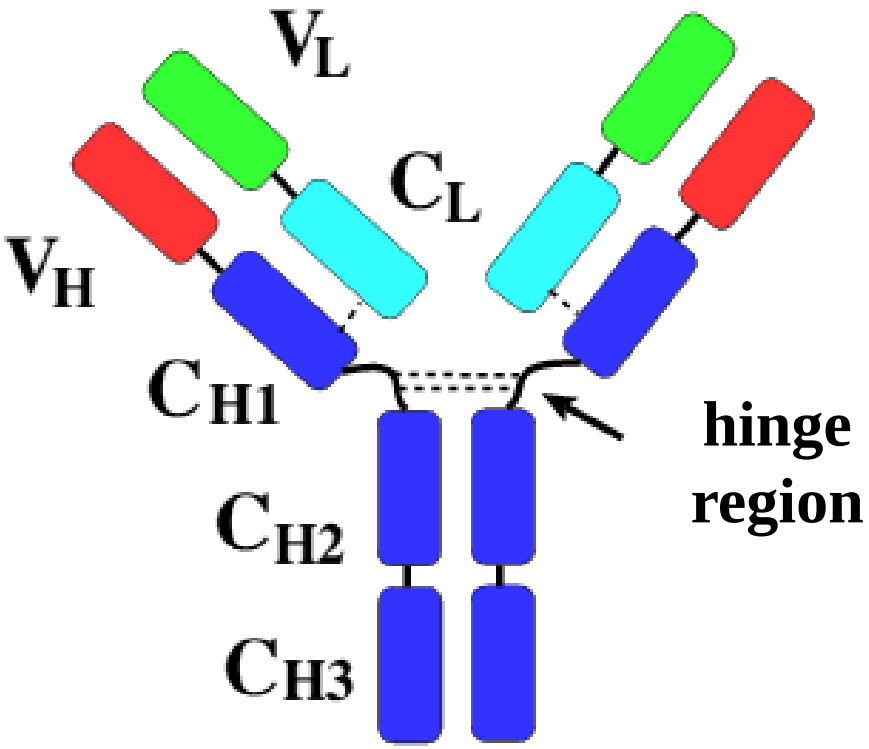
Antibodies

Ig structure: light and heavy chains



Ig structure: light and heavy chains

Light chains:

- κ, λ (65 : 35 in humans)
- 23 kDa
- 215 amino acids

Ig structure: light and heavy chains

Heavy chains:

- 5 isotype classes
- various molecular mass
- 4 domains (IgG, IgD, IgA) or 5 domains (IgM, IgE)
- 440 - 450 amino acids

Ig structure: flexibility

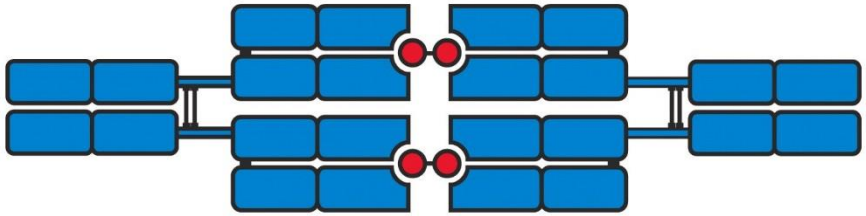


Figure 3-4 part 2 of 4 Immunobiology, 6/e. (© Garland Science 2005)

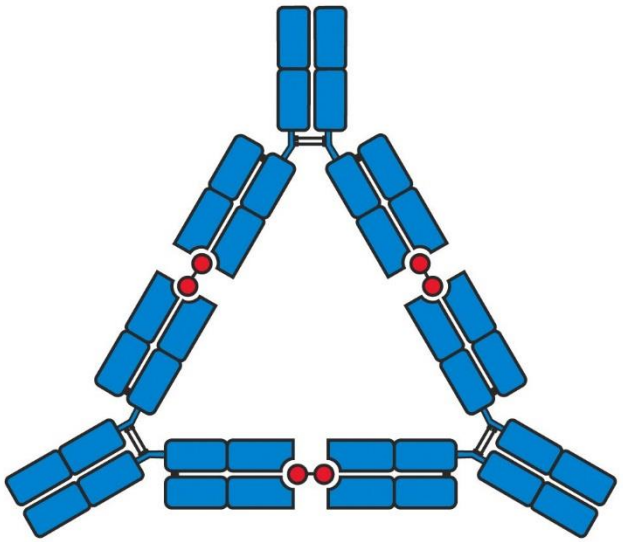


Figure 3-4 part 3 of 4 Immunobiology, 6/e. (© Garland Science 2005)

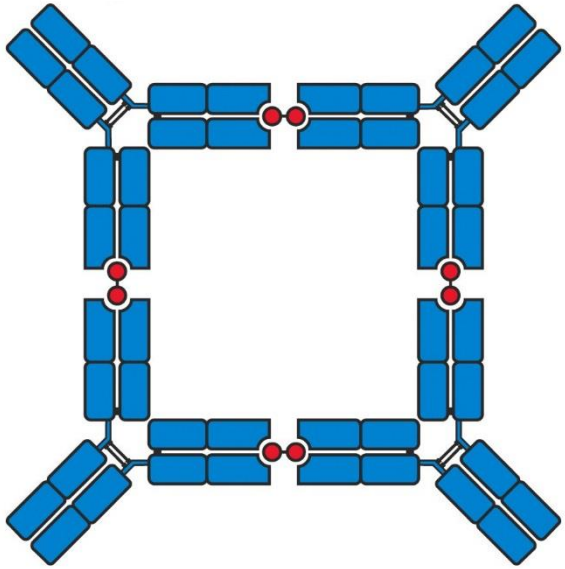


Figure 3-4 part 4 of 4 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: proteolytic cleavage

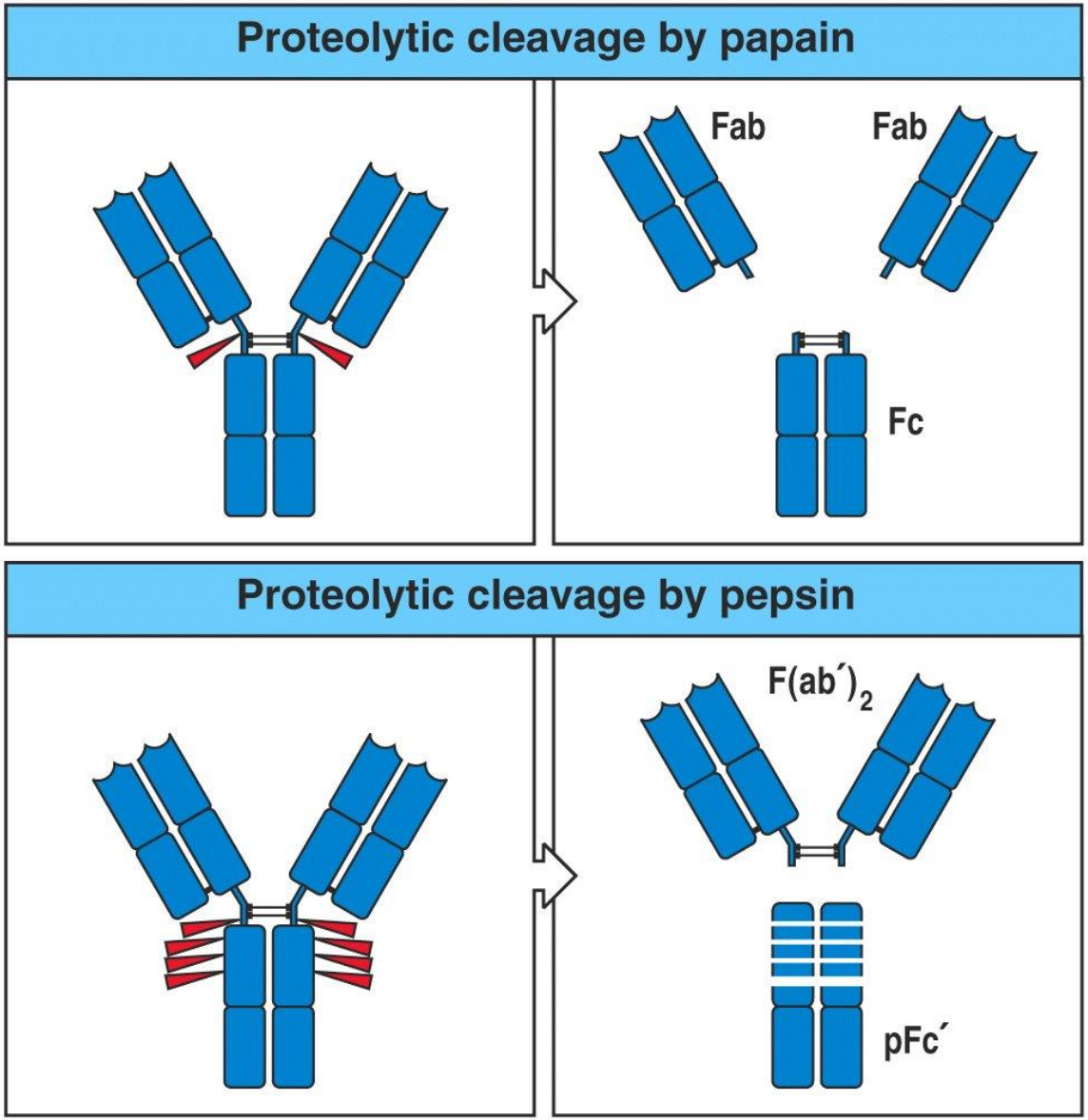
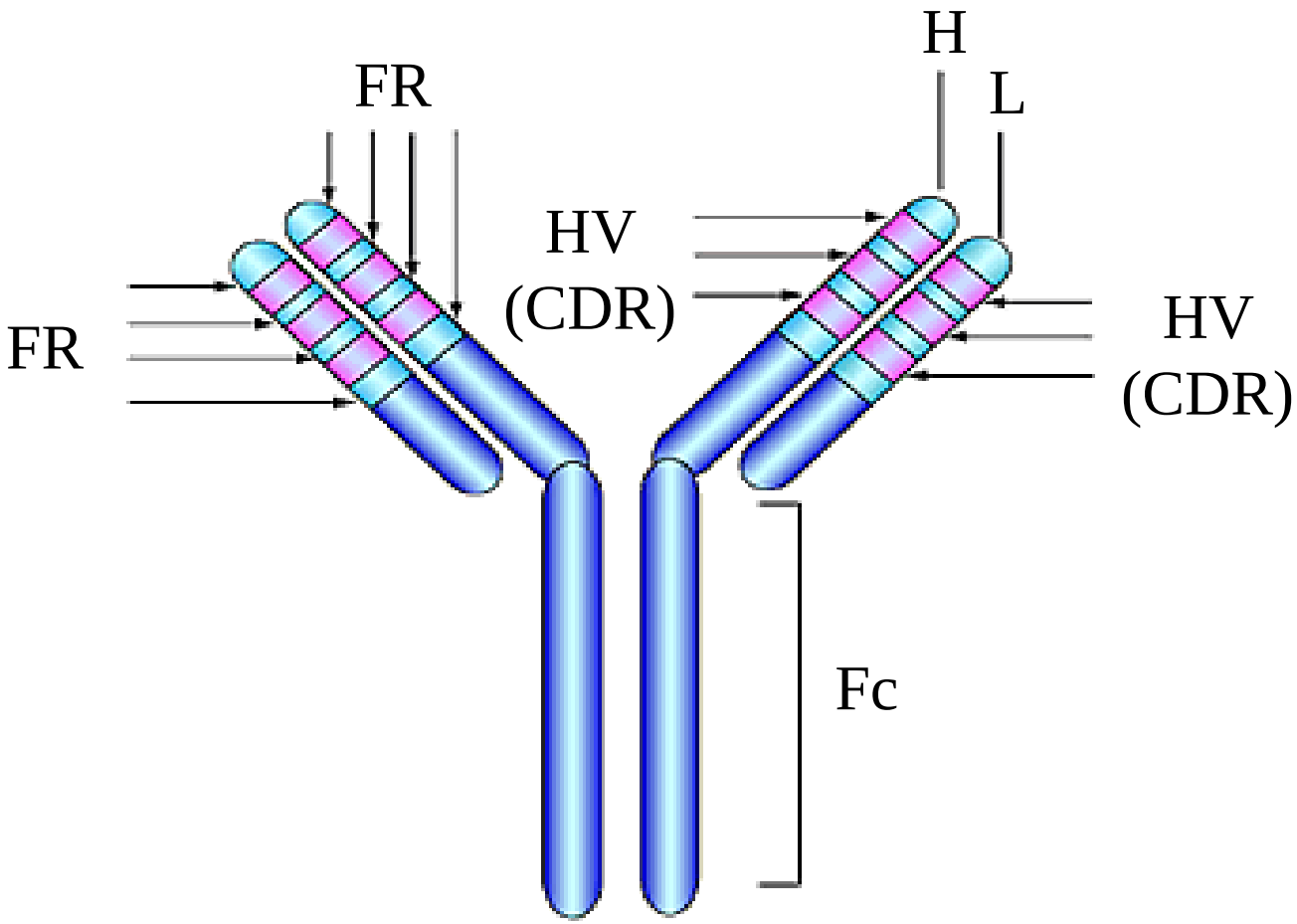


