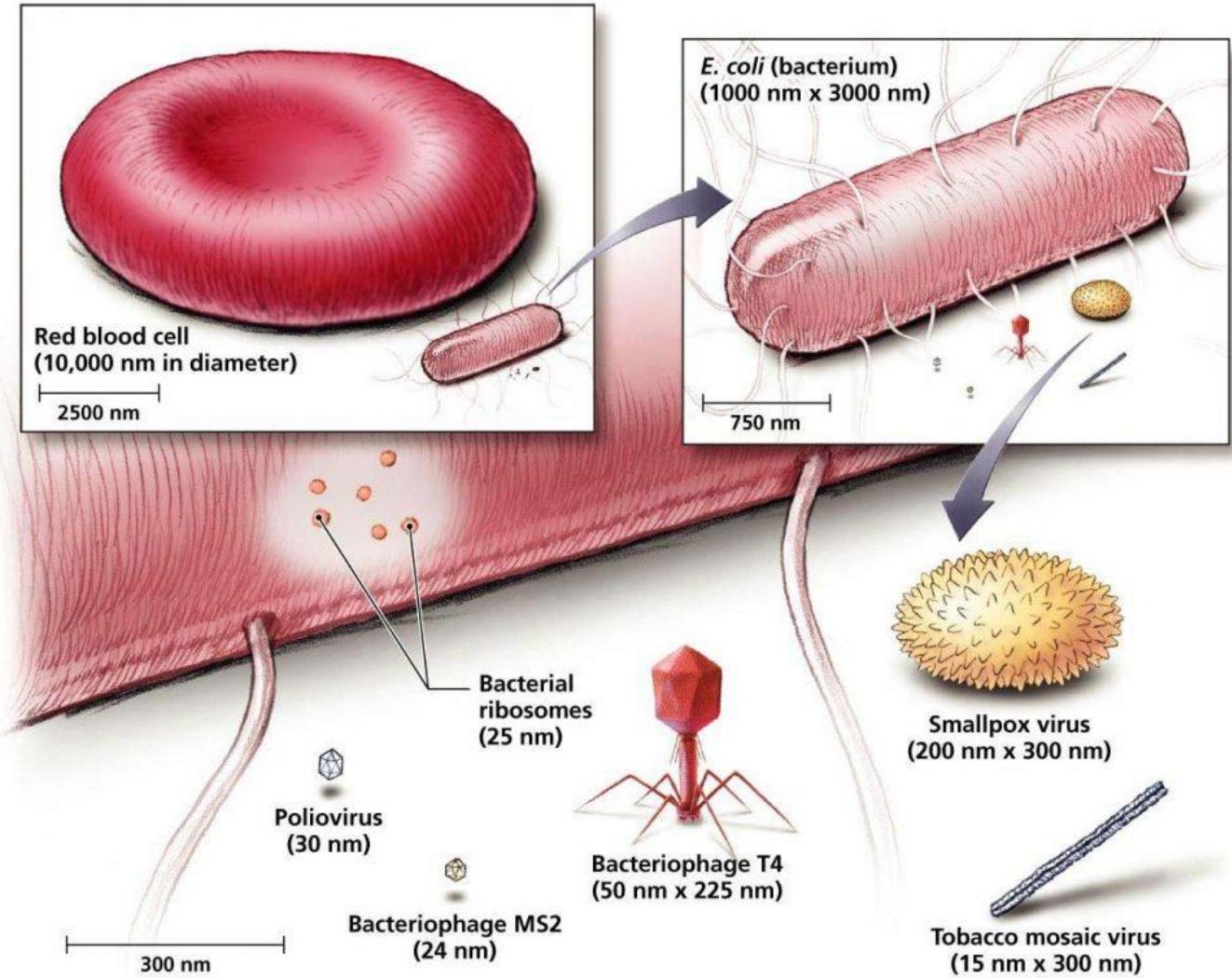
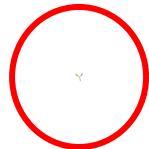
4. Th cells secrete cytokines that determine class switching



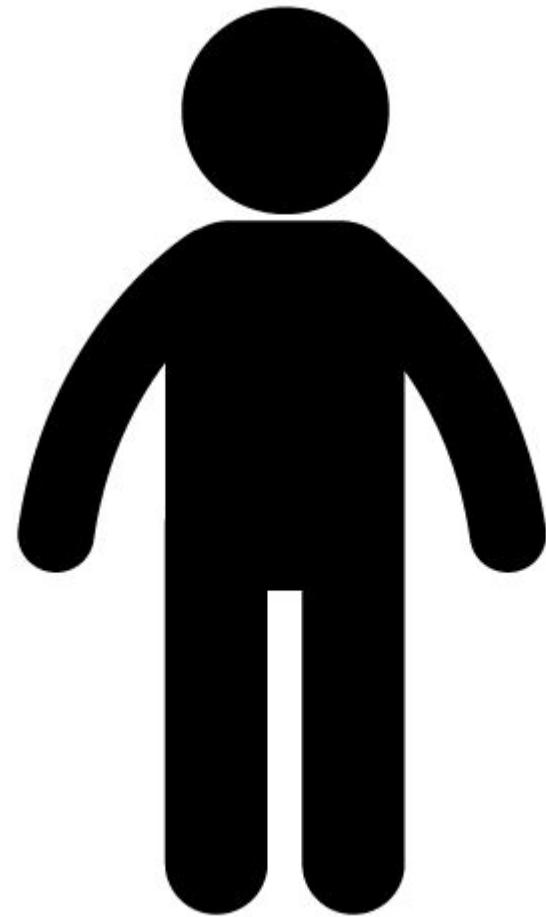
12nm x 12nm

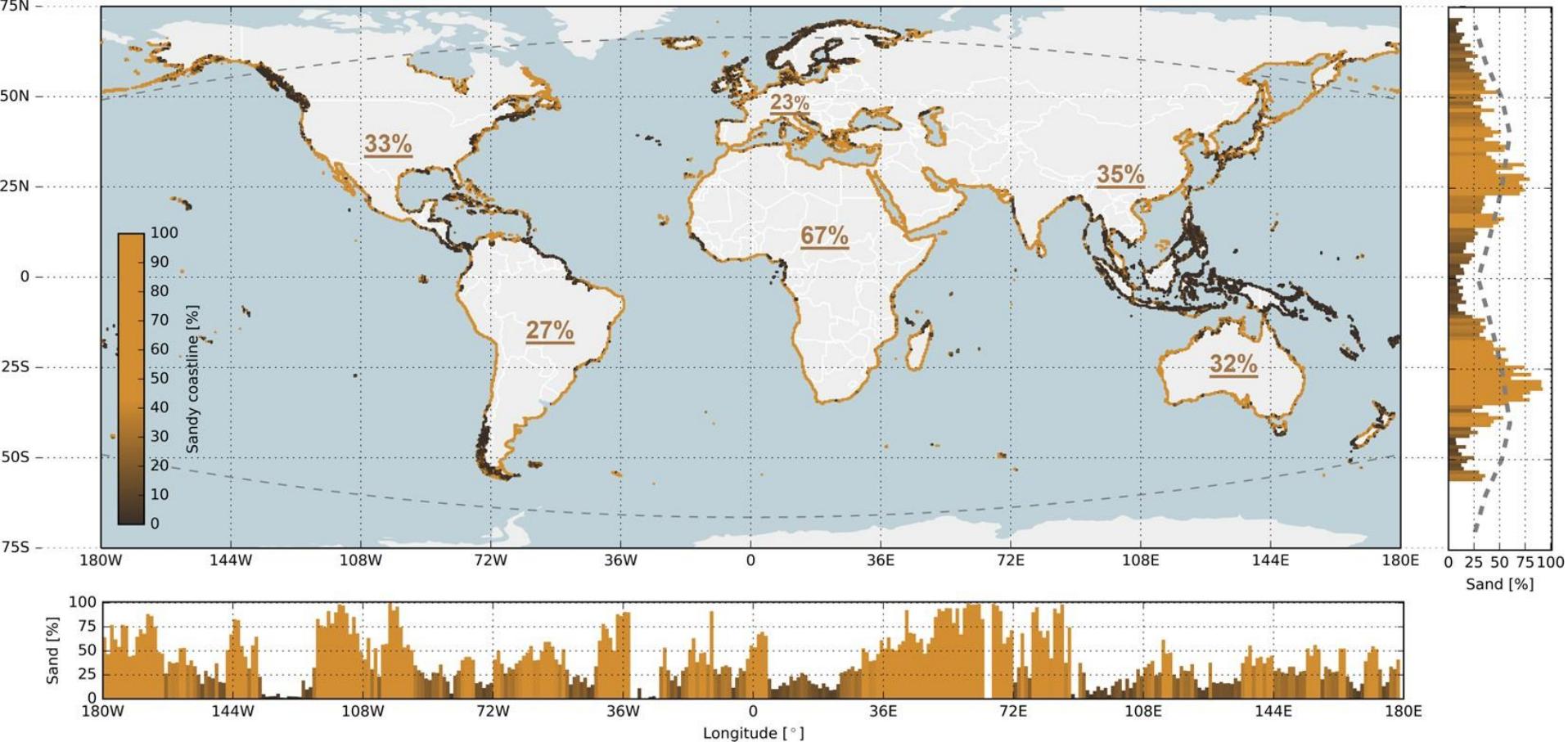


12nm x 12nm





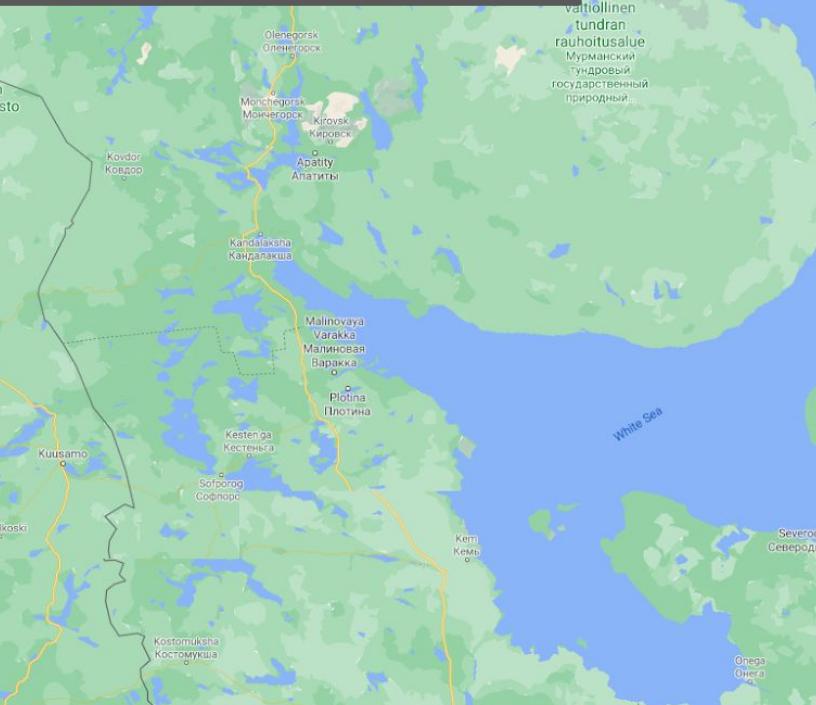




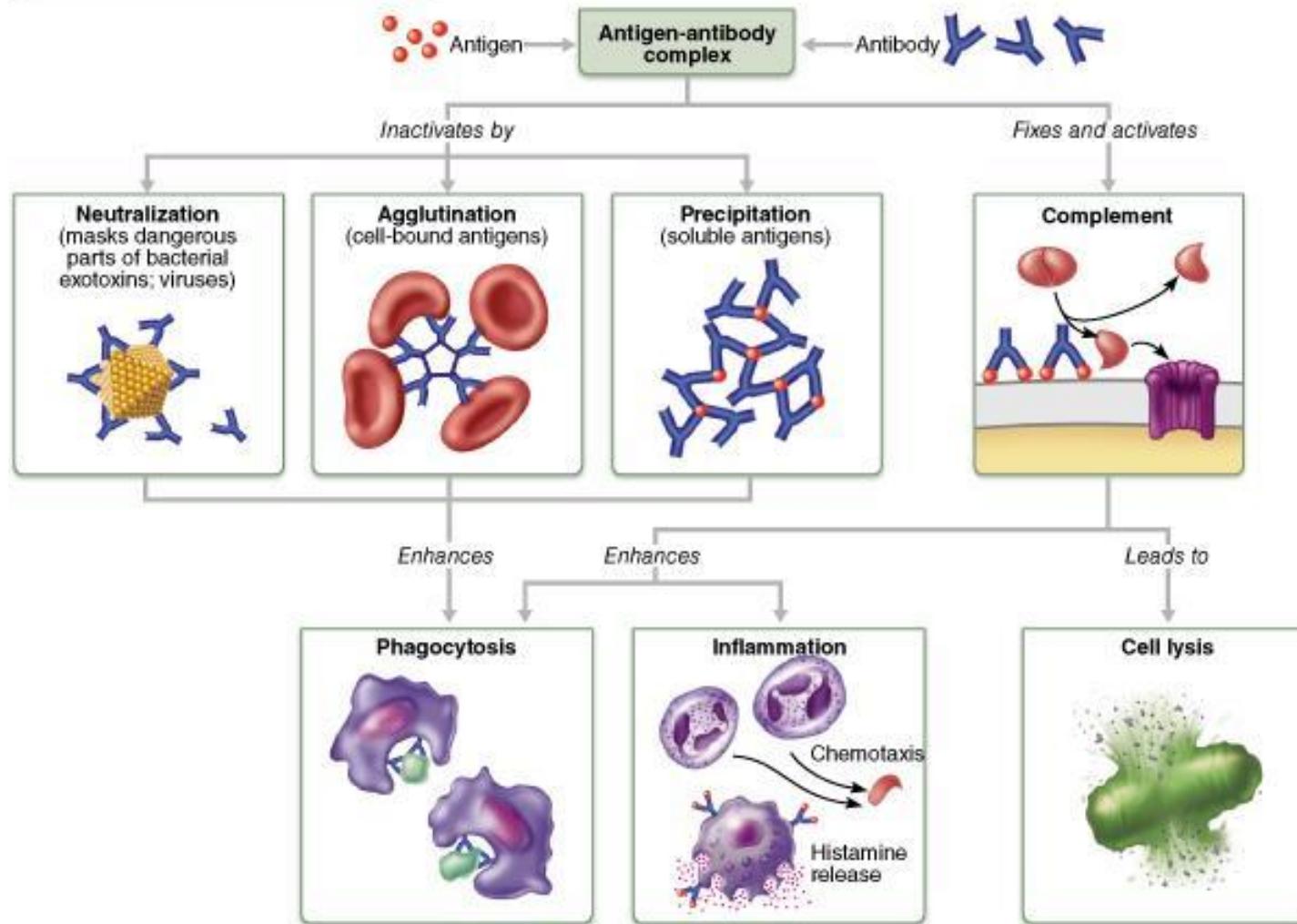
The State of the World's Beaches
April 2018

<https://doi.org/10.1038/s41598-018-24630-6>

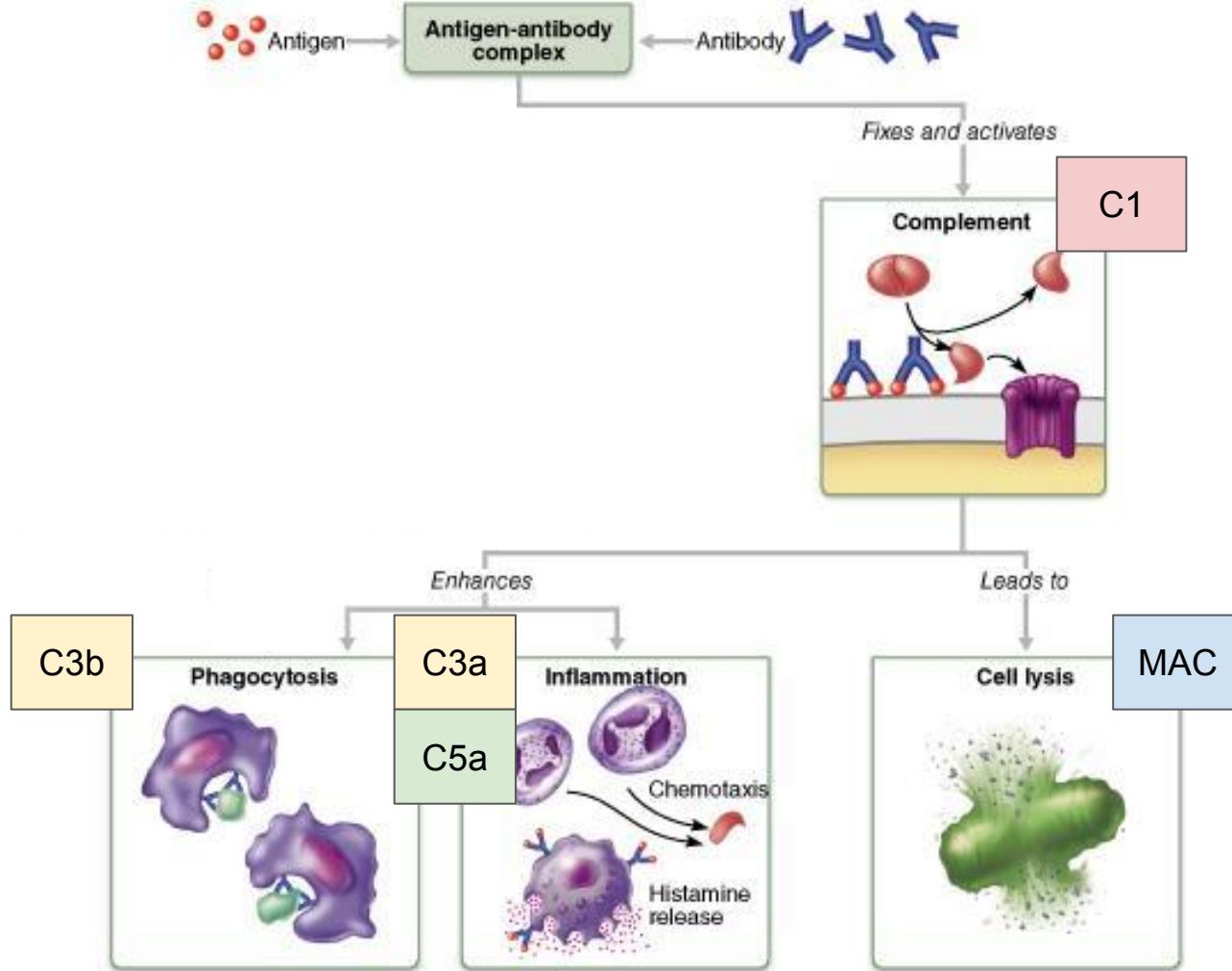
Find



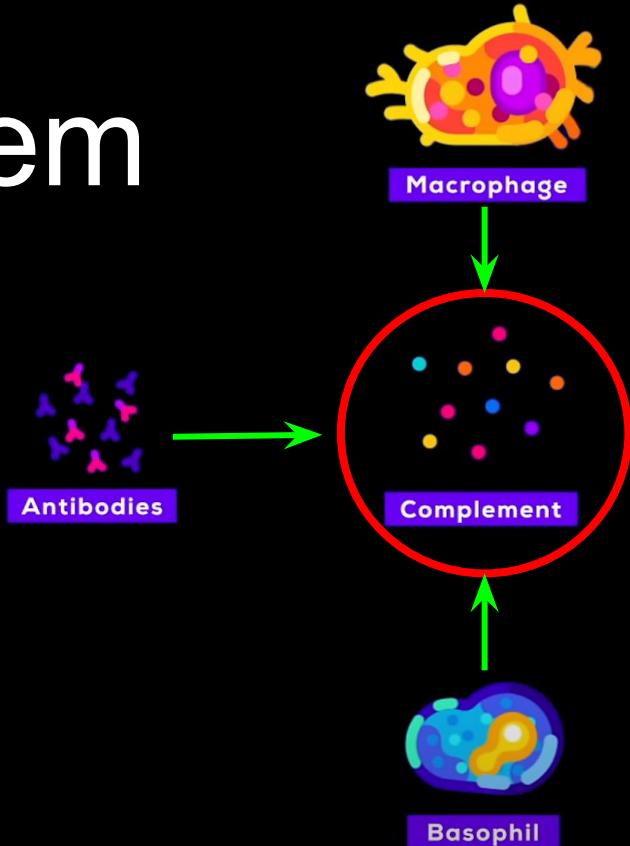
Adaptive defenses → Humoral immunity



Adaptive defenses → Humoral immunity



Complement System



Initiation

PHASE - A

Activation

Amplification

Termination

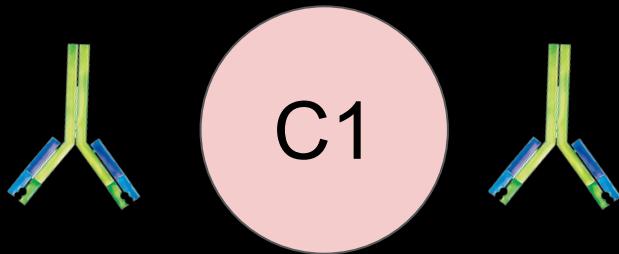
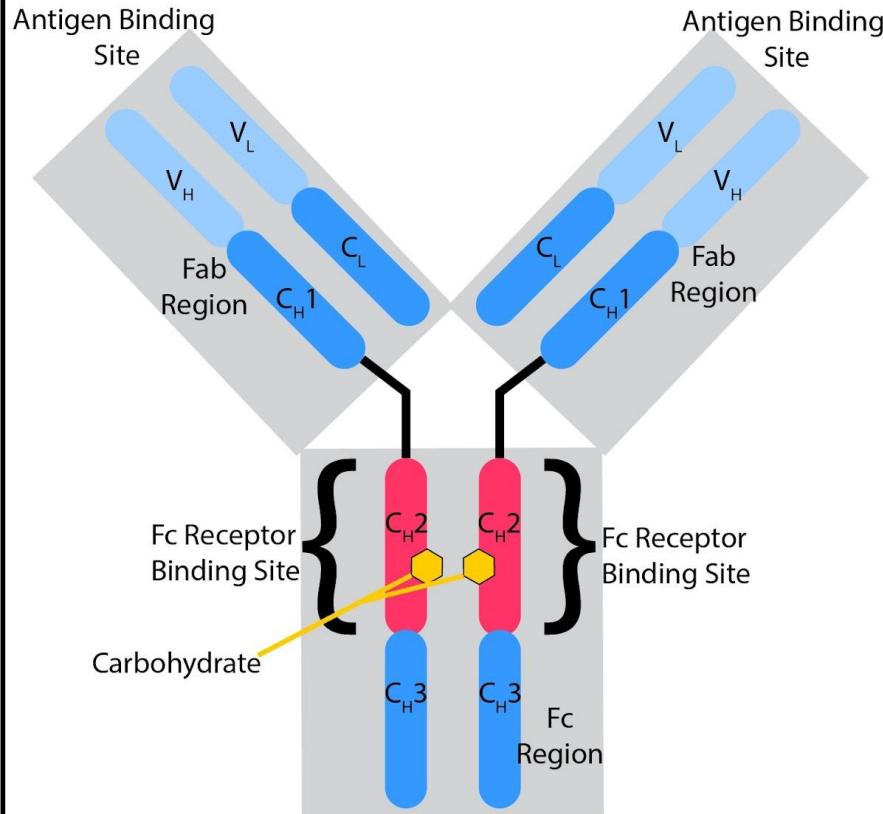
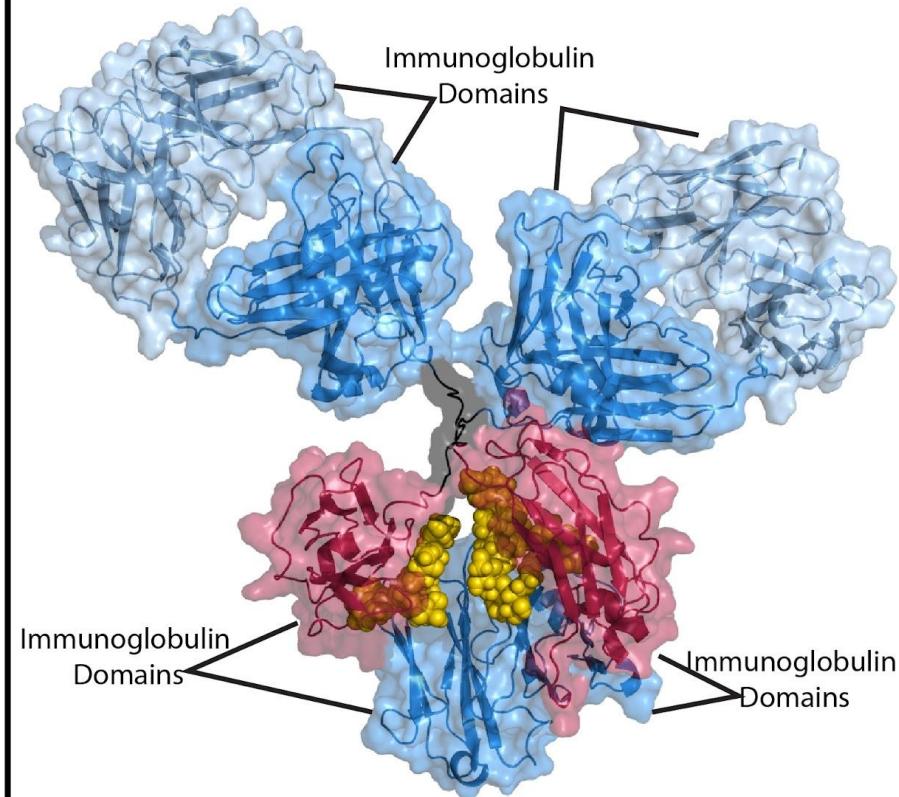


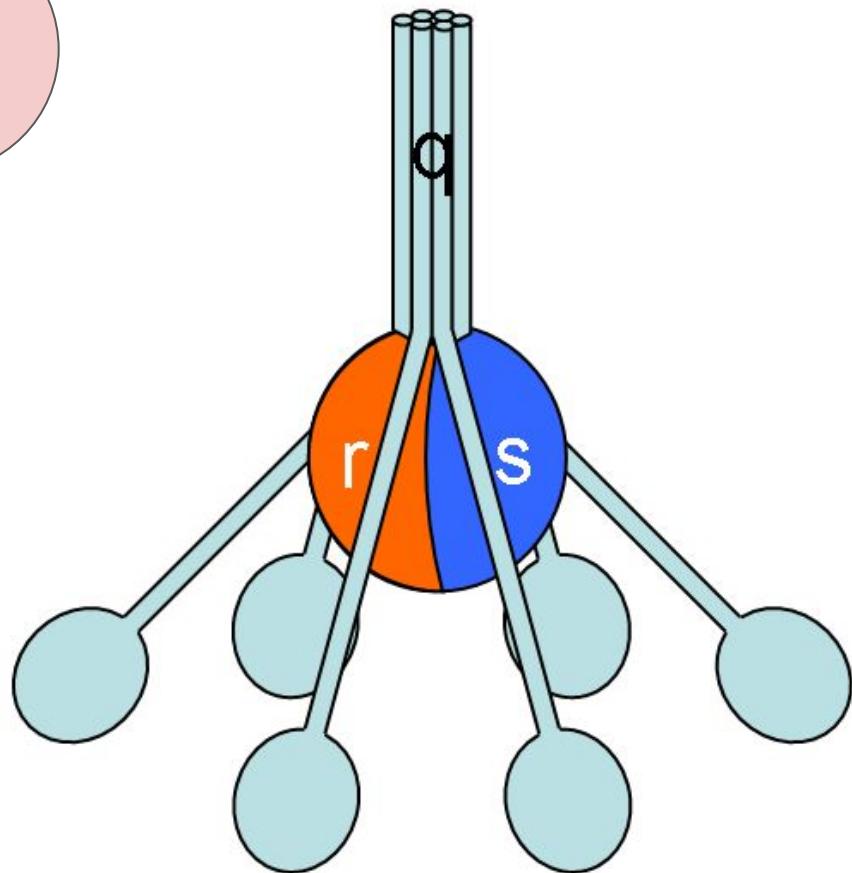
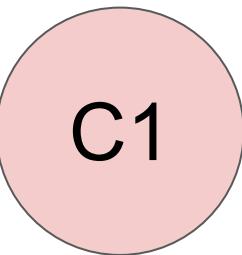
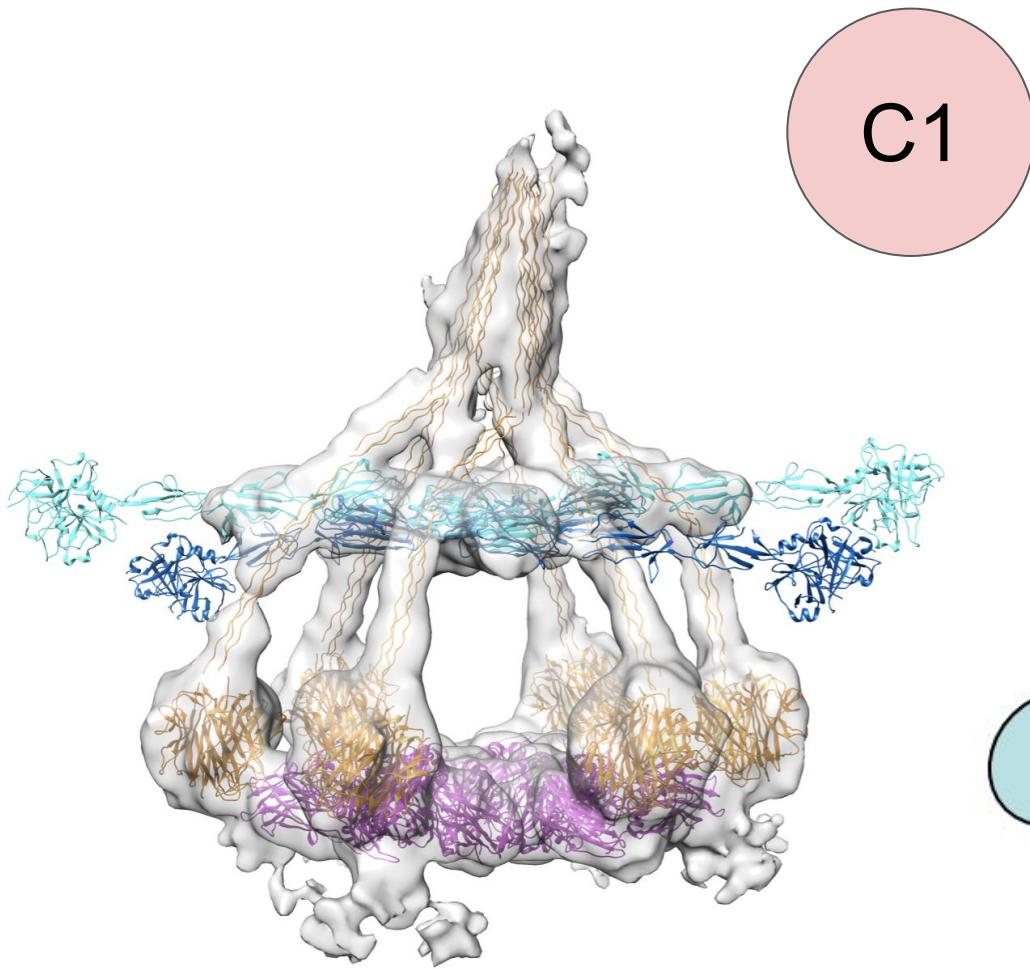
Figure 1: Antibody Structure

