Lecture 17
11 Sept 2023

The complement system

- Important effector in both innate and acquired immunity

- Over 30 circulating and membrane-bound proteins
(synthesized in liver and other cells- immune and epithelial)

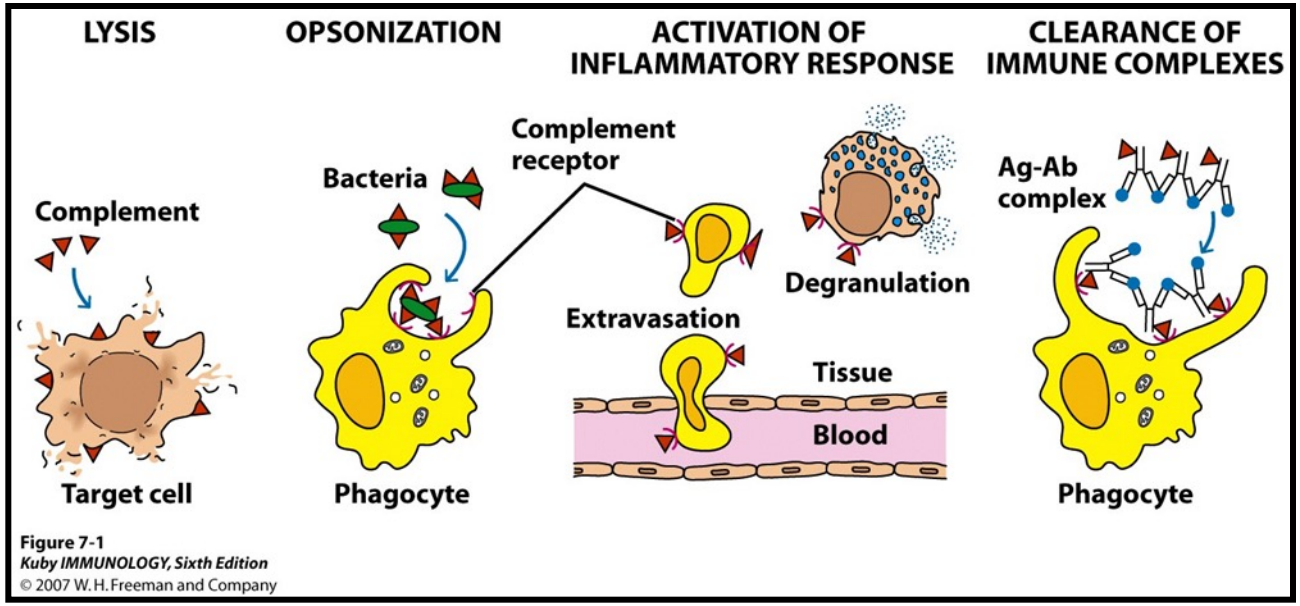
- Acts as a cascade
(one event must occur before another takes place)

Cascade:

- Many of the components are enzymes that become activated when cleaved into two peptides
- One peptide binds to the immune complex and becomes a functional part of it
- The other peptide diffuses away and can become an inflammatory mediator (binds to a receptor)

Four important functions of complement system

- Lysis
- Opsonization
- Activation of inflammatory response
- Clearance of immune complexes



