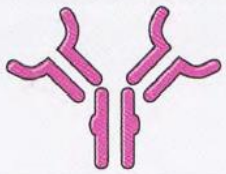
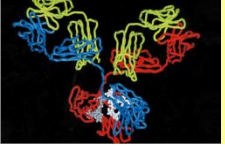
TABLE 5–1 Features of Antigen Binding by the Antigen-Recognizing Molecules of the Immune System

Feature	Antigen-Binding Molecule		
	Immunoglobulin (Ig) 	T cell receptor (TCR)* 	MHC molecules* 
Antigen-binding site	Made up of three CDRs in V_H and three CDRs in V_L domains	Made up of three CDRs in V_α and three CDRs in V_β domains	Peptide-binding cleft made of $\alpha 1$ and $\alpha 2$ (class I) and $\alpha 1$ and $\beta 1$ (class II) domains
Nature of antigen that may be bound	Macromolecules (proteins, lipids, polysaccharides) and small chemicals	Peptide-MHC complexes	Peptides
Nature of antigenic determinants recognized	Linear and conformational determinants of various macromolecules and chemicals	Linear determinants of peptides; only 2 or 3 amino acid residues of a peptide bound to an MHC molecule	Linear determinants of peptides; only some amino acid residues of a peptide
Affinity of antigen binding	K_d 10^{-7}-10^{-11} M; average affinity of Igs increases during immune response	K_d 10^{-5}-10^{-7} M	K_d 10^{-6}-10^{-9} M; extremely stable binding
On-rate and off-rate	Rapid on-rate, variable off-rate	Slow on-rate, slow off-rate	Slow on-rate, very slow off-rate

*The structures and functions of MHC and TCR molecules are discussed in Chapters 6 and 7, respectively.

CDR, complementarity-determining region; K_d, dissociation constant; MHC, major histocompatibility complex; (only class II molecules depicted); V_H, variable domain of heavy chain Ig; V_L, variable domain of light chain Ig.



Structure of IgG and IgM

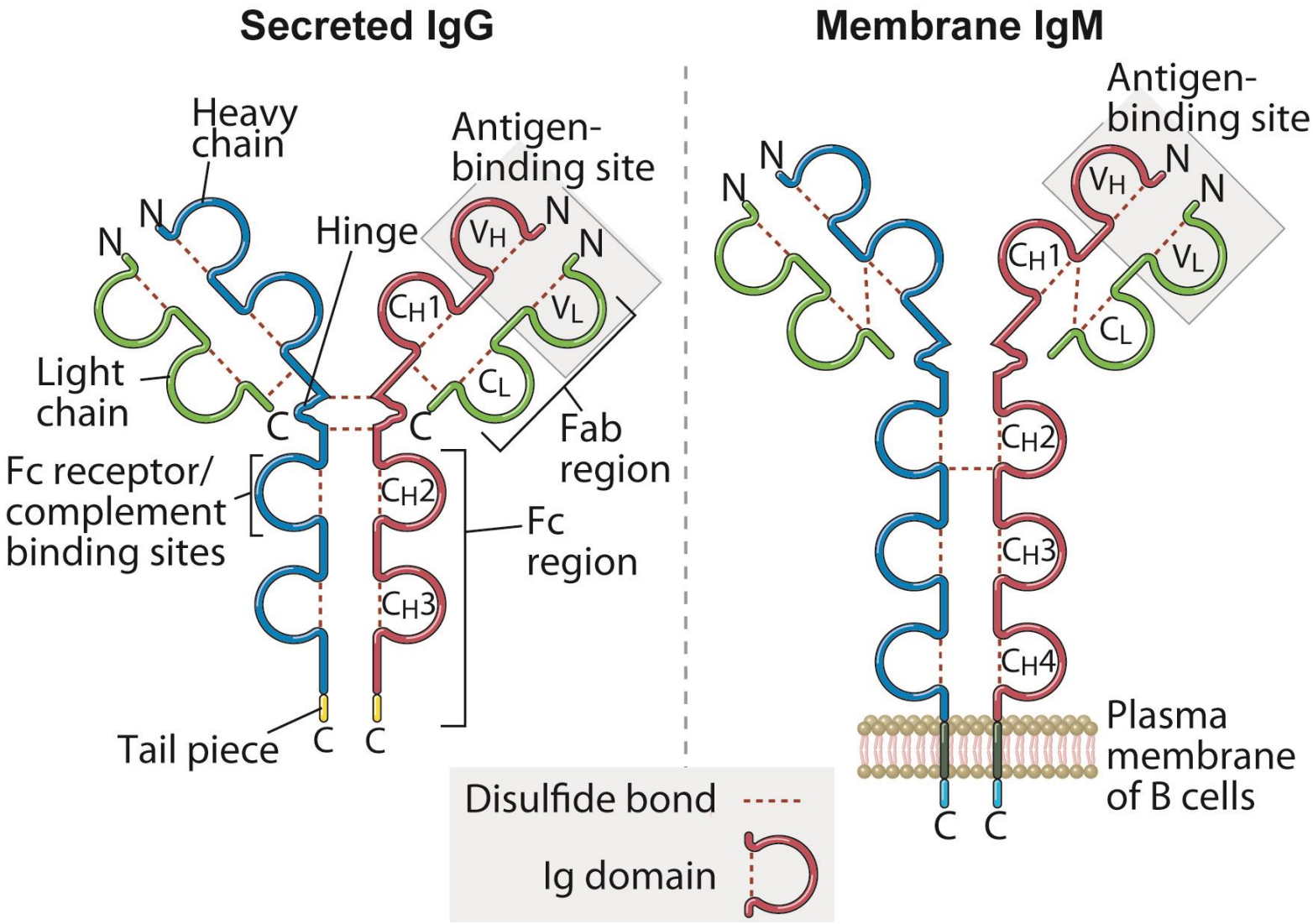


Fig. 5-1 A,B

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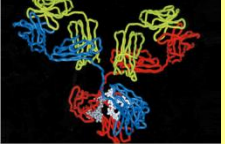

Crystal Structure of Secreted IgG

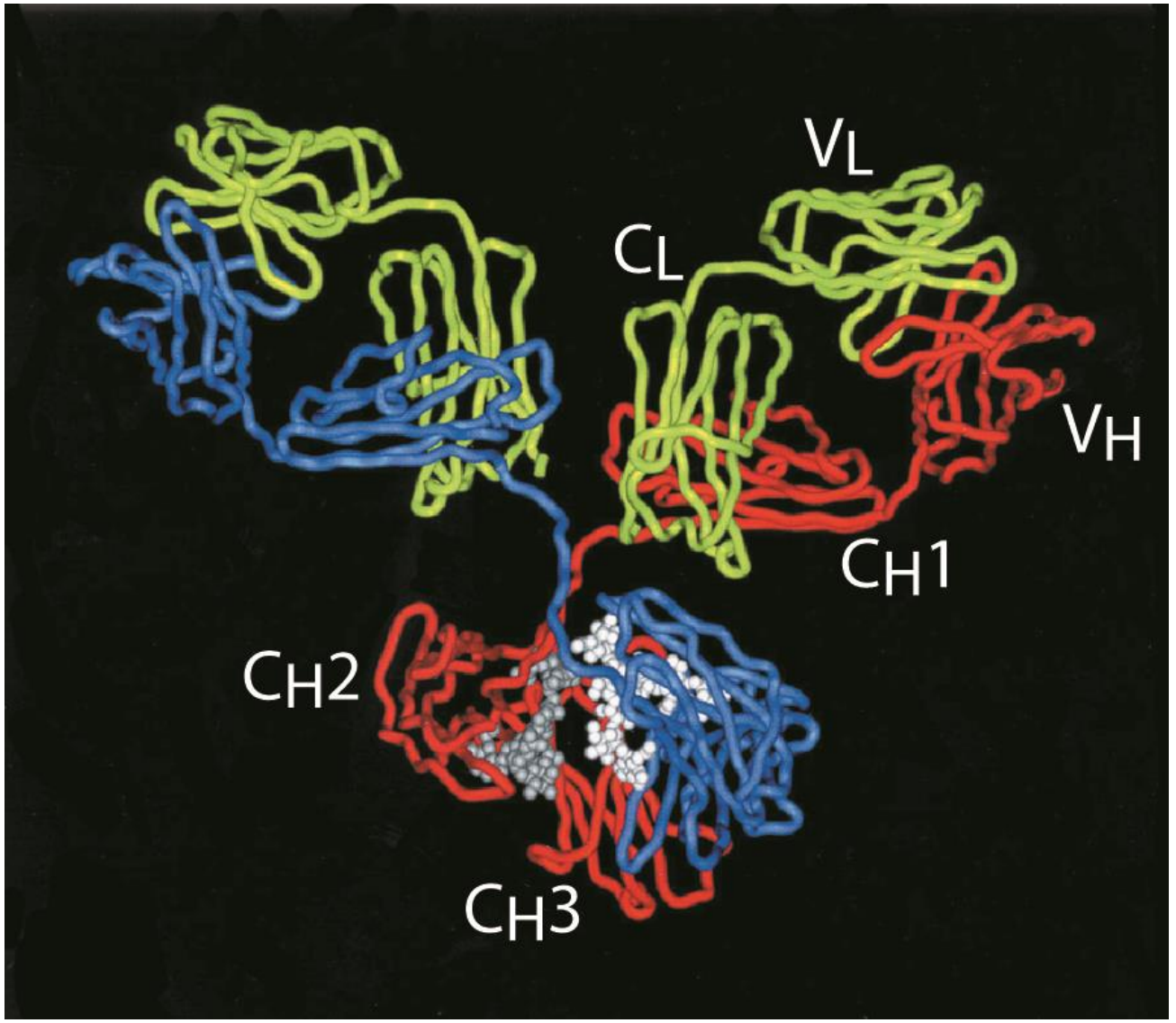

Fig. 5-1 C

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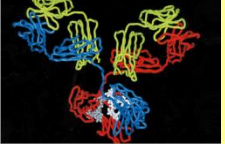