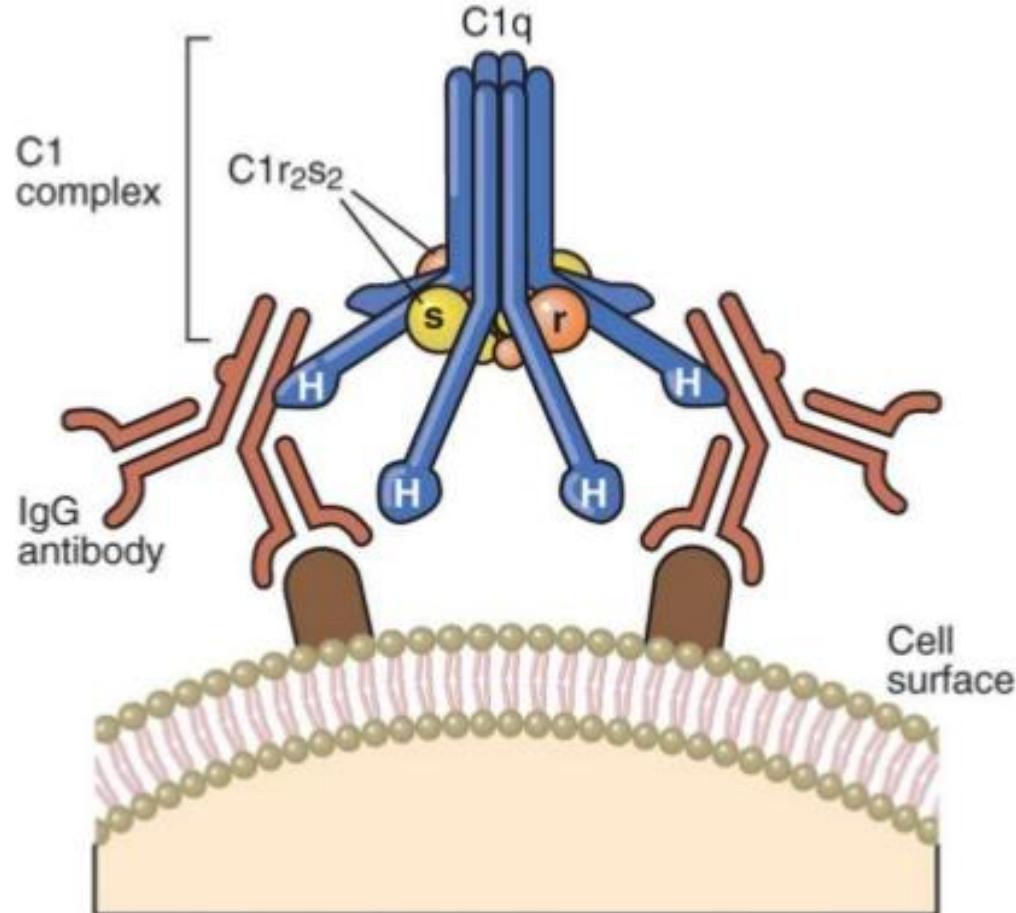
a: Architecture of an IgG Antibody

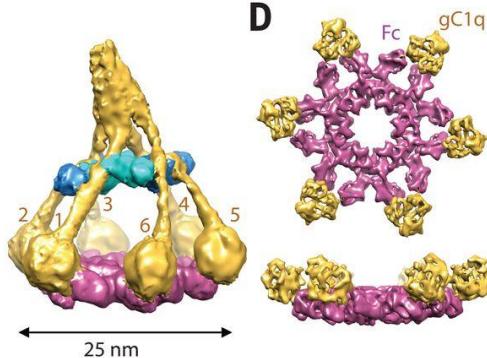
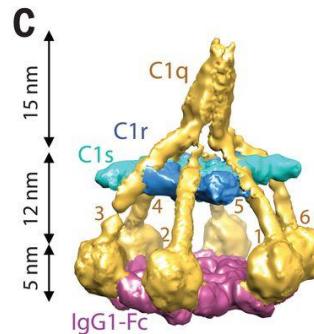
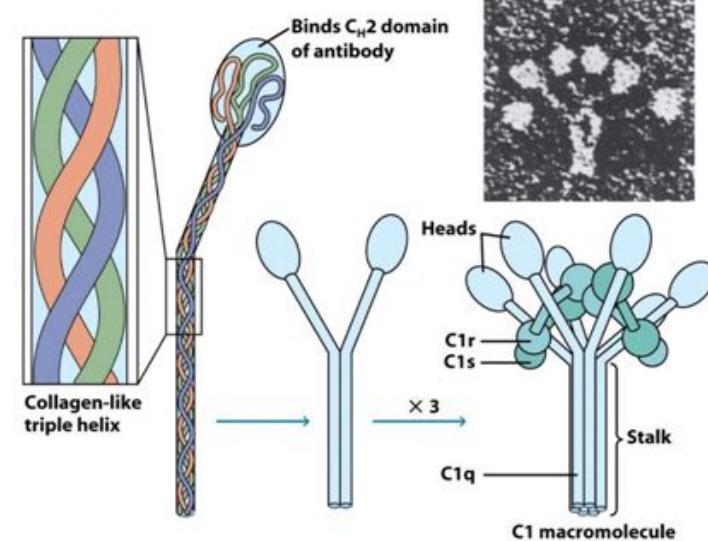
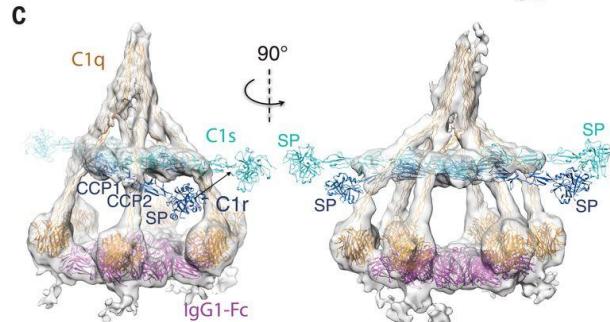
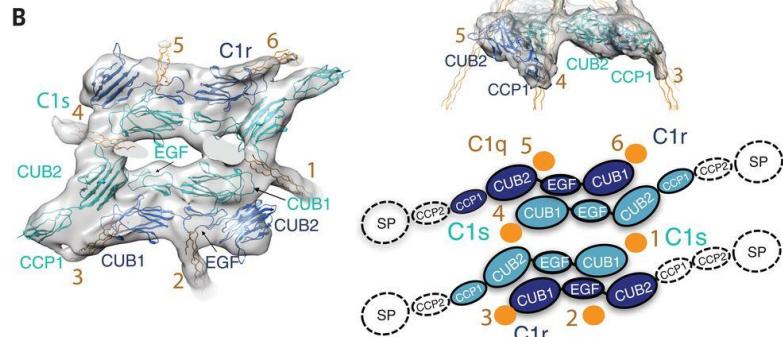
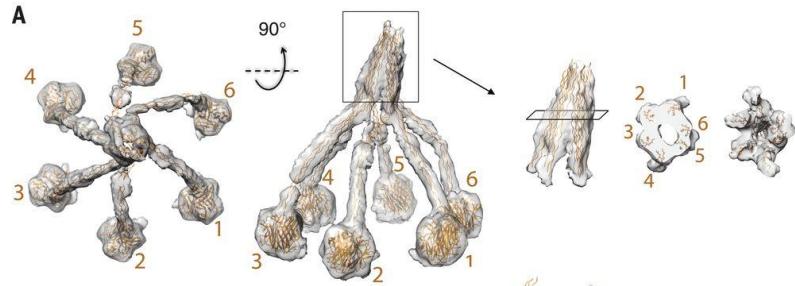


b: Crystal Structure of an IgG Antibody (1IGY)



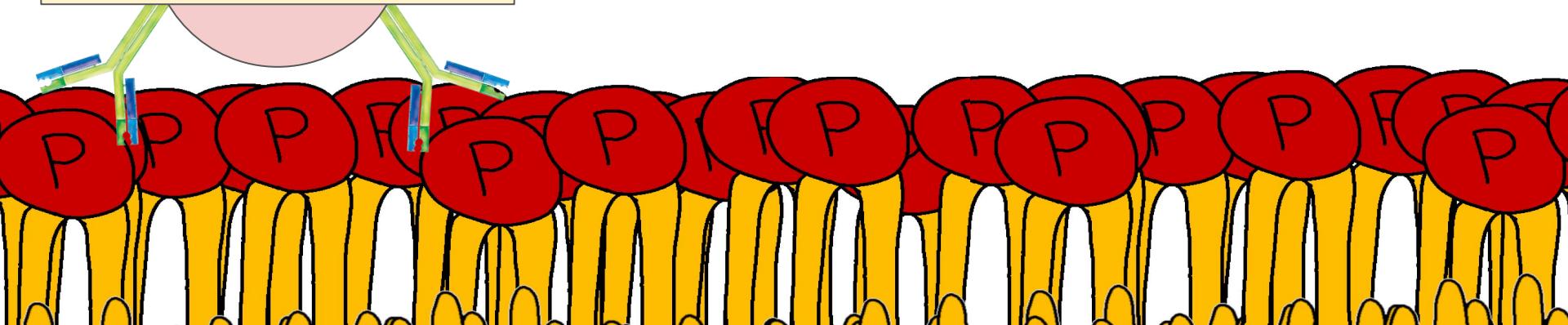






C1q

C1-r/s



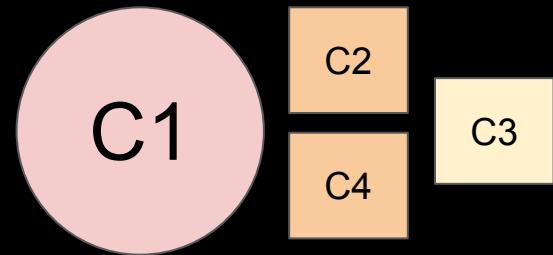
Initiation

Activation

Amplification

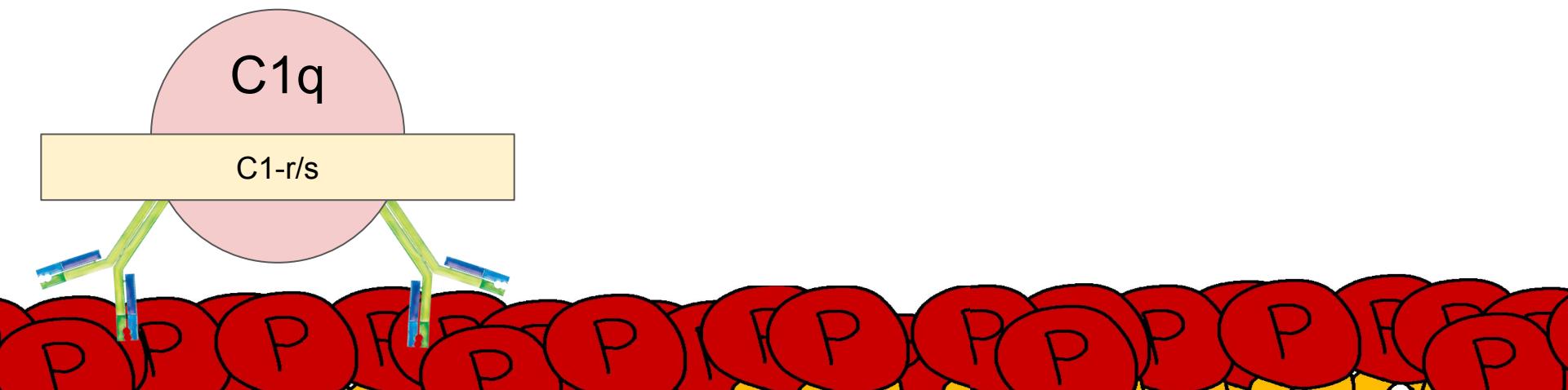
Termination

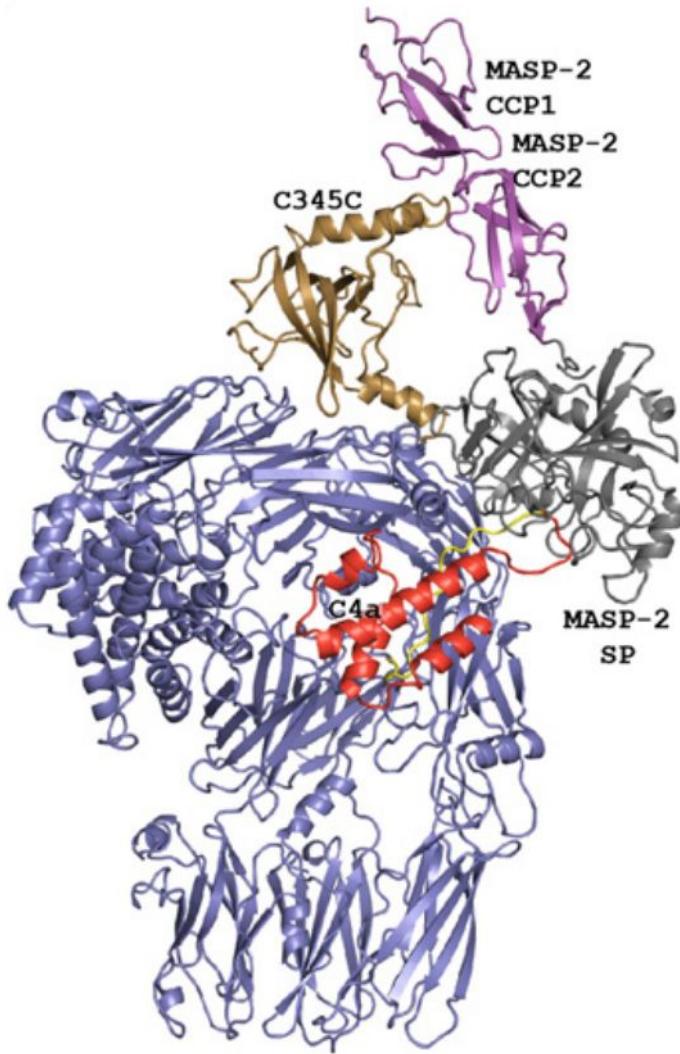
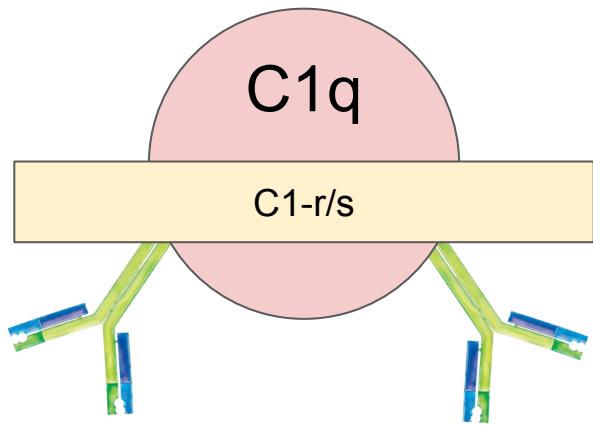
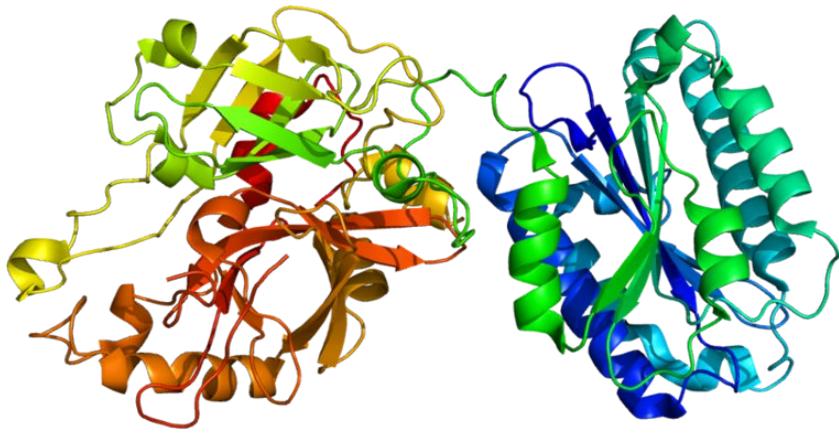
PHASE - B

