

Antigen Recognition by B and T Lymphocytes

Dr. Aws Alshamsan
Department of Pharmaceutics
Office: AA87
Tel: 4677363
aalshamsan@ksu.edu.sa

Learning Objectives

By the end of this lecture you will be able to:

- ① Describe the structure and genetics of TCR
- ② Describe the structure and genetics of BCR and **antibodies**
- ③ Differentiate between **monoclonal** and **polyclonal** antibodies

T Cell Receptor (TCR)

- TCR exist either in α/β or γ/δ forms
- The α/β is the most abundant type

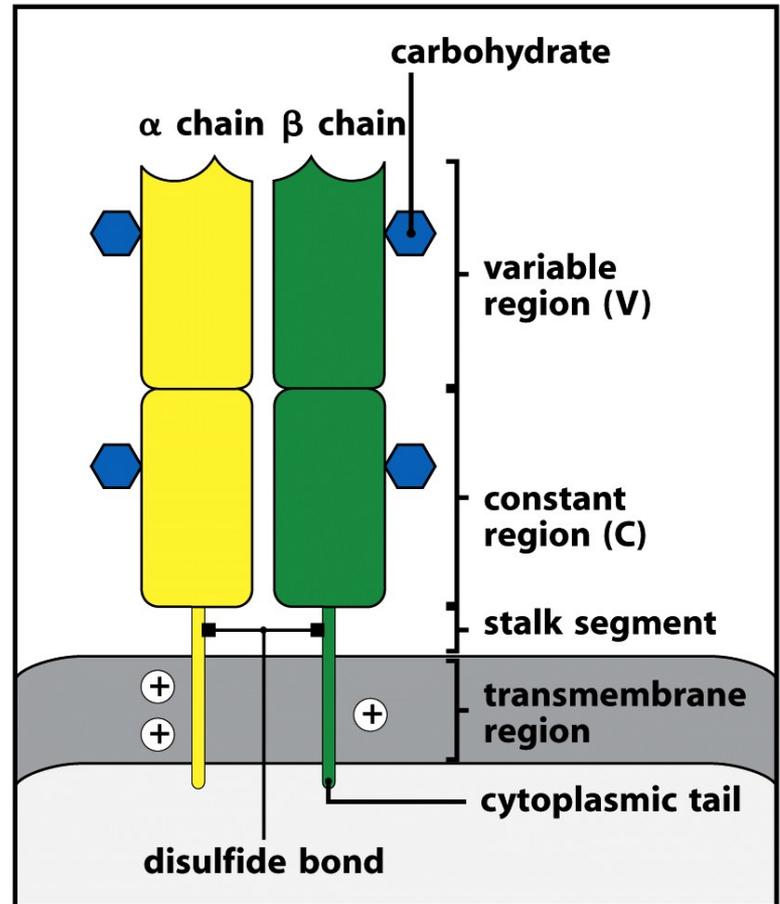
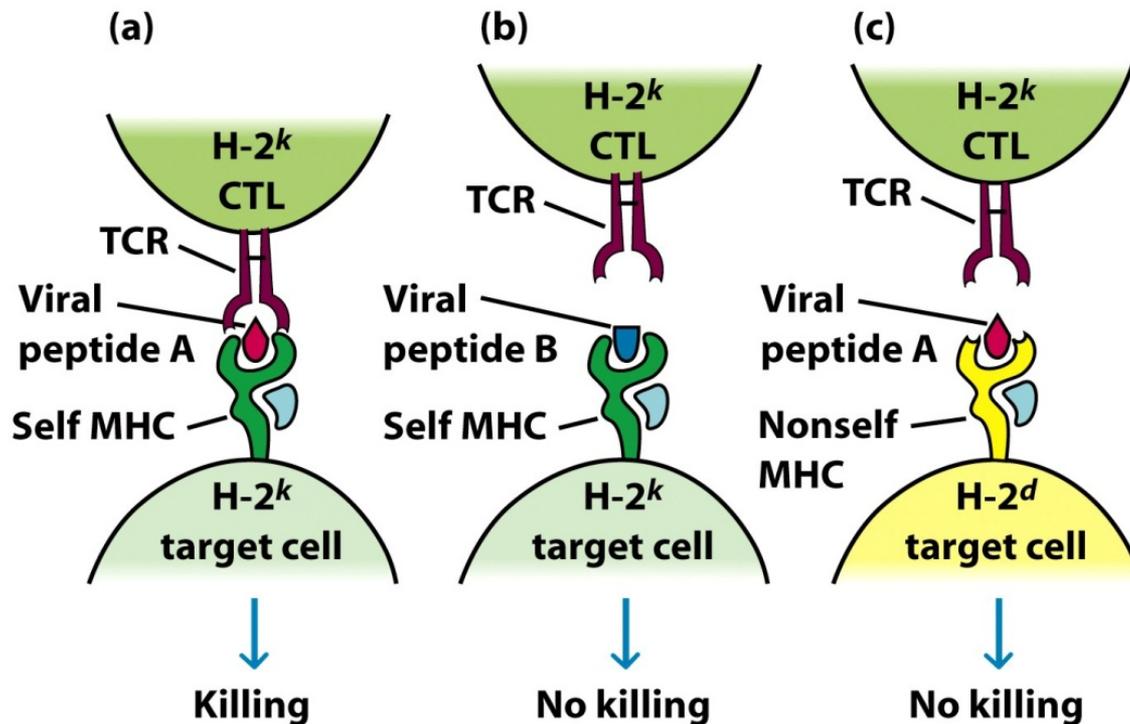


