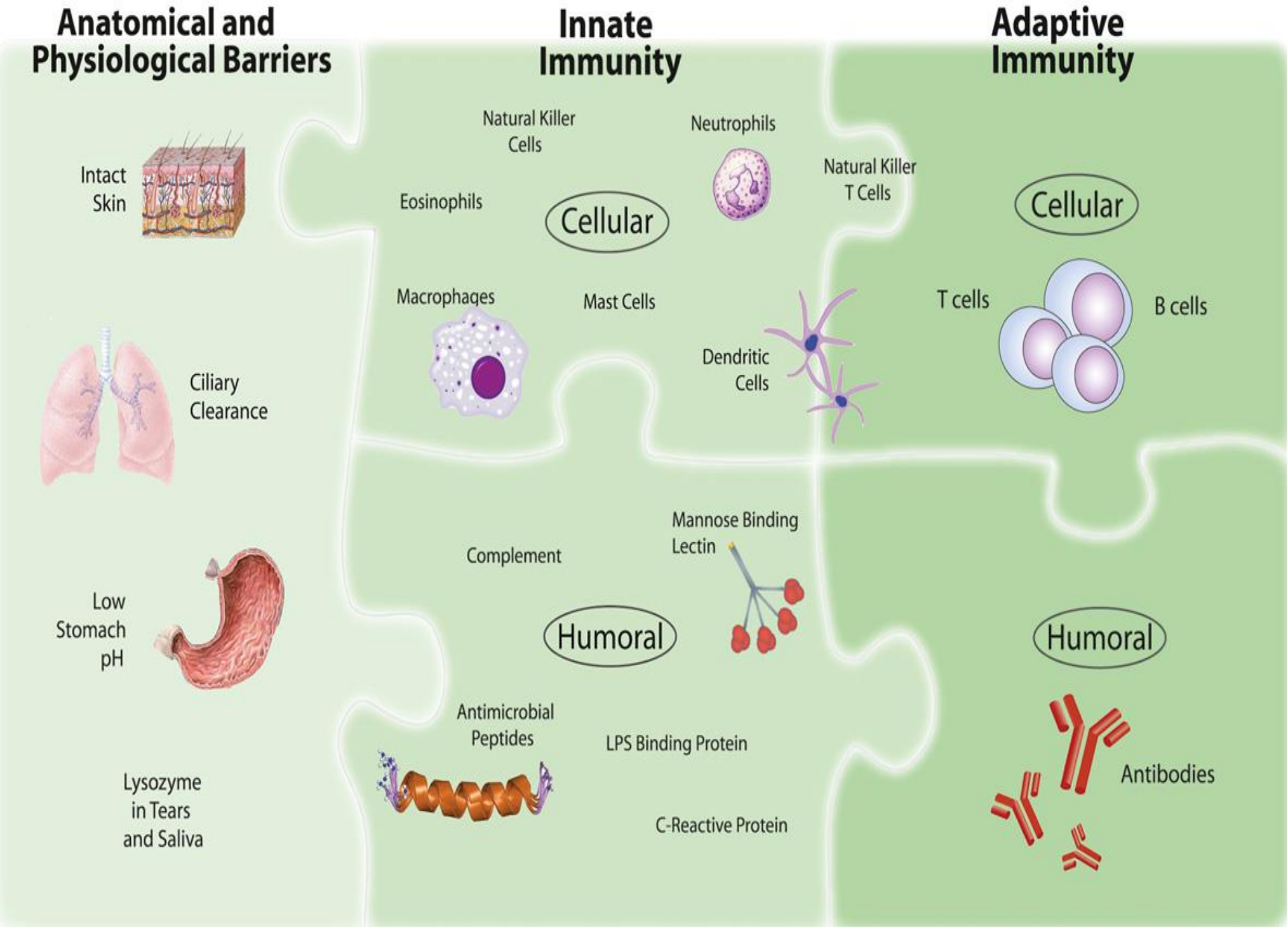
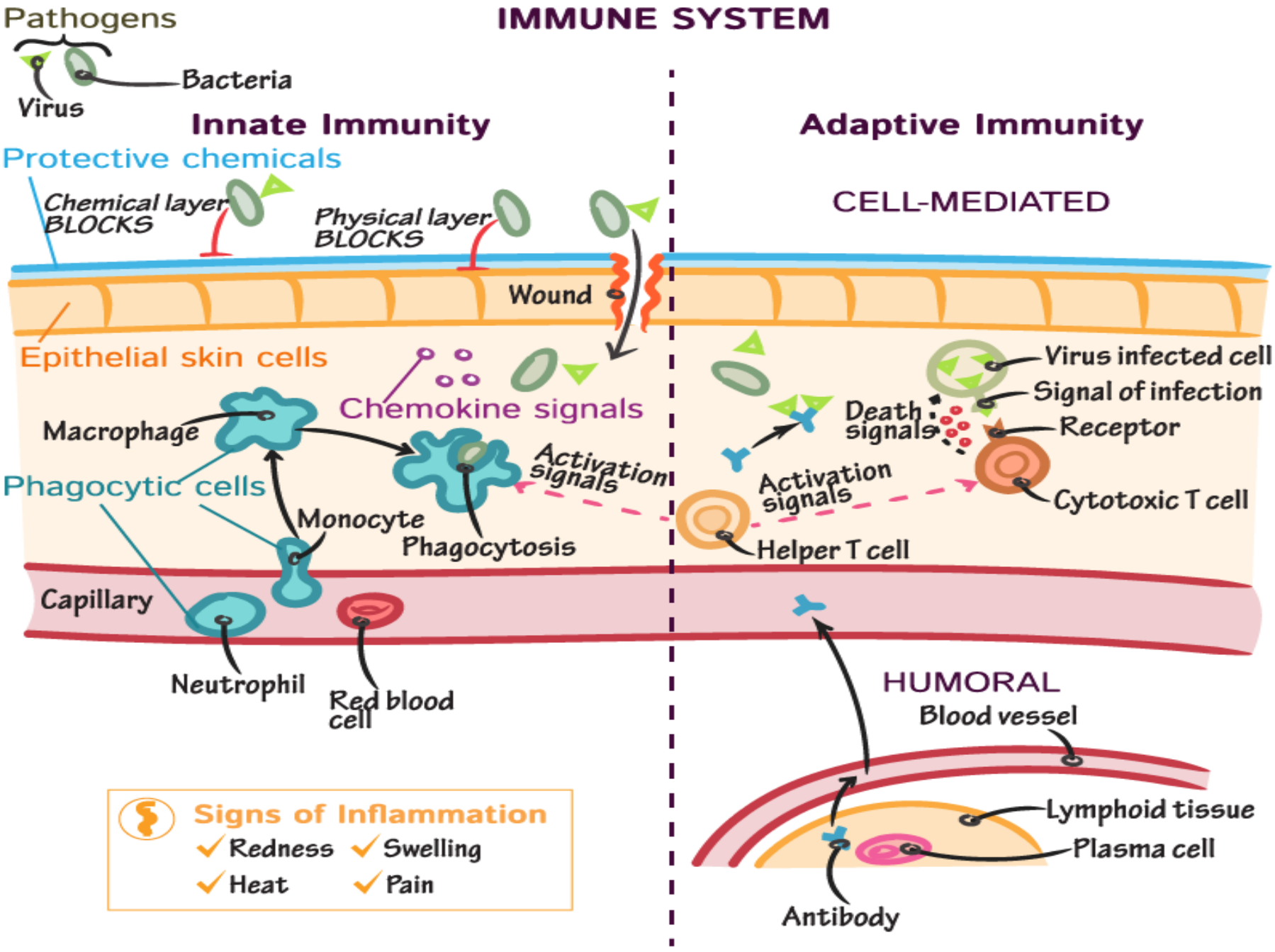

Anatomical and Physiological Barriers
Innate Immunity
Adaptive Immunity
Intact Skin
Ciliary Clearance
Low Stomach pH
Lysozyme in Tears and Saliva
Natural Killer Cells
Neutrophils
Natural Killer T Cells
Eosinophils
Cellular
Macrophages
Mast Cells
Dendritic Cells
Cellular
T cells
B cells
Mannose Binding Lectin
Complement
Humoral
Humoral
Antimicrobial Peptides
LPS Binding Protein
C-Reactive Protein
Antibodies


IMMUNE SYSTEM
Pathogens
Bacteria
Virus
Innate Immunity
Adaptive Immunity
Protective chemicals
Chemical layer BLOCKS
Physical layer BLOCKS
CELL-MEDIATED
Wound
Epithelial skin cells
Chemokine signals
Virus infected cell
Signal of infection
Death signals
Receptor
Macrophage
Activation signals
Activation signals
Phagocytic cells
Monocyte
Phagocytosis
Cytotoxic T cell
Helper T cell
Capillary
Neutrophil
Red blood cell
HUMORAL
Blood vessel
Lymphoid tissue
Plasma cell
Antibody
Signs of Inflammation
Redness
Swelling
Heat
Pain

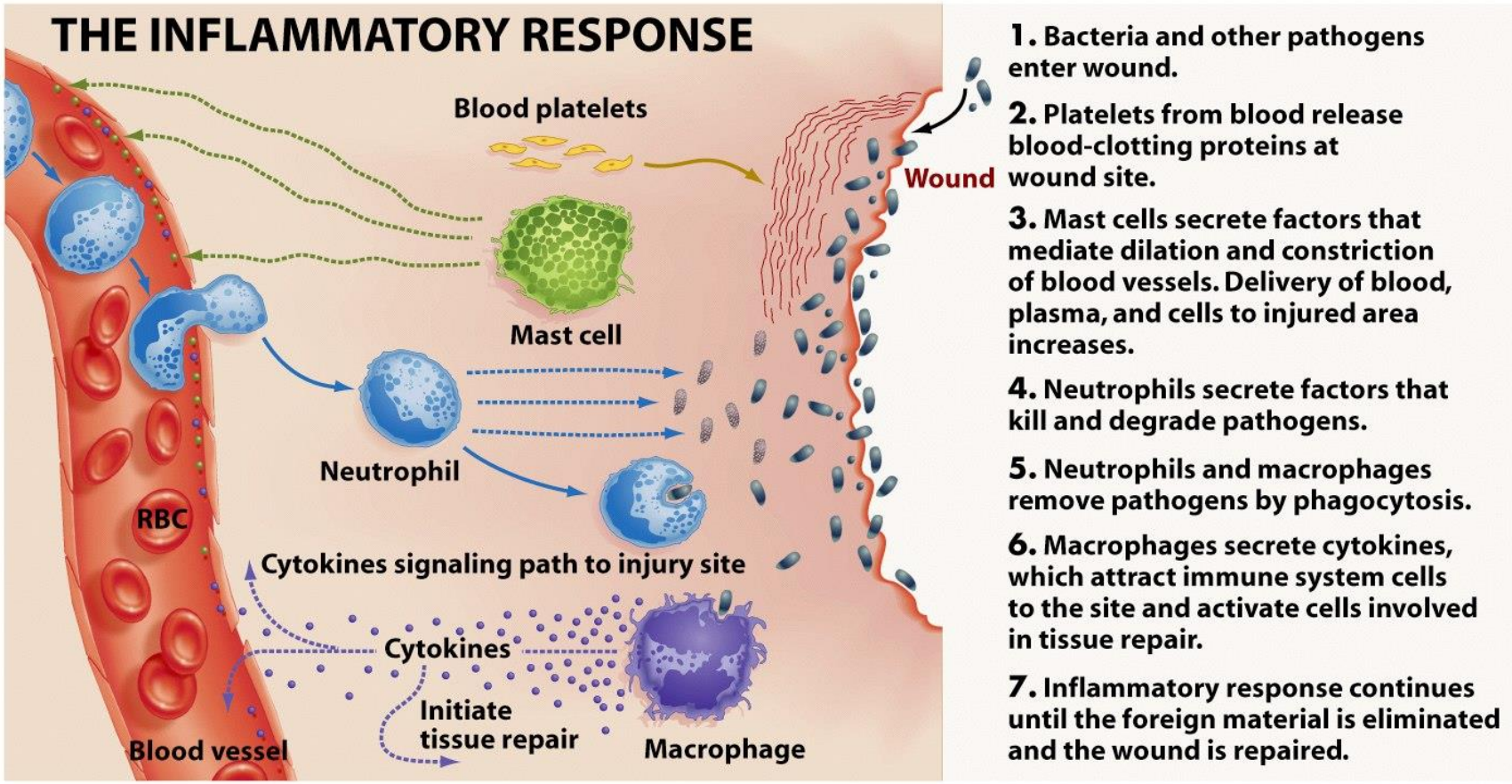
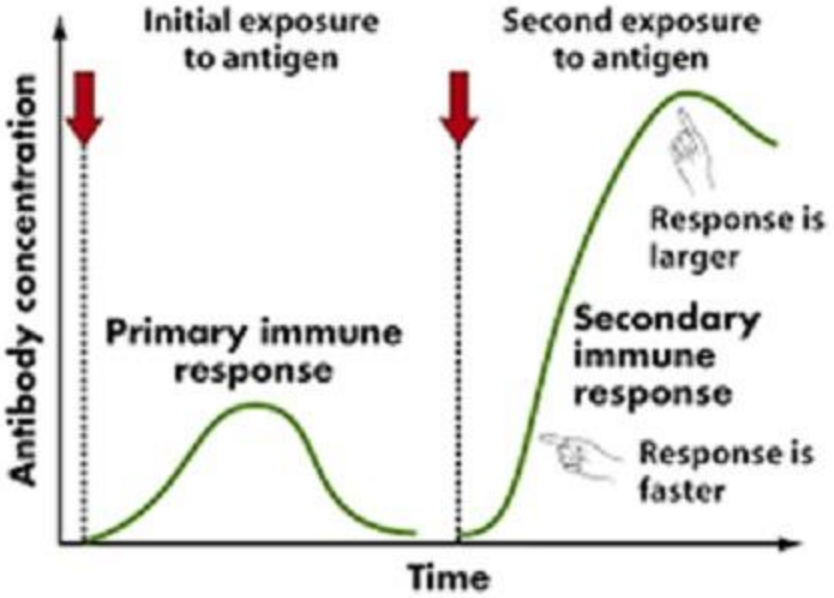
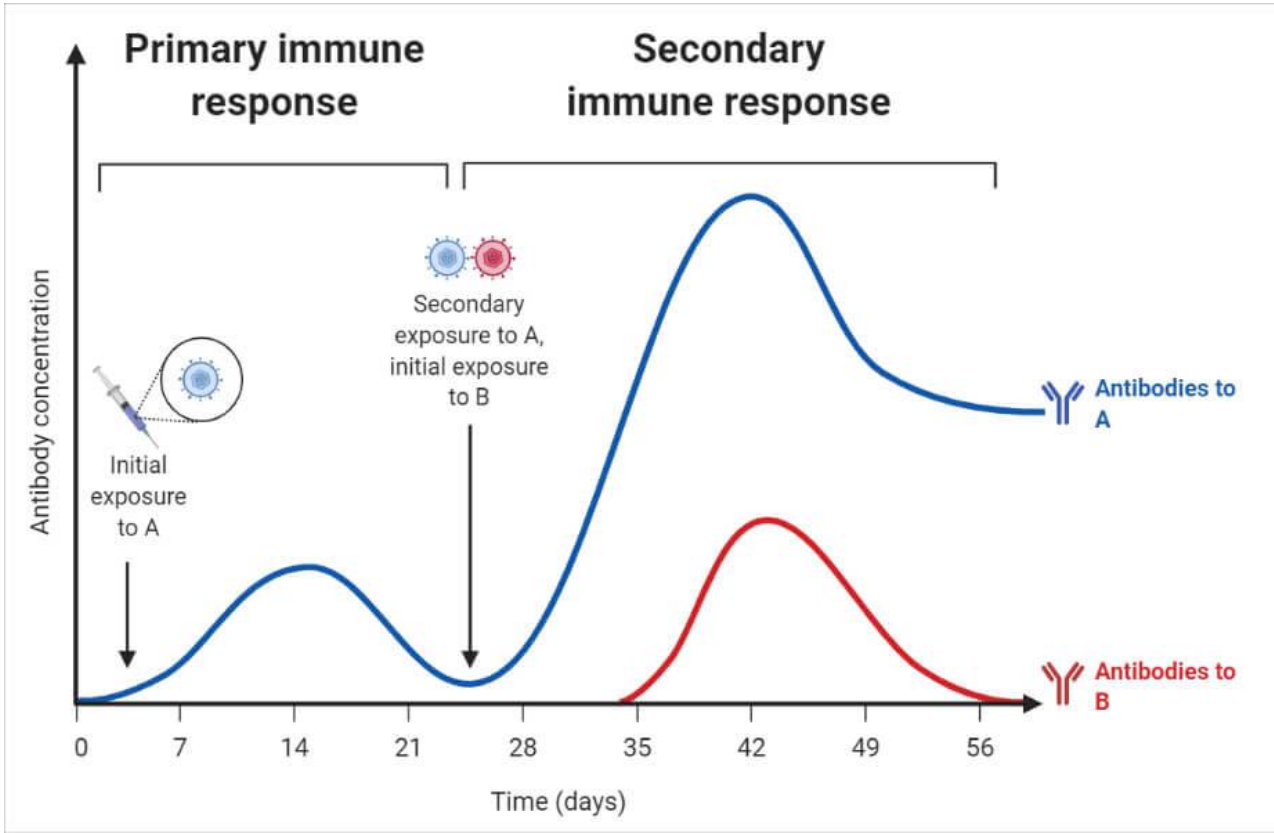
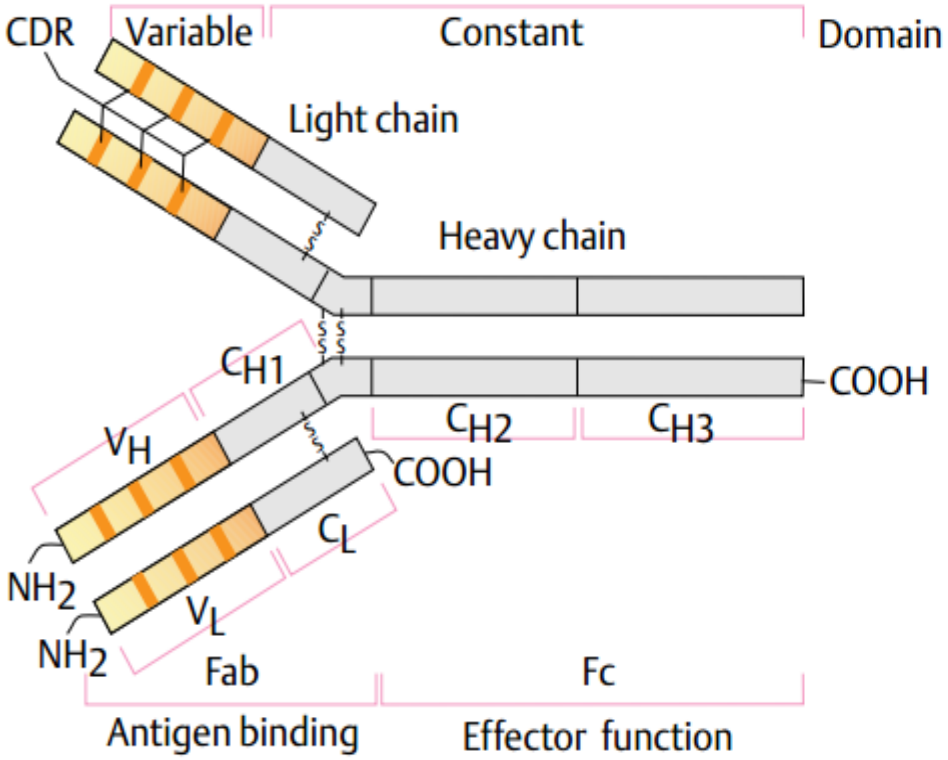
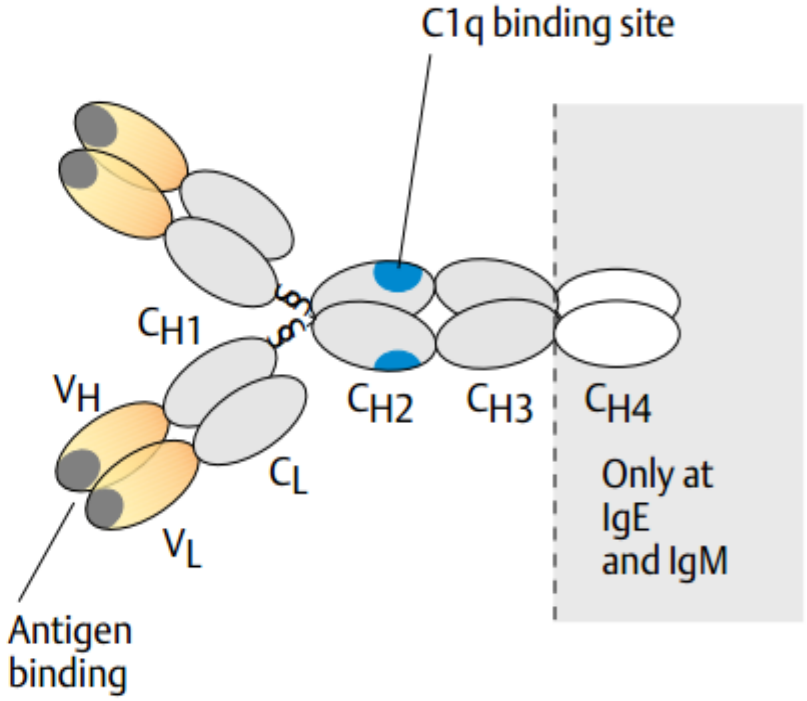