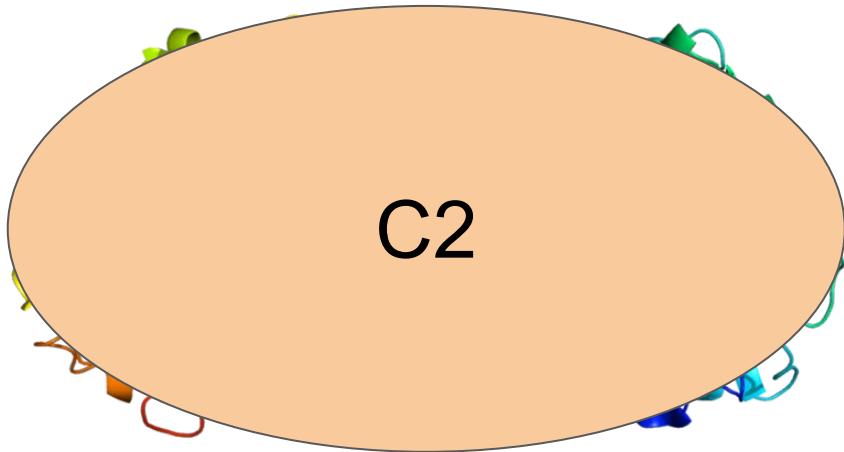


C1q

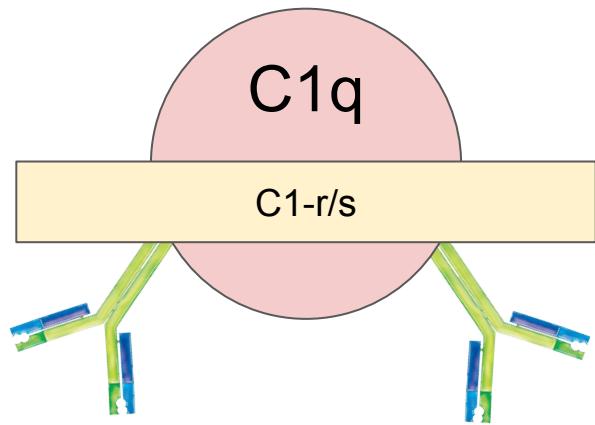
C1-r/s





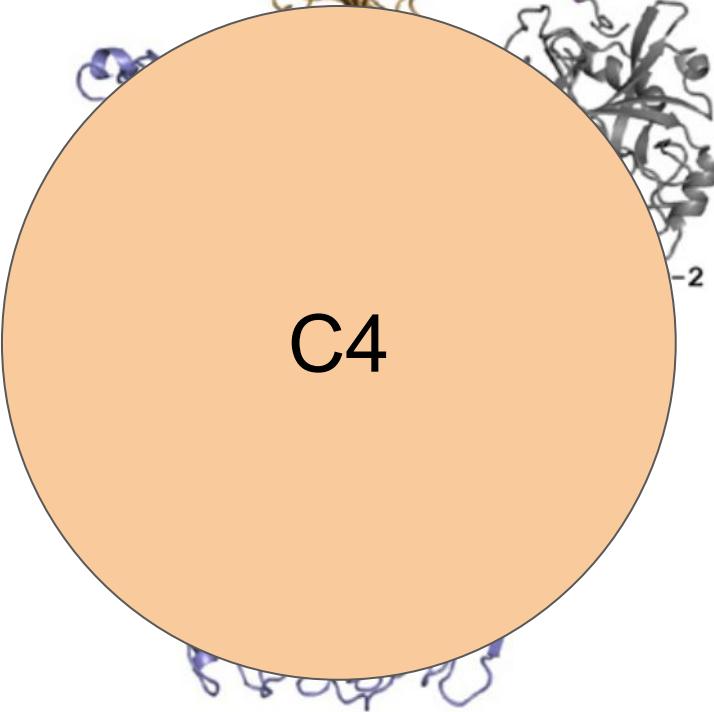


C2



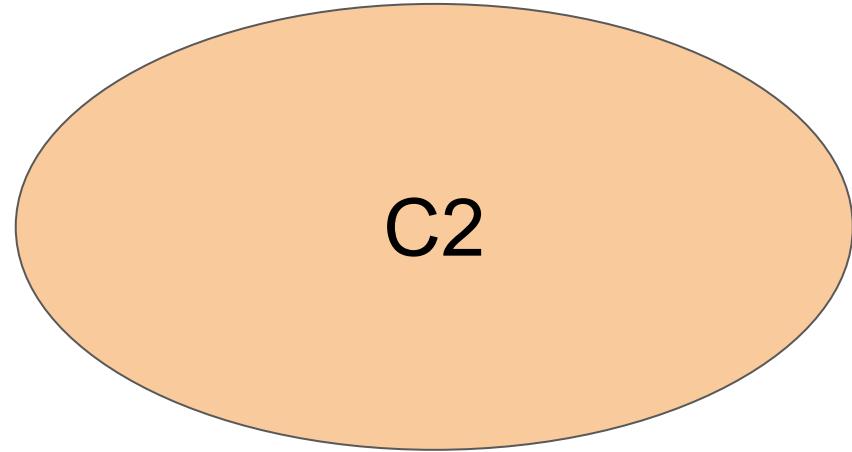
C1q

C1-r/s

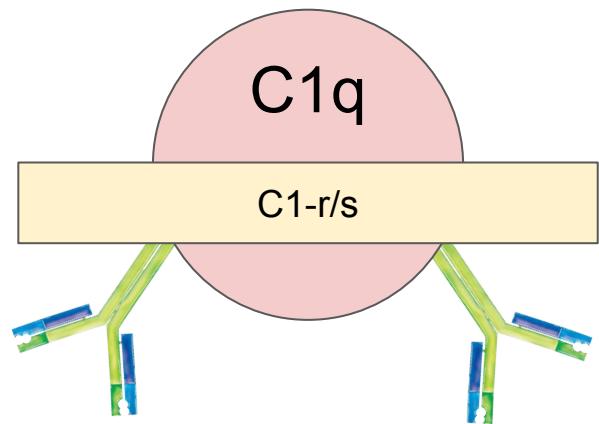


C4

-2

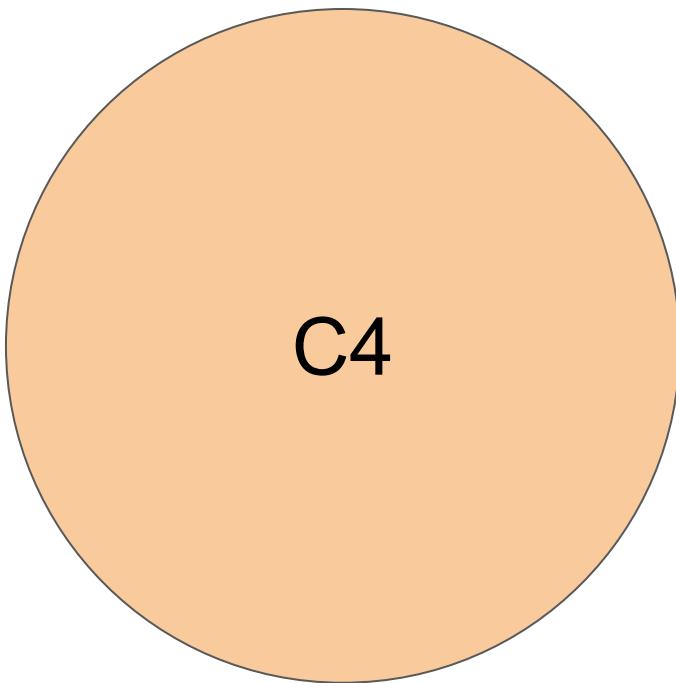


C2

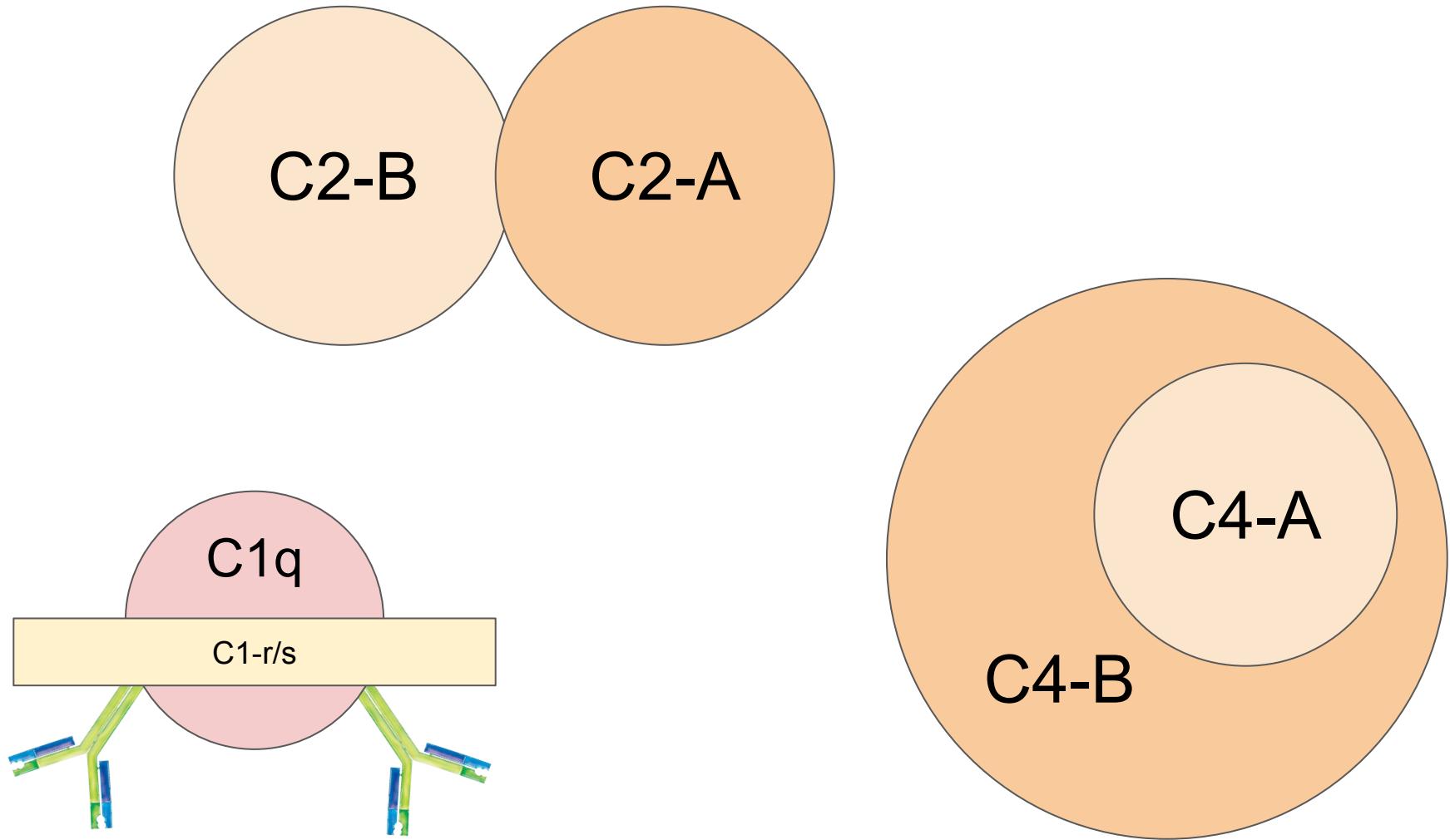


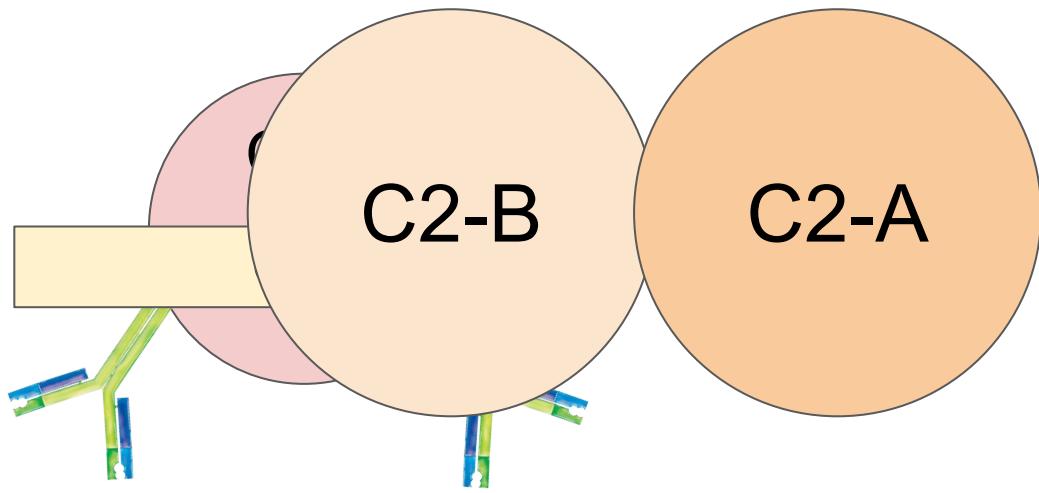
C1q

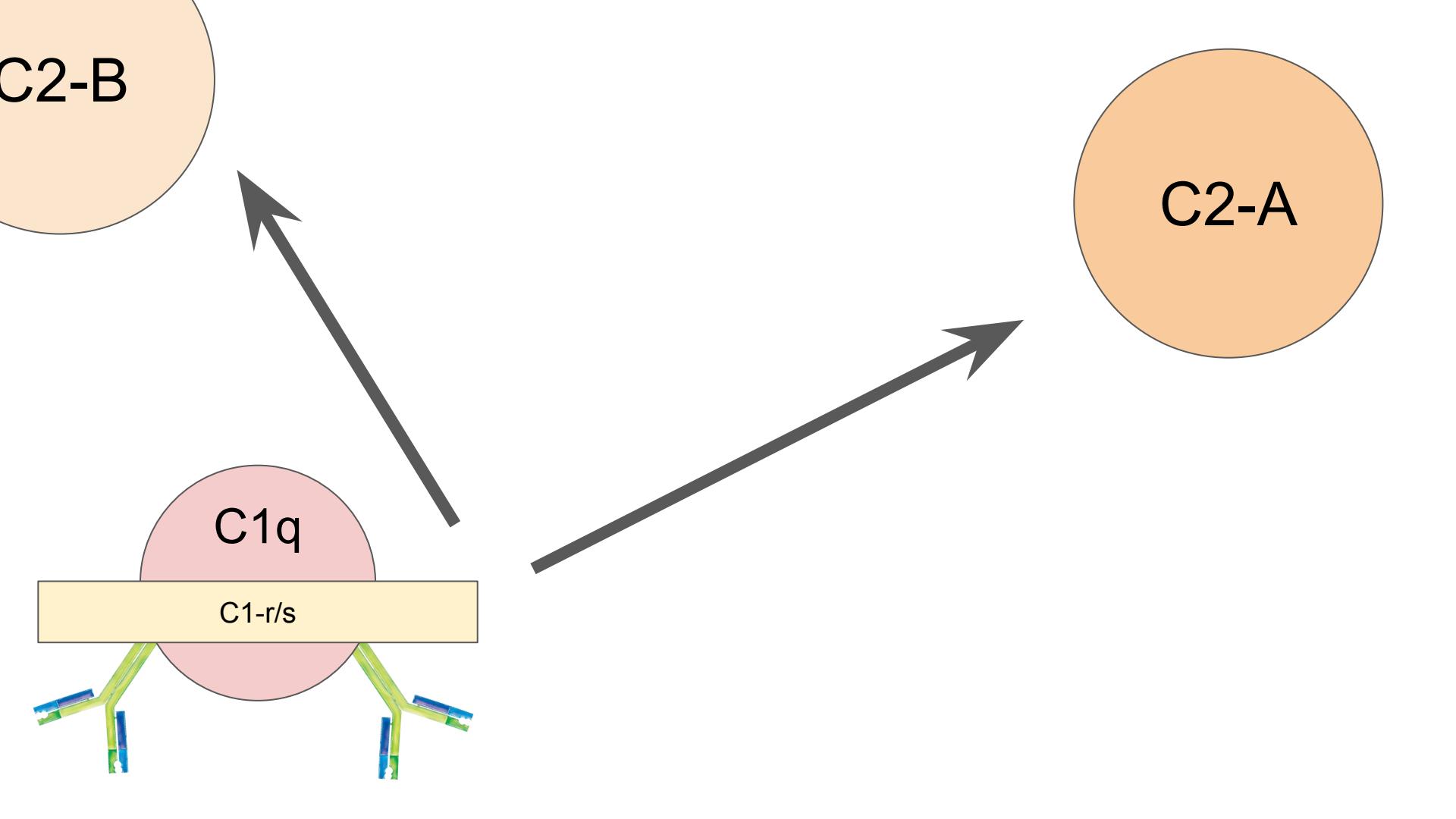
C1-r/s



C4





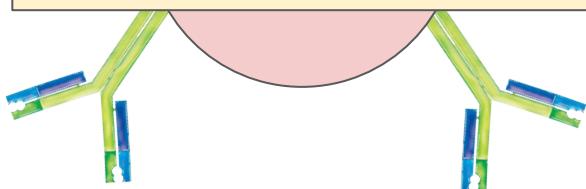


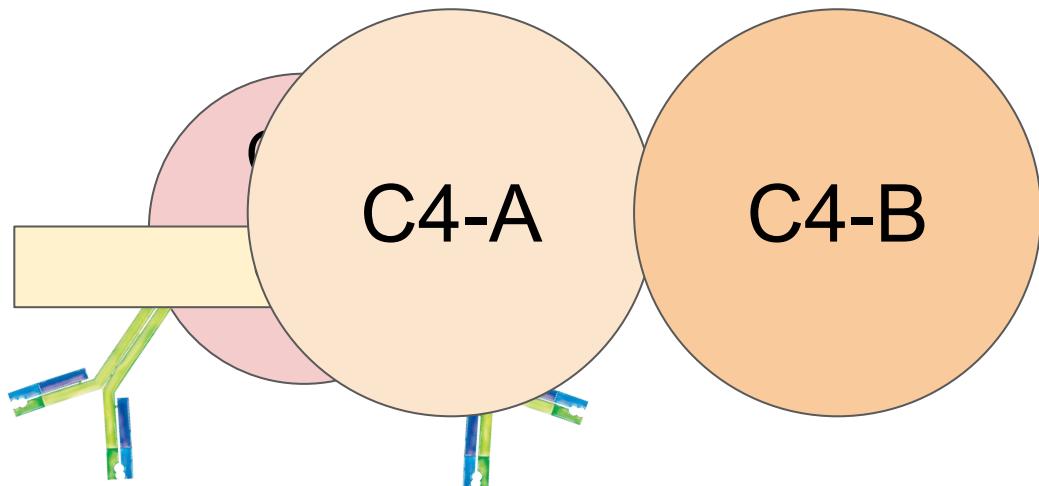
C2-B

C2-A

C1q

C1-r/s





C2-B

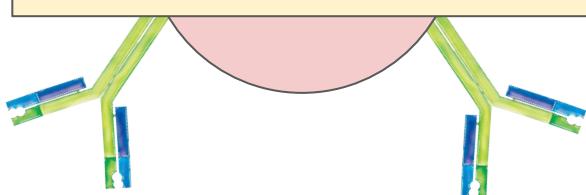
C4-A

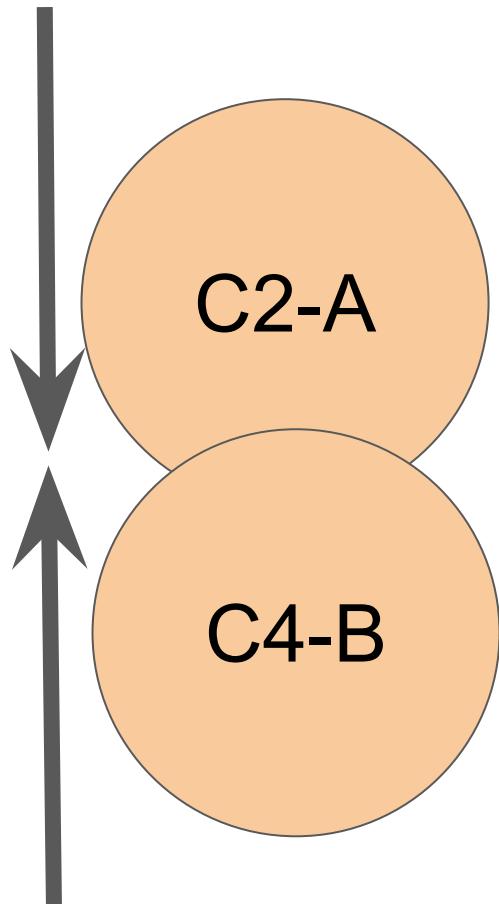
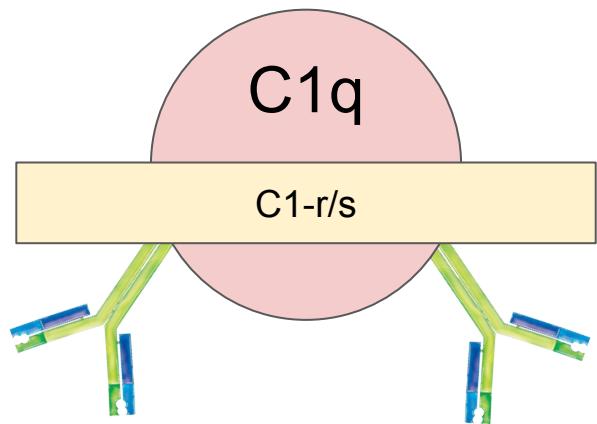
C2-A

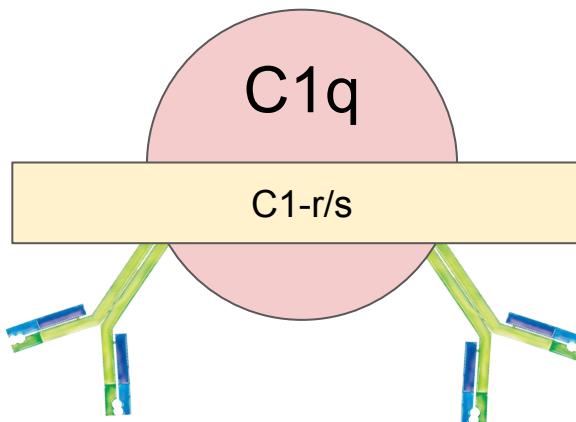
C4-B

C1q

C1-r/s



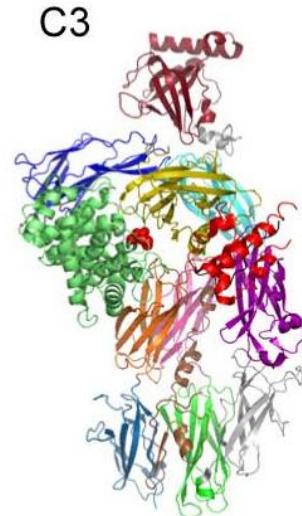




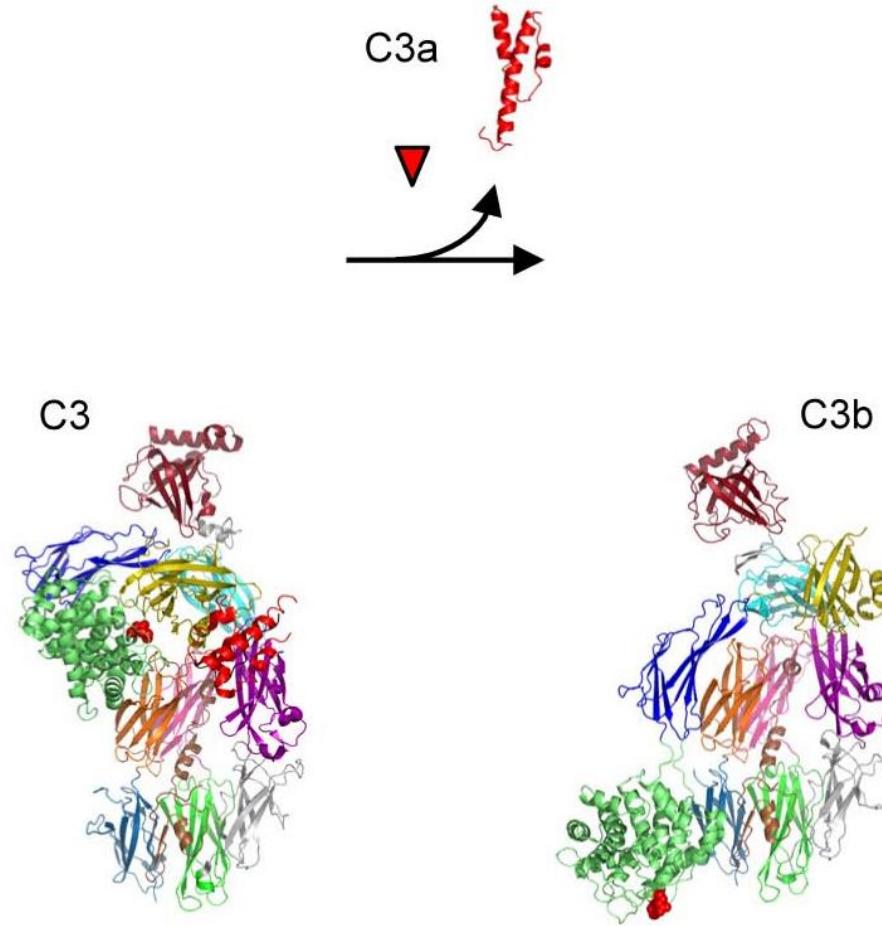
The diagram illustrates the C4bC2a complex. It features a large, light orange rectangular box on the right side containing the text "C4bC2a Complex". To the left of this box, there is a schematic representation of the complex. At the top, a pink circle labeled "C1q" is positioned above a yellow horizontal bar labeled "C1-r/s". Below this, two green Y-shaped structures represent the C4b2a subunits, each with blue and white components at their tips.

