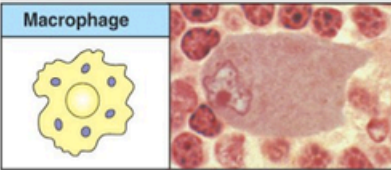
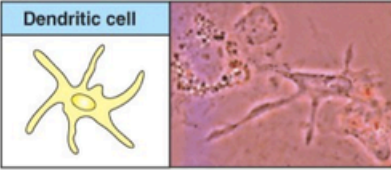
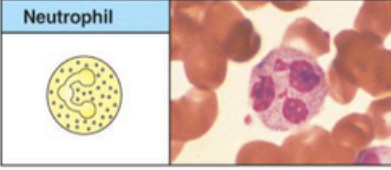
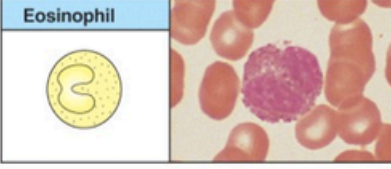
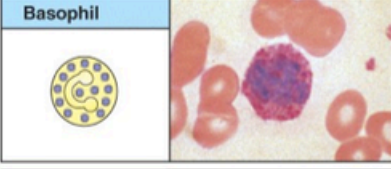
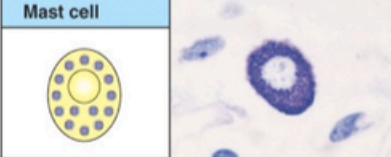


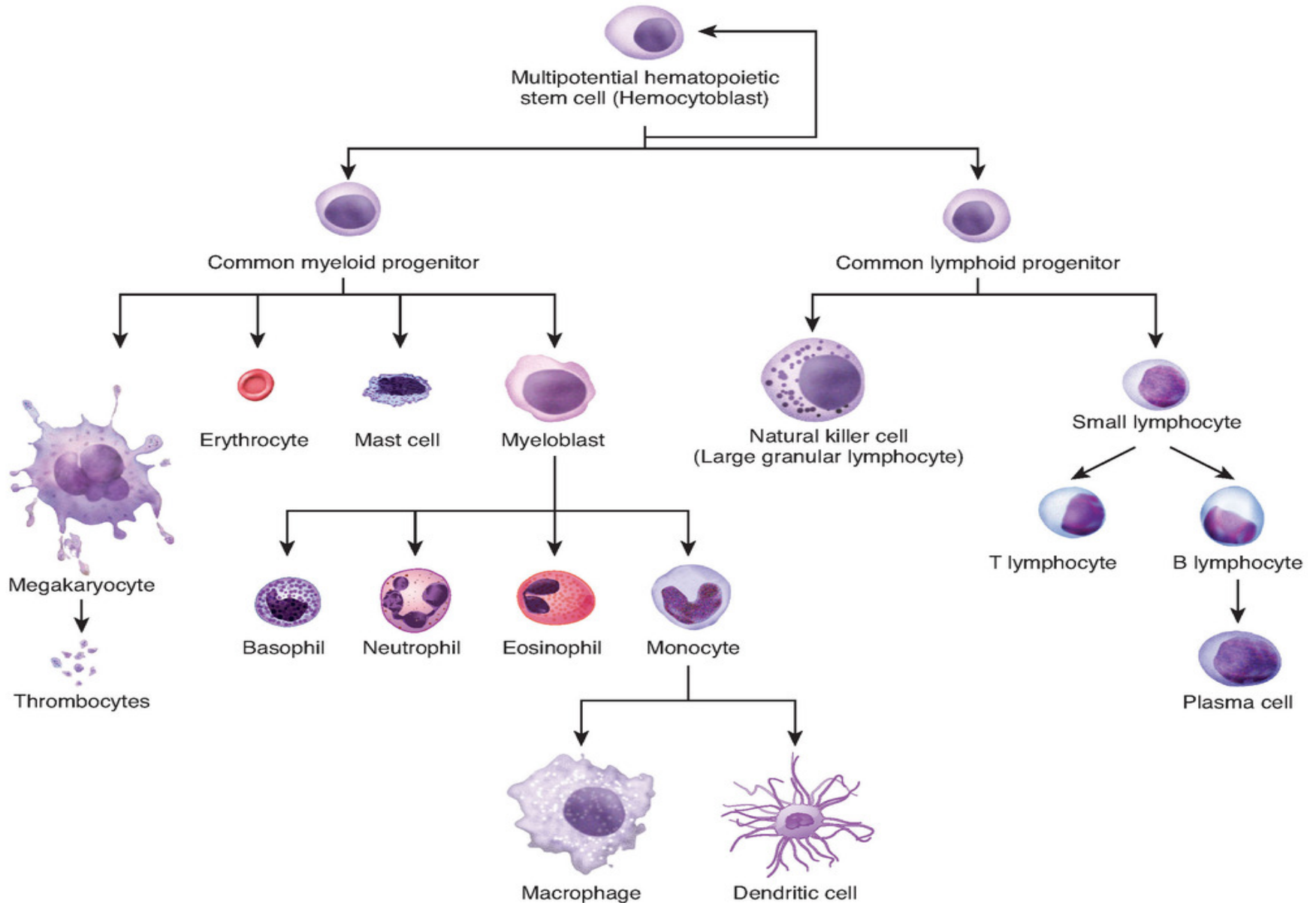
Components of the Immune System (Innate immunity)

Definition

- The innate immunity represents the first line of defense against an intruding pathogen.
- All these cells exhibit a rapid non-specific response to either foreign cells or to tumor cells.

Cell		Activated function
Macrophage		Phagocytosis and activation of bactericidal mechanisms Antigen presentation
Dendritic cell		Antigen uptake in peripheral sites Antigen presentation in lymph nodes
Neutrophil		Phagocytosis and activation of bactericidal mechanisms
Eosinophil		Killing of antibody-coated parasites
Basophil		Unknown
Mast cell		Release of granules containing histamine and other active agents

Haematopoietic Cell Lineages



Molecular Mediators of the Innate Immune Response (1)

- Directly bactericidal molecules

1- Lysozyme → glycosidase that breaks down bacterial cell walls

2- Lactoferrin → inhibits bacterial growth

3- Complement → alternative pathway
activated directly by bacteria

Molecular Mediators of the Innate Immune Response (2)

Soluble molecules that enhance phagocytosis

1. Complement alternative pathway vs. bacteria
2. Collectins vs. terminal mannose residues
3. C-reactive protein vs. phosphorylcholine
4. LPS-binding protein vs. lipopolysaccharide (endotoxin)
5. Defensin

