

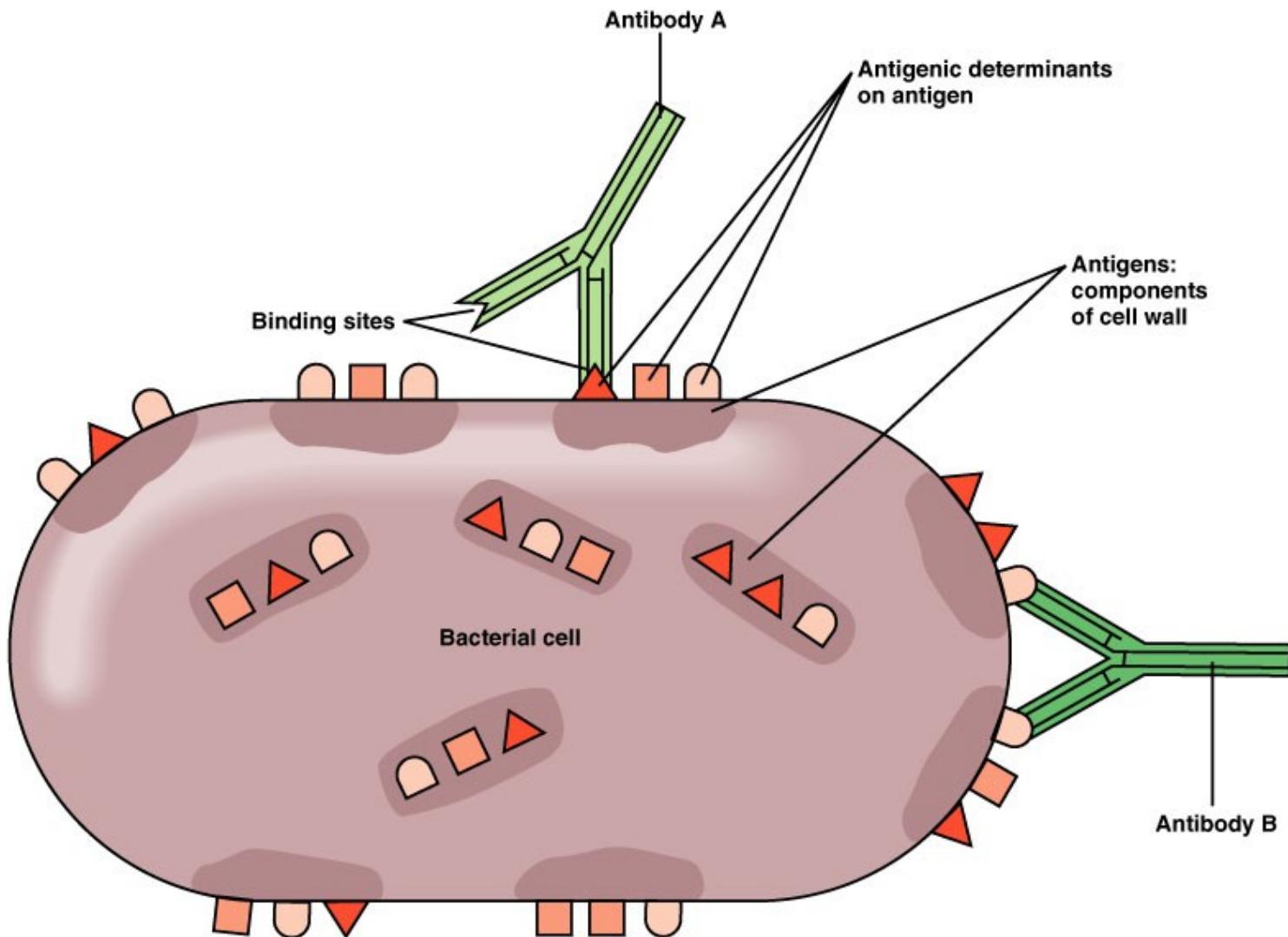
Imunoglobulins – structure and function

Production of immunoglobulins

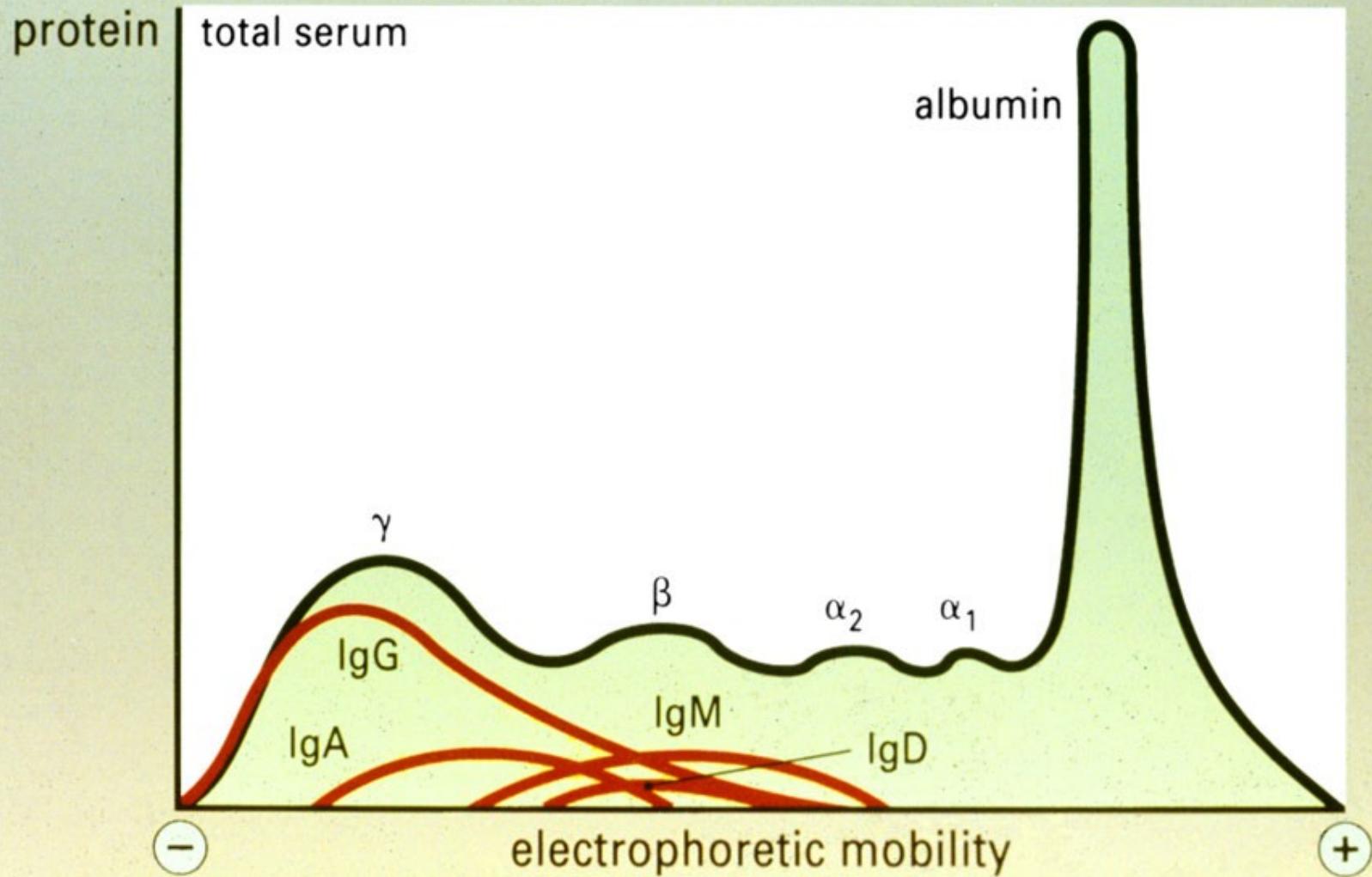
Genetic determination of immunoglobulin production

