The Complement System

An overview

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The Complement System

A major system of innate immunity

and one of the main effector mechanisms

of antibody-mediated immunity

The Complement System

A. Complement components

Inert soluble proteins that upon activation exert enzymatic activity whose the substrate is the next protein of the cascade

B. Complement receptors

Ligands of the CRs are the cleavage products and/or the protein complexes produced during complement activation

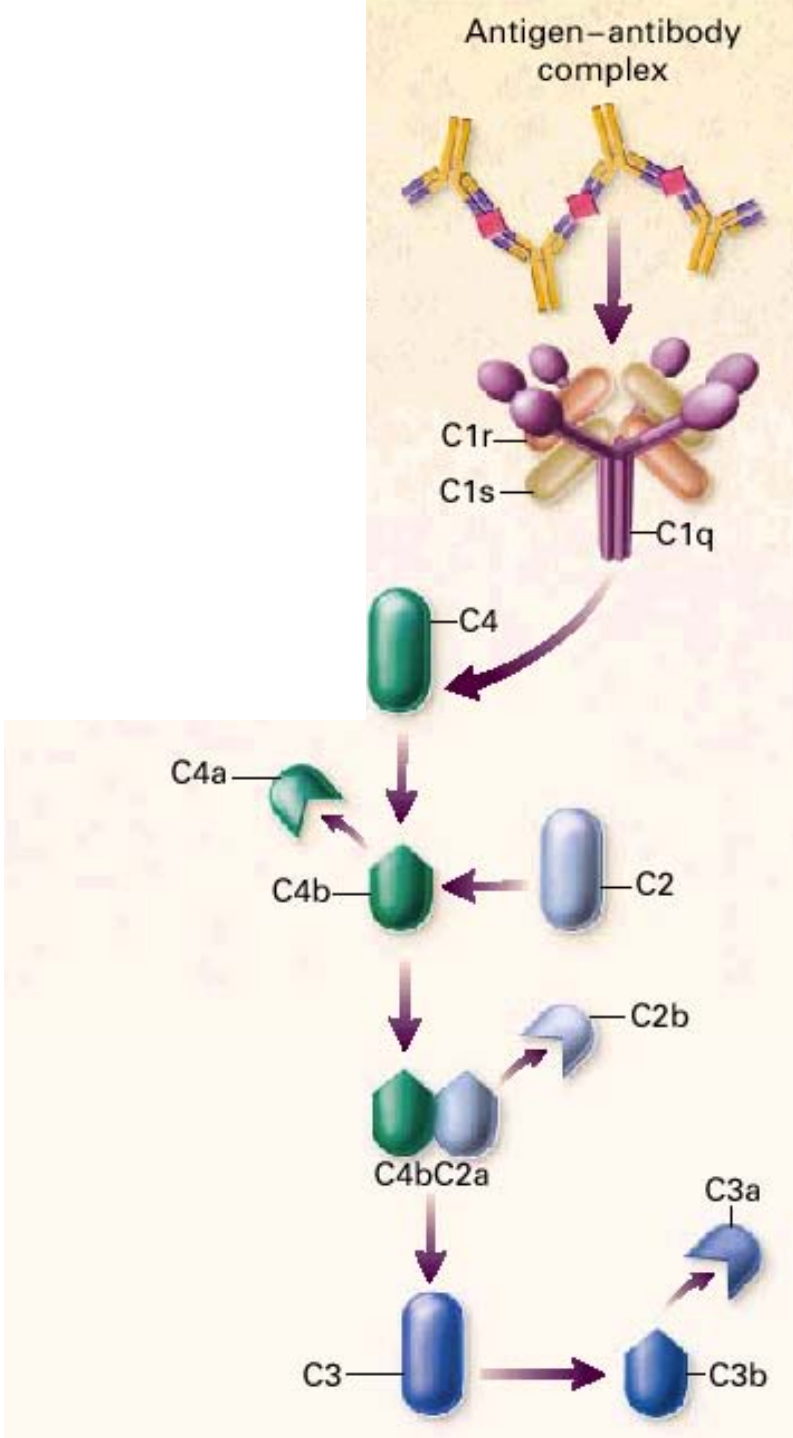
C. Regulatory proteins (soluble and membrane-associated)

Along with a series of physicochemical regulatory mechanisms, aim to:

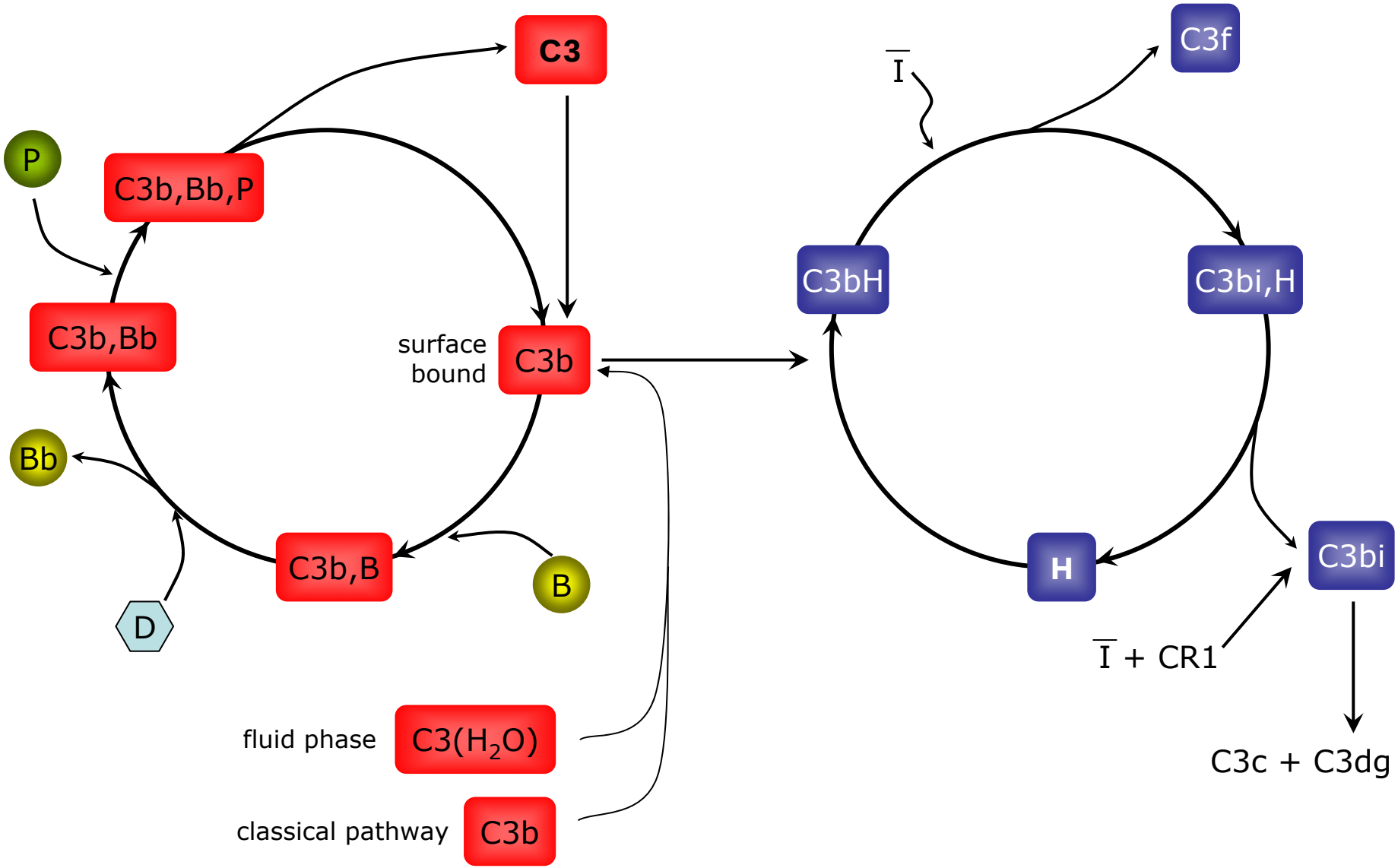
- focus the complement activation on the surface of invading pathogens
- limit the deposition of complement on normal/homologous cells and tissues