Figure 3-12 Immunobiology, 7ed. (© Garland Science 2008)

T Cell Receptor (TCR)

- Each T cell has more than one TCR that recognize a **single antigen (epitope)** in context of self MHC



T Cell Receptor (TCR)

- TCR has recognition part and signaling part through CD3 complex
- CD3 contains signal transduction motifs known as **immunoreceptor tyrosine-based activation motifs (ITAMs)**

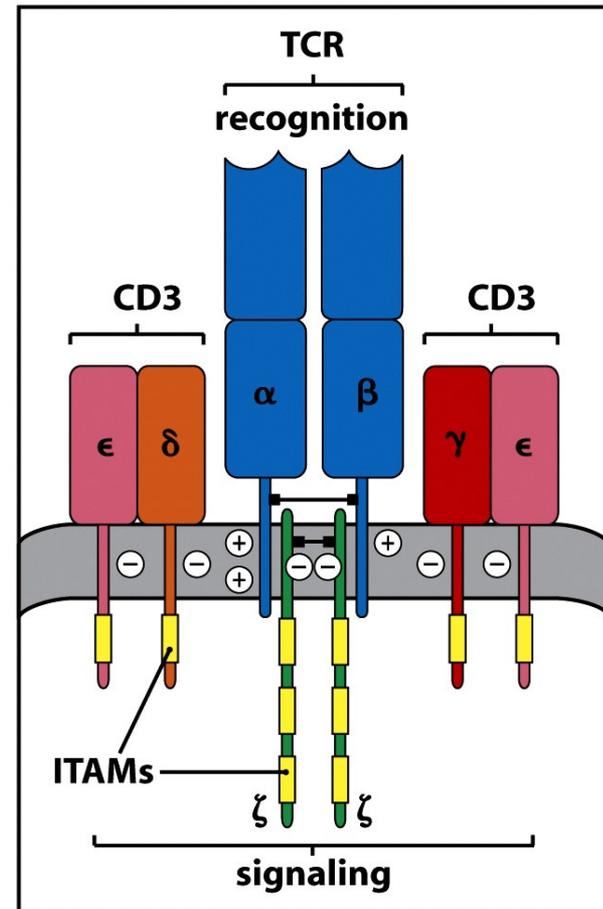


Figure 6-10 Immunobiology, 7ed. (© Garland Science 2008)

T Cell Receptor (TCR)

- Antigen binding to TCR is weak. Therefore, **co-receptors** are required
- CD4 is monomer
- CD8 is dimer