Clonal selection theory

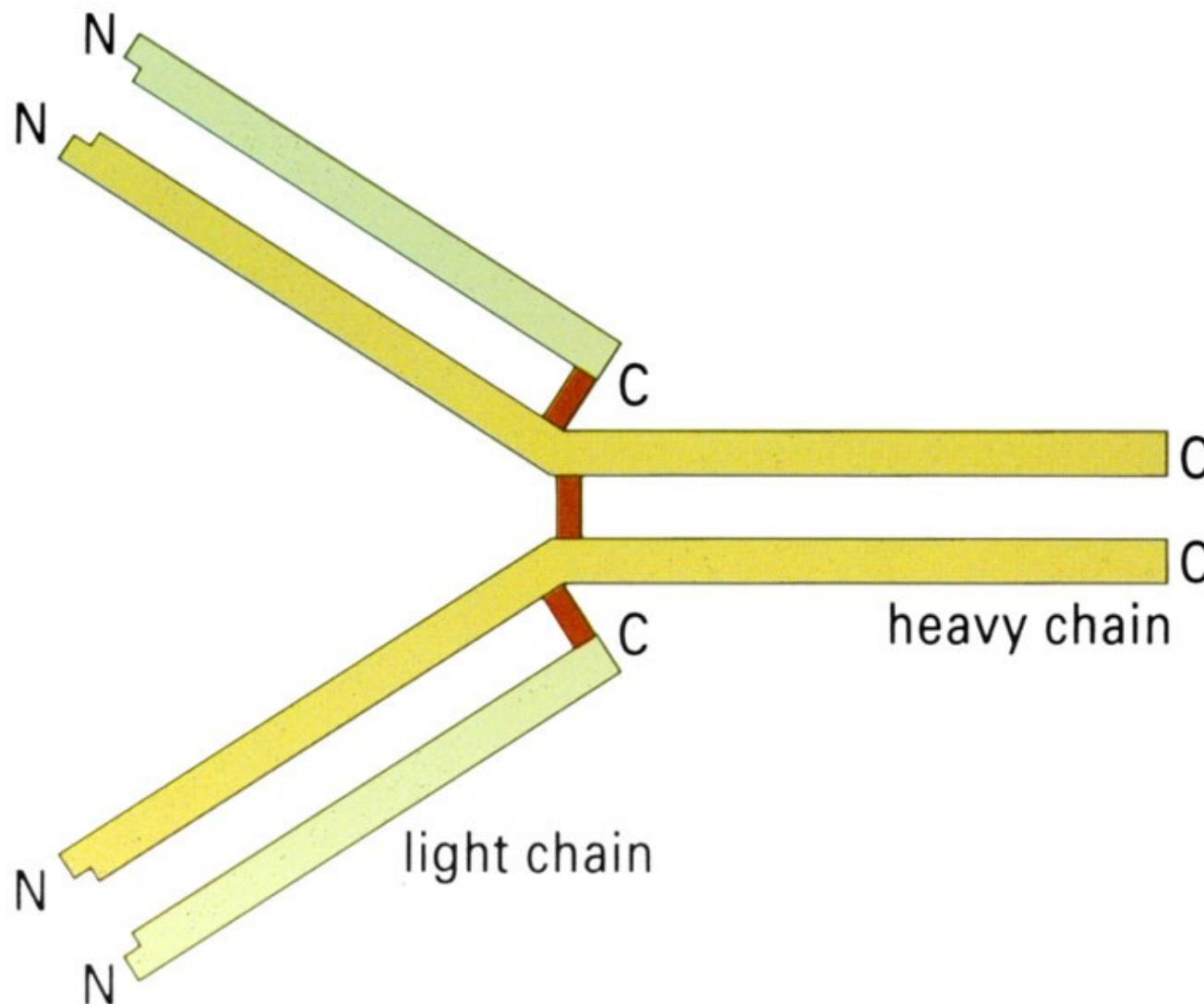
Antigen and epitope



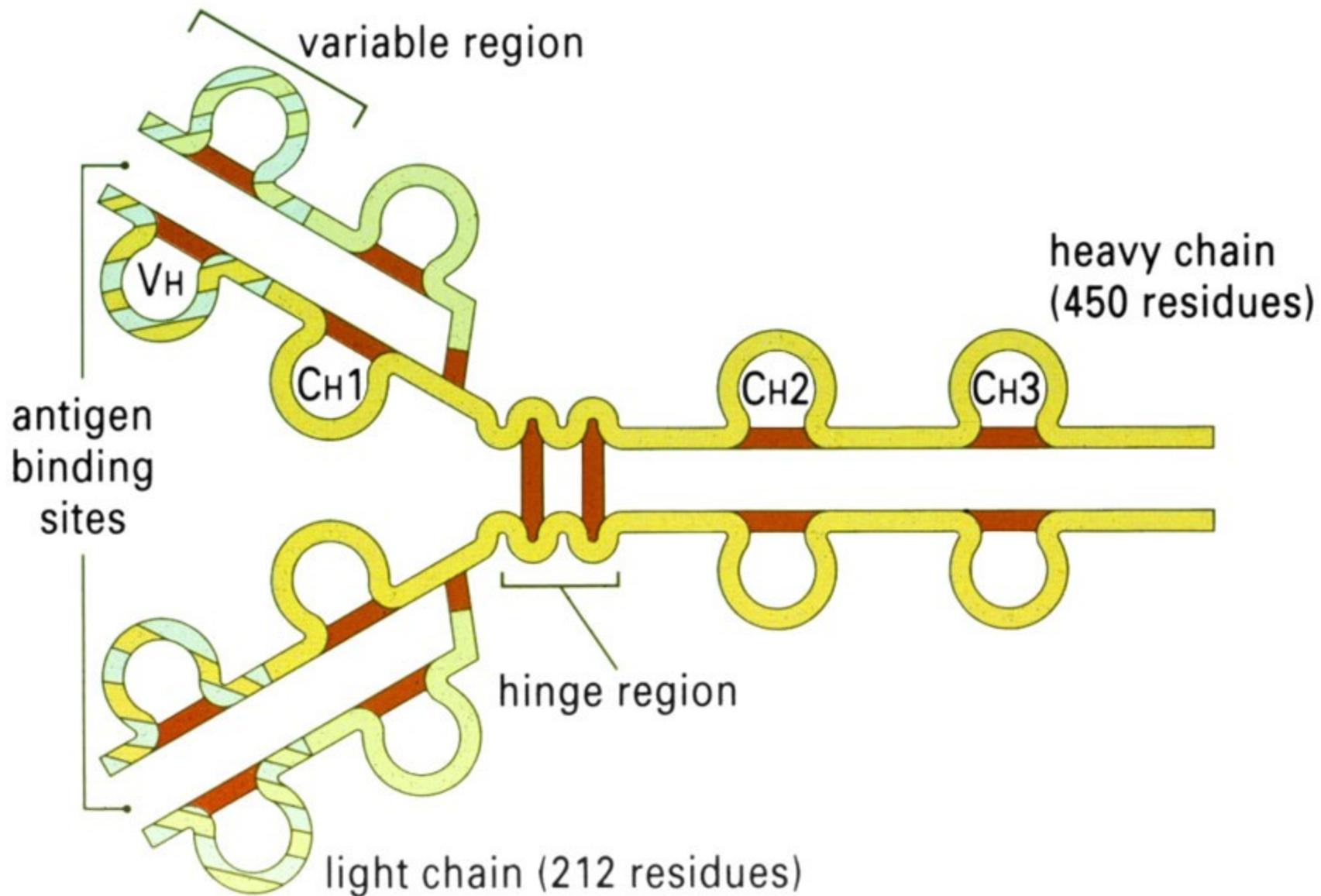
Distribution of the major human immunoglobulins



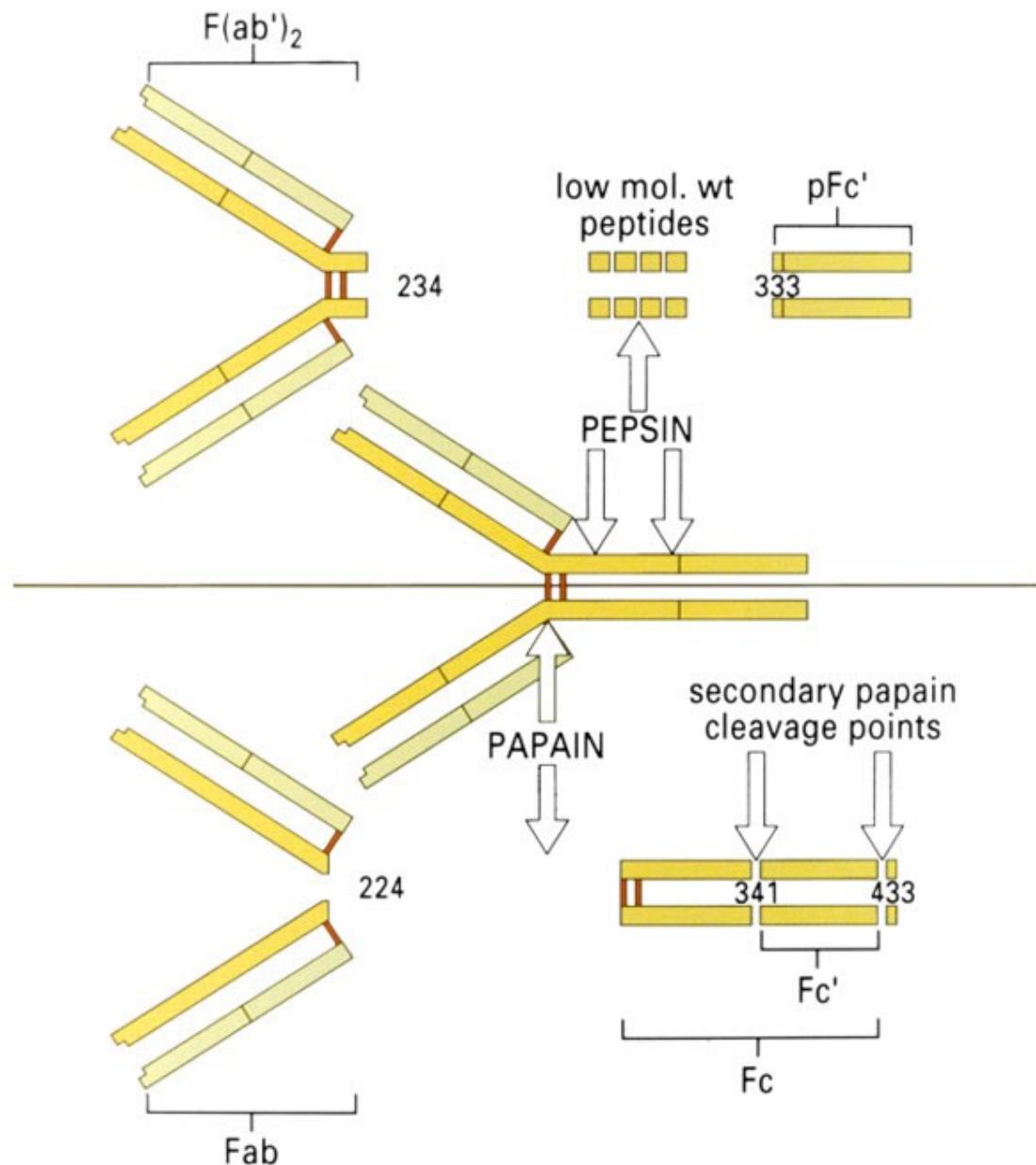
The basic chain structure of immunoglobulins