Structure of an Ig Domain

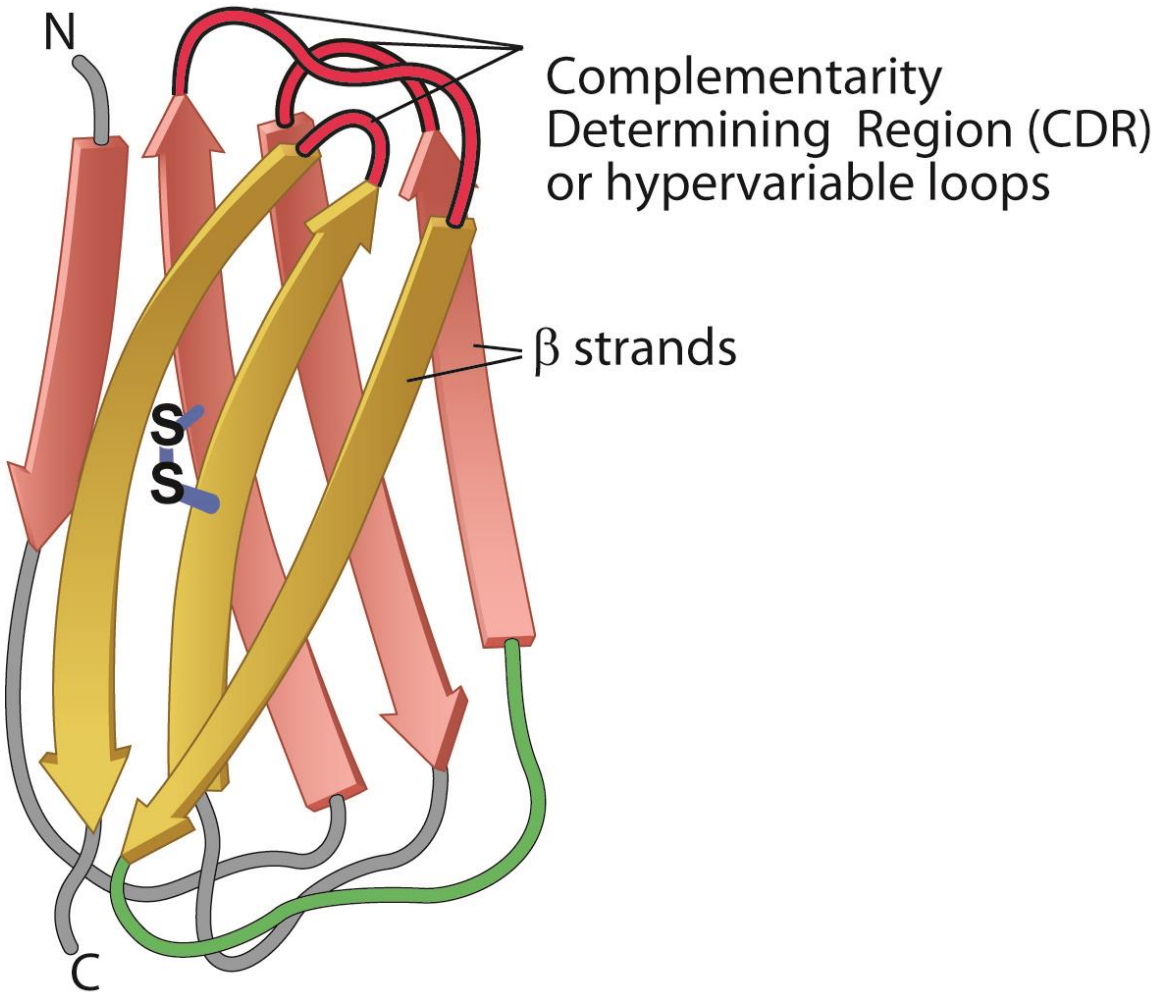

Fig. 5-2

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Proteolytic Fragments of IgG (1)

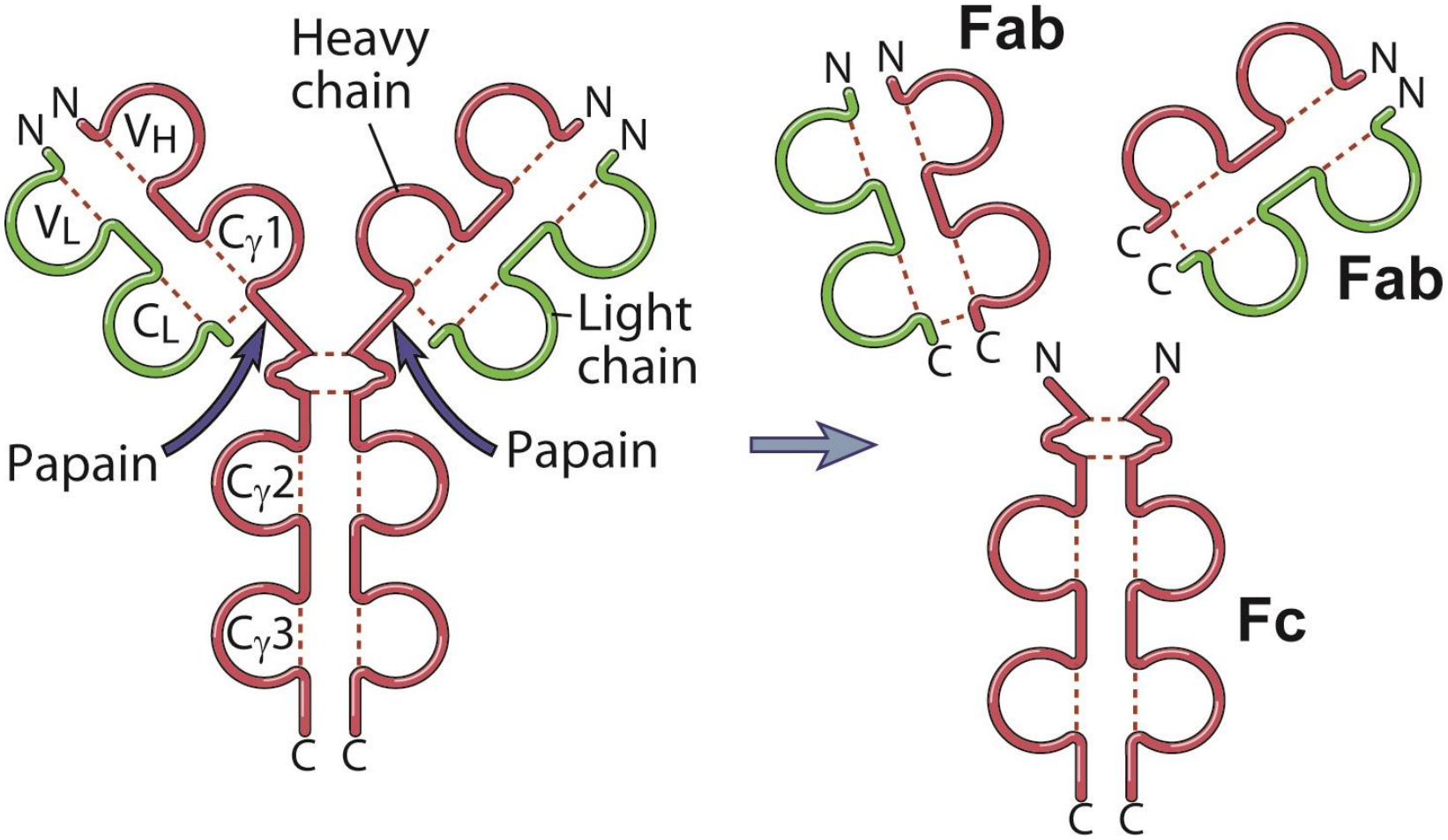

Fig. 5-3A

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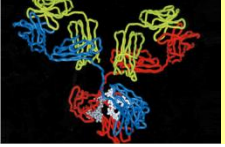

Proteolytic Fragments of IgG (2)