Figure 3-3 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: hypervariable regions



CDR = complementarity-determining regions

FR = frame region

Ig structure: hypervariable regions

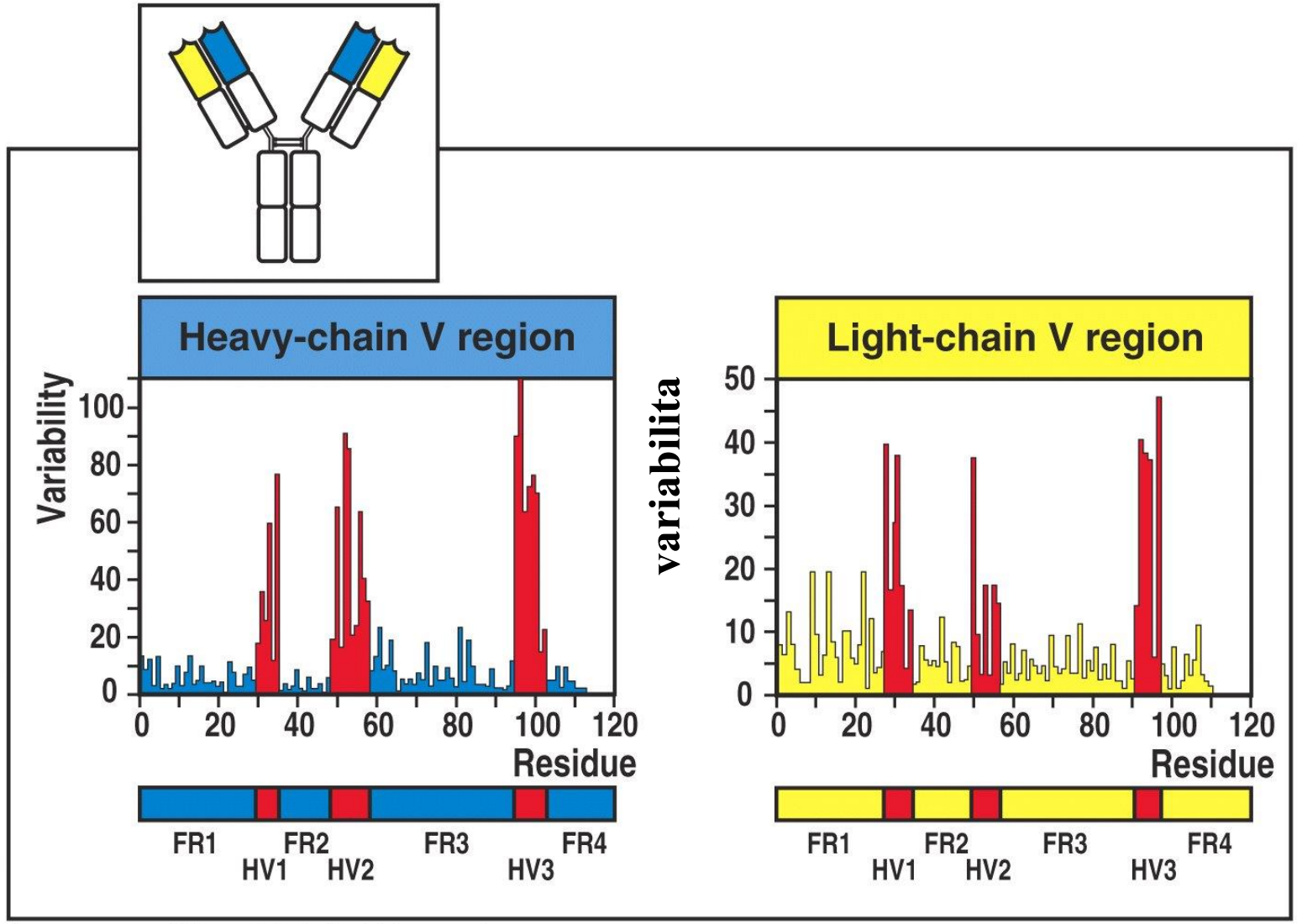
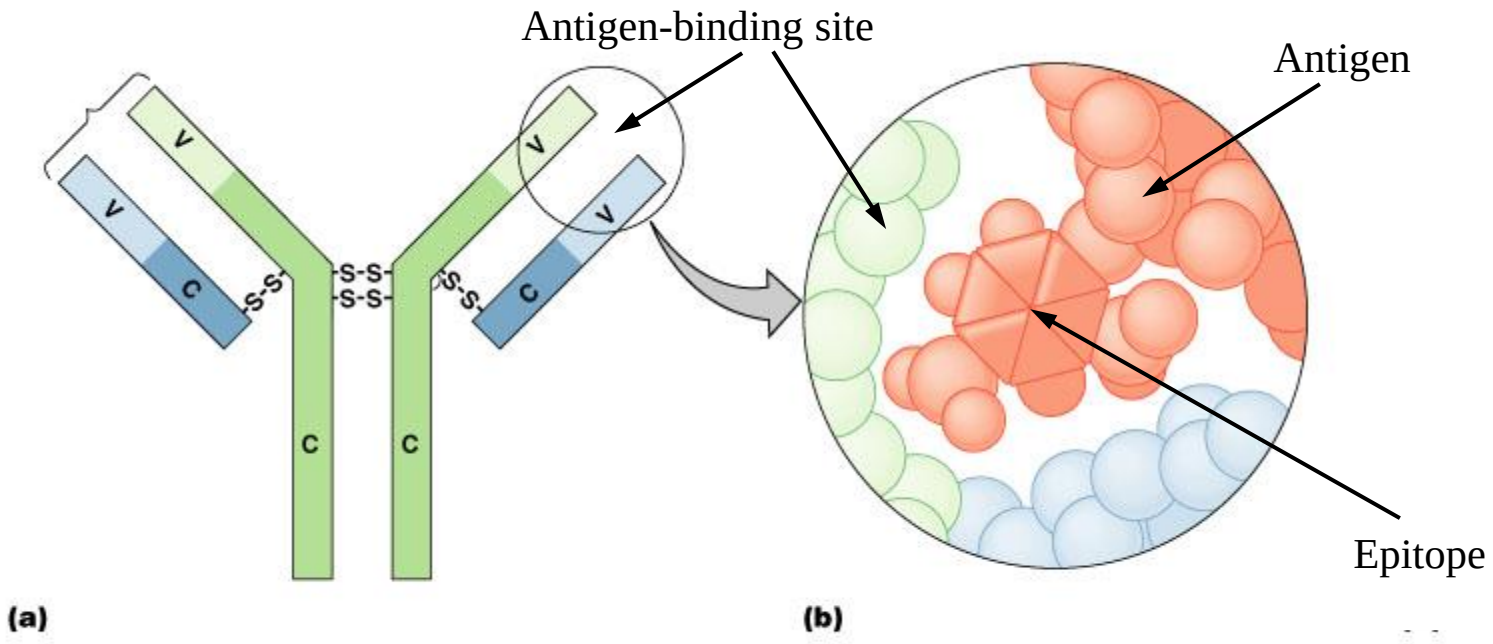
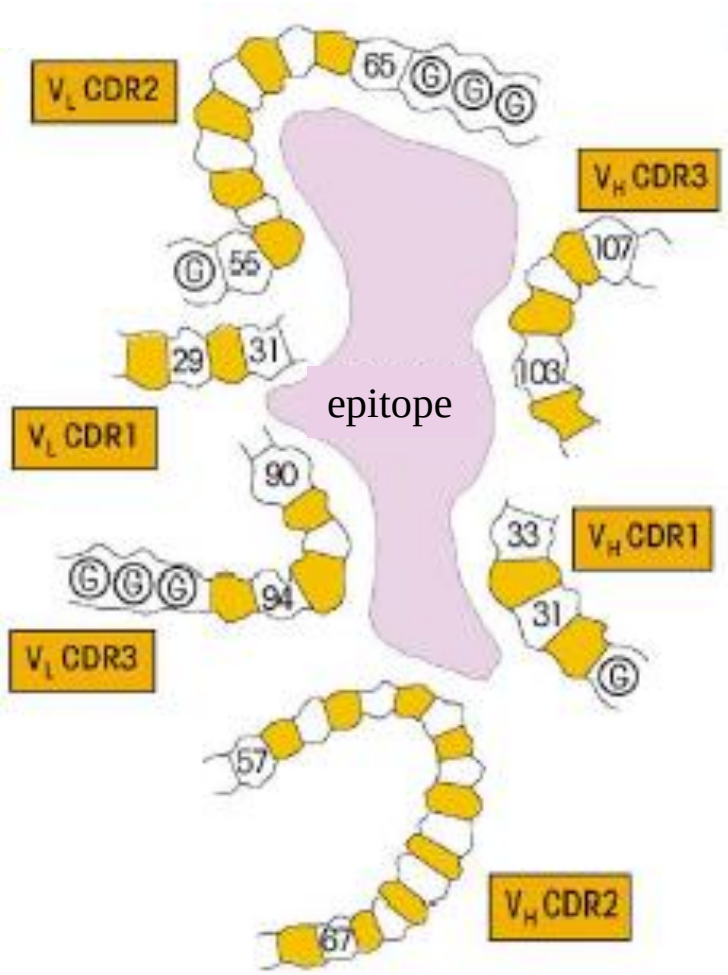


Figure 3-6 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: antigen-binding site