Three pathways: classical, alternative, & lectin

Final steps identical in all 3 pathways

Classical - Initiated by formation of an Ag-Ab complex

Alternative - Antibody-independent

- ✓ Part of innate immunity
- ✓ Initiated by foreign cell surfaces

Lectin - Initiated by host proteins binding microbial surfaces

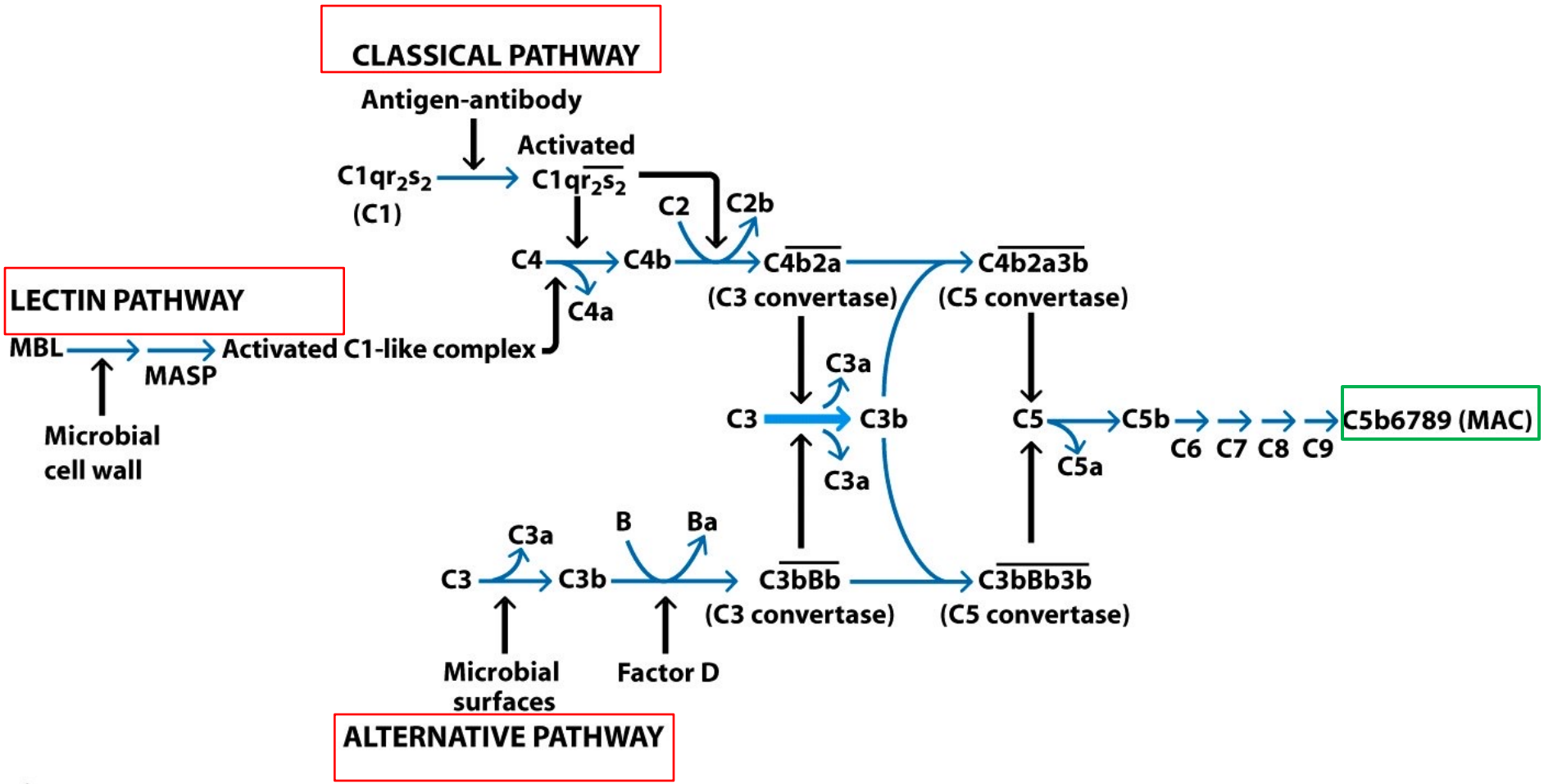


Figure 7-2
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- MBL: mannose binding lectins
- MASP: MBL associated serine proteases