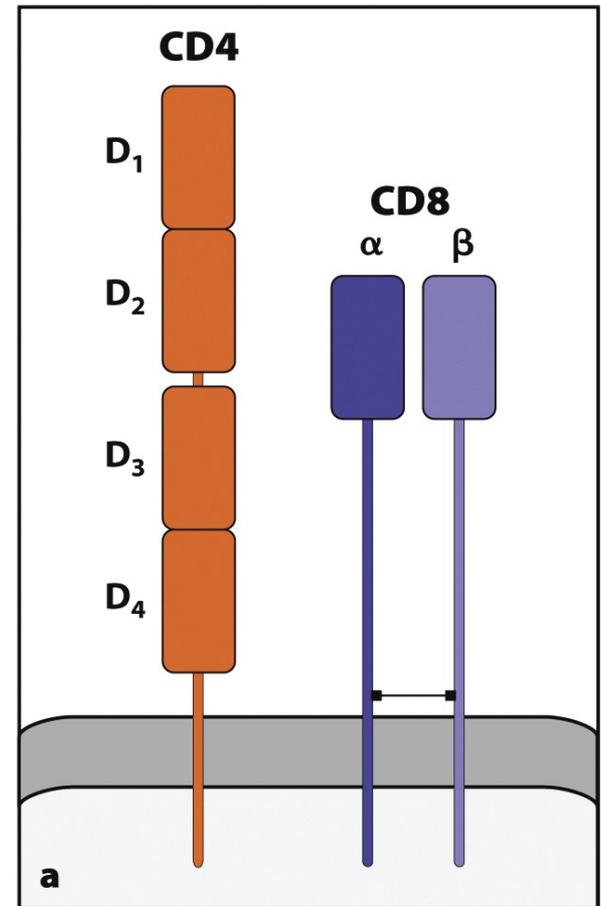


Figure 3-24 Immunobiology, 7ed. (© Garland Science 2008)

T Cell Receptor (TCR)

- Roles of co-receptors:
 - ① Stabilization of TCR-MHC interaction
 - ② Signal transduction

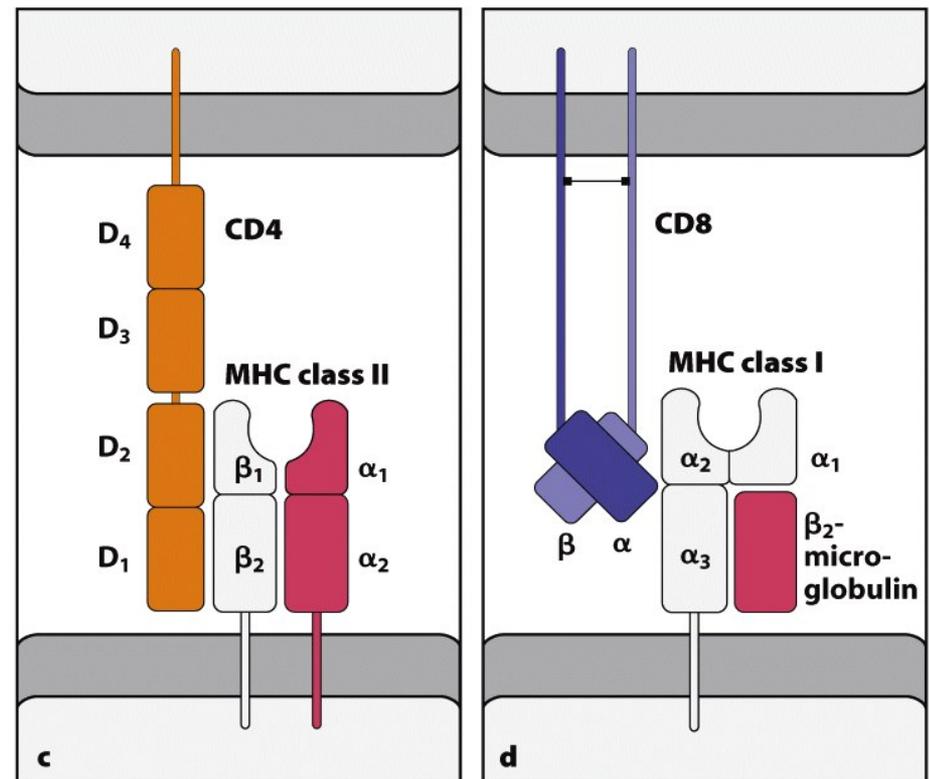


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T Cell Receptor (TCR)

Affinity of TCR for peptide-MHC complexes is enhanced by co-receptors and the formation of **Immunological Synapse**