Figure 49-3 Biological Science, 2/e


Initial exposure to antigen
Second exposure to antigen
Antibody concentration
Response is larger
Primary immune response
Secondary immune response
Response is faster
Time


Primary immune response
Secondary immune response
Secondary exposure to A, initial exposure to B
Initial exposure to A
Antibody concentration
Antibodies to A
Antibodies to B
0
7
14
21
28
35
42
49
56
Time (days)

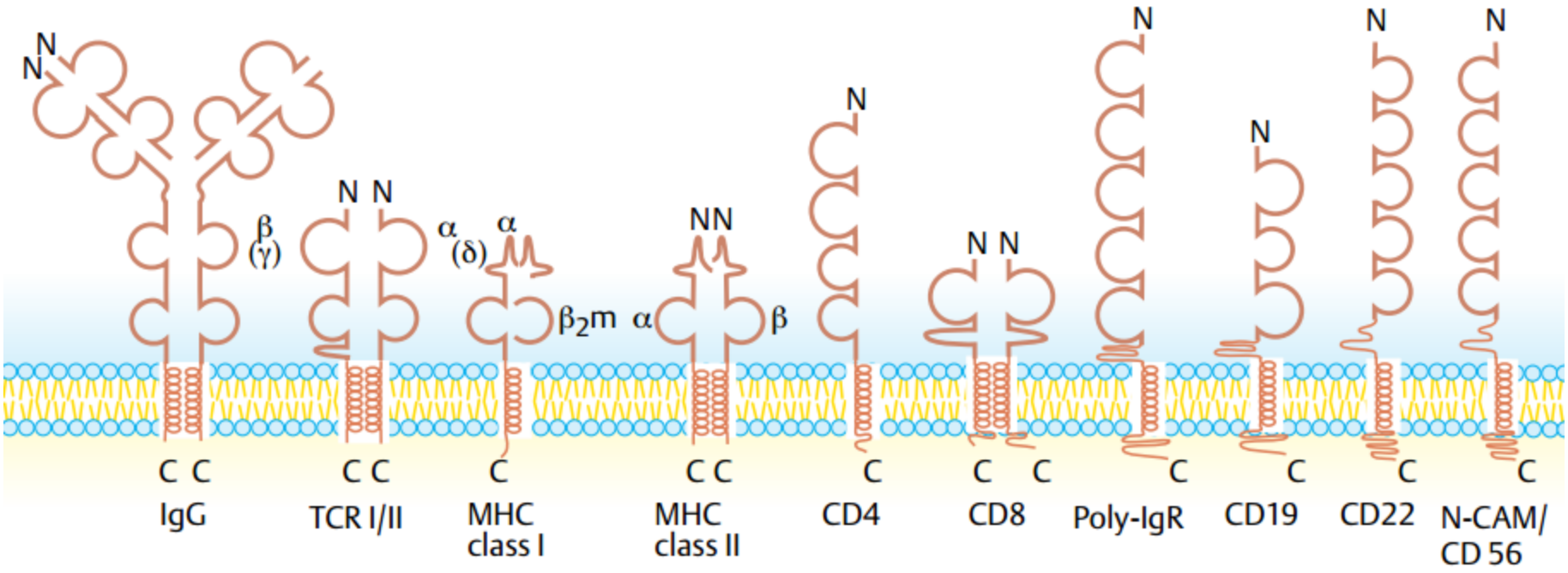


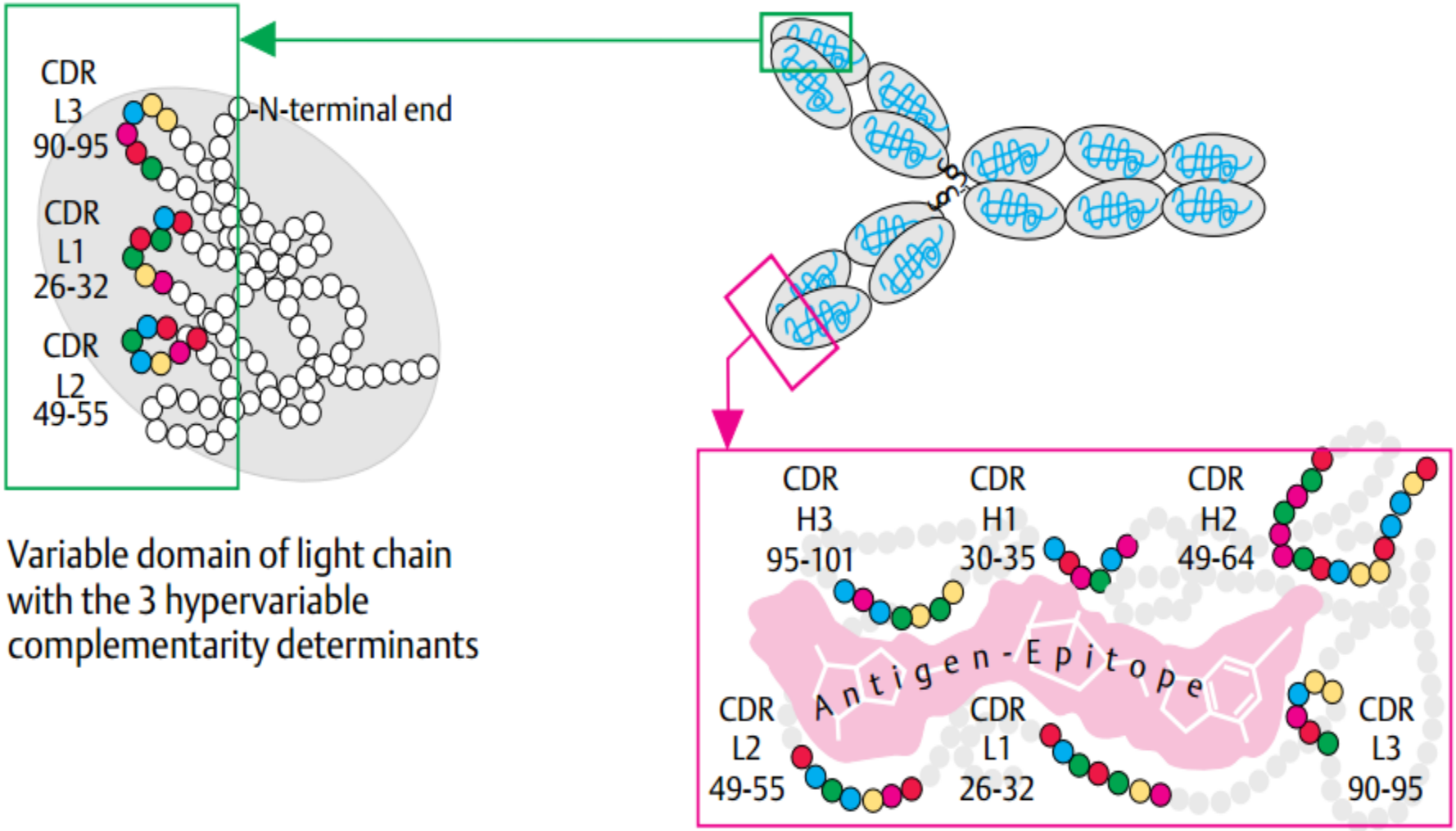

CDR = complementarity-determining region
Fab = antigen-binding fragment
Fc = crystallizable fragment

$V_H$ = variable domain of heavy chains
$V_L$ = variable domain of light chains
$C_{H/L}$ = constant domain of heavy / light chains

**A. Immunoglobulin structure**




**B. Immunglobulin-“superfamily”**




Variable domain of light chain with the 3 hypervariable complementarity determinants

**C. Hypervariable regions determine the antigen specificity**

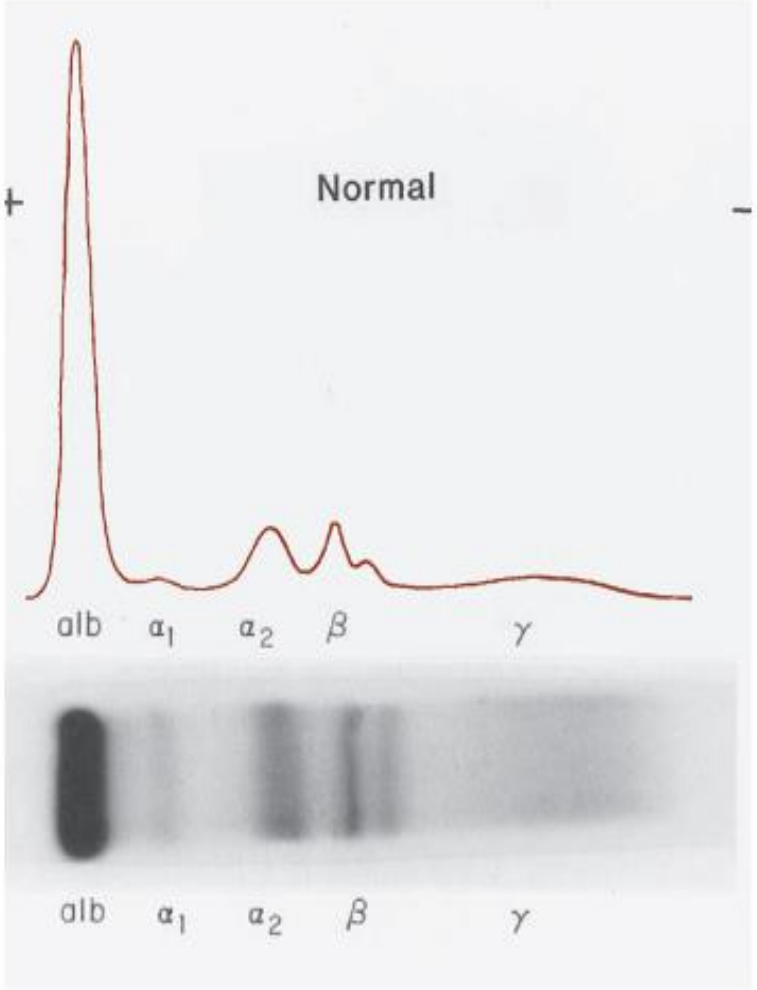
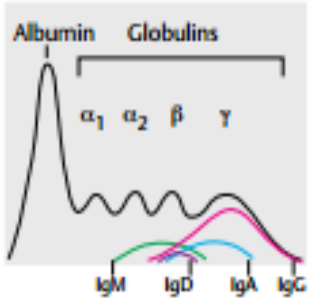
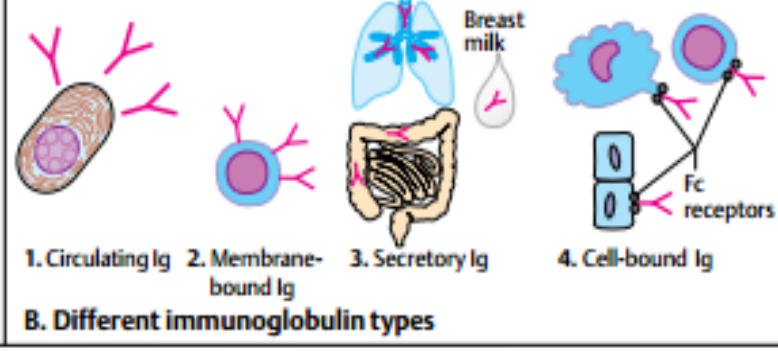


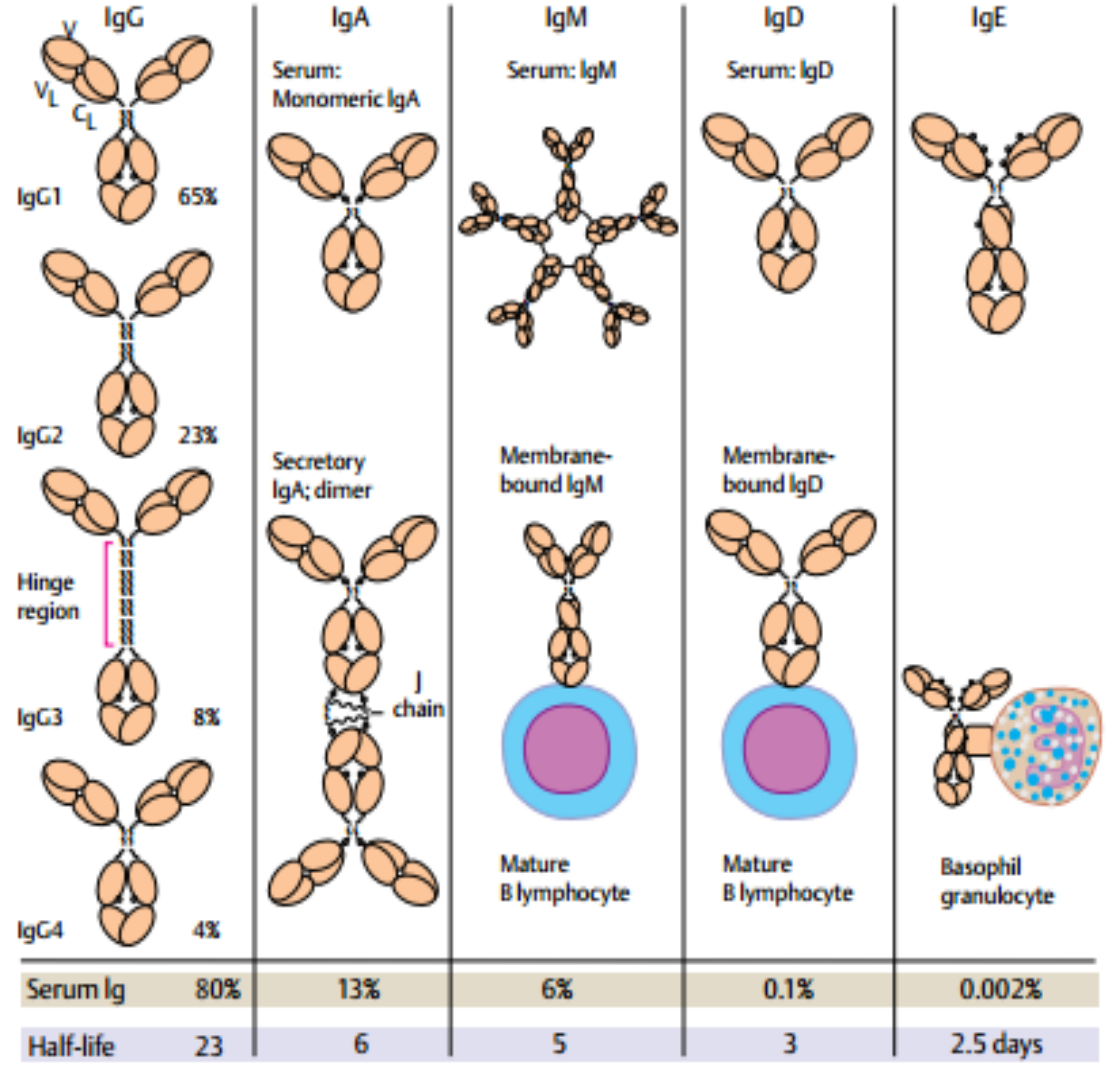

FIGURE 4–1. Serum electrophoresis. *(From Widmann, FK. An Introduction to Clinical Immunology. FA Davis, Philadelphia, 1989, with permission.)*