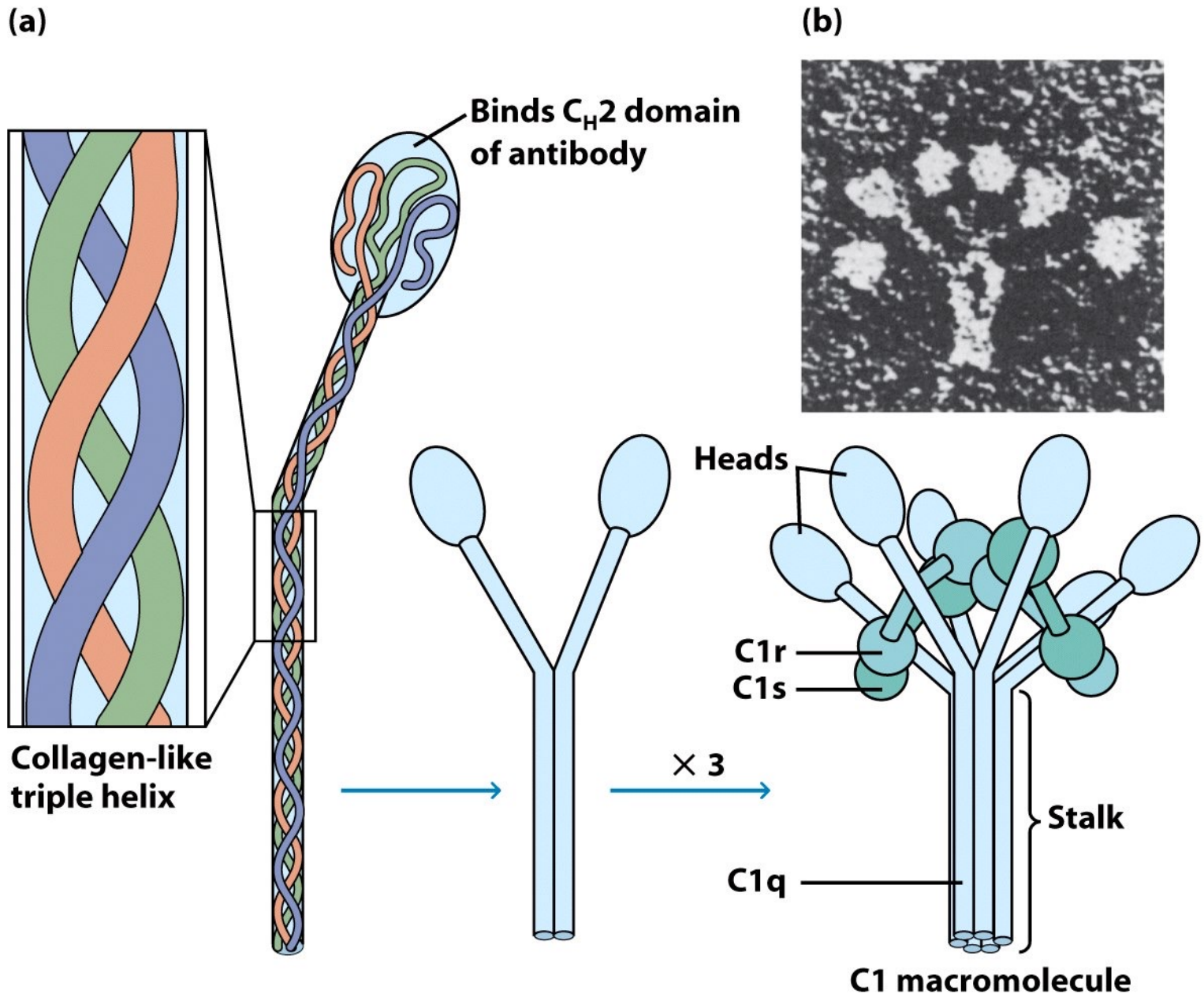

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Figure 7-3
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Classical pathway

- Classical was discovered first (but actually evolved later)

- Initiated by:

-formation of a soluble Ag-Ab complex

-binding of antibody to a target such as a bacterial cell

- Only certain antibodies can initiate this

(IgM, some classes of IgG)

Classical pathway

1 **C1q binds antigen-bound antibody. C1r activates auto-catalytically and activates the second C1r; both activate C1s.**