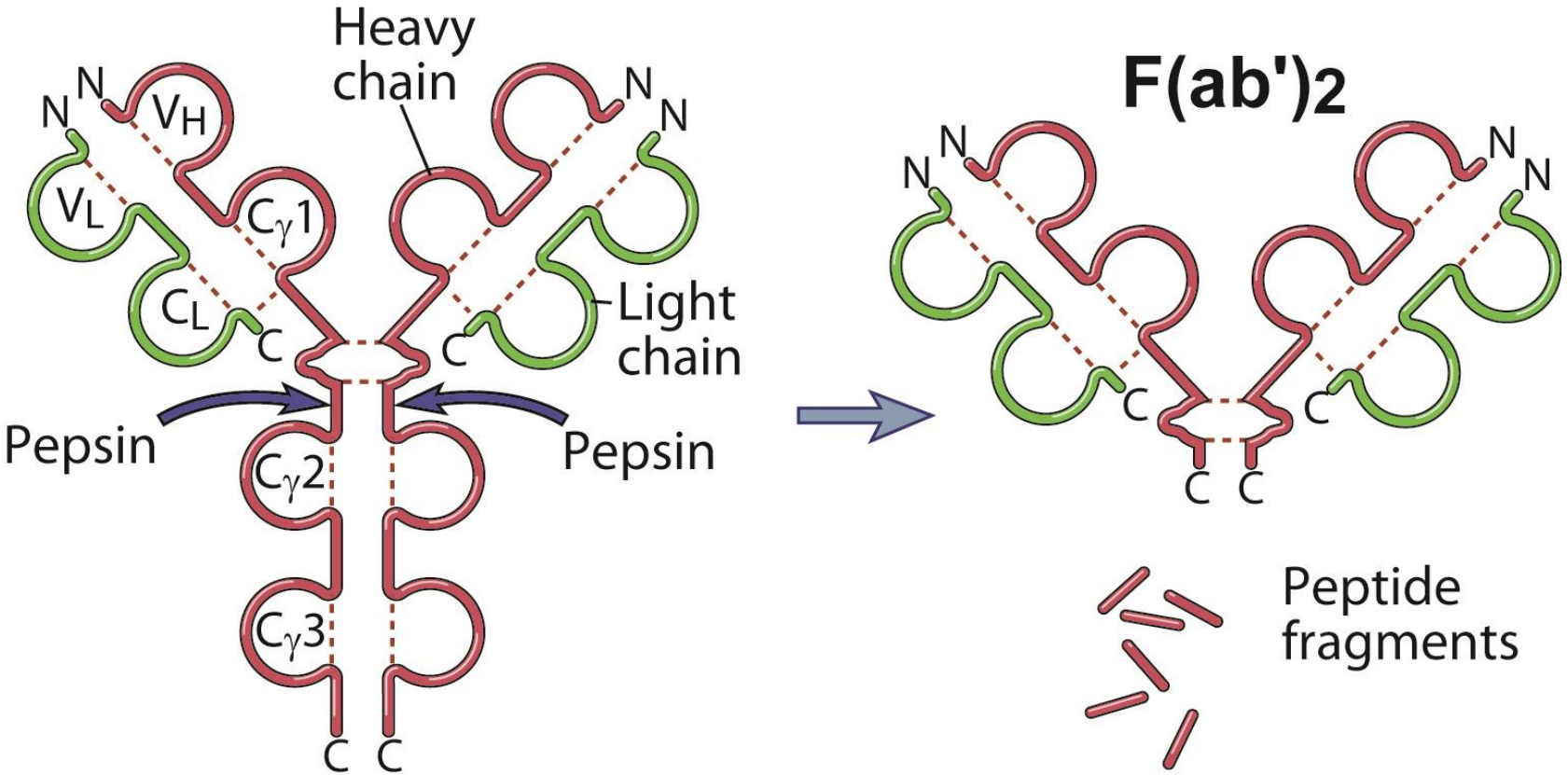

Fig. 5-3B

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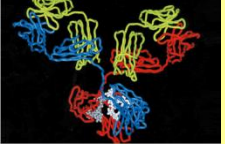
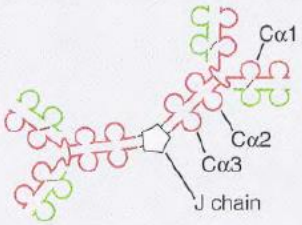
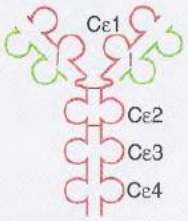
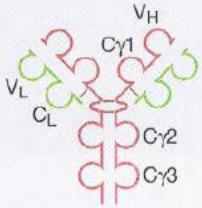
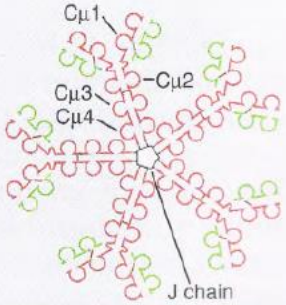


Human antibody isotypes

Isotope of Antibody	Subtypes (H Chain)	Serum Concentration (mg/mL)	Serum Half-life (days)	Secreted Form		Functions
IgA	IgA1,2 (α1 or α2)	3.5	6	IgA (dimer) Monomer, dimer, trimer		Mucosal immunity
IgD	None (δ)	Trace	3	None		Naive B cell antigen receptor
IgE	None (ε)	0.05	2	IgE Monomer		Defense against helminthic parasites, immediate hypersensitivity
IgG	IgG1-4 (γ1, γ2, γ3, or γ4)	13.5	23	IgG1 Monomer		Opsonization, complement activation, antibody-dependent cell-mediated cytotoxicity, neonatal immunity, feedback inhibition of B cells
IgM	None (μ)	1.5	5	IgM Pentamer		Naive B cell antigen receptor, complement activation

Tab. 5-2

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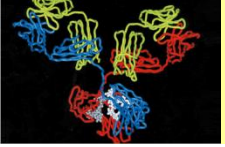

Examples of Ig Superfamily Proteins

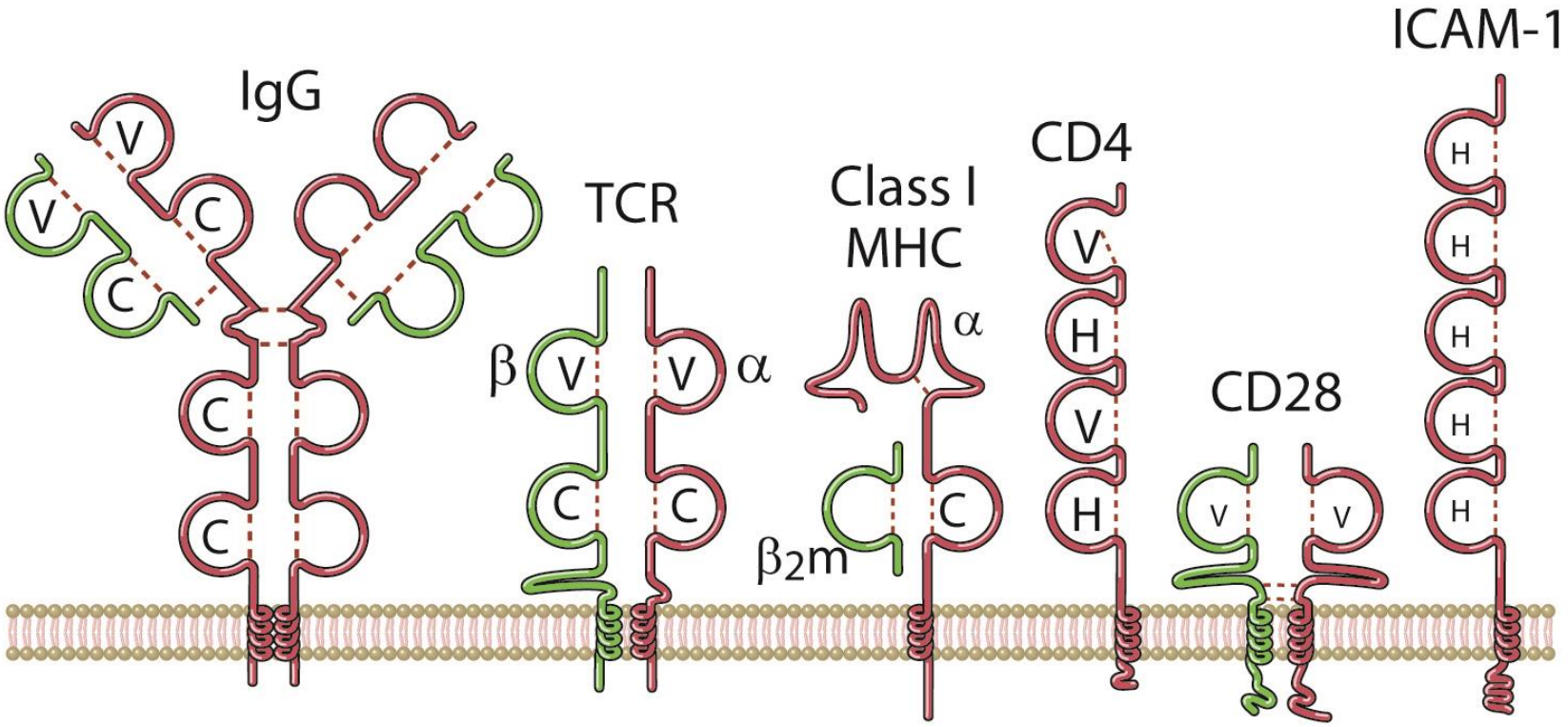

Fig. 5-4

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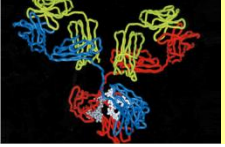
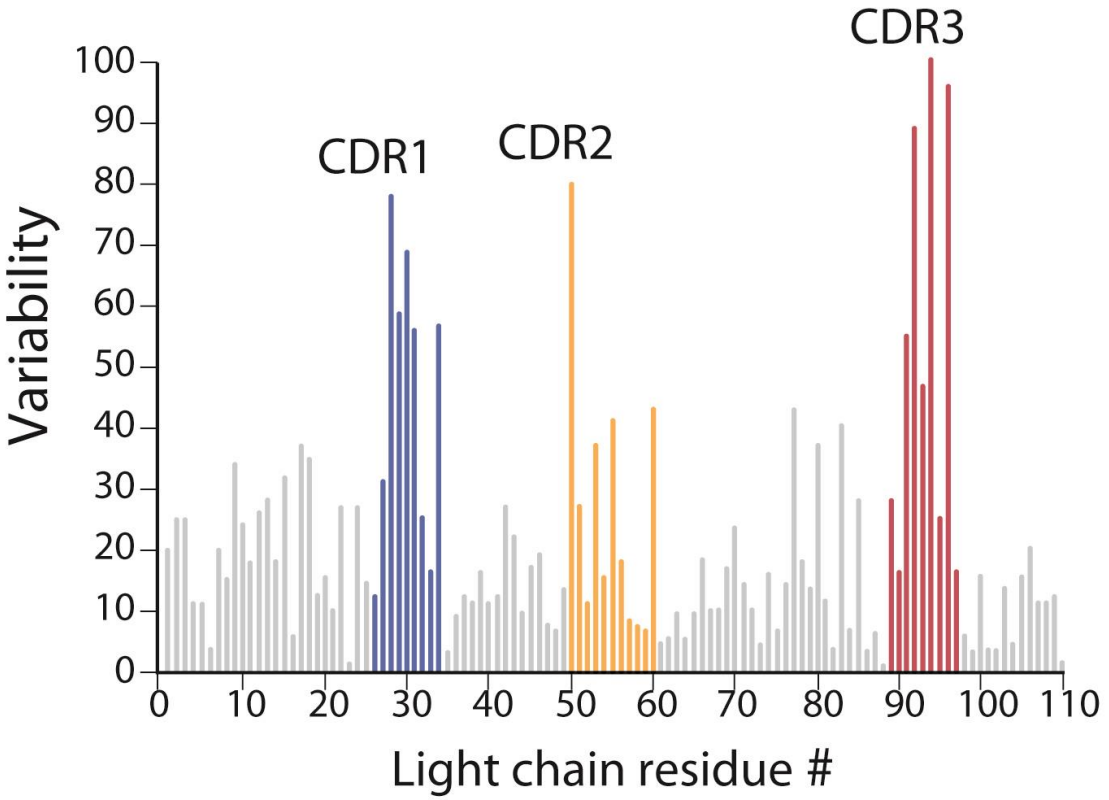