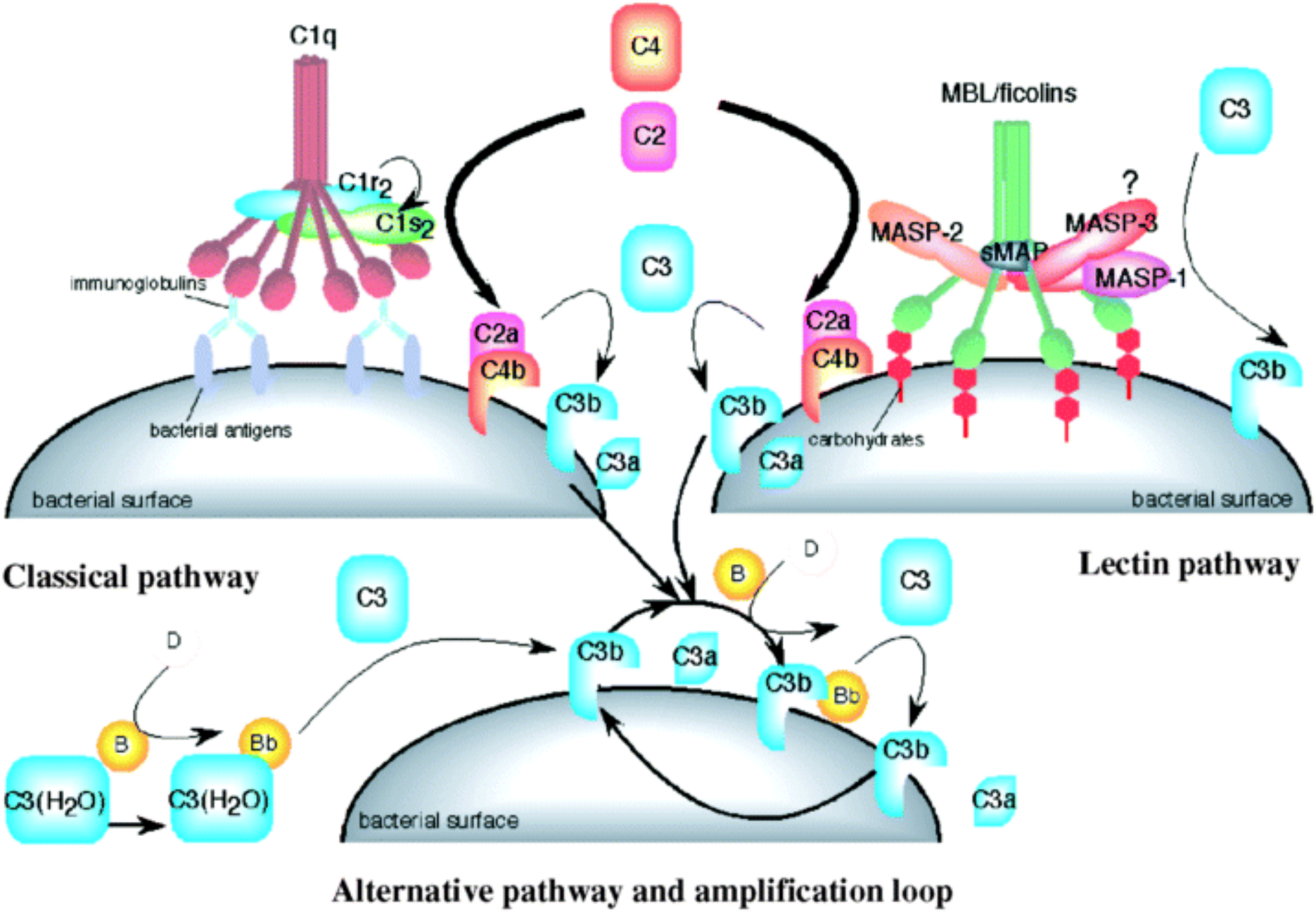
Lectin pathway

Classical pathway

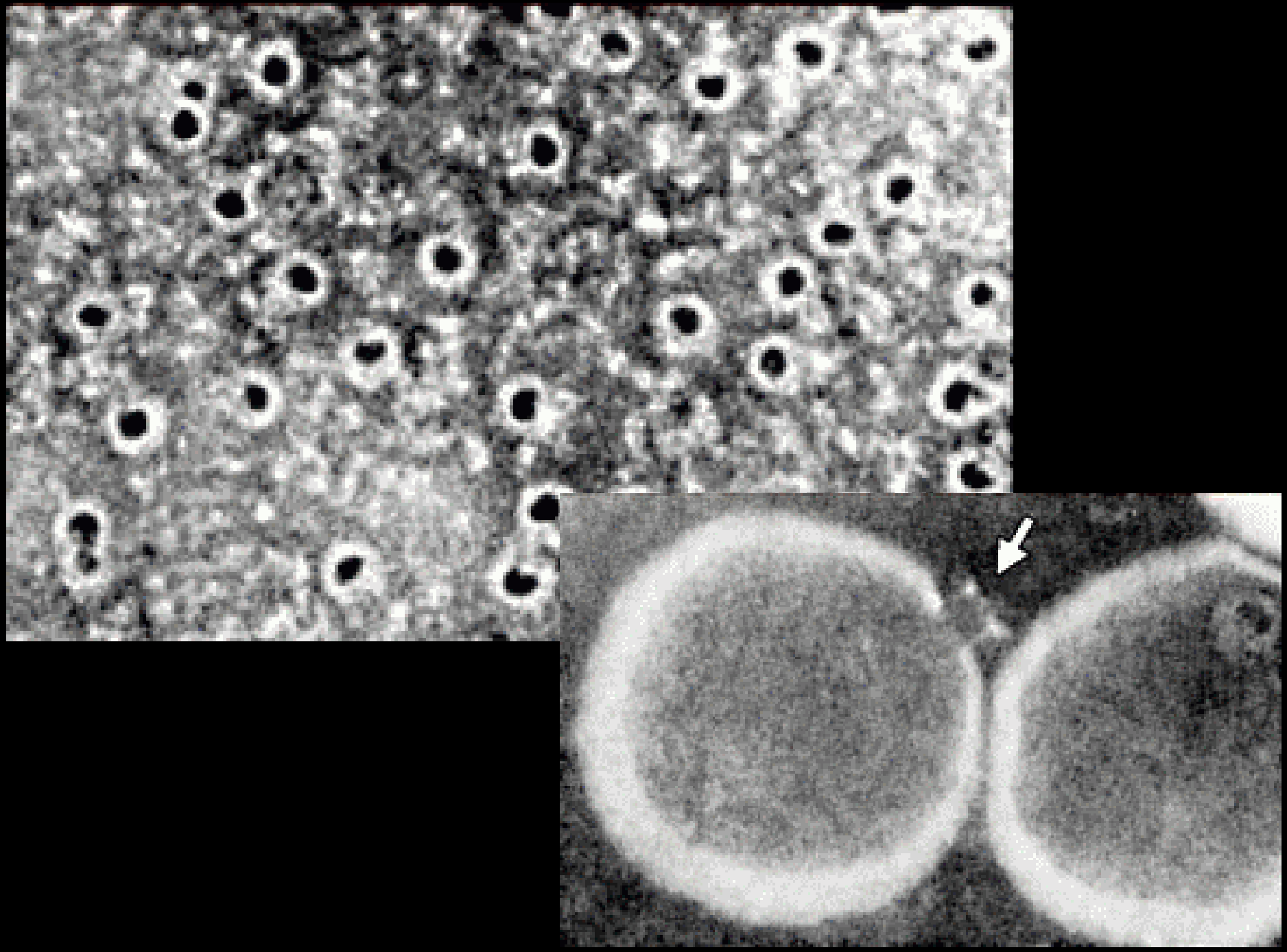


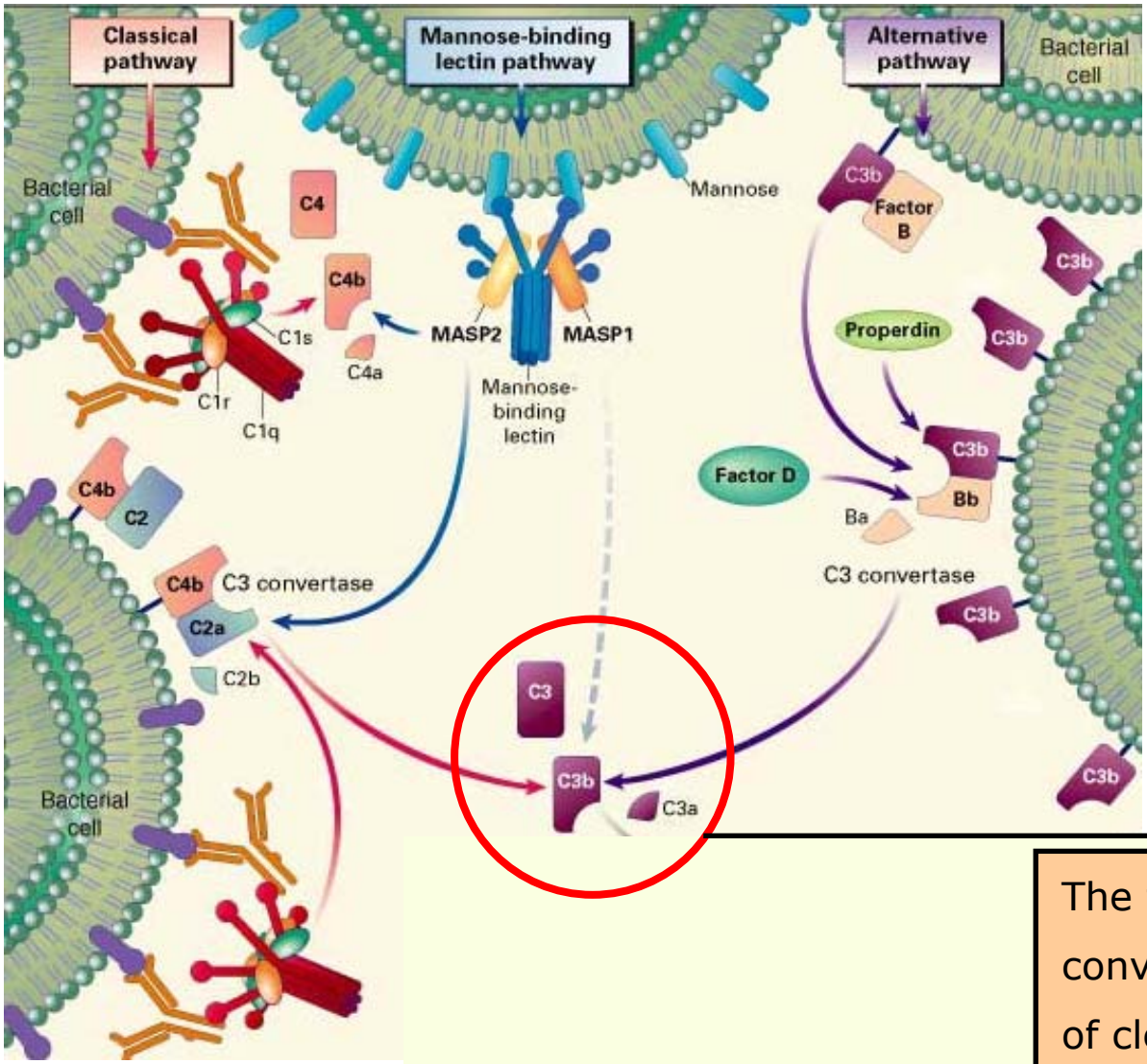
Alternative pathway and amplification loop