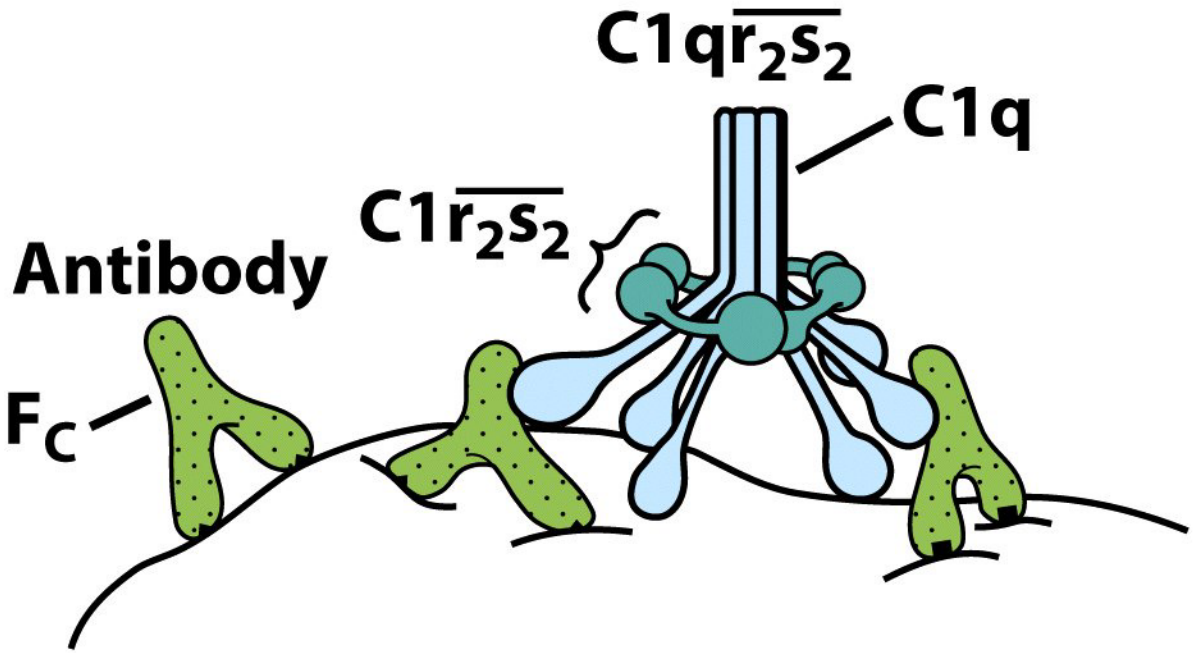

Figure 7-5 part 1
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2

C1s cleaves C4 and C2. Cleaving C4 exposes the binding site for C2. C4 binds the surface near C1 and C2 binds C4, forming C3 convertase.