Macrophage



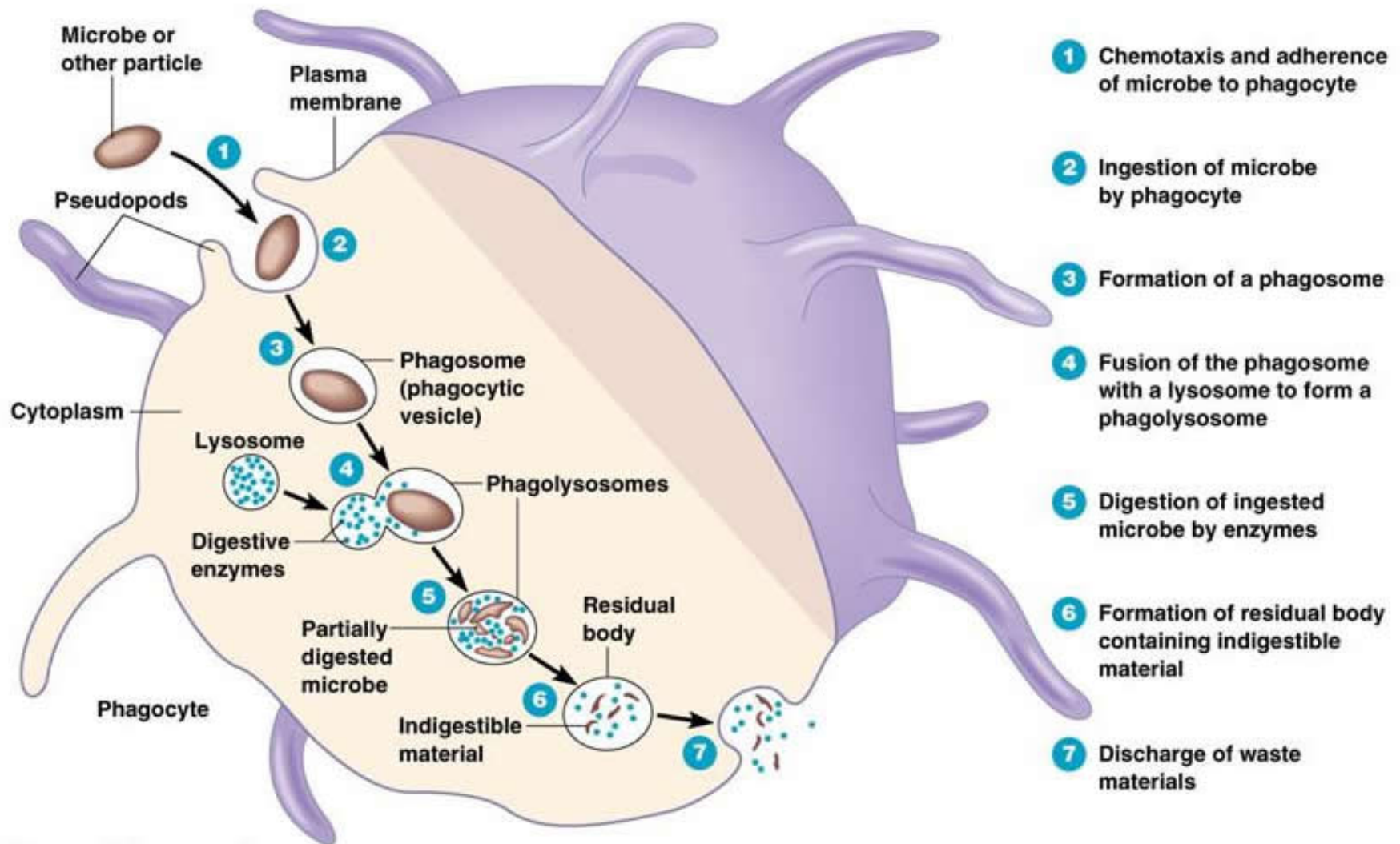
Macrophage

Bacterium

SEM

2 μ m

Mechanism of phagocytosis



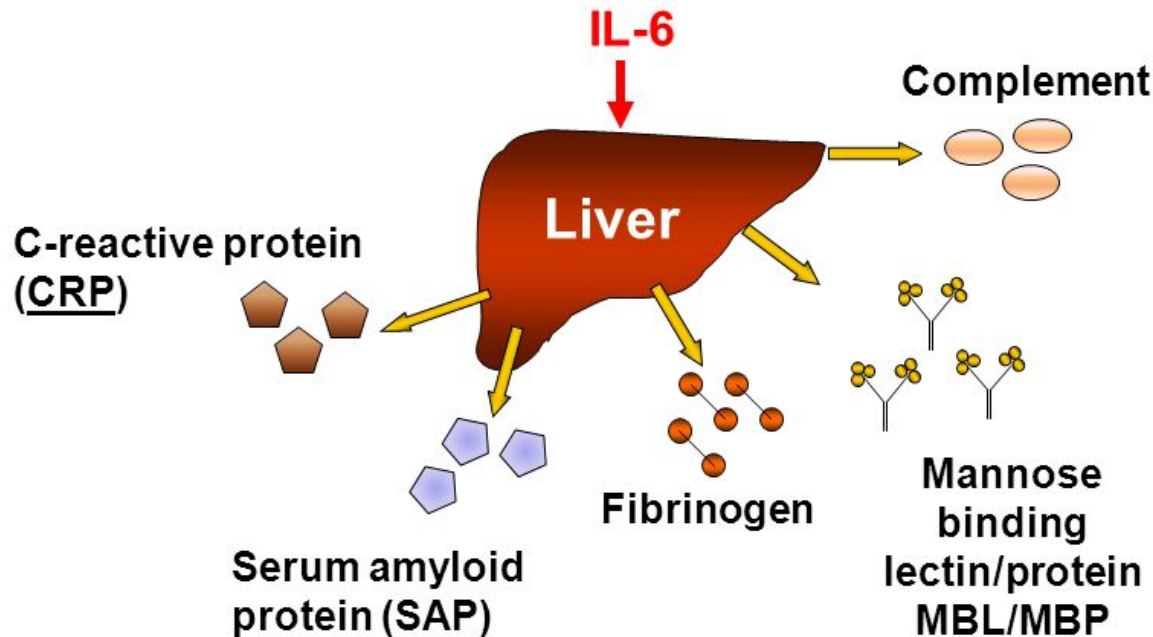
Phases of phagocytosis

Collectins

- Soluble proteins of innate immunity
- Acute phase proteins
- Produced in lung, liver and g/i tract
- Bind bacterial and yeast saccharides
- Activate the complement pathway ...alternative pathway
- Stimulate phagocytosis

Acute Phase Protein (APP)