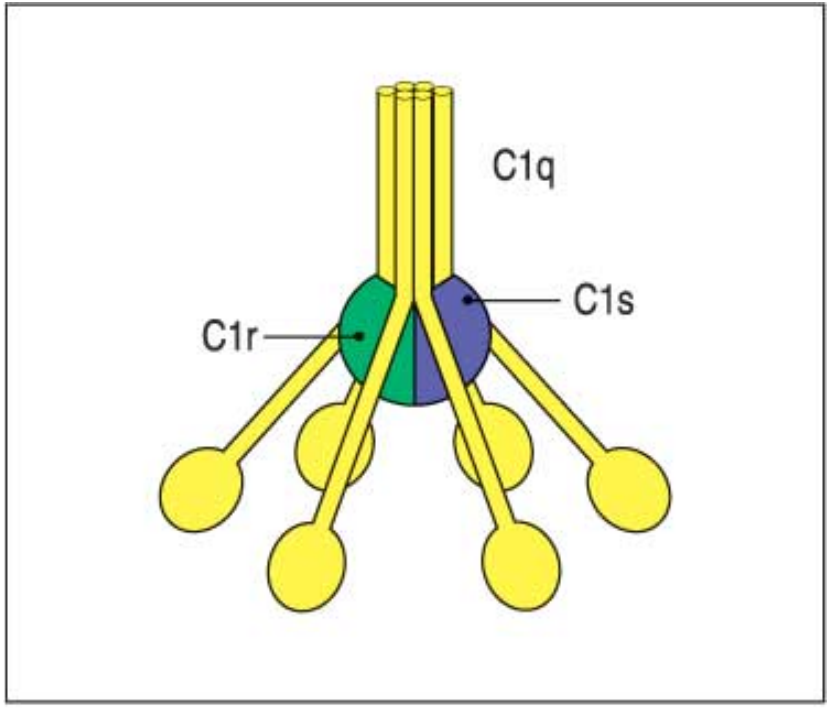


Alternative pathway and amplification loop





The three complement pathways converge at the point of cleavage of C3


C1q