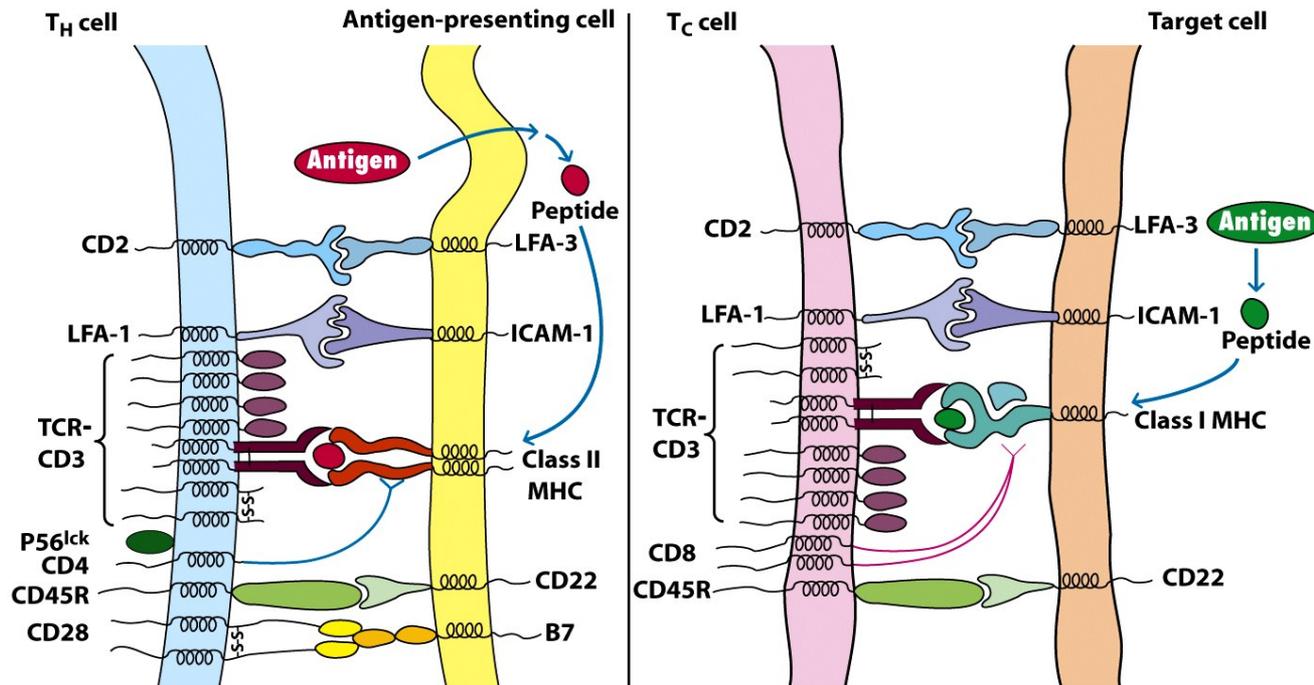


Figure 9-12b
Kuby IMMUNOLOGY, Sixth Edition
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T Cell Accessory Molecules

TABLE 9-4 Selected T-cell accessory molecules

Name	Ligand	FUNCTION		Member of Ig superfamily
		Adhesion	Signal transduction	
CD4	Class II MHC	+	+	
CD8	Class I MHC	+	+	+
CD2 (LFA-2)	CD58 (LFA-3)	+	+	+
LFA-1 (CD11a/CD18)	ICAM-1 (CD54)	+	?	+/(-)
CD28	B7	?	+	+
CTLA-4	B7	?	+	-
CD45R	CD22	+	+	+
CD5	CD72	?	+	-

Table 9-4
Kuby IMMUNOLOGY, Sixth Edition
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T Cell Receptor (TCR)

- **Complementarity determining regions (CDRs)** are hypervariable regions in the TCR. The role of CDRs is binding with MHC
- CDR3 has the most sequence variability

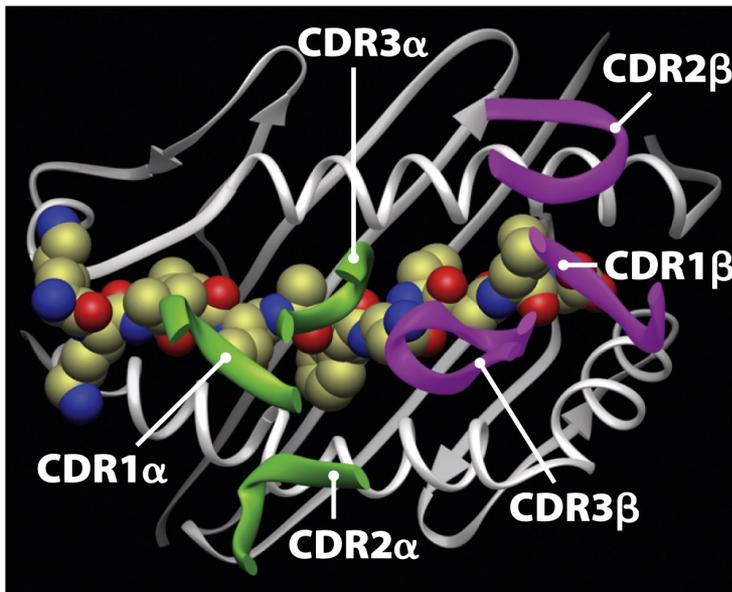


Figure 4-13 Immunobiology, 7ed. (© Garland Science 2008)