Ig structure: antigen-binding site



Ig structure: isotype classes

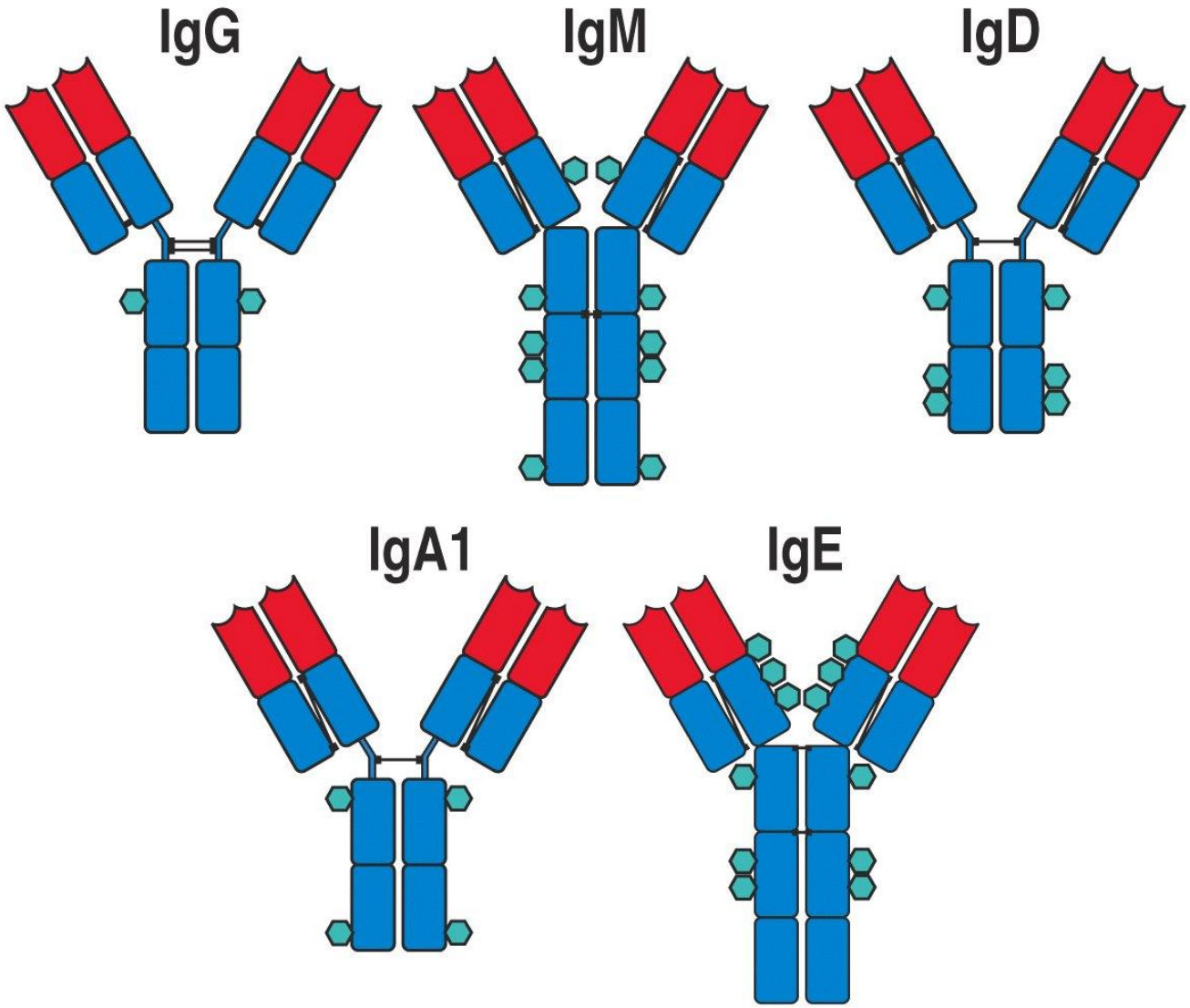
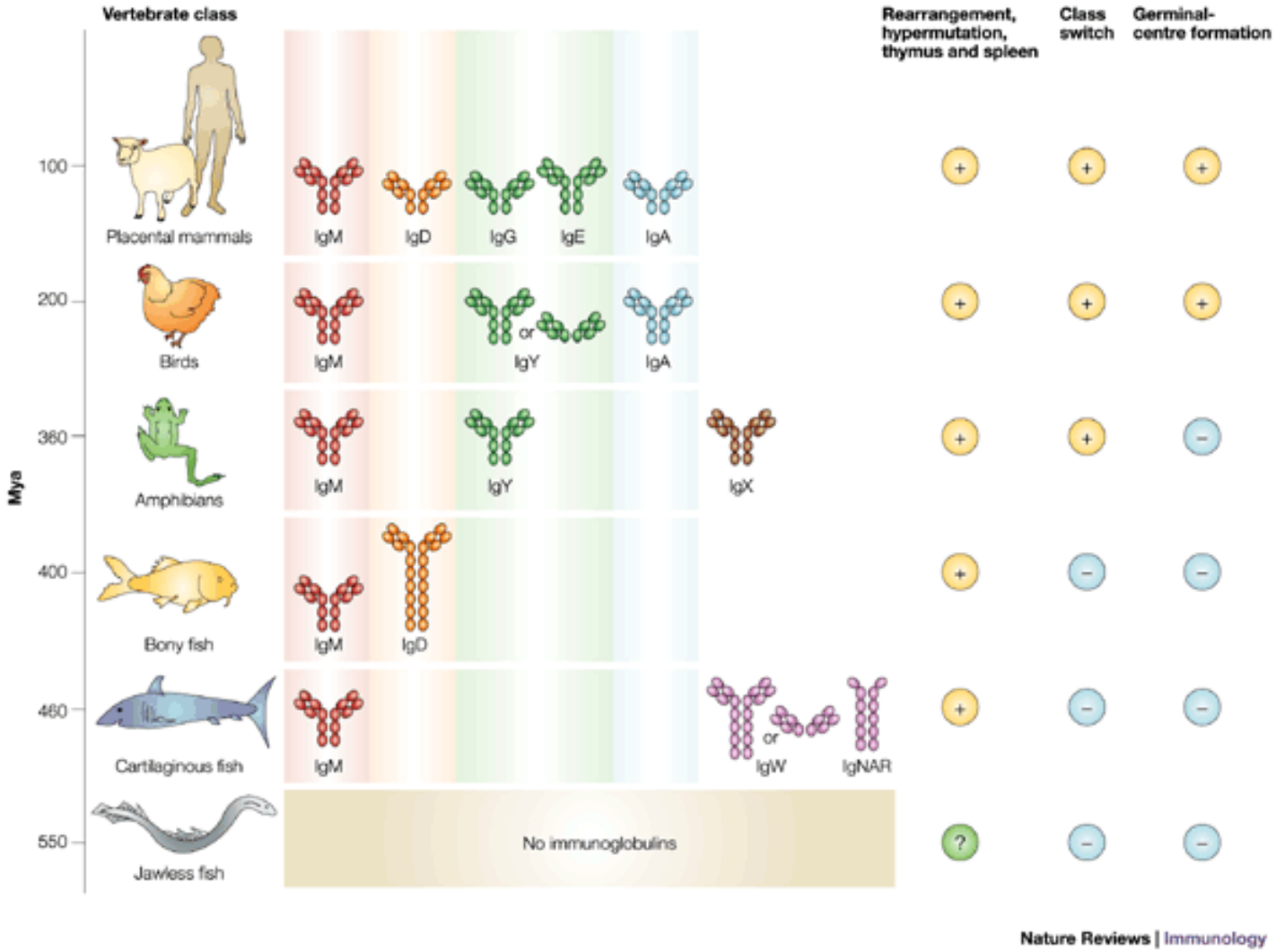


Figure 4-18 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: isotype classes



Ig structure: isotype classes

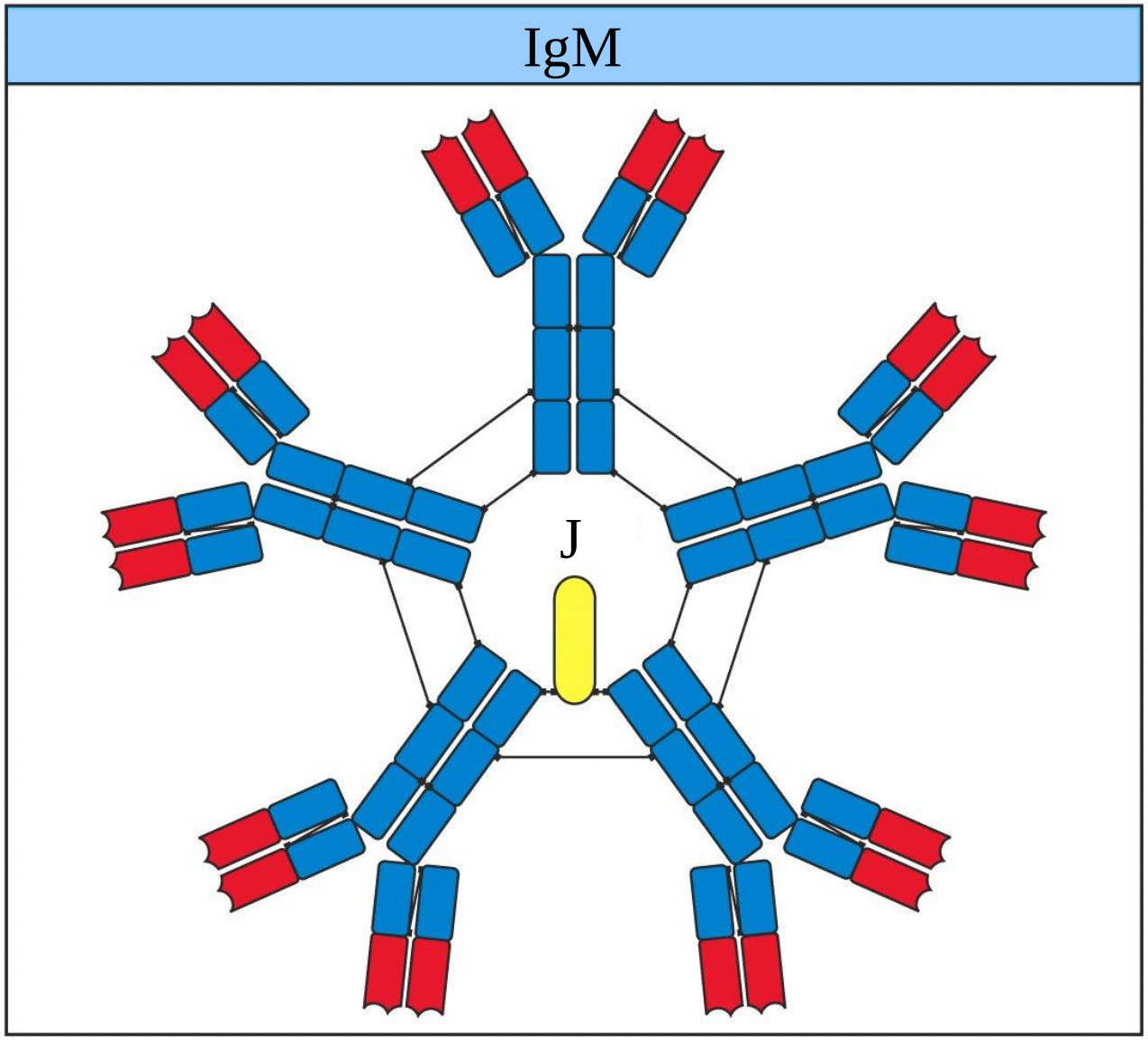


Figure 4-23 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: isotype classes

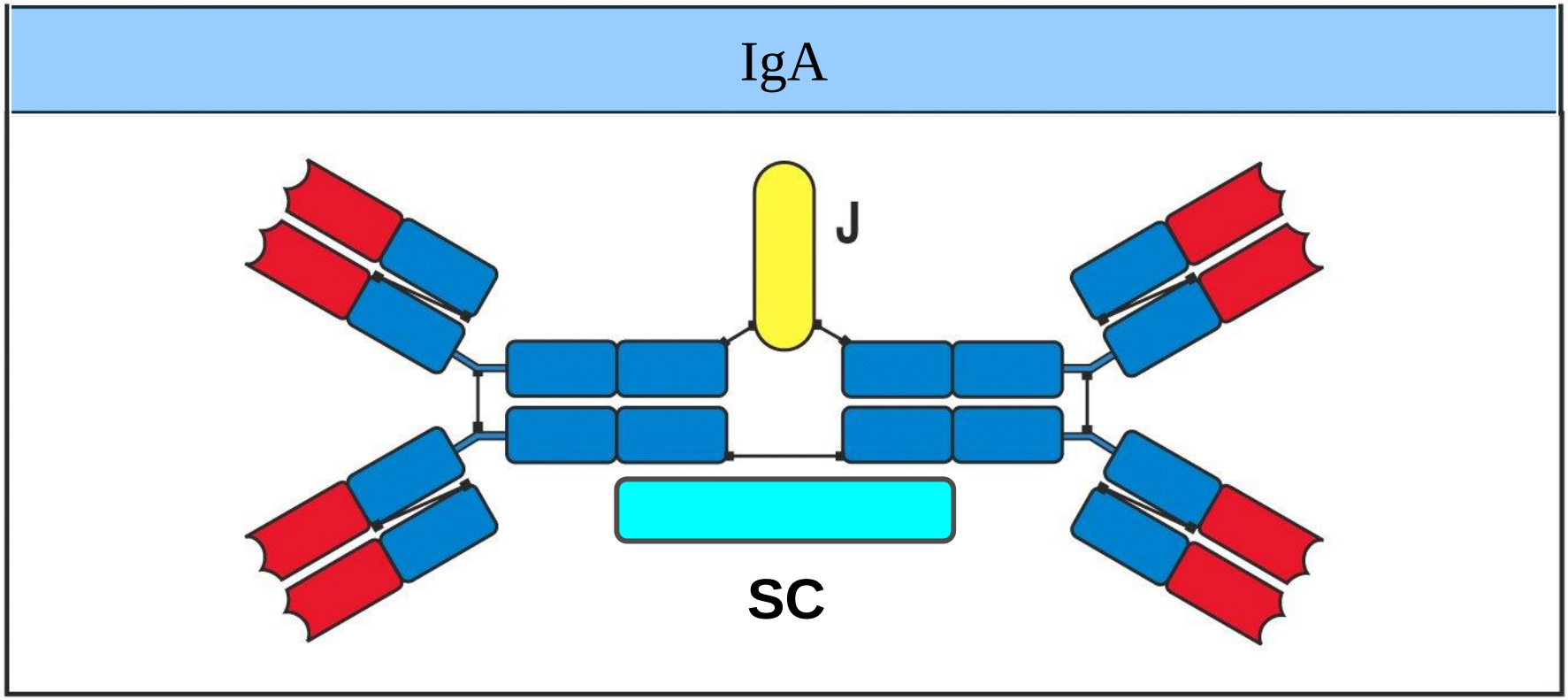


Figure 4-23 part 2 of 3 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: isotype classes

	Ig								
	IgG1	IgG2	IgG3	IgG4	IgM	IgA1	IgA2	IgD	IgE
Heavy chain	γ_1	γ_2	γ_3	γ_4	μ	α_1	α_2	δ	ϵ
Molecular weight (kDa)	146	146	165	146	970	160	160	184	188
Serum level (mean adult mg ml^{-1})	9	3	1	0.5	1.5	3.0	0.5	0.03	5×10^{-5}
Half-life in serum (days)	21	20	7	21	10	6	6	3	2