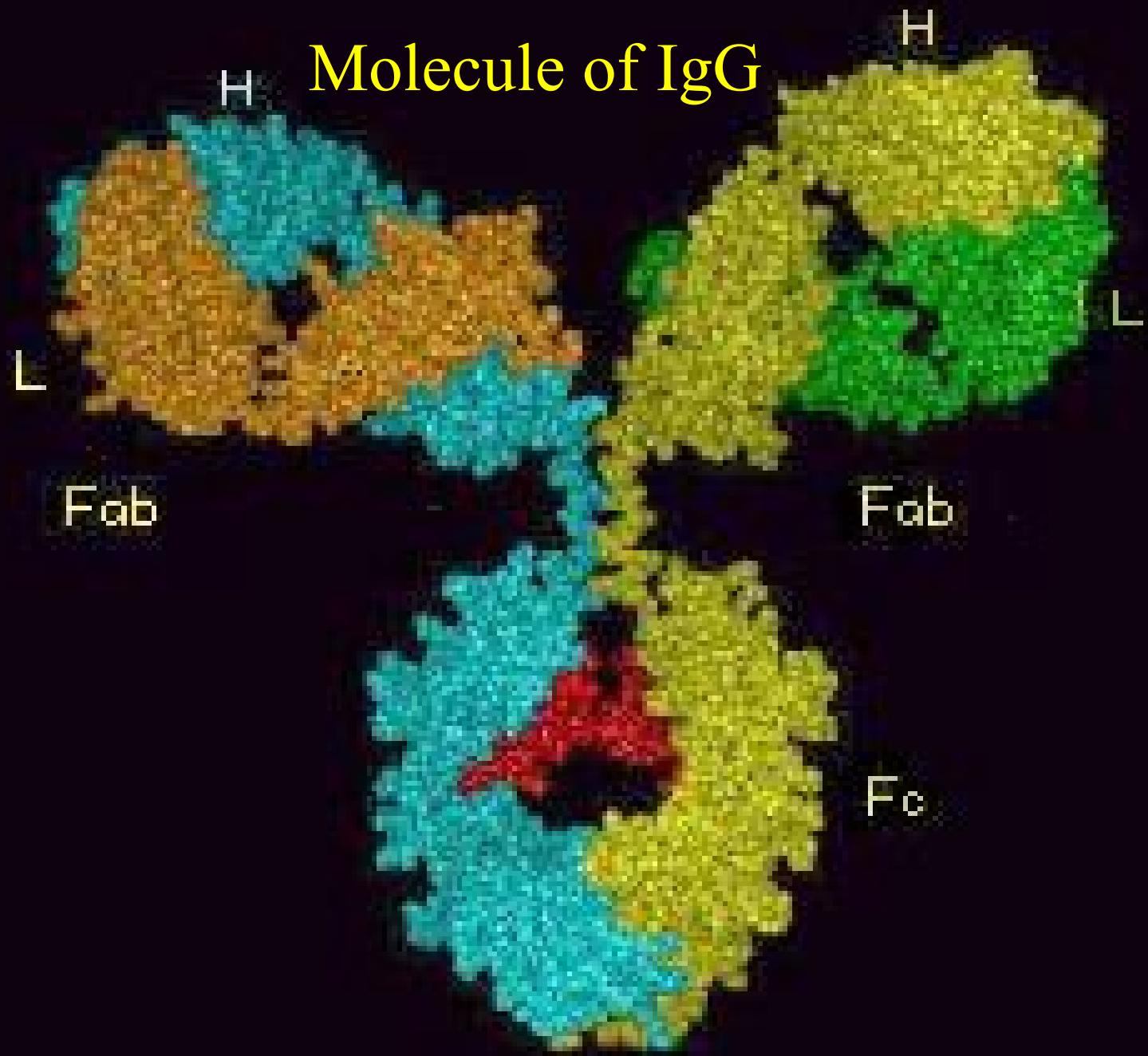


The basic structure of IgG1

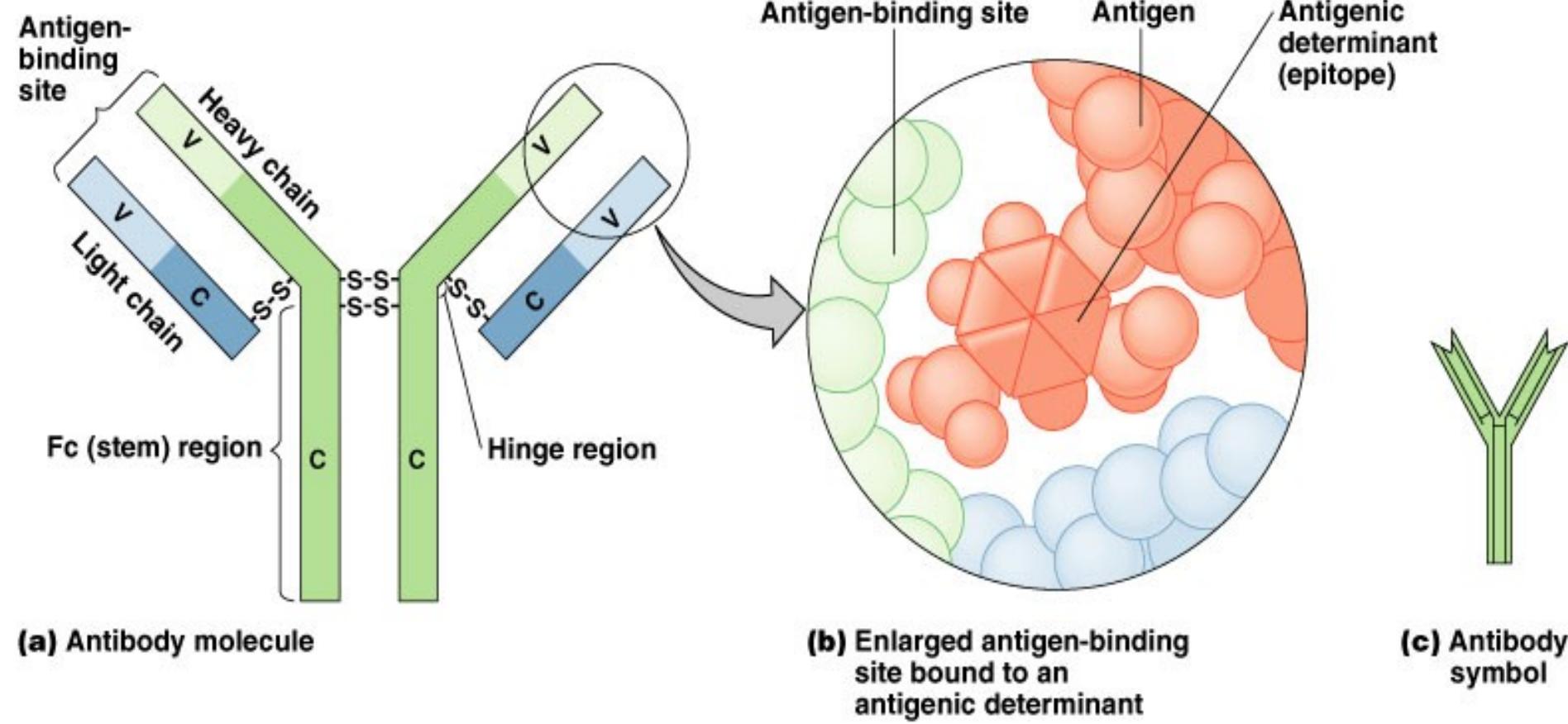


Enzymic cleavage of human IgG1



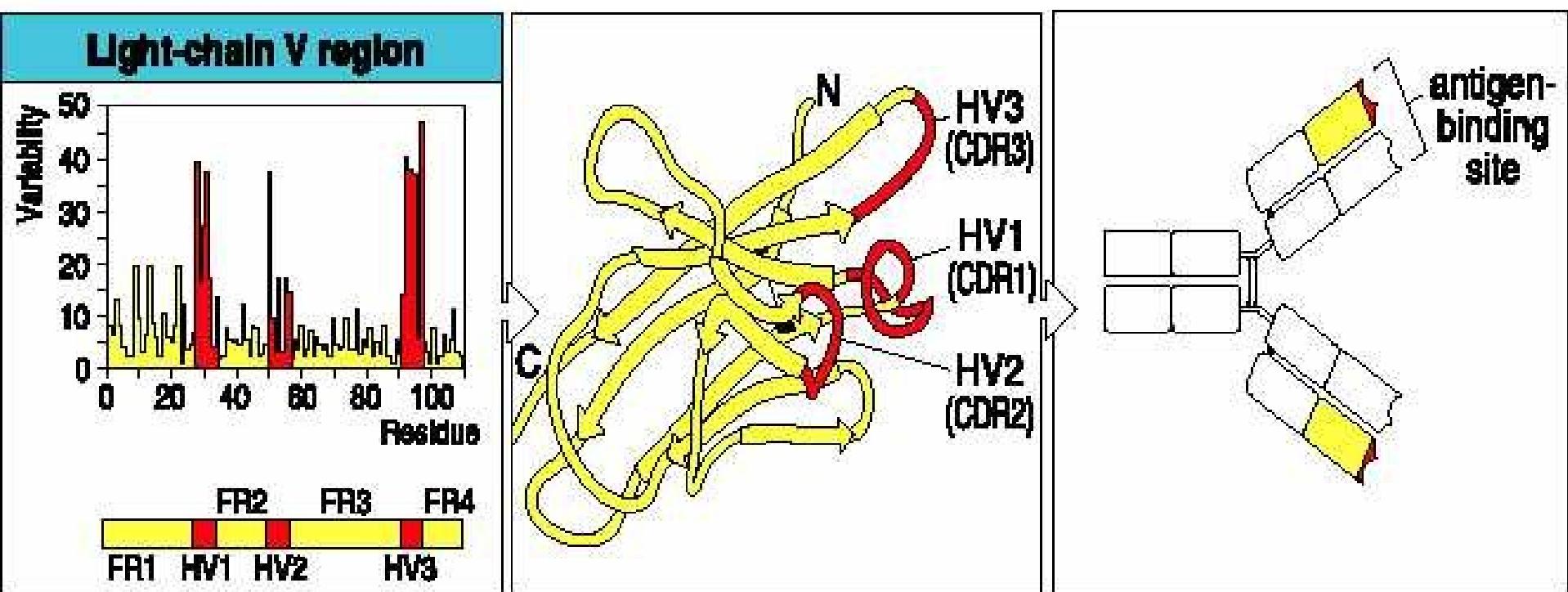


Hypervariable region of immunoglobulin molecule binds epitope of the antigen

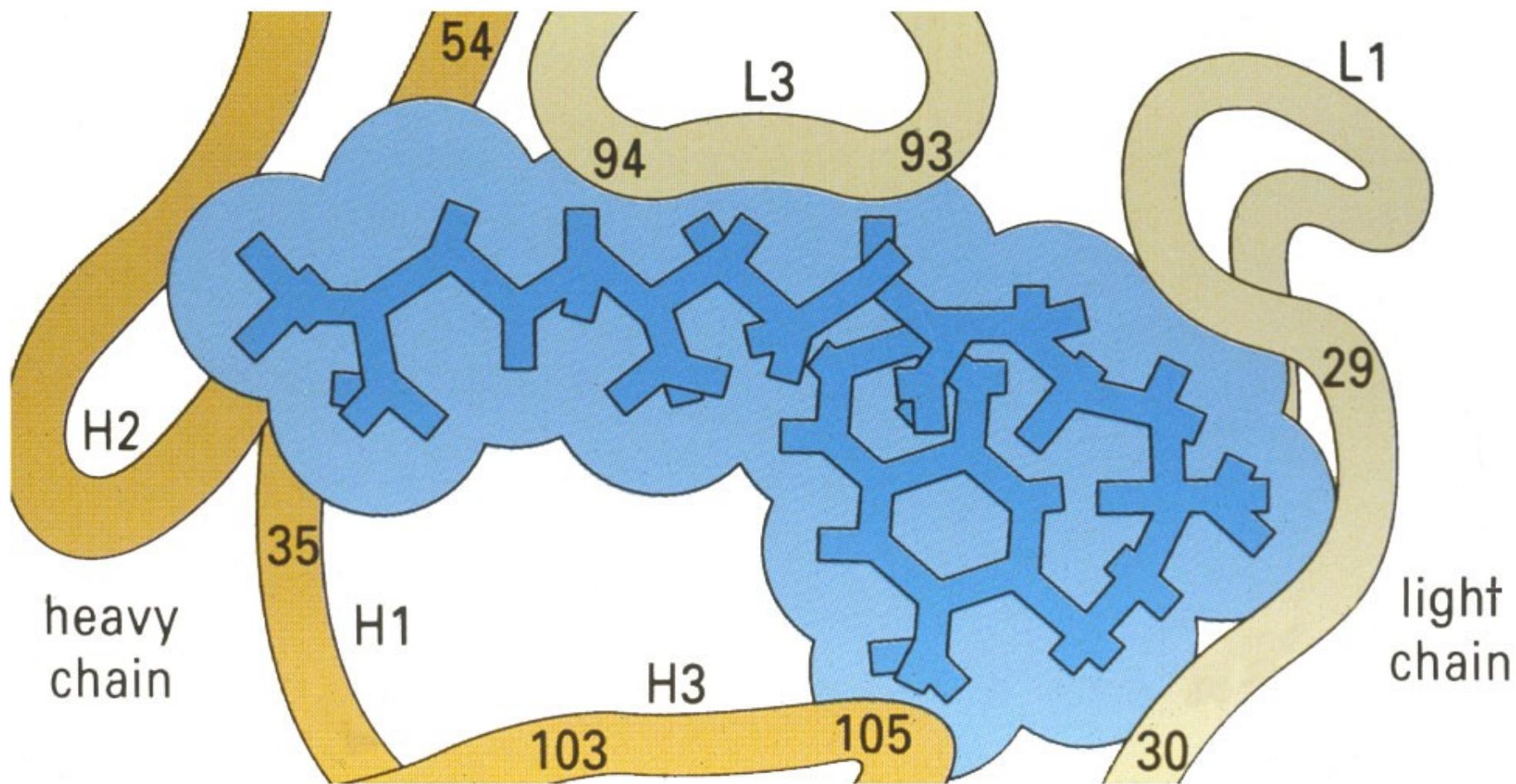


Variable region of immunoglobulin molecule

Figure 2.7



The antibody combining site



VDJ Recombination

Germline configuration V segments D segments J segments Constant region exons



D to J recombination



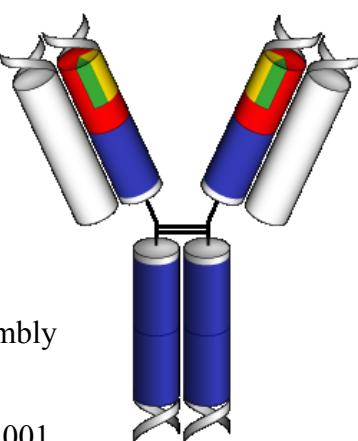
V to DJ recombination



transcription, splicing