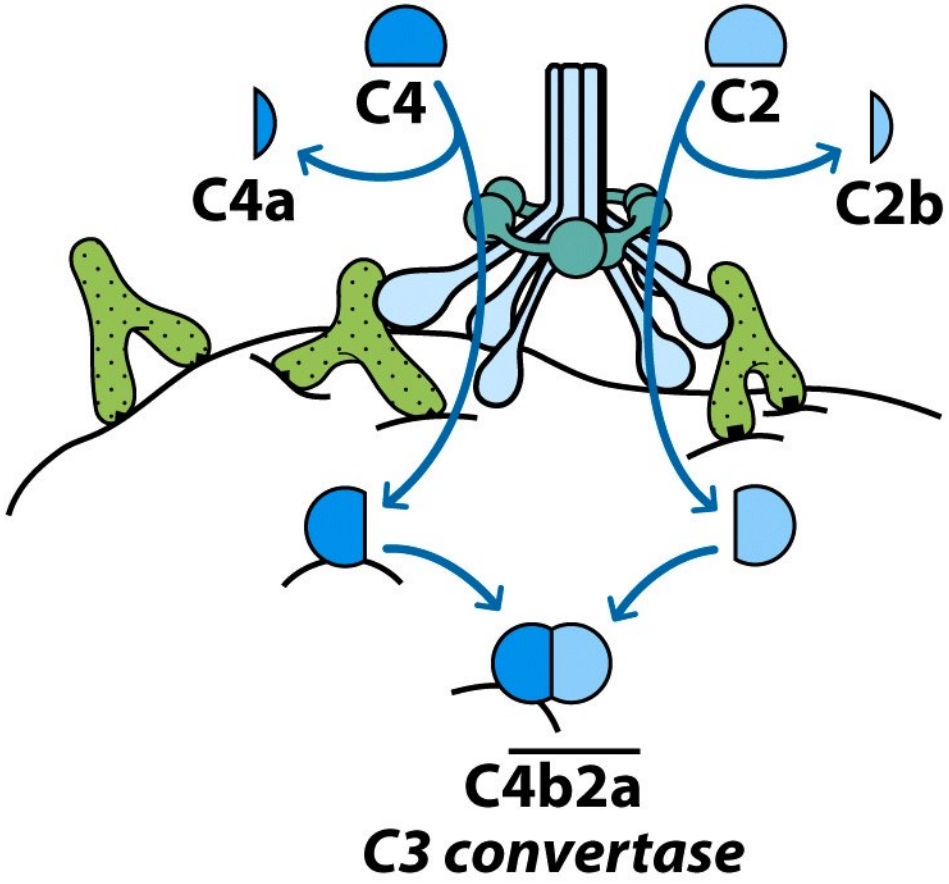

Figure 7-5 part 2
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3

C3 convertase hydrolyzes many C3 molecules. Some combine with C3 convertase to form C5 convertase.