C1s
C1r

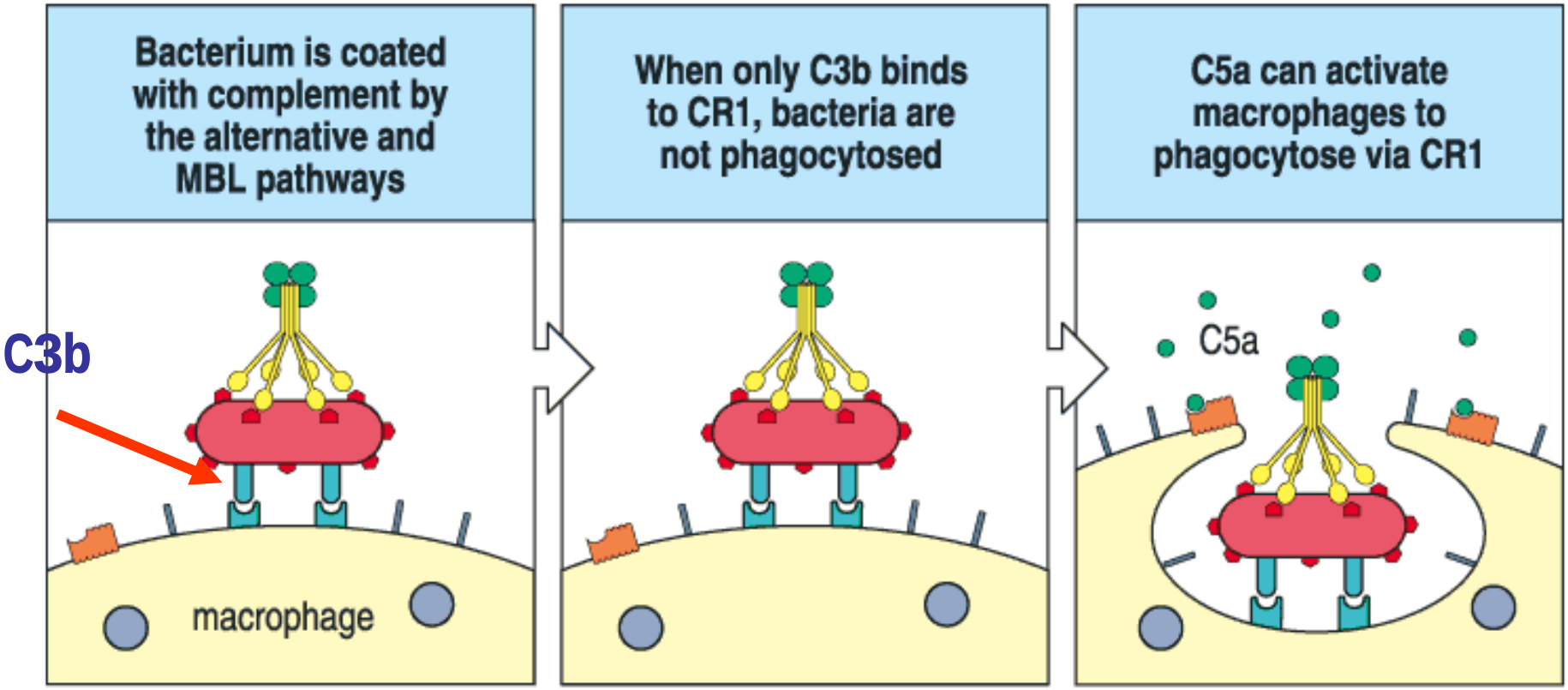


Fig 2.21 © 2001 Garland Science

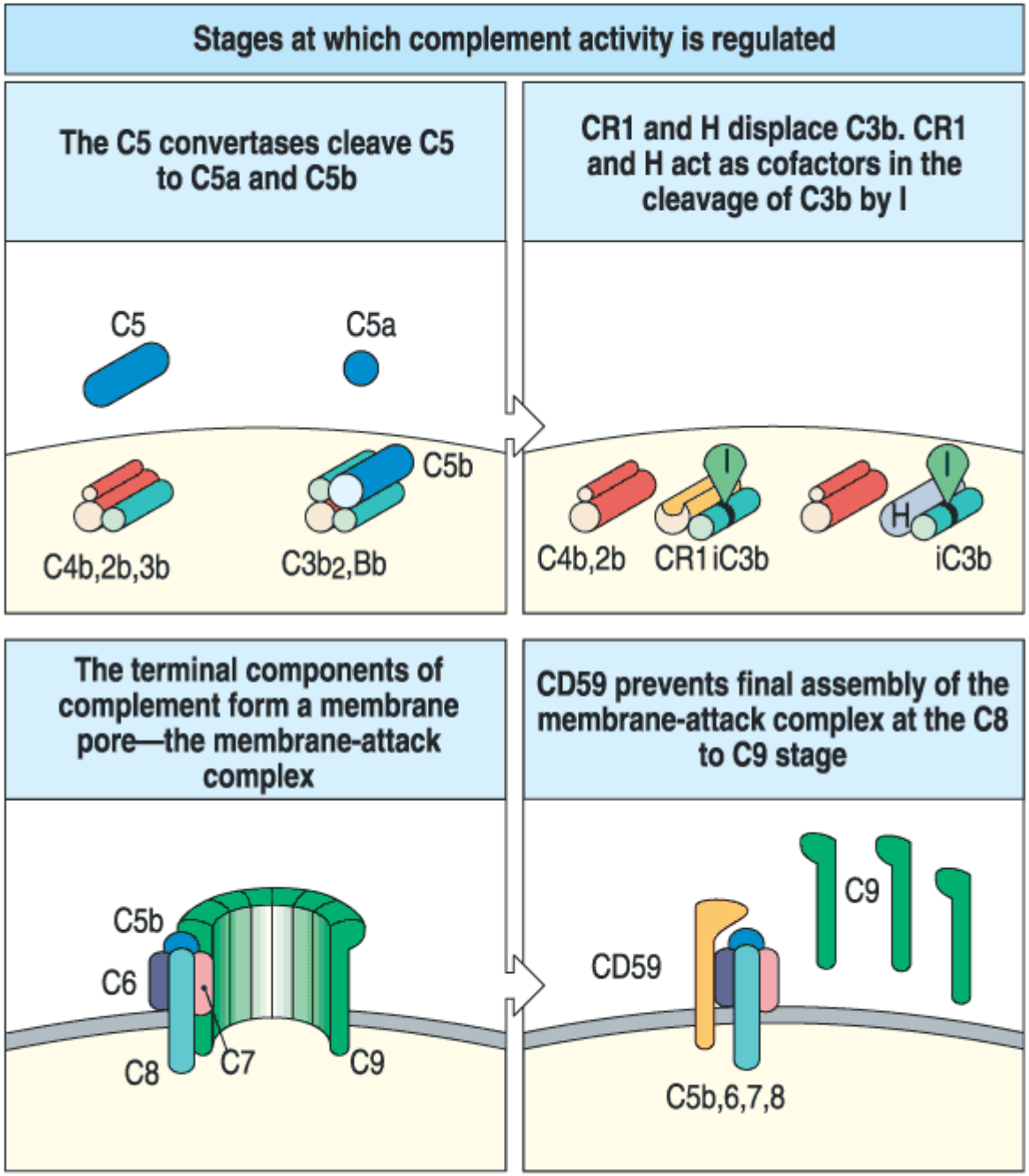
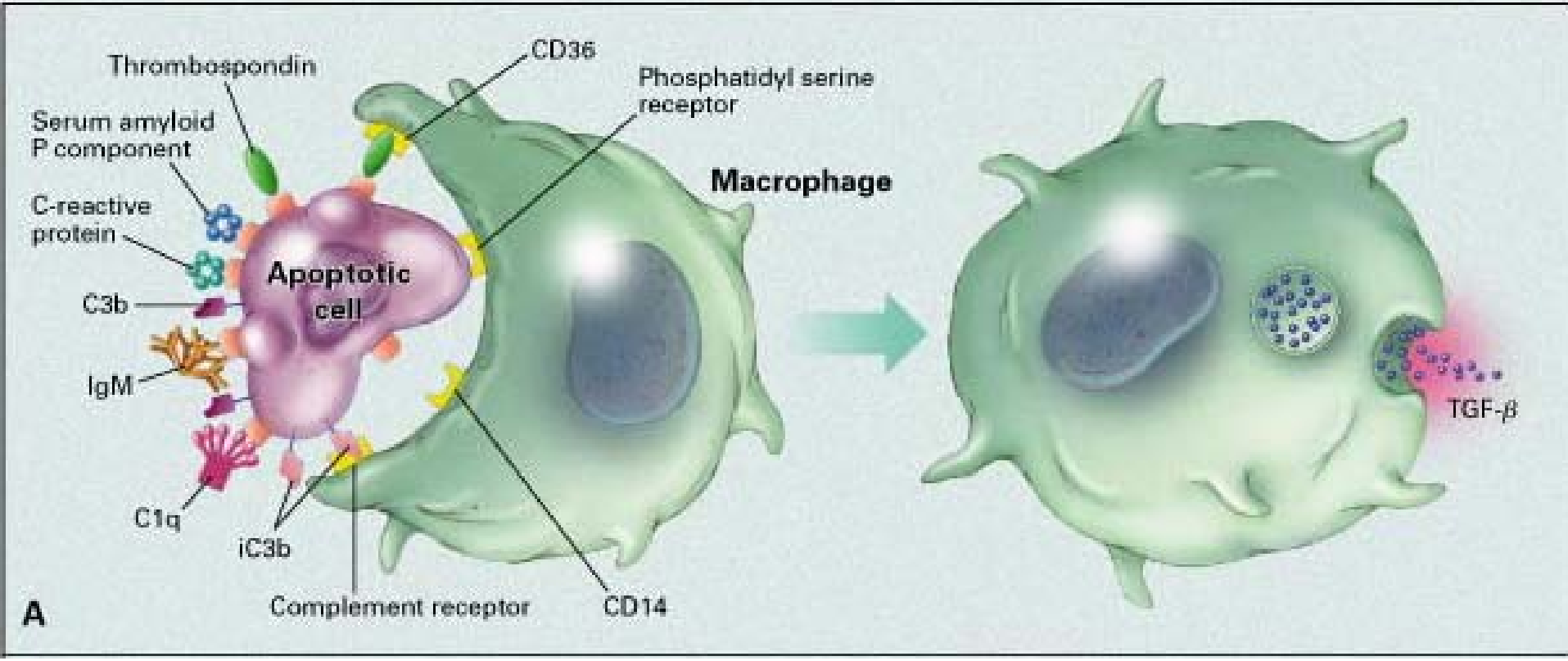