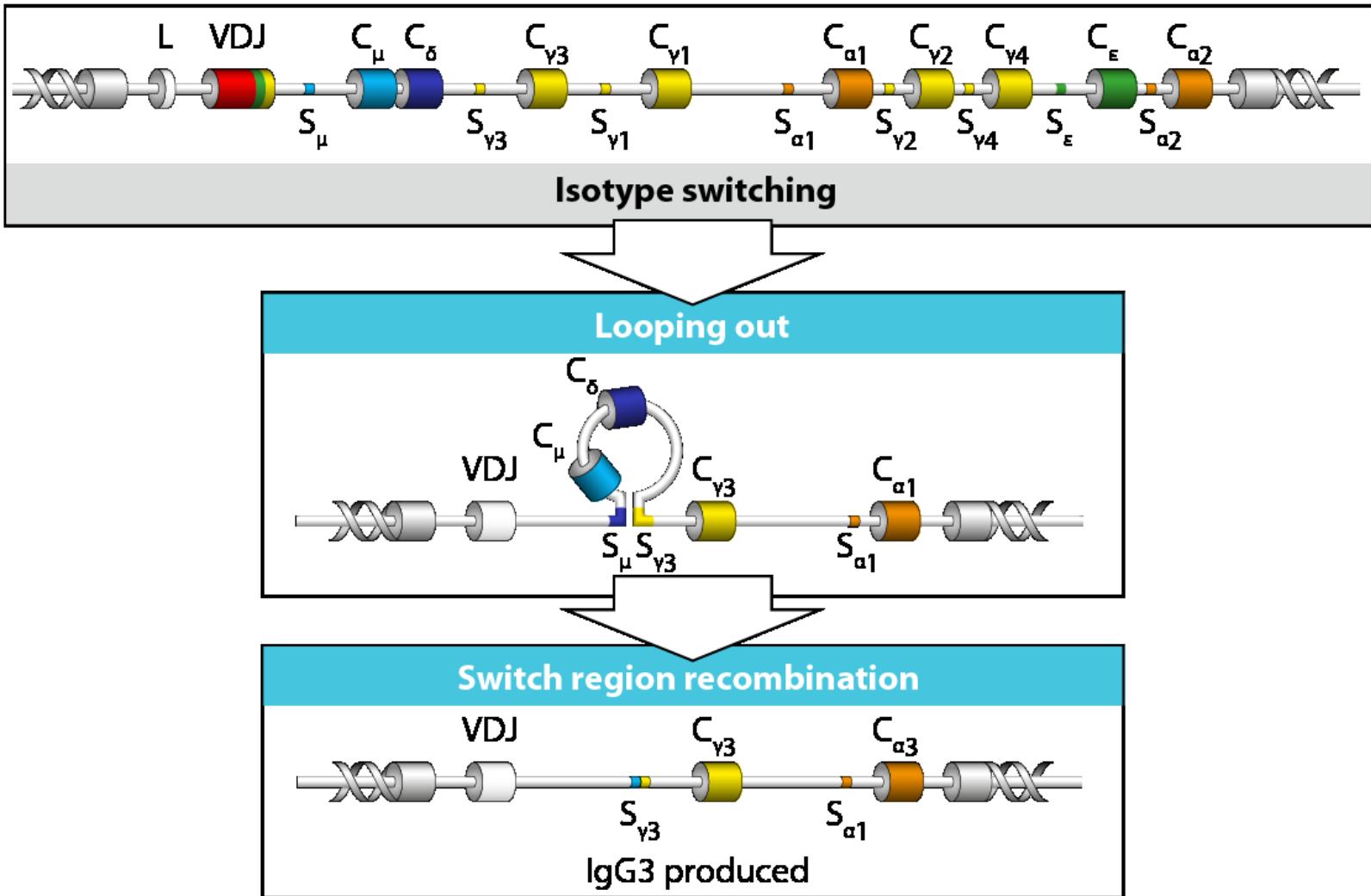


Assembly



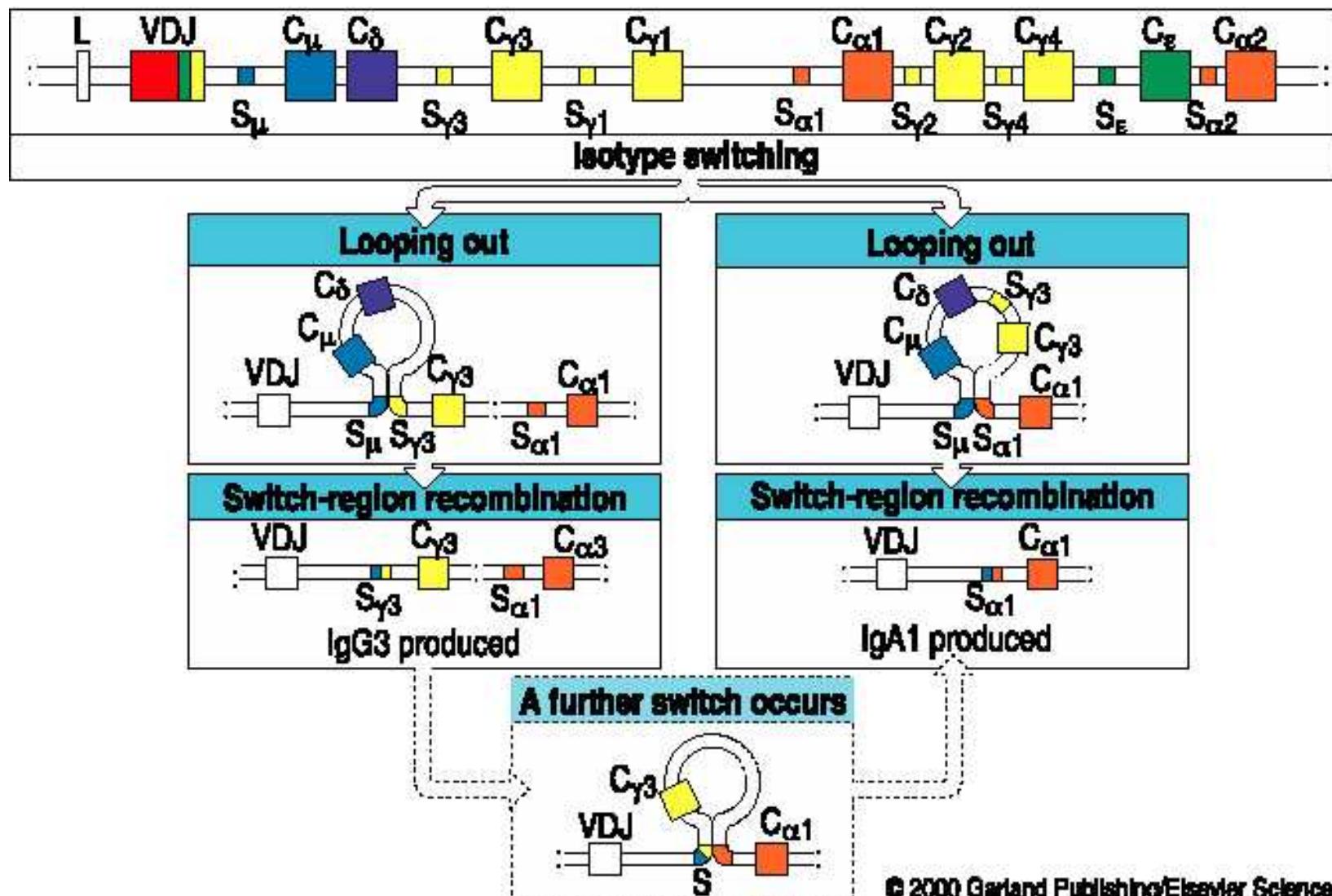
Adapted from Janeway 2001

Isotype switching



Isotype switching

Figure 2.26

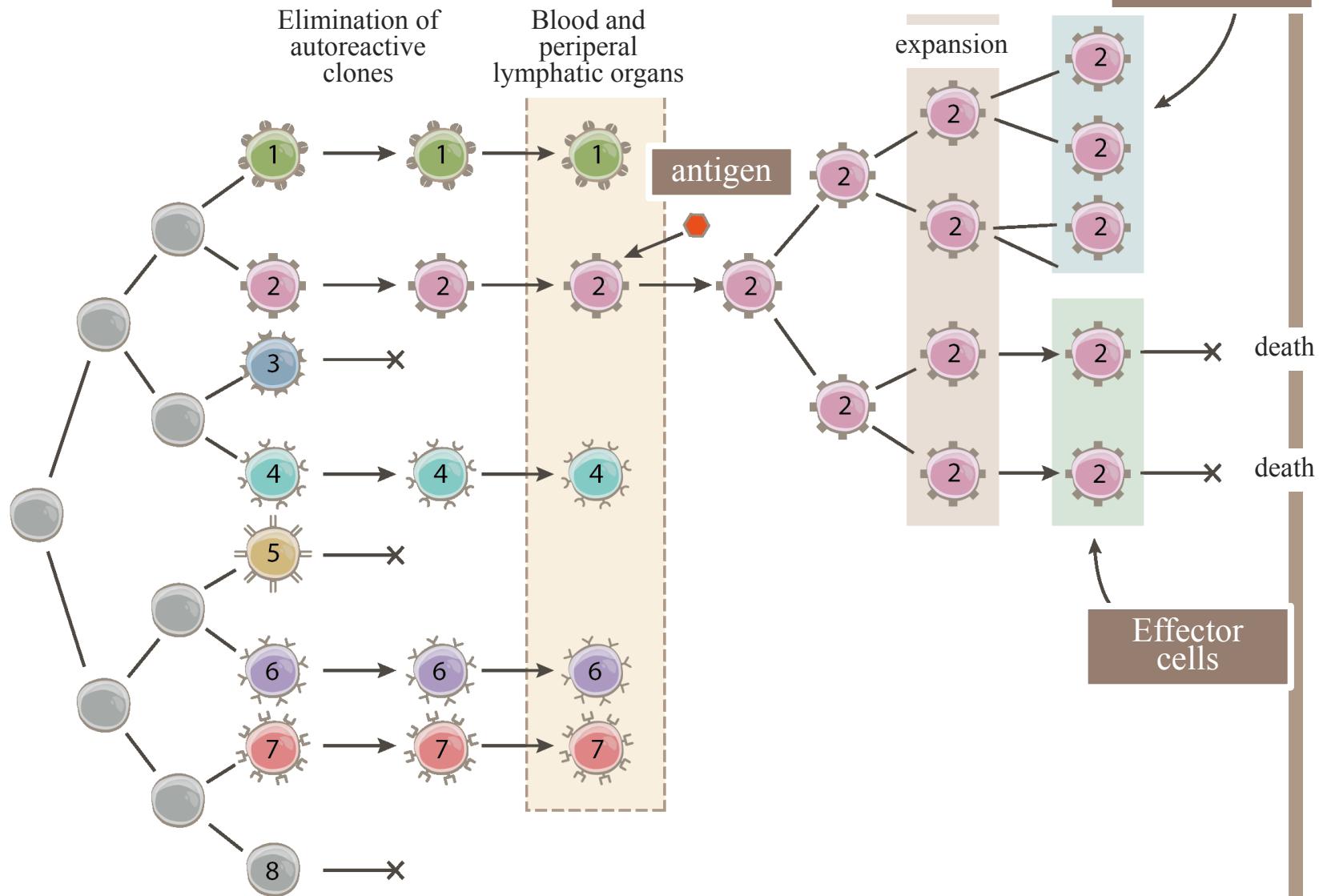


Clonal selection theory

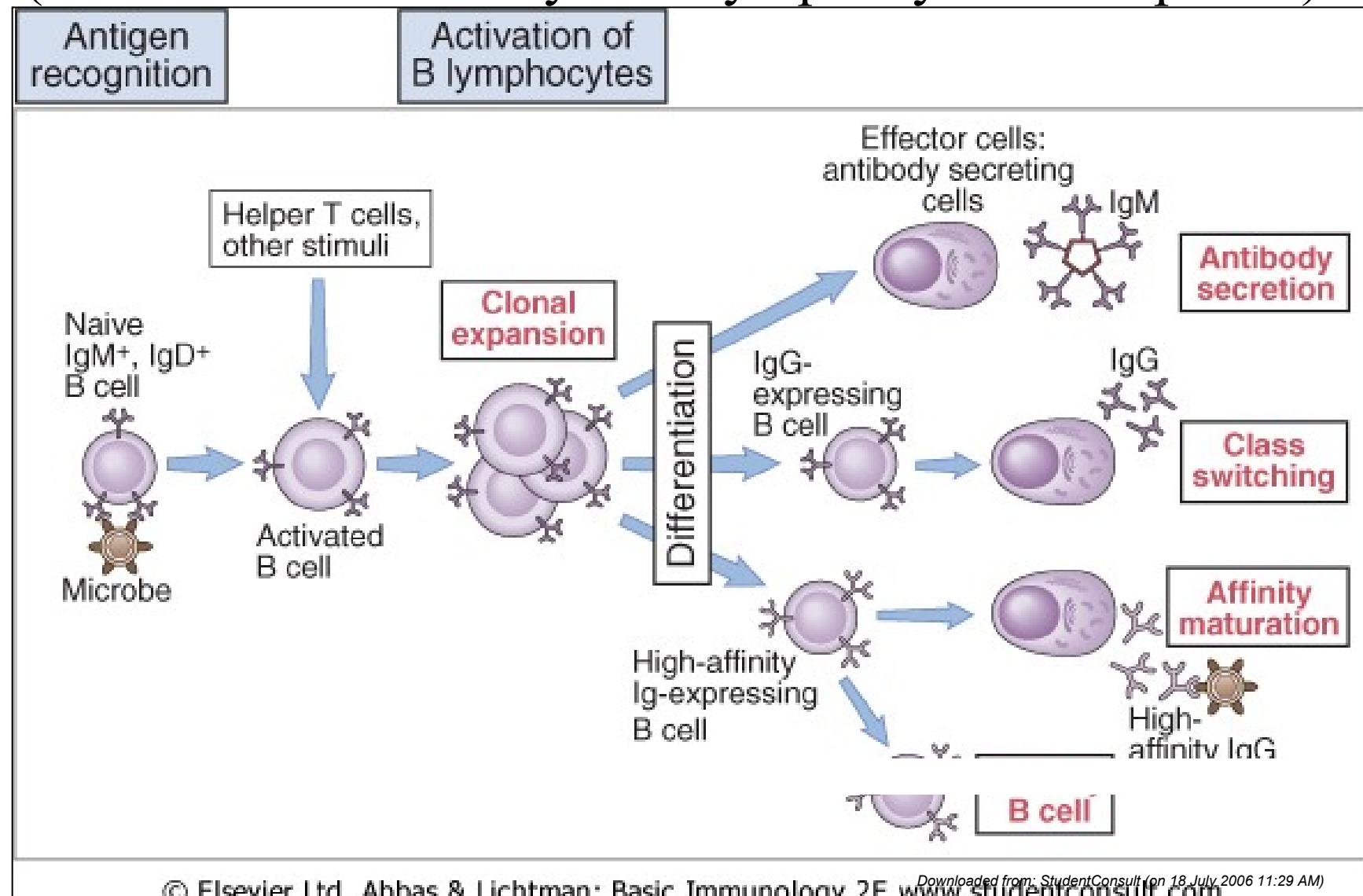
F.M. Burnet, 1957

- During (mainly fetal) development immunocompetent cells of the immune system develop. Each cell is characterized by its own antigen specific receptor. Each cell reacts only with one concrete specific antigen.
- After exposure to autoantigen during fetal life autoreactive clones are eliminated („forbidden clones“).