A. Protein electrophoresis




B. Different immunoglobulin types




| | | | | | |
|---|---|---|---|---|---|
| Serum Ig | 80% | 13% | 6% | 0.1% | 0.002% |
| Half-life | 23 | 6 | 5 | 3 | 2.5 days |

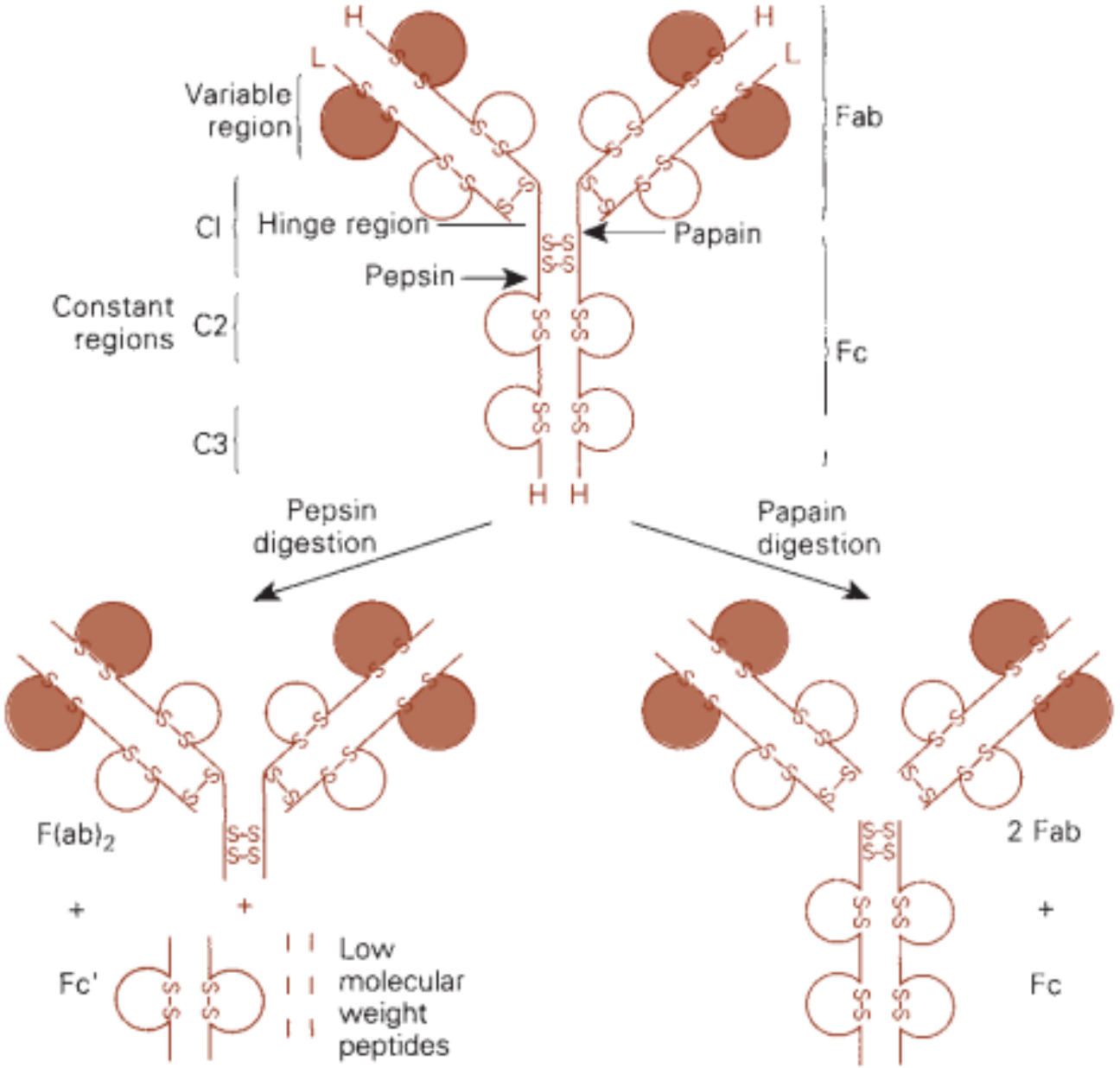
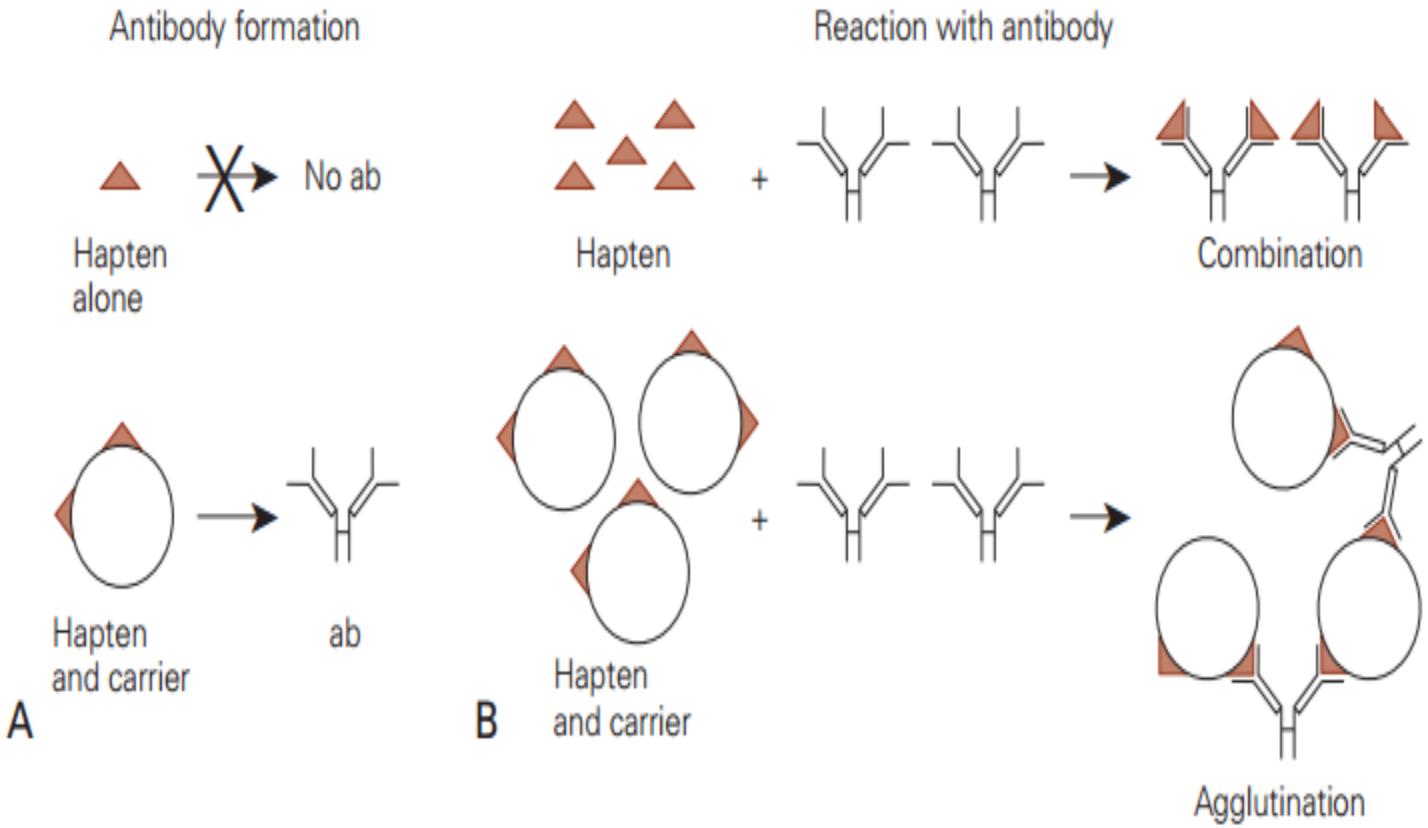



**FIGURE 4–2.** Generalized structure of an immunoglobulin molecule.


Antibody formation
No ab
Hapten alone
Hapten and carrier
ab
A
Reaction with antibody
Hapten
+
Combination
Hapten and carrier
+
Agglutination
B

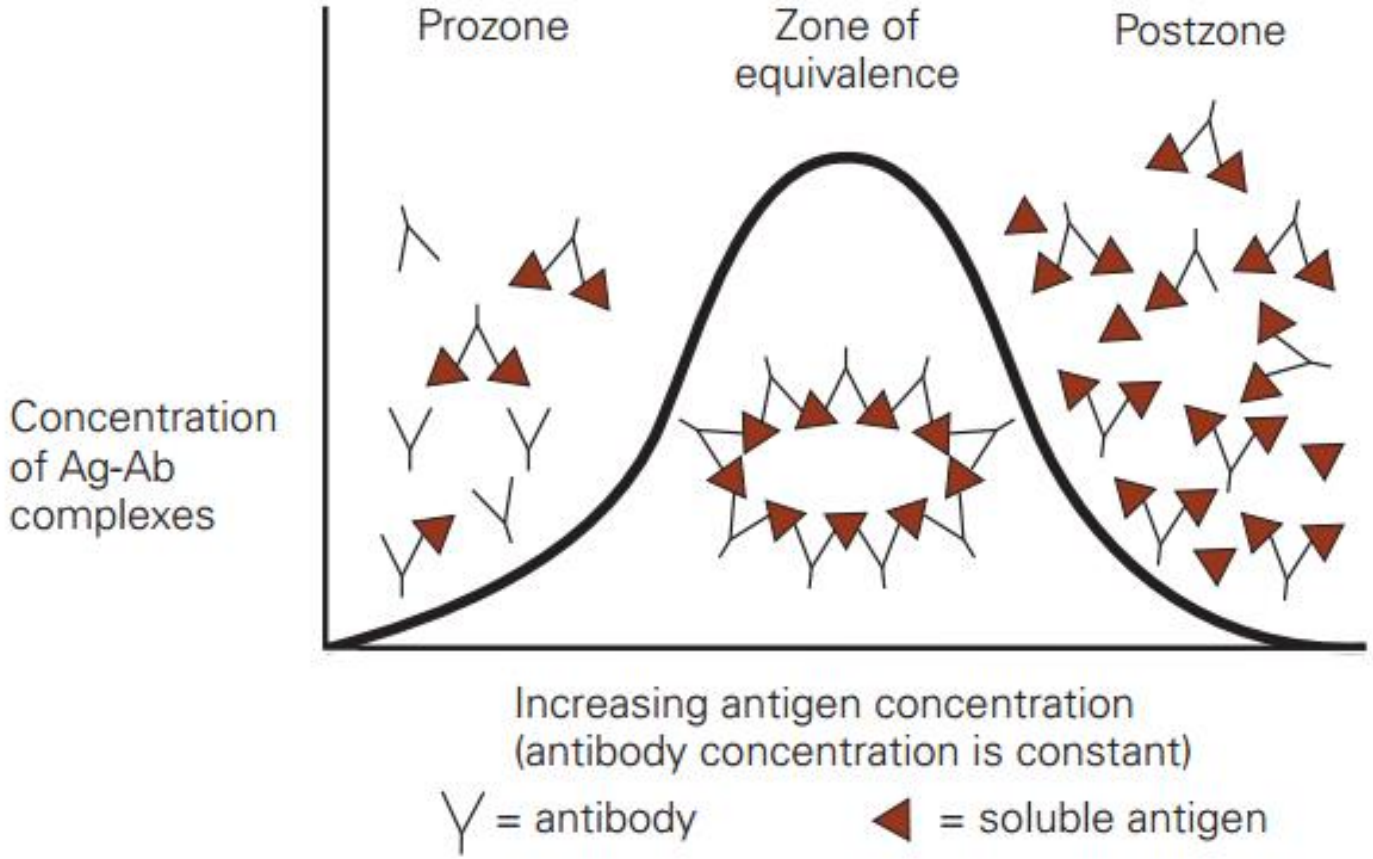



**FIGURE 8–2.** Precipitin curve. The precipitin curve shows how the amount of precipitation varies with varying antigen concentration when the antibody concentration is kept constant. Excess antibody is called the *prozone*, and excess antigen concentration is called the *postzone*.

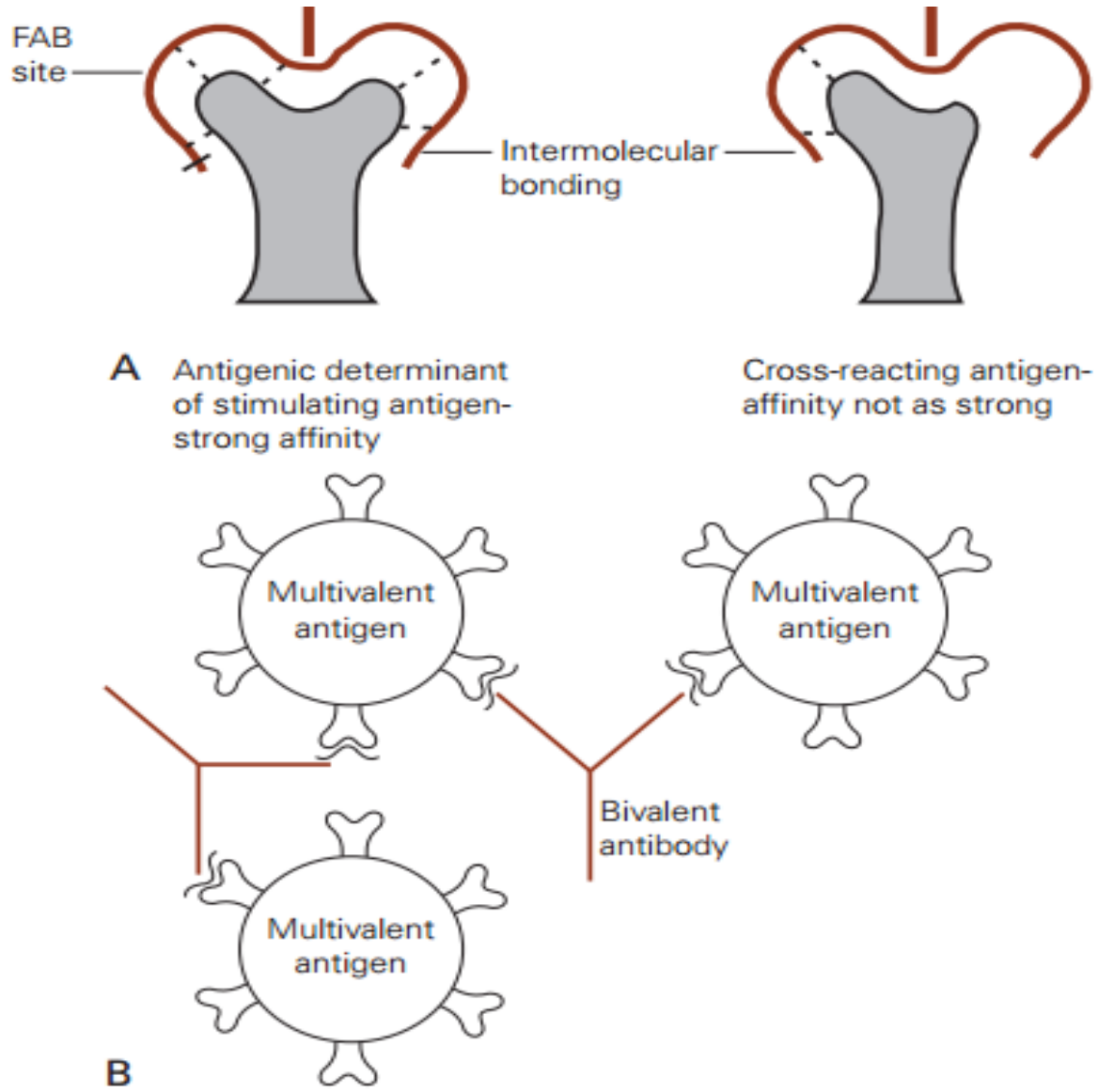



FIGURE 8–1. Affinity and avidity. *(A)* Affinity is the fit of one antigenic determinant with one antibody binding site. The original stimulating antigen is a better fit than cross-reacting antigen. *(B)* Avidity is the sum of the forces binding multivalent antigens to multivalent antibodies.