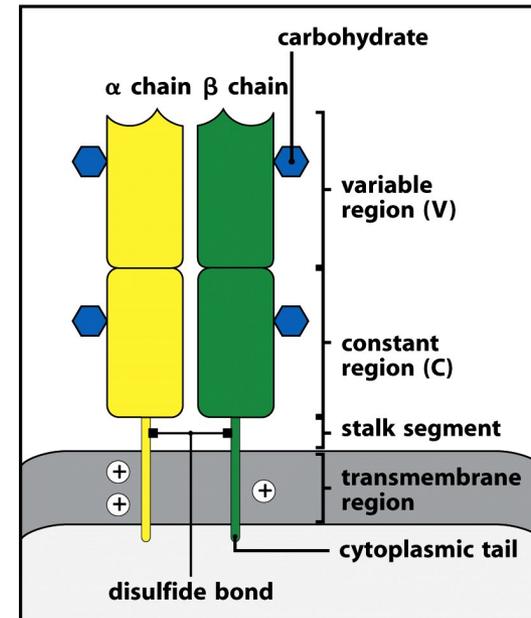


Figure 3-12 Immunobiology, 7ed. (© Garland Science 2008)

TCR Rearrangement

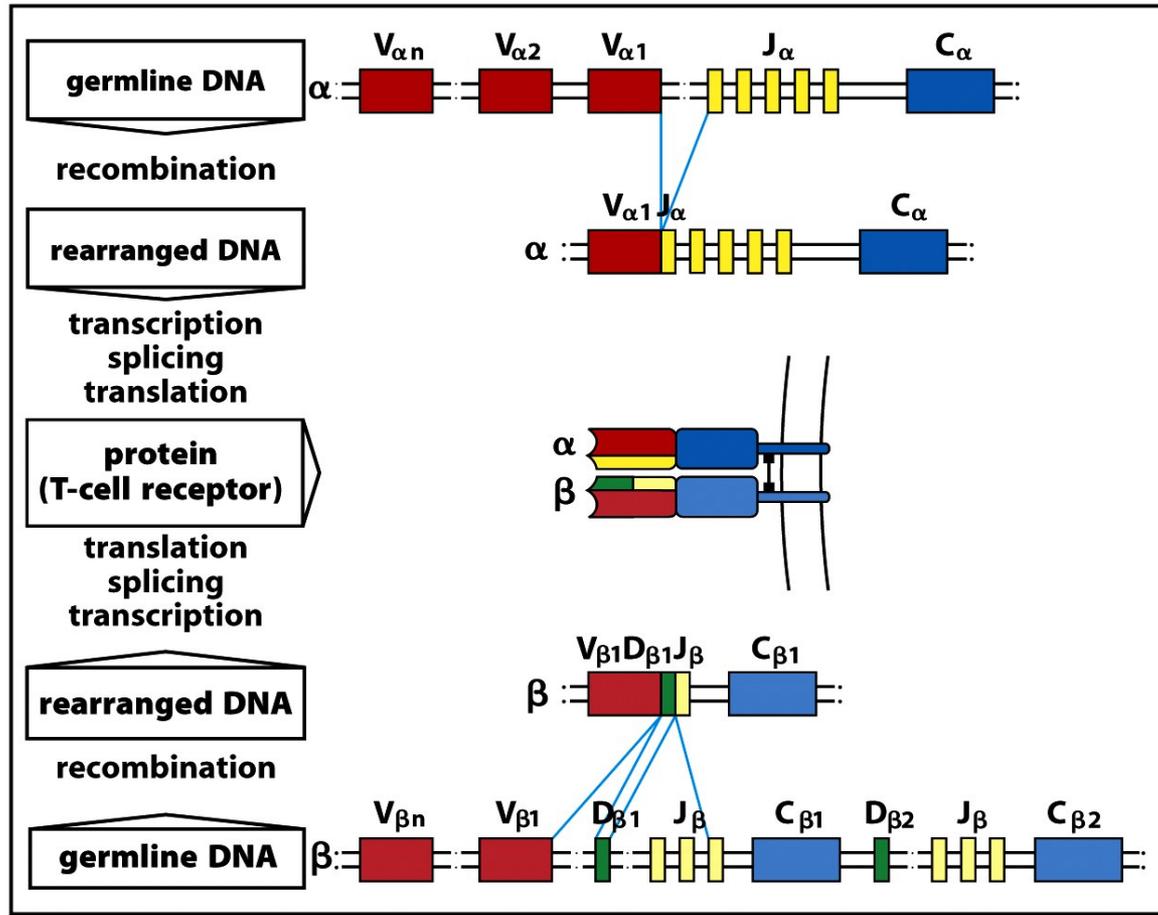


Figure 4-10 Immunobiology, 7ed. (© Garland Science 2008)