Fig 2.26 part 2 of 2

The Waste-Disposal Hypothesis for Systemic Lupus Erythematosus



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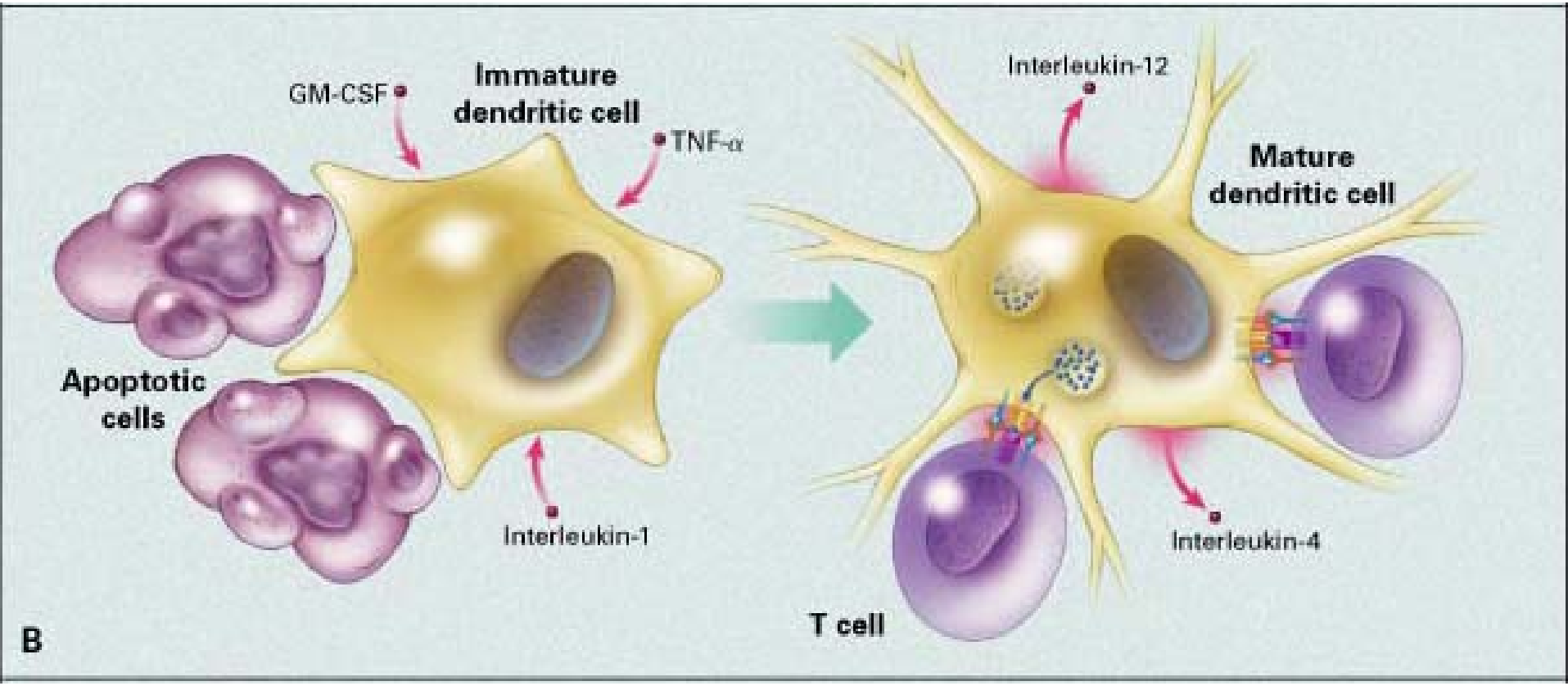