Ig Light Chain Hypervariable Regions



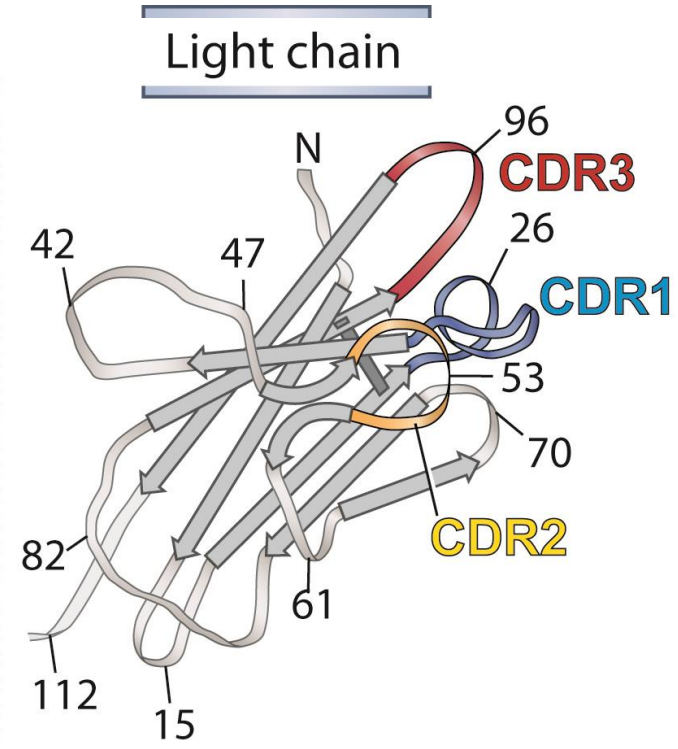


Fig. 5-5

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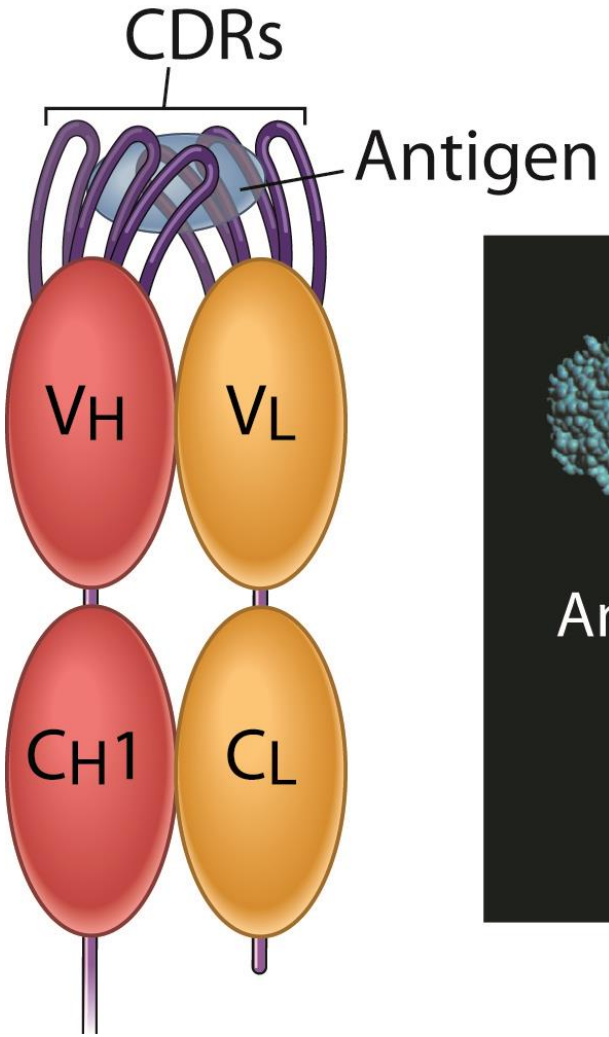
Binding of an Antigen by an Antibody



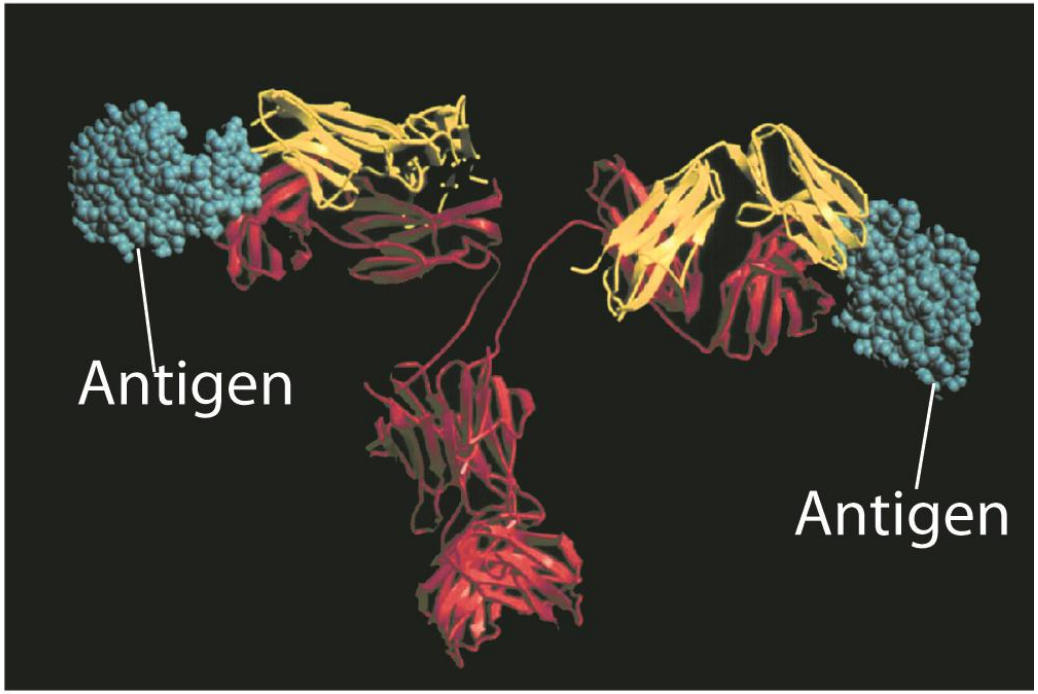


Fig. 5-6 A,B

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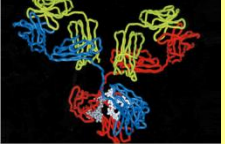

Antigen and Antibody Binding Surfaces

Antigen

Residues interacting with antibody

Ig light chain

Ig heavy chain

Residues interacting with antigen

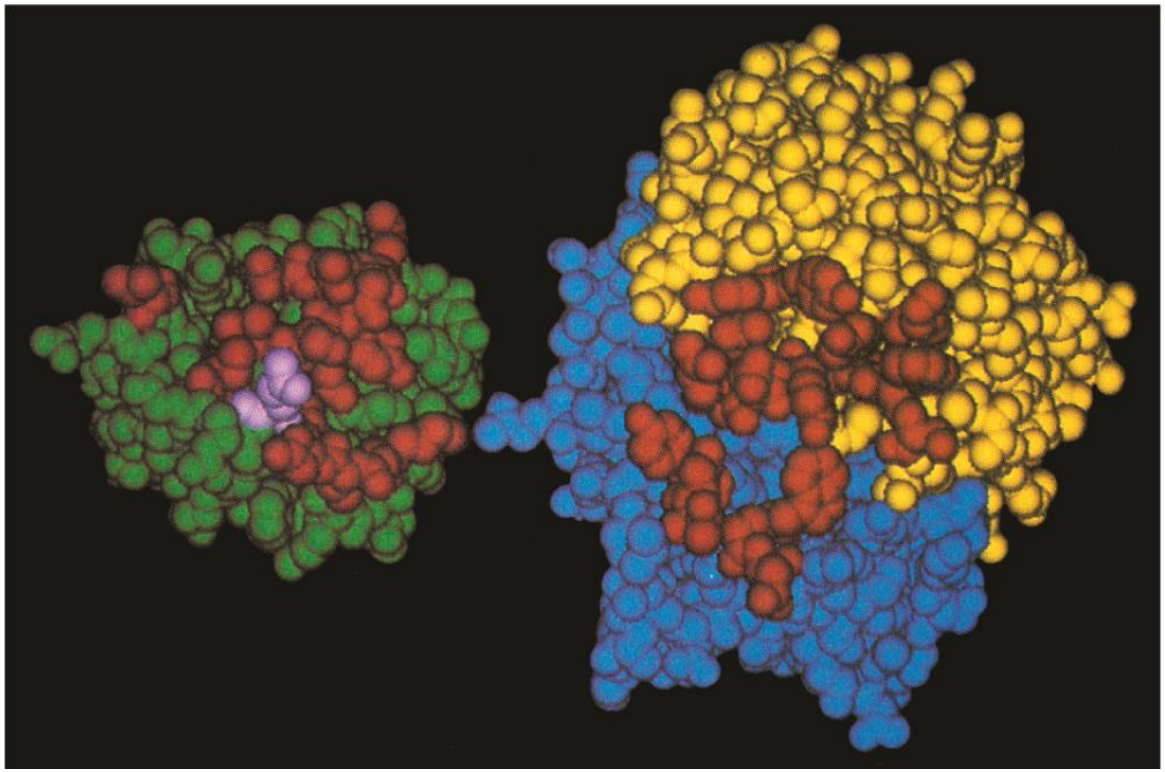

Fig. 5-6 C

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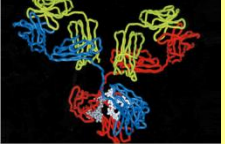