Figure 4-17 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

Ig structure: isotypes, allotypes, idiotypes

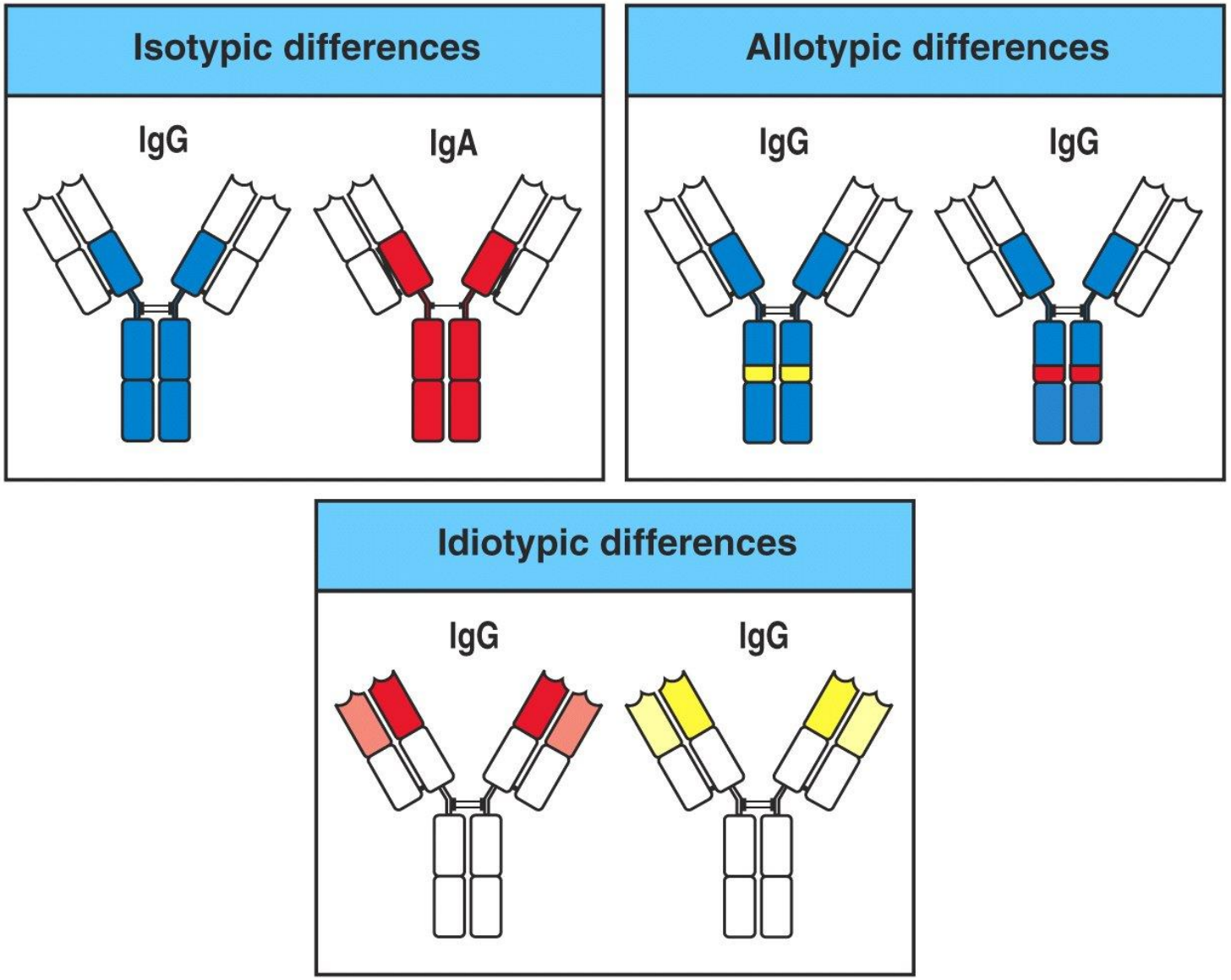
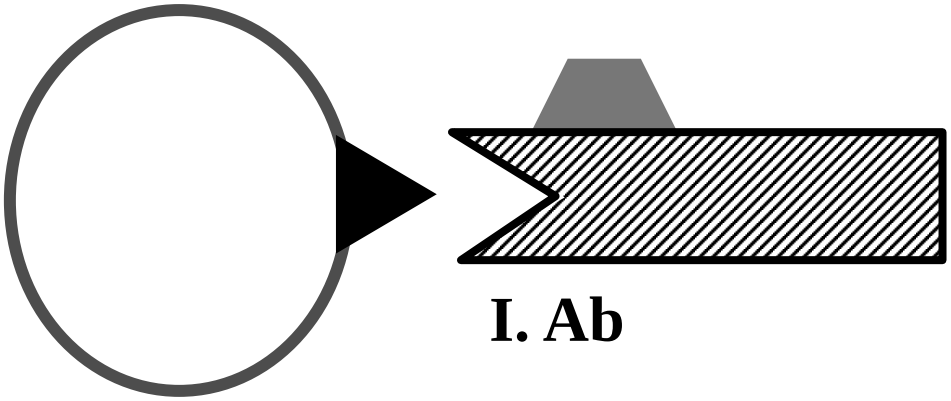
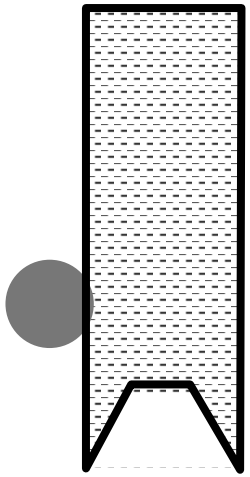


Figure 4-24 Immunobiology, 6/e. (© Garland Science 2005)

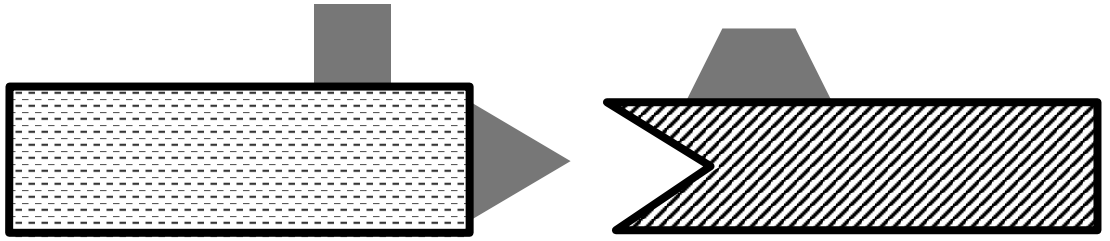
Ig structure: idiotypes



I. Ab



II. Ab (α)



II. Ab (β)

IgG

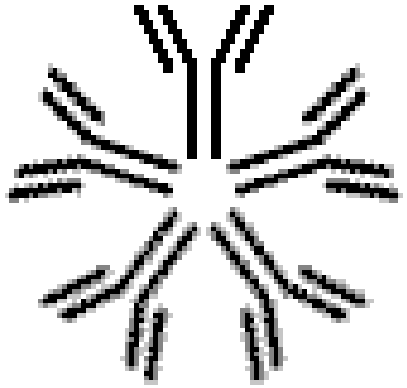
IgG

- Major portion of serum Ig
- Fundamental part of antibody activities
- Repeated immunization
- Major anti-infective defense of newborns

IgM

IgM

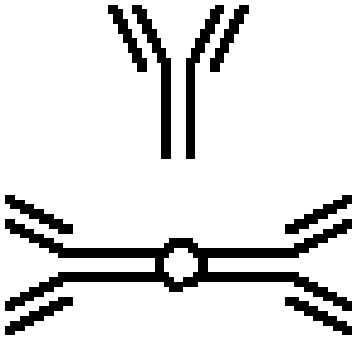
- First Ig in phylogenesis
- Produced after first contact with Ag
- Mainly corpuscular Ag
- Membrane BCR



IgA

IgA

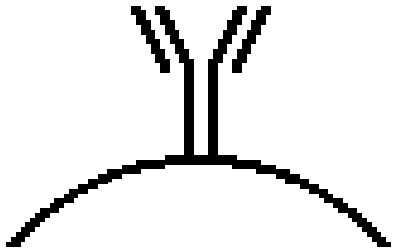
- Secretory IgA (saliva, tears, nasal secretion, sweat, colostrum, lung secretion, urogenital and gastrointestinal tracts)
- Protection of mucosa and body surfaces
- Secretory component
- Serum IgA