**C4bC2a
Complex**

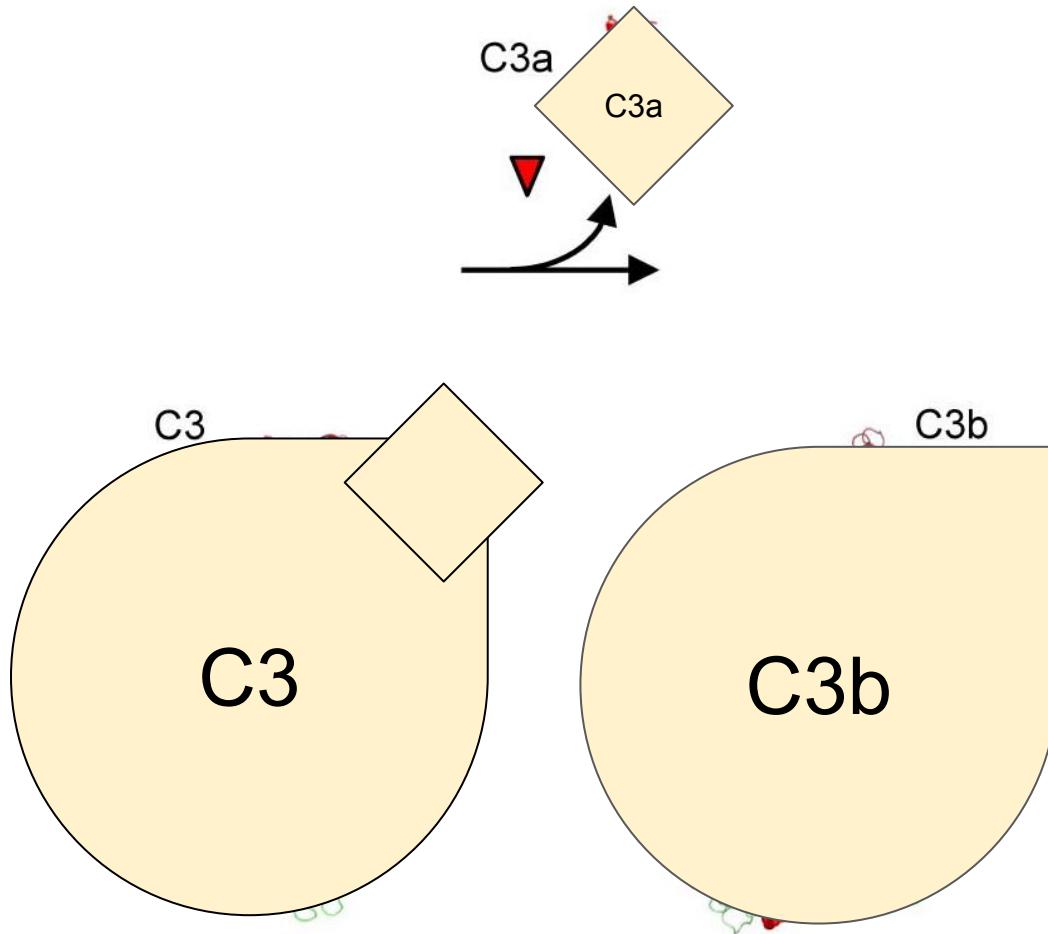
C4bC2a
Complex



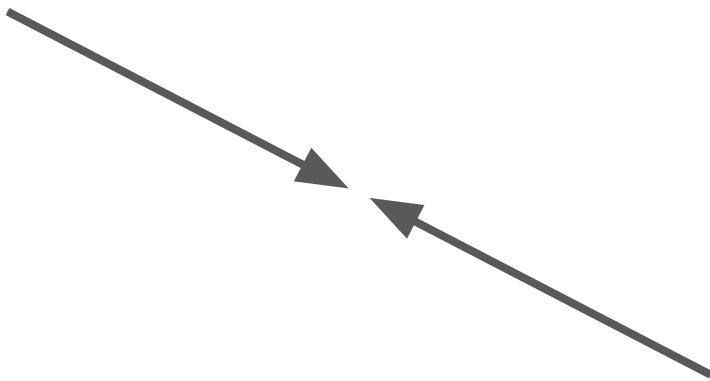
C4bC2a Complex



C4bC2a Complex

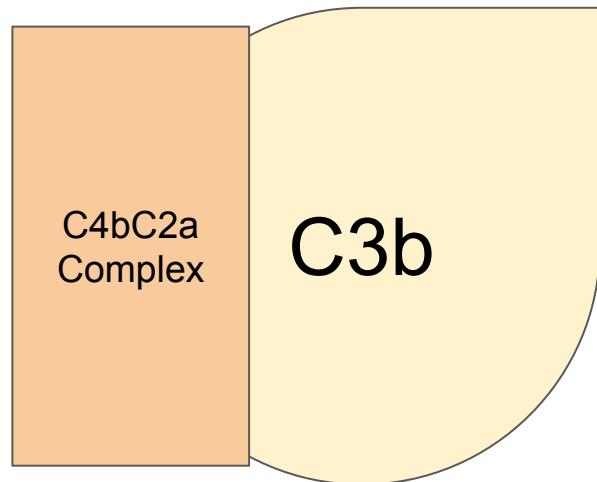


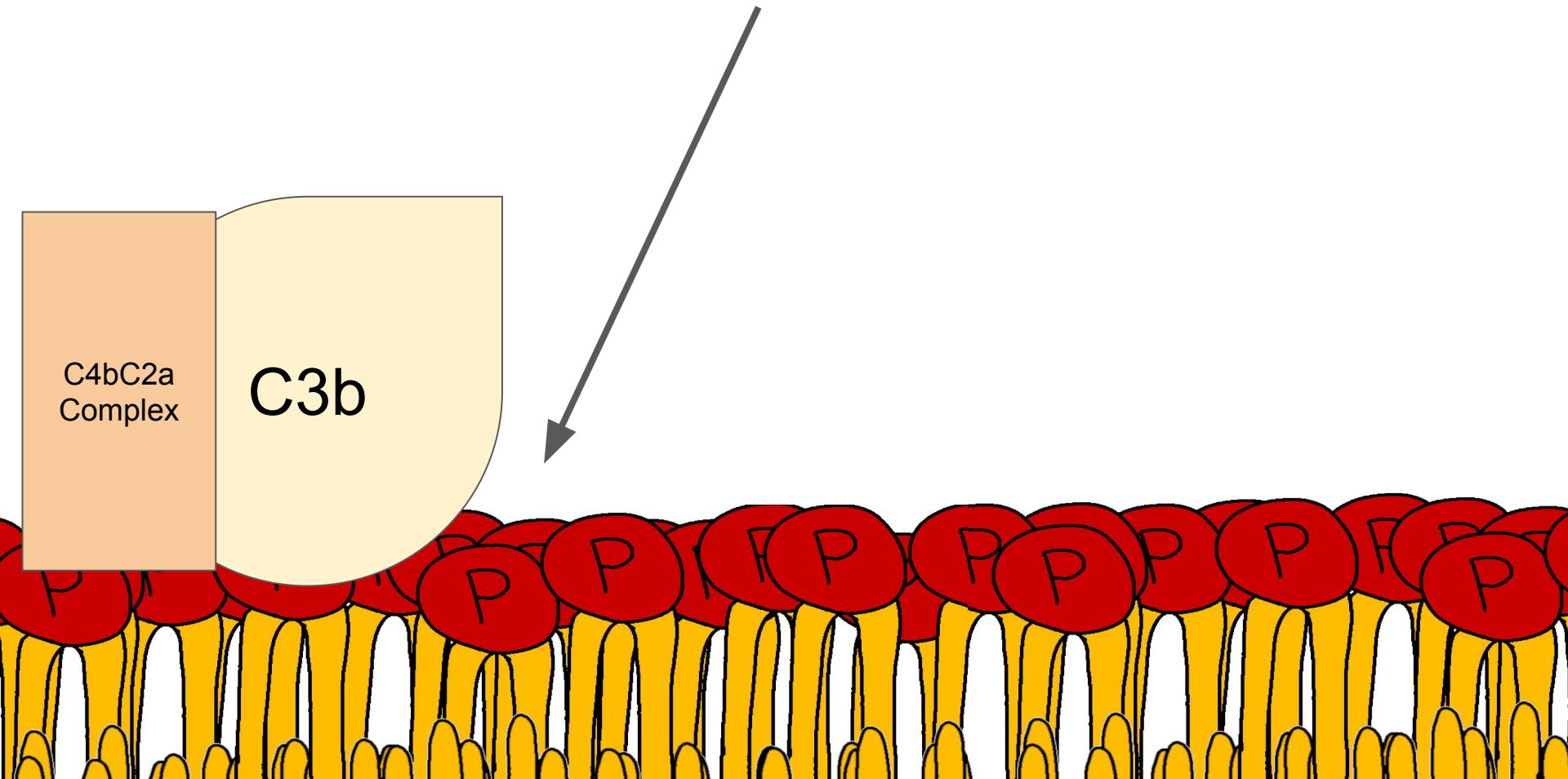
**C4bC2a
Complex**



C3b

**C4b2a3b
Convertase**





C4bC2a
Complex

C3b

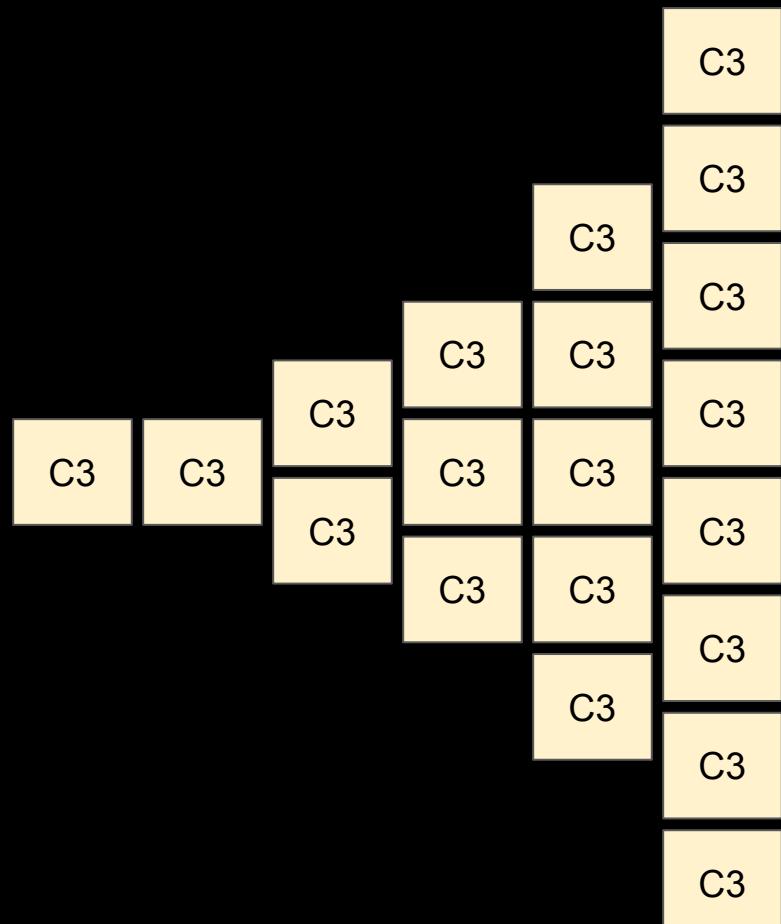
Initiation

Activation

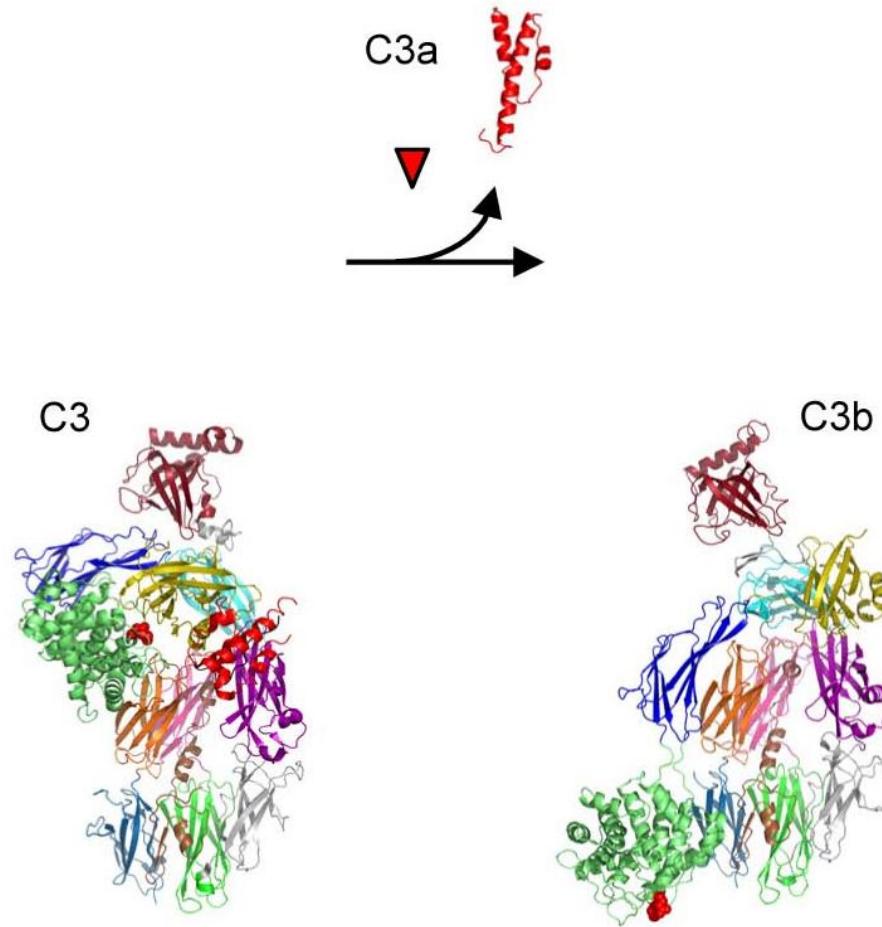
Amplification

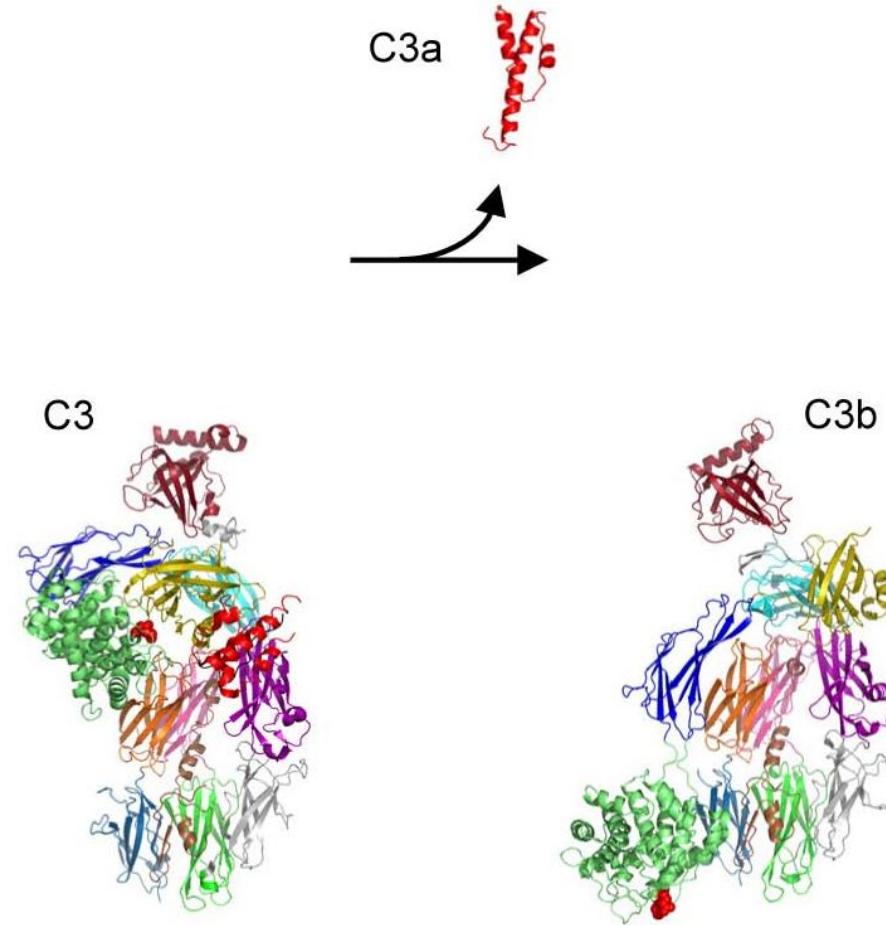
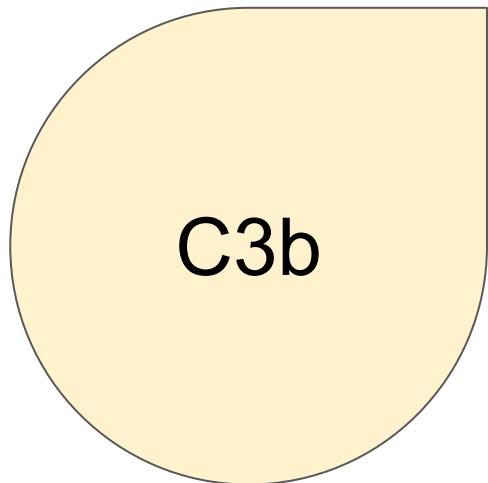
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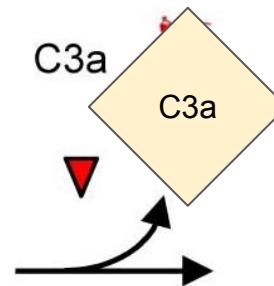
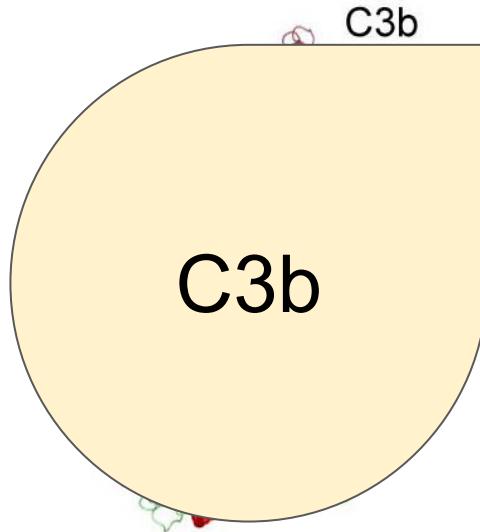
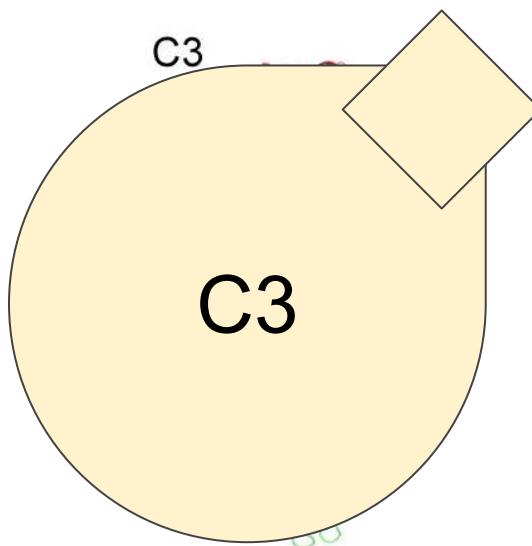
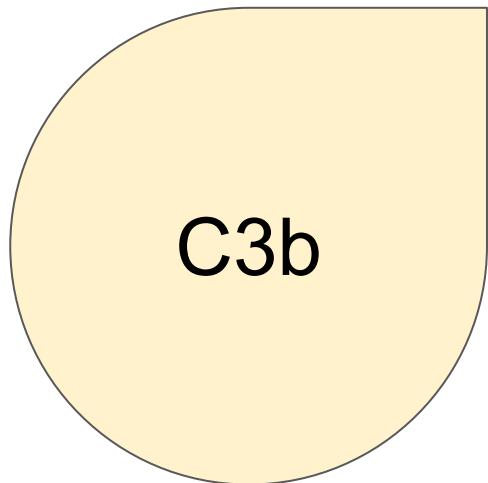
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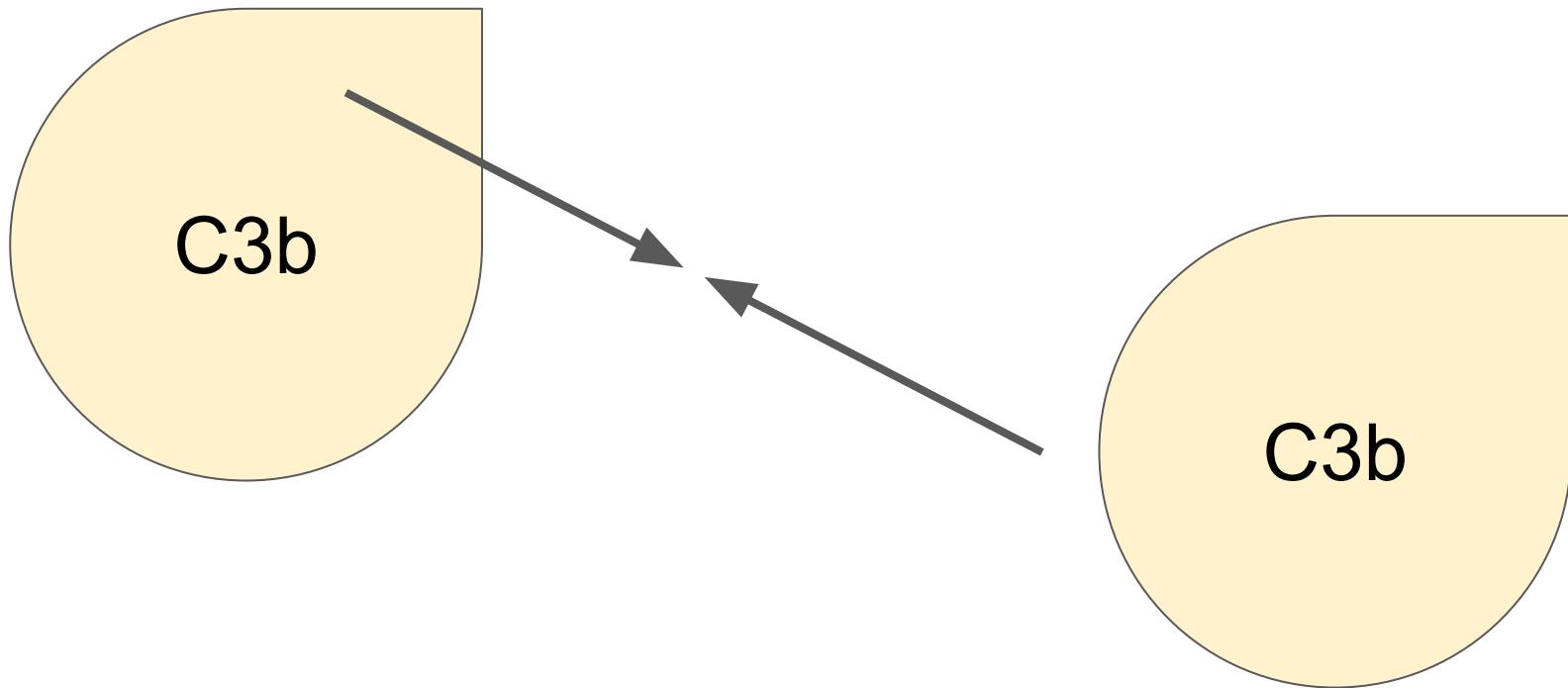


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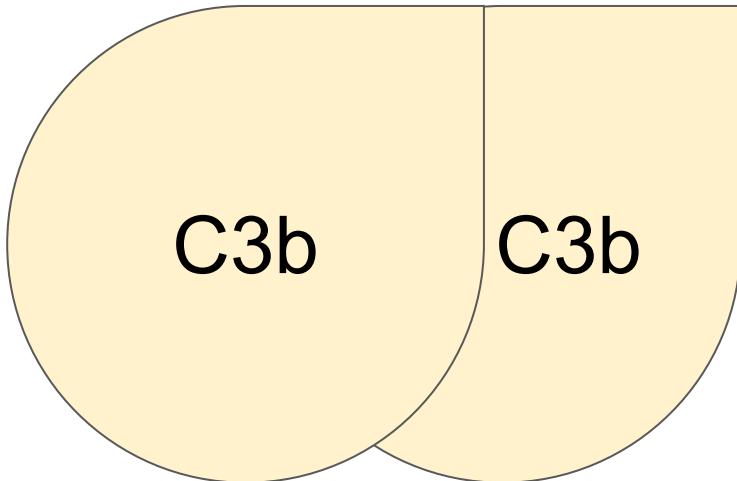






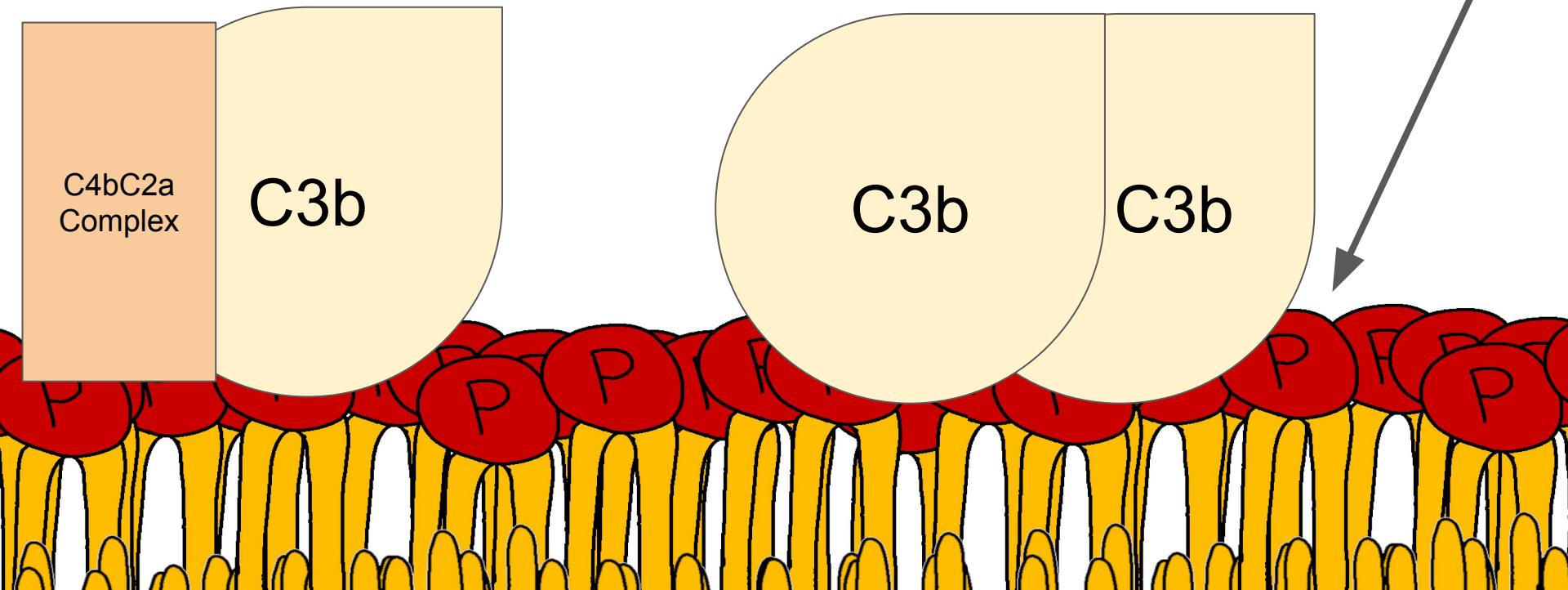


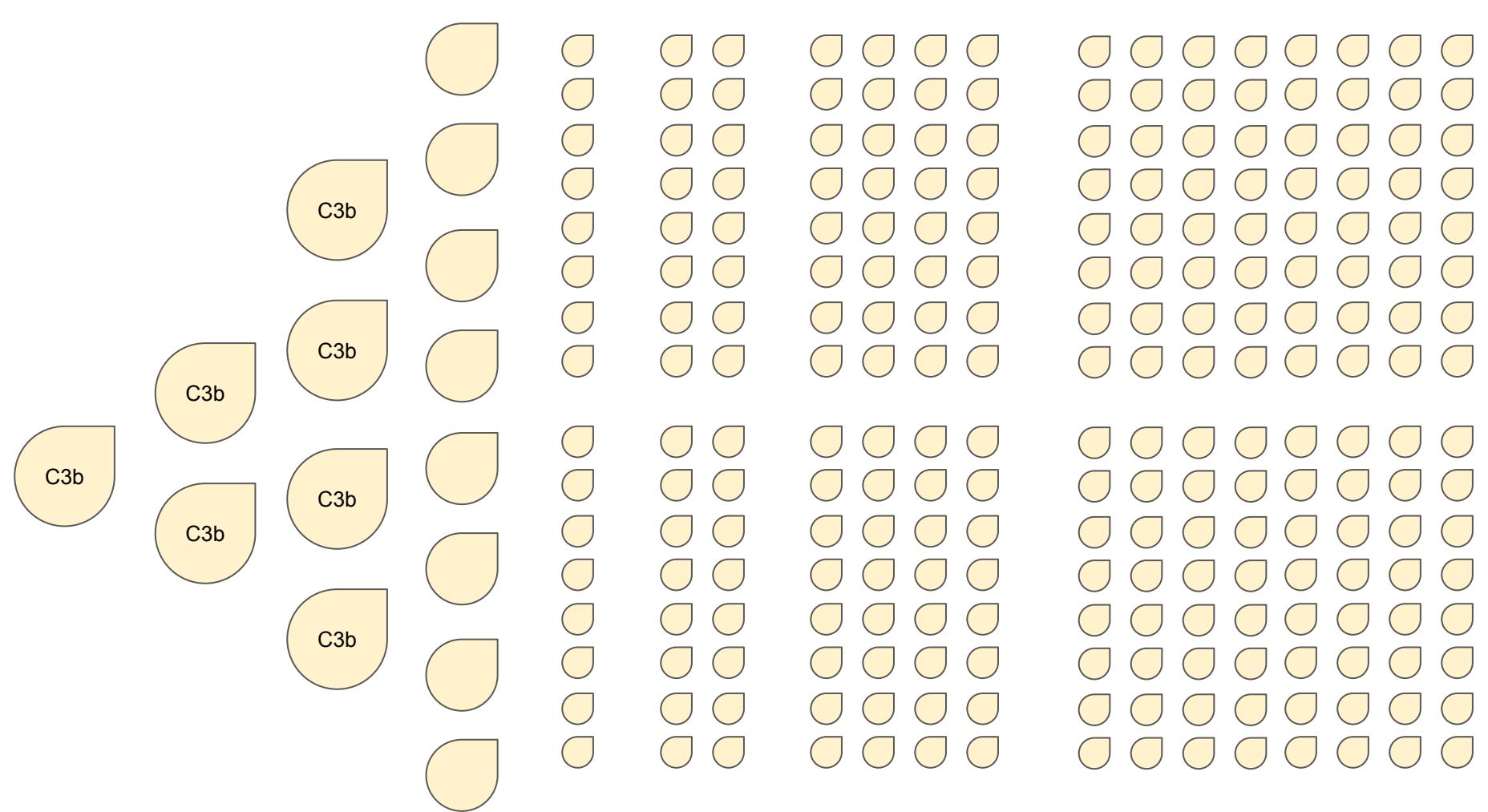
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Convertase

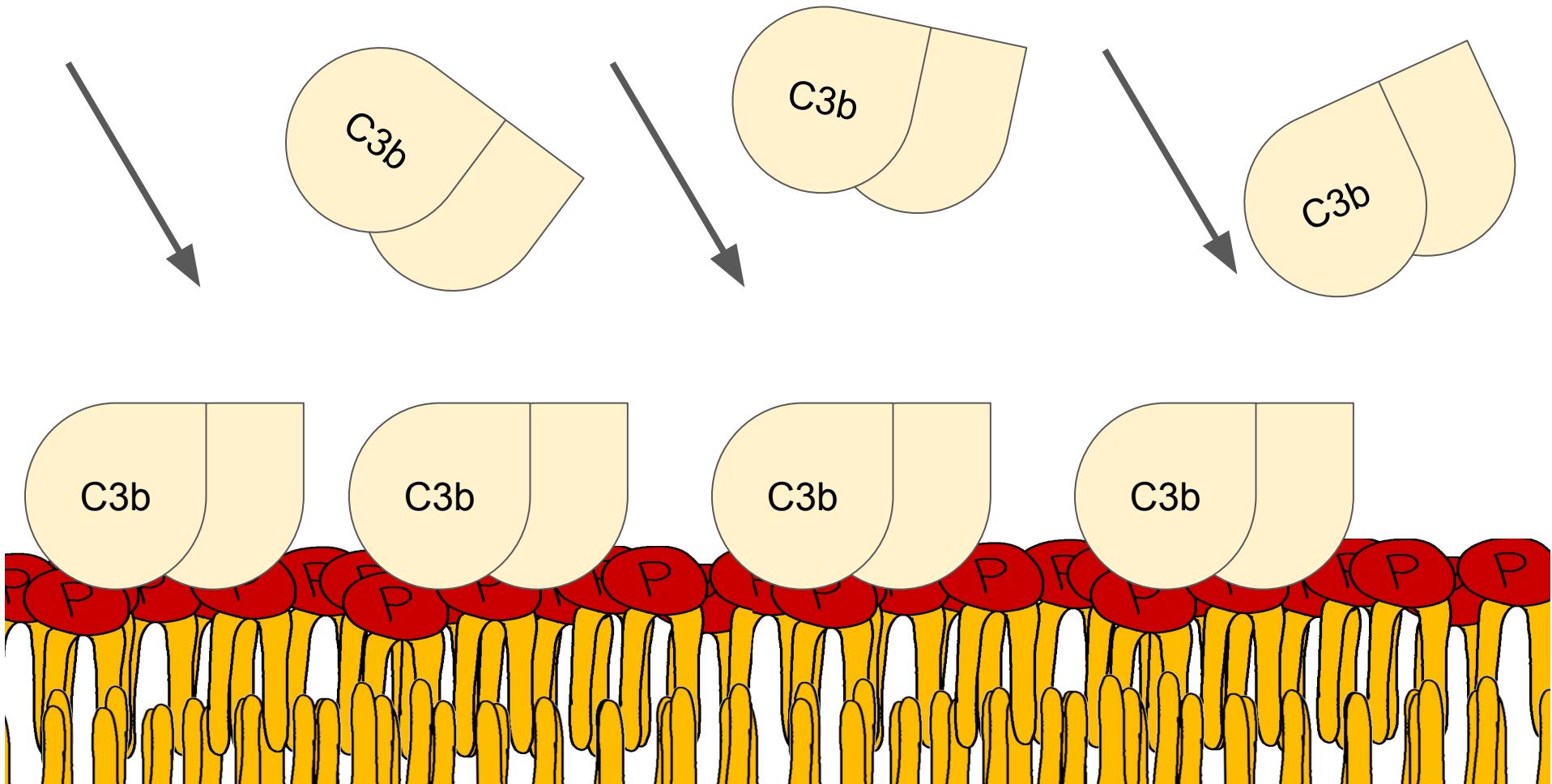


Activation

Amplification

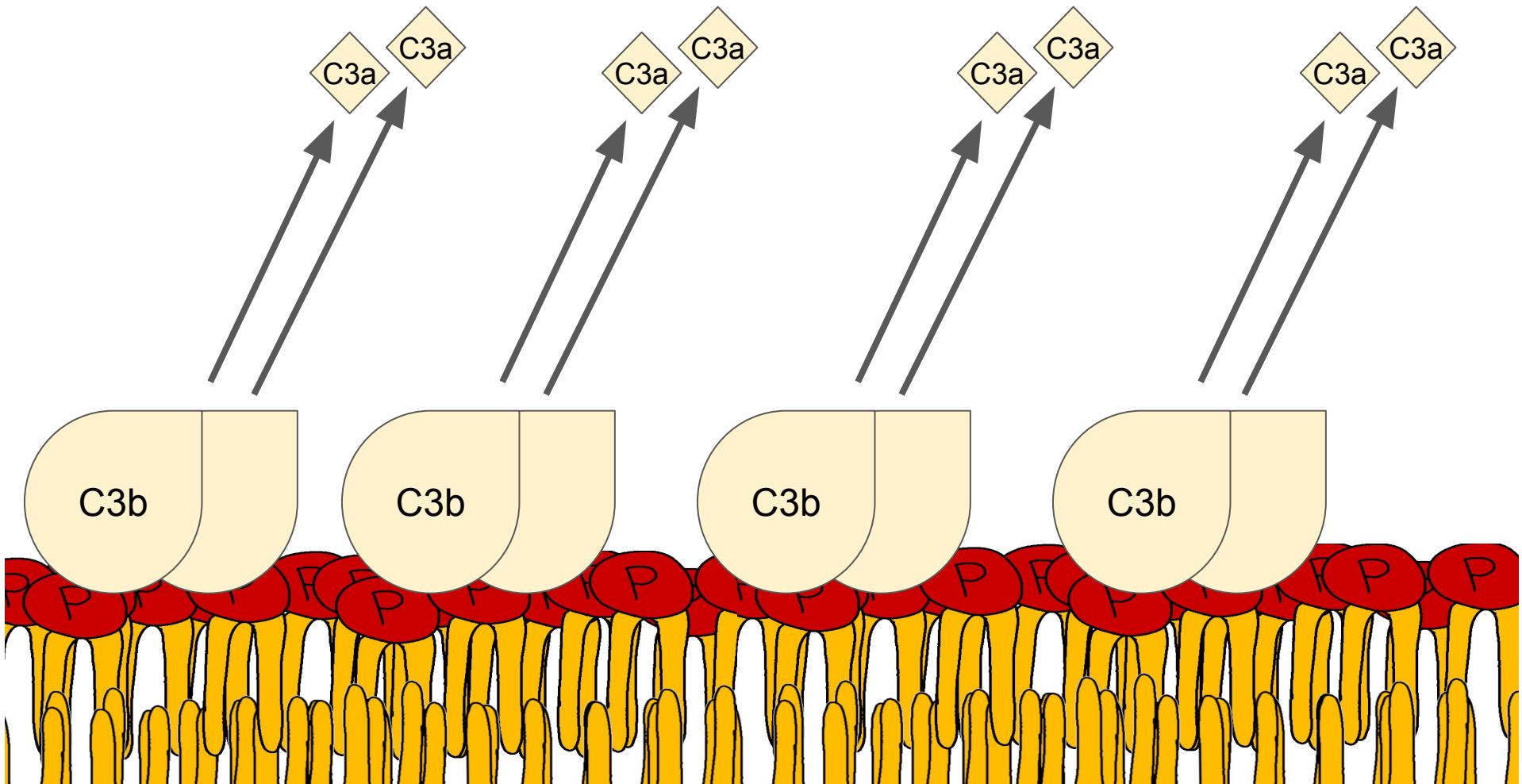




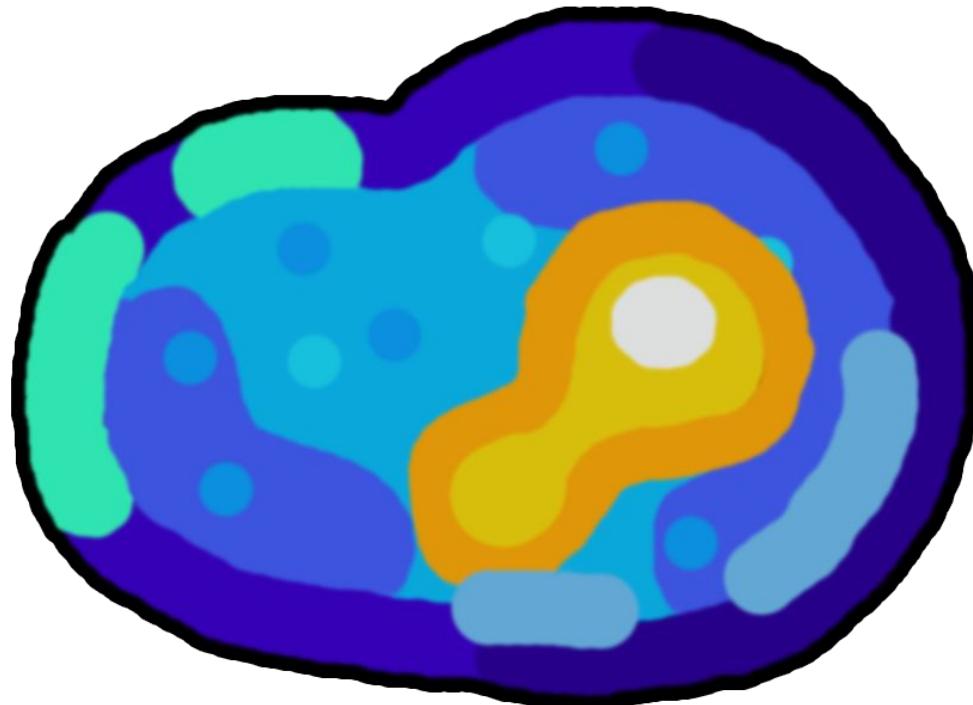


Bacteria: finally, the bloodstream. time t-
Complement system attacks
Bacteria:





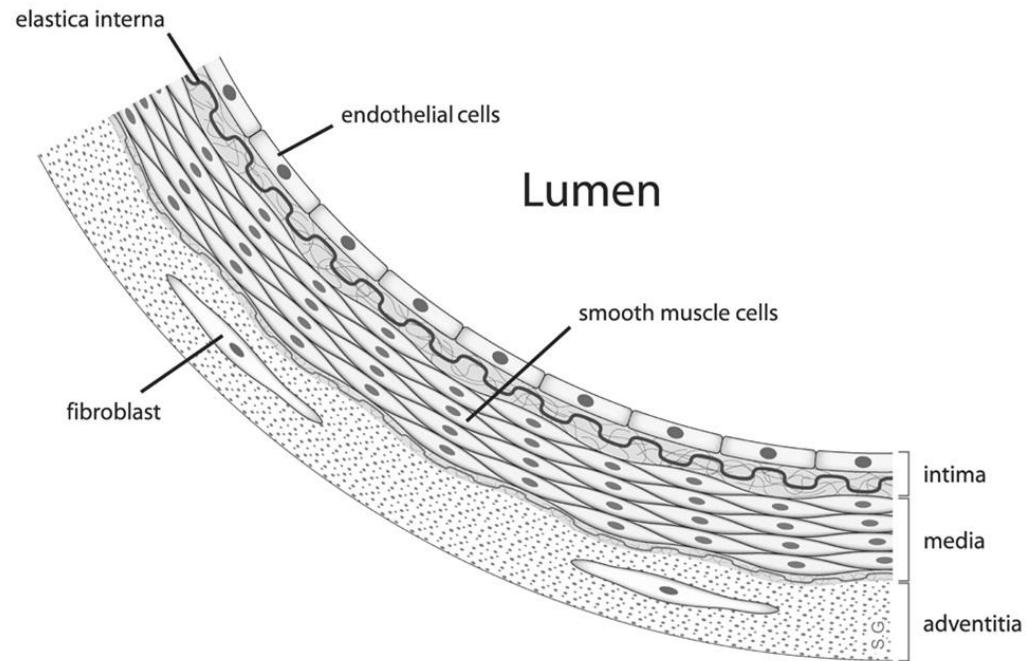
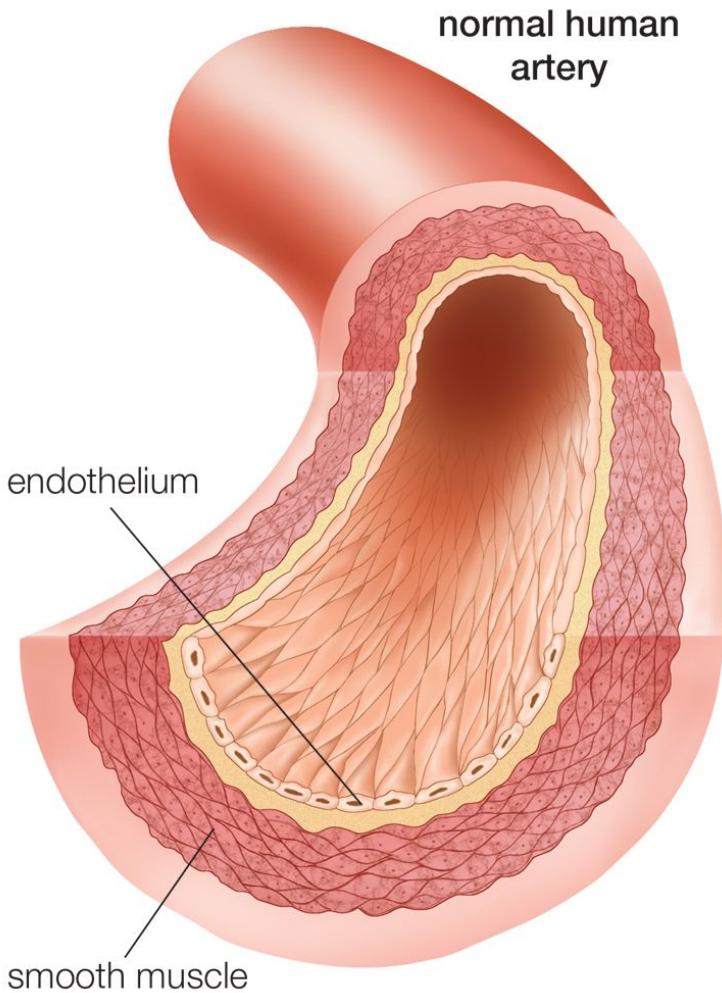
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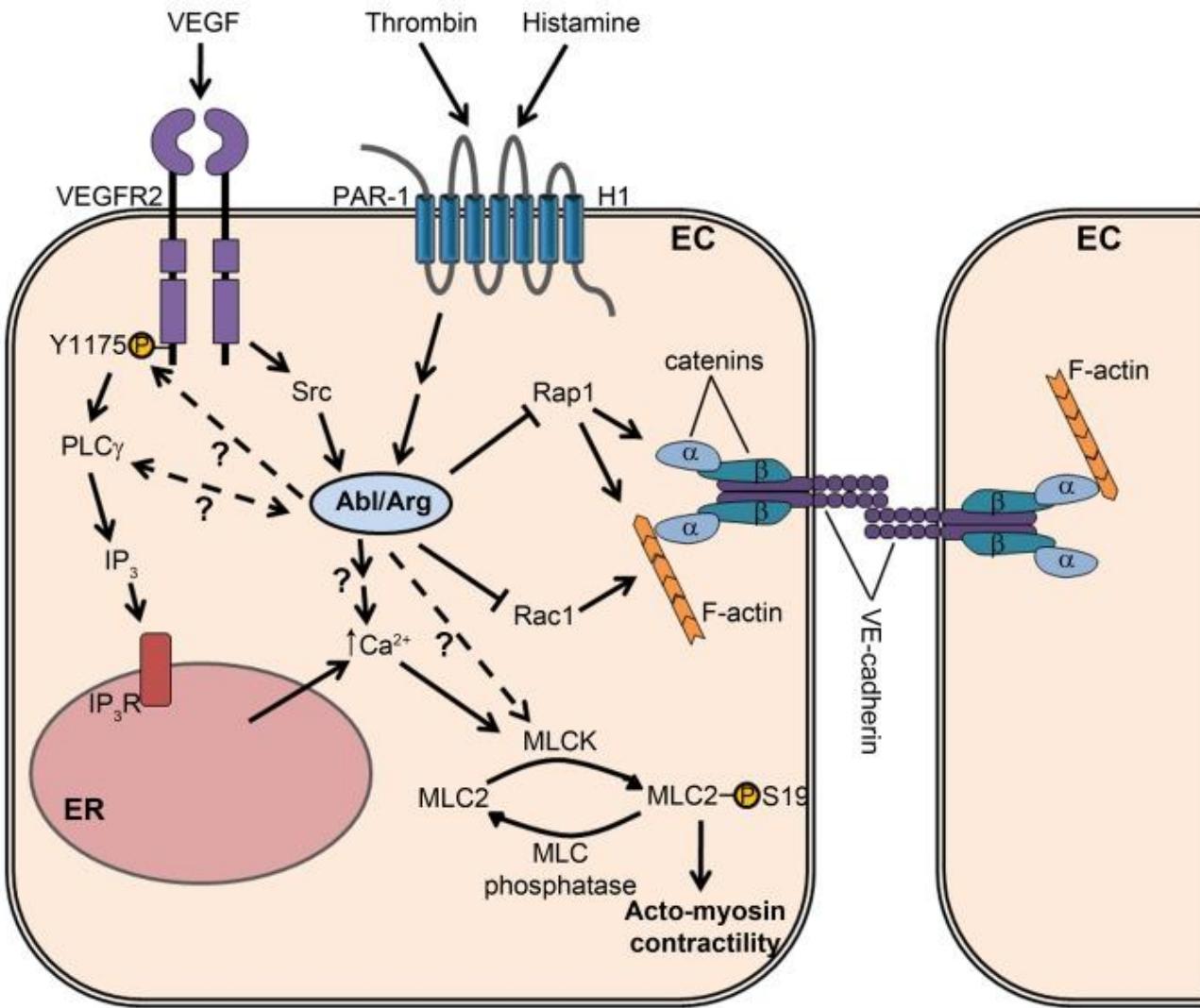