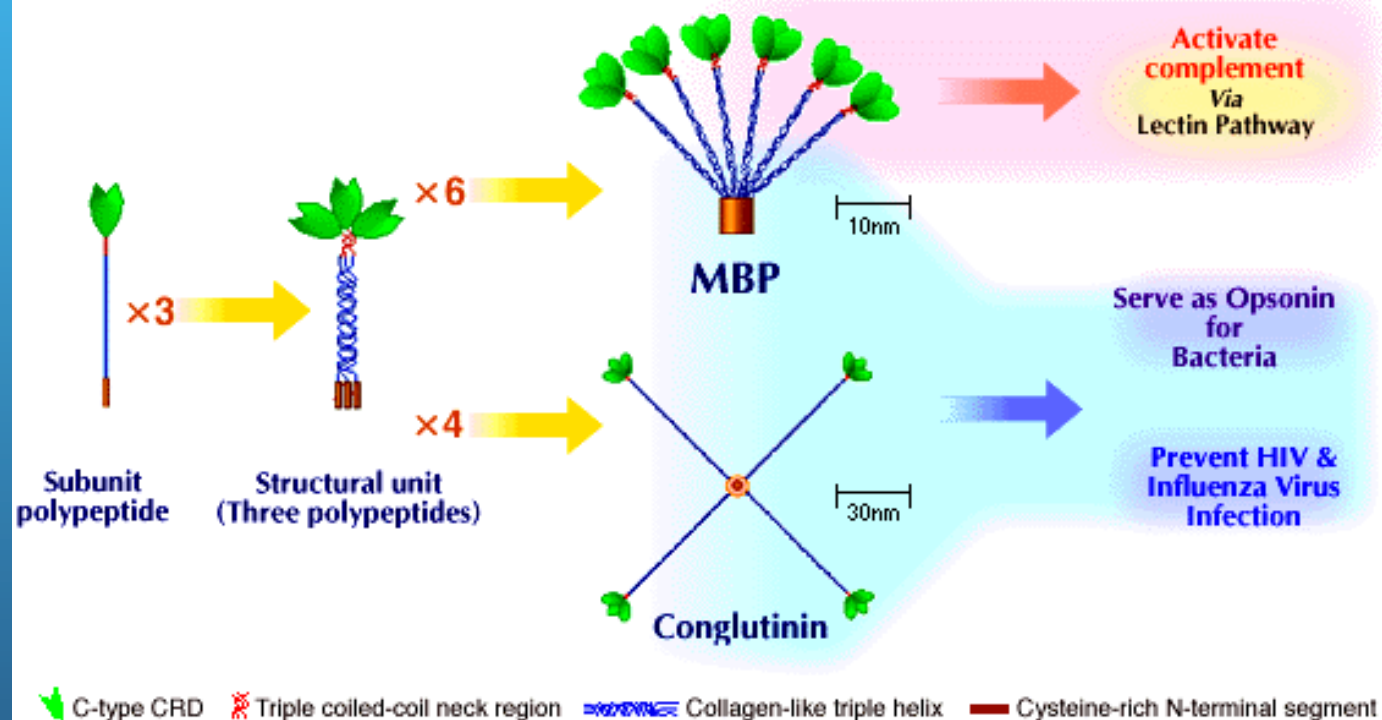
ACUTE PHASE REACTION

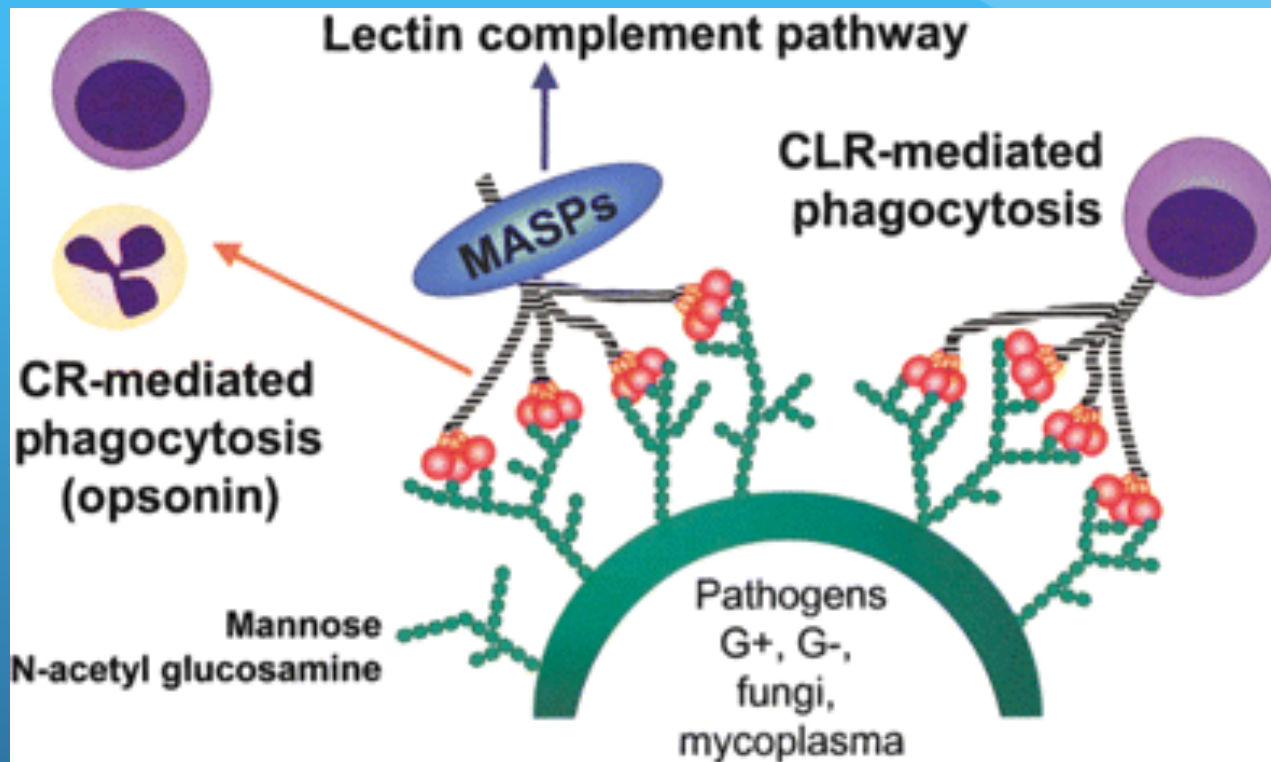


UNDER THE INFLUENCE OF IL-6 THE LIVER PRODUCES A BUNCH OF ACUTE-PHASE PROTEINS

Mannose Binding Protein/Lectin

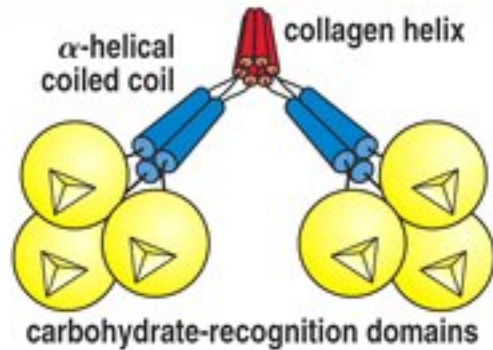
Molecular structures and biological activities of collectins (MBP and conglutinin)



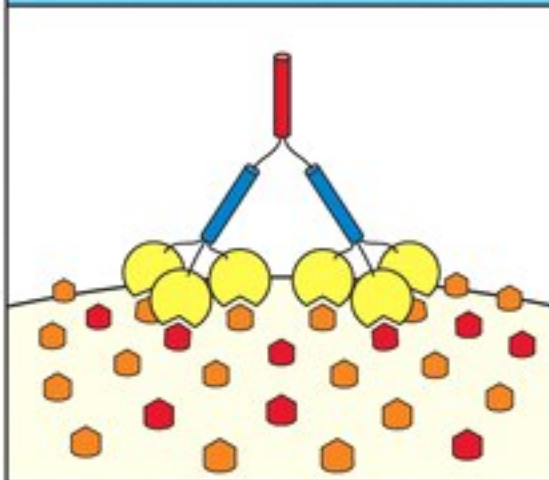


Hoffmann et al. (1999)

Mannose-binding lectin (MBL) has two to six clusters of carbohydrate-recognition domains. Within each of the clusters the carbohydrate-binding sites have a fixed orientation



MBL binds with high affinity to mannose and fucose residues with correct spacing



Mannose and fucose residues that have different spacing are not bound by MBL

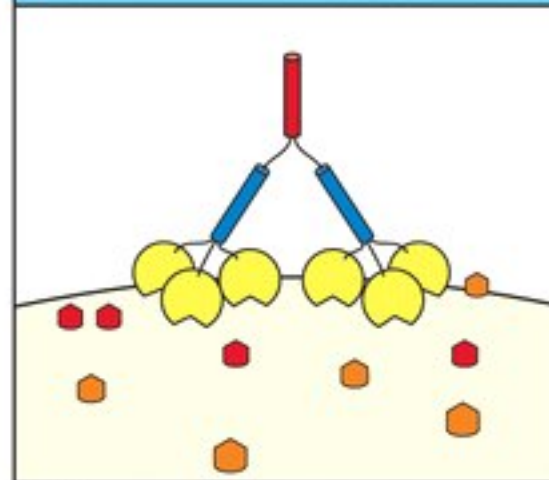


Figure 2-11 Immunobiology, 6/e. (© Garland Science 2005)

Mannose Binding Protein/Lectin

- Serum protein produced in the liver
- Binds terminal mannose
- Activates C3 in Ab independent manner
- Opsonises bacteria for phagocytosis
- Deficiency leads to serious infections

C-reactive protein (CRP)

- Acute phase protein
- Made in liver
- Binds phosphoryl choline on pneumococcal C-polysaccharide.
- Also binds damaged cell membranes and nuclei
- Activates complement classical pathway

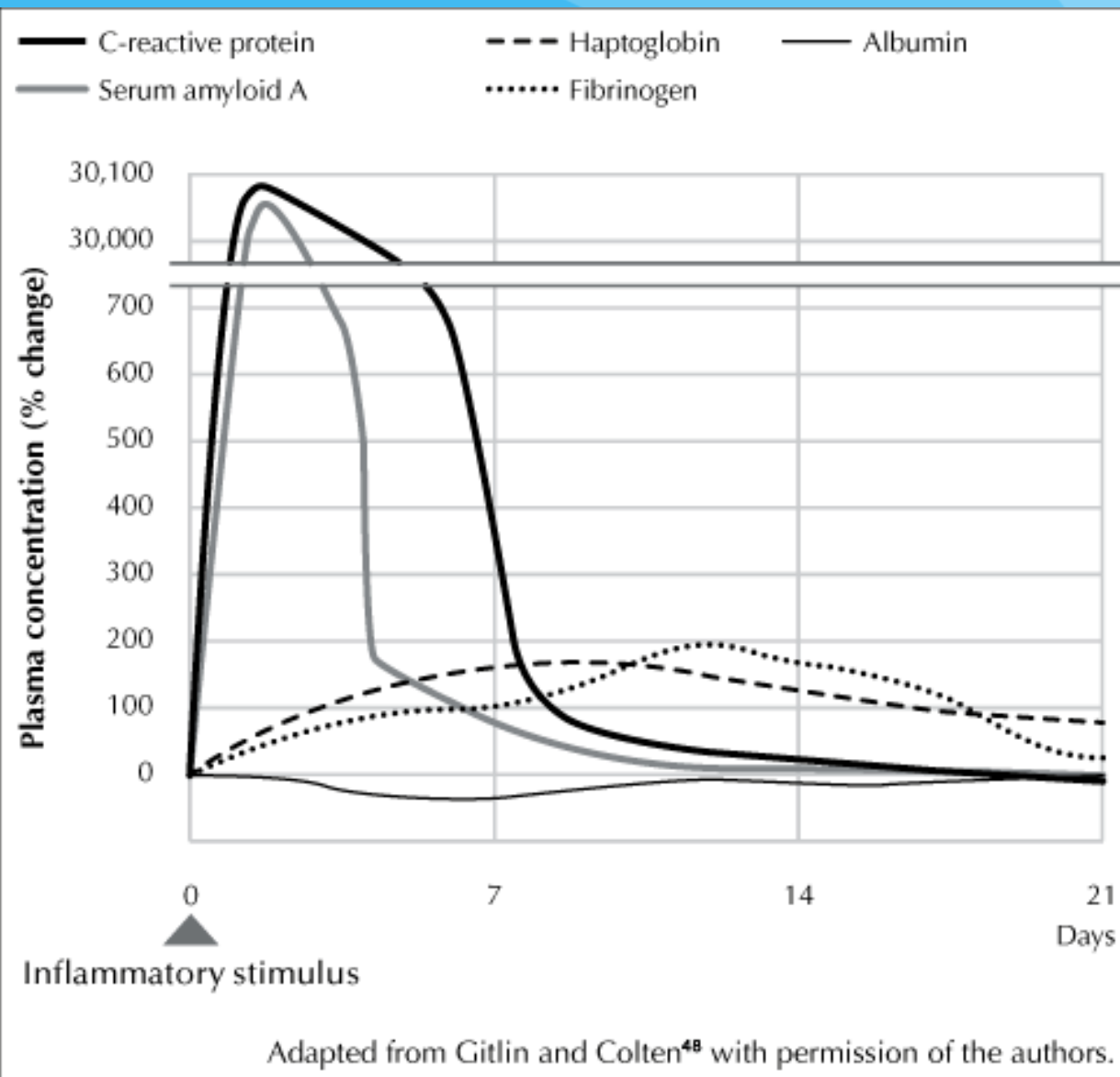


Figure 1. Characteristic pattern of inflammatory biomarkers in tissue damage.