Flexibility of Antibody Molecules

Widely spaced cell surface determinants

Closely spaced cell surface determinants

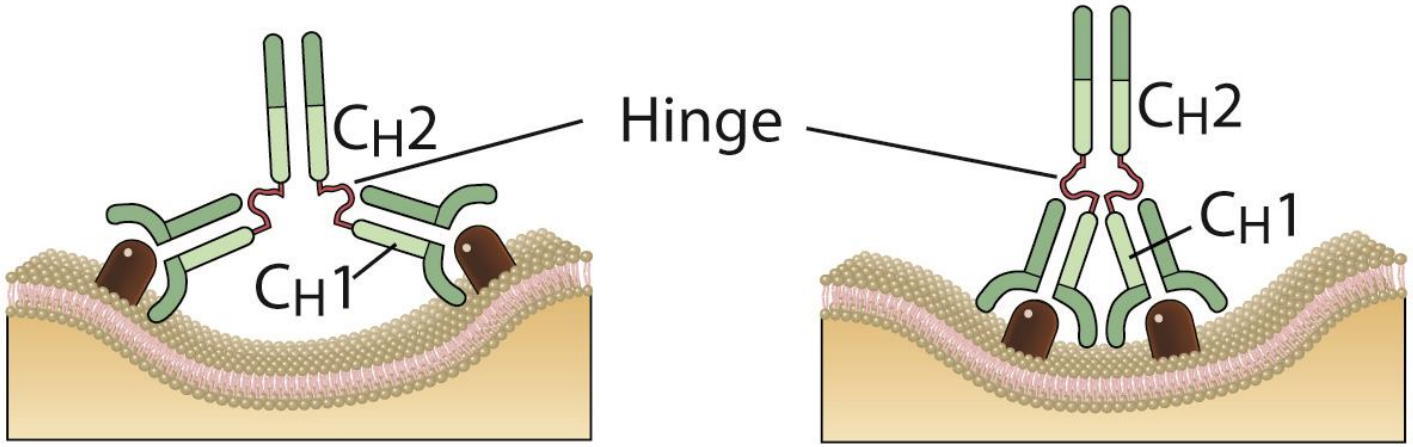

Fig. 5-7

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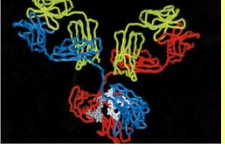

Membrane and Secreted Forms of IgG

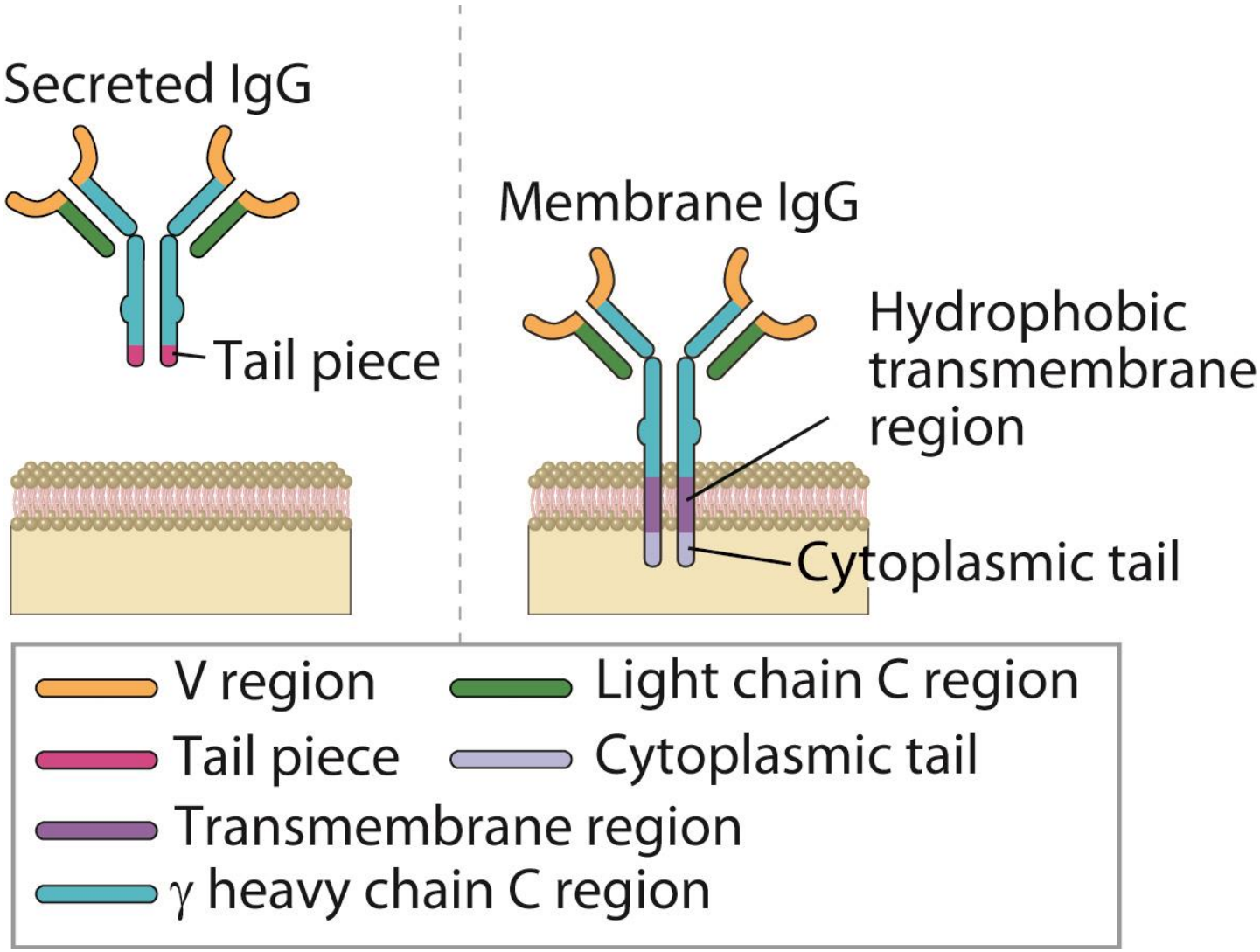

Fig. 5-8

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- Identification of phenotypic markers unique to particular cell types. The basis for the modern classification of lymphocytes and other leukocytes is the recognition of individual cell populations by specific monoclonal antibodies. These antibodies have been used to define clusters of differentiation (CD) markers for various cell types
- Immunodiagnosis. The diagnosis of many infectious and systemic diseases relies on the detection of particular antigens or antibodies in the circulation or in tissues by use of monoclonal antibodies in immunoassays Tumor detection. Tumor-specific monoclonal antibodies are used for detection of tumors by imaging techniques and by staining tissues with labeled antibodies.

- Therapy. Advances in medical research have led to the identification of cells and molecules that are involved in the pathogenesis of many diseases. Monoclonal antibodies, because of their exquisite specificity, provide a means of targeting these cells and molecules. A number of monoclonal antibodies are used therapeutically today. Some examples include antibodies against the cytokine tumor necrosis factor (TNF) used to treat rheumatoid arthritis and other inflammatory diseases, antibodies against CD20 for the treatment of B cell leukemias and for depleting B cells in certain autoimmune disorders, antibodies against the type 2 epidermal growth factor receptor to target breast cancer cells, antibodies against vascular endothelial growth factor (a cytokine that promotes angiogenesis) in patients with colon cancer, and so on

- Tumor detection. Tumor-specific monoclonal antibodies are used for detection of tumors by imaging techniques and by staining tissues with labeled antibodies.
- Functional analysis of cell surface and secreted molecules. In biologic research, monoclonal antibodies that bind to cell surface molecules and either stimulate or inhibit particular cellular functions are invaluable tools for defining the functions of surface molecules, including receptors for antigens. Monoclonal antibodies are also widely used to purify selected cell populations from complex mixtures to facilitate the study of the properties and functions of these cells.