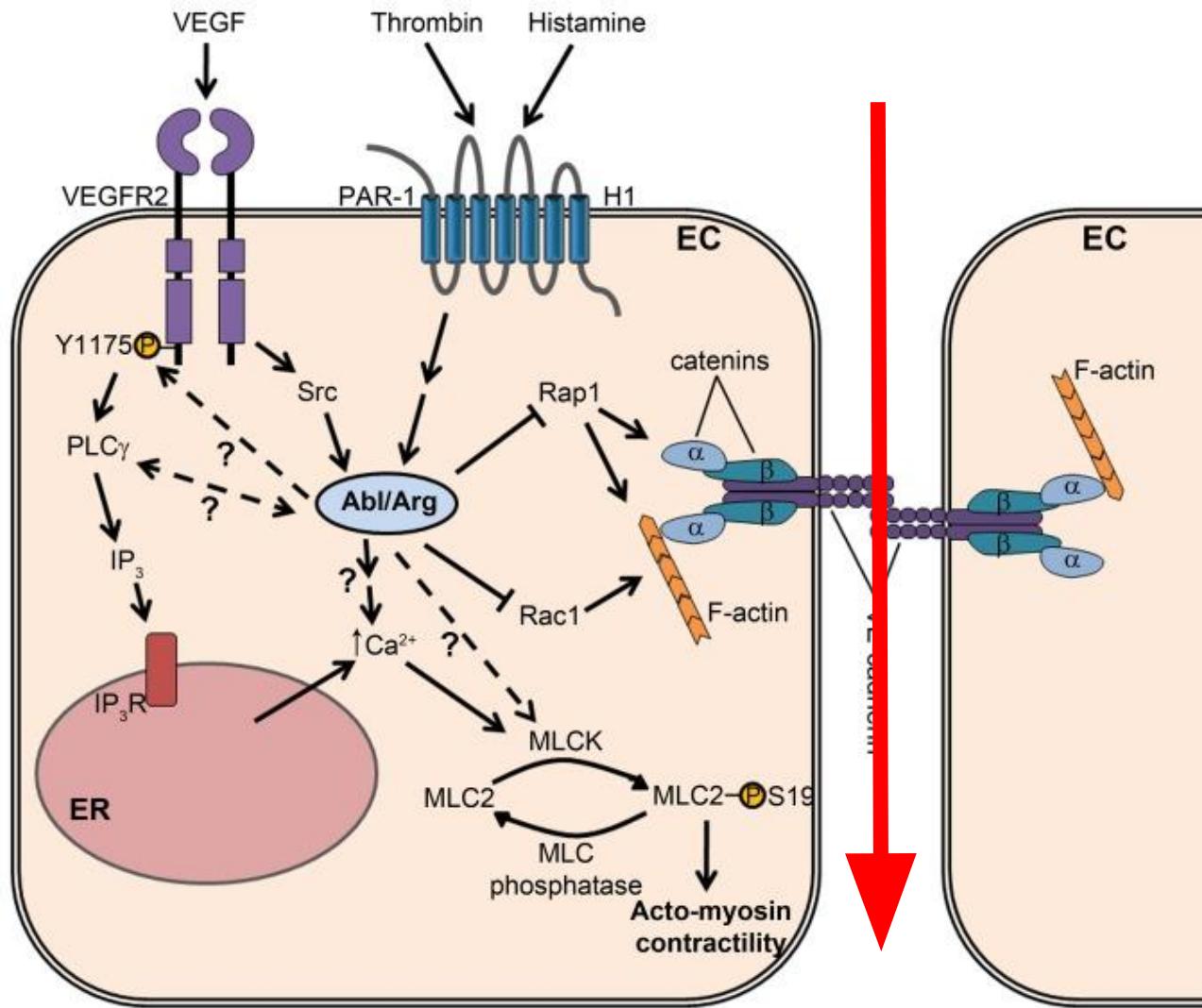
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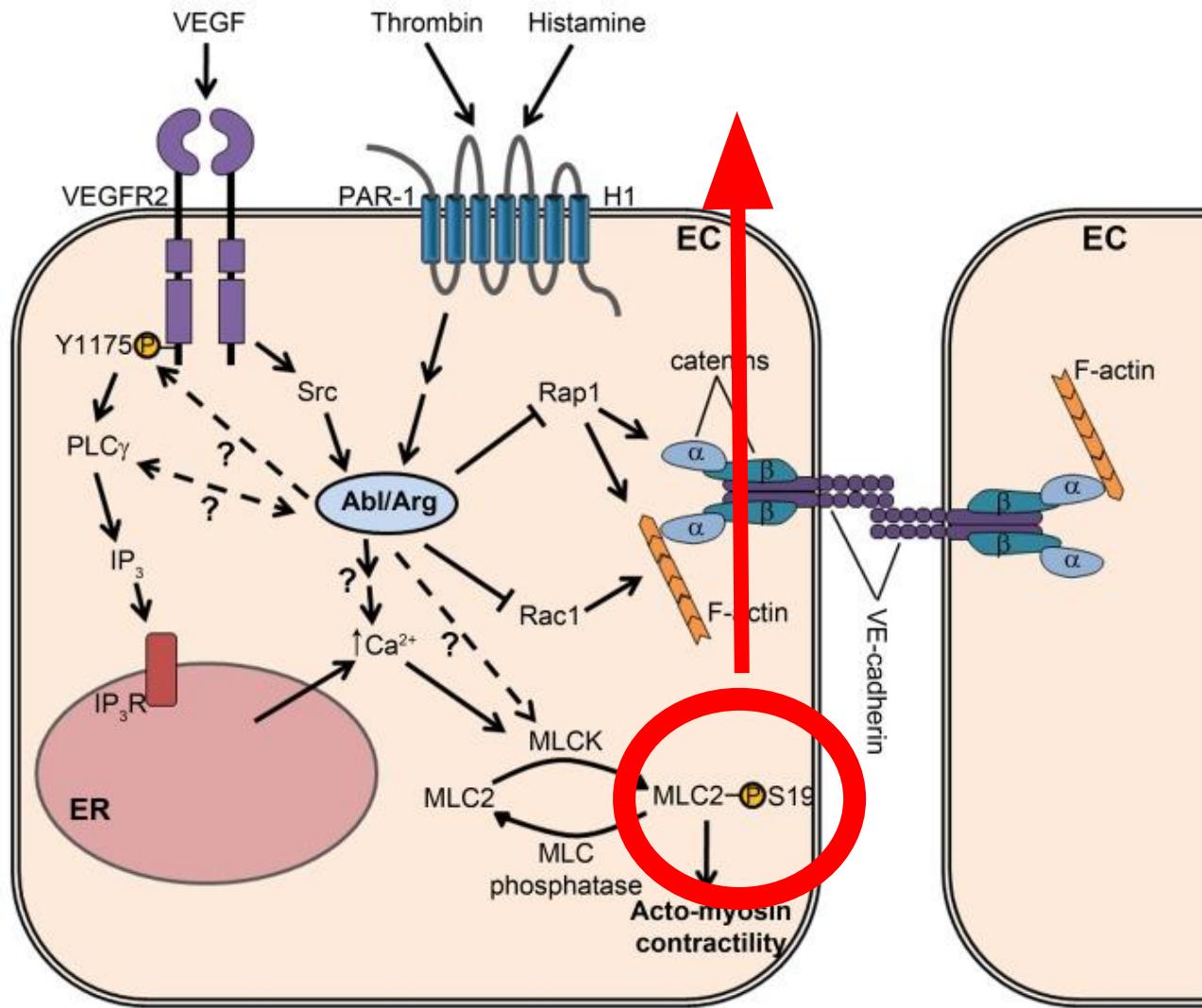


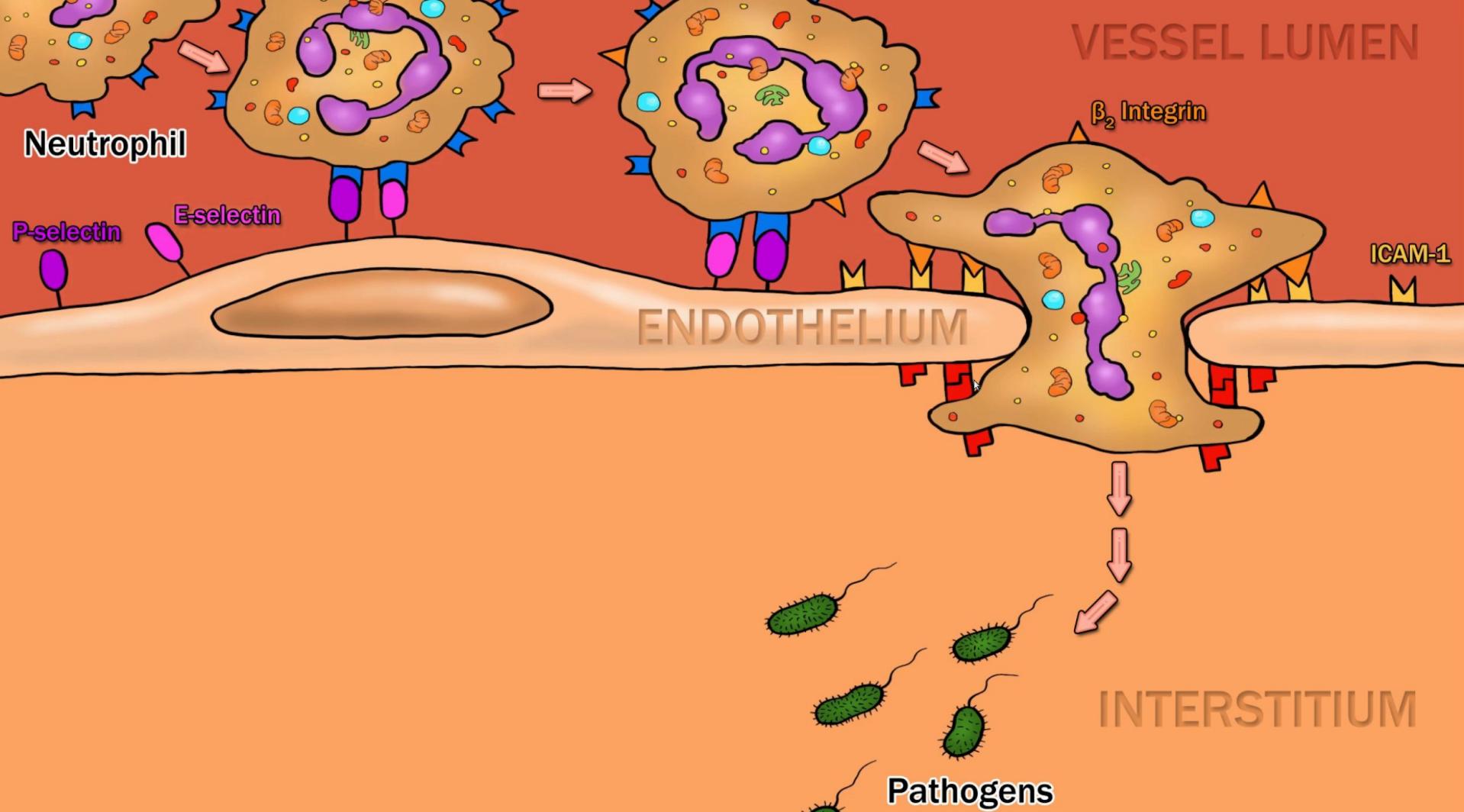


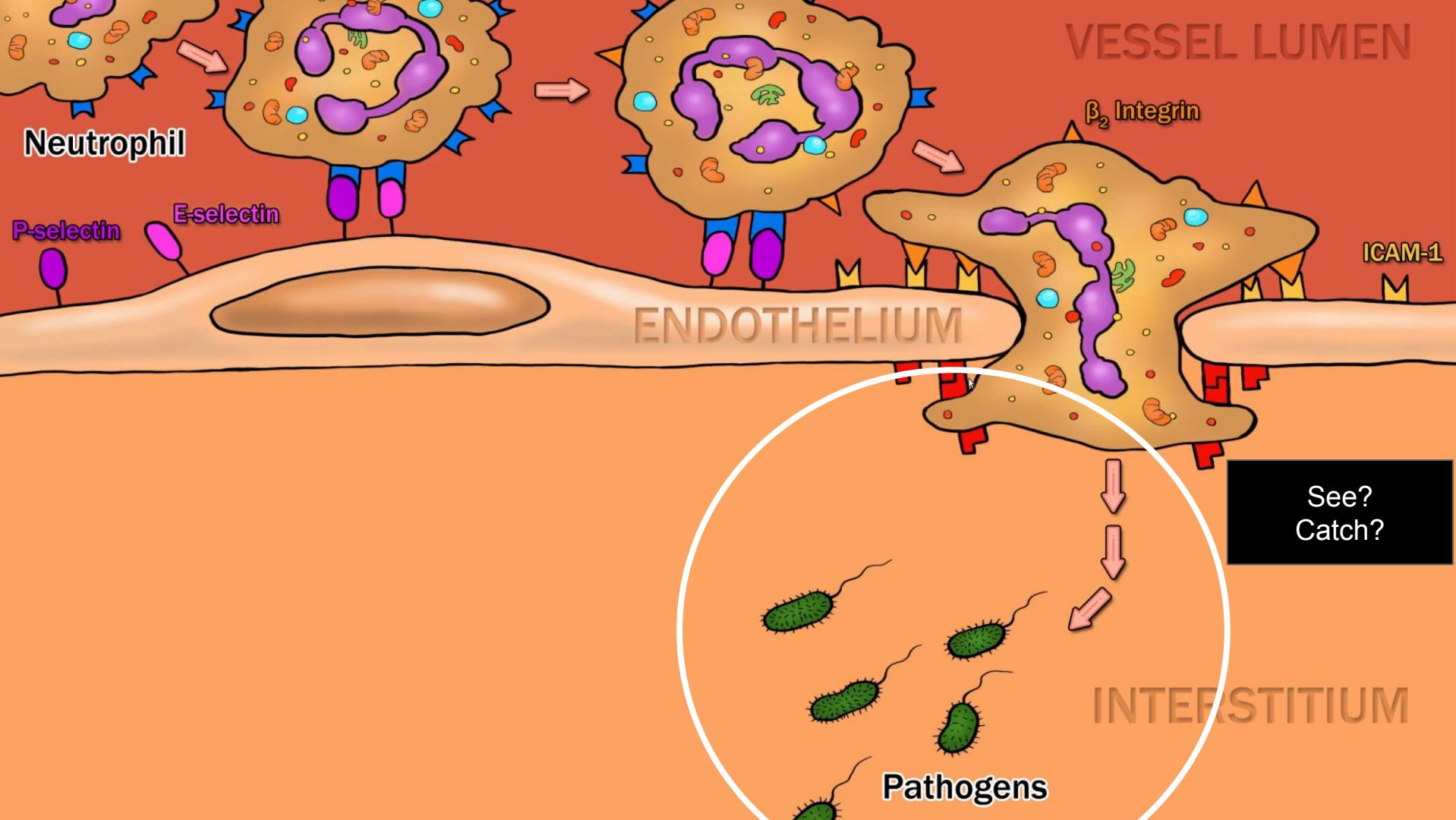












Initiation

Activation

Amplification

Termination

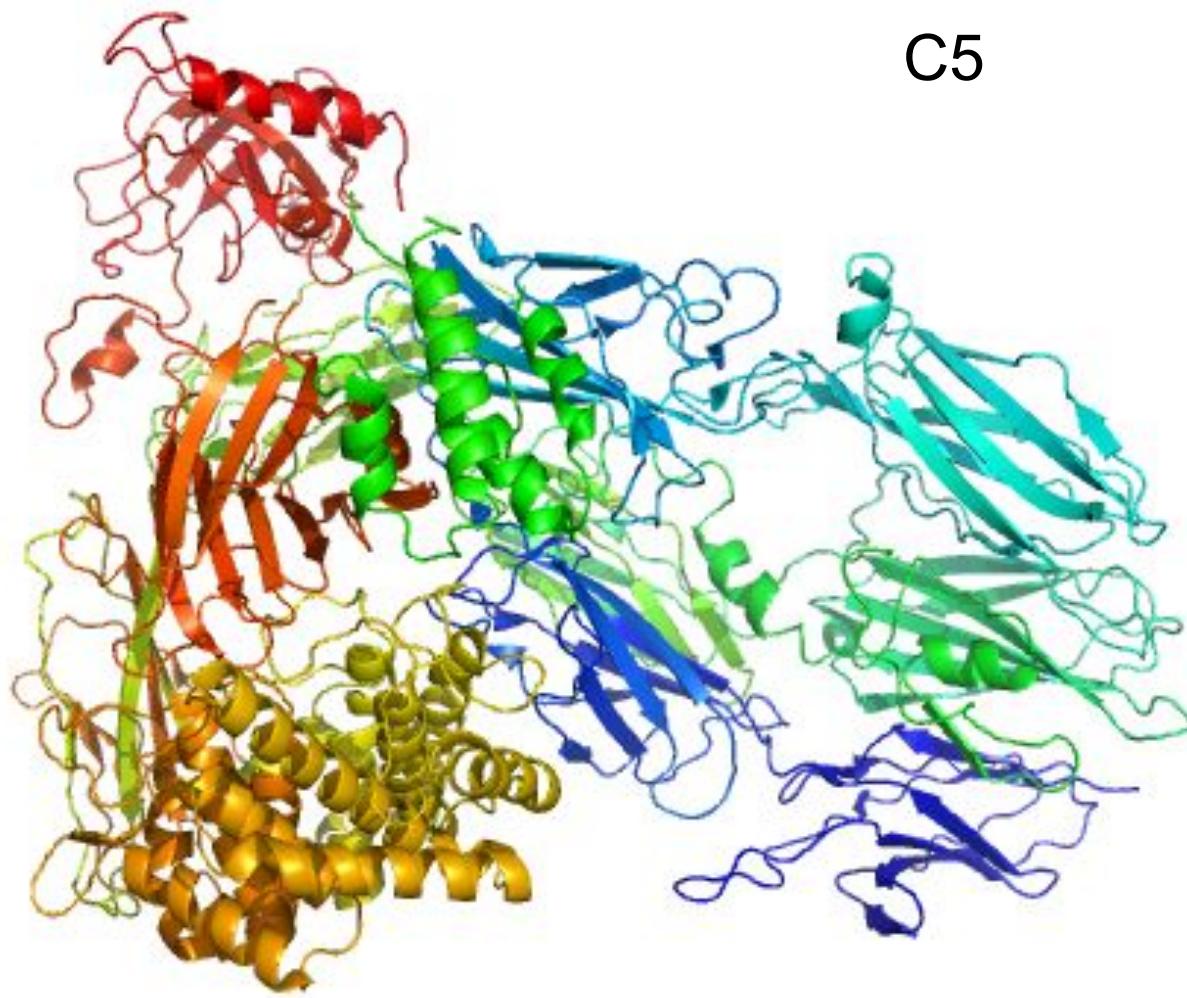
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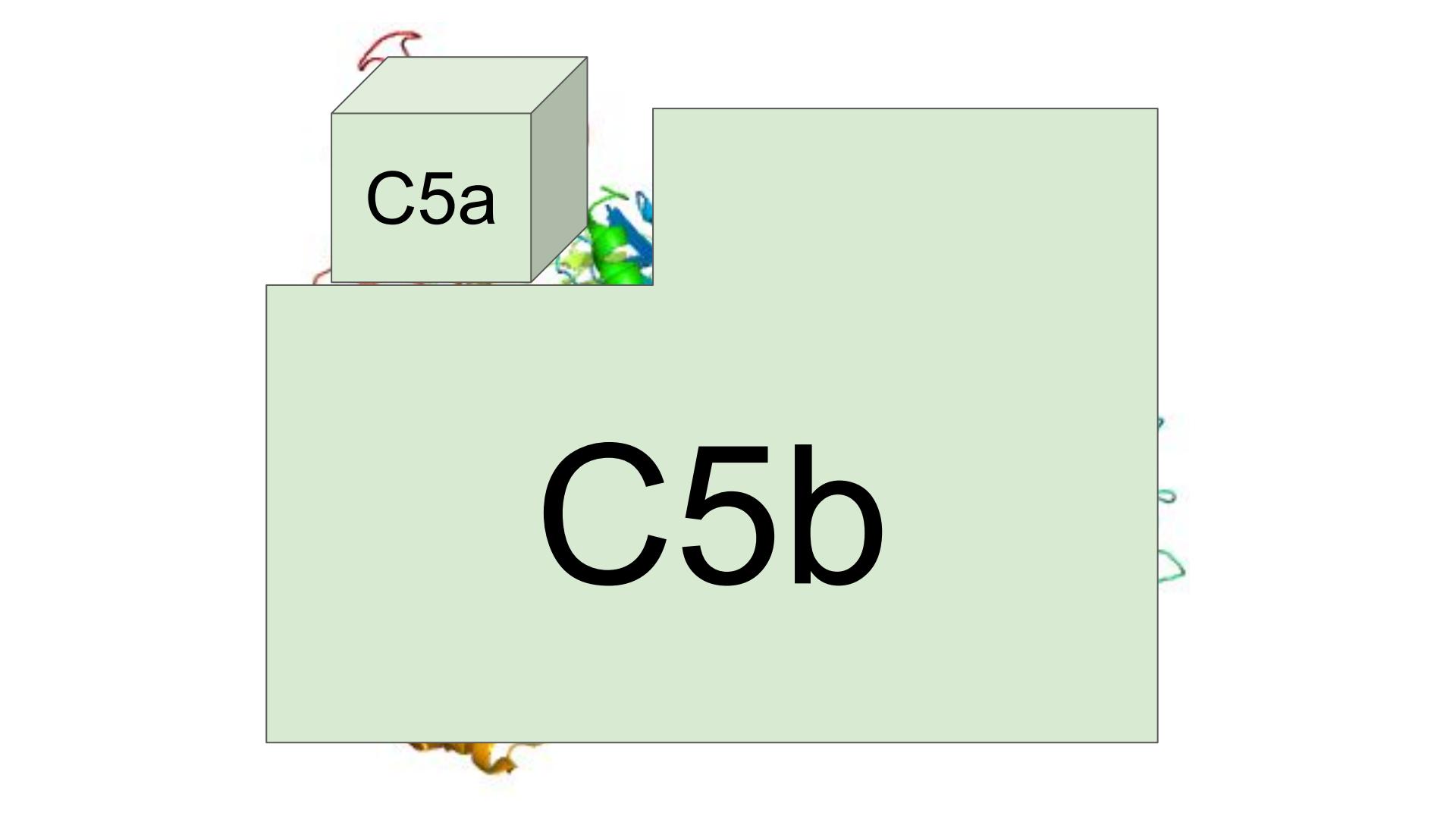
C5