Defensins

- Cysteine rich endogenous peptides vs. bacteria, fungi & viruses
- Present in skin and mucous membranes
- Stored in neutrophil & Paneth cell granules and secreted in response to bacteria
- Lead to permeabilisation of bacterial membranes and leucocyte chemotaxis

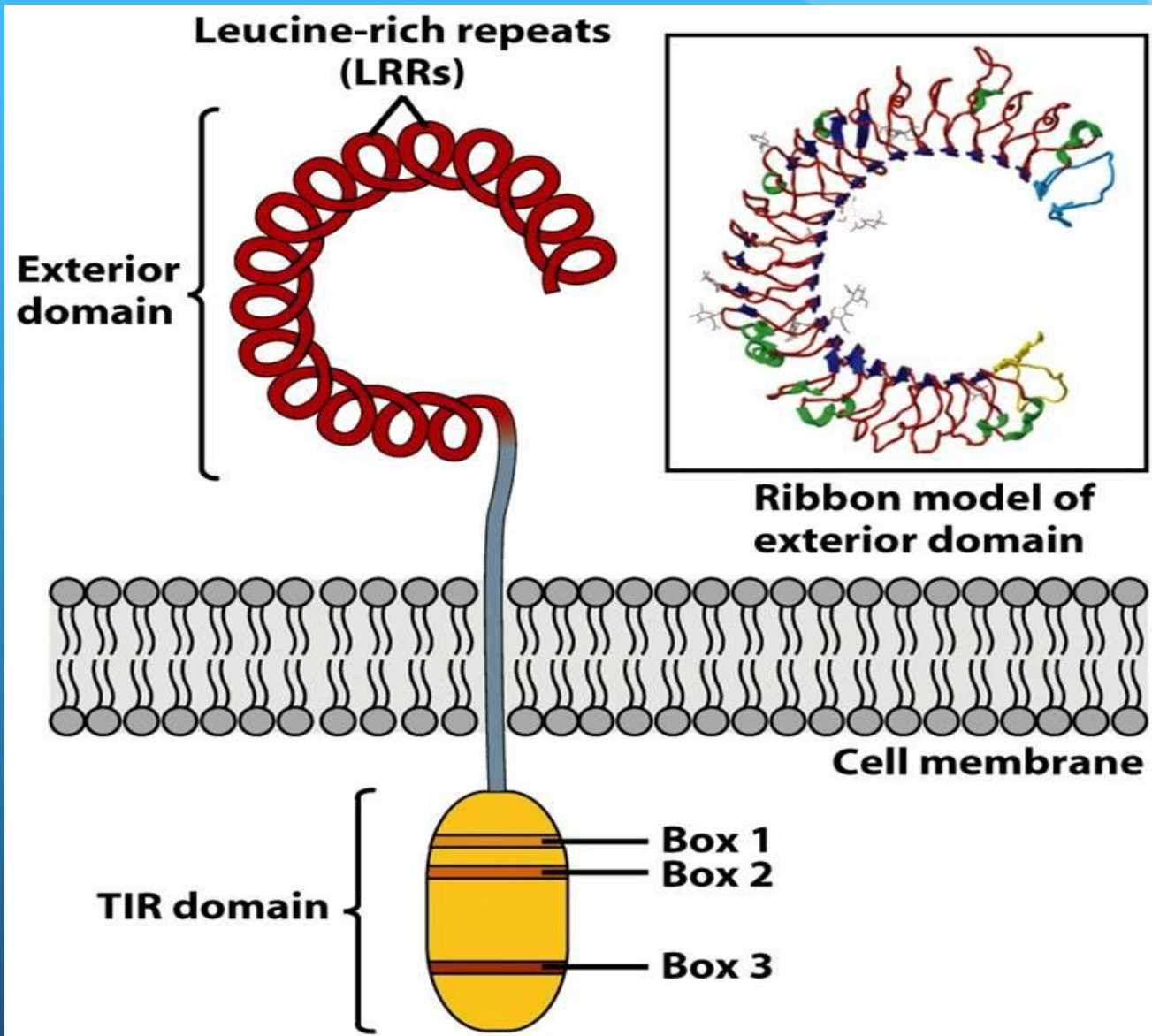
Interferon (IFN)

- Antiviral proteins produced by the cells in response to viral infections
 1. Type I IFN: IFN- α and IFN- β
 2. Type II IFN: IFN- γ
- What are the main Functions of IFN?

Pattern Recognition Receptors (PRRs)

- Cell surface receptors for pathogens
- Expressed by phagocytic cells/APCs
- Bind saccharides / lipids absent from host
- Recognise bacteria, viruses and yeasts via PAMPs (Pathogen Associated Molecular Patterns)

PRR structure



PRRs and their Specificities

Phagocyte PRR

Bacterial ligand (PAMP)

1- Mannose receptor

Terminal mannose

2-Toll-like receptors

Different bacterial/viral/ fungal
components

Cell surface and intracellular TLRs

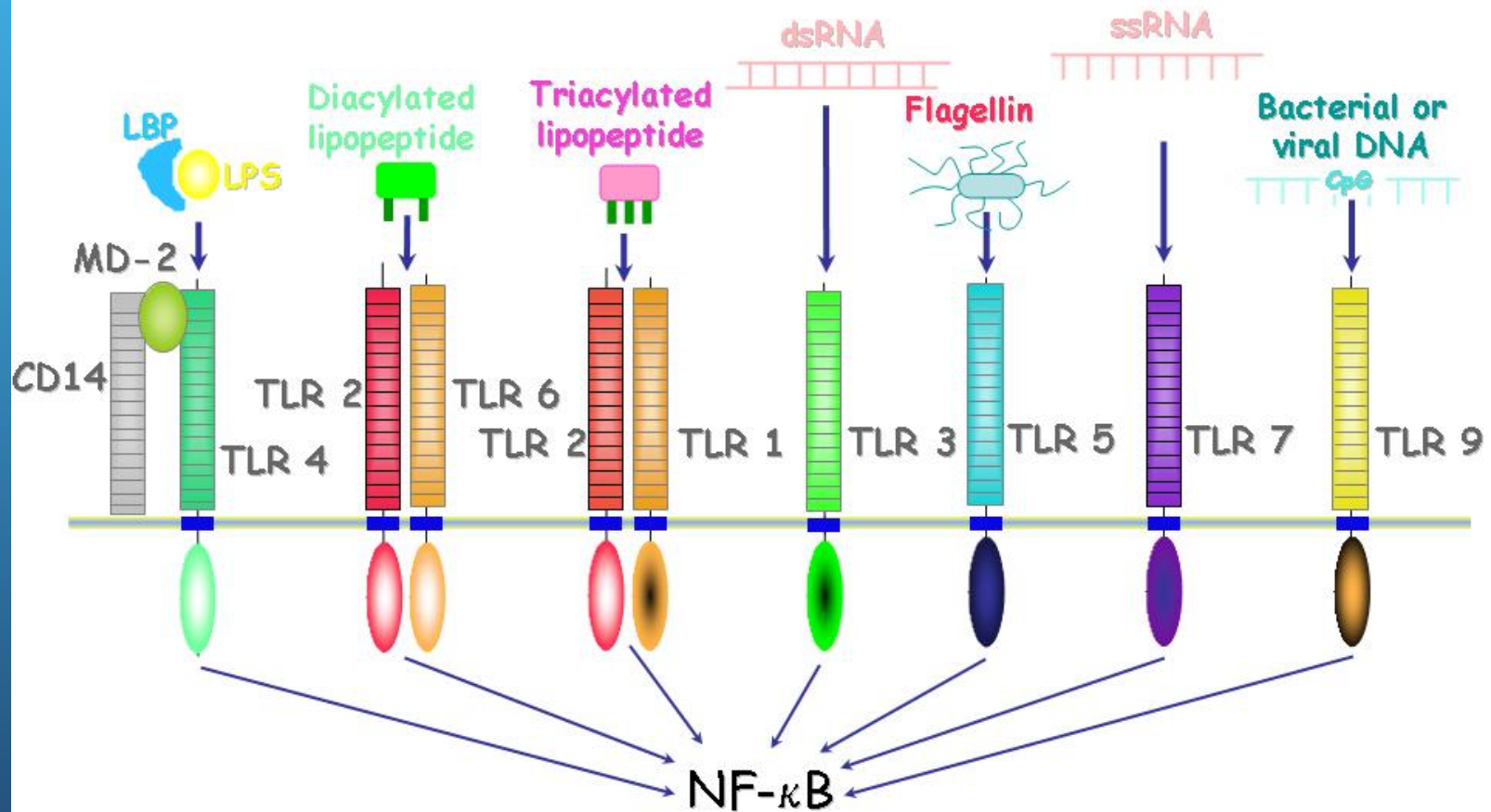
1- Cell surface receptors

TLRs 1, 2, 4, 5, 6, 10 & 11

2- Intracellular receptors

TLRs 3, 7, 8 & 9

Activation of TLRs by microbial molecules



Inflammation

What does it means?

What are the major symptoms of inflammation?

What are the functions of inflammation?

The Complement System

Definition:

A cascade of plasma proteins (30 proteins) that provide rapid defence against infectious agents.

- Synthesized mainly by liver hepatocytes and other cell types (monocyte, macrophage, GI epithelial cells)
- Circulate as inactive proenzymes

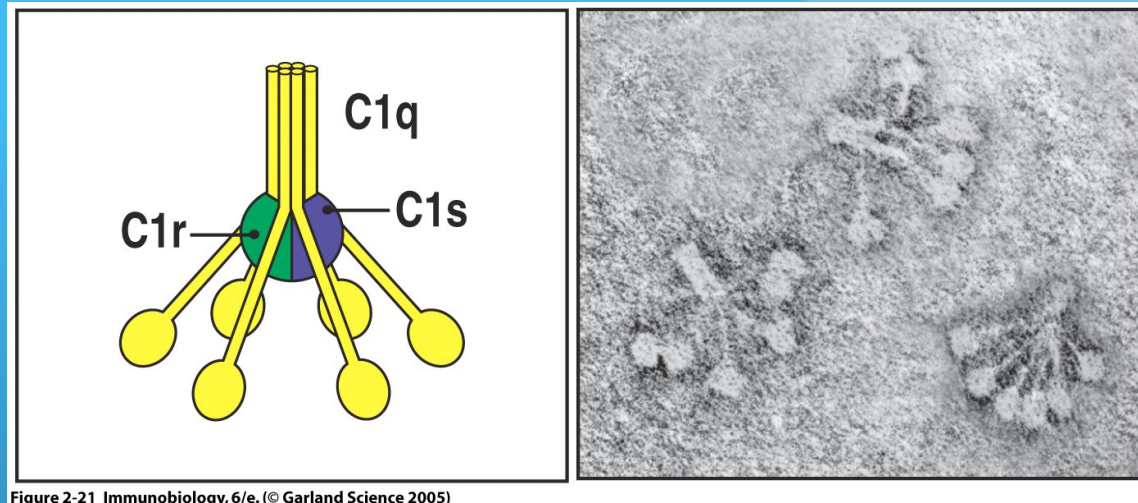


Figure 2-21 Immunobiology, 6/e. (© Garland Science 2005)