- If a concrete cell recognizes its specific antigen, it is stimulated, proliferates and forms a clone = clonal selection.
- After repeated divisions the cell becomes a terminally differentiated cell, that does not proliferate and after some time dies.
- The cells of the clone that do not differentiate into the terminal stage become a memory cells which will quickly react after the second exposure to the antigen.

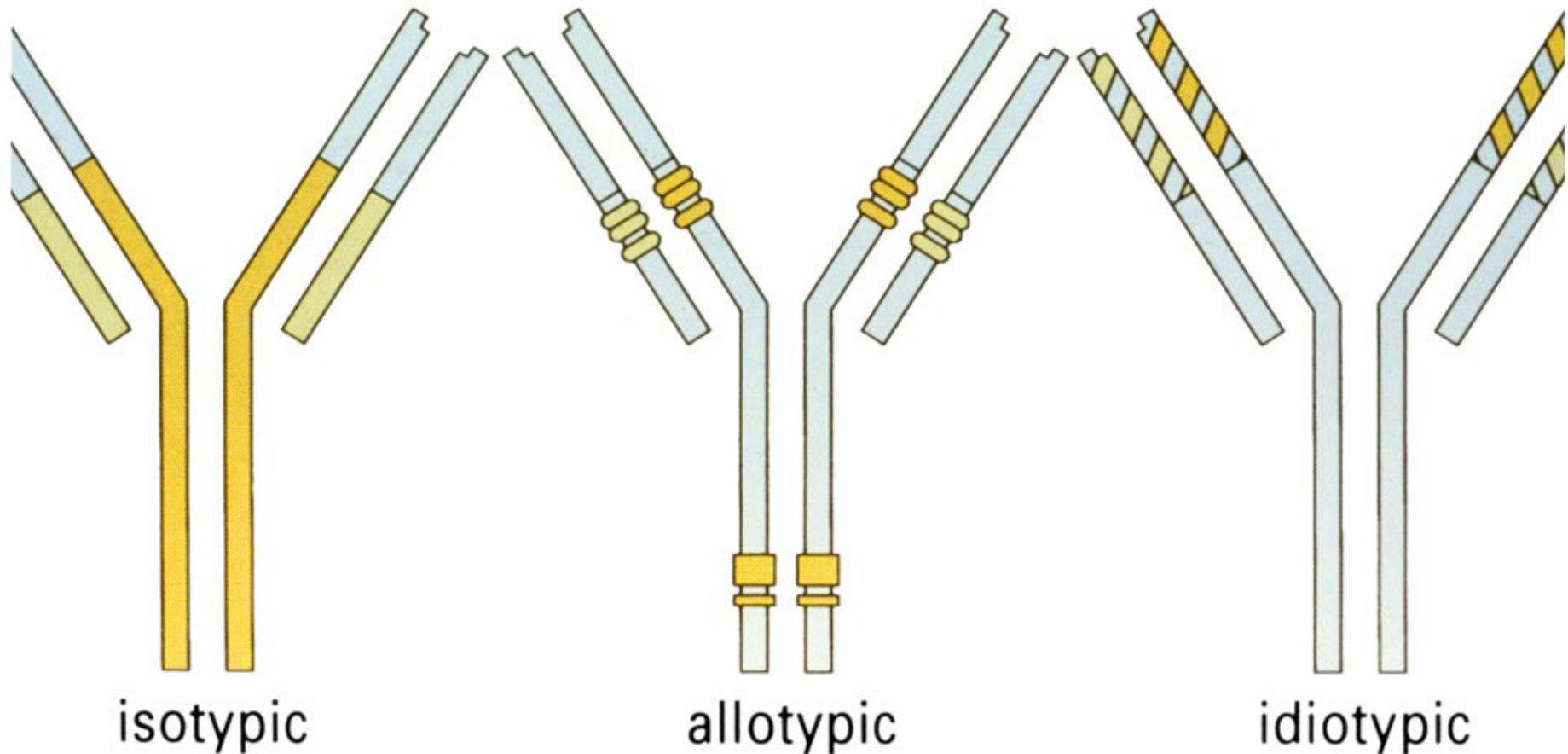
Clonal selection theory



Activation and differentiation of B-lymphocytes (clonal selection theory in B-lymphocyte development)