MAC



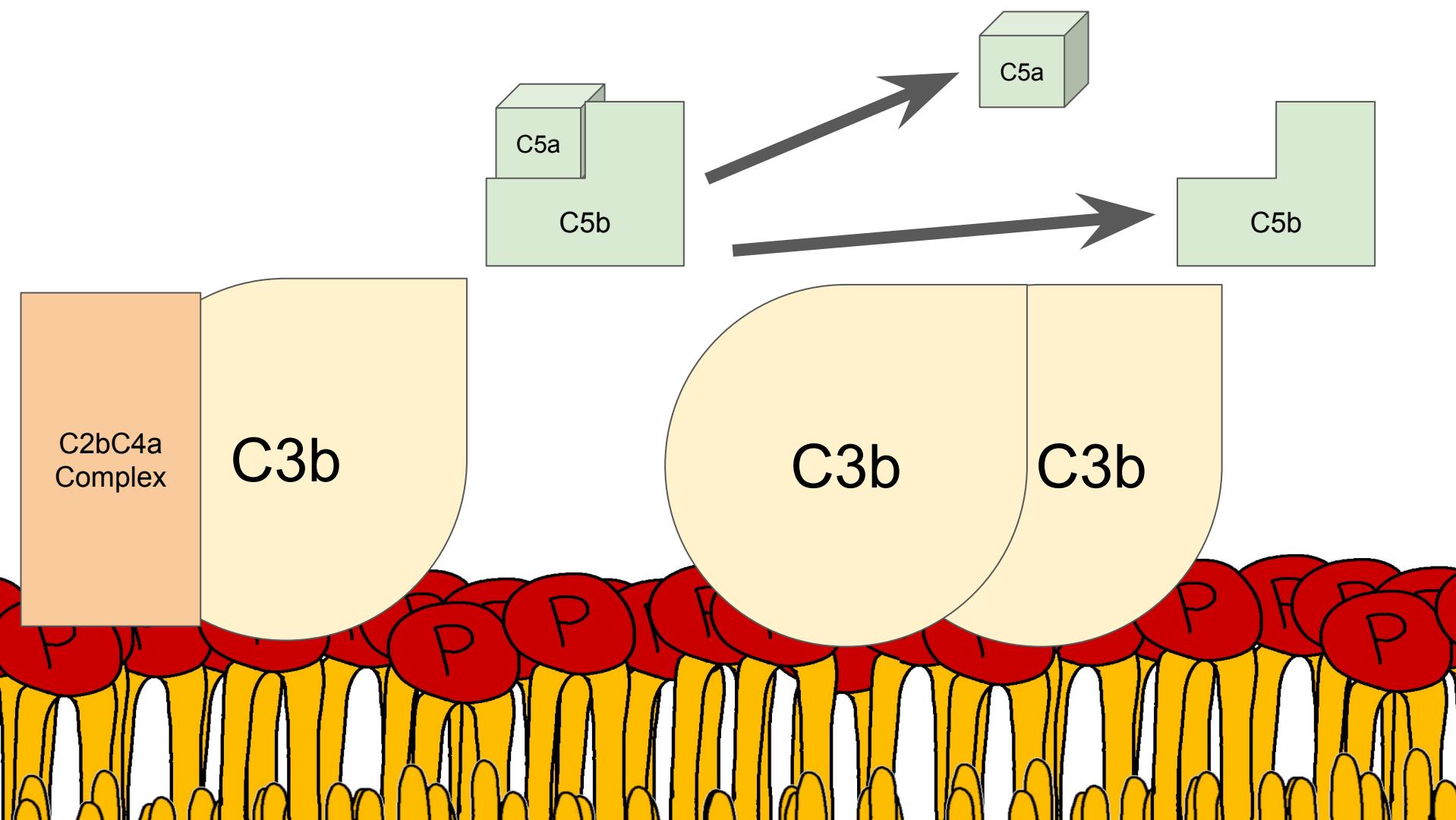
C5

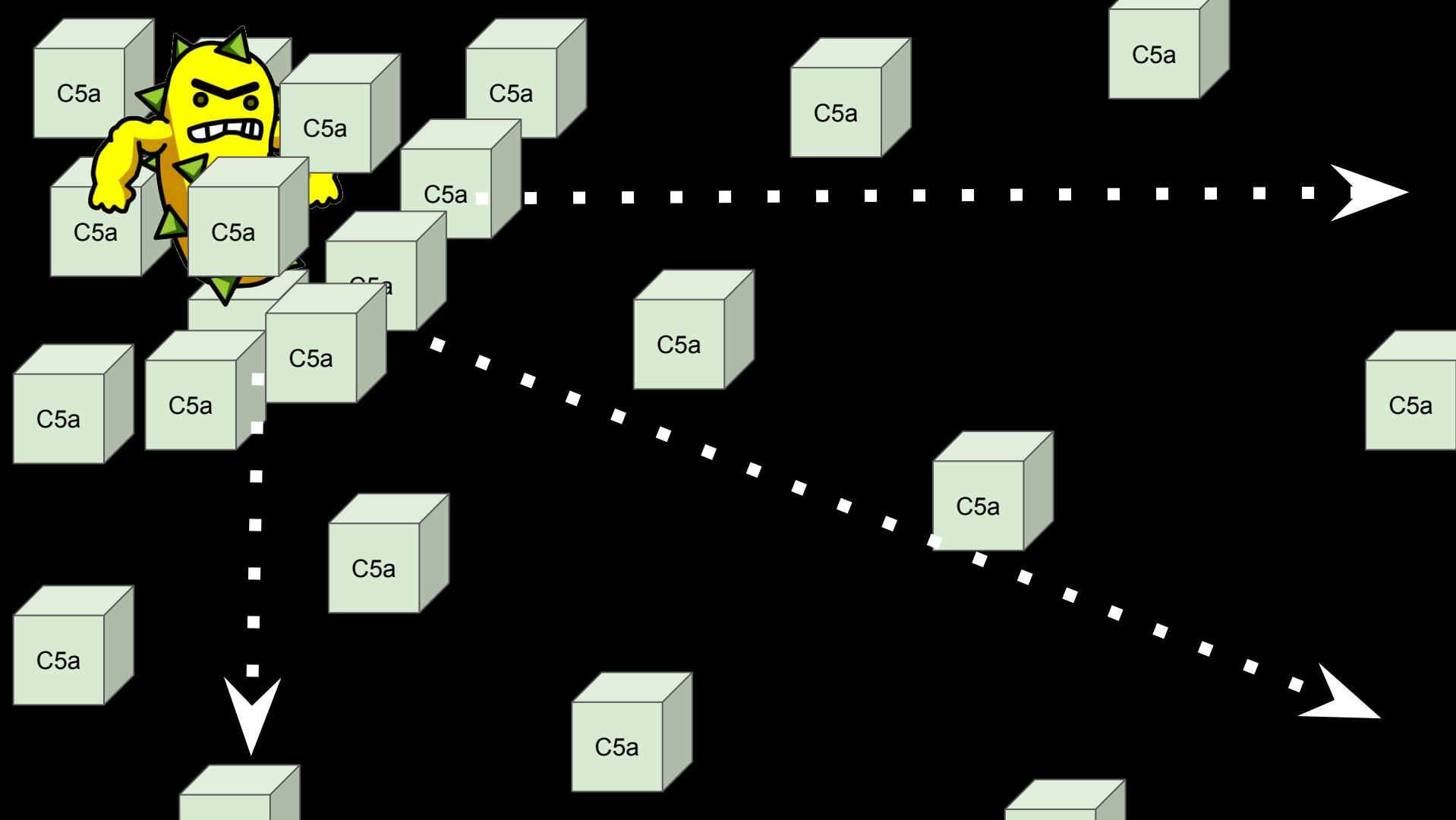




C5a

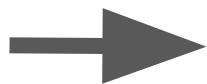
C5b







C5a



Macrophage



Macrophage



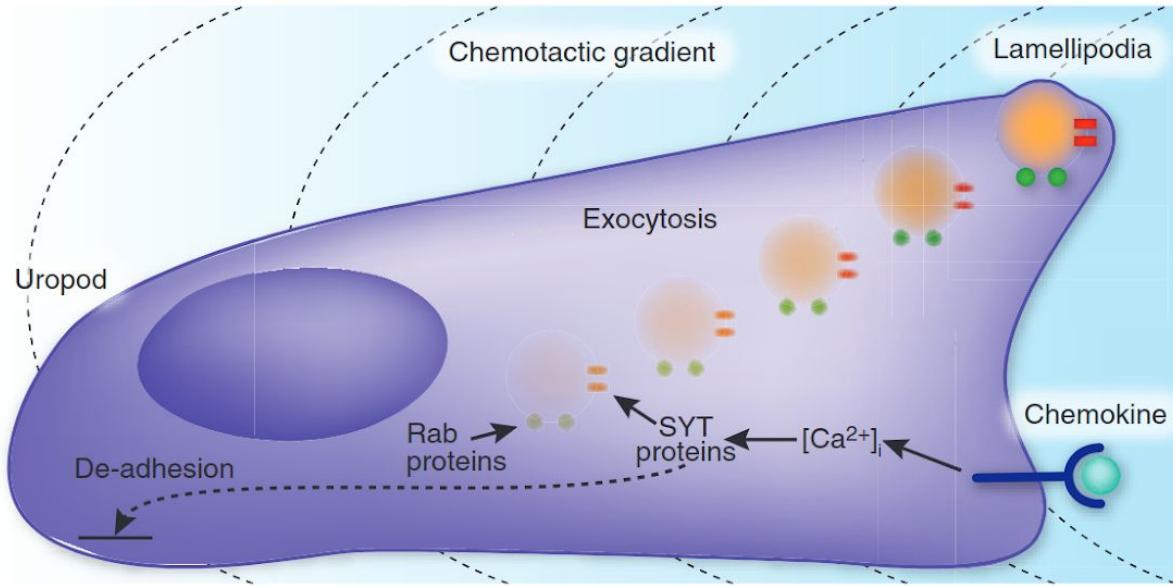


Figure 1 Leukocytes follow a chemotactic stimulus by sensing the gradient and generating a continuous cycling of adhesive events, cytoskeleton polymerization and plasma membrane remodeling. Colvin *et al.* now demonstrate the critical role of synaptotagmins (SYT proteins) and Rab small GTPases (Rab proteins) in controlling the permanent flow of preformed endomembranes to the plasma membrane, thus allowing continuous cell-shape changes. Chemokines trigger an increase in intracellular calcium ($[Ca^{2+}]_i$). This acts together with synaptotagmins and Rab small GTPases in controlling vesicle trafficking and exocytosis during chemotaxis. Exocytosis delivers to the cell surface the preformed layers of lipid membrane necessary for continuous plasma membrane turnover and extension toward the gradient. Synaptotagmins also participate in the adhesion–de-adhesion cycling that leads to uropod release.

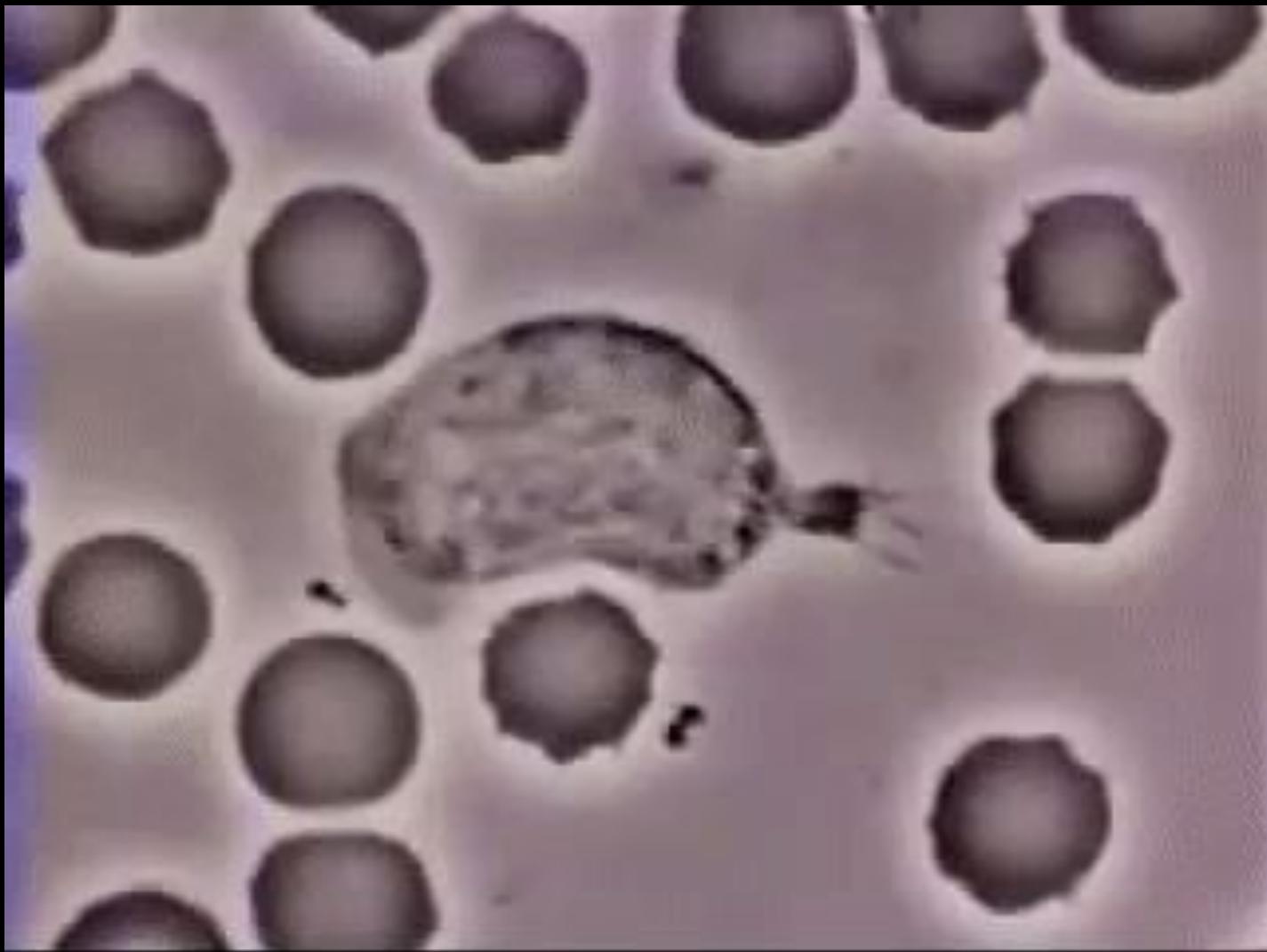
Published: June 2010

Leukocyte chemotaxis: from lysosomes to motility

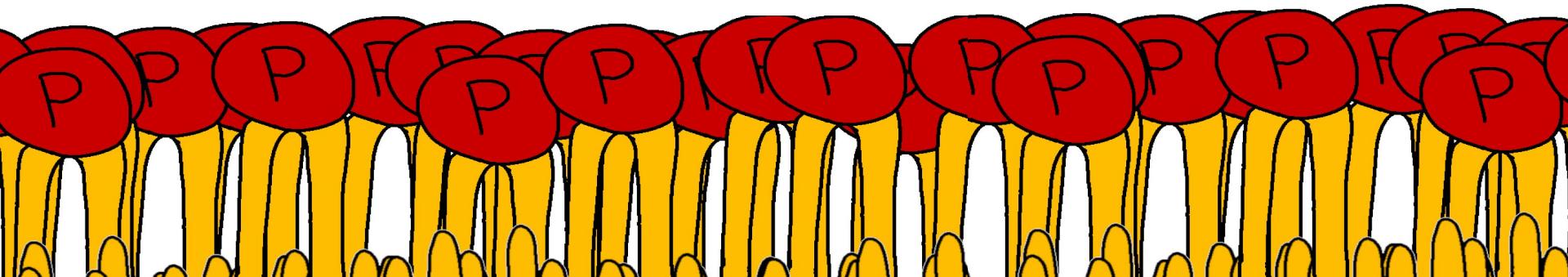
Gabriela Constantin & Carlo Laudanna [✉](#)

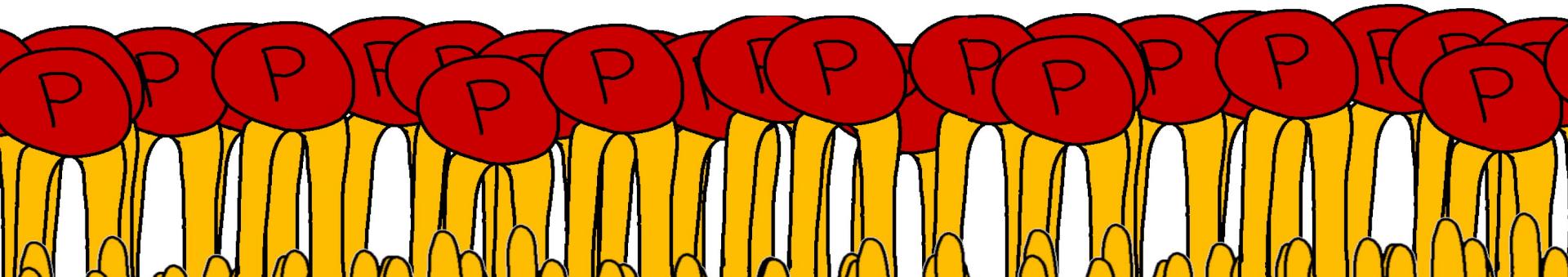
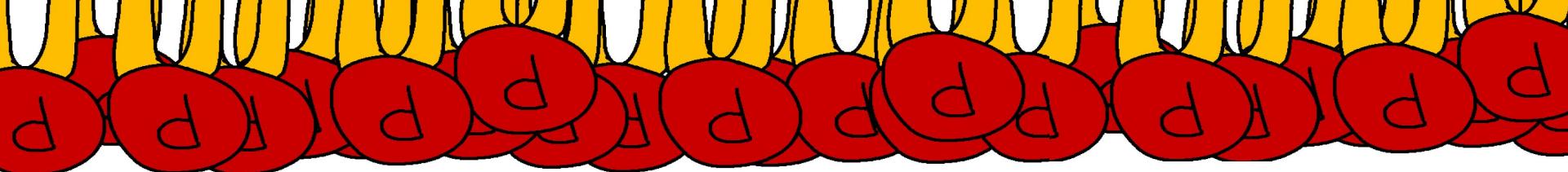
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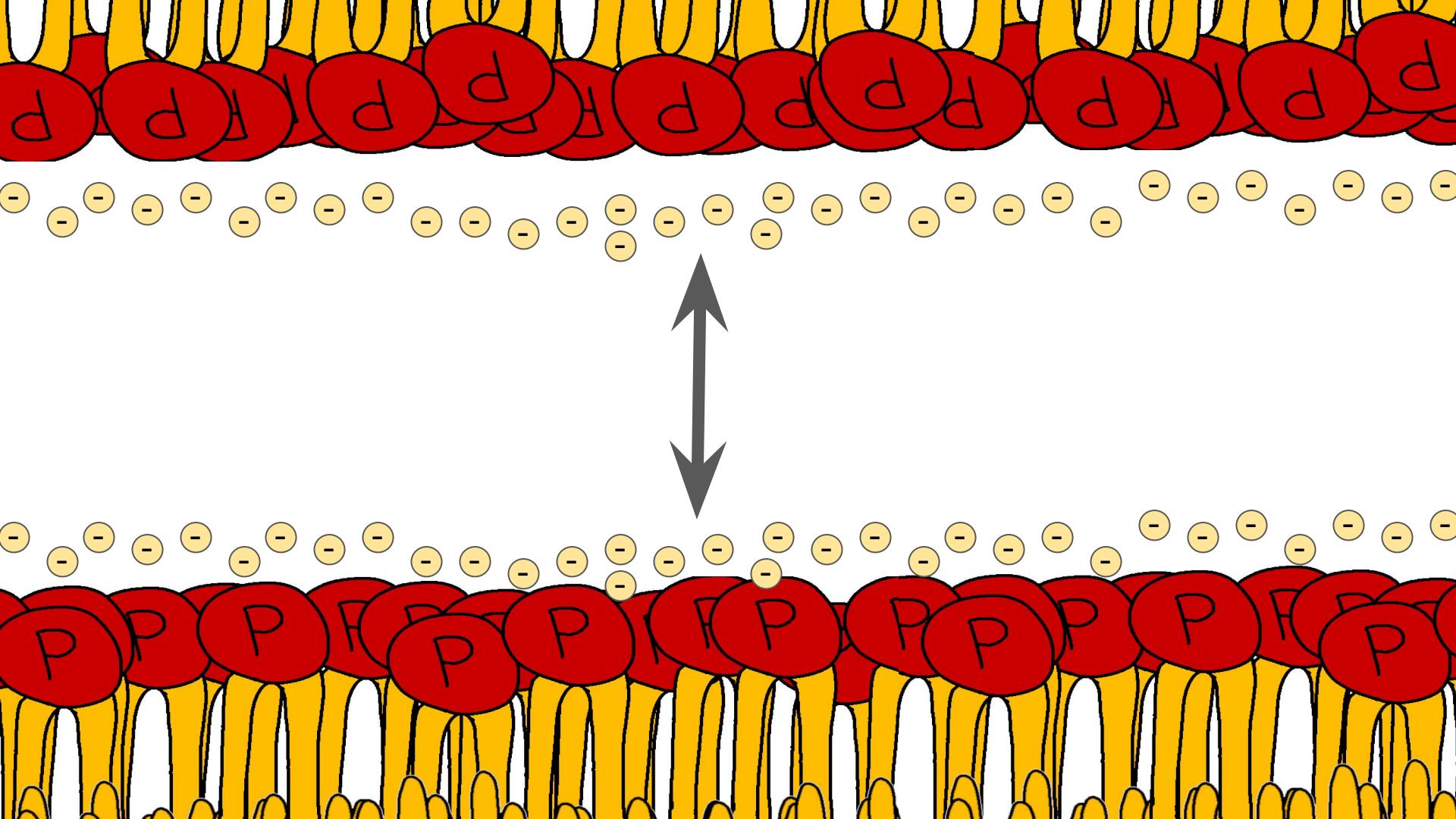
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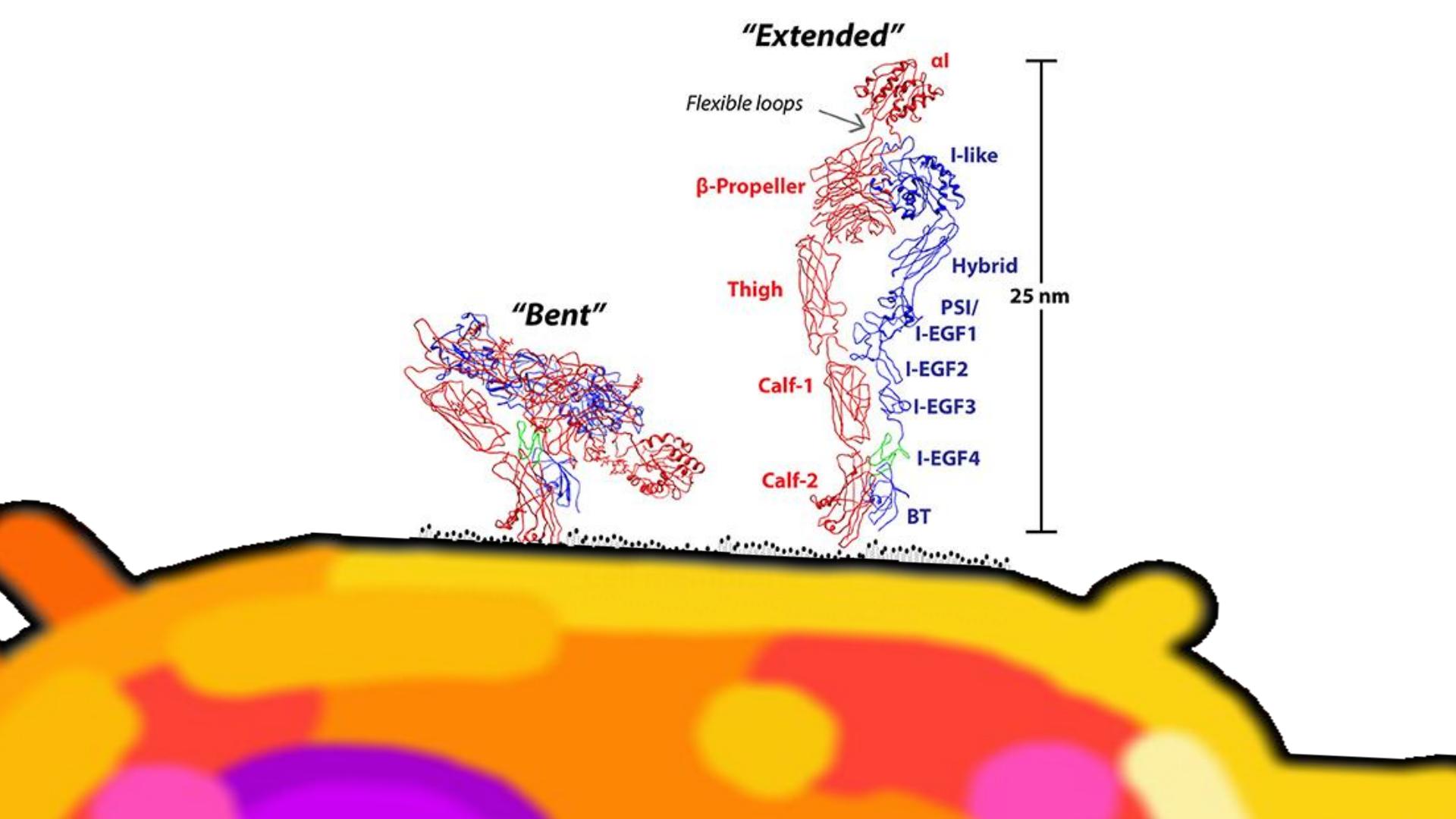


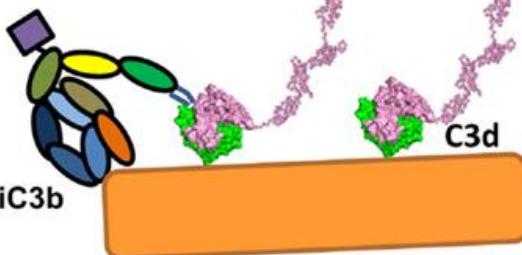
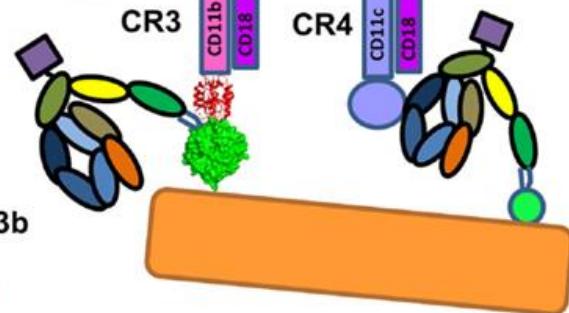
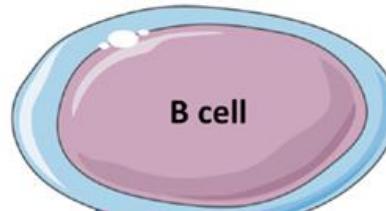
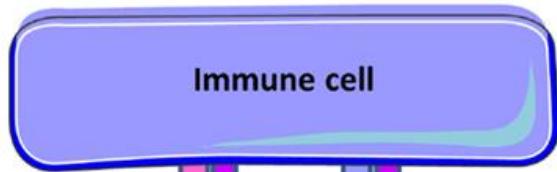
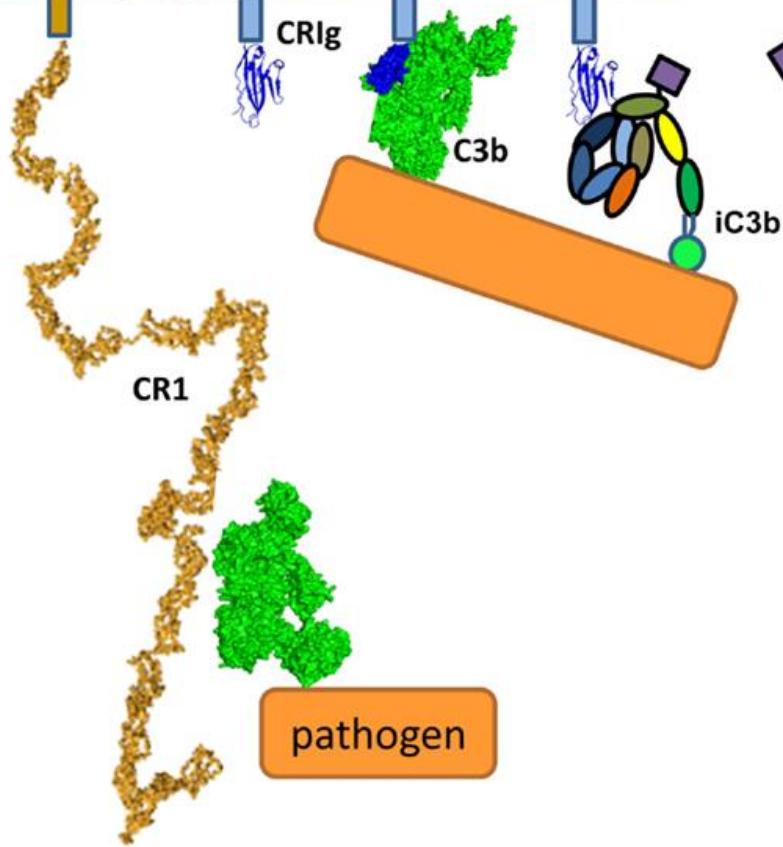


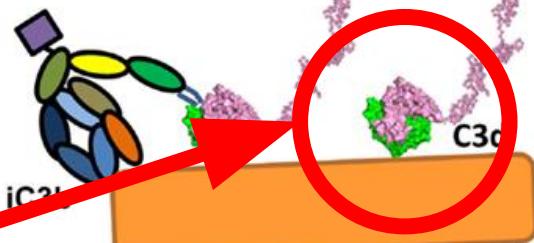
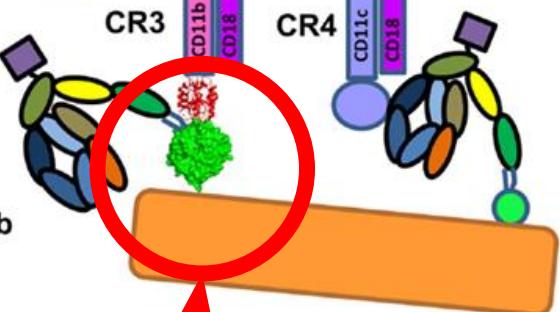
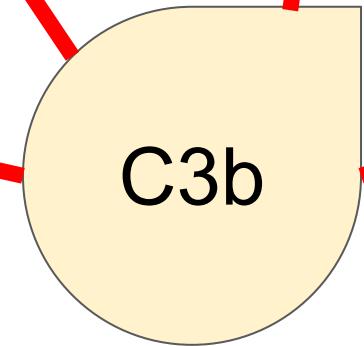
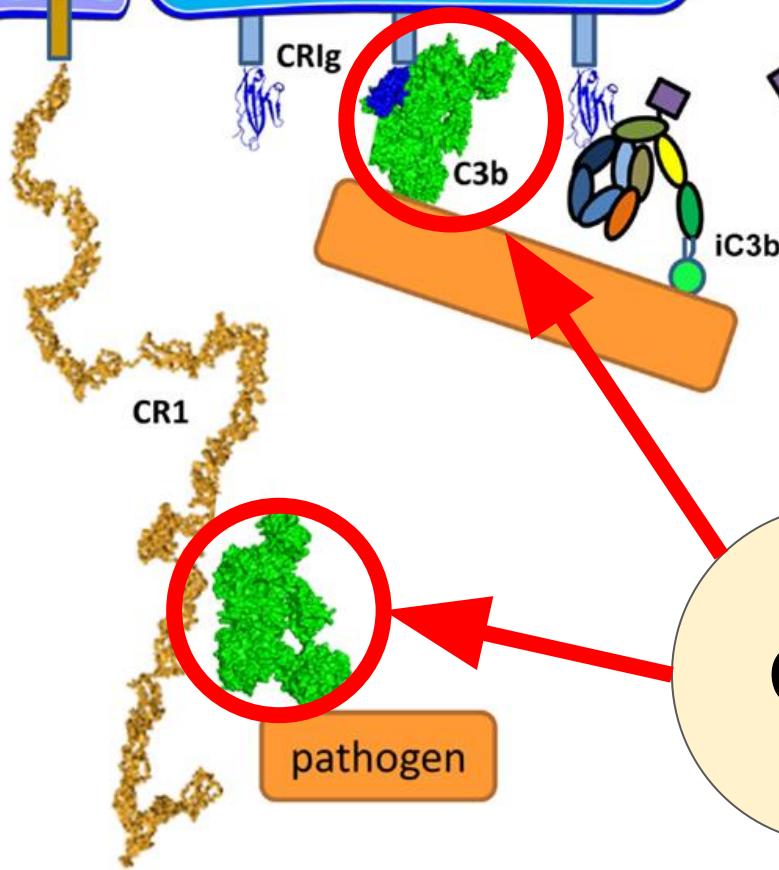
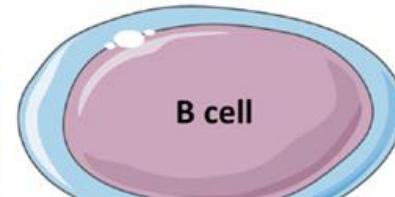








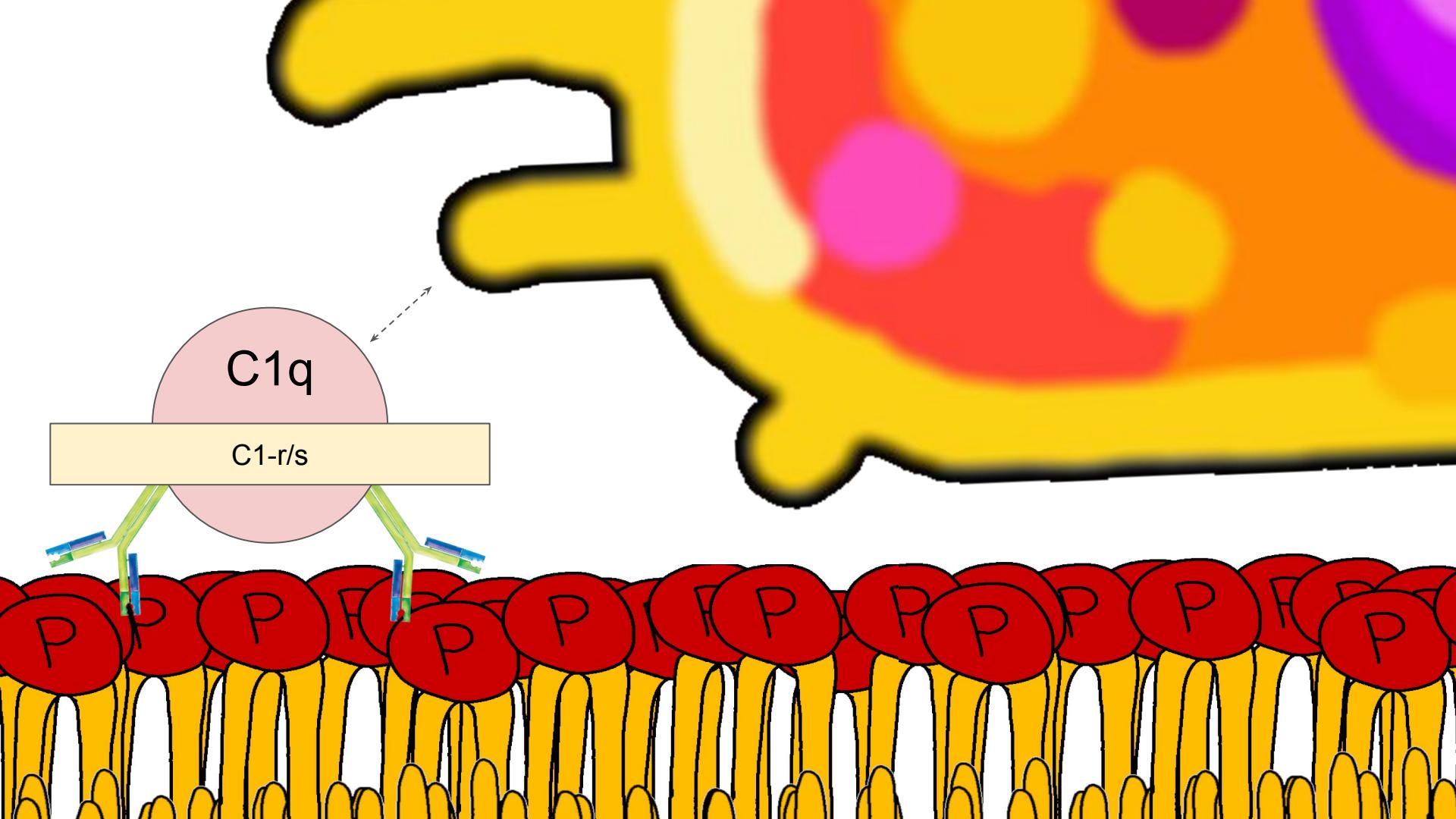




A diagram illustrating the C3b Receptor pathway of the complement system. At the top, three purple, irregularly shaped proteins labeled "C3b" are shown. One of these C3b molecules is bound to a yellow, elongated protein labeled "C1q". Below this, a blue rectangular box contains the text "C3b Receptor". In the bottom half of the image, a green and blue striped surface represents a bacterial membrane. Three yellow and red protein complexes, each consisting of a yellow "C1q" domain and a red "C3b" domain, are shown bound to the membrane. The text "Bacterium" is located at the bottom right of the membrane.