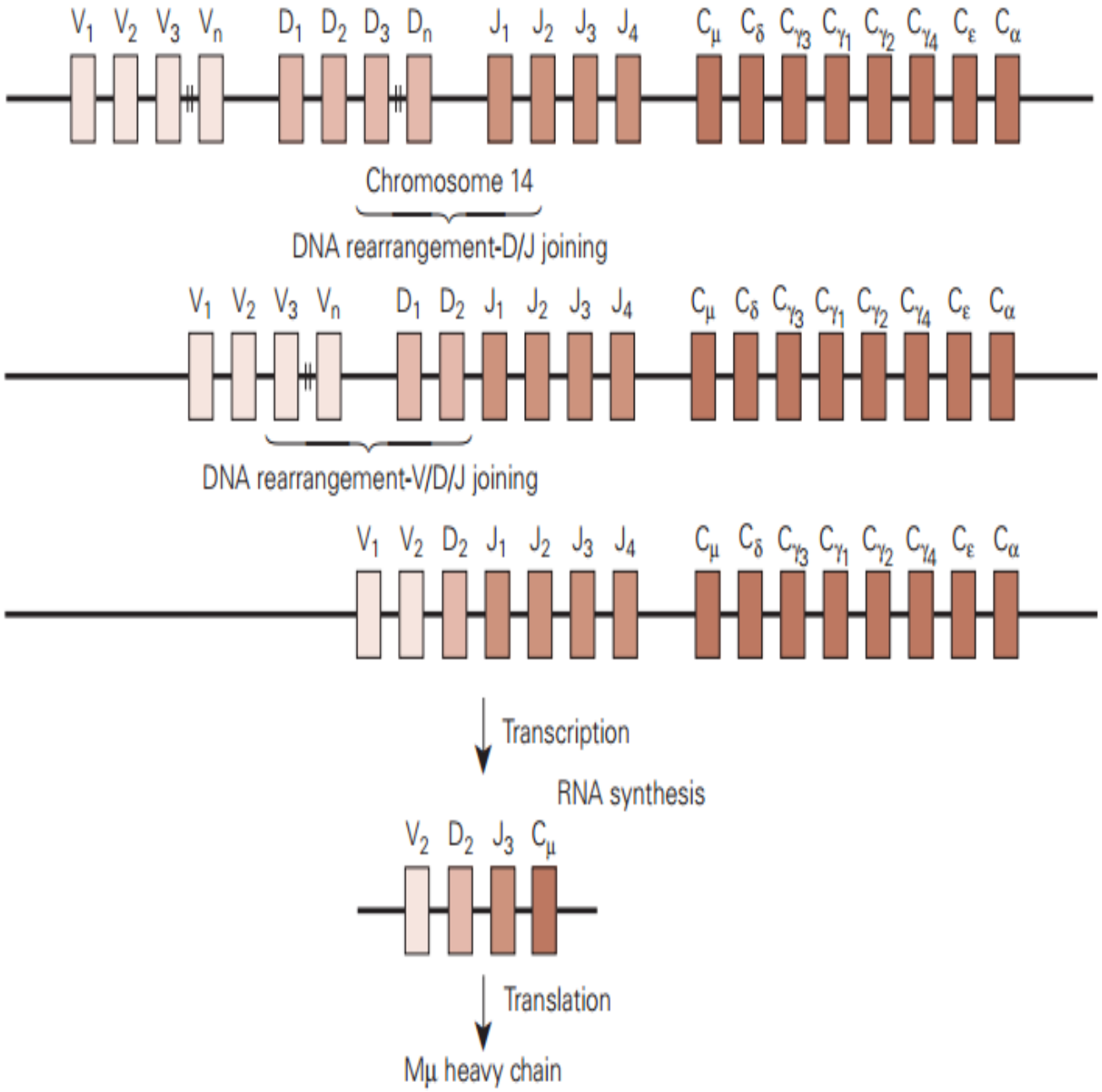



FIGURE 4–10. Coding for immunoglobulin H chains. Four separate regions on chromosome 14 code for H chains. DJ regions are spliced first, and then this segment is joined to a variable region. When RNA synthesis occurs, one constant region is attached to the VDJ combination. μ H chains are made first, but the cell retains its capacity to produce immunoglobulin of another class.

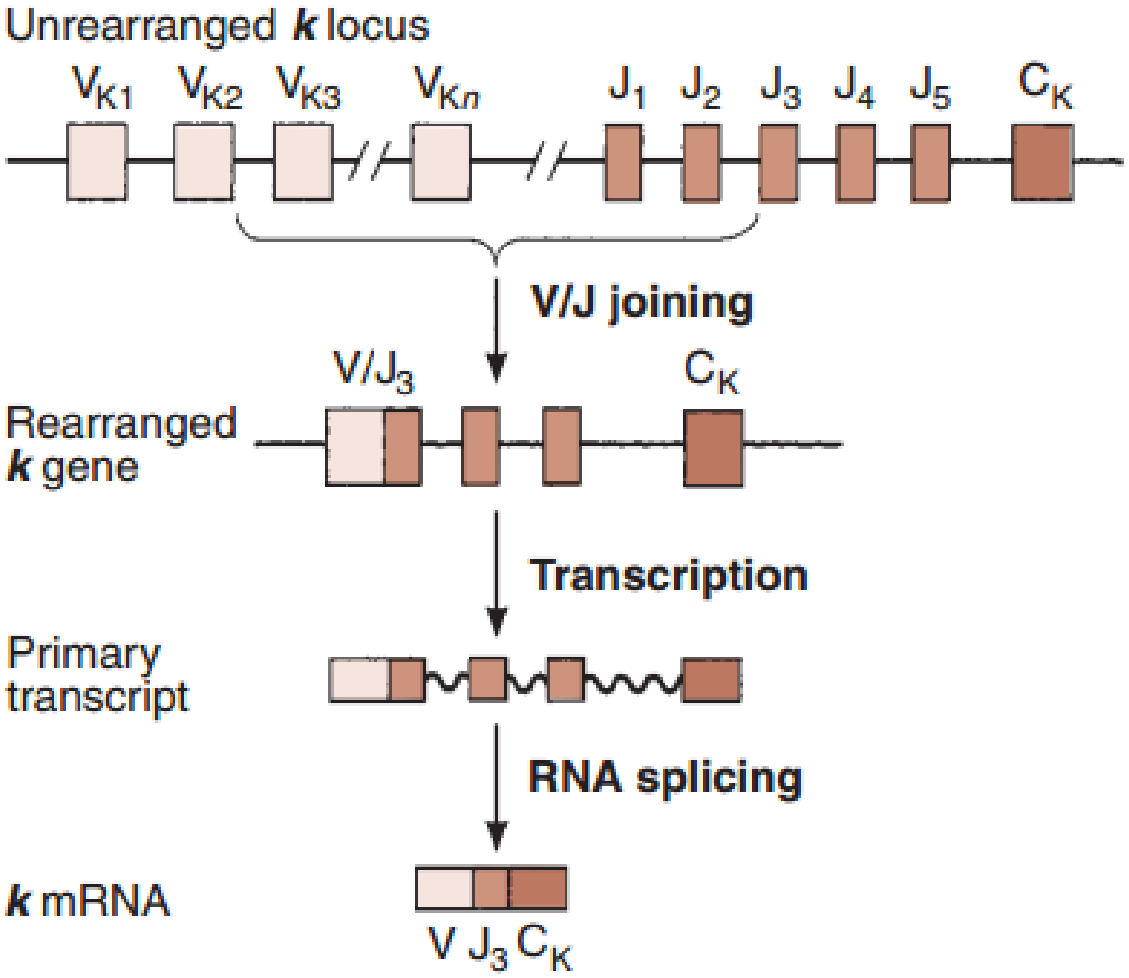
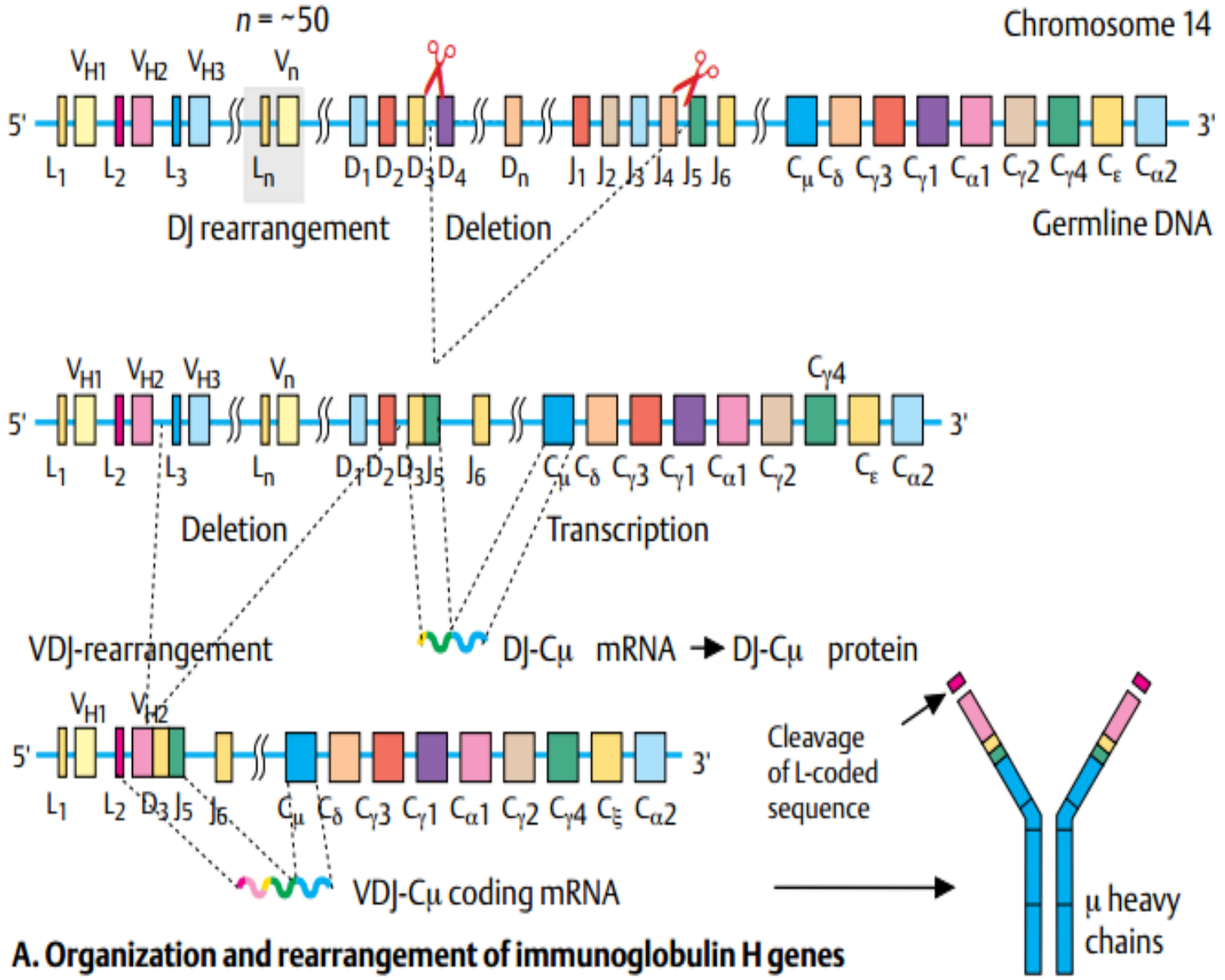
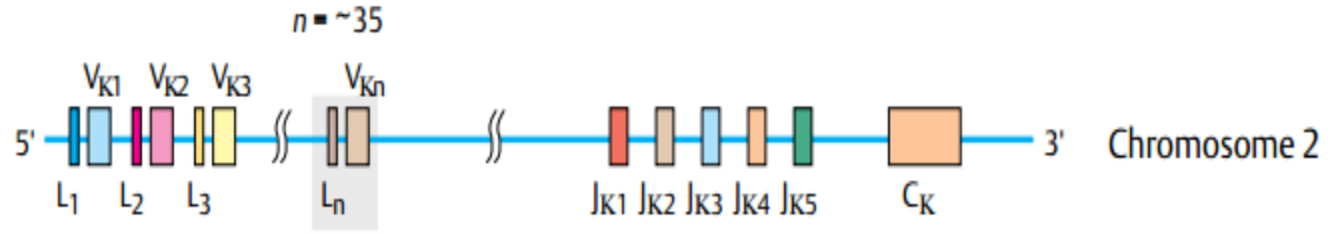



FIGURE 4–11. Assembly and expression of the κ L chain locus. A DNA rearrangement fuses one V segment to one J segment. The VJ segment is then transcribed along with a unique C region to form mature κ mRNA. Unarranged J segments are removed during RNA splicing. *(From Parslow, TG, et al. Medical Immunology, ed. 10. McGraw-Hill/Appleton & Lange, 2001, with permission.)*