Antibody variants



isotypic

allotypic

idiotypic

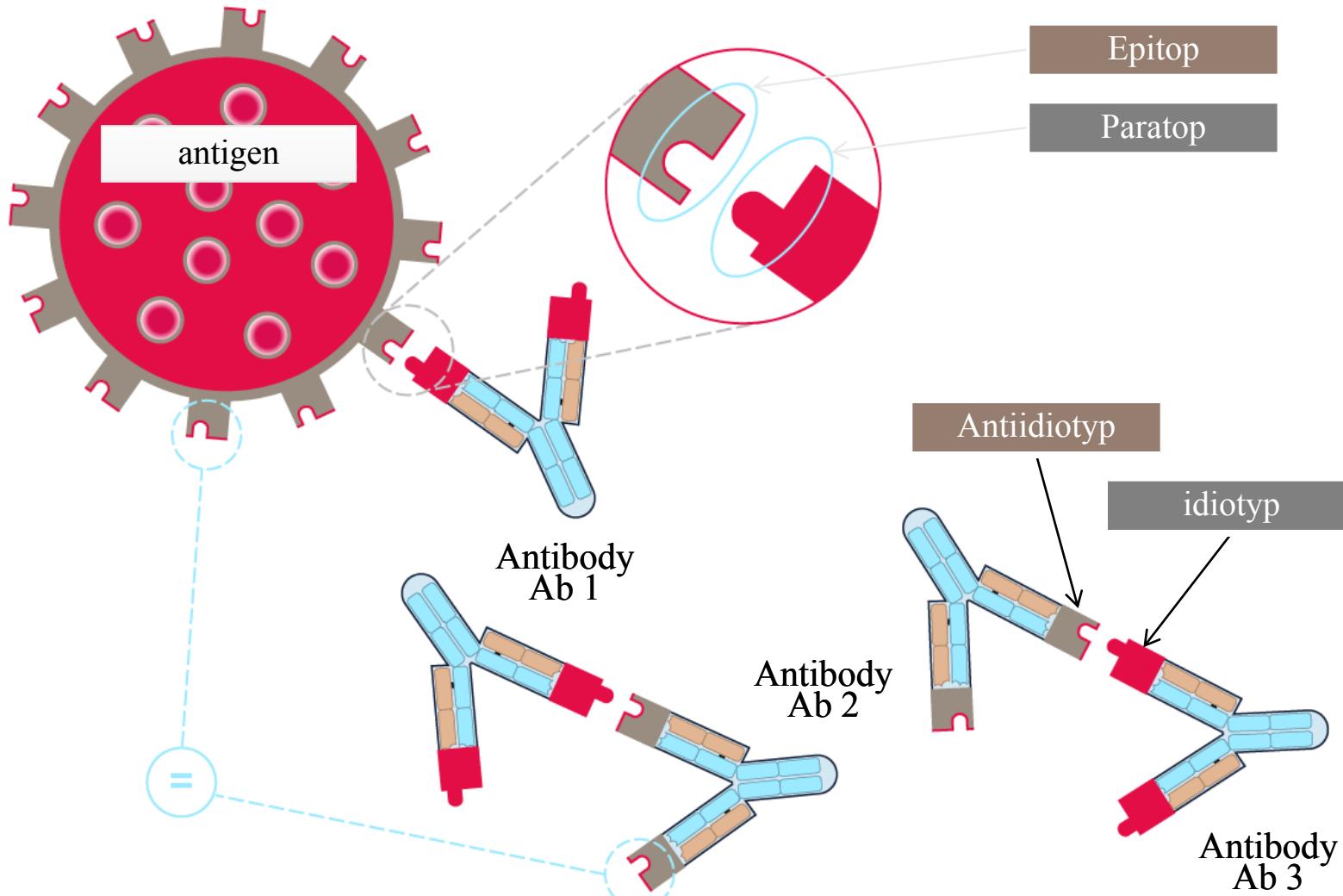
Isotype

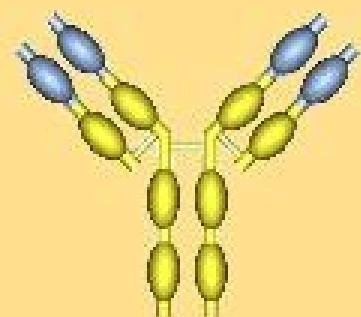
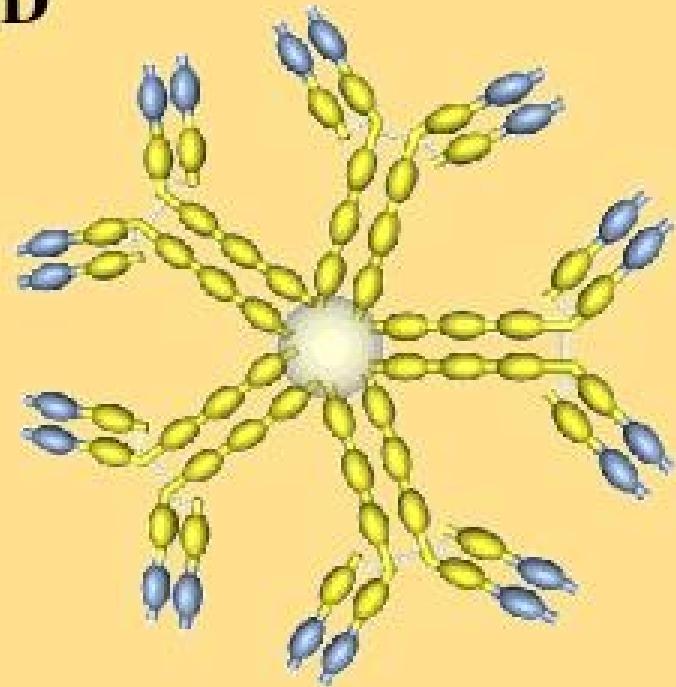
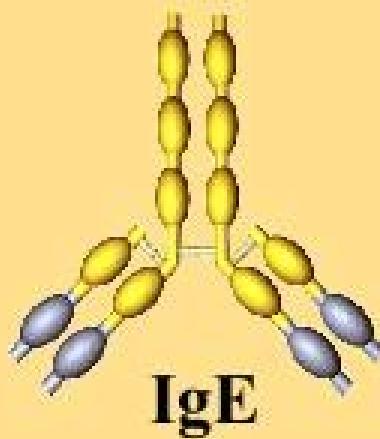
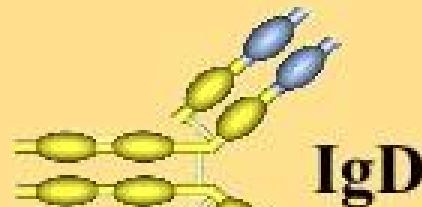
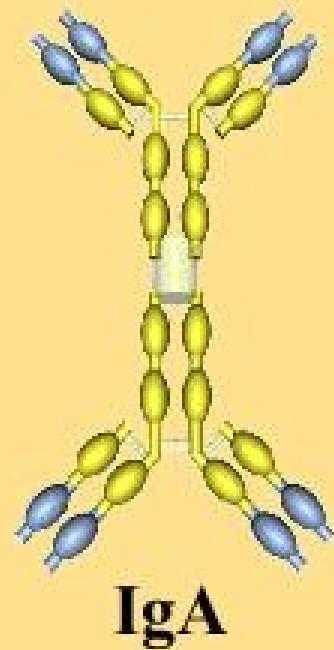
- The class or subclass of an immunoglobulin.
- Antigenic determinants are on constant part of immunoglobulin molecule.

Idiotype

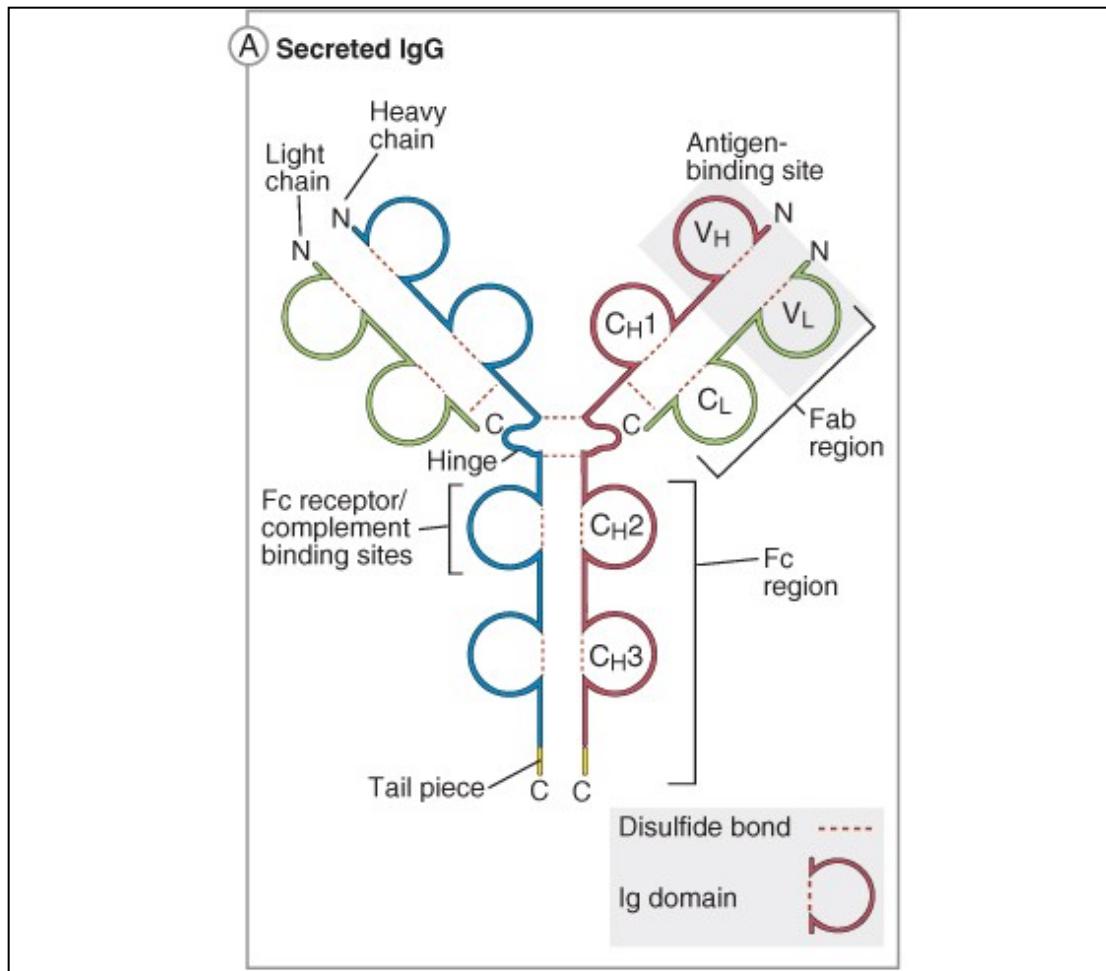
- An antigenic determinant on the variable region of a specific antibody.