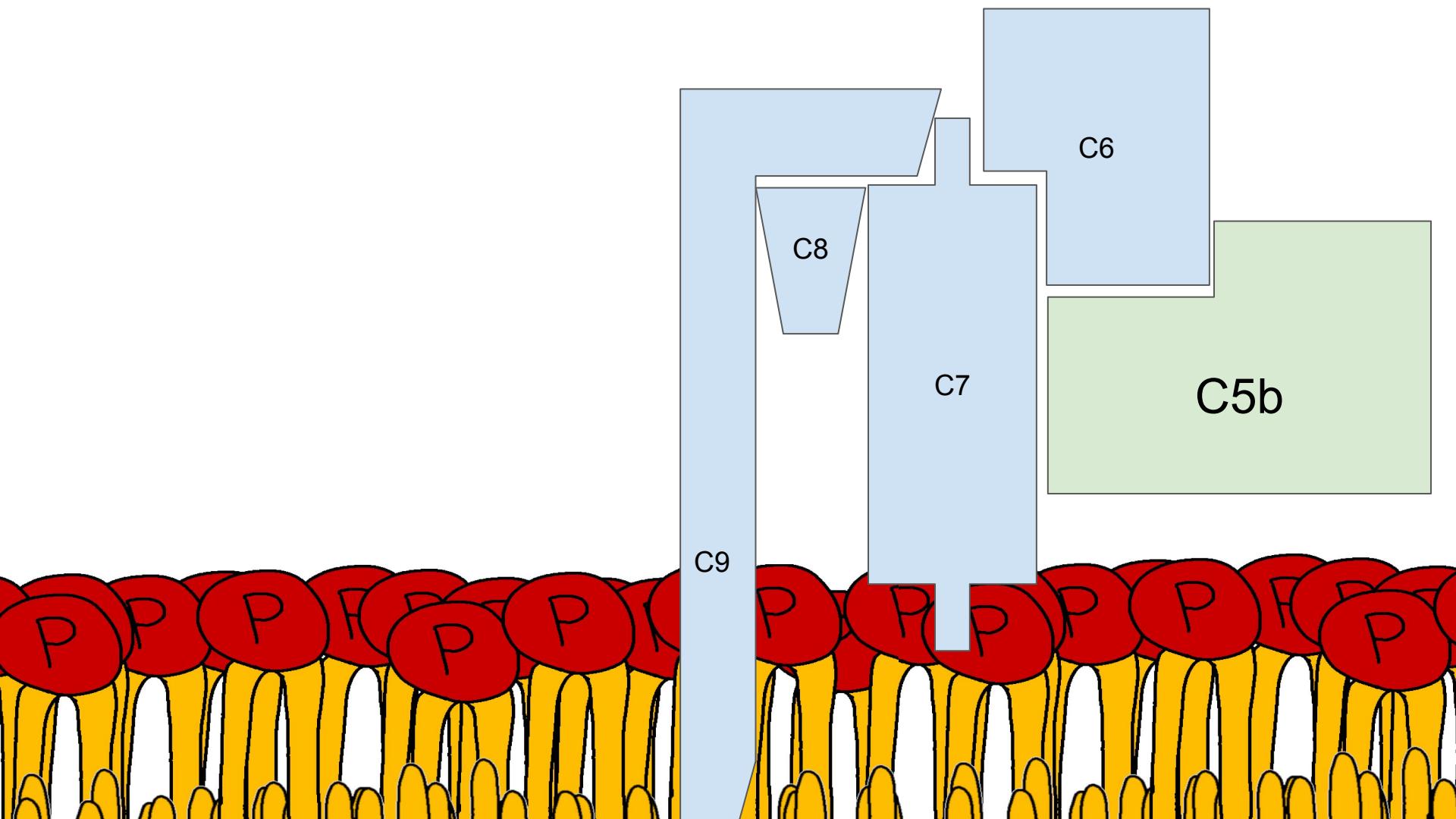
C3b Receptor

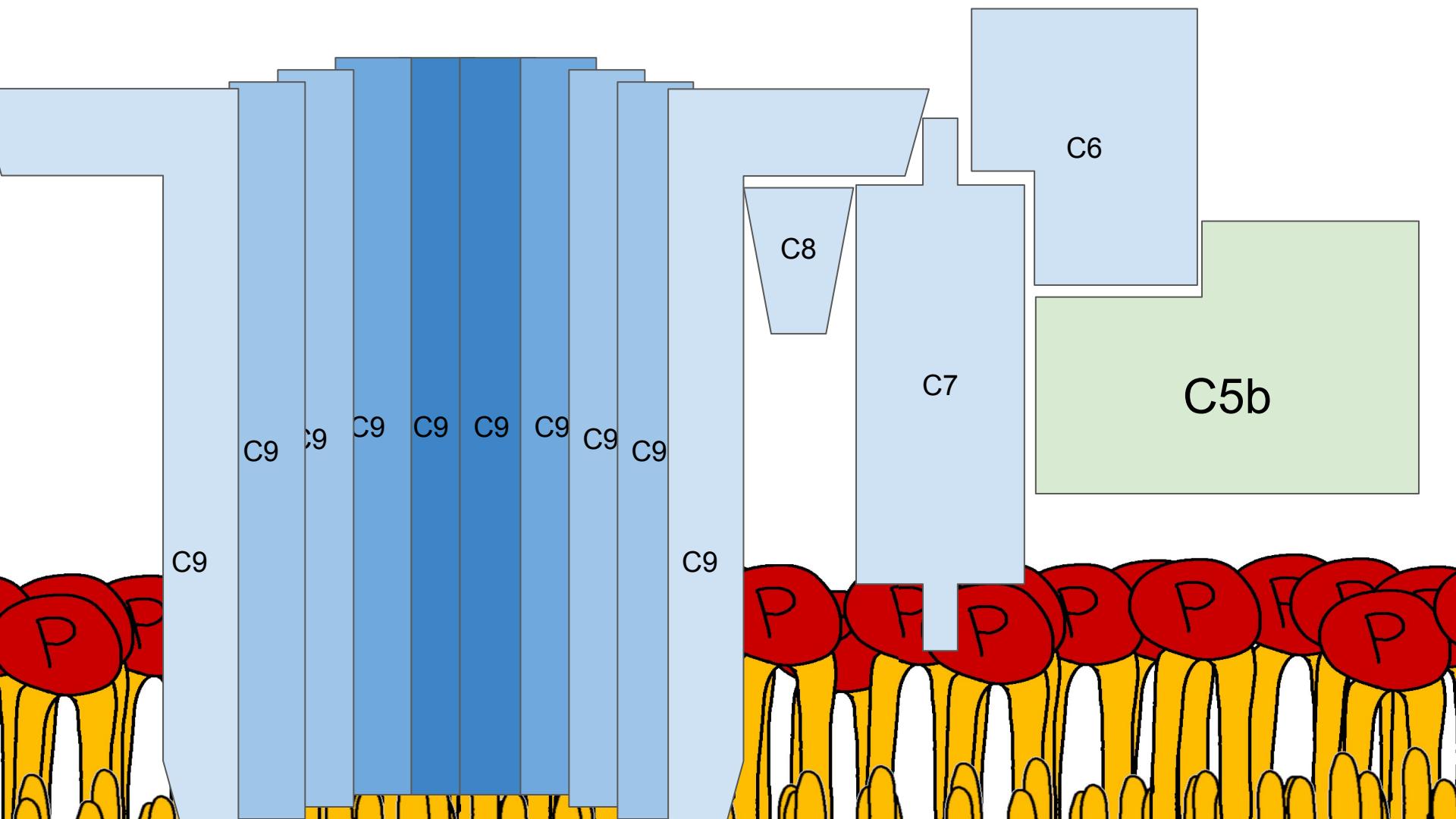
Bacterium

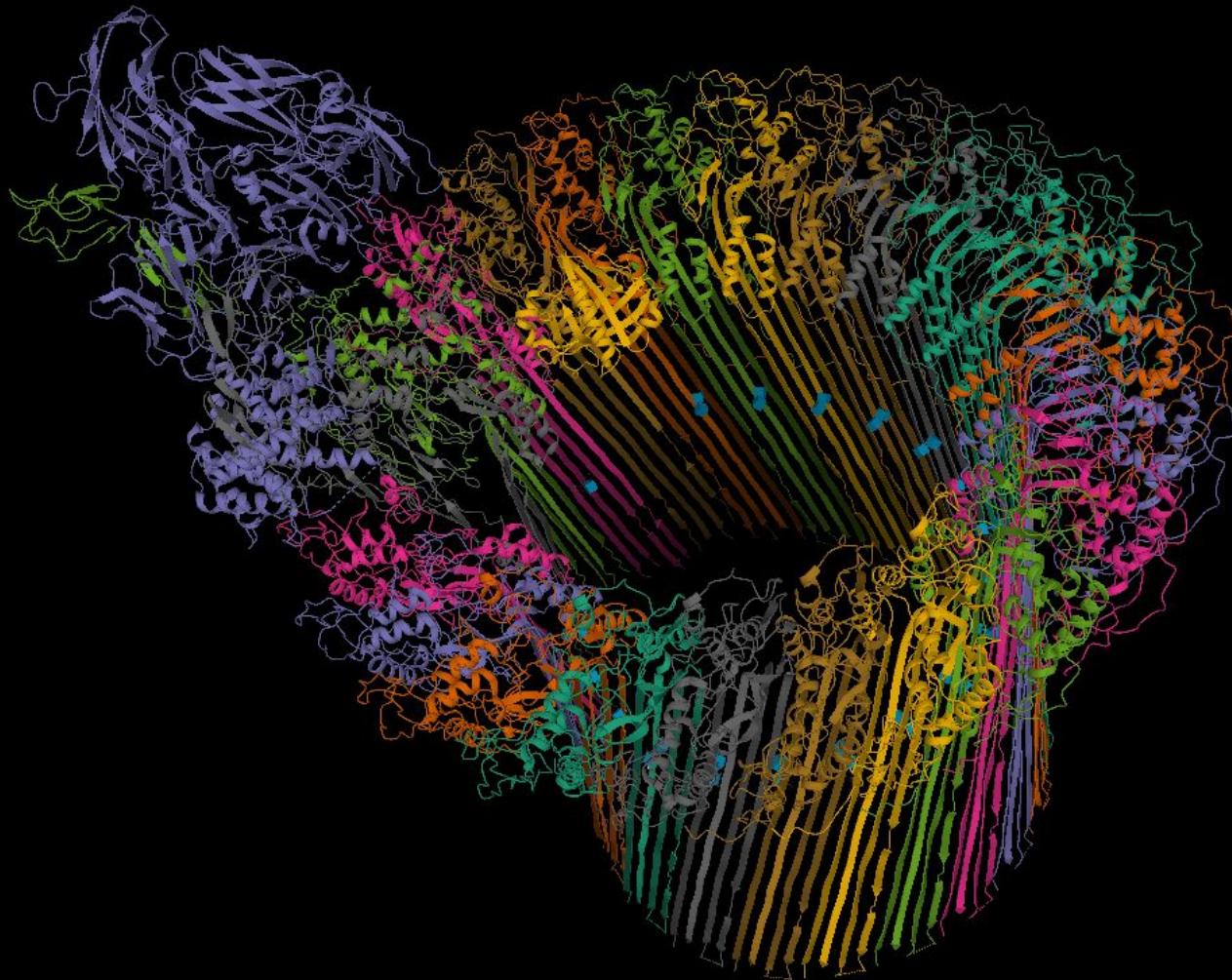


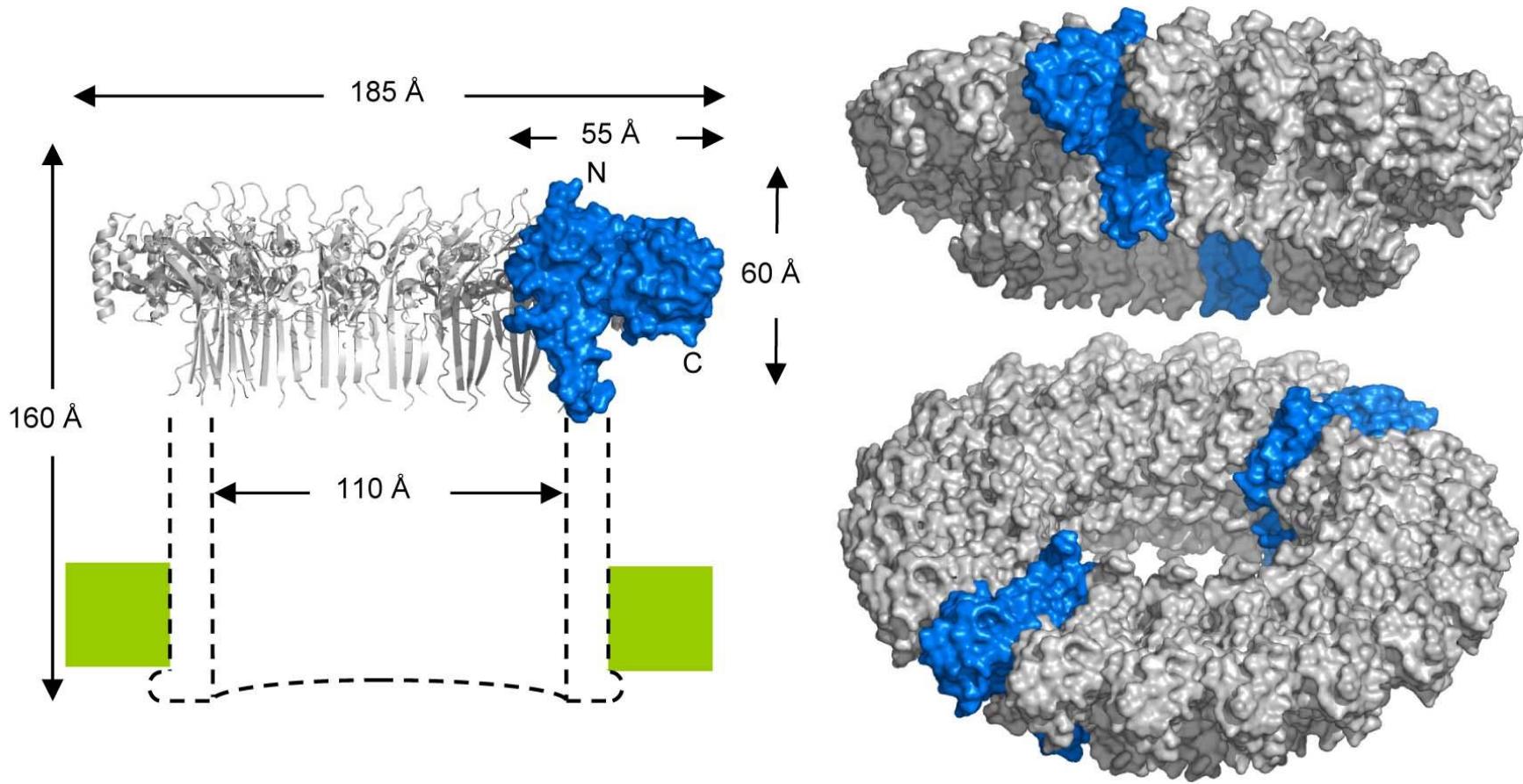
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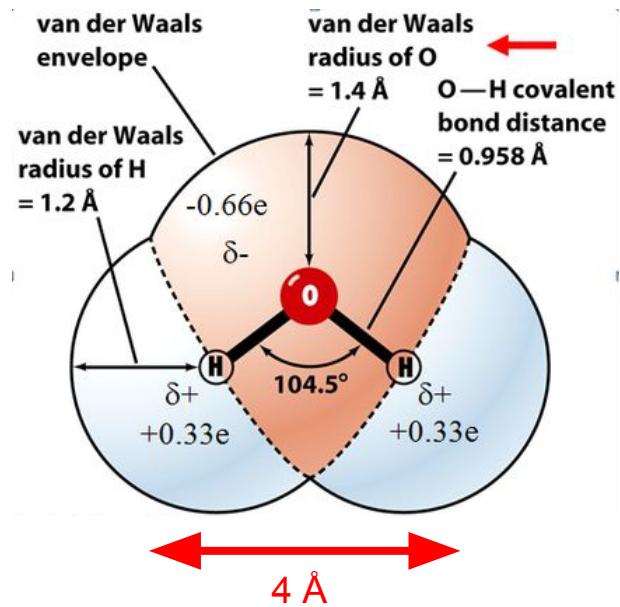
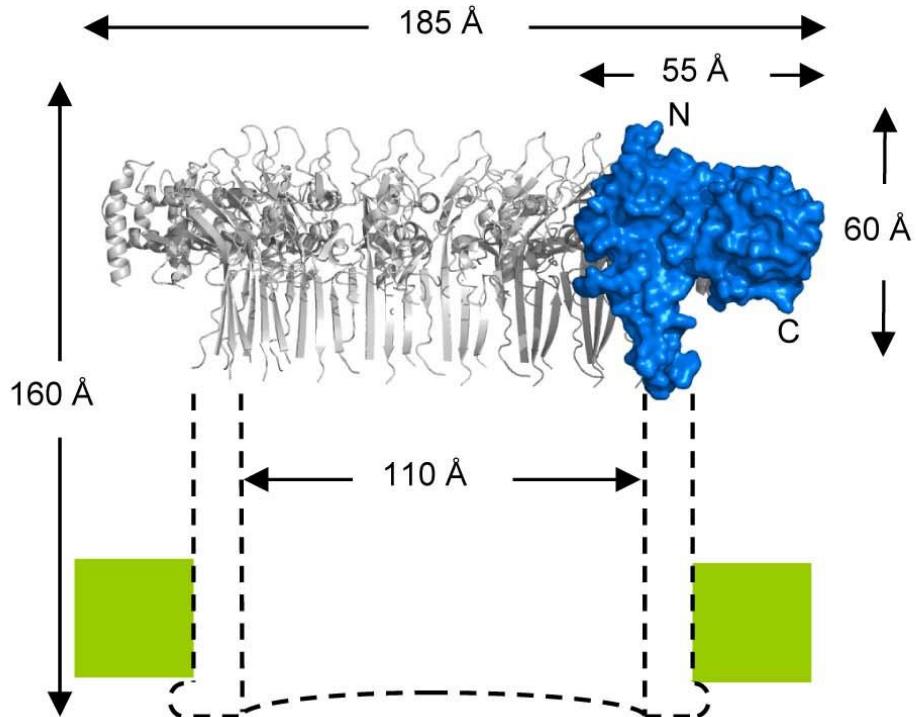