Generation of Monoclonal Antibodies (1)

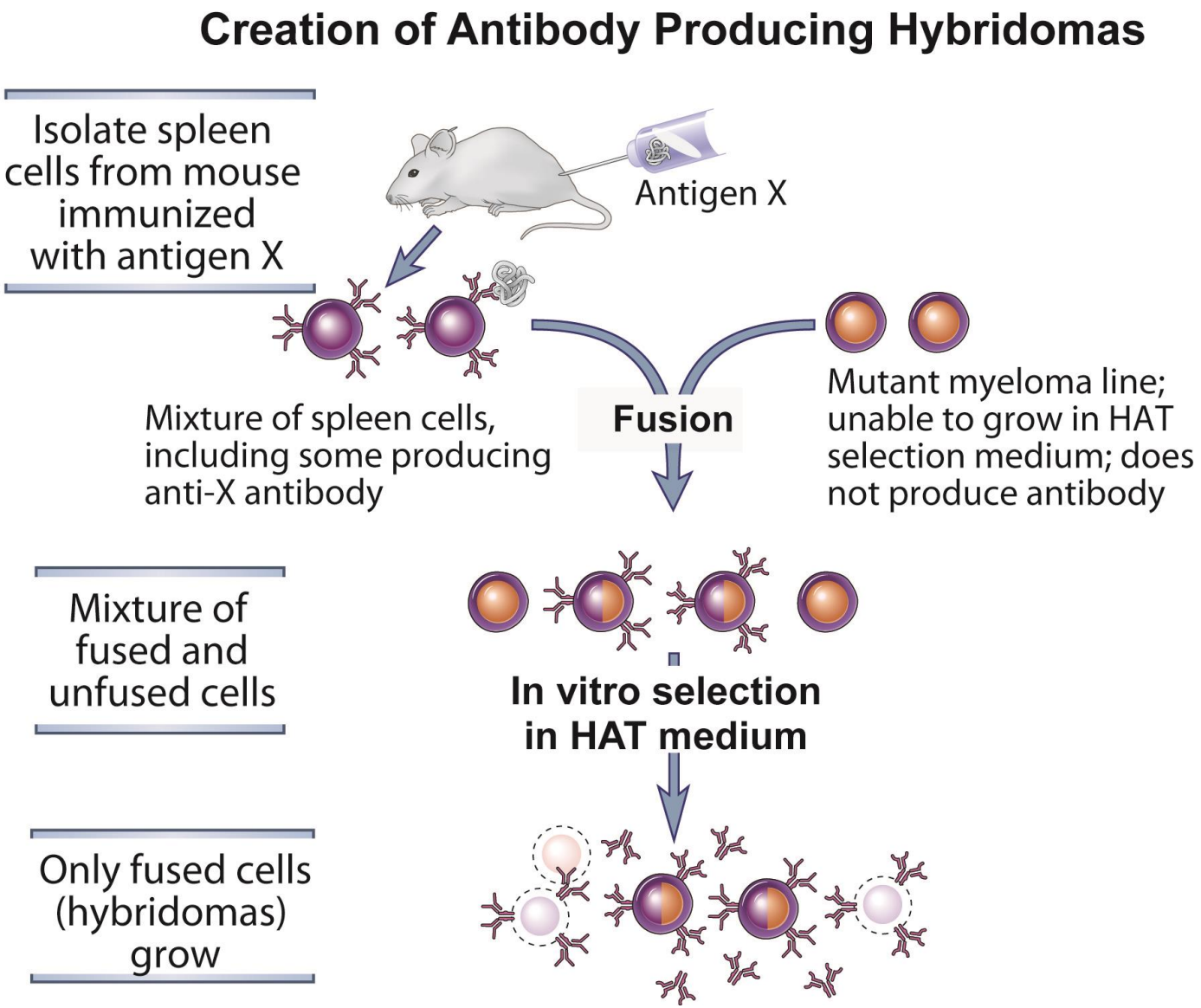

Fig. 5-9

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Generation of Monoclonal Antibodies (2)

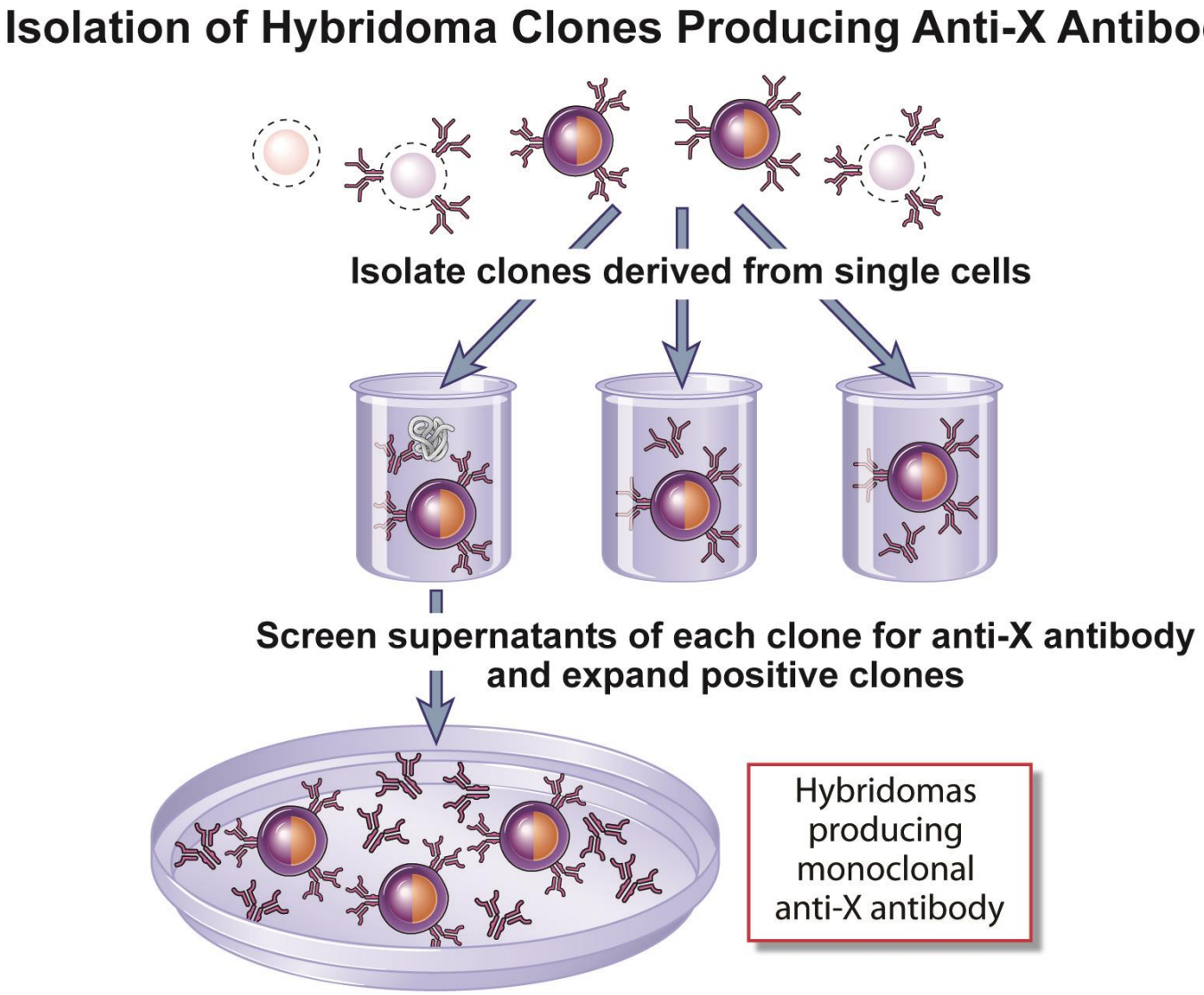

Fig. 5-9

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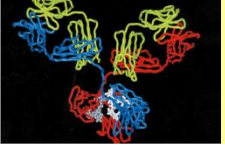
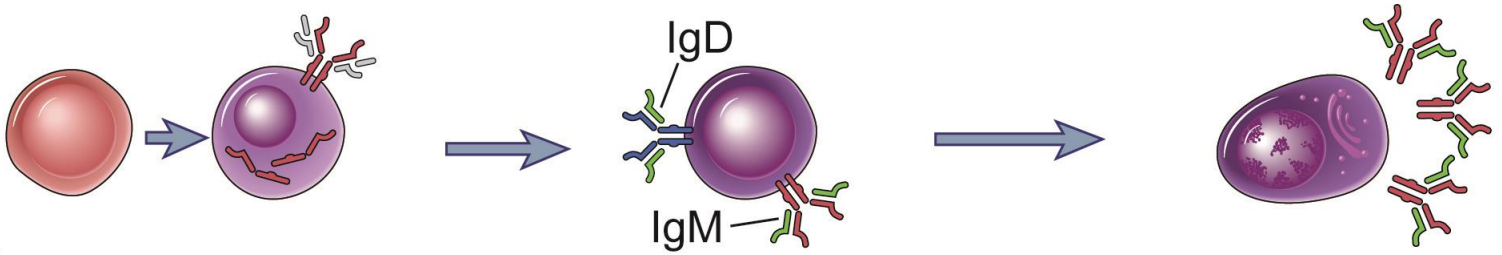


Ig Expression During B Cell Maturation



Stage of maturation	Stem cell	Pre-B cell	Immature B cell	Mature B cell	Activated B cell	Antibody-secreting cell
Pattern of Ig production	None	Cytoplasmic μ heavy chain and pre-B receptor	Membrane IgM	Membrane IgM, IgD	Low rate Ig secretion; heavy chain isotype switching; affinity maturation	High rate Ig secretion; reduced membrane Ig

Fig. 5-10

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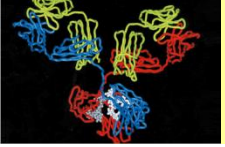