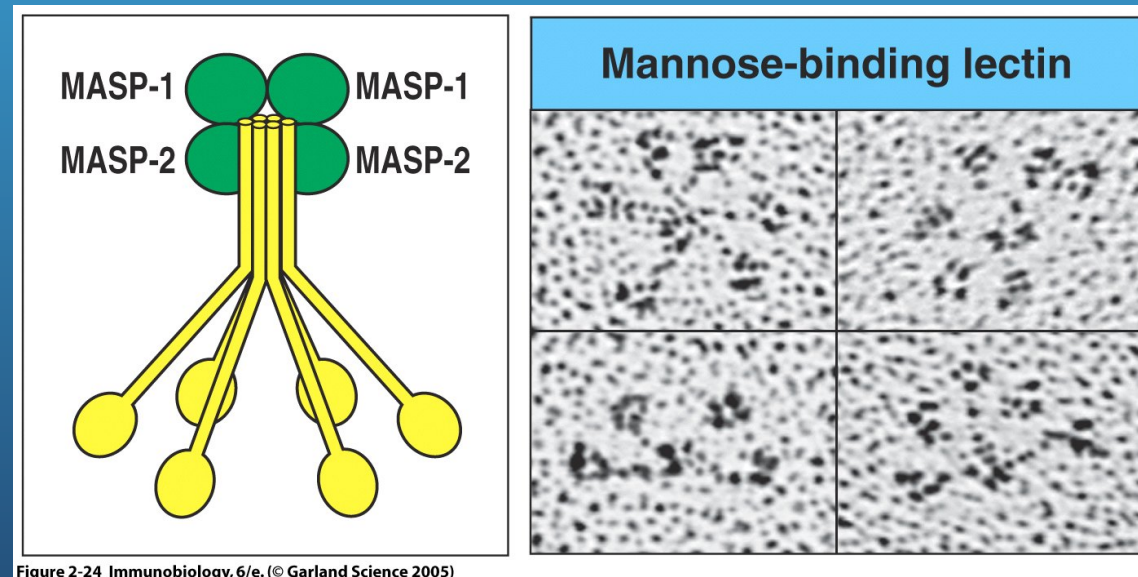


Figure 2-24 Immunobiology, 6/e. (© Garland Science 2005)