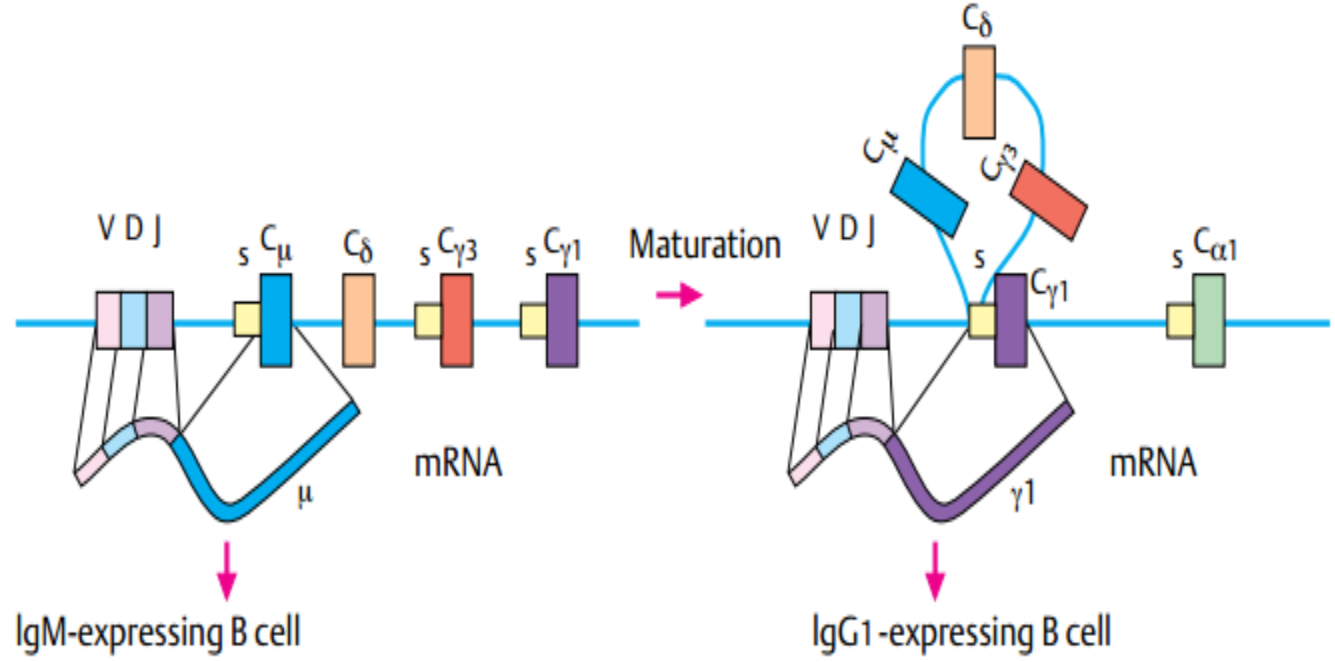



**A. Organization and rearrangement of immunoglobulin H genes**

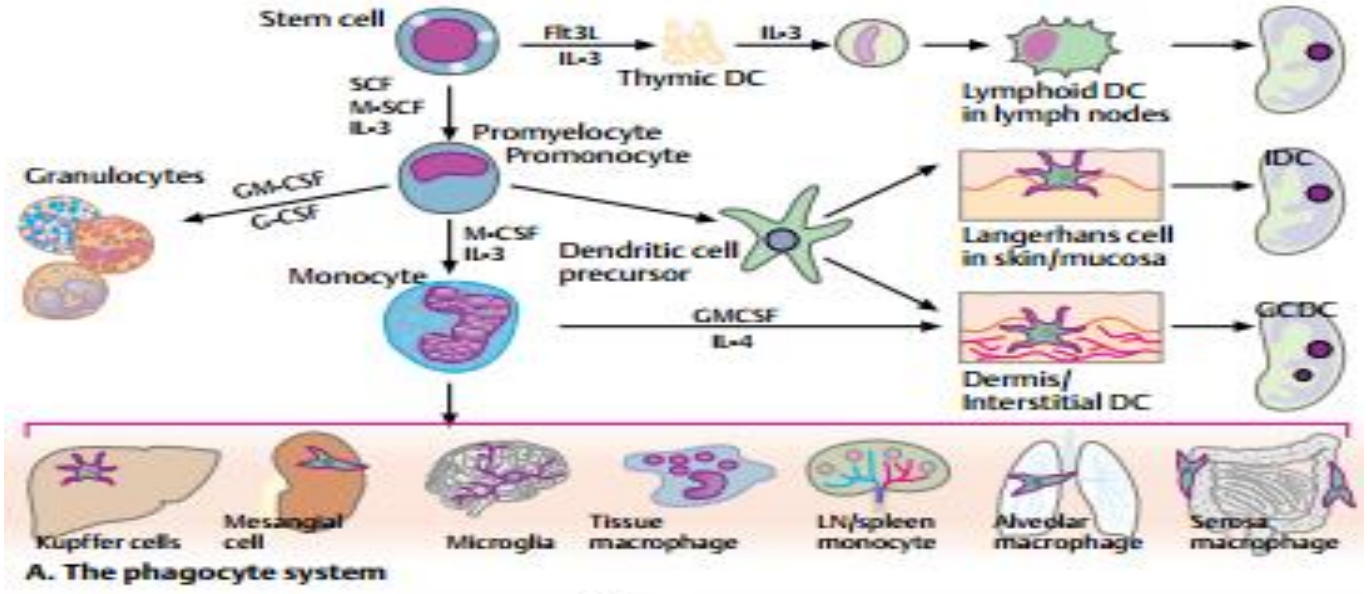



**B. Organization of κ light chain genes**

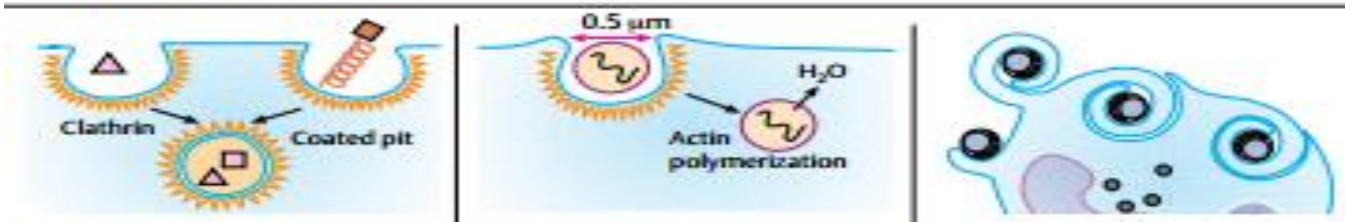

**C. Organization of λ light chain genes**




**D. Immunoglobulin class-switching**

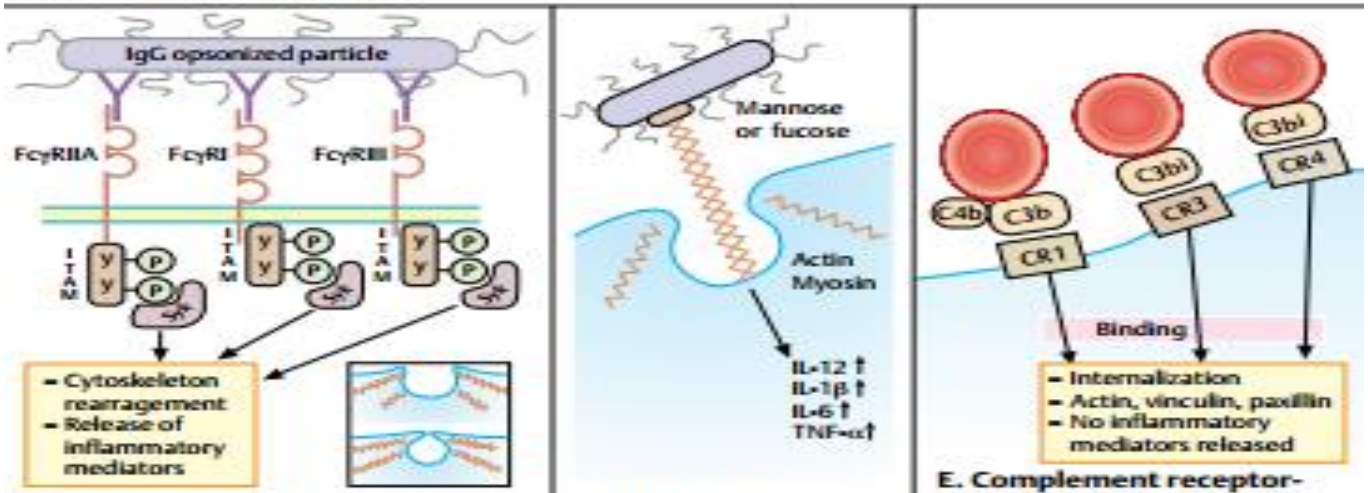



A. The phagocyte system




1. Pinocytosis
2. Phagocytosis
3. Coiling phagocytosis

B. Mechanism of endocytosis

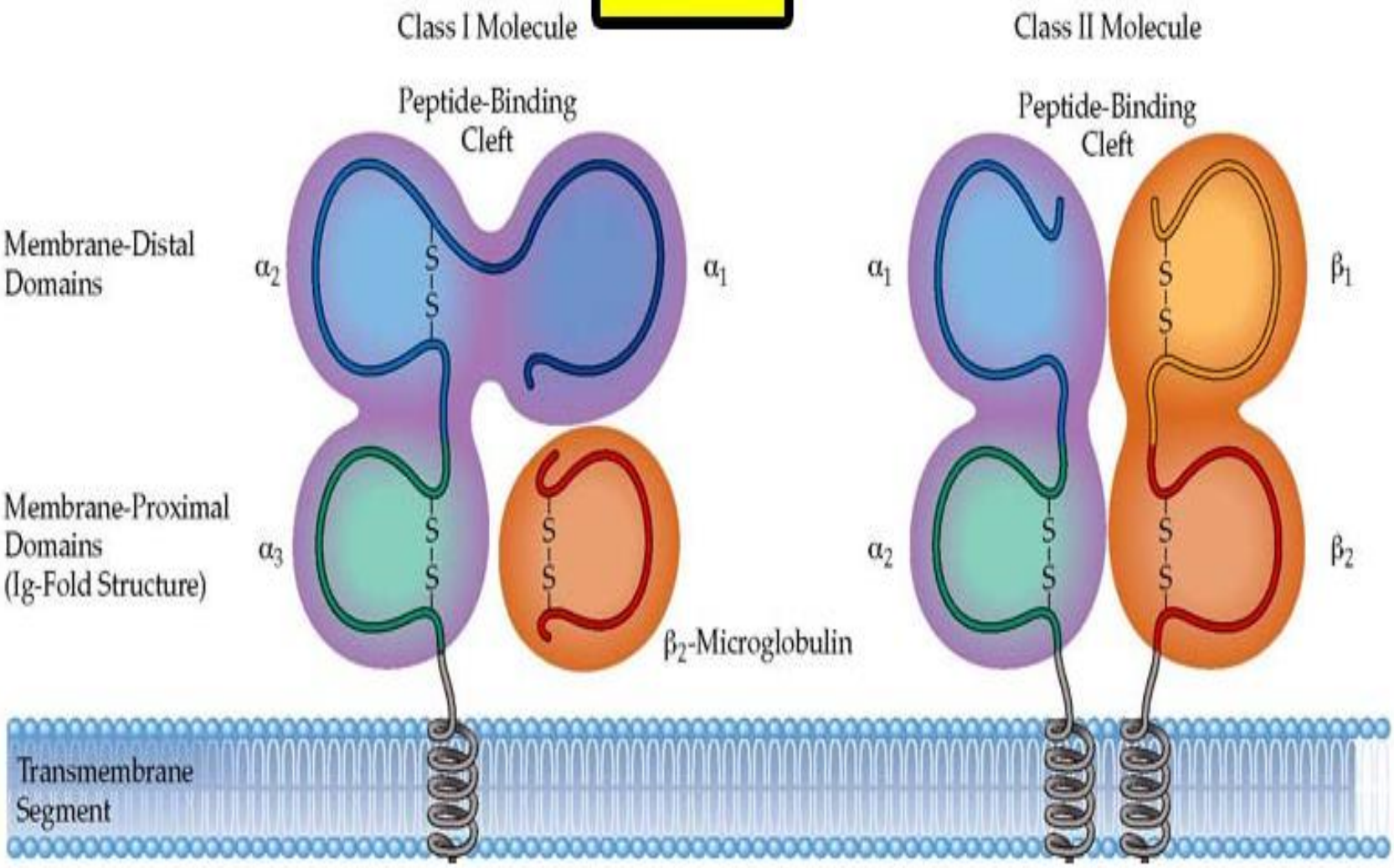



C. Fc-mediated phagocytosis

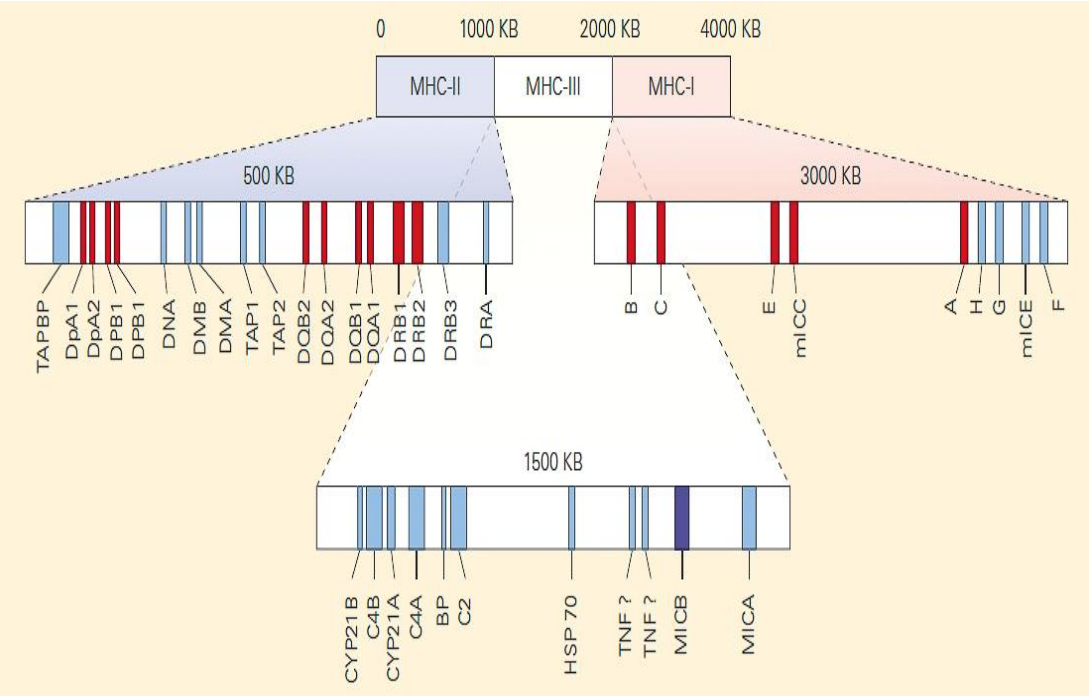
D. Mannose receptor

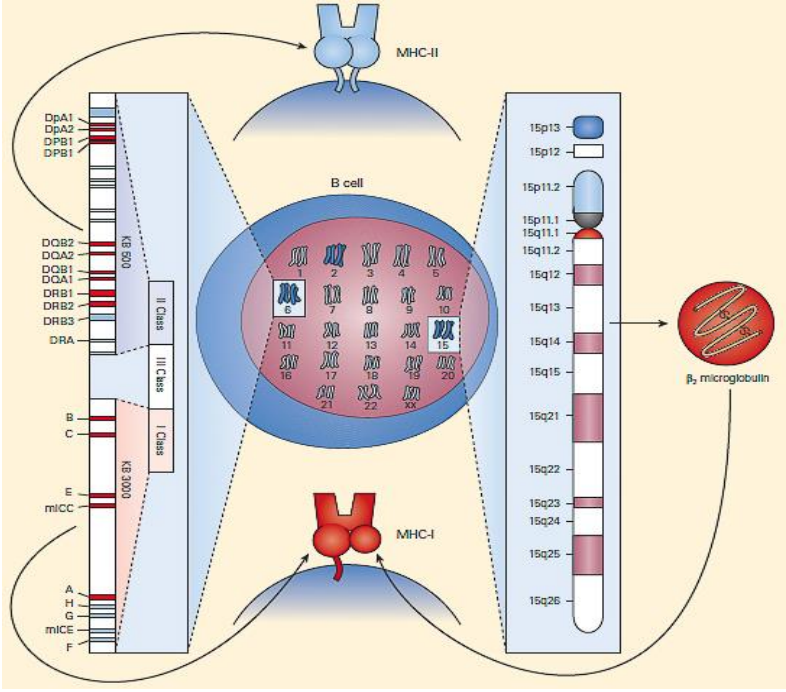
E. Complement receptor-mediated phagocytosis

# MHC Class I VS MHC Class II



# Genetic map of the MHC regions

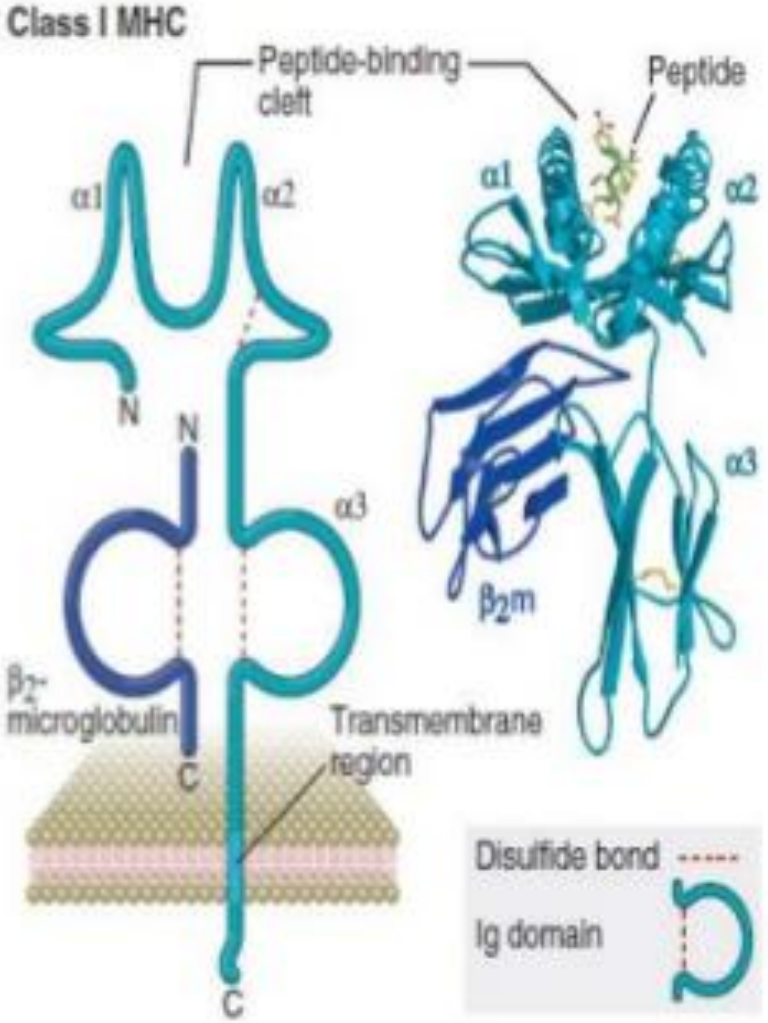



Schematic representation of the chromosomal location and genetic loci responsible for MHC-I and MHC-II synthesis.

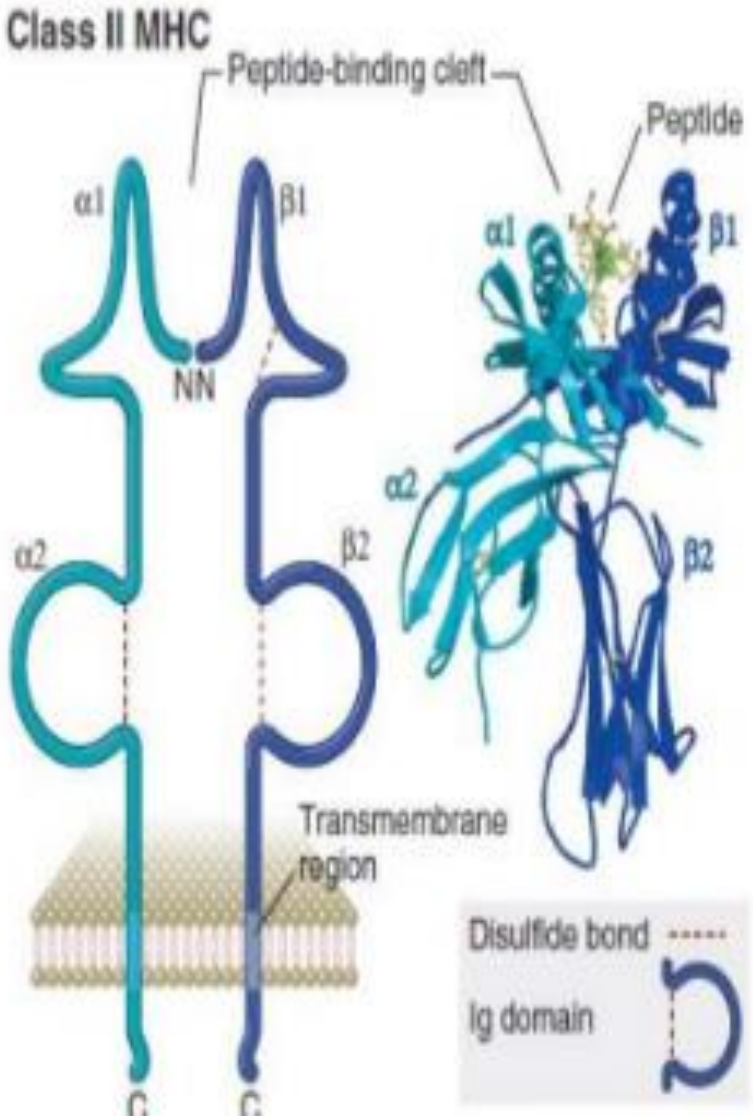
# Class I MHC Molecules

- 2 noncovalently linked polypeptide chain, an MHC encoded **44-47 kD α chain** (heavy) and a non-MHC encoded **12kD β-2 microglobulin** (light).
- α chain is encoded by genes in A,B and C region in HLA complex.
- A chain has 3 parts:-
  - Cytoplasmic domain(α1, α2 and α3, each contain about 90 A. As)
  - Transmemembrane domain( 25 A.As)
  - Cytoplasmic terminal (30 A.As)

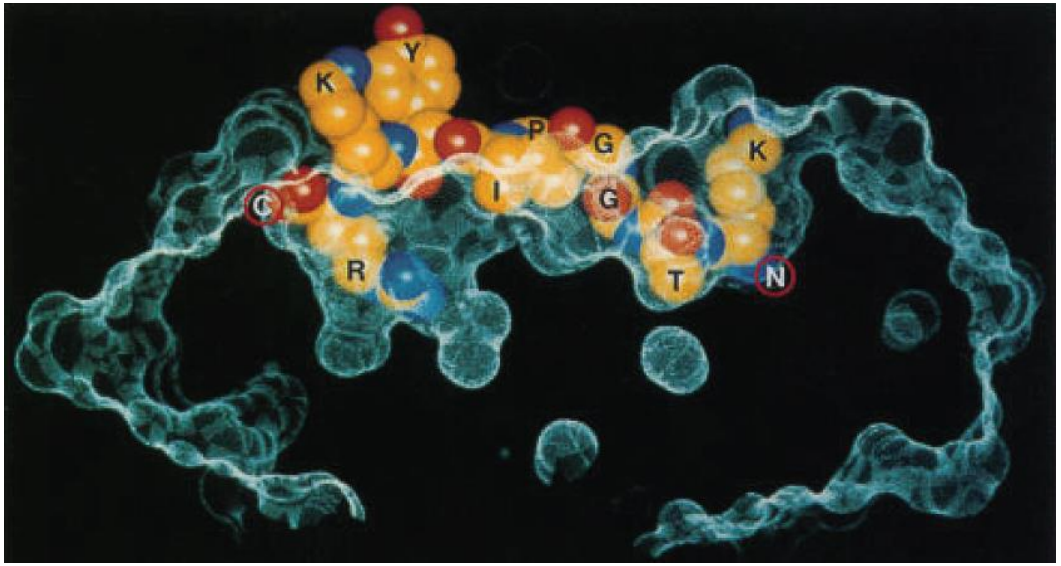


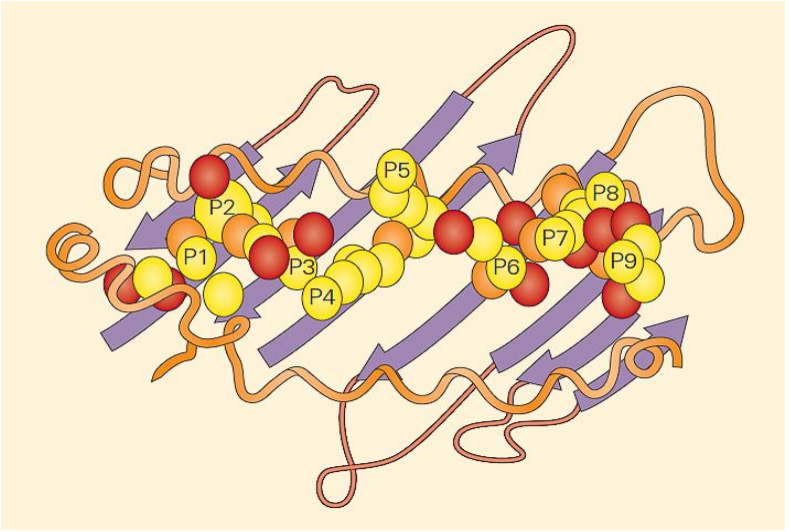
# Class II MHC Molecules

- Similar to class I molecule.
- 2 non covalently associated chain :- **32-34 kD α chain (α1 and α2) and 29-32 kD β chain (β1 and β2).**
- Both α and β chain is encoded by DP,DQ and DR region In HLA complex.
- Each α2 and β2 domain is followed by transmembrane domain and cytoplasmic domain.
- α1 and β2 domain form antigen binding cleft which is open at both ends and binds peptide antigen of 10-30 A.As.