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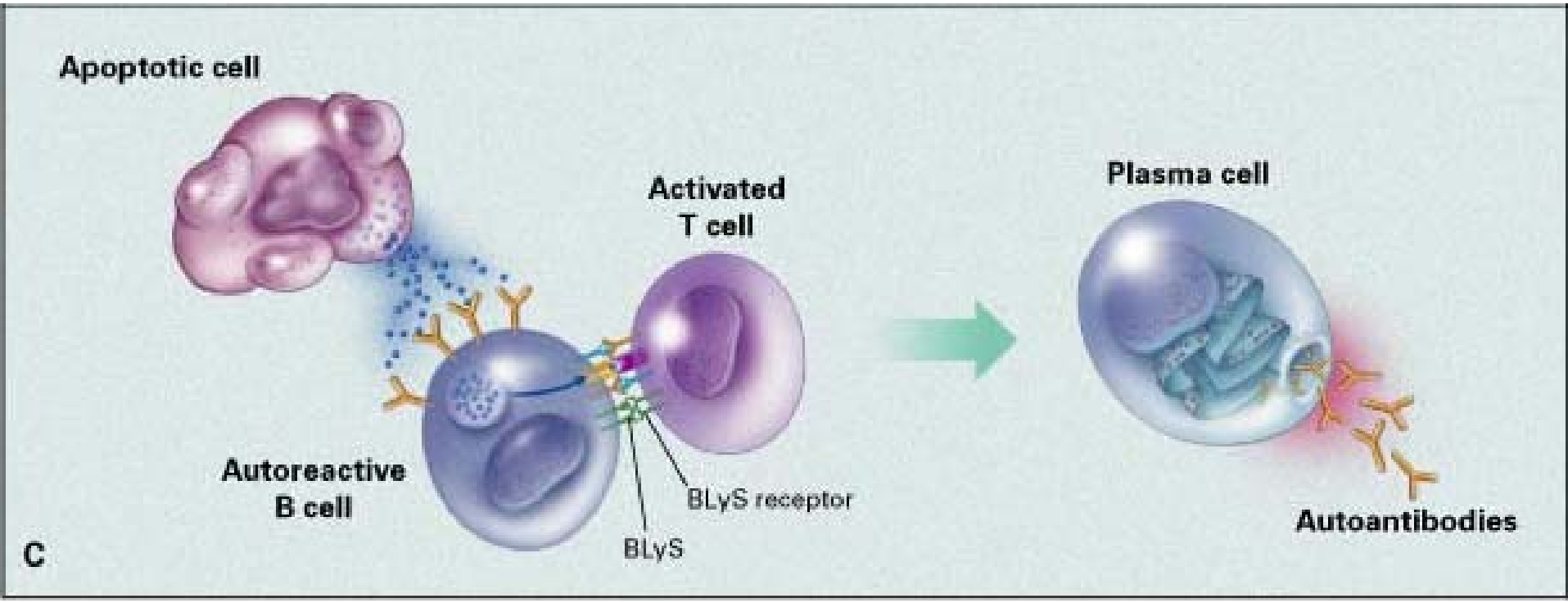