Complement pathways

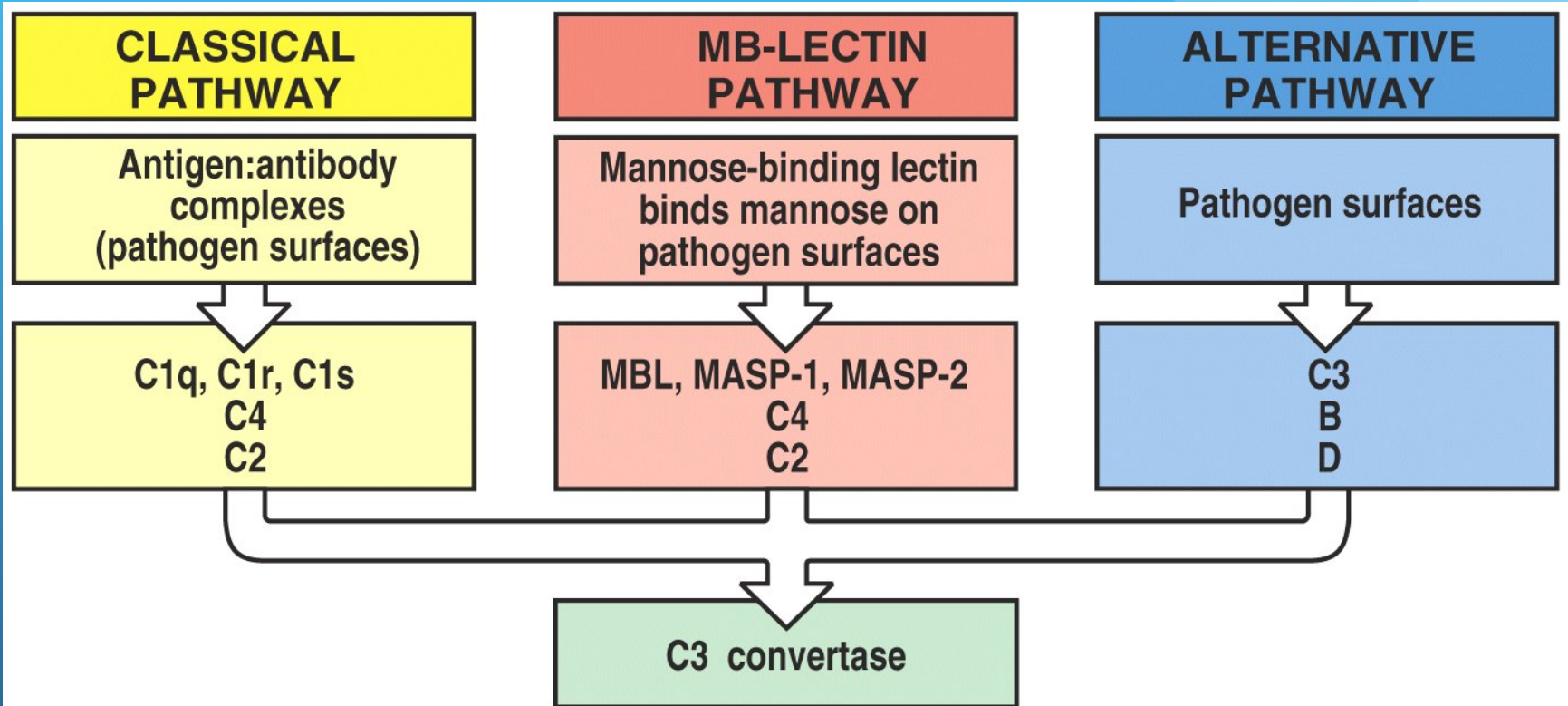


Figure 2-19 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

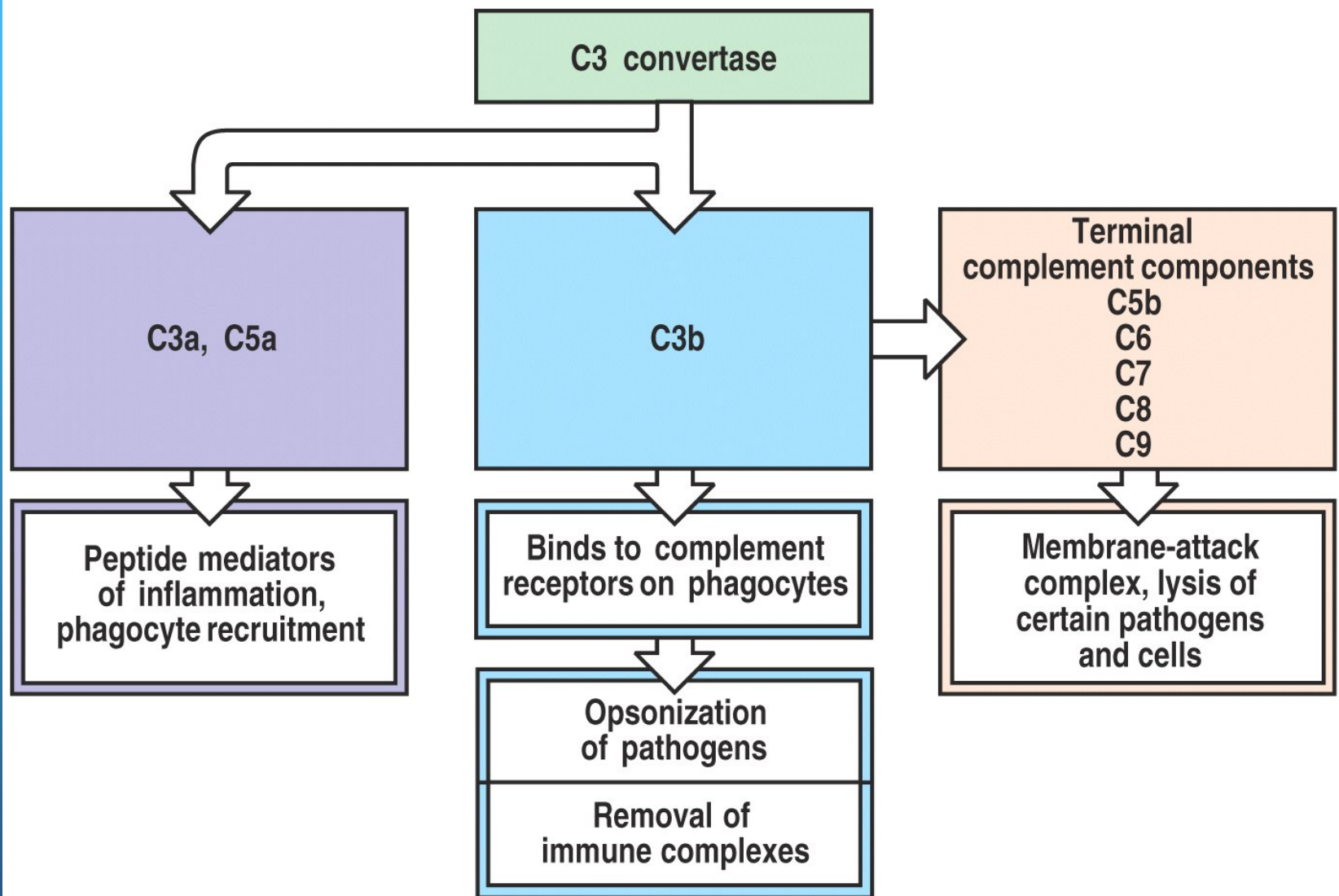


Figure 2-19 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

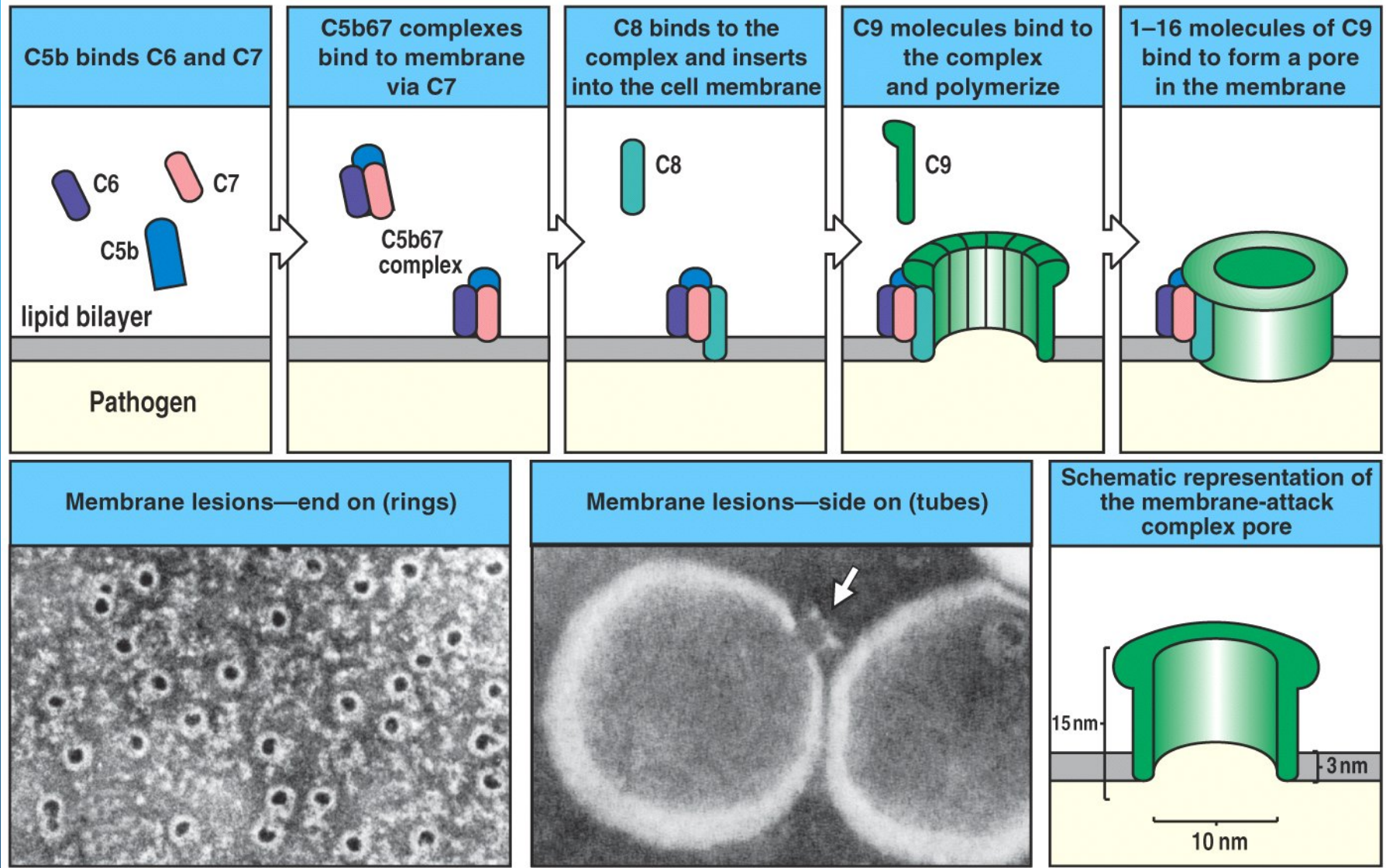
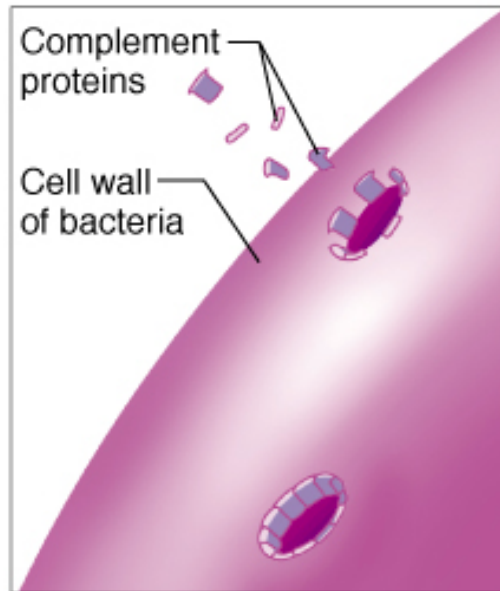
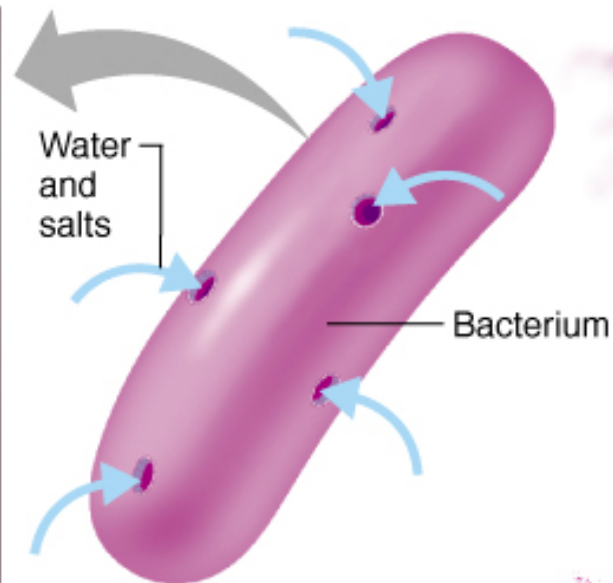


Figure 2-35 Immunobiology, 6/e. (© Garland Science 2005)

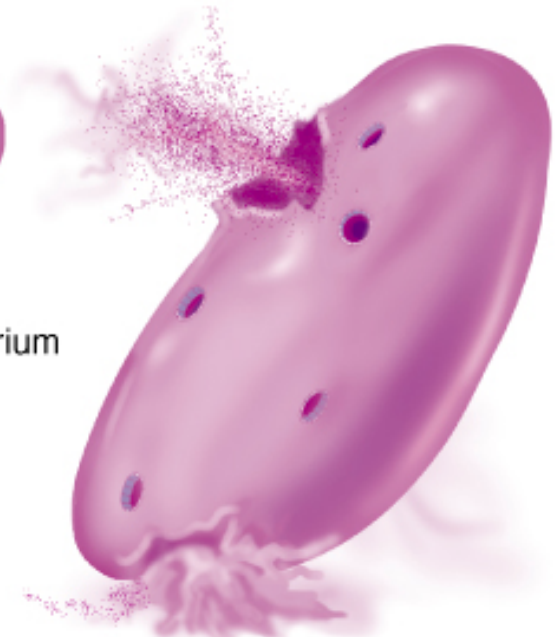
Membrane Attack Complex (MAC)



- ① Activated complement proteins form complexes of proteins that create holes in the bacterial cell wall.



- ② Water and salts diffuse into the bacterium through the holes.



- ③ The bacterium swells and eventually bursts.

Classical pathway

Immune complexes etc.