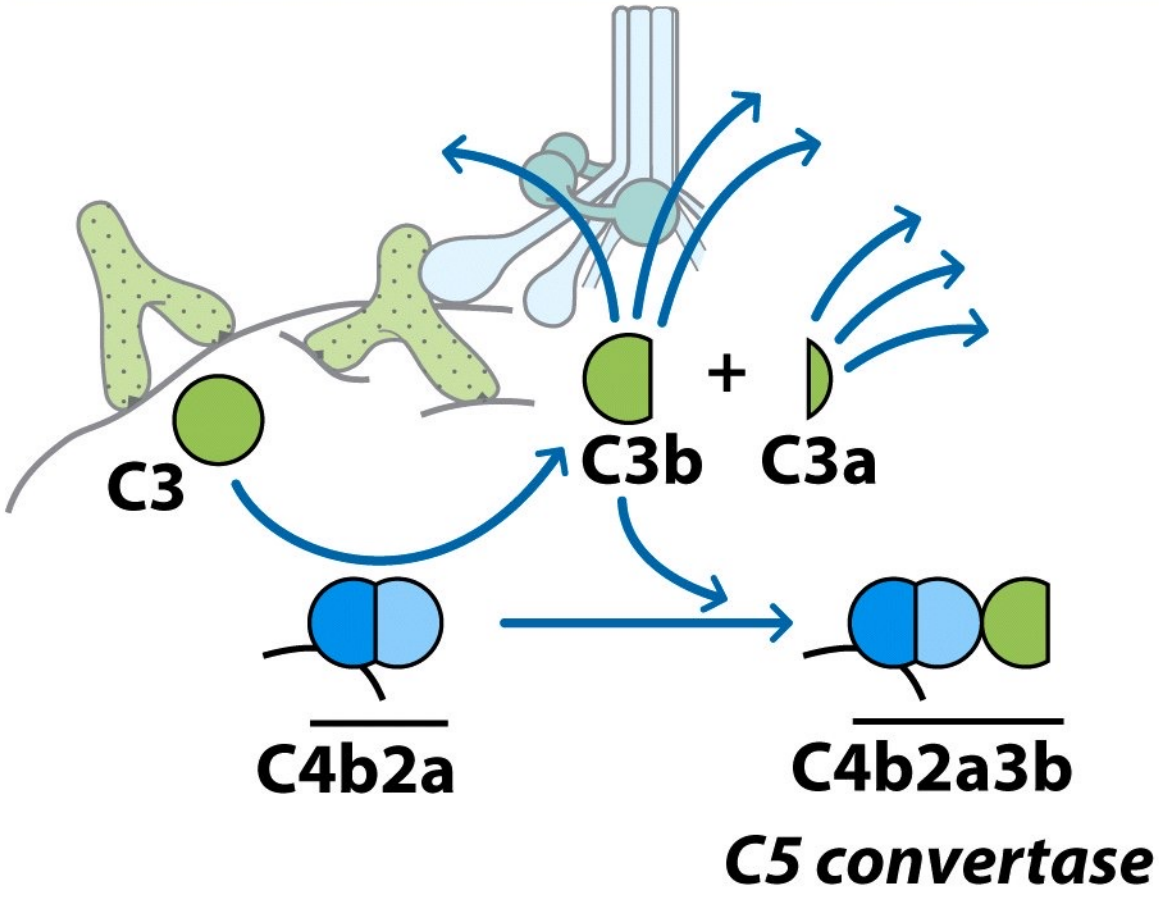

Figure 7-5 part 3
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4

The C3b component of C5 convertase binds C5, permitting $\overline{C4b2a}$ to cleave C5.