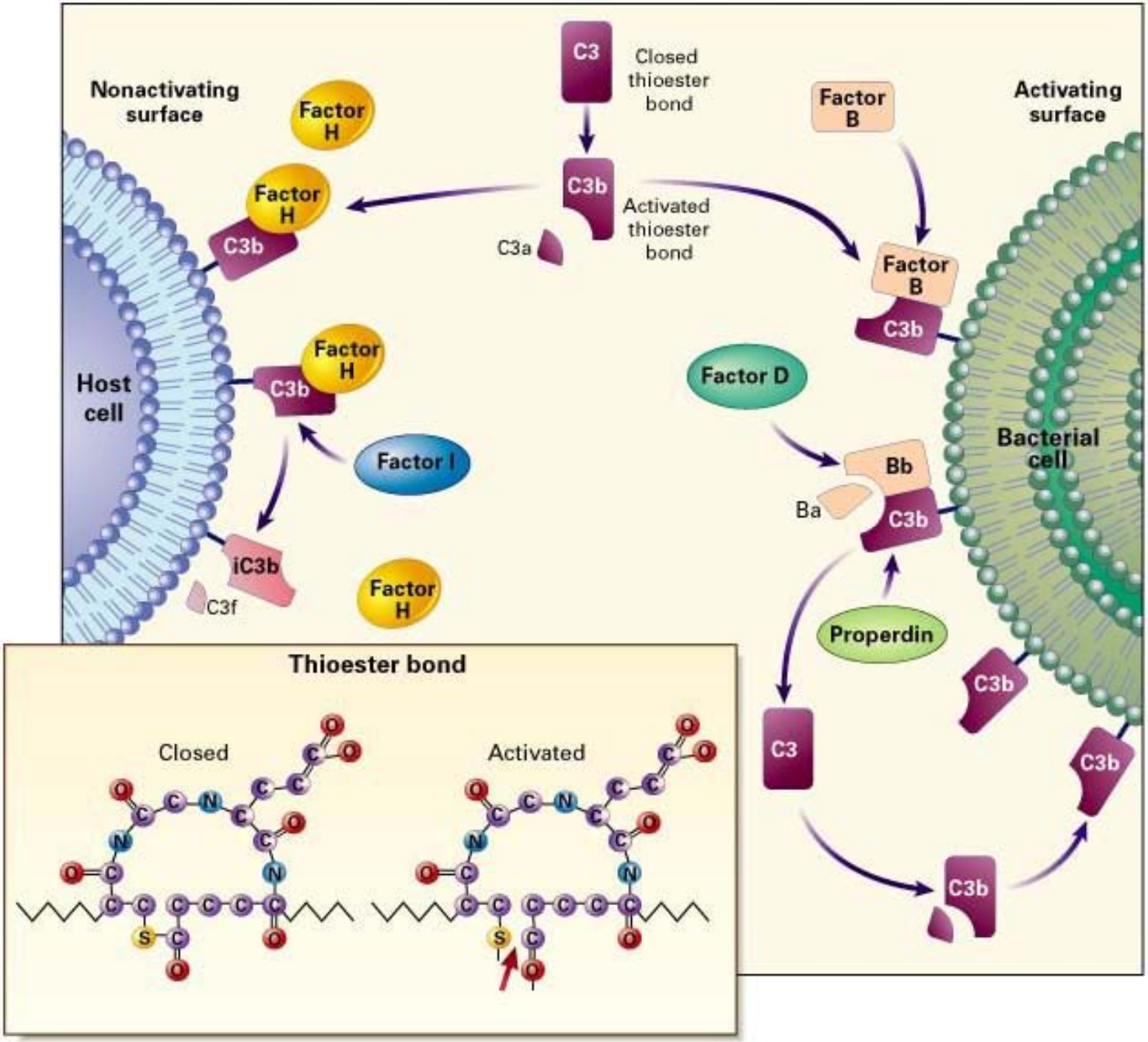
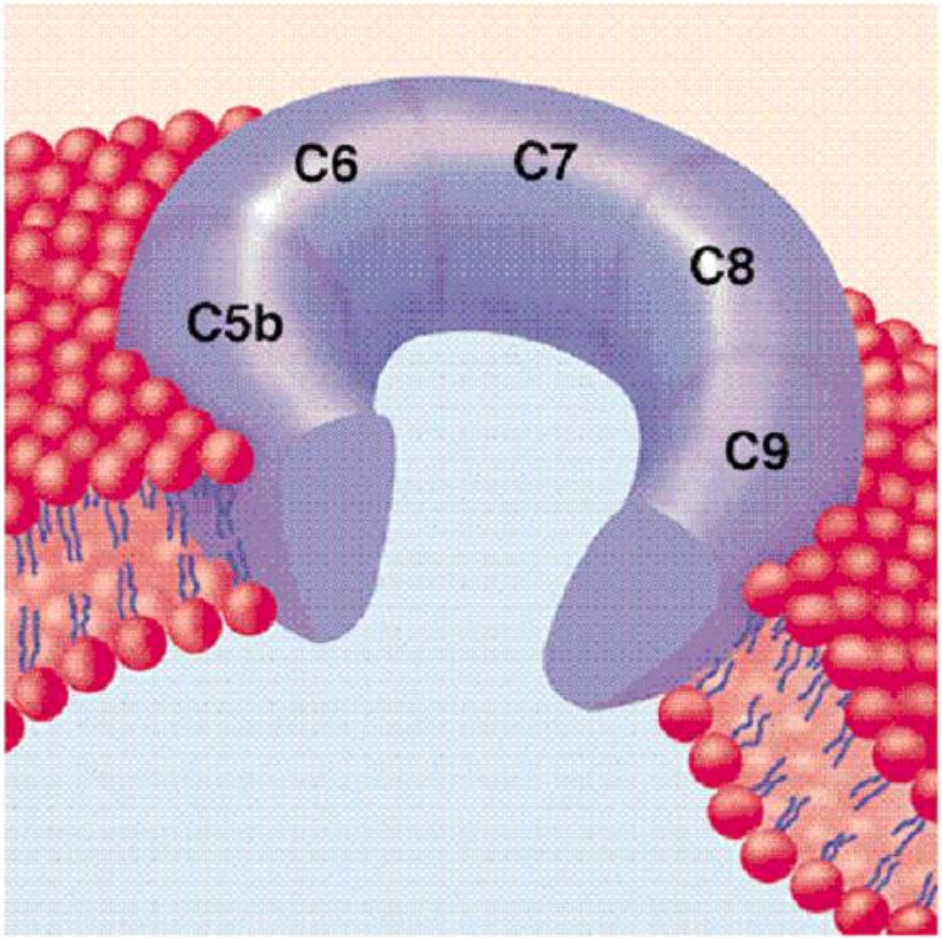
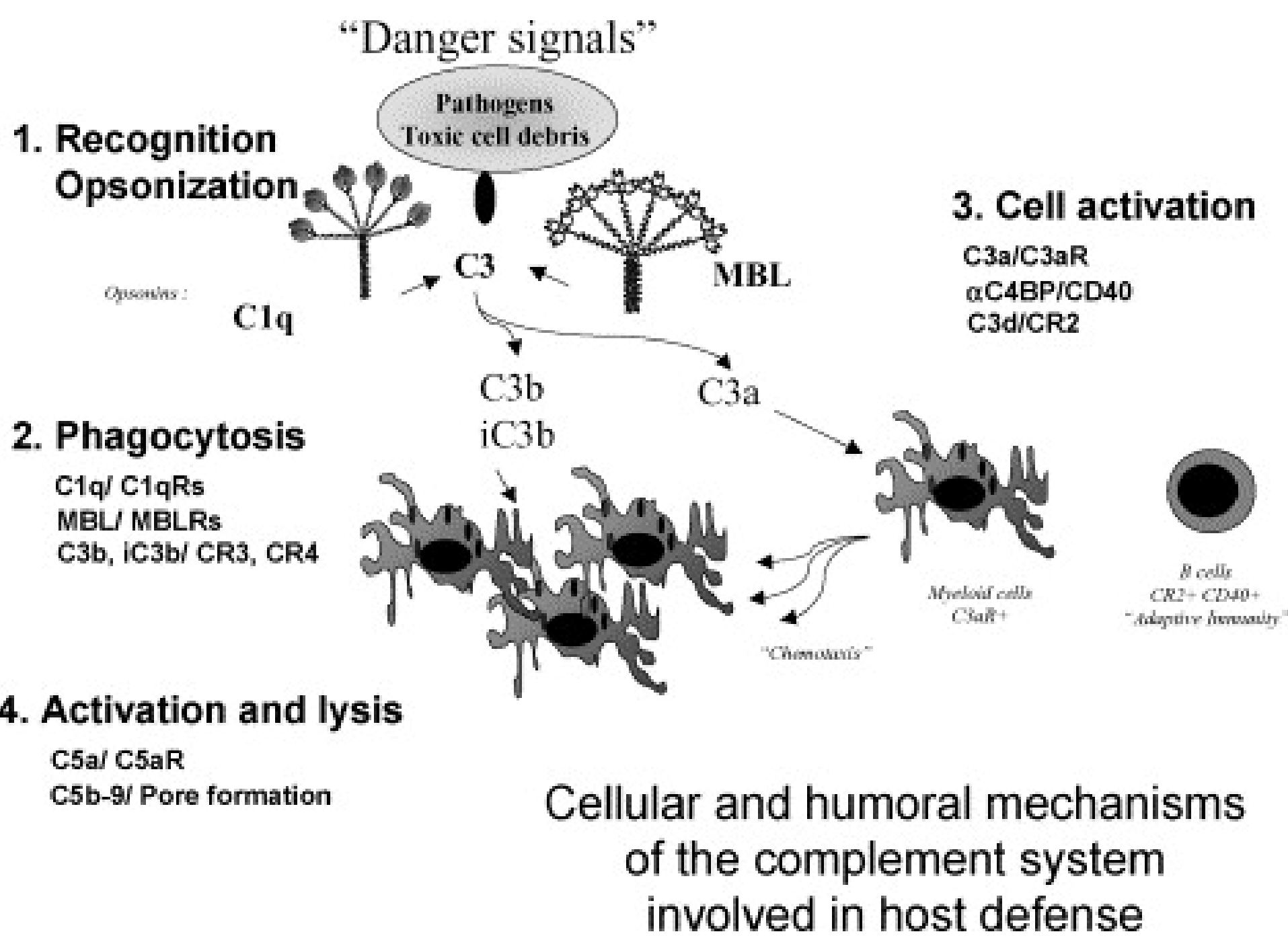