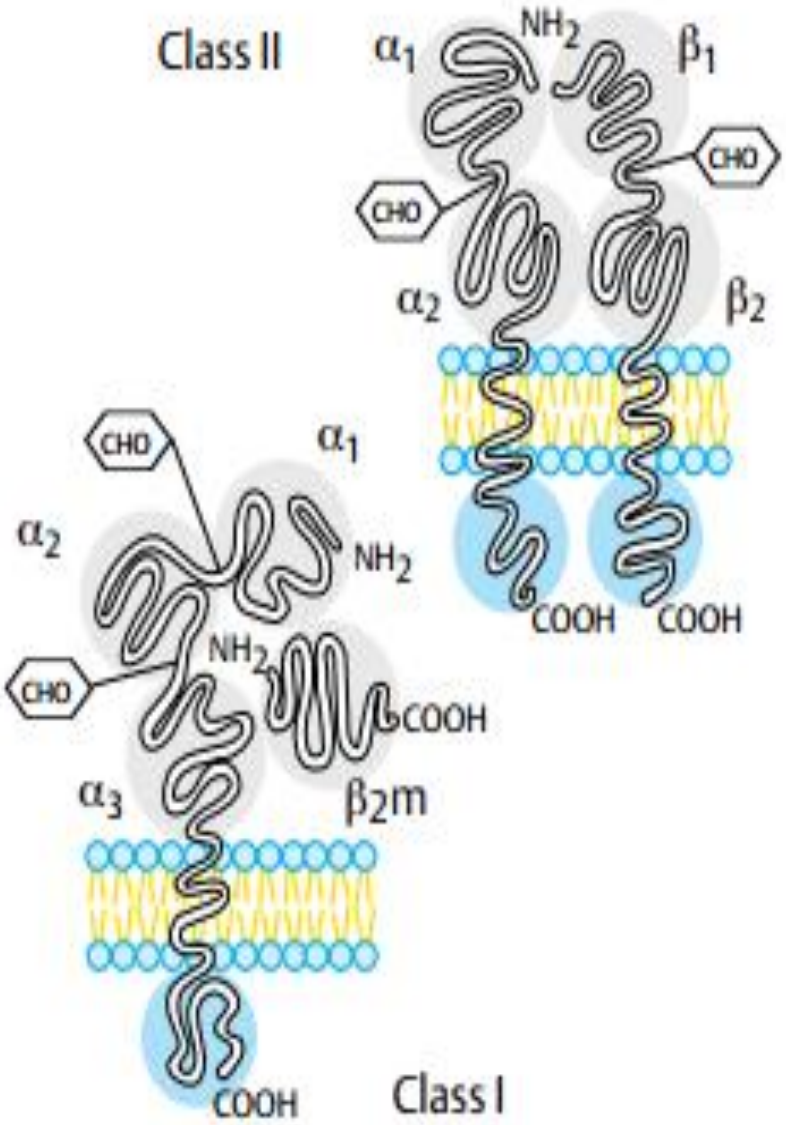


An influenza virus nucleoprotein peptide (KTGGPIYKR) bound to HLA-A*6801, shows insertion of Thr (T) and Arg (R) buried in specificity pockets of the HLA molecule.

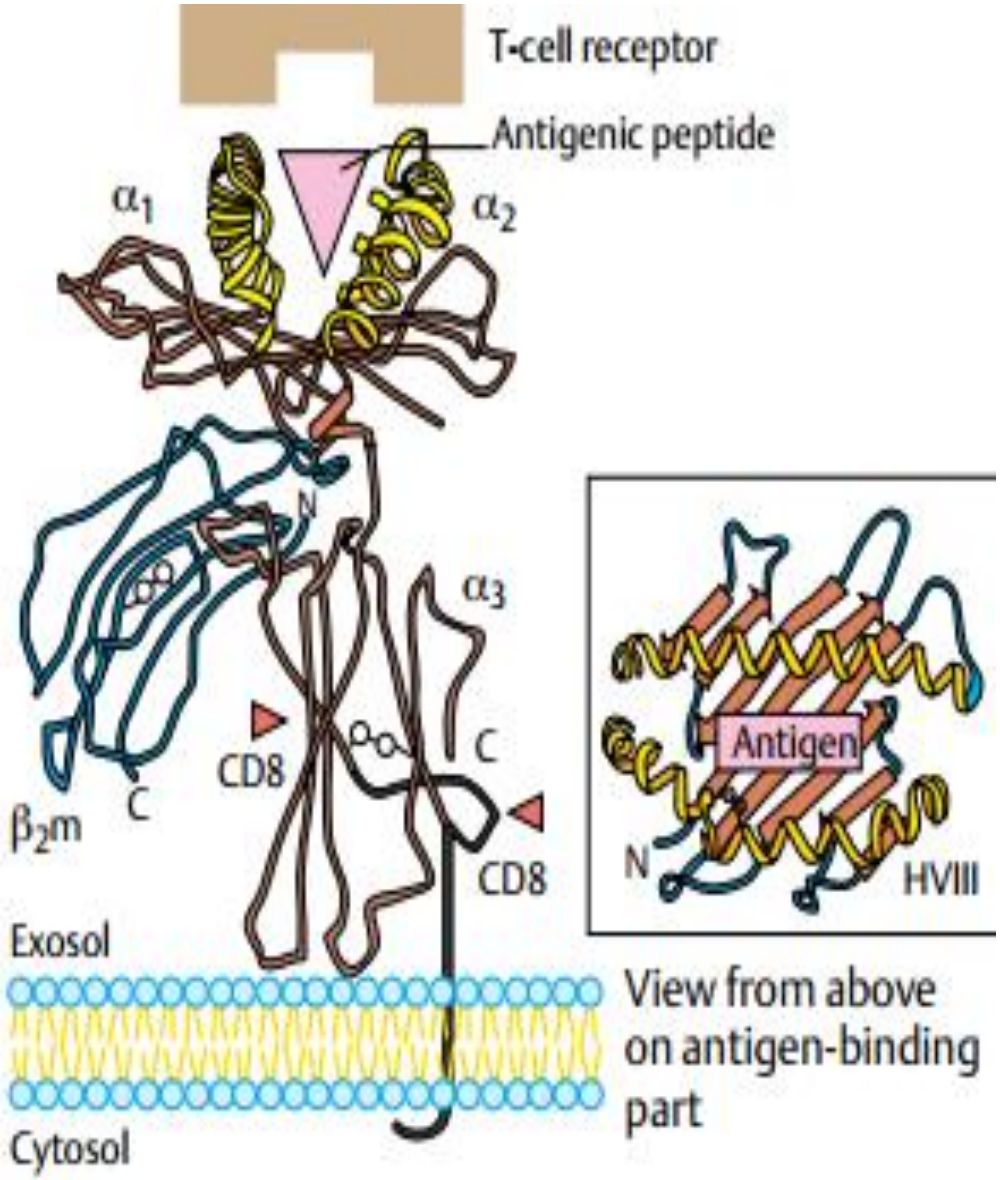



- An example of a peptide held within an MHC-II groove. The fit of the peptide within the groove is very specific.

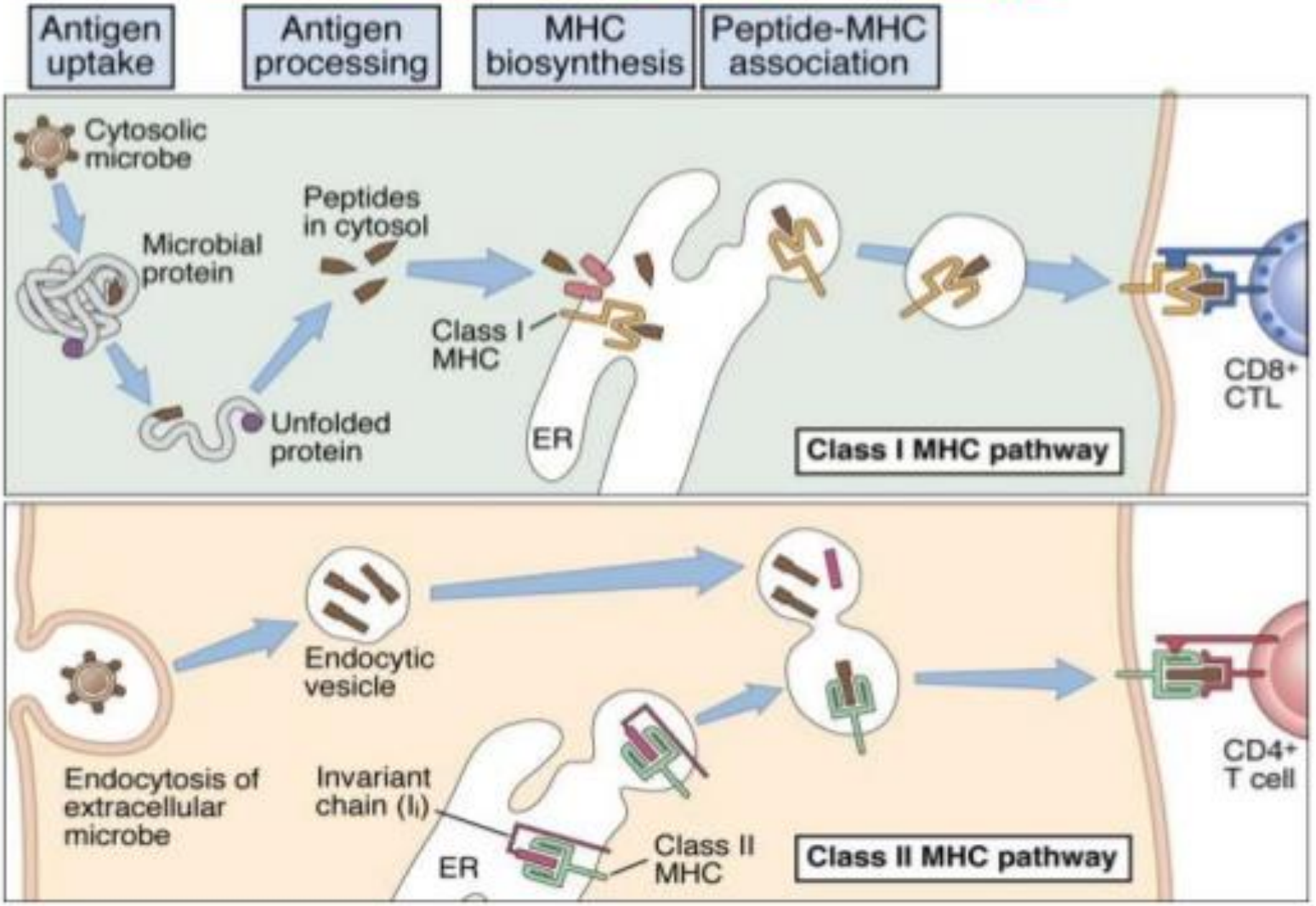



A. HLA molecules (schematic)



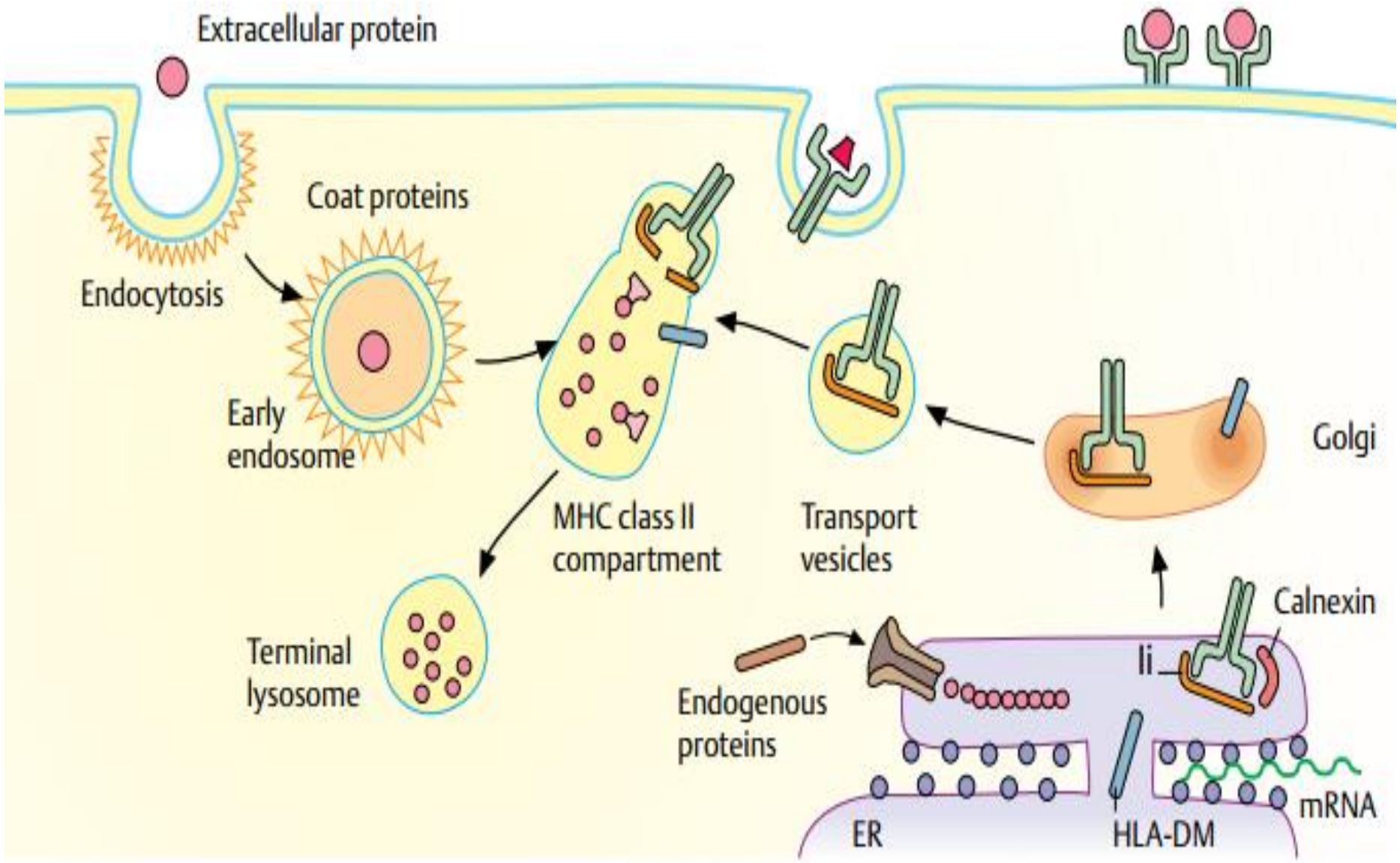

B. Structure of an HLA class I molecules

# Pathways of antigen processing

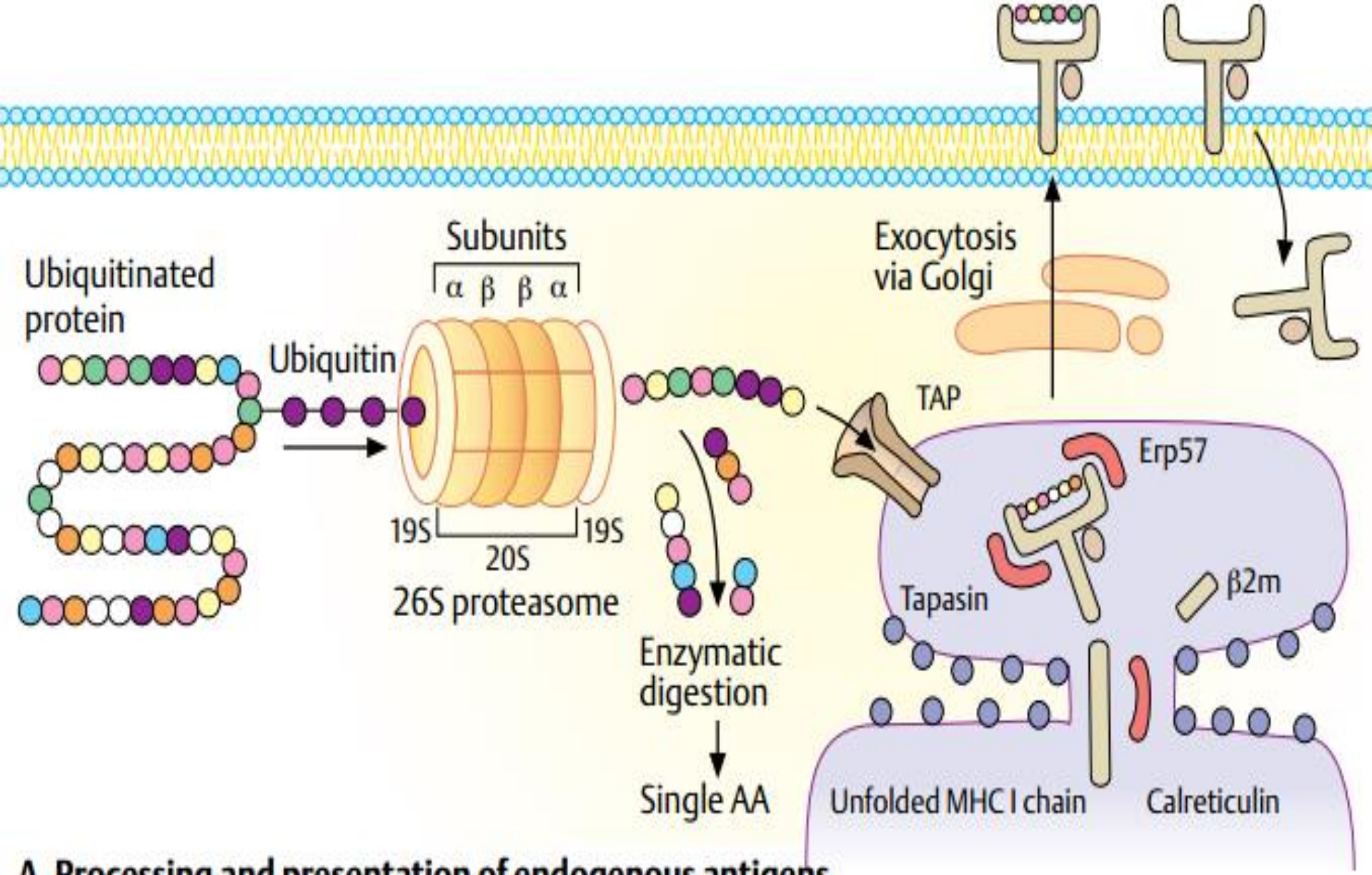



***Protein antigen in cytosol (cytoplasm) --> class I MHC pathway***

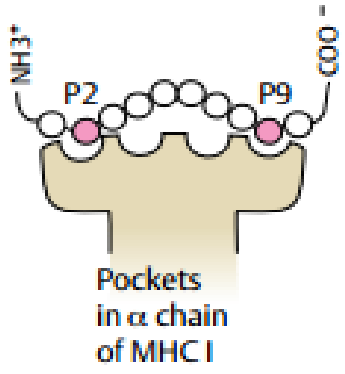
***Protein antigen in vesicles --> class II MHC pathway***