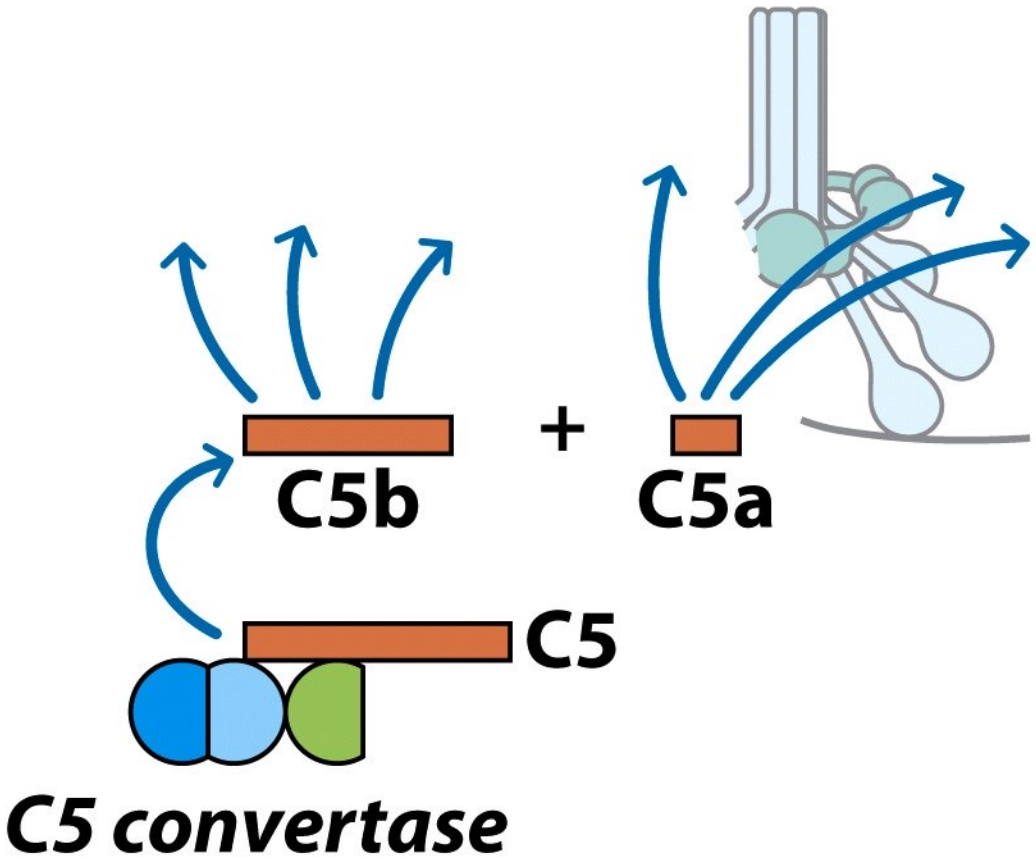

Figure 7-5 part 4
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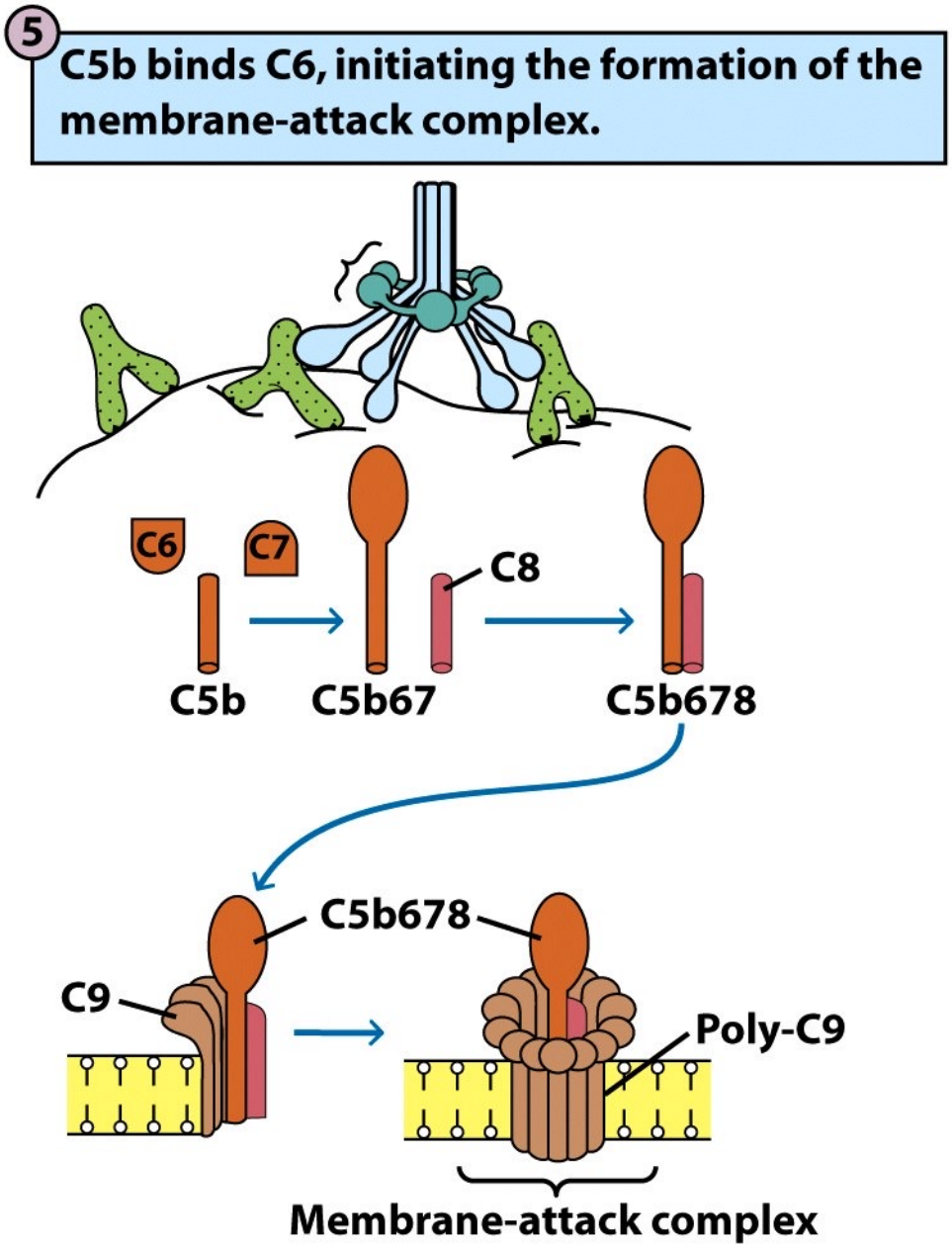