TABLE 1. THE THREE MAIN PHYSIOLOGIC ACTIVITIES OF THE COMPLEMENT SYSTEM.

ACTIVITY	COMPLEMENT PROTEIN RESPONSIBLE FOR ACTIVITY
Host defense against infection	
Opsonization	Covalently bound fragments of C3 and C4
Chemotaxis and activation of leukocytes	Anaphylatoxins (C5a, C3a, and C4a); anaphylatoxin receptors on leukocytes
Lysis of bacteria and cells	Membrane-attack complex (C5b–C9)
Interface between innate and adaptive immunity	
Augmentation of antibody responses	C3b and C4b bound to immune complexes and to antigen; C3 receptors on B cells and antigen-presenting cells
Enhancement of immunologic memory	C3b and C4b bound to immune complexes and to antigen; C3 receptors on follicular dendritic cells
Disposal of waste	
Clearance of immune complexes from tissues	C1q; covalently bound fragments of C3 and C4
Clearance of apoptotic cells	C1q; covalently bound fragments of C3 and C4


C3
Closed thioester bond
Nonactivating surface
Factor H
Factor H
C3b
C3b
Activated thioester bond
C3a
Factor B
Activating surface
Factor B
C3b
Host cell
Factor H
C3b
Factor D
Factor I
Bb
Ba
C3b
Bacterial cell
iC3b
C3f
Factor H
Properdin
C3b
C3
C3b
C3b
Thioester bond
Closed
Activated


C6
C7
C8
C5b
C9



Cellular and humoral mechanisms of the complement system involved in host defense

The regulatory proteins