IgD

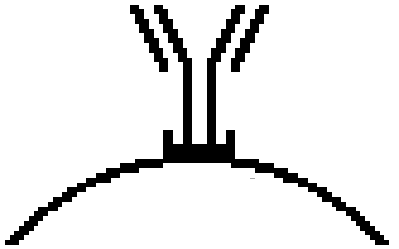
IgD

- Plasma membrane of B lymphocytes
- Weak antibody activity

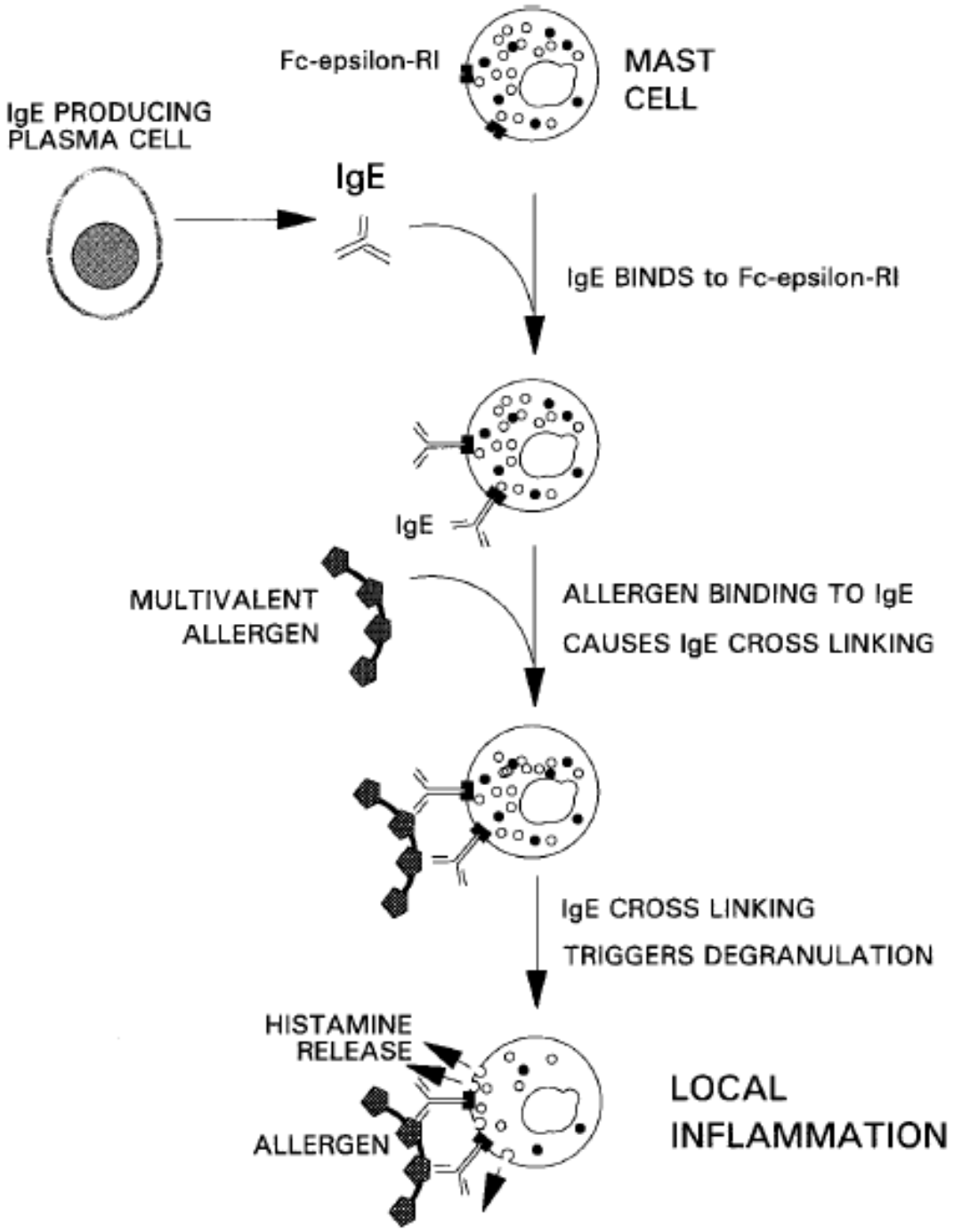


IgE

IgE

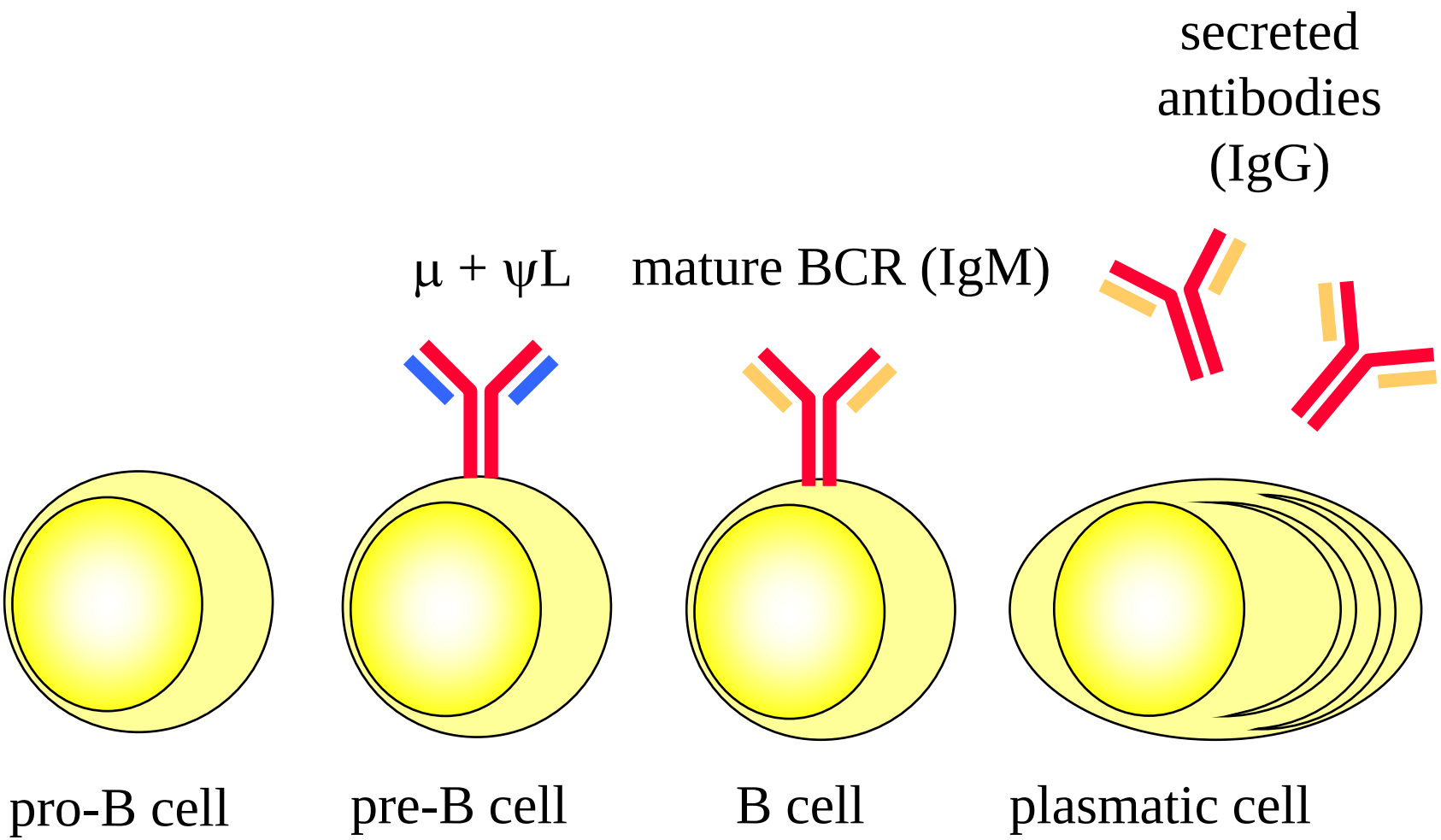


- The lowest concentration in serum
- The shortest biological half-life
- Mast cells and basophils (Fcε receptors)
- Immediate allergic reactions (type I)
- Indigenous biological function – protection against parasites?

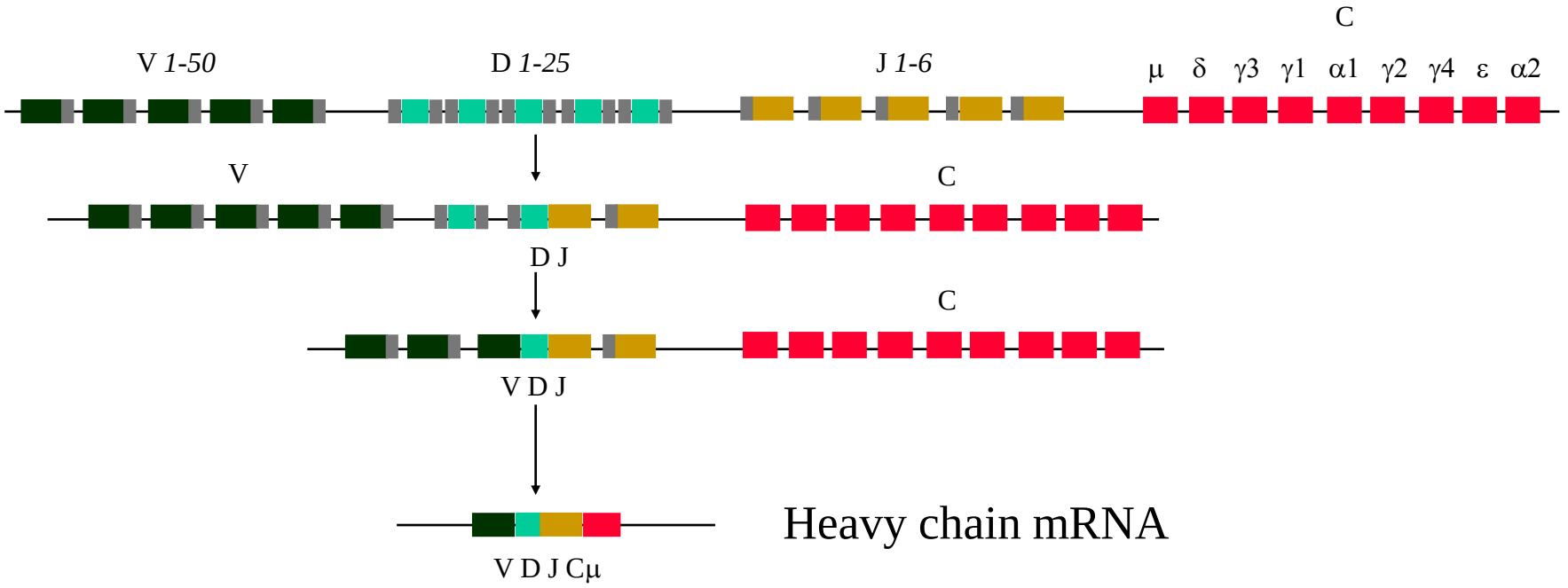

Fc-epsilon-RI
MAST CELL
IgE PRODUCING PLASMA CELL
IgE
IgE BINDS to Fc-epsilon-RI
IgE
MULTIVALENT ALLERGEN
ALLERGEN BINDING TO IgE
CAUSES IgE CROSS LINKING
IgE CROSS LINKING
TRIGGERS DEGRANULATION
HISTAMINE RELEASE
ALLERGEN
LOCAL INFLAMMATION

IgE

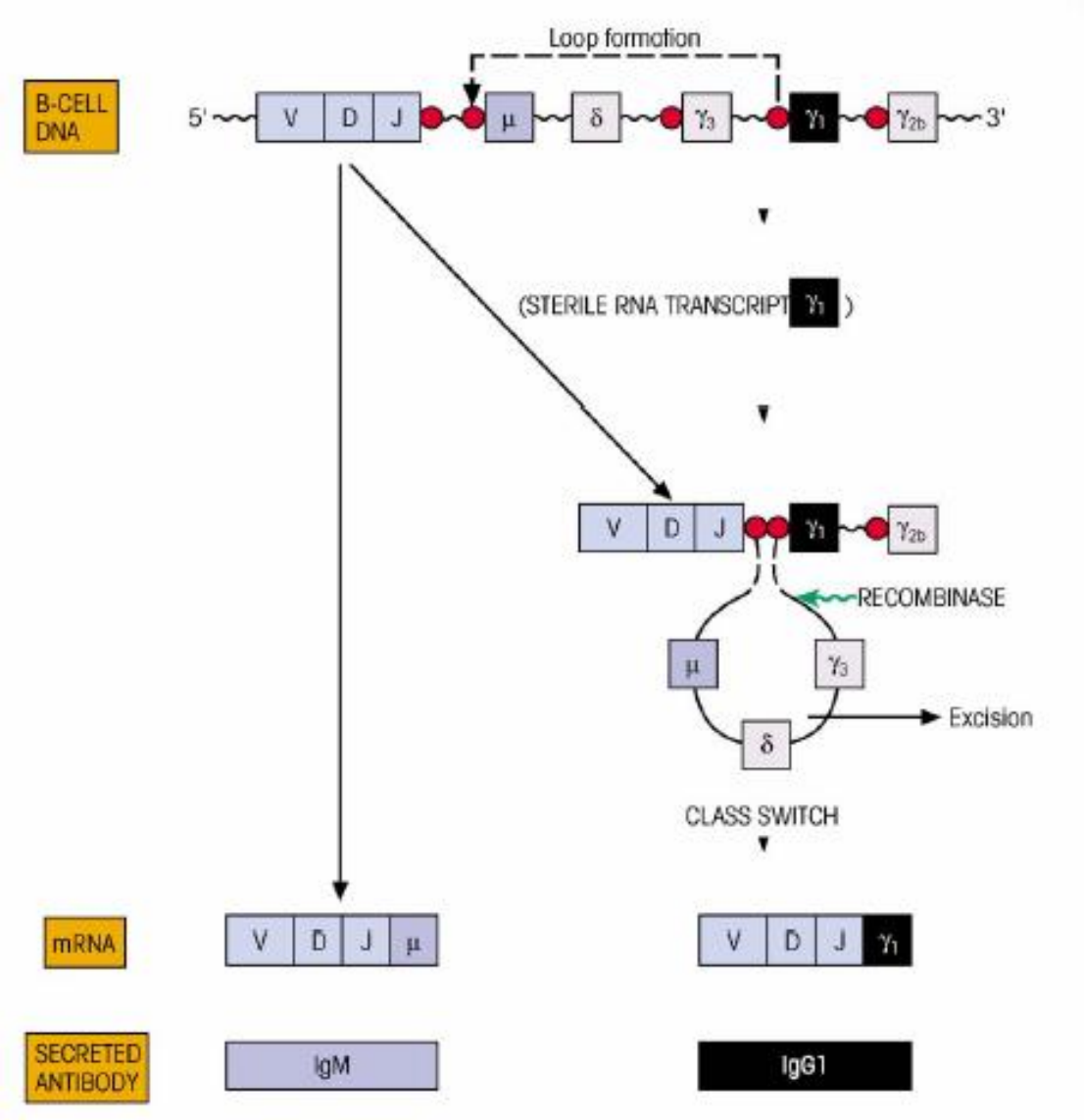
Ig production: B lymphocyte maturation



Ig production: Ig gene segment rearrangement



Ig production: isotype switching



Allelic exclusion

- is a process by which only one allele of a gene is expressed while the other allele is silenced
- holds for both heavy and light chains
- successful chain gene rearrangement of the genetic material from one chromosome results in the shutting down of rearrangement of genetic material from the second chromosome
- every B-lymphocyte produces only one type of heavy and one type og light chains

Clonal restriction

- every B-lymphocyte expresses antibodies specific only to one epitope
- if B-lymphocyte further divides, there is no more V/J or V/D/J rearrangement
- B-lymphocyte and its progeny are identical in their antigenic specificity and in κ or λ chain isotype

Functions of antibodies

- Antibodies are directly protective if they inhibit binding of a microorganism or a toxin to a matching cell receptor.
- Antibodies do not act separately, but they tightly cooperate with other components of immune system.

- neutralization
- opsonization
- complement activation

Functions of antibodies

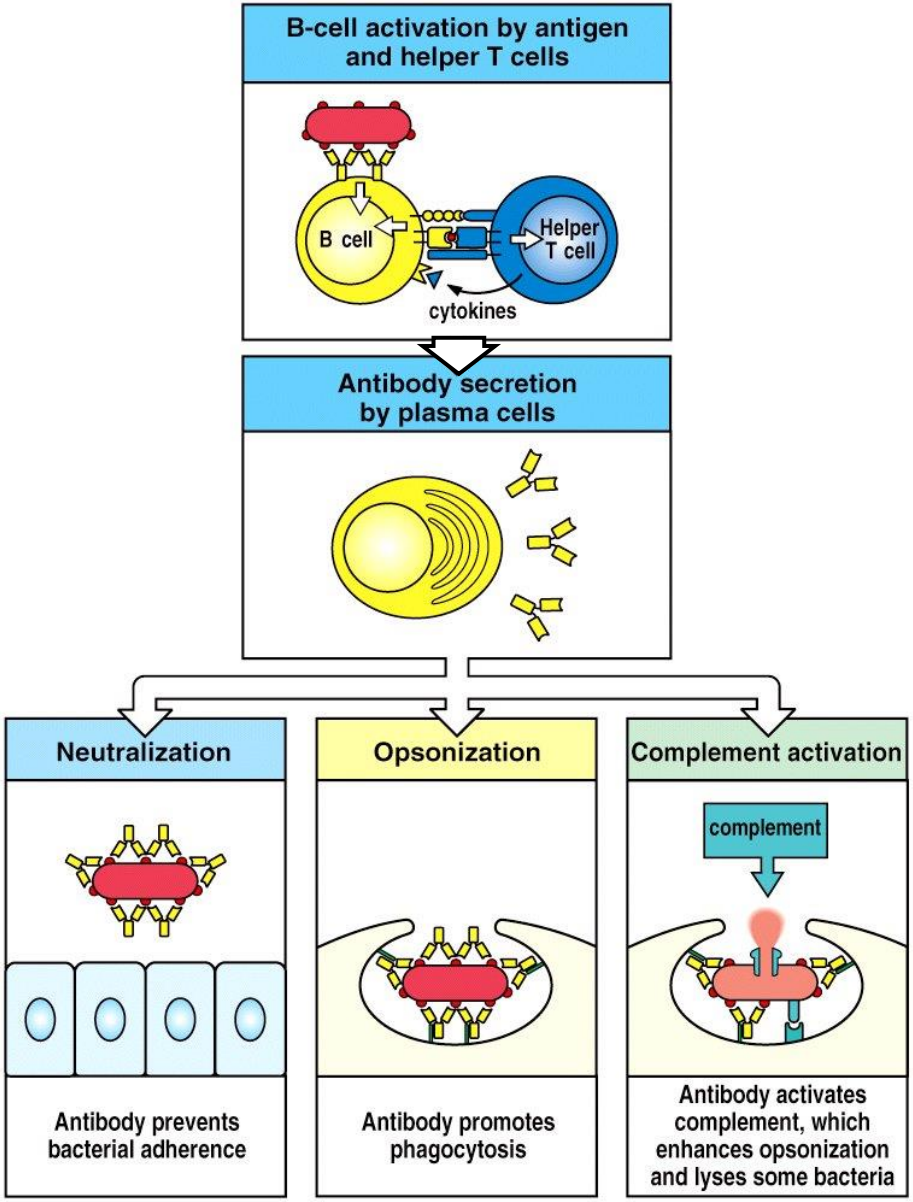


Figure 9-1 Immunobiology, 6/e. (© Garland Science 2005)