B Cell Receptor (BCR)

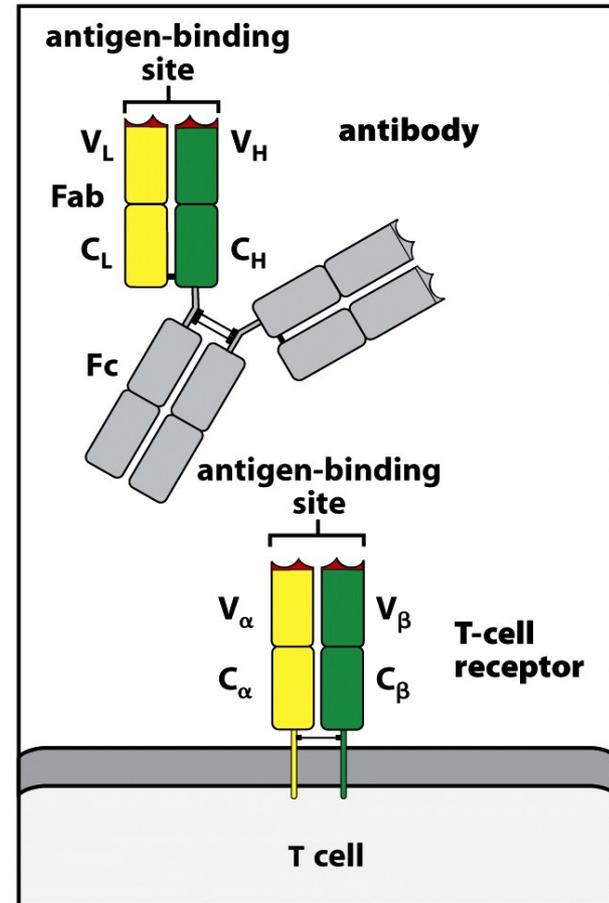
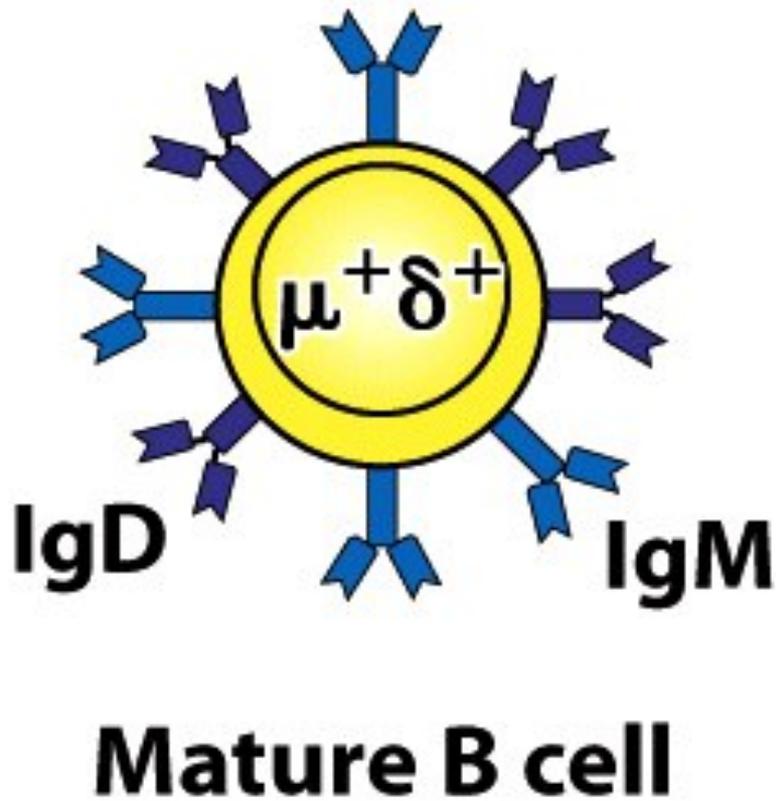


Figure 3-11 Immunobiology, 7ed. (© Garland Science 2008)

B Cell Receptor (BCR)