**A. MHC class II-dependant antigen processing**




**A. Processing and presentation of endogenous antigens**

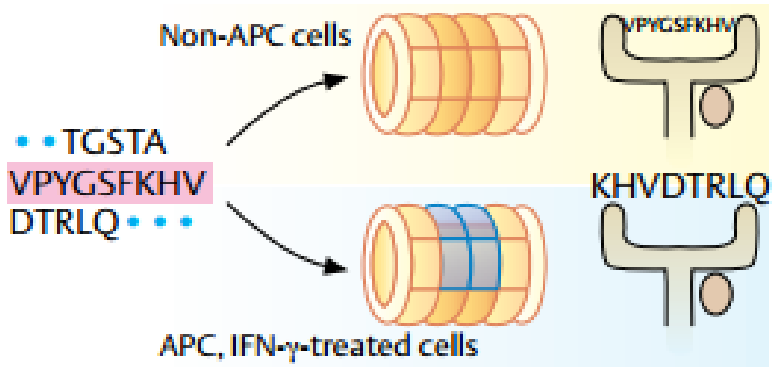



| | |
|---|---|
| HLA-A*0201 | P2=Leucine<br>P9=Valine,<br>Tyrosine |
| HLA-A3: | P2=Leucine<br>P9=Lysine |
| HLA-B7: | P2=Leucine<br>P9=Proline |

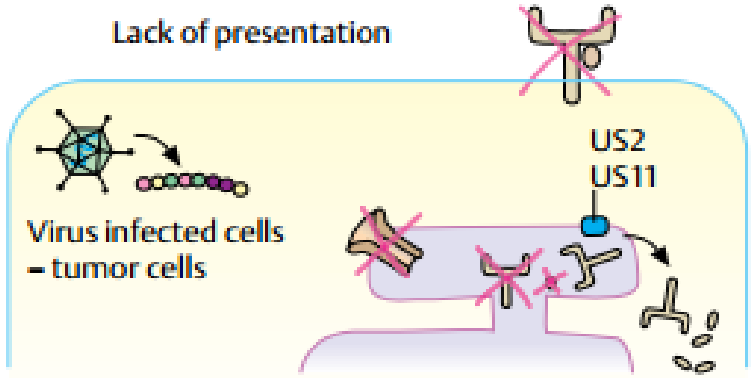
**B. Binding motifs**

MAPPQVLAFGLLLAAATATFAAAQEECVLENY
KLAVNCFVNNNRQCQCTSVGAQNTVICSKL
AAKCLVMKAEMNGSKLGRRAKPEGALQNND
GLYDPDCDESGLFKAKQCNGTSTCWCVNTA
GVRRTDKDTEITCSERVRTYWIIIELKHKAREK
PYDSKSLRTALQKEITTRYGLDPKFITSILYENN
VITIDLVQNSQQKTQNDVDIADVAYYVEKDV
KGESLFSHKKMDLTVNGEQLDLDPGQTLIYY
VDEKAPEFSMQGLKAGVIAVIVVVVIAVVAGI
VVLVISRKKRMAKIEKAEIKEMGEMHRELNA

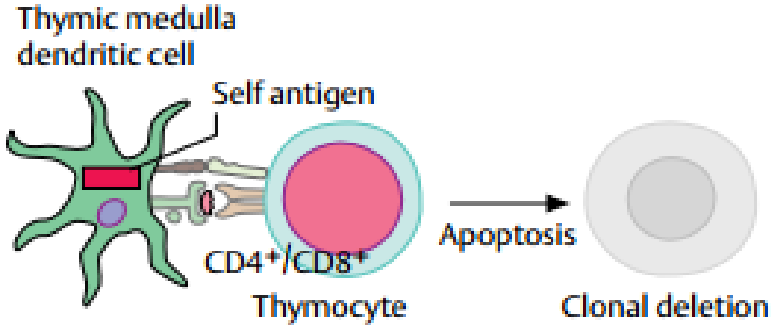
**C. HLA-A2-binding epitopes of a 314 AA protein**