Functions of antibodies

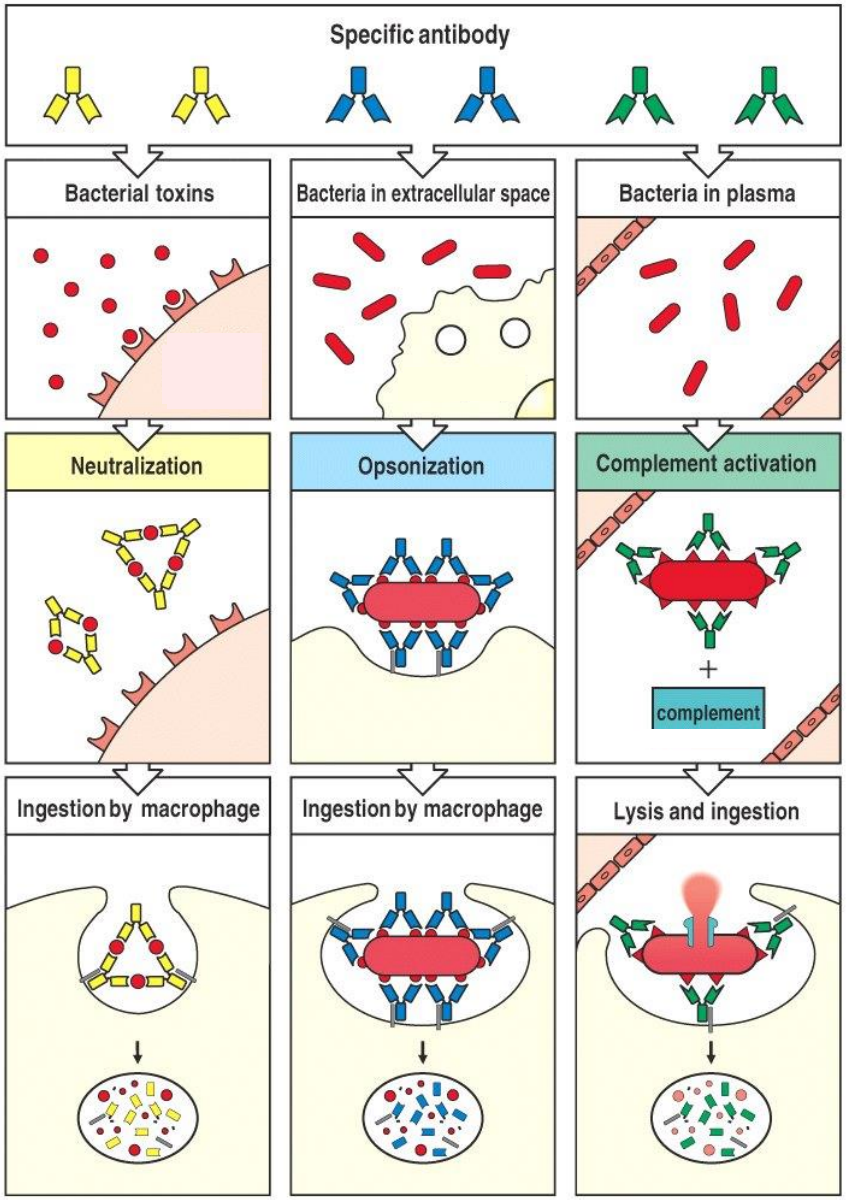


Figure 1-24 Immunobiology, 6/e. (© Garland Science 2005)

Functions of antibodies

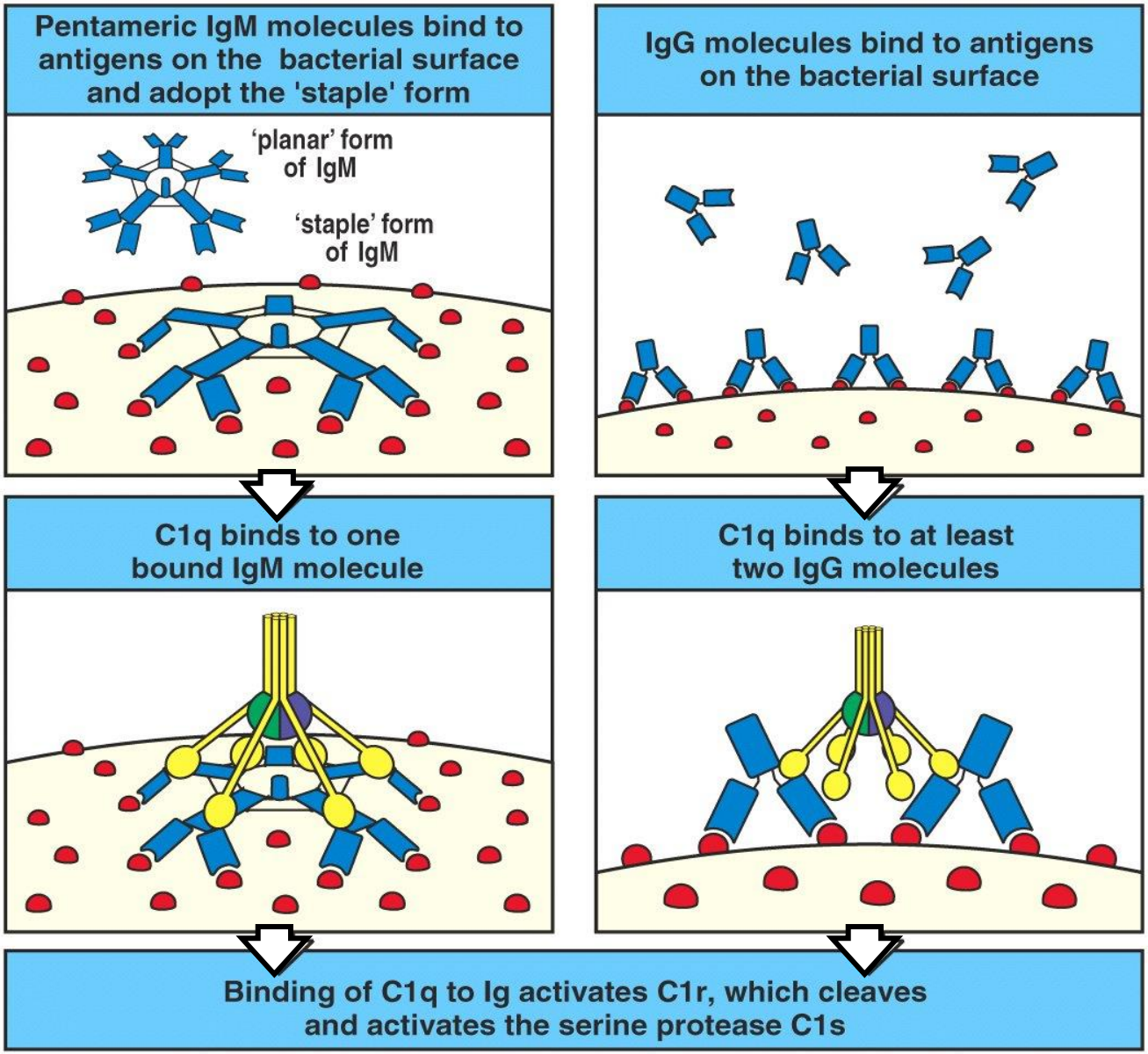


Figure 9-28 Immunobiology, 6/e. (© Garland Science 2005)

Functions of antibodies: ADCC
(Antibody-dependent cell-mediated cytotoxicity)

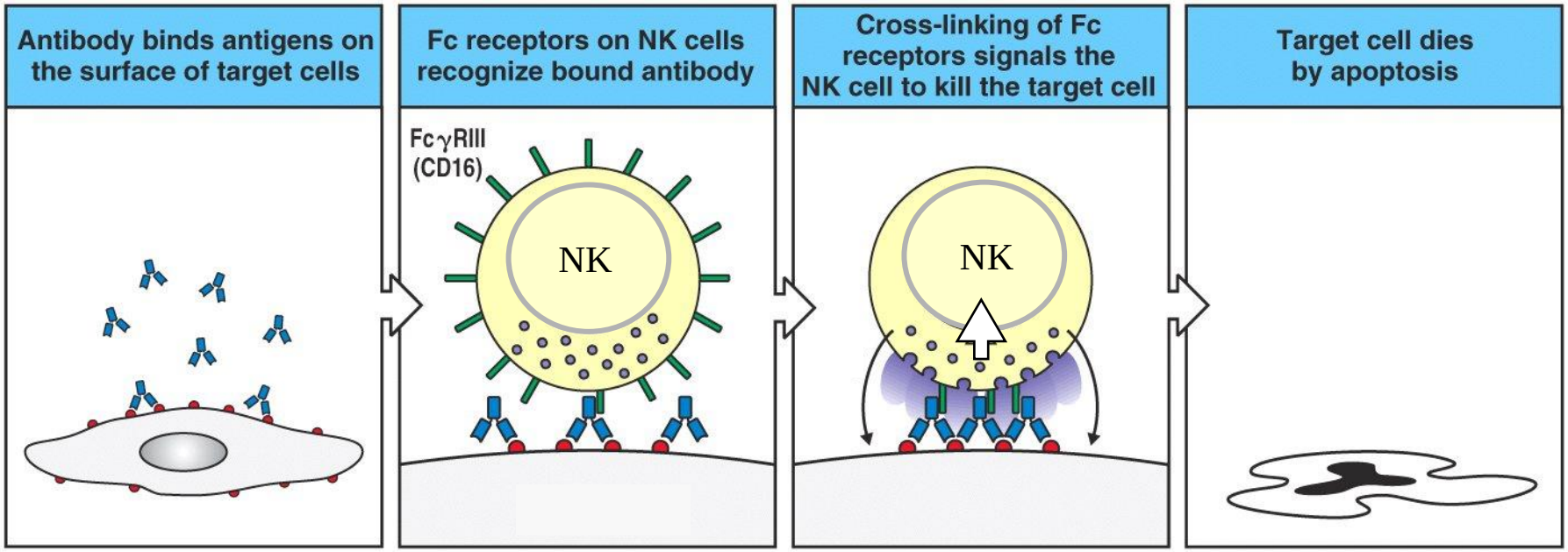
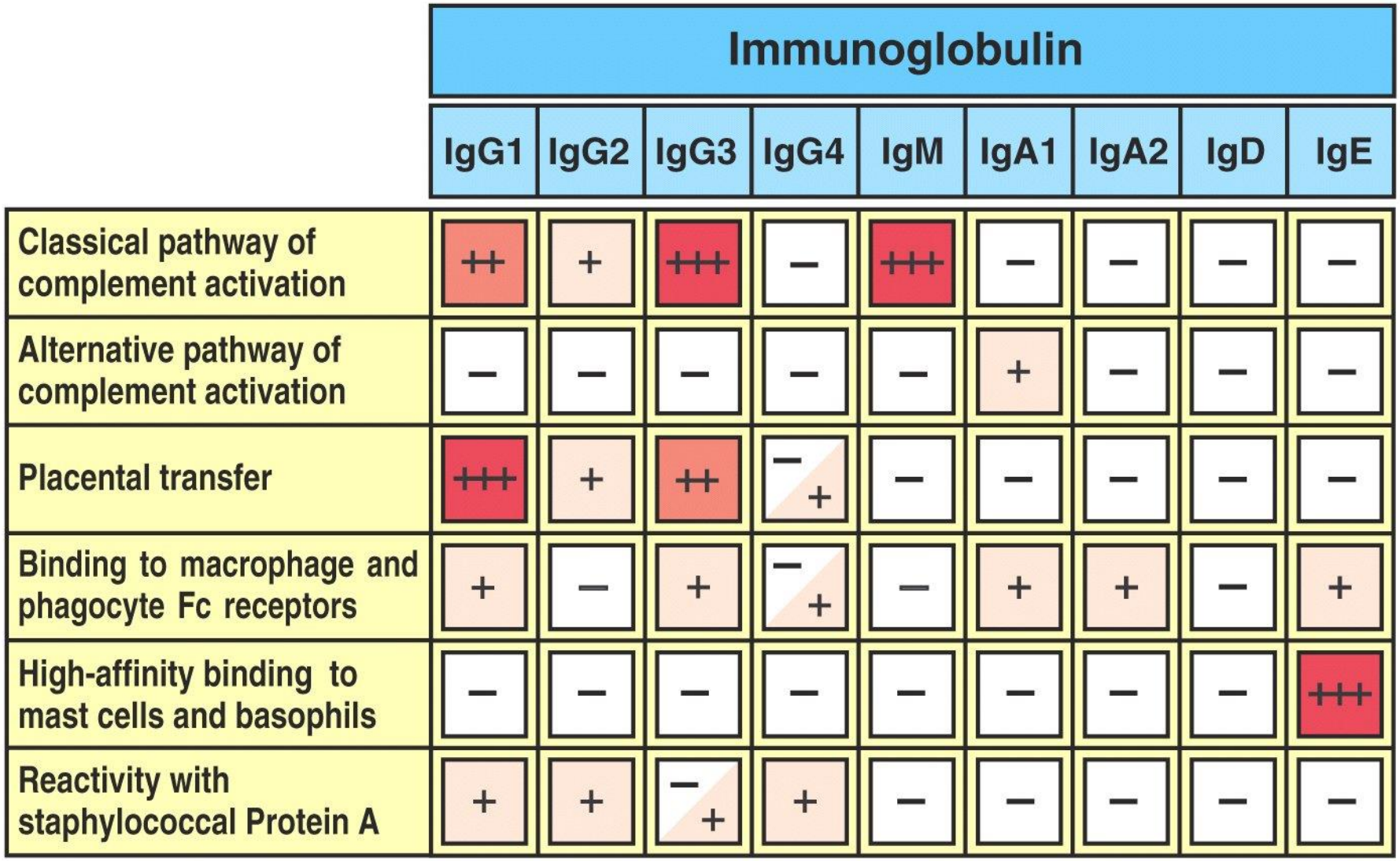