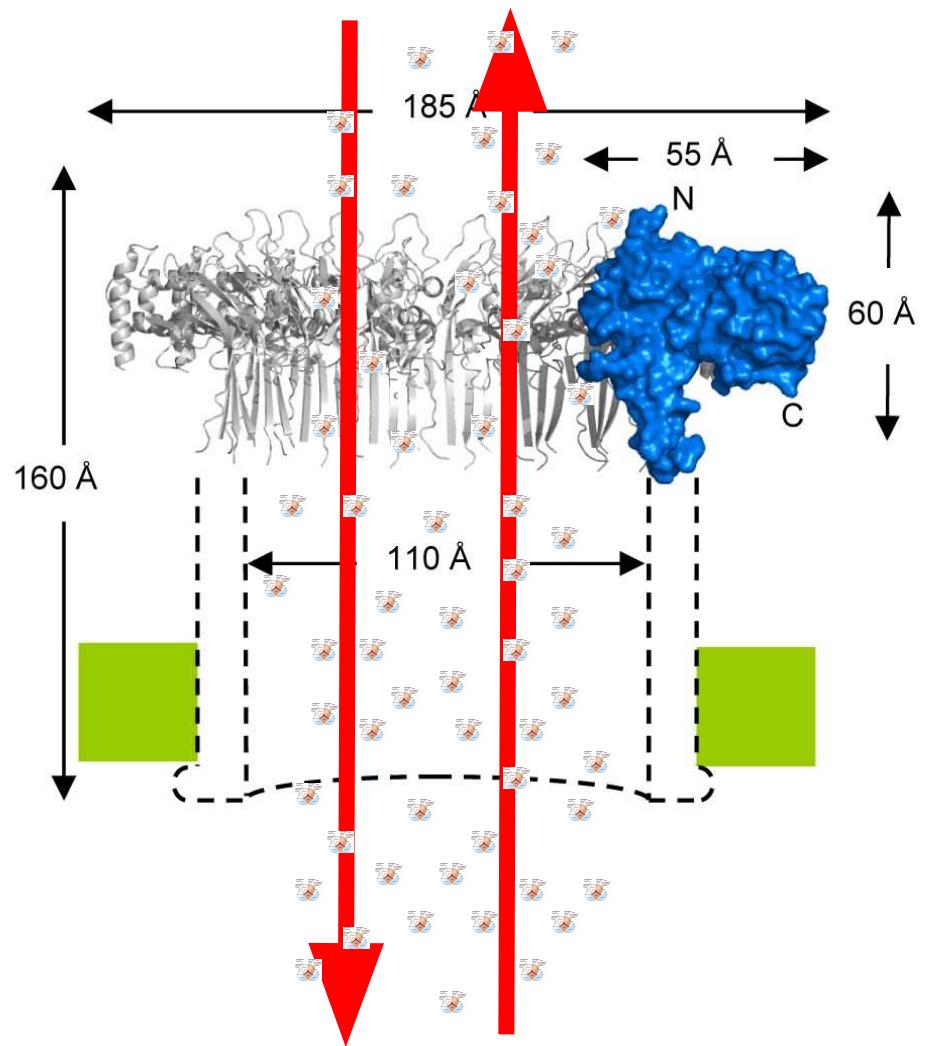


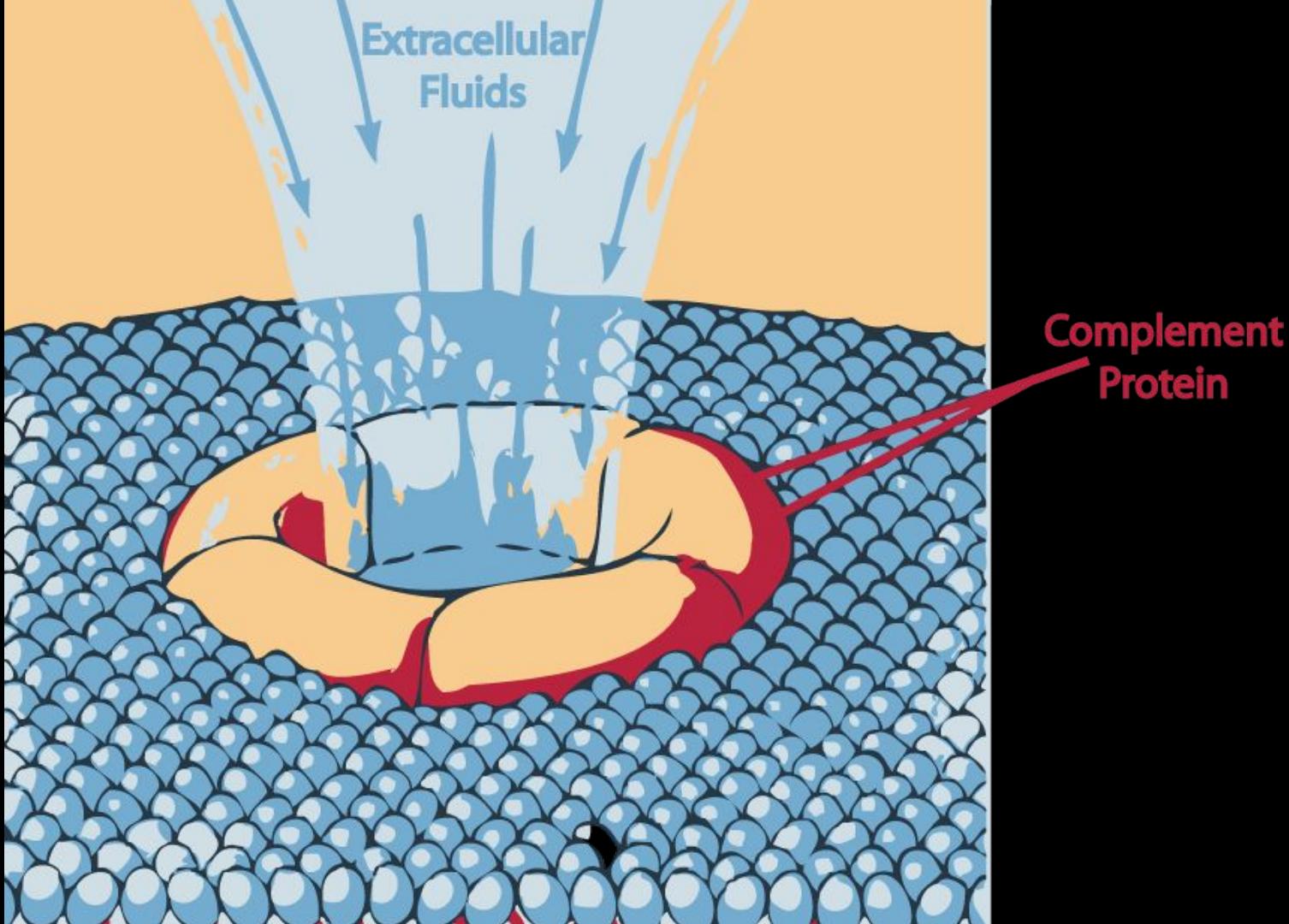


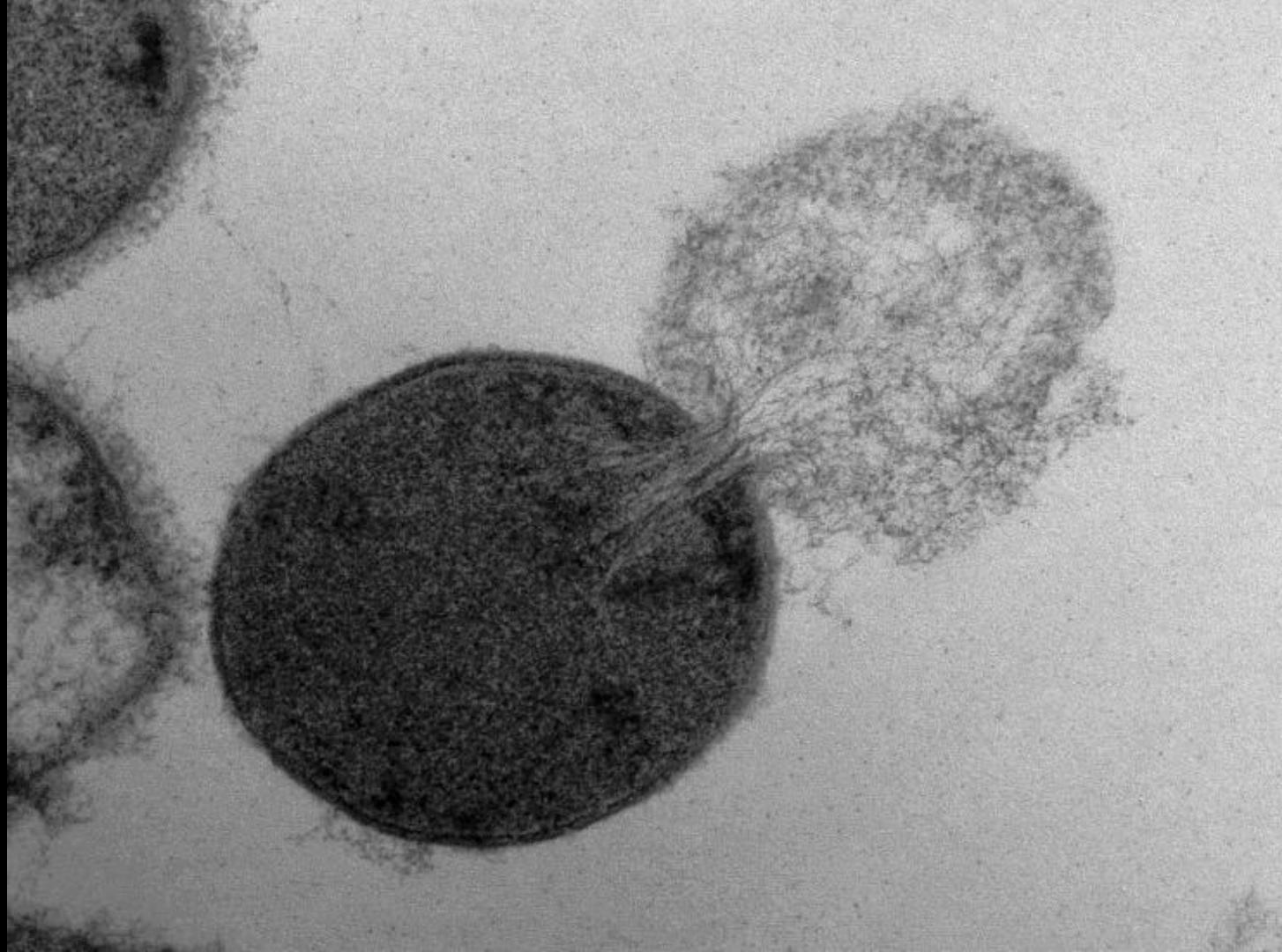




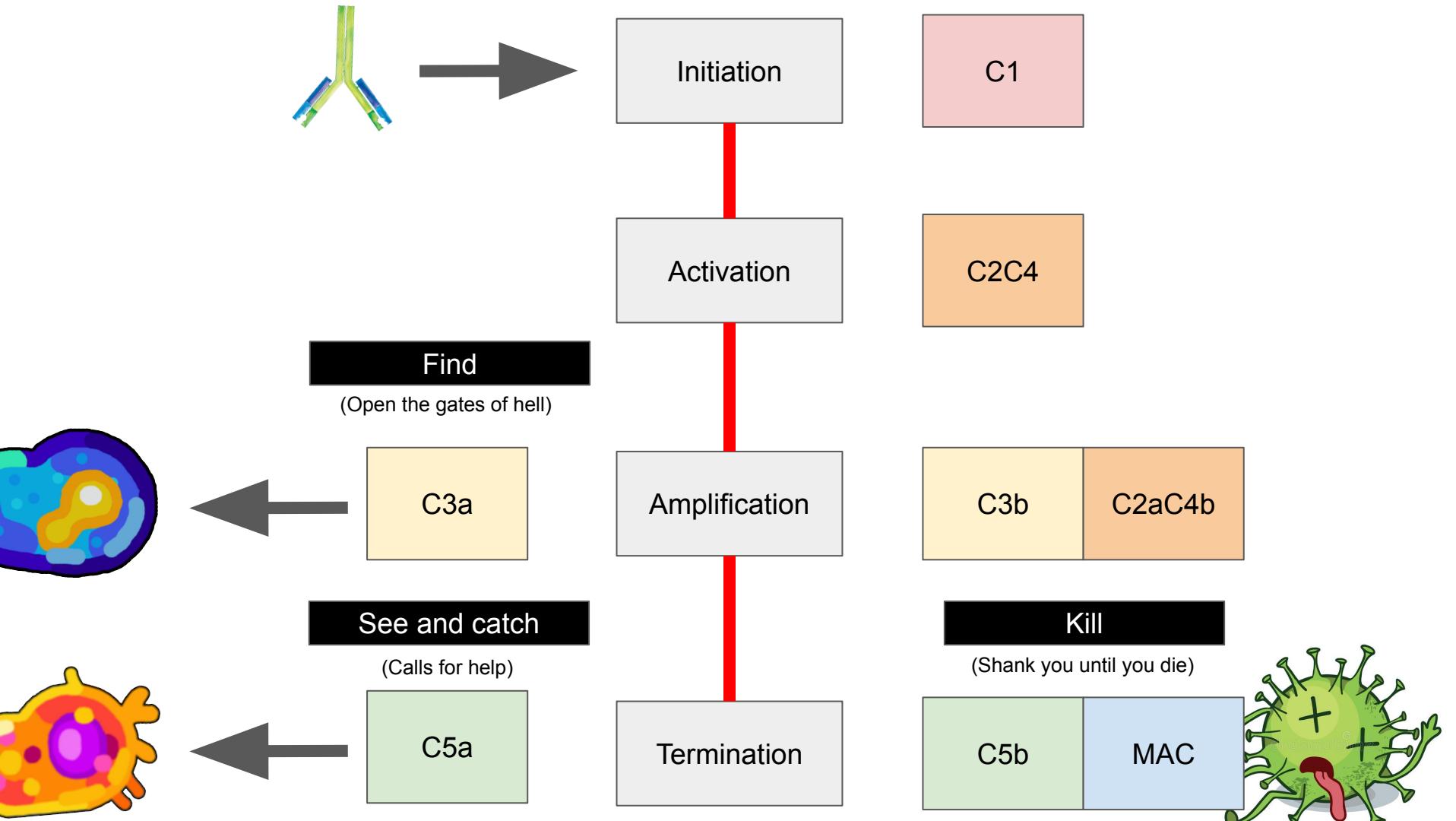












Initiation

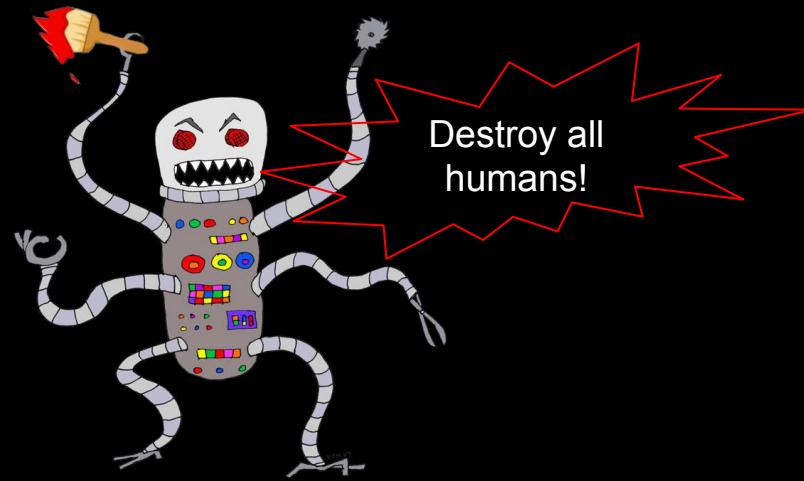
Activation

Amplification

Termination

PHASE - ?

When everything goes horribly wrong





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REVIEW

Complementopathies

Andrea C. Baines, Robert A. Brodsky *



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ARTICLE INFO

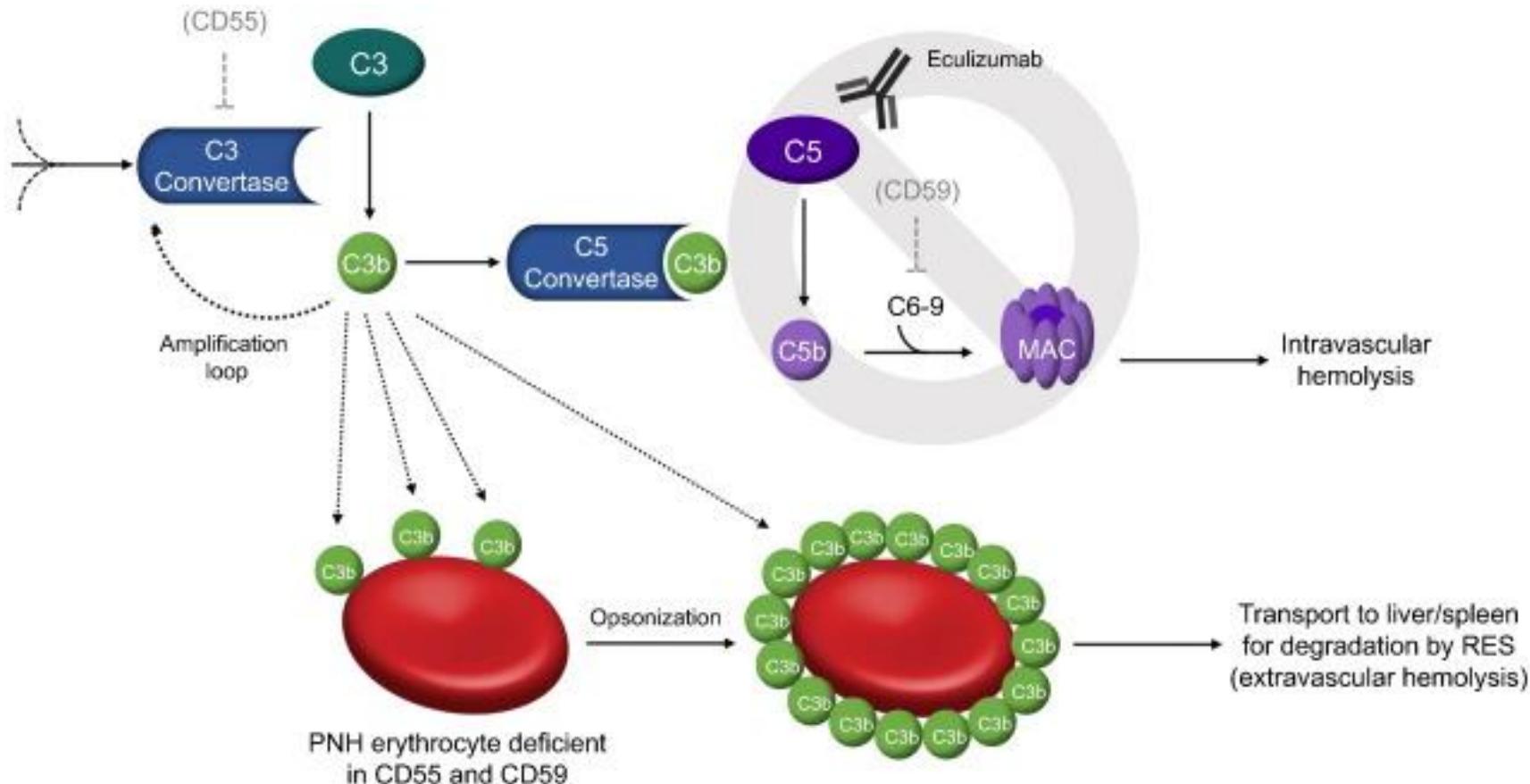
Keywords:

Alternative pathway of complement
Paroxysmal nocturnal hemoglobinuria
Atypical hemolytic uremic syndrome
HELLP syndrome
Cold agglutinin disease
Complementopathy

ABSTRACT

The complement system is an essential part of the innate immune system that requires careful regulation to ensure responses are appropriately directed against harmful pathogens, while preventing collateral damage to normal host cells and tissues. While deficiency in some components of the complement pathway is associated with increased susceptibility to certain infections, it has also become clear that inappropriate activation of complement is an important contributor to human disease. A number of hematologic disorders are driven by complement, and these disorders may be termed "complementopathies". This includes paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), cold agglutinin disease (CAD) and other related disorders, which will be the focus of this review. A better understanding of the central role of the complement system in the pathophysiology of these disorders may allow for application of therapies directed at blocking the complement cascade.

- Classical Pathway
- Alternative Pathway
- Lectin Pathway



Fundamental role of C1q in autoimmunity and inflammation

Myoungsun Son ¹, Betty Diamond ², Frances Santiago-Schwarz ¹

Affiliations + expand

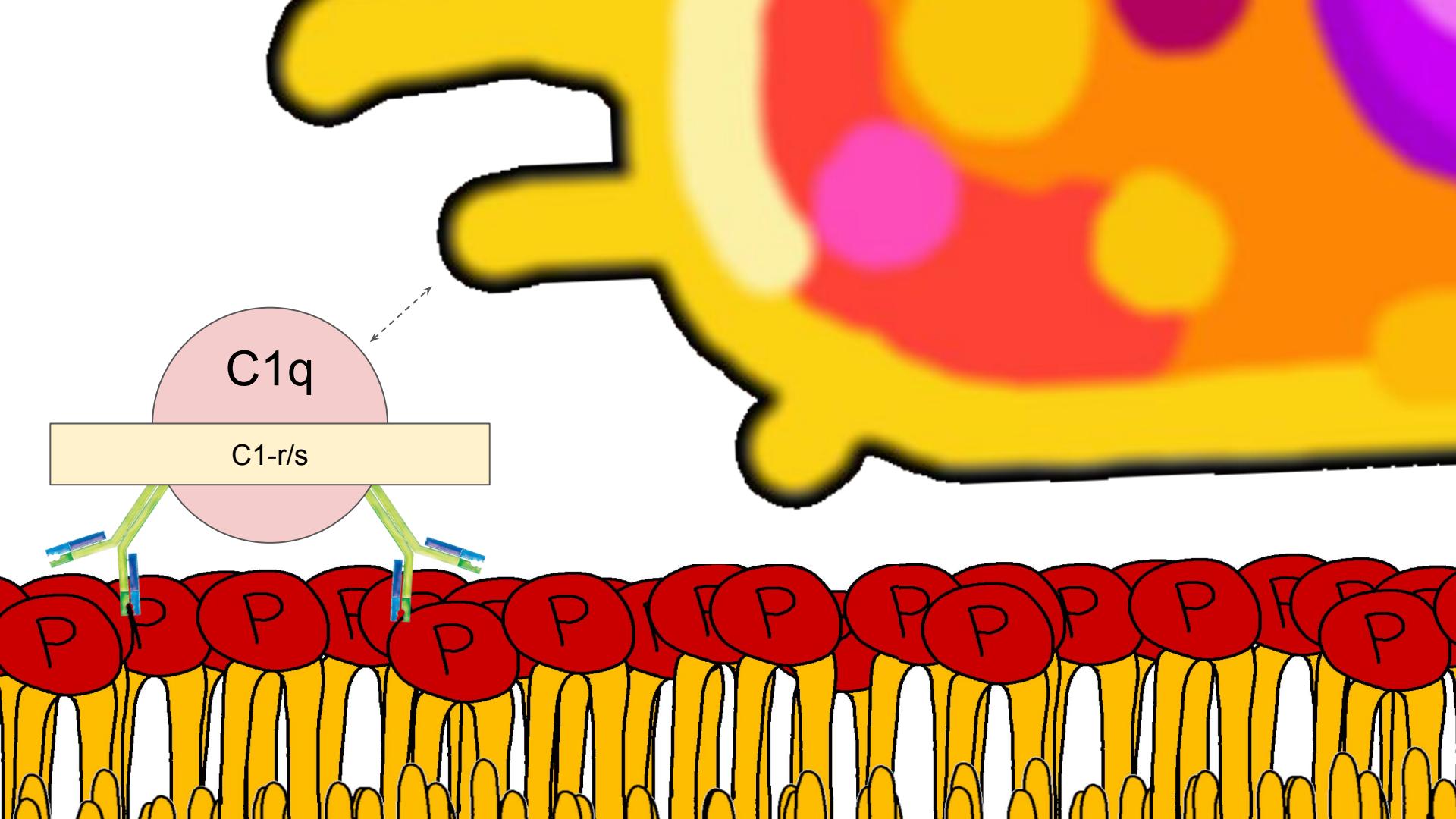
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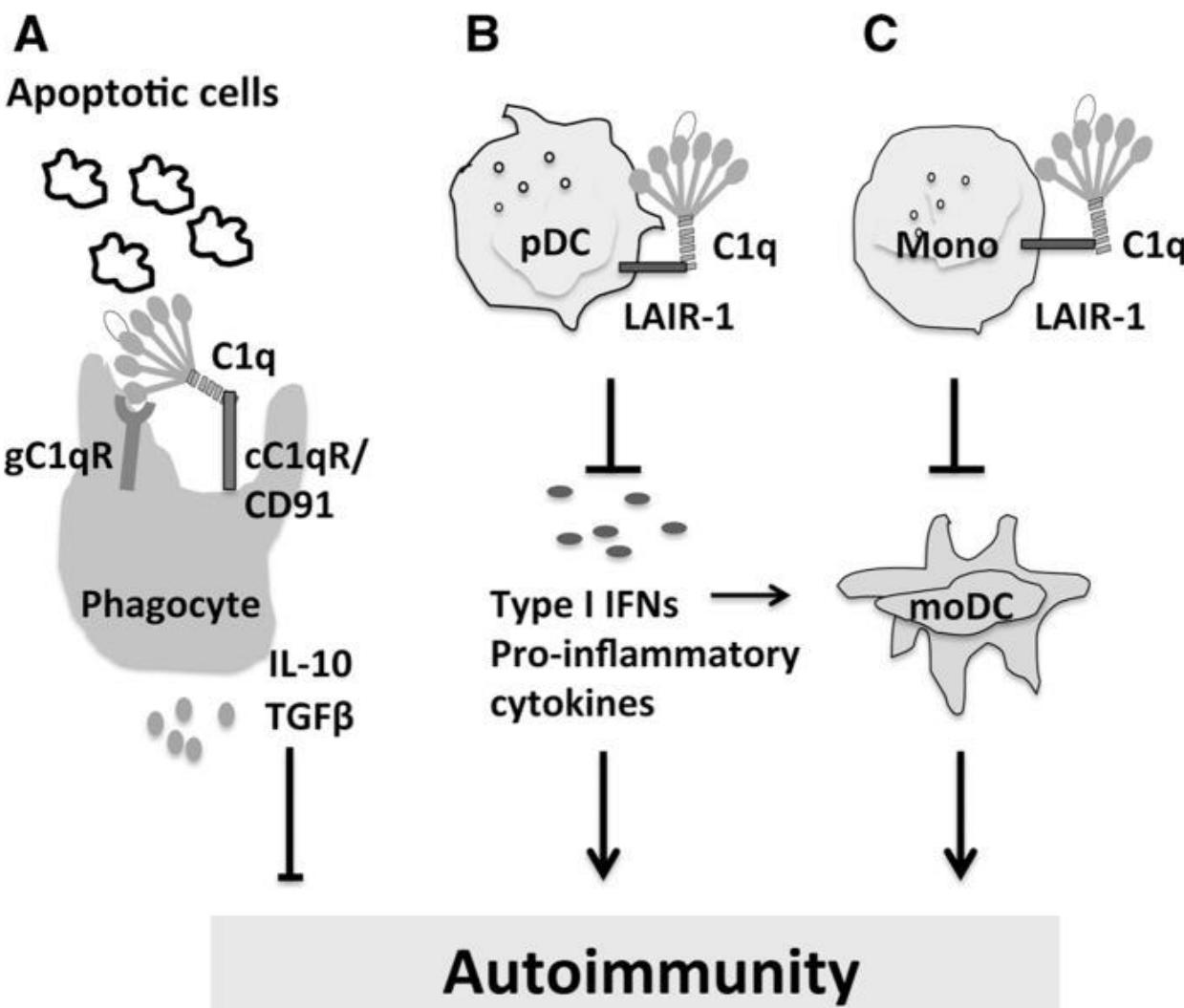
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Abstract

C1q, historically viewed as the initiating component of the classical complement pathway, also exhibits a variety of complement-independent activities in both innate and acquired immunity. Recent studies focusing on C1q's suppressive role in the immune system have provided new insight into how abnormal C1q expression and bioactivity may contribute to autoimmunity. In particular, molecular networks involving C1q interactions with cell surface receptors and other ligands are emerging as mechanisms involved in C1q's modulation of immunity. Here, we discuss the role of C1q in controlling immune cell function, including recently elucidated mechanisms of action, and suggest how these processes are critical for maintaining tissue homeostasis under steady-state conditions and in preventing autoimmunity.

Keywords: Autoimmunity; C1q; Complement; Inflammation; SLE.





Cancer Cell Int. 2019; 19: 300.

PMCID: PMC6858723

Published online 2019 Nov 15. doi: [10.1186/s12935-019-1027-3](https://doi.org/10.1186/s12935-019-1027-3)

PMID: [31787848](#)

Role of the complement system in the tumor microenvironment

Ronghua Zhang,[#] Qiaofei Liu,[#] Tong Li,[#] Quan Liao,[✉] and Yupei Zhao[✉]

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Abstract

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The complement system has traditionally been considered a component of innate immunity against invading pathogens and “nonself” cells. Recent studies have demonstrated the immunoregulatory functions of complement activation in the tumor microenvironment (TME). The TME plays crucial roles in tumorigenesis, progression, metastasis and recurrence. Imbalanced complement activation and the deposition of complement proteins have been demonstrated in many types of tumors. Plasma proteins, receptors, and regulators of complement activation regulate several biological functions of stromal cells in the TME and promote the malignant biological properties of tumors. Interactions between the complement system and cancer cells contribute to the proliferation, epithelial-mesenchymal transition, migration and invasion of tumor cells. In this review, we summarize recent advances related to the function of the complement system in the TME and discuss the therapeutic potential of targeting complement-mediated immunoregulation in cancer immunotherapy.

Keywords: Complement system, Tumor microenvironment, Immunoregulation, Immunotherapy

Table 1

Effects of complement system on the TME and their therapeutic potential for cancer treatment

Complement protein	Malignancy types/models	Functions in the TME	Example drugs	Refs.
C1q	Melanoma (murine models and cell lines), cervical cancer (murine models), breast cancer (cell lines), pancreatic cancer (cell lines), colon cancer (cell lines) and lung cancer (cell lines)	Promote angiogenesis, cell adhesion, proliferation and metastasis independent of complement activation, and inhibit the inflammatory response of macrophages and DCs	No correlational studies	[23, 25, 27, 98]
C3a	Melanoma (murine models, patient samples and cell lines), lung cancer (murine models, patient samples and cell lines), gastric cancer (murine models, patient samples and cell lines), colon cancer (murine models, patient samples and cell lines), breast cancer (patient samples and cell lines), pancreatic cancer (patient samples and cell lines)	Promote tumor growth, metastasis, EMT and angiogenesis; regulate the function of TAMs, MDSCs, DCs and Tregs; and serve as a predictive biomarker for cancer diagnosis and response to cancer treatment	Compstatin (C3-targeted complement inhibitor)	[13, 15, 58, 67, 77, 81]
C3d	Lymphoma (murine models and patient samples)	Serve as a predictive biomarker for response to cancer treatment or the tumor stage	No correlational studies	[121]
C4d	Oral squamous cell carcinoma (patient samples), lung cancer (patient samples)	Serve as a diagnostic and prognostic biomarker for cancer progression	No correlational studies	[19, 20]
C5a	Lung cancer (murine models, patient samples and cell lines), gastric cancer (murine models, patient samples and cell lines), hepatocellular carcinoma (murine models and cell lines), colorectal cancer (murine models and cell lines), breast cancer (murine models and cell lines), ovarian cancer (murine models and cell lines), melanoma (murine models), ovarian cancer (murine models), cervical cancer (murine models)	Promote tumorigenesis, tumor growth, angiogenesis, cell motility and invasiveness and inhibit immune function by inducing MDSCs or decreasing CD8 ⁺ T cells. Blockade of C5aR significantly reduced MDSCs and the immunomodulators ARG1, CTLA-4, IL-6, IL-10, LAG3, and PDL-1	Eculizumab (C3-targeted complement inhibitor) PMX-53 (C5a/C5aR inhibition)	[17, 39, 44, 66, 73, 109]
C7	Liver cancer (murine models, patient samples and cell lines)	Promote the stemness of liver cancer cells	No correlational studies	[93]
mCRPs	Many types of cancers (murine models, patient samples and cell lines)	Protect cancer cells from MAC-mediated CDC and regulate the response of T cells	Bispecific antibodies	[39, 101, 103, 104]
MBL-MASP	Glioblastoma multiforme (patient samples), colorectal cancer (patient samples), hepatocellular carcinoma (murine models)	Protect against the initiation and progression of glioblastoma and colorectal cancer, while suppressing	No correlational studies	[112–114]

The Complement System in Flavivirus Infections

Jonas N Conde ¹, Emiliana M Silva ¹, Angela S Barbosa ², Ronaldo Mohana-Borges ¹

Affiliations + expand

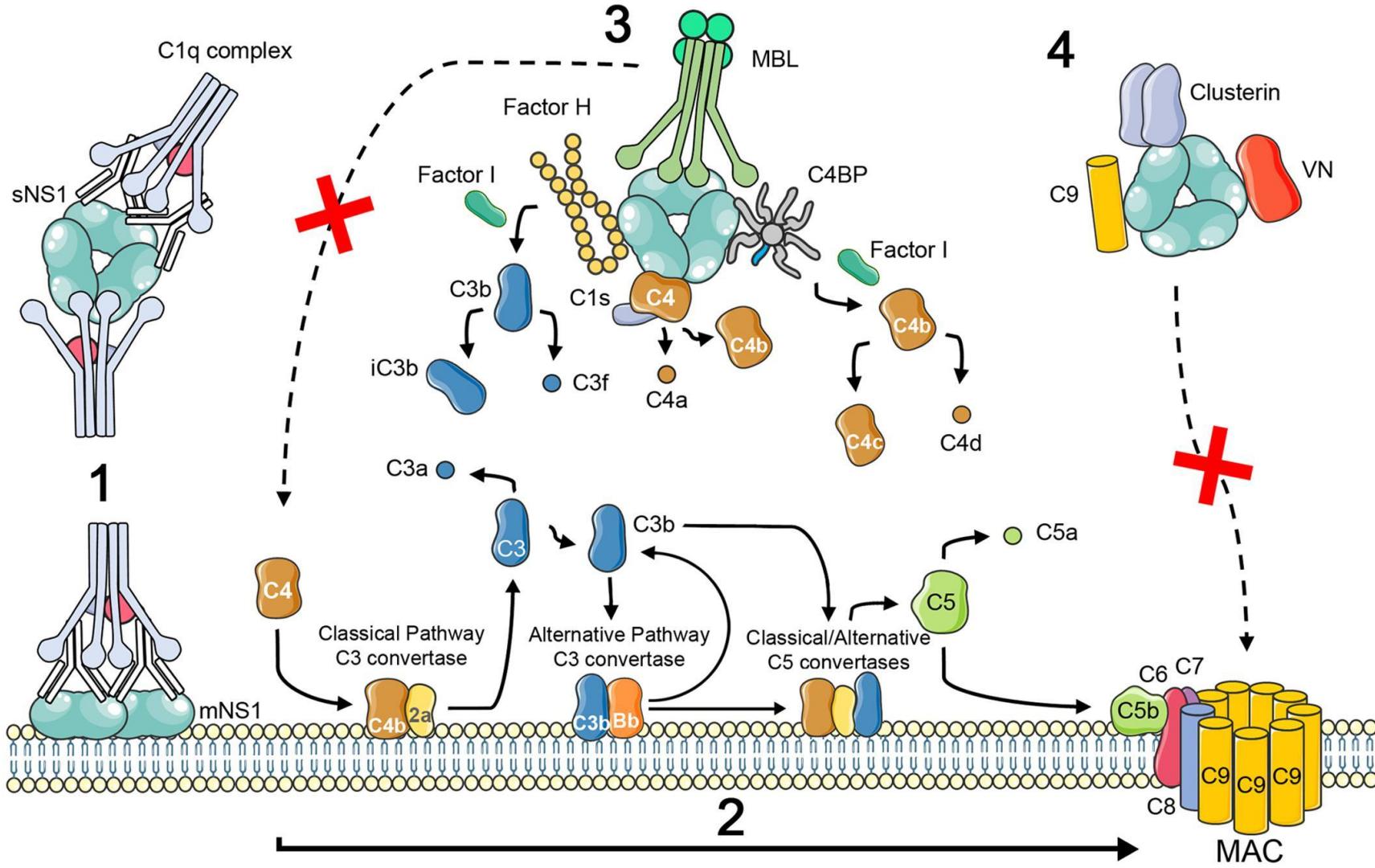
PMID: 28261172 PMCID: PMC5306369 DOI: 10.3389/fmicb.2017.00213

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Abstract

The incidence of flavivirus infections has increased dramatically in recent decades in tropical and sub-tropical climates worldwide, affecting hundreds of millions of people each year. The *Flaviviridae* family includes dengue, West Nile, Zika, Japanese encephalitis, and yellow fever viruses that are typically transmitted by mosquitoes or ticks, and cause a wide range of symptoms, such as fever, shock, meningitis, paralysis, birth defects, and death. The flavivirus genome is composed of a single positive-sense RNA molecule encoding a single viral polyprotein. This polyprotein is further processed by viral and host proteases into three structural proteins (C, prM/M, E) and seven non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5) that are involved in viral replication and pathogenicity. The complement system has been described to play an important role in flavivirus infection either by protecting the host and/or by influencing disease pathogenesis. In this mini-review, we will explore the role of complement system inhibition and/or activation against infection by the *Flavivirus* genus, with an emphasis on dengue and West Nile viruses.

Keywords: NS1 protein; complement system; dengue; flavivirus; immune evasion.



THE END