FcRn Prolongs Half-Life of IgG Molecules

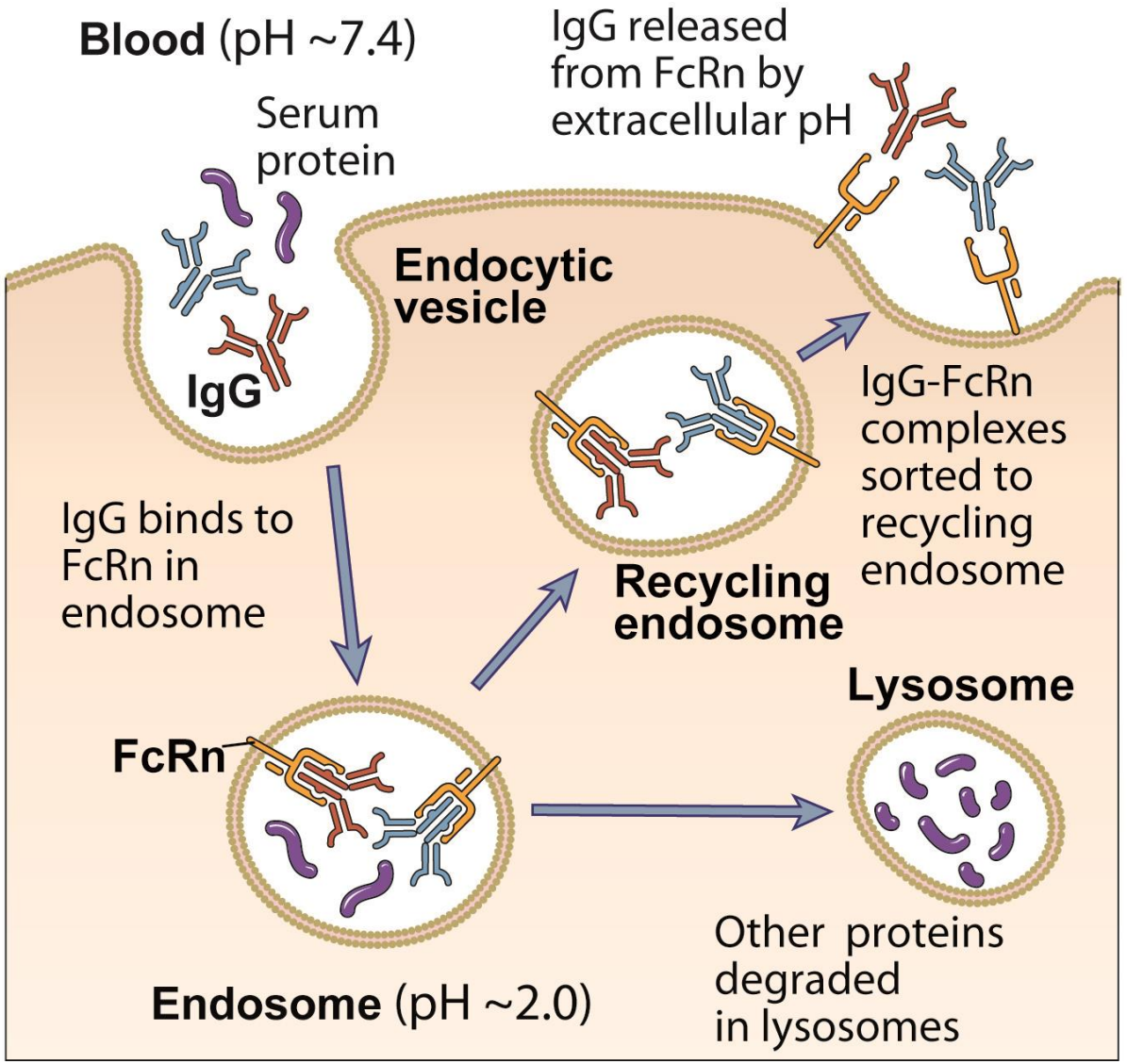

Fig. 5-11

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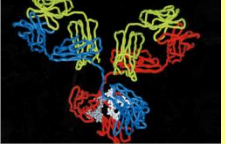

Types of Antigenic Determinants (1)

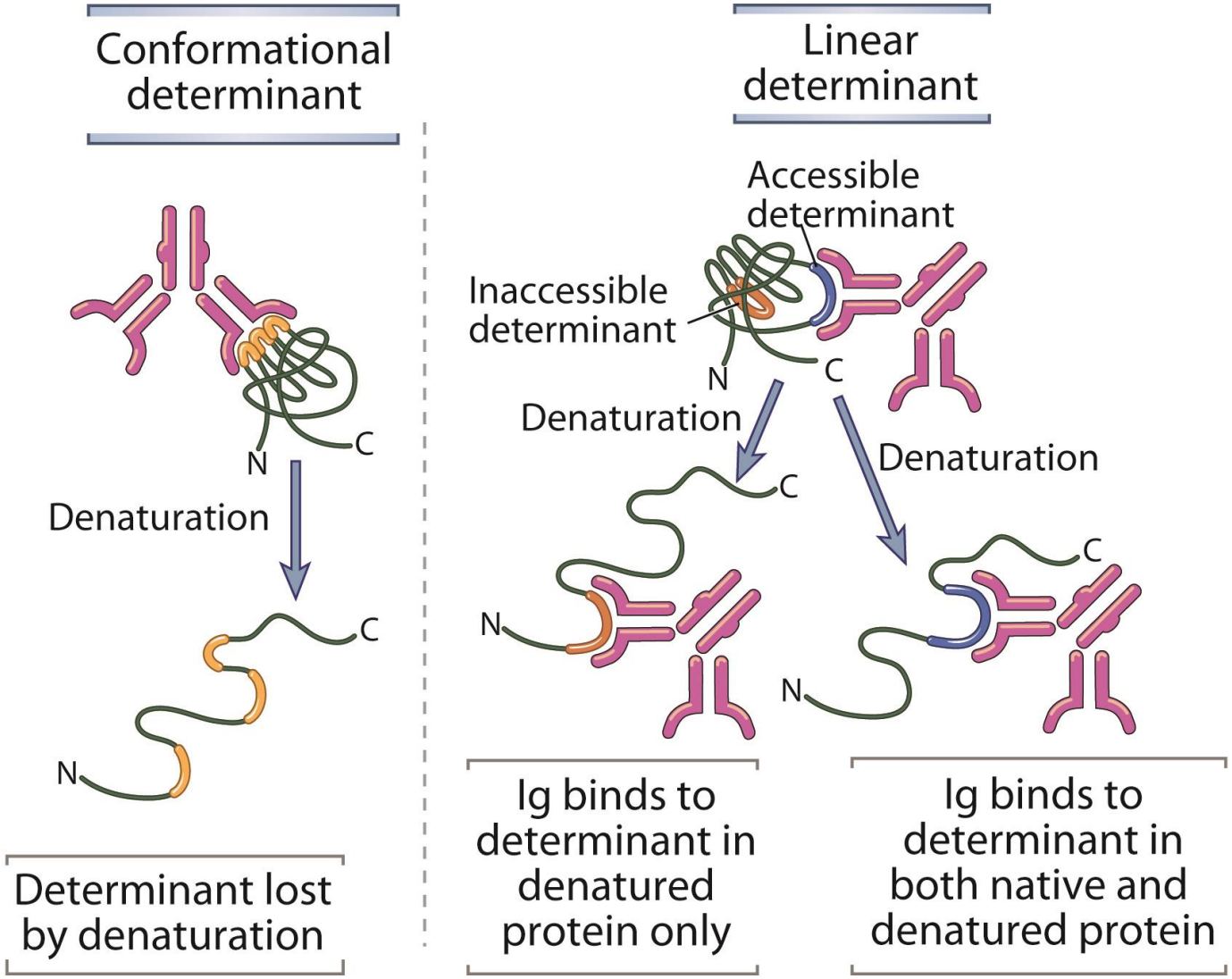

Fig. 5-12 A,B

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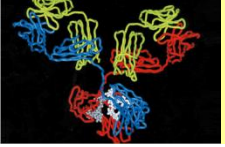

Types of Antigenic Determinants (2)