Figure 9-34 Immunobiology, 6/e. (© Garland Science 2005)

Functions of antibodies: isotype classes



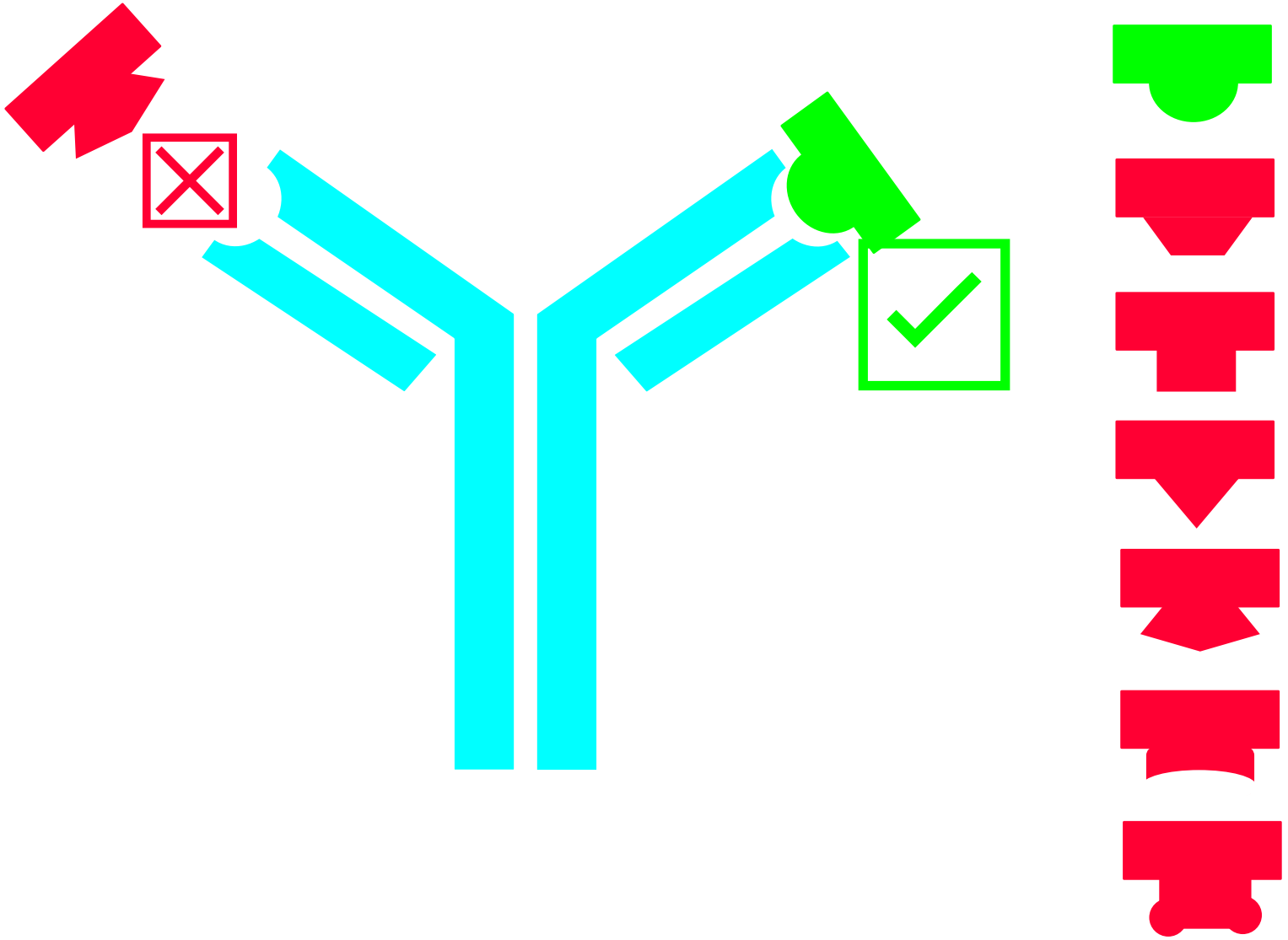
	Immunoglobulin								
	IgG1	IgG2	IgG3	IgG4	IgM	IgA1	IgA2	IgD	IgE
Classical pathway of complement activation	++	+	+++	–	+++	–	–	–	–
Alternative pathway of complement activation	–	–	–	–	–	+	–	–	–
Placental transfer	+++	+	++	–/+	–	–	–	–	–
Binding to macrophage and phagocyte Fc receptors	+	–	+	–/+	–	+	+	–	+
High-affinity binding to mast cells and basophils	–	–	–	–	–	–	–	–	+++
Reactivity with staphylococcal Protein A	+	+	–/+	+	–	–	–	–	–

Figure 4-17 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

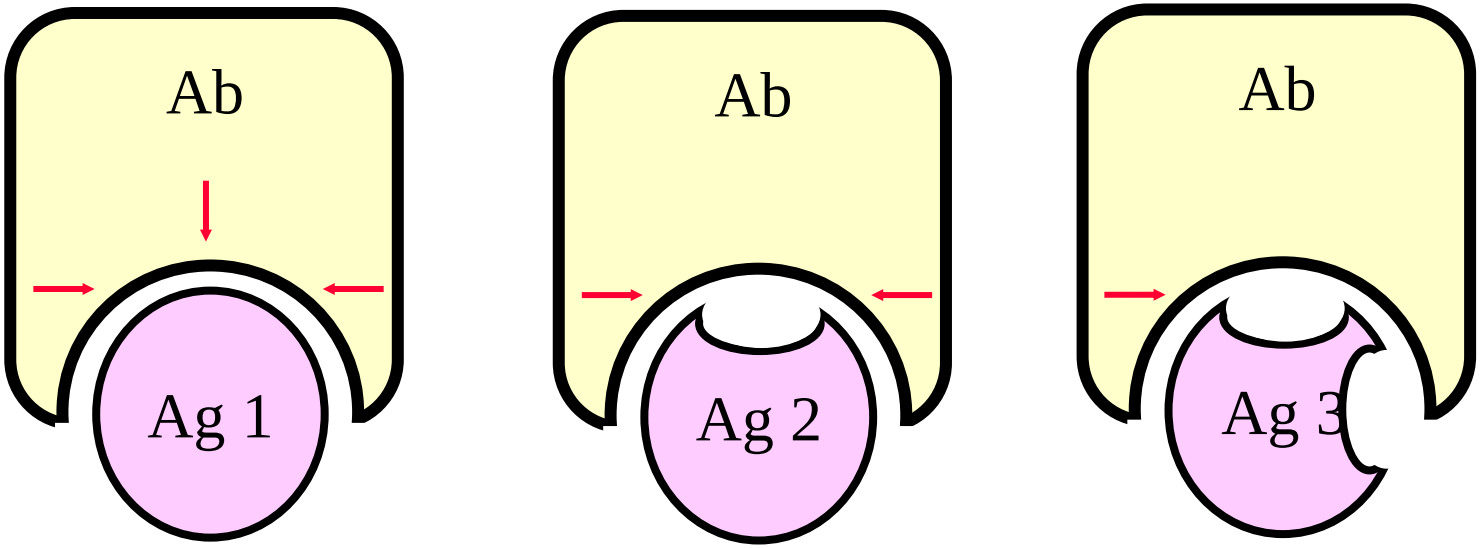
Antigen-antibody reactions: basic terms

- **Affinity** - measures the strength of interaction between an epitope and an antibody's antigen binding site.
- **Avidity** - gives a measure of the overall strength of an antibody-antigen complex. It is dependent on three major parameters:
    - Affinity of the antibody for the epitope
    - Valency of both the antibody and antigen
    - Structural arrangement of the parts that interact
- **Specificity** – the ability of the antibody to discriminate between similar or even dissimilar antigens
- **Cross-reactivity** - occurs when an antibody raised against one specific antigen has a competing high affinity toward a different antigen. This is often the case when two antigens have similar structural regions that the antibody recognizes.