Figure 7-5 part 5
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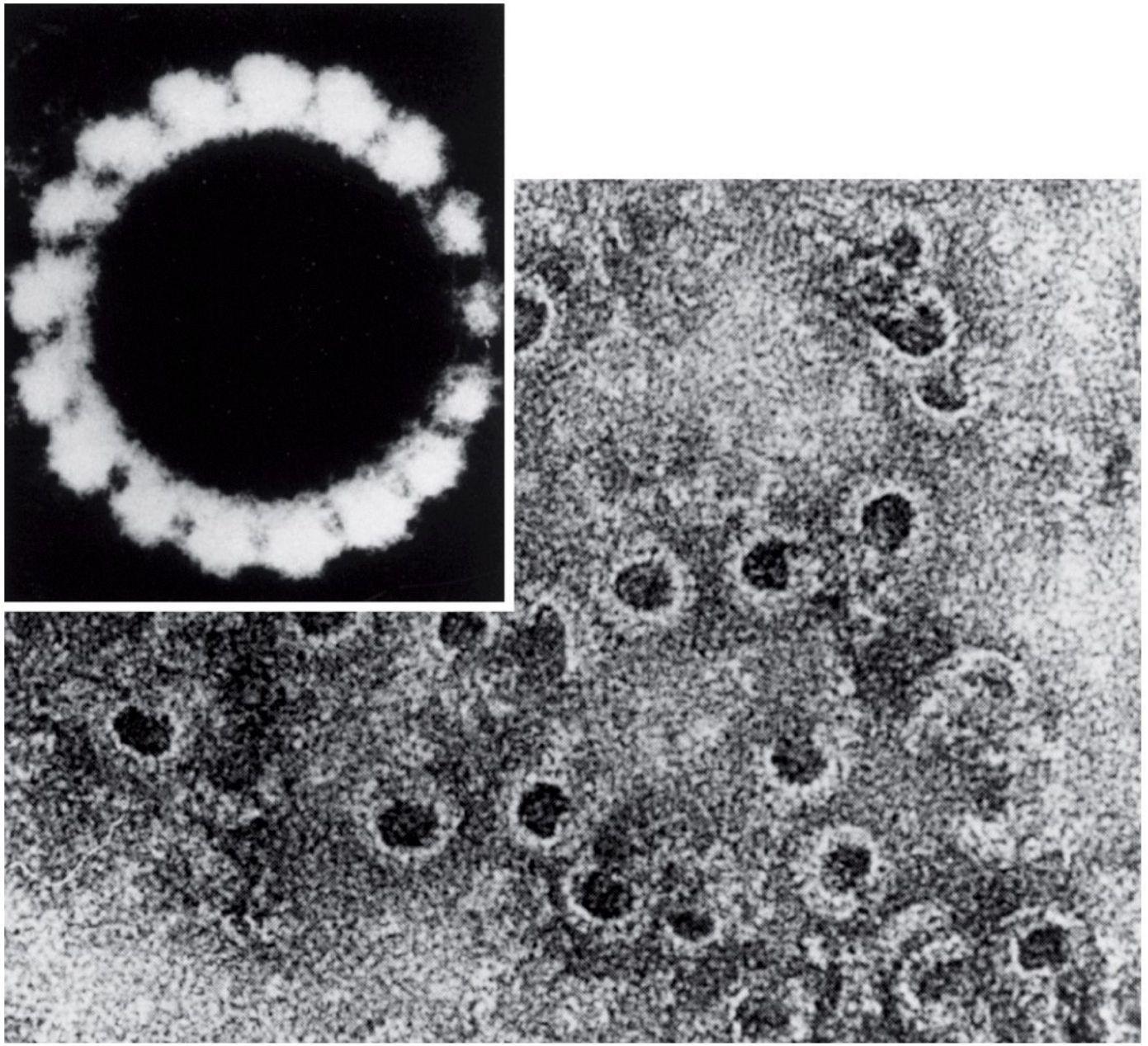

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Figure 7-8
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