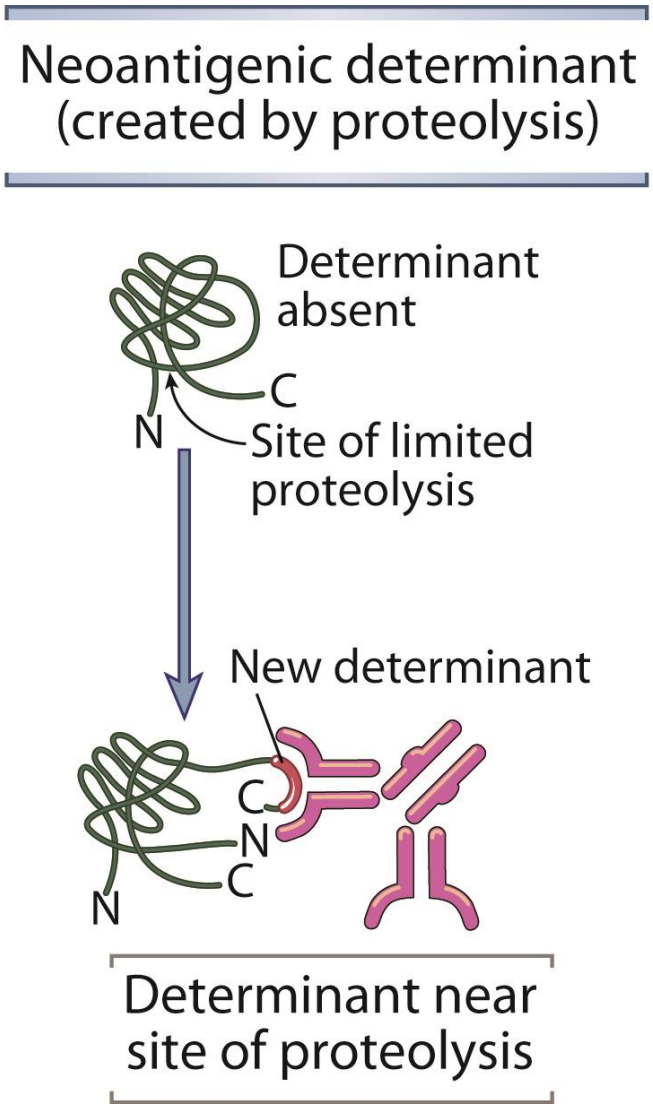

Fig. 5-12 C

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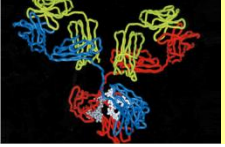
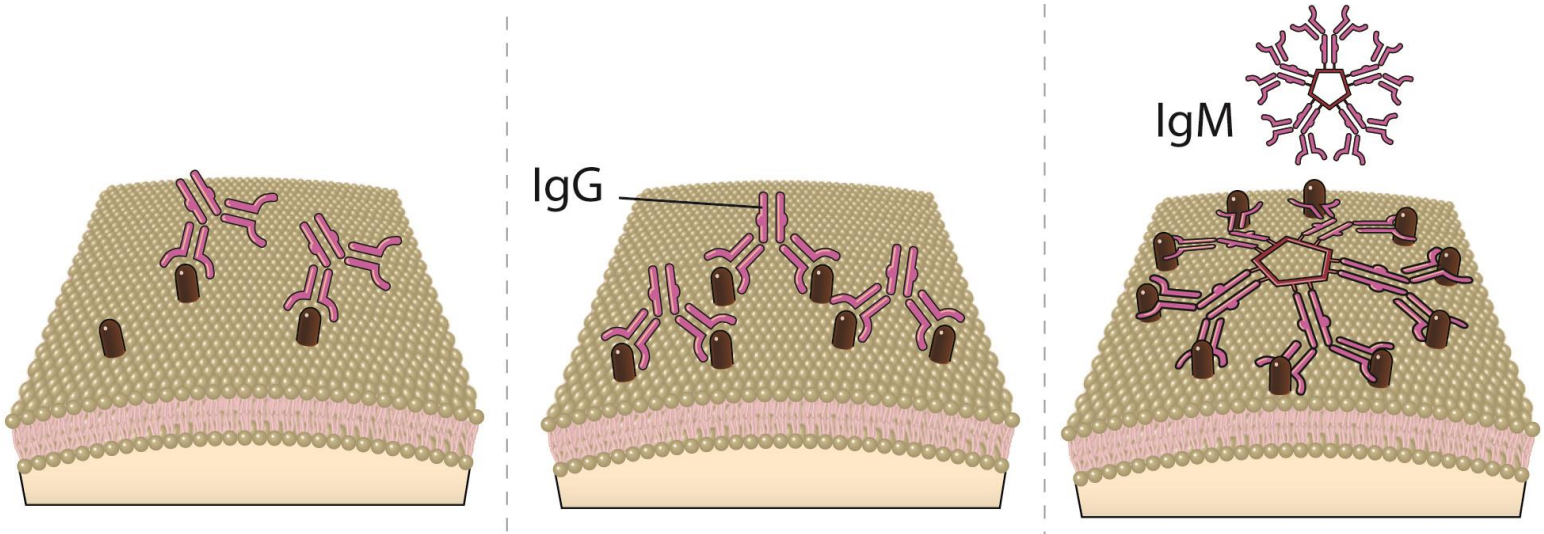


Valency and Avidity of Antibodies



Valency of interaction	Monovalent	Bivalent	Polyvalent
Avidity of interaction	Low	High	Very high

Fig. 5-13

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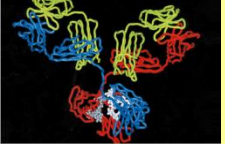
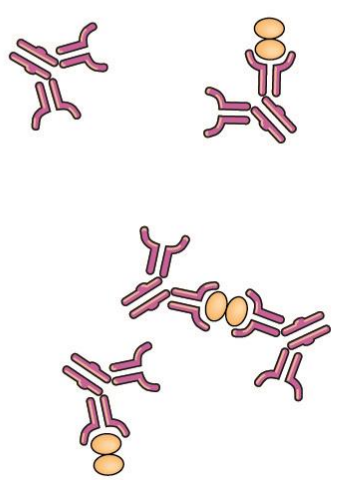


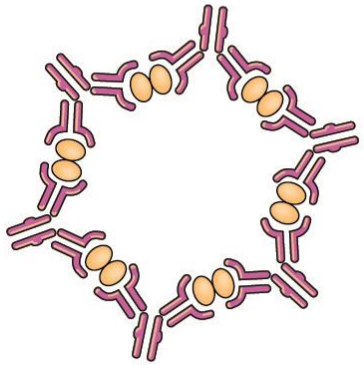
Antigen-Antibody Complexes

Zone of antibody excess (small complexes)

Zone of equivalence (large complexes)

Zone of antigen excess (small complexes)





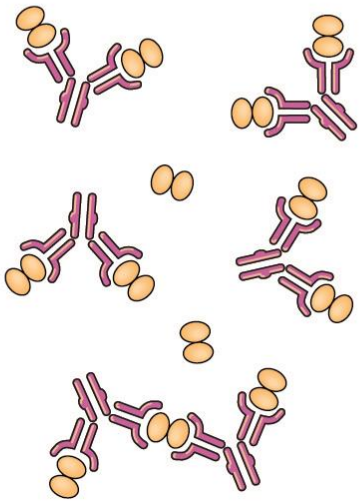


Fig. 5-14

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Changes in Ig During Humoral Responses

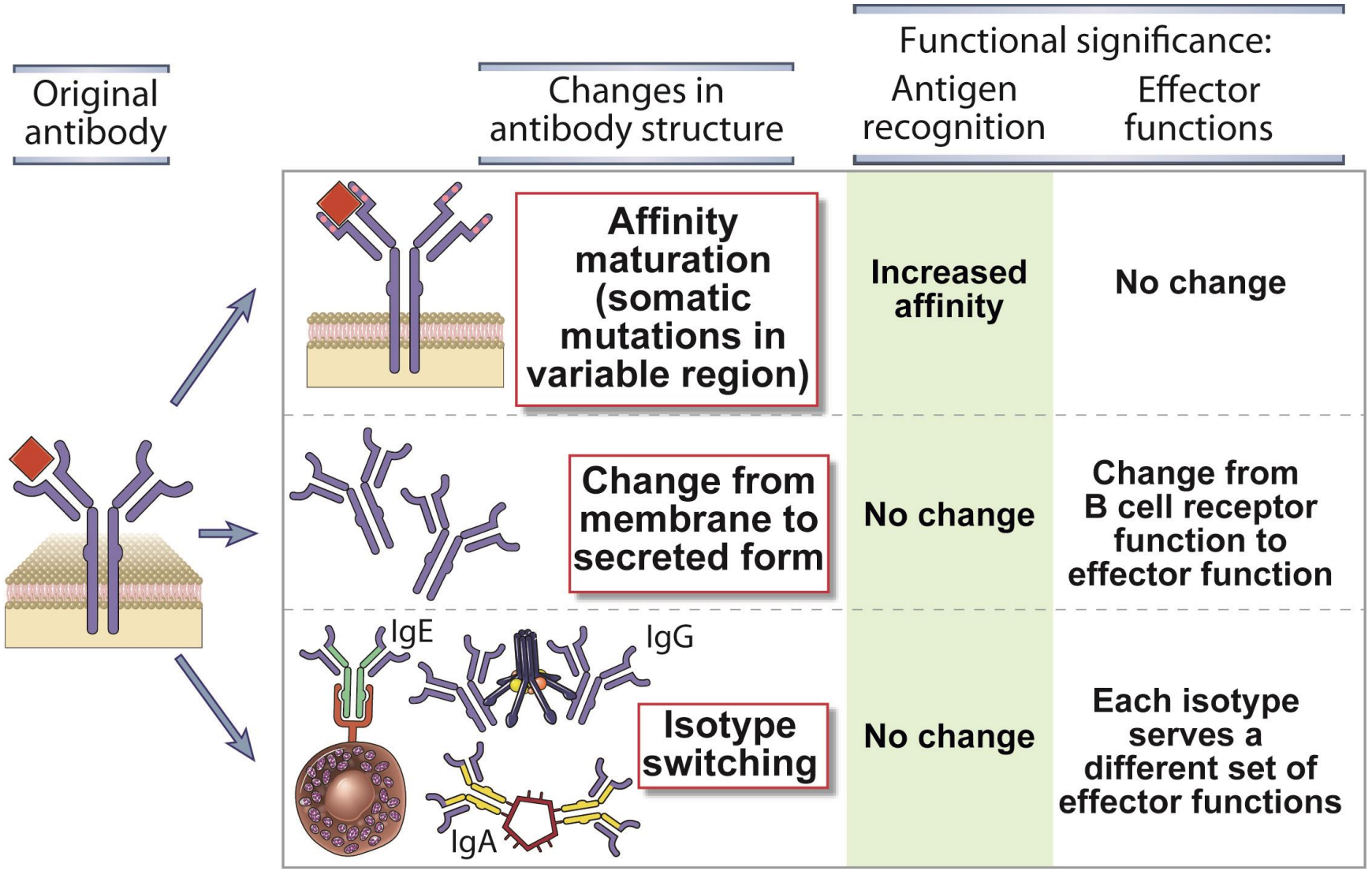

Fig. 5-15

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