Interaction idiotype-antiidiotype

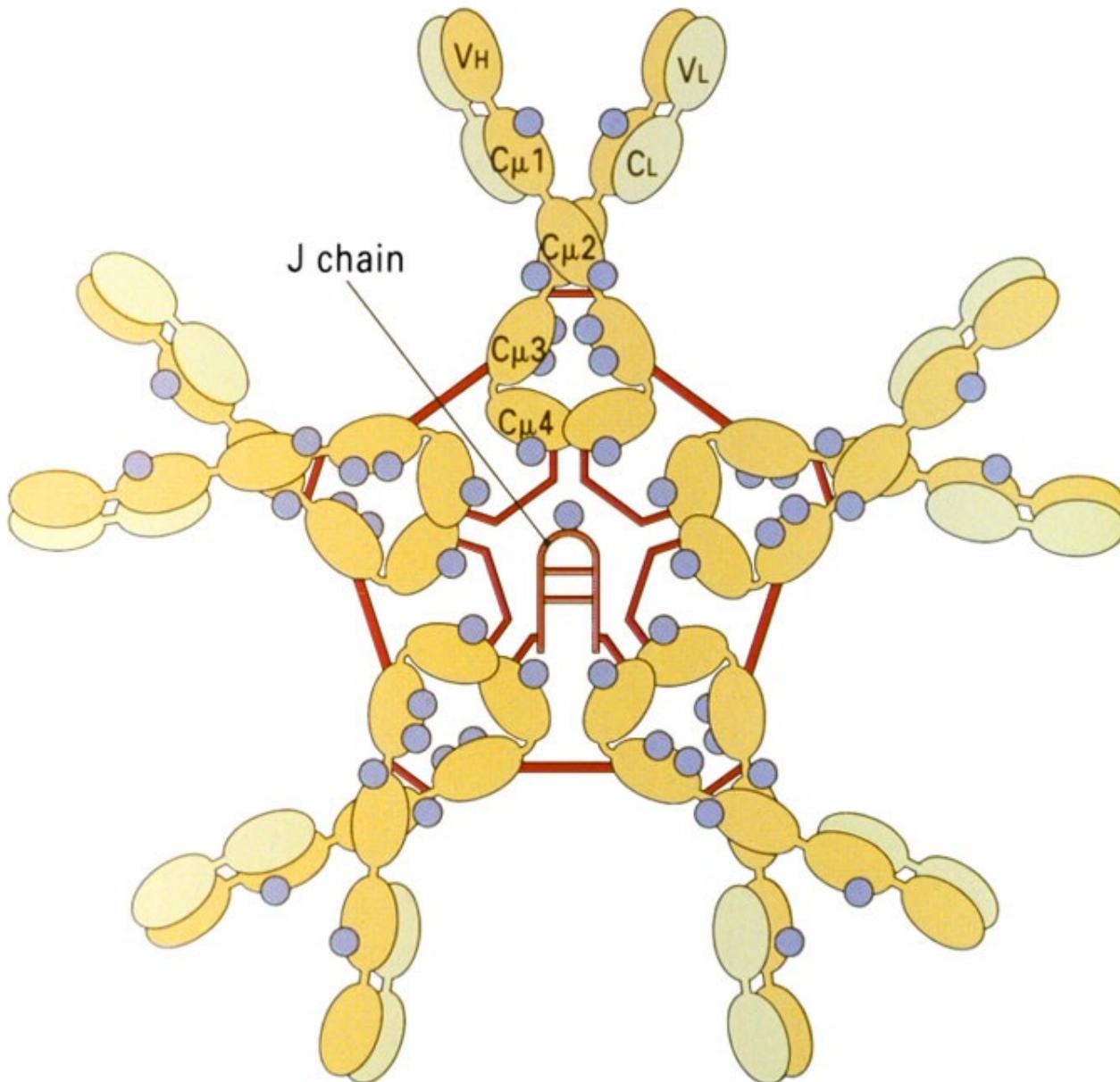




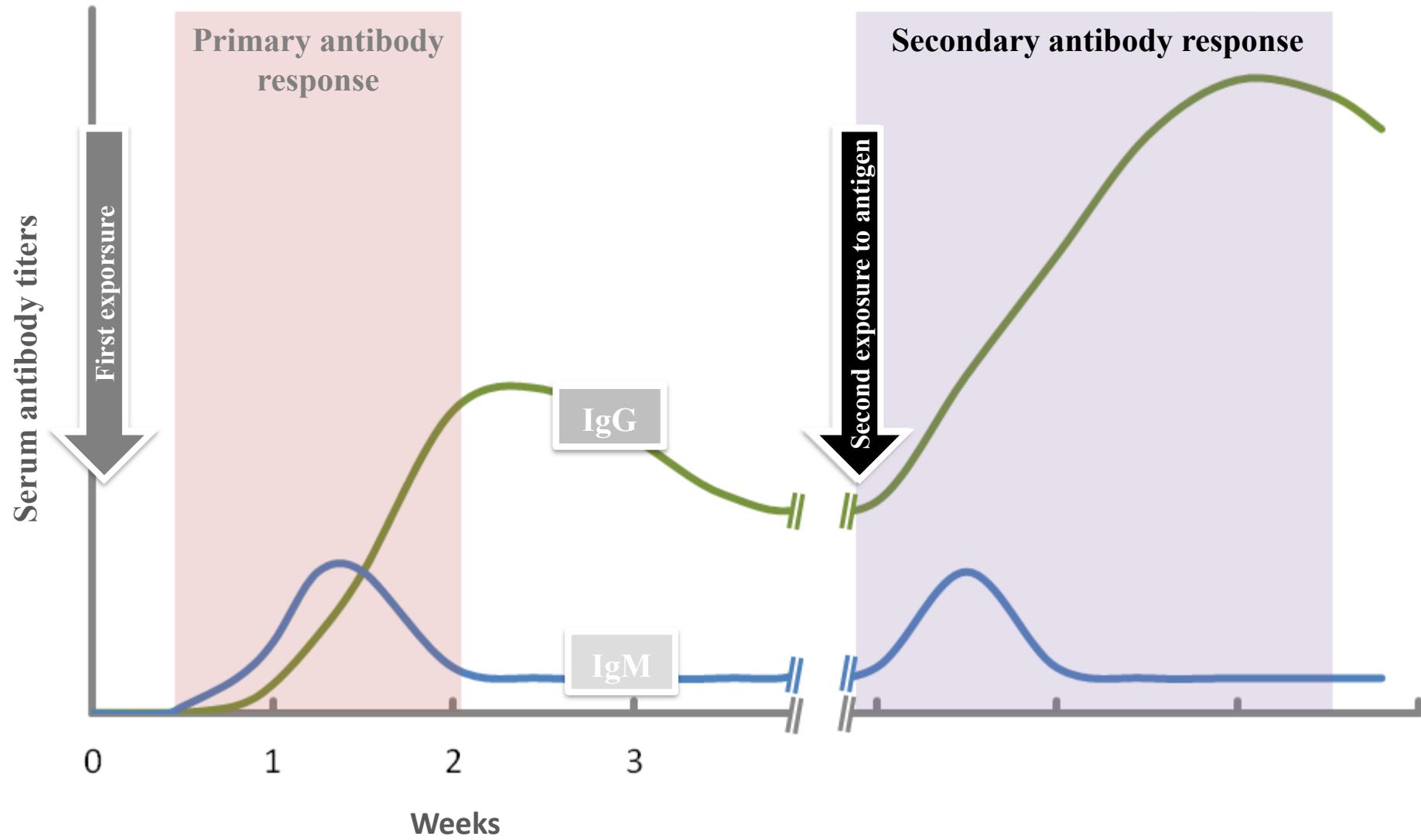
IgG

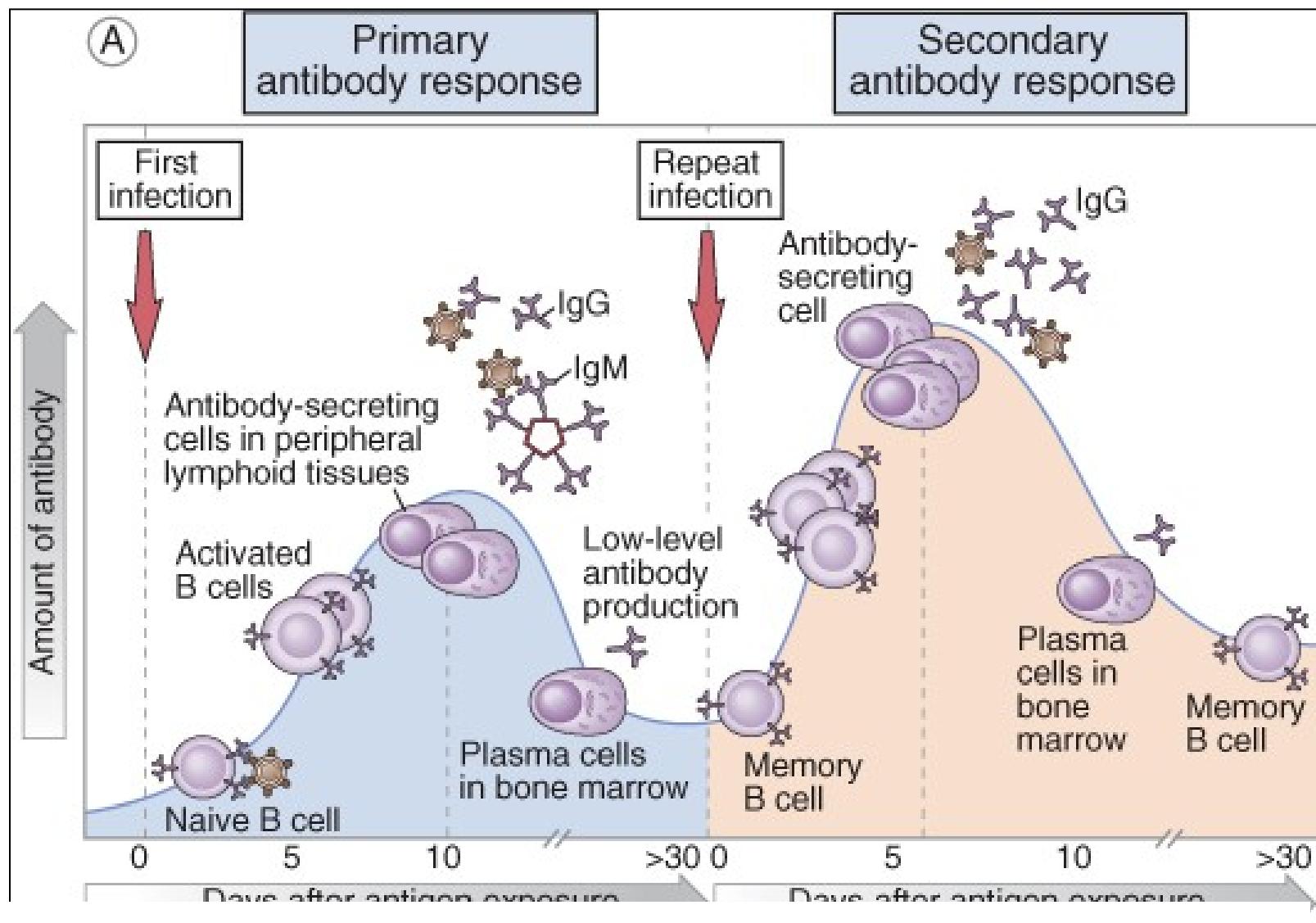


Structure of human IgM

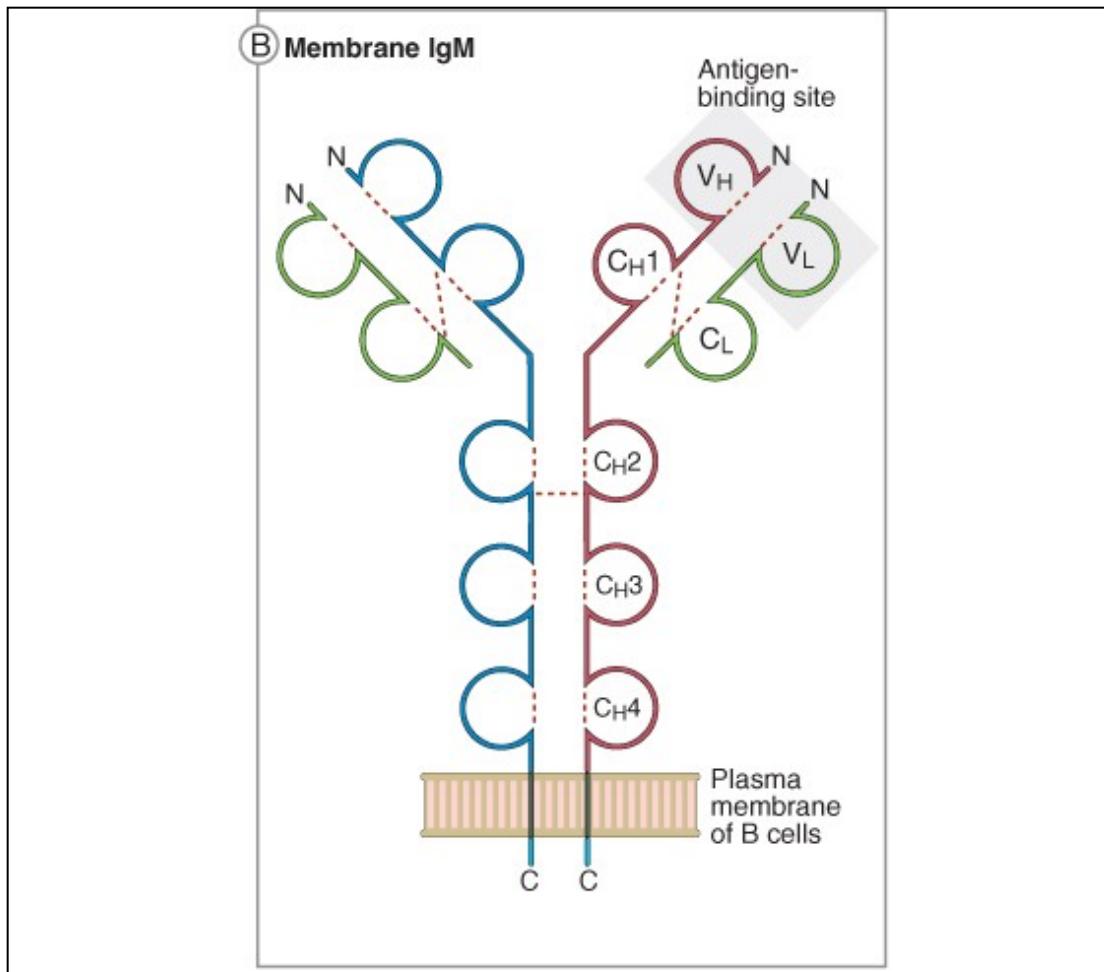


Primary and secondary antibody immune response





IgM on B-cell membrane



Expression of surface immunoglobulins on B-cells

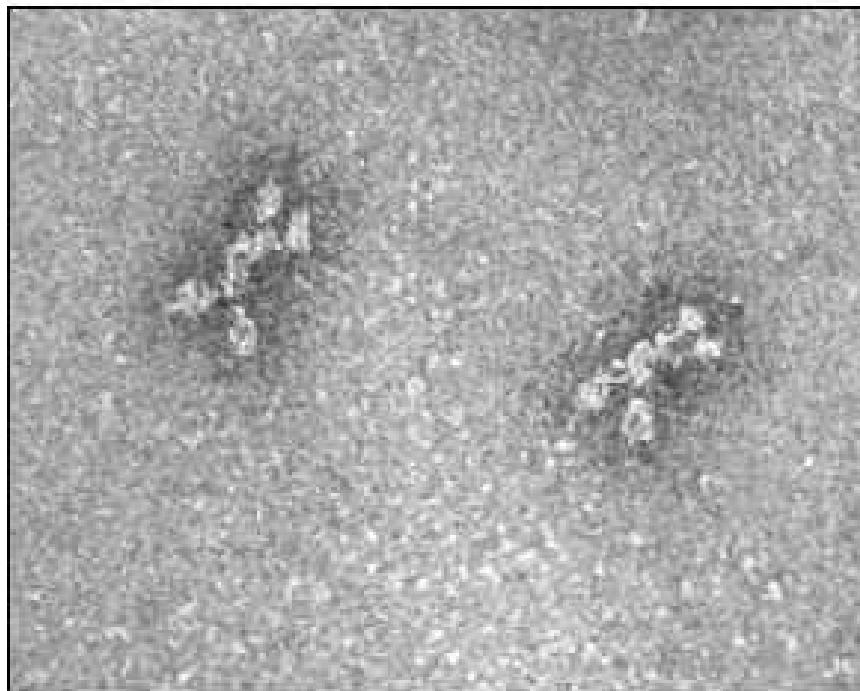
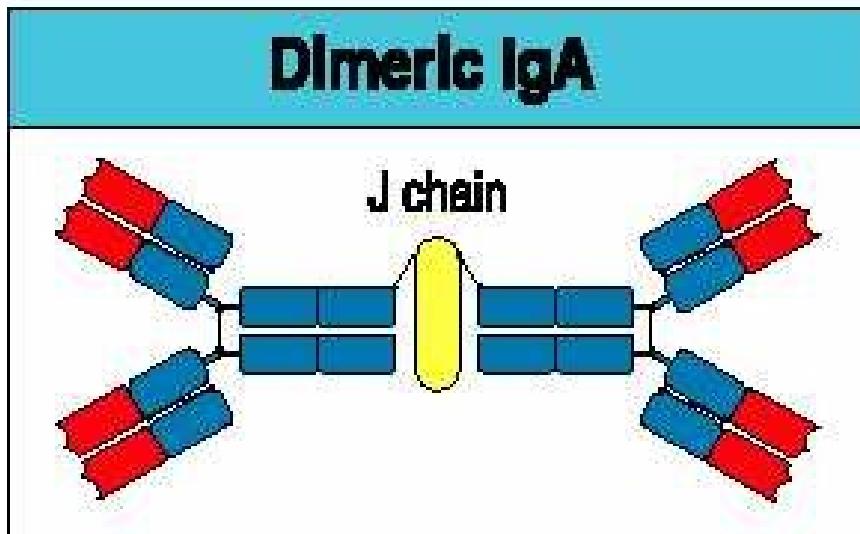
The diagram illustrates the sequential stages of B-cell maturation:

- Stem cell:** Undifferentiated cell.
- Pre-B cell:** Expresses a single chain of the heavy IgM chain.
- Immature B cell:** Expresses membrane IgM and IgD.
- Mature B cell:** Expresses membrane IgM, IgD, and IgG.
- Activated B cell:** Expresses membrane IgG and IgA, and undergoes low-rate Ig secretion, heavy chain isotype switching, and affinity maturation.
- Antibody-secreting cell:** Expresses membrane IgG and IgA, and undergoes high-rate Ig secretion, reduced membrane Ig.