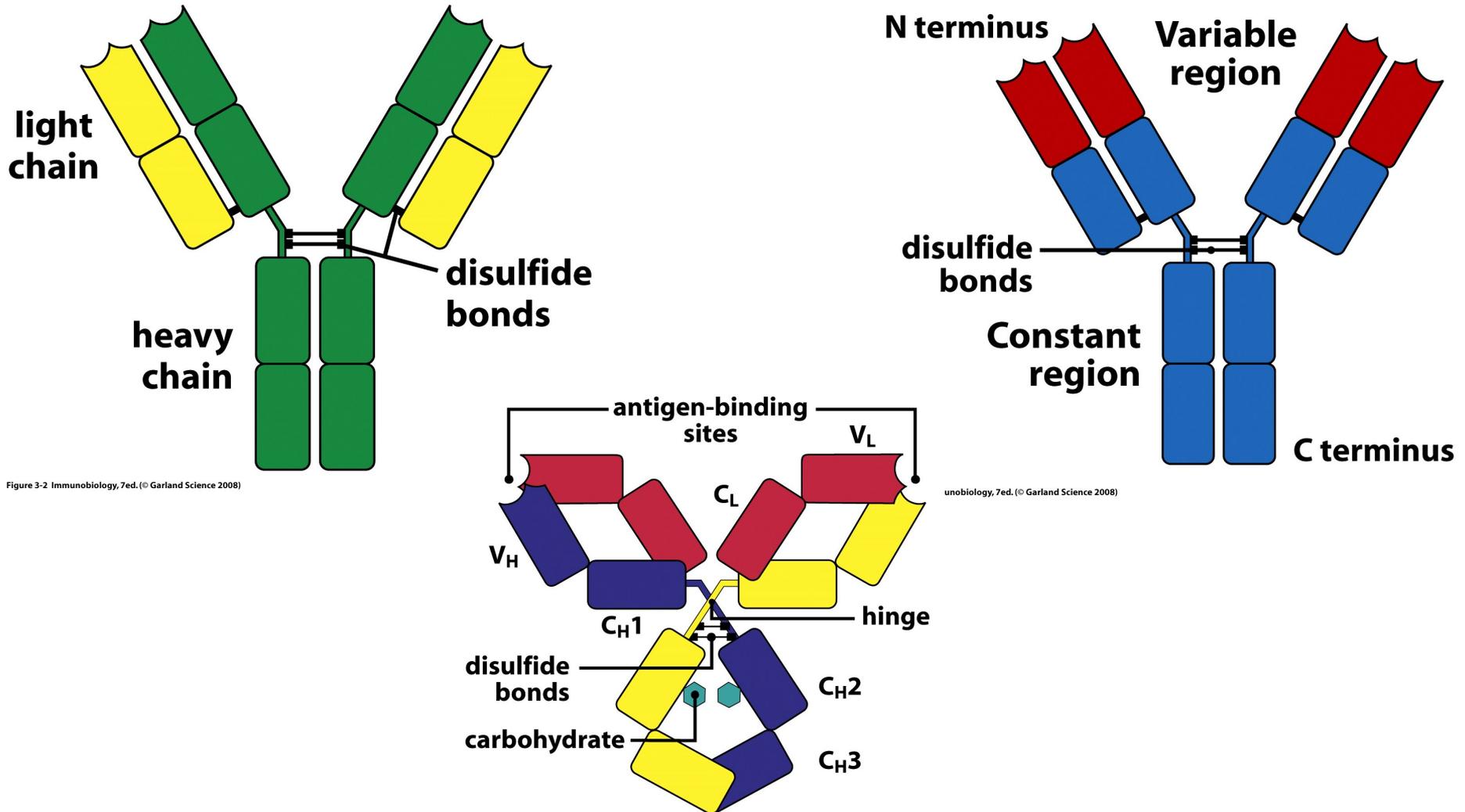


Figure 3-2 Immunobiology, 7ed. (© Garland Science 2008)

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Figure 3-1b Immunobiology, 7ed. (© Garland Science 2008)

B Cell Receptor (BCR)