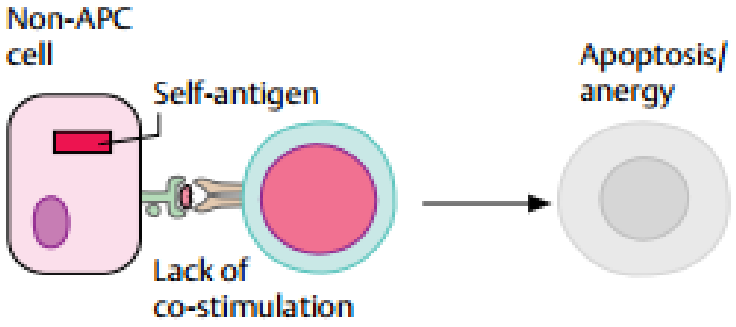

**D. Immunoproteasome**



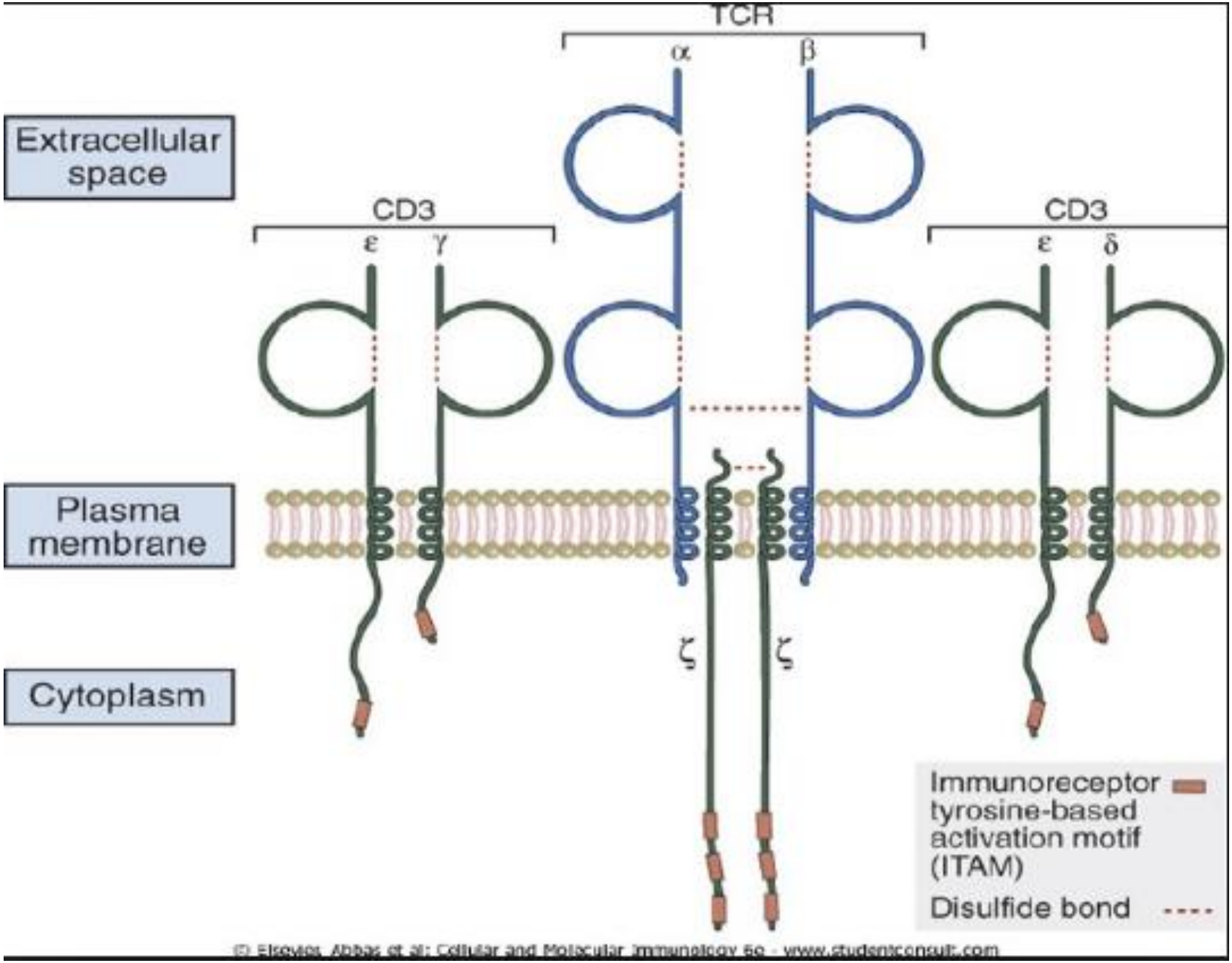

**E. Immune escape mechanisms**

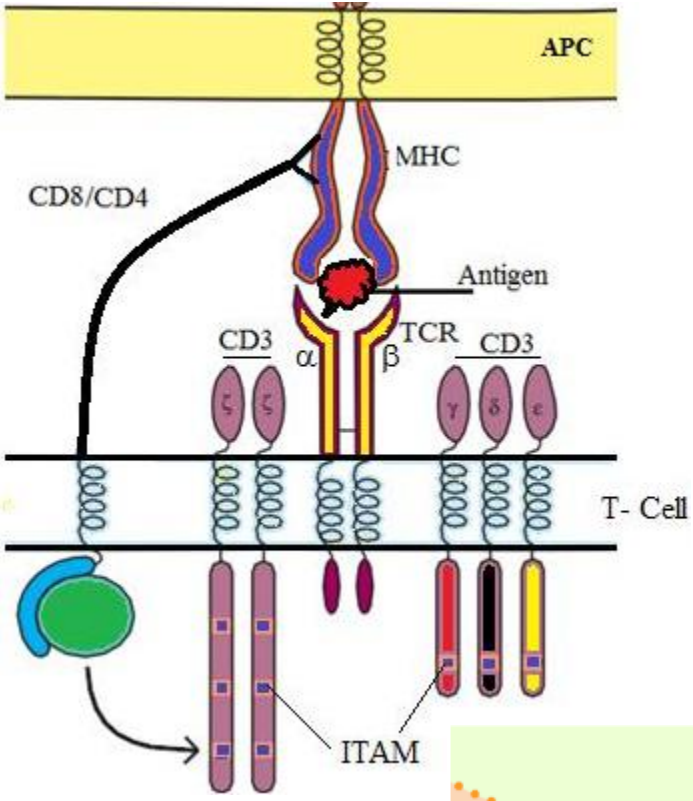


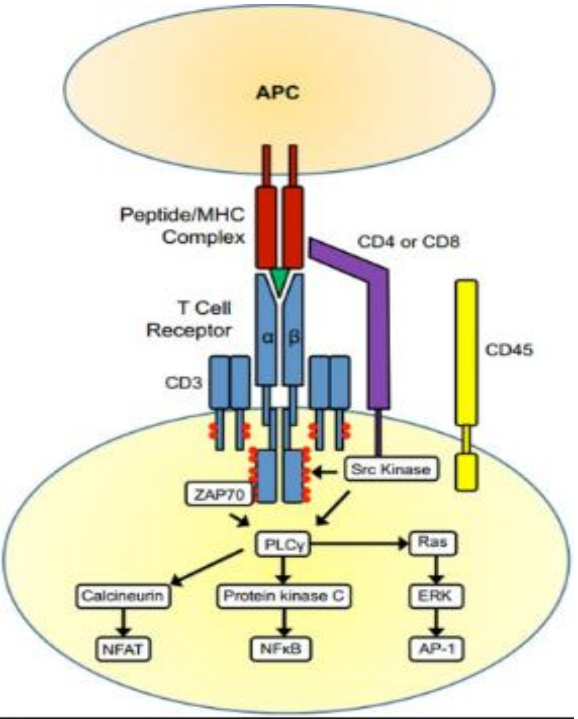

**F. Central tolerance to self antigens**

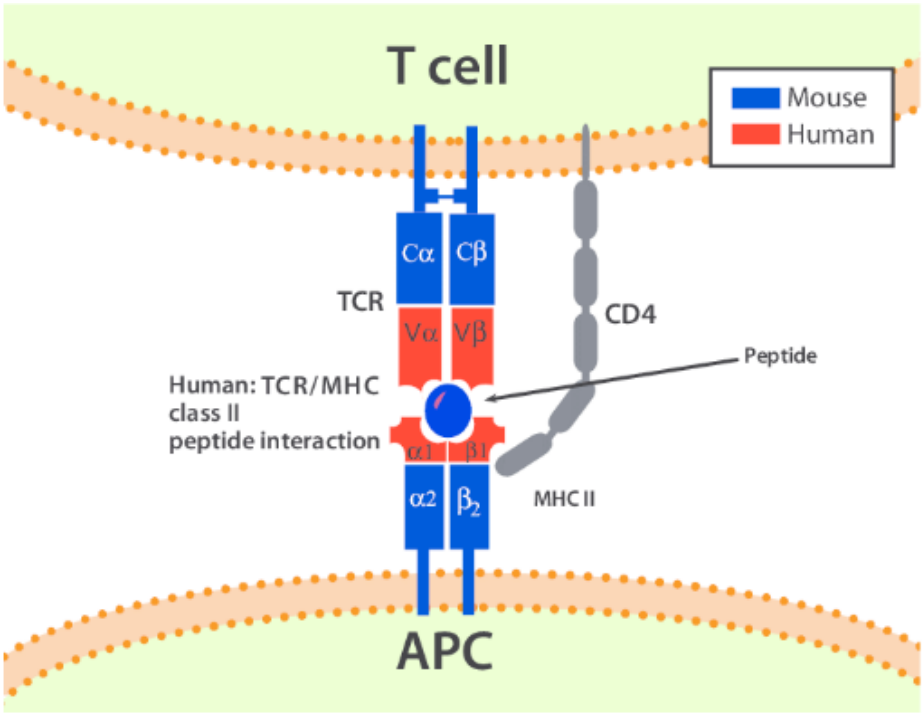



**G. Peripheral tolerance to self-antigens**

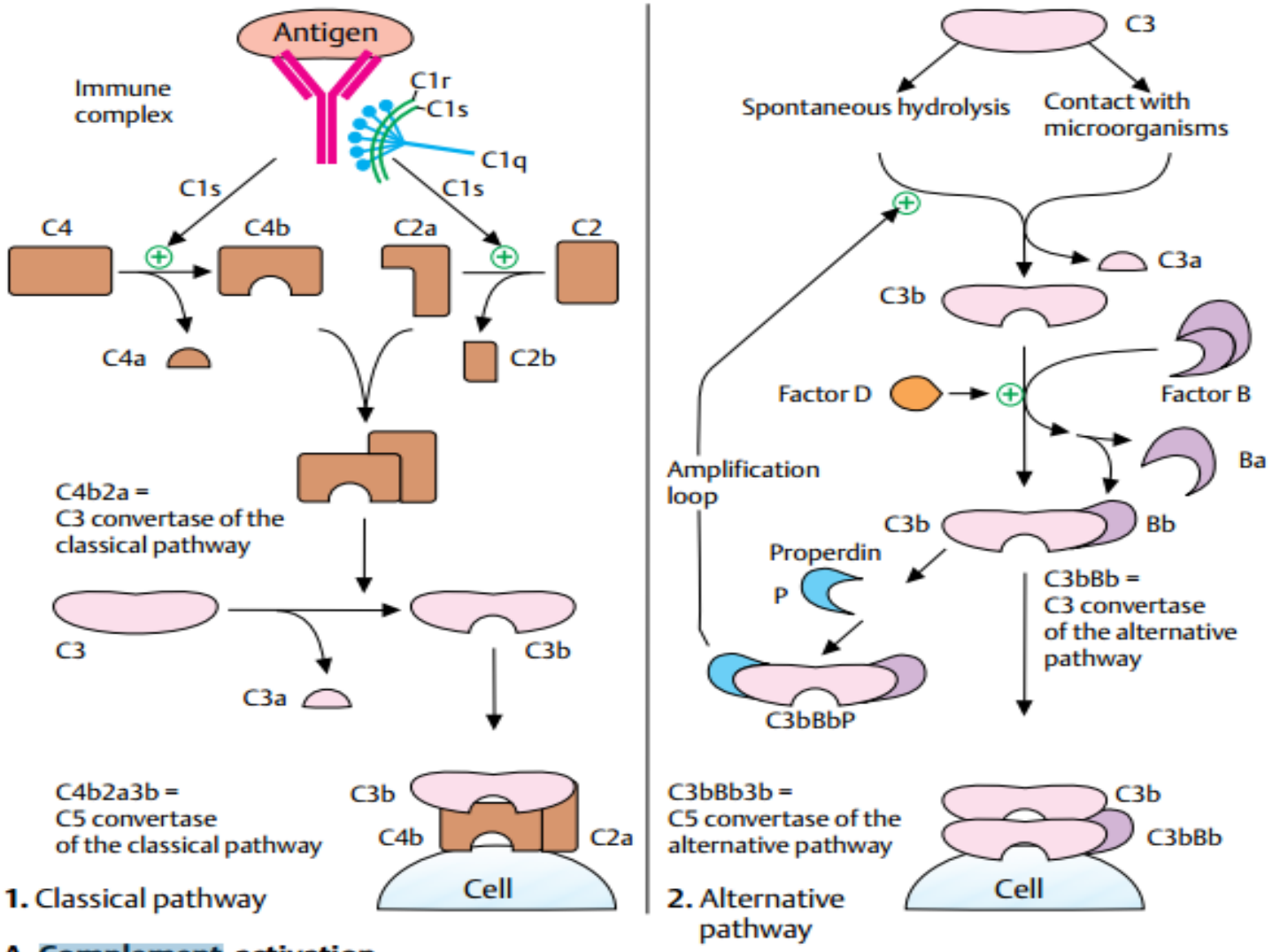


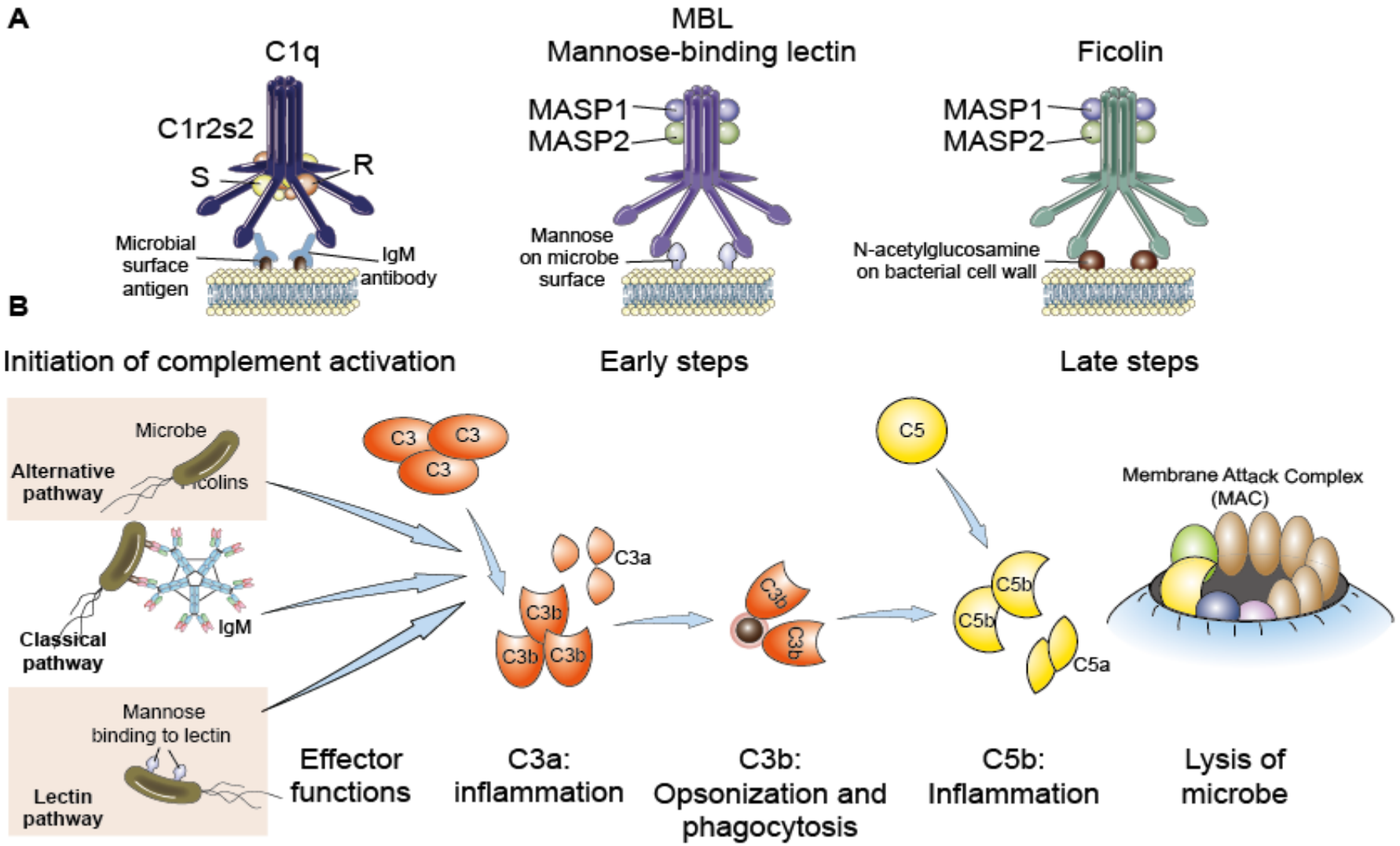

APC
MHC
CD8/CD4
Antigen
CD3
TCR
CD3
α
β
ζ
ζ
γ
δ
ε
T- Cell
ITAM


APC
Peptide/MHC Complex
CD4 or CD8
T Cell Receptor
α
β
CD3
CD45
Src Kinase
ZAP70
PLCγ
Ras
Calcineurin
Protein kinase C
ERK
NFAT
NFκB
AP-1

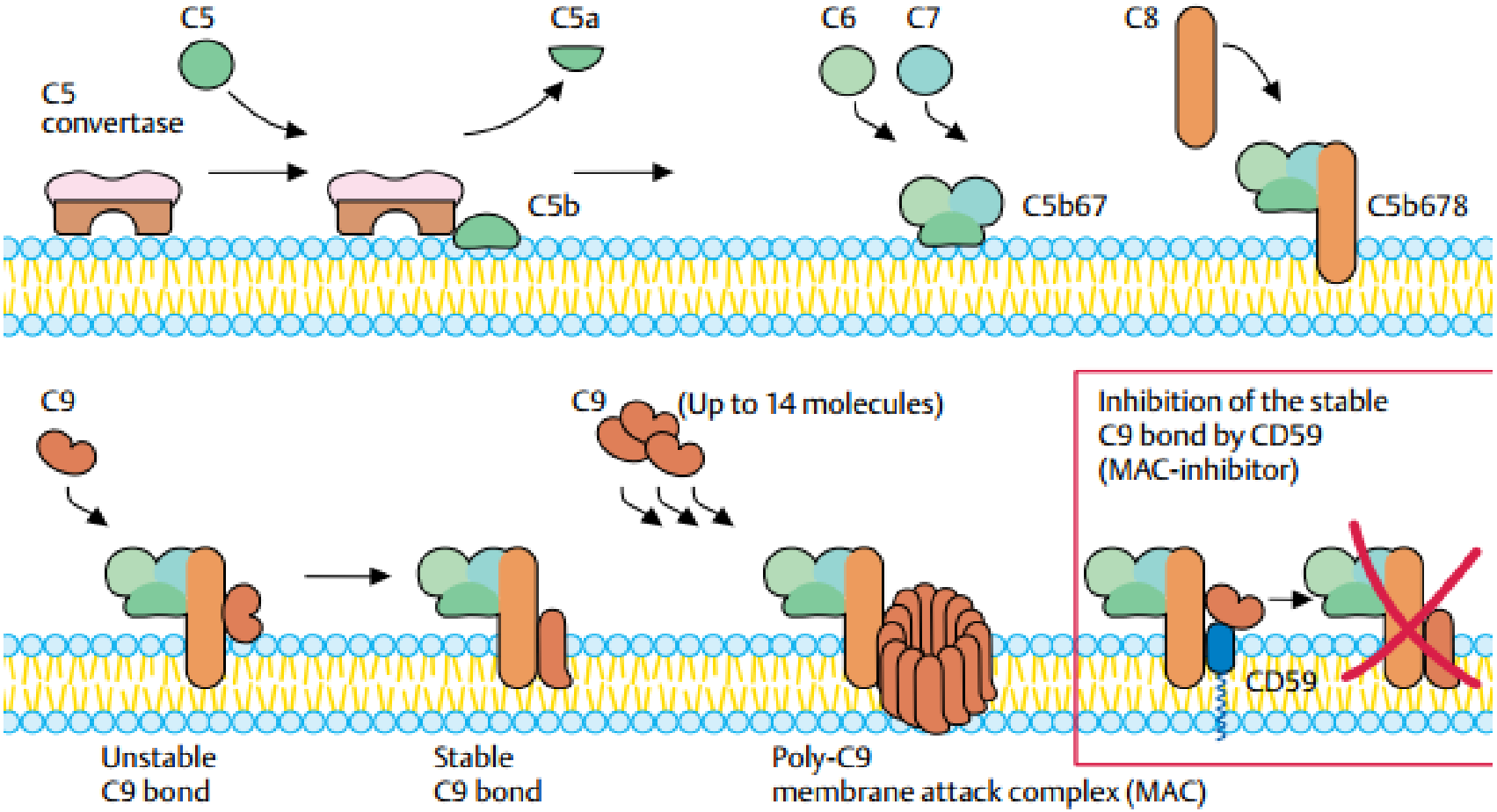

T cell
Mouse
Human
Cα
Cβ
TCR
Vα
Vβ
CD4
Peptide
Human: TCR/MHC class II peptide interaction
α1
β1
α2
β2
MHC II
APC

# Complement System



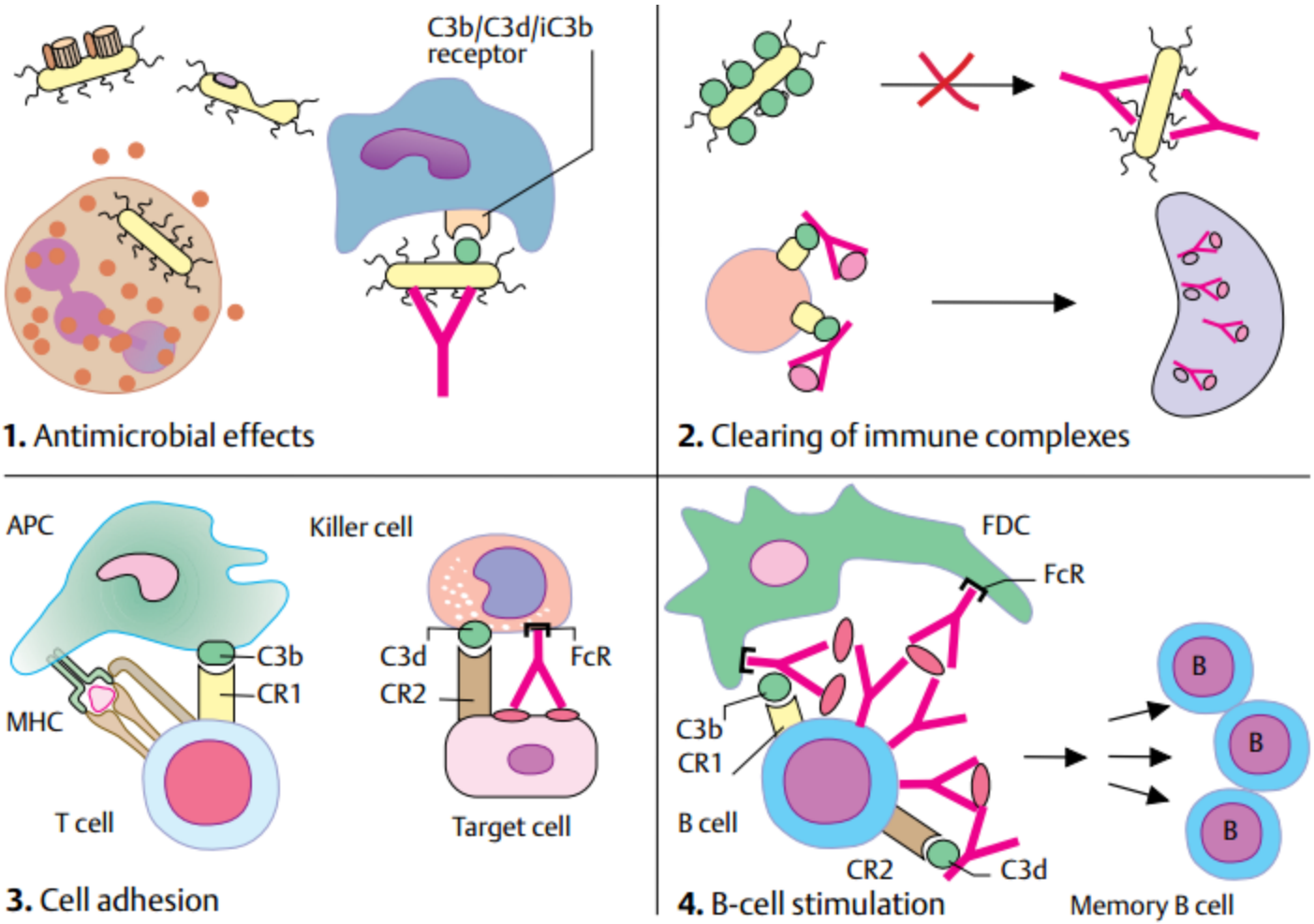

A
C1q
C1r2s2
S
R
Microbial surface antigen
IgM antibody
MBL
Mannose-binding lectin
MASP1
MASP2
Mannose on microbe surface
Ficolin
MASP1
MASP2
N-acetylglucosamine on bacterial cell wall
B
Initiation of complement activation
Early steps
Late steps
Microbe
Alternative pathway
Ficolins
Classical pathway
IgM
Mannose binding to lectin
Lectin pathway
C3
C3
C3
C3a
C3b
C3b
C3b
C3b
C3b
C5
C5b
C5b
C5a
Membrane Attack Complex (MAC)
Effector functions
C3a: inflammation
C3b: Opsonization and phagocytosis
C5b: Inflammation
Lysis of microbe

# Complement System

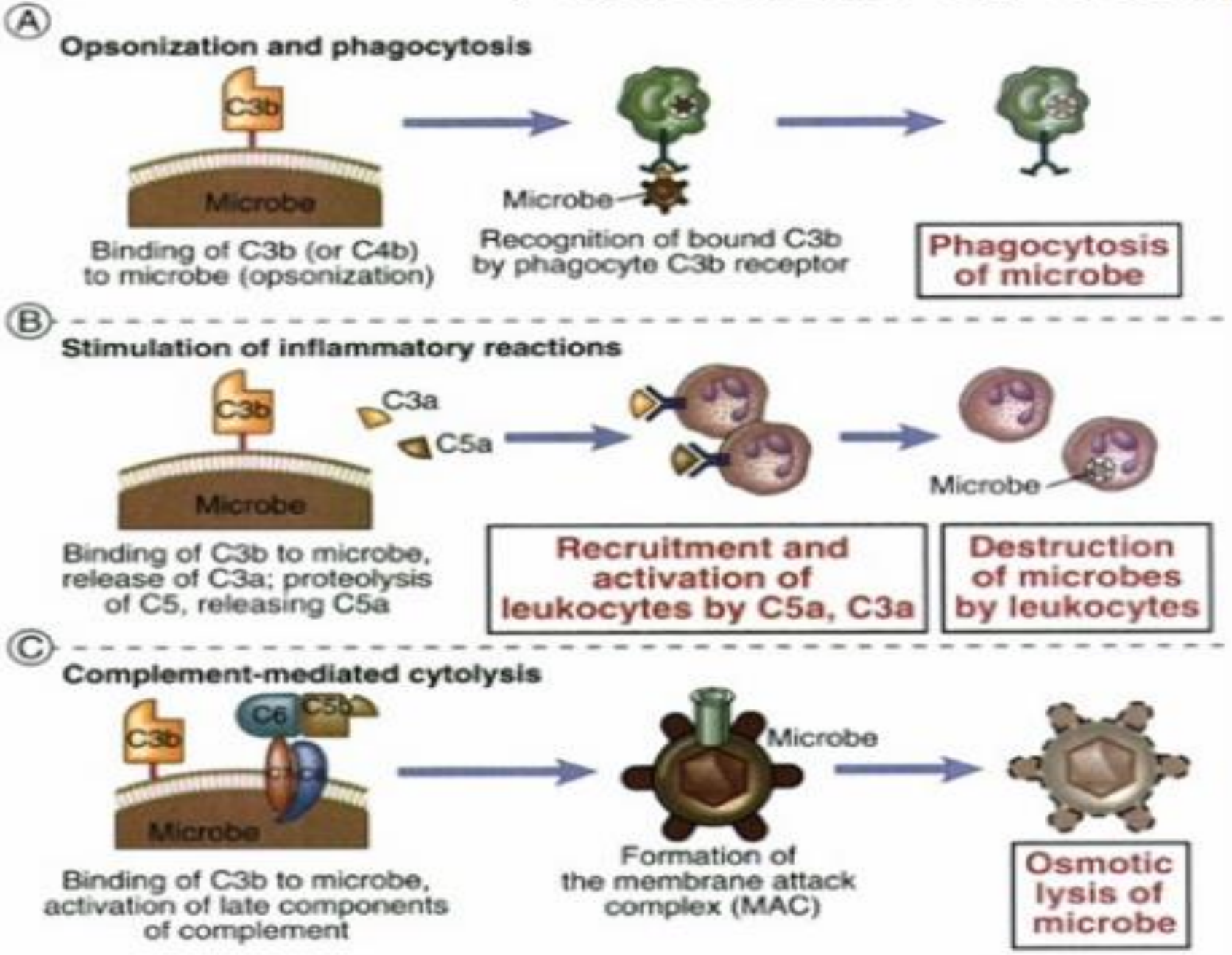



**B. Lytic terminal sequence**

# Complement System




**C. Biological effects of complement: immunological effects**


A
Opsonization and phagocytosis
C3b
Microbe
Binding of C3b (or C4b) to microbe (opsonization)
Microbe
Recognition of bound C3b by phagocyte C3b receptor
Phagocytosis of microbe
B
Stimulation of inflammatory reactions
C3b
Microbe
C3a
C5a
Microbe
Binding of C3b to microbe, release of C3a; proteolysis of C5, releasing C5a
Recruitment and activation of leukocytes by C5a, C3a
Destruction of microbes by leukocytes
C
Complement-mediated cytolysis
C3b
C6
C5b
Microbe
Binding of C3b to microbe, activation of late components of complement
Microbe
Formation of the membrane attack complex (MAC)
Osmotic lysis of microbe