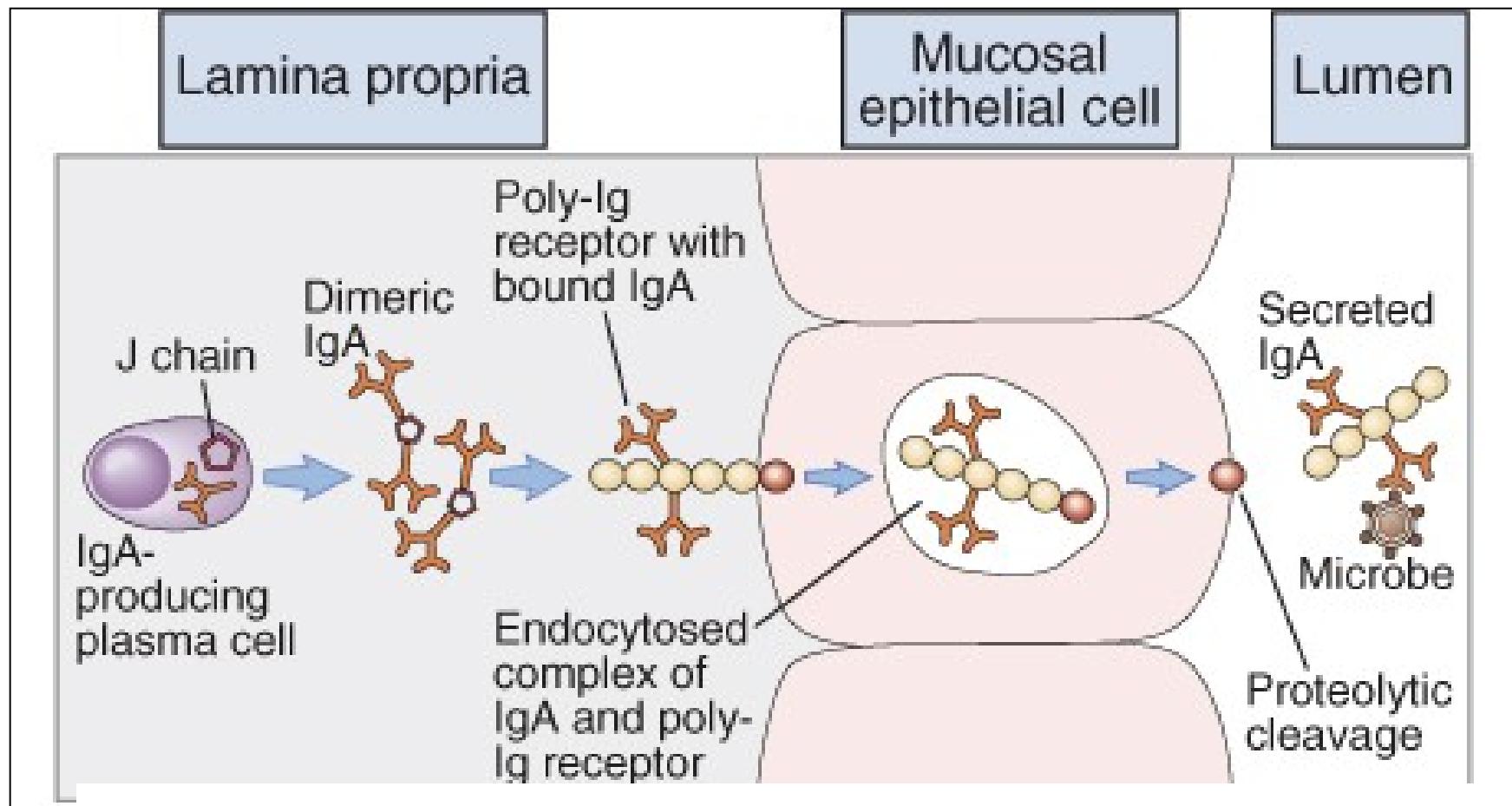
Stage of maturation	Stem cell	Pre-B cell	Immature B cell	Mature B cell	Activated B cell	Antibody-secreting cell
Pattern of immunoglobulin production	None	Cytoplasmic μ heavy chain	Membrane IgM	Membrane IgM, IgD	Low-rate Ig secretion; heavy chain isotype switching; affinity maturation	High-rate Ig secretion;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

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Figure 2.29



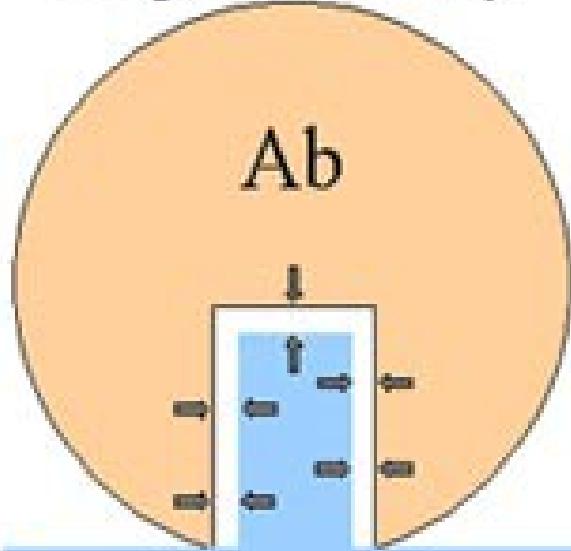
Formation of Secretory IgA



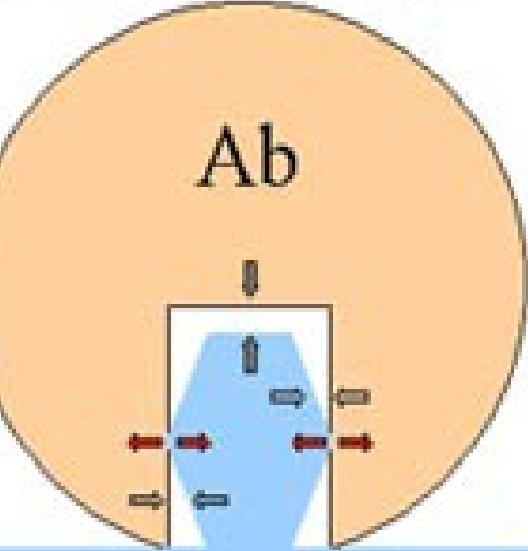
- **Affinity:** The strength of the binding between a single site of an antibody (one variable region) and an epitope.
- **Avidity:** The overall strength of interaction between antibody and antigen. The avidity depends on affinity and the valency of interactions.

Antibody affinity

High Affinity

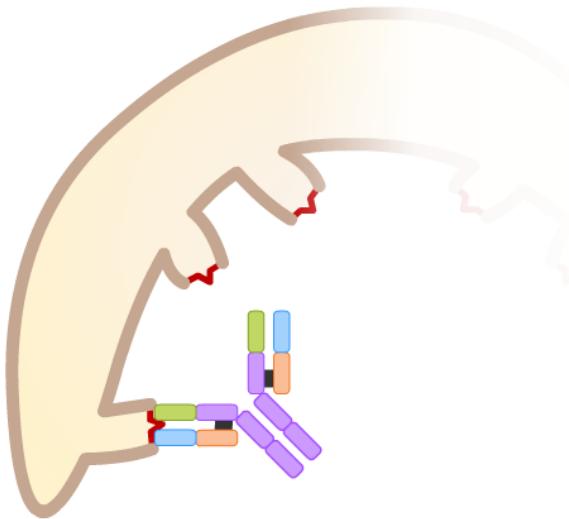


Low Affinity

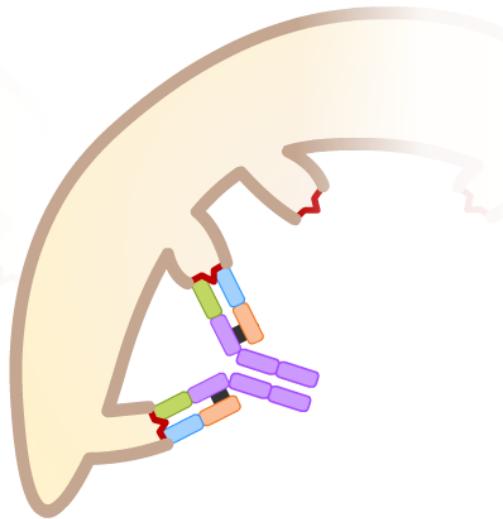


Affinity and avidity

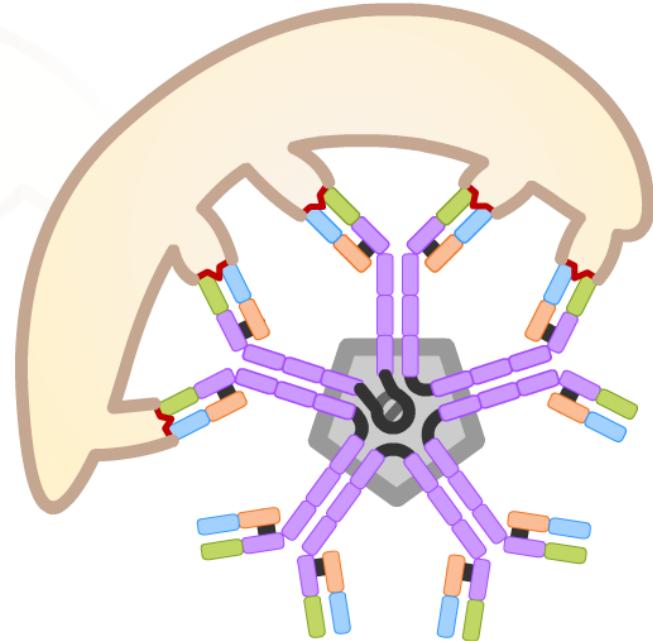
IgA



IgG



IgM



Biological functions of immunoglobulin molecules

- Activation of complement system (IgG, IgM)
- Opsonization (particularly IgG)
- Neutralization of antigens (IgG, IgA, IgM)
- Adherence interference (IgA, IgG)
- Antibody dependent cellular cytotoxicity (ADCC)
- Agglutination, precipitation (IgG, IgM)
- Mast cells degranulation (IgE)
- Transport through placenta (IgG)
- Immunoregulation (mainly IgG)

Antibody dependent cellular cytotoxicity (ADCC)