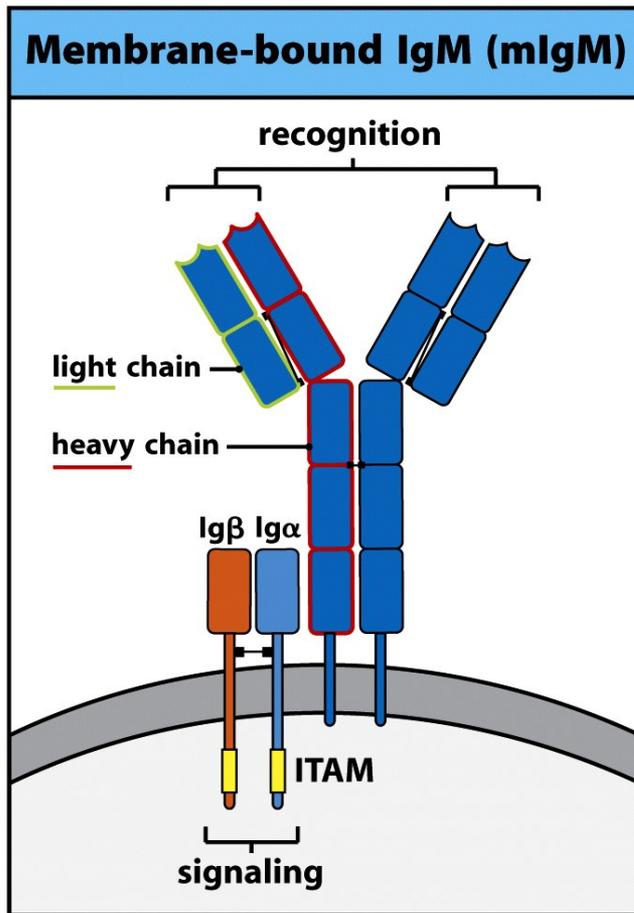


Figure 6-9 Immunobiology, 7ed. (© Garland Science 2008)

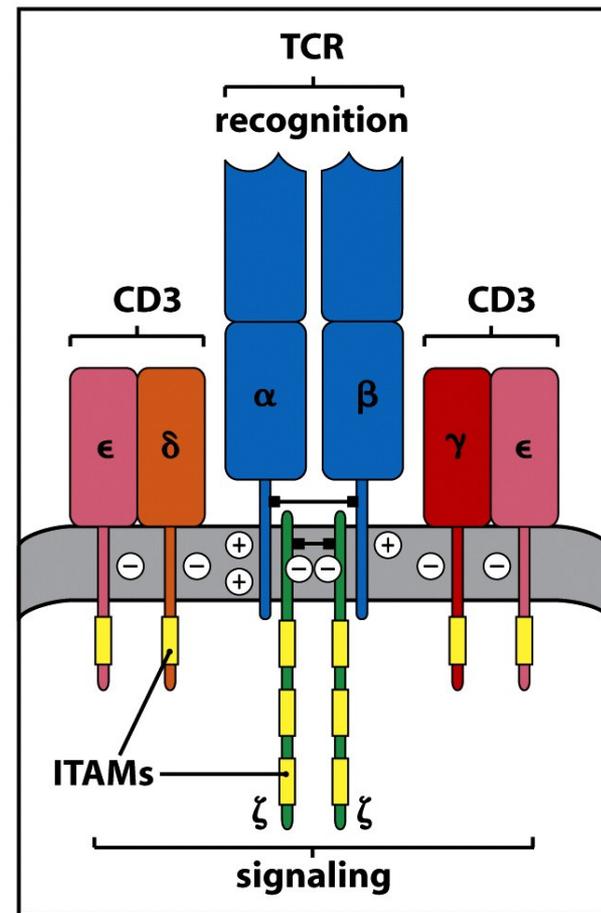


Figure 6-10 Immunobiology, 7ed. (© Garland Science 2008)

B Cell Receptor (BCR)

- BCR has the ability of direct recognition and binding to antigens

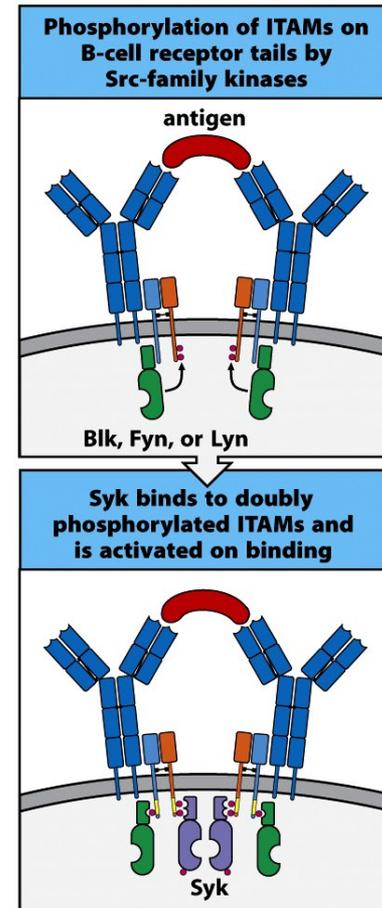


Figure 6-24 Immunobiology, 7ed. (© Garland Science 2008)

BCR Rearrangement