C1q

C1r

C1s

C4

C2

C3

Lectin pathway

Bacterial carbohydrate

MBL

MASP-1

MASP-2

C4

C2

C3

Alternative pathway

Bacterial carbohydrate

C3b

fB

fD

Properdin

C3

C3b

C5

C6

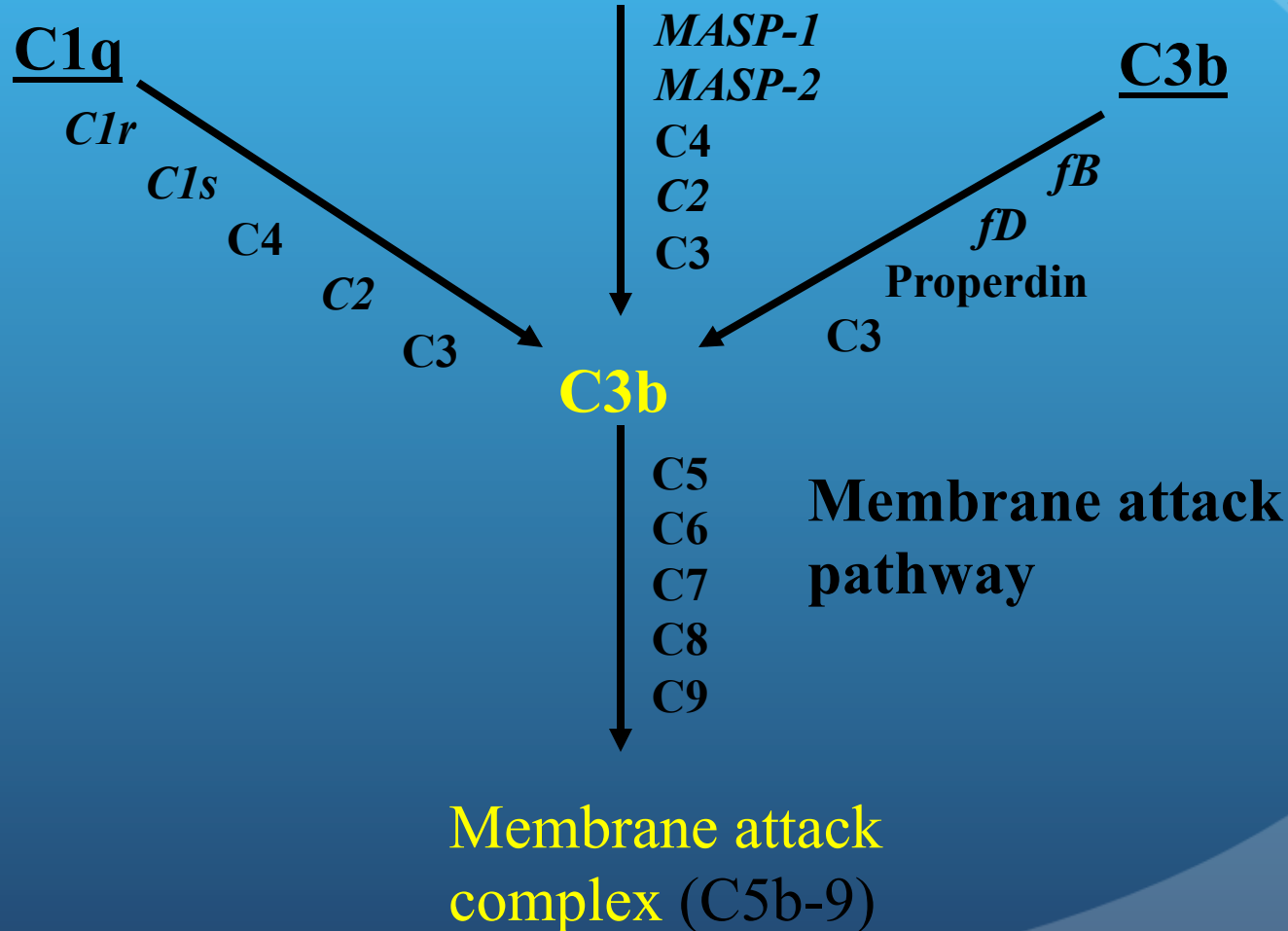
C7

C8

C9

Membrane attack
pathway

Membrane attack
complex (C5b-9)