Antigen-antibody reactions: specificity



Antigen-antibody reactions: cross-reactivity



Primary and secondary antibody response

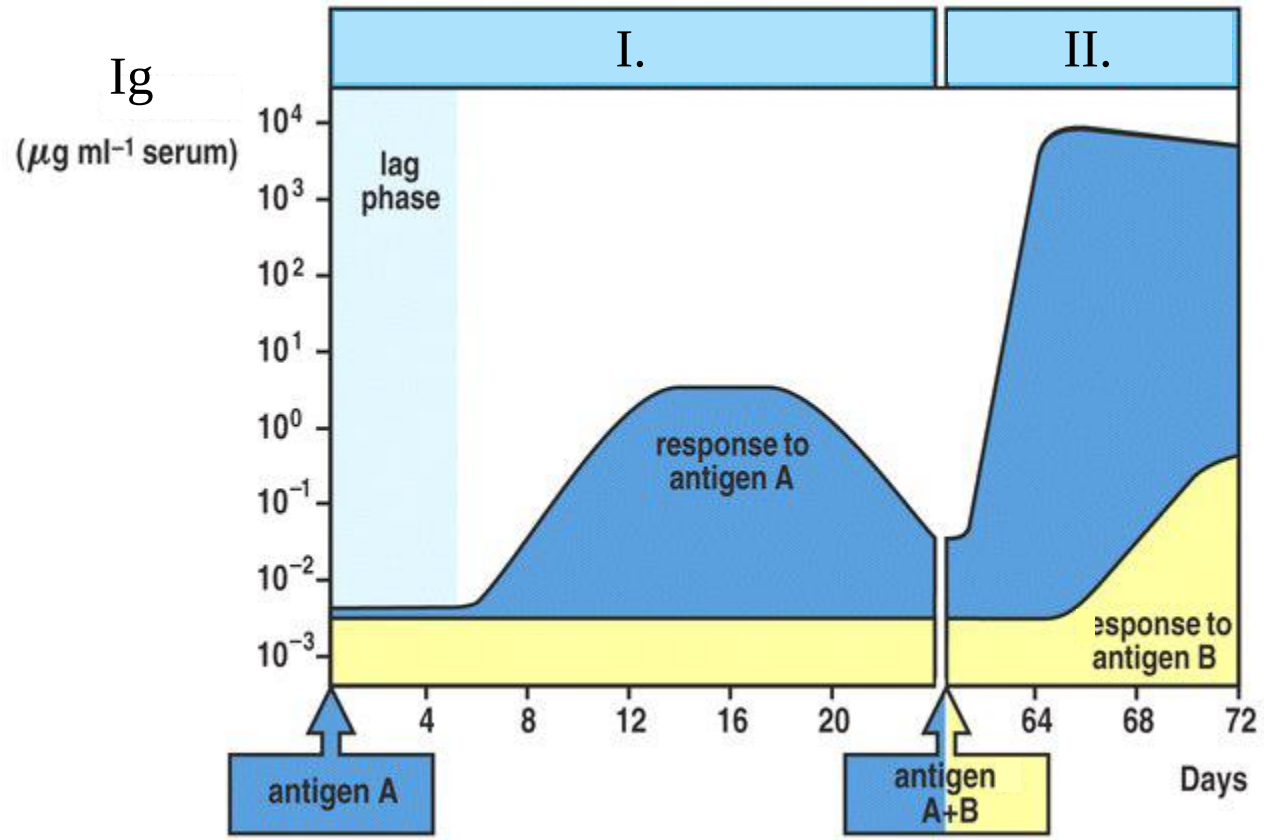
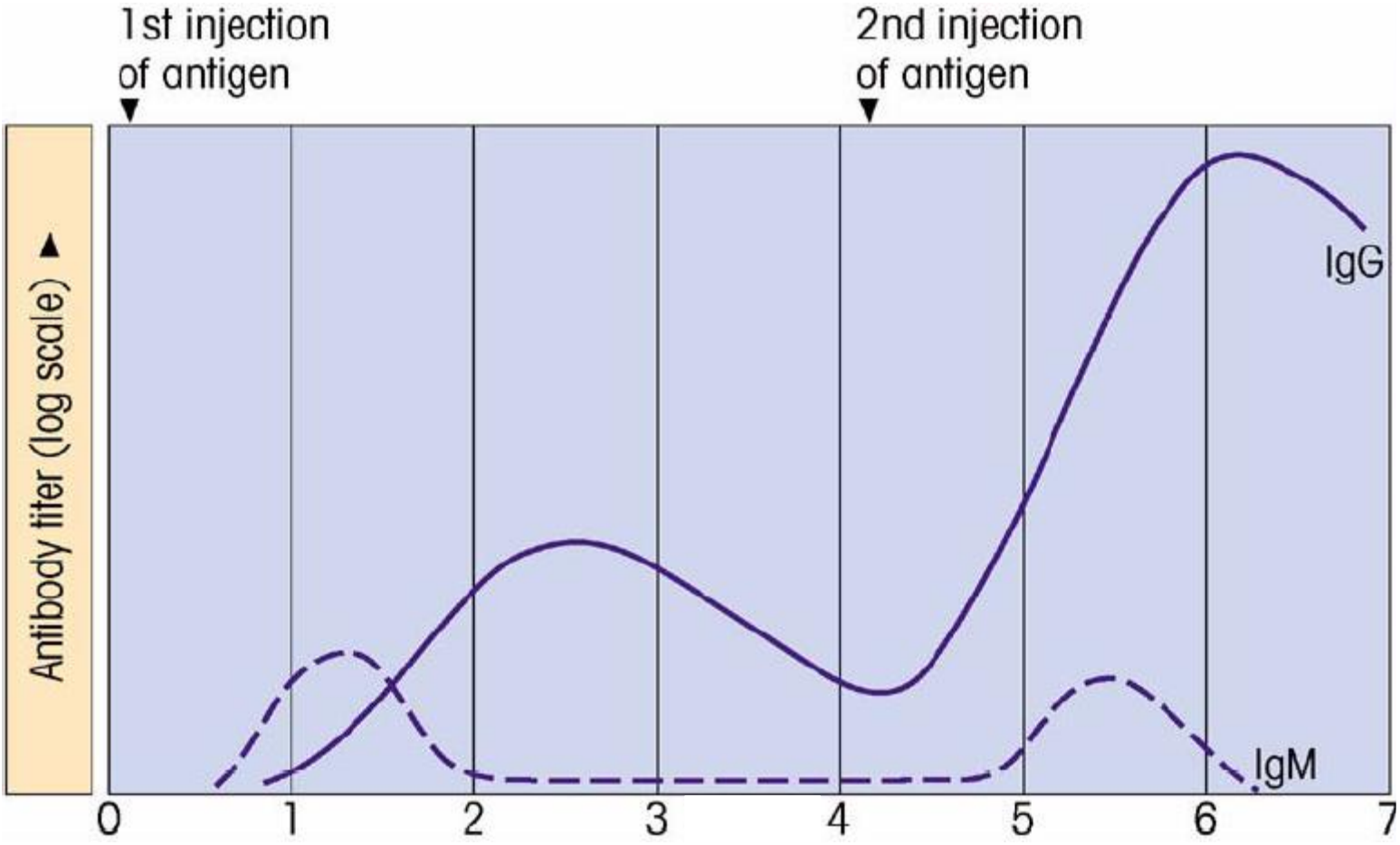


Figure 1-20 Immunobiology, 6/e. (© Garland Science 2005)

Primary and secondary antibody response



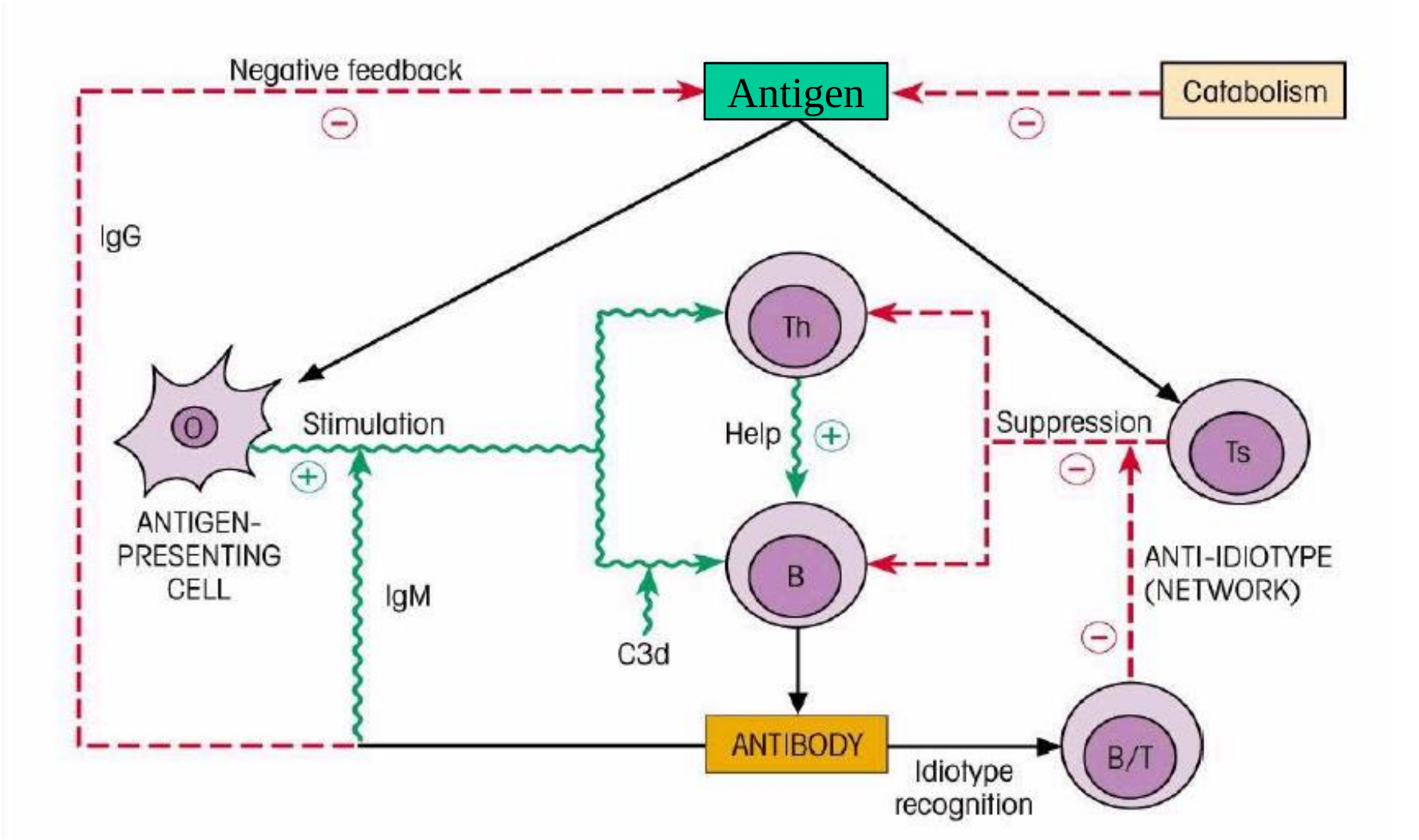
Primary antibody response

- 3-4 days after immunization
- Located in secondary lymphatic organs
- type of response – IgM isotype, low affinity to antigen, hinder antigen spreding
- Ab+Ag immunocomplexes stored on FDC in lymph nodes (for a very long time, perhaps years!) – primary lymphoid follicles
- FDC repeatedly stimulate B lymphocytes (clonal expansion of cells primarily stimulated by Ag)

Secondary antibody response

- requirements: recognition of antigens on FDC in primary lymphoid follicle, signals from Th lymphocytes
- newly divided and differentiated B lymphocytes, mutations in V gene segments for H, L chains
- only B lymphocytes with very high affinity survive, cells with low affinity (non-productive mutations) die
- increased selection and competition of cells, as the amount of antigens (on FDC) decreases
- intensive proliferation and dying
- located in secondary lymphoid follicles in germinal centers
- affinity by 4-6 orders higher than in IgM during primary response

Antibody response regulation

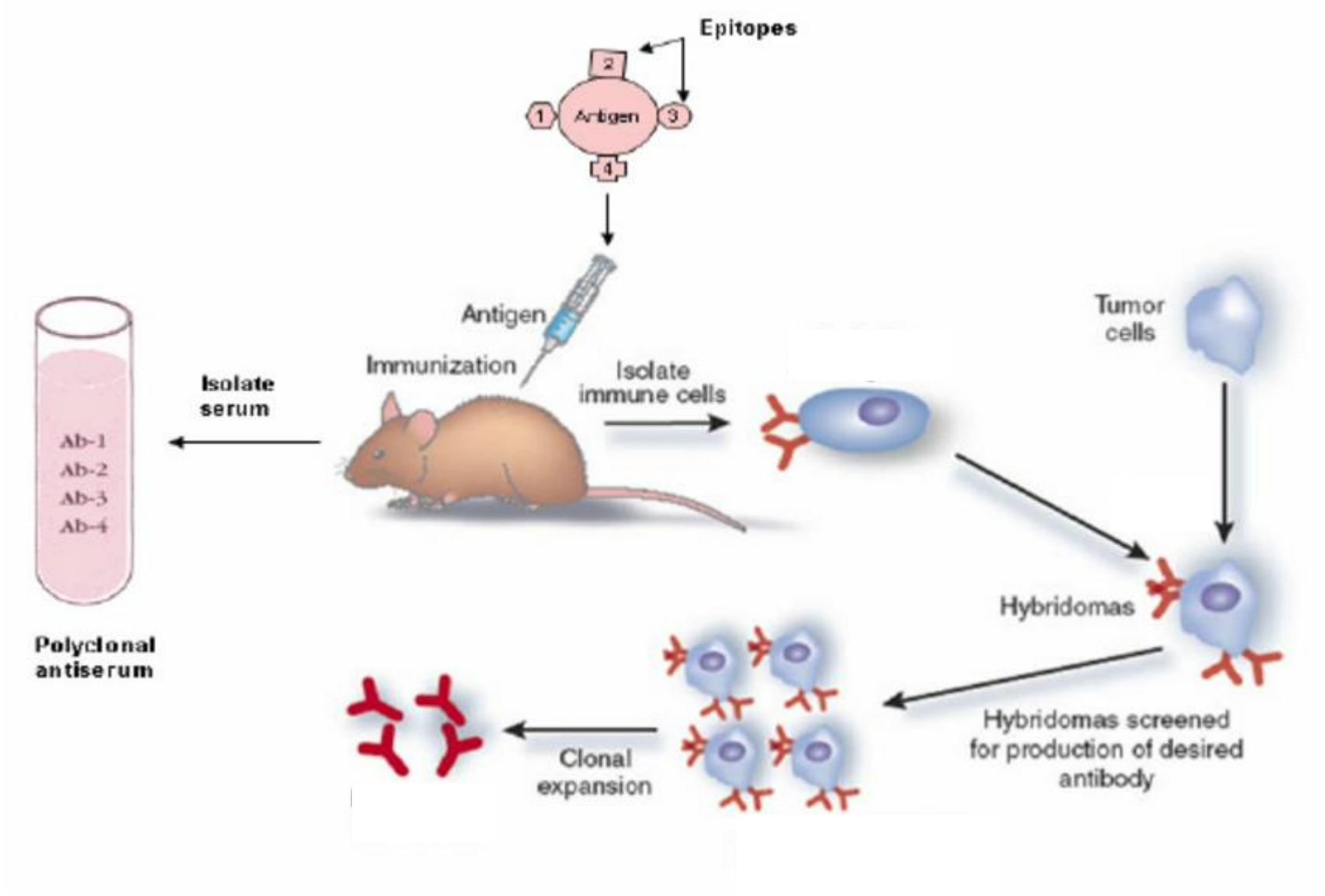


Monoclonal antibodies

- antibodies produced by one B-lymphocyte clone
- artificially generated by hybridization of B-lymphocytes with certain antigen specifity (= produce Ig with the same antigen specifity) and tumor cells (= are „immortal“)
    - tumor cells are $HGPRT^-$ (hypoxanthine-guanine phosphoribosyltransferase)
    - cultivation in HAT-medium (hypoxanthine, aminopterin a thymidine)

- Use of monoclonal antibodies
    - diagnostics (eg. Flow-cytometry, ELISA)
    - therapy (anti-IgE, anti-TNF-α, anti-CD3)

Monoclonal antibodies



Monoclonal antibodies