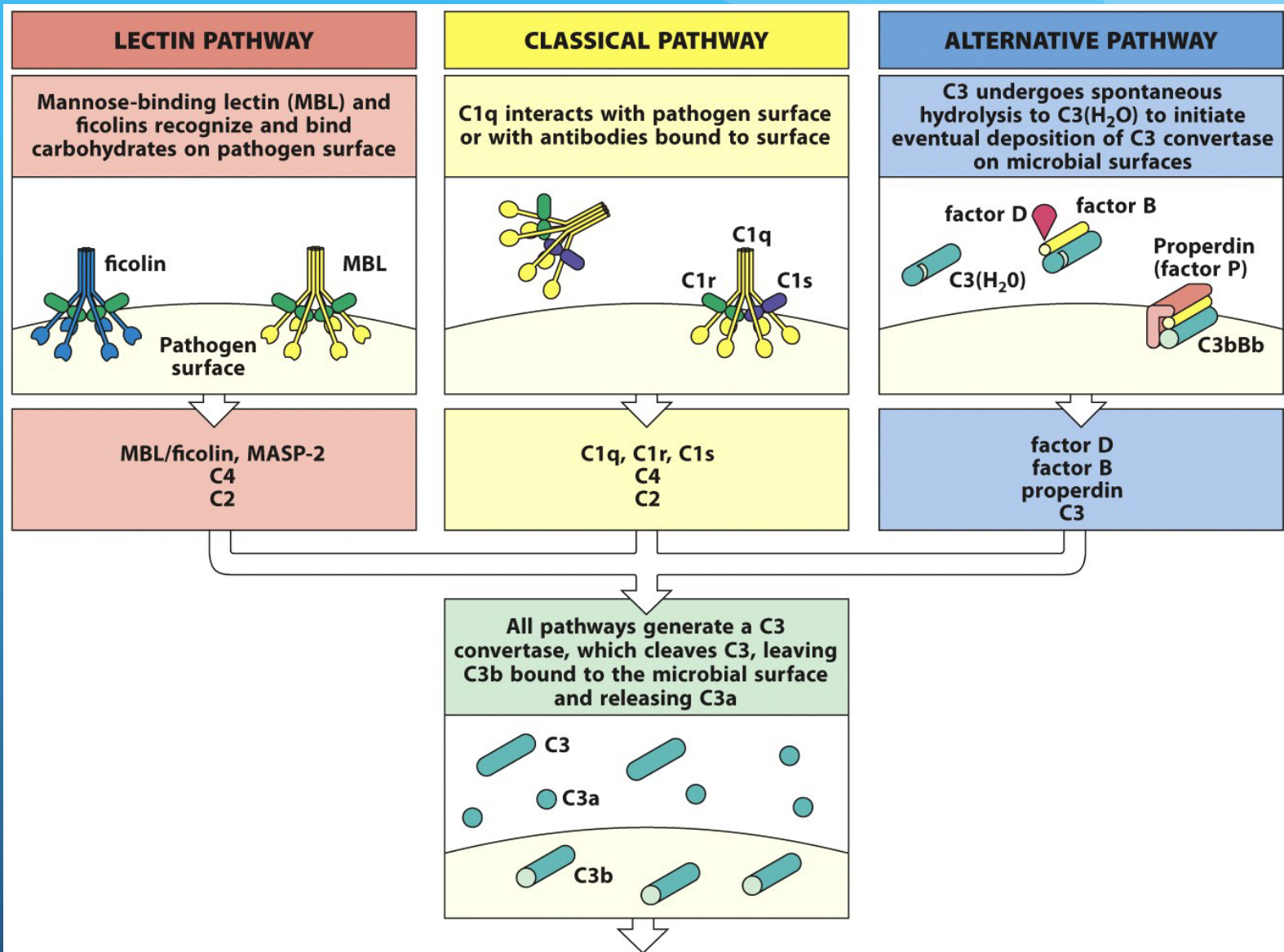


Figure 2.12 part 1 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

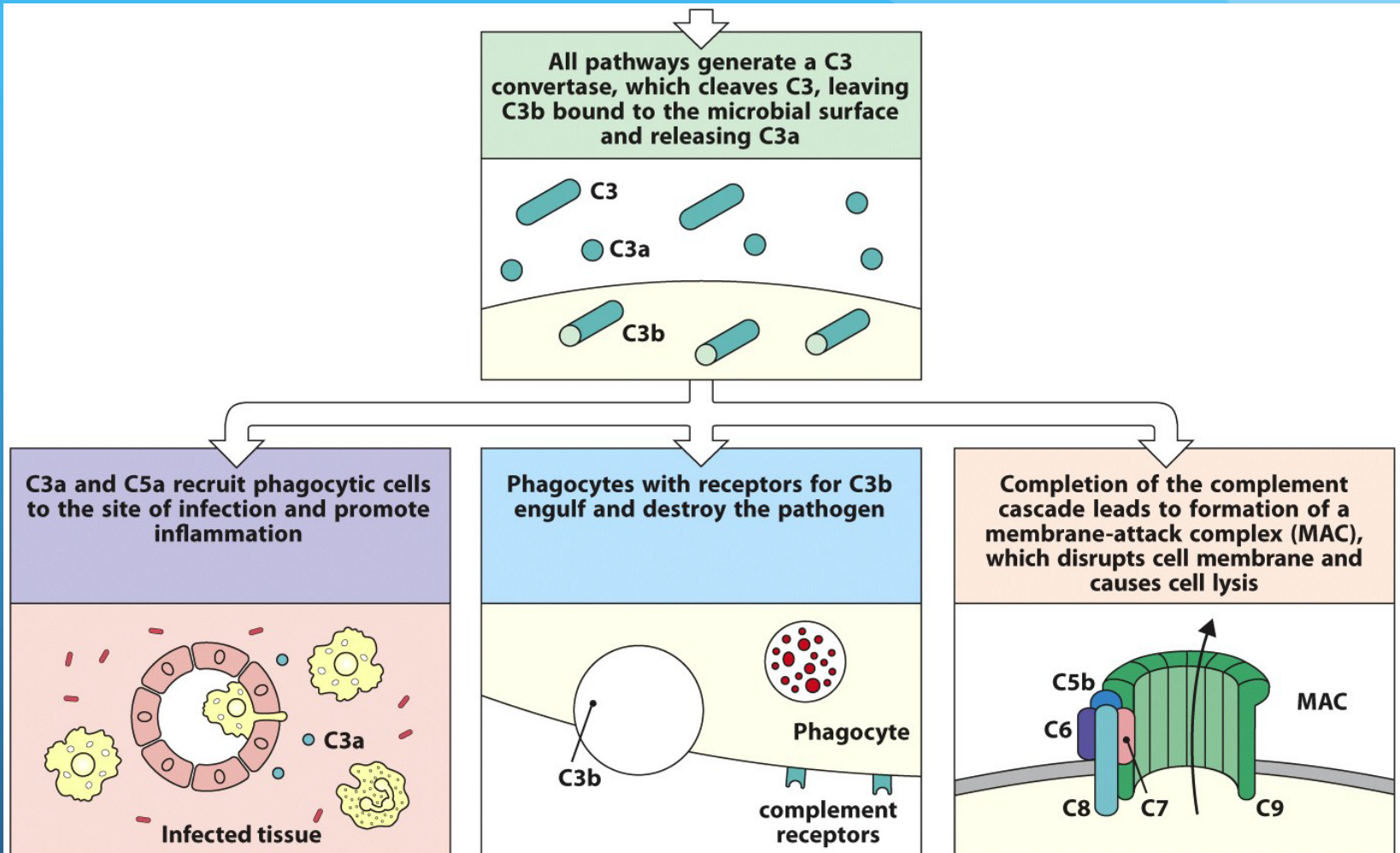
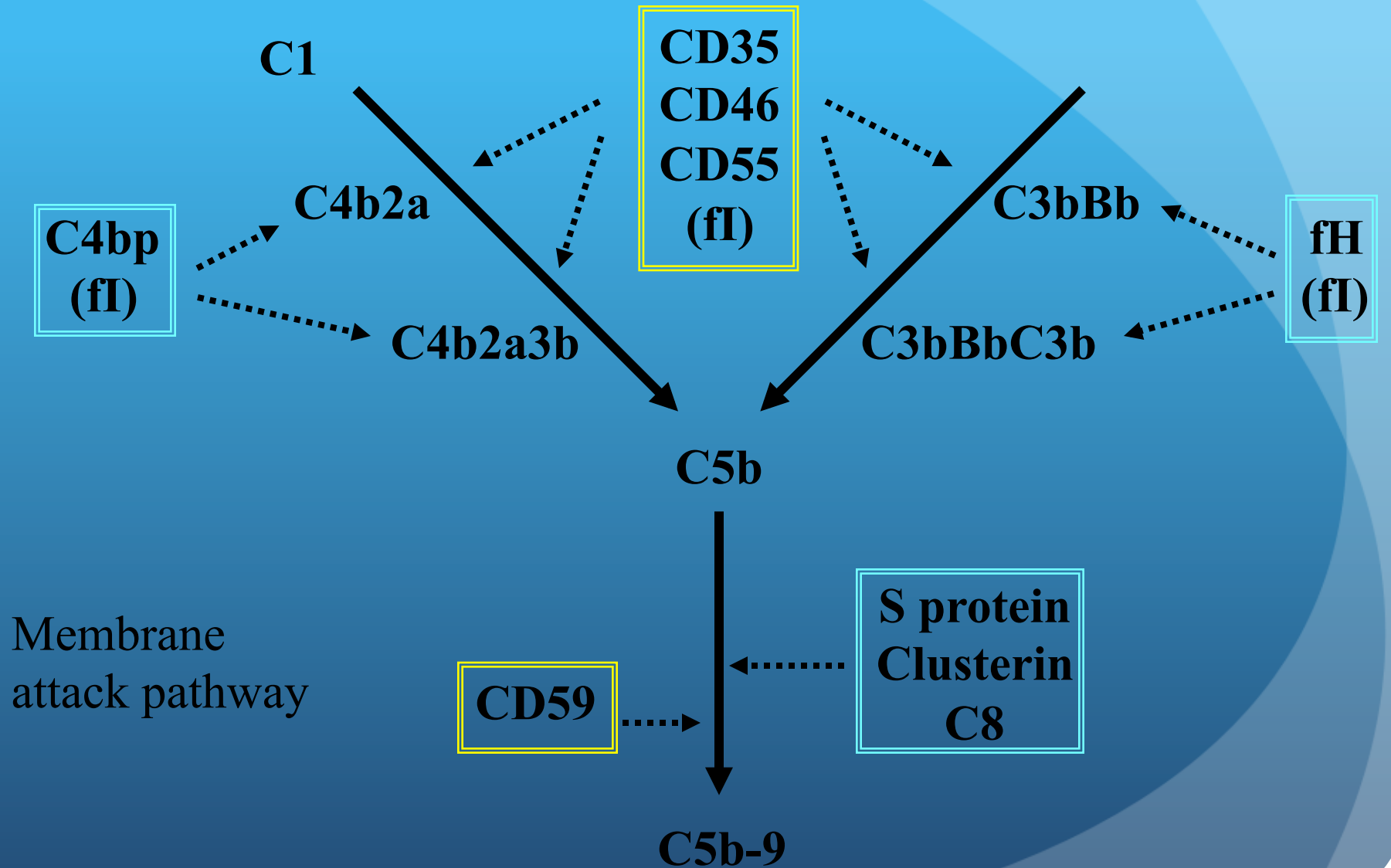


Figure 2.12 part 2 of 2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

INHIBITORS

Classical pathway

Alternative pathway



Complement functions

Activation

Macrophages
Neutrophils
inflammation

Cytolysis

target cell
death

COMPLEMENT

```
graph TD; C[COMPLEMENT] --> A[Activation]; C --> Cy[Cytolysis]; C --> O[Opsonisation]; C --> R[Ab/Ag complex removal]; C --> IAI[Increased Adaptive immunity T and B cell]
```

Ab/Ag complex
removal

Increased Adaptive
immunity T and B cell

Opsonisation

Bacteria
phagocytosis

Complement functions

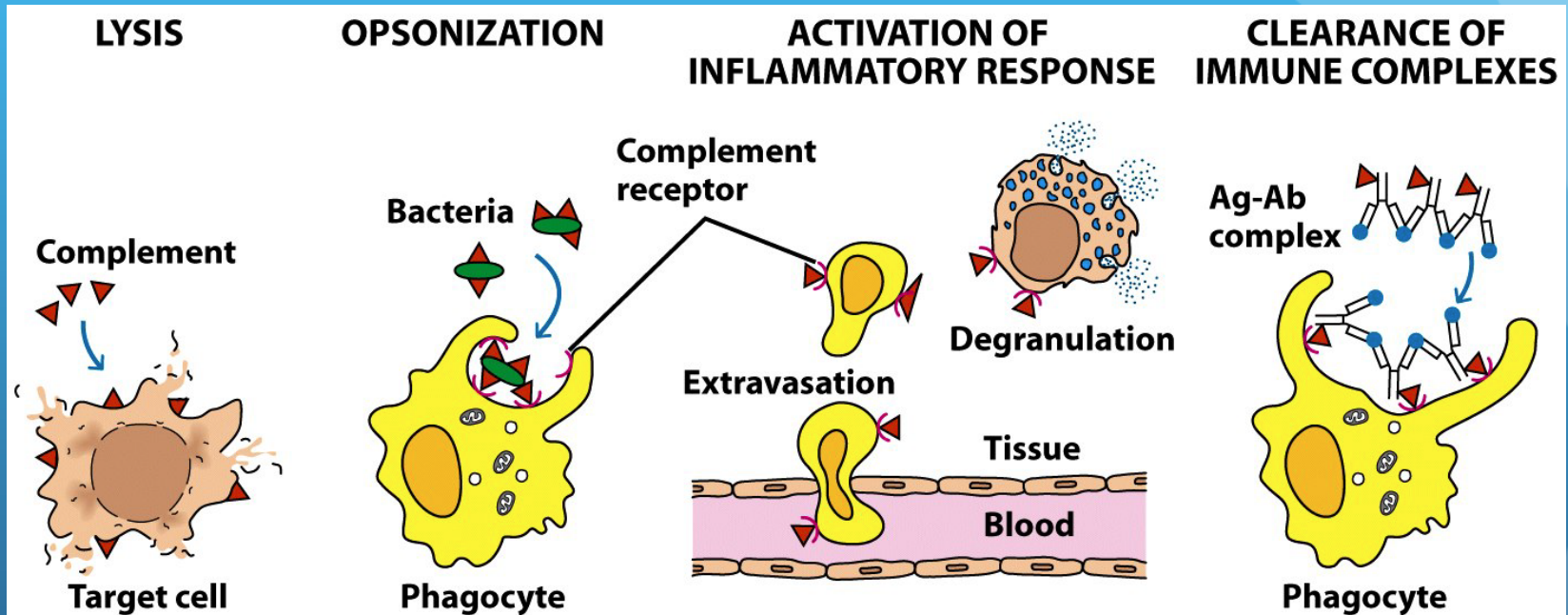


Figure 7-1
Kuby IMMUNOLOGY, Sixth Edition
© 2007 W. H. Freeman and Company

Why so many innate soluble mediators and receptors?

- Vast range of pathogens potentially able to attack us
- Bacteria and viruses have ability to evade immune response

Interaction between Innate & Adaptive Immune Response

- Soluble mediators facilitate antigen uptake by antigen presenting cells (APC)
- Cell surface receptors also enhance uptake of antigen
- Triggers adaptive immune response

Summery

- 1- A wide variety of molecules are involved in the development of immune response.
- 2- Soluble protein mediators normally present in the serum.
- 3- The concentration of these protein mediators increase rapidly during and following infections.
- 4- Innate immune components enhance opsonisation/phagocytosis and stimulate the Adaptive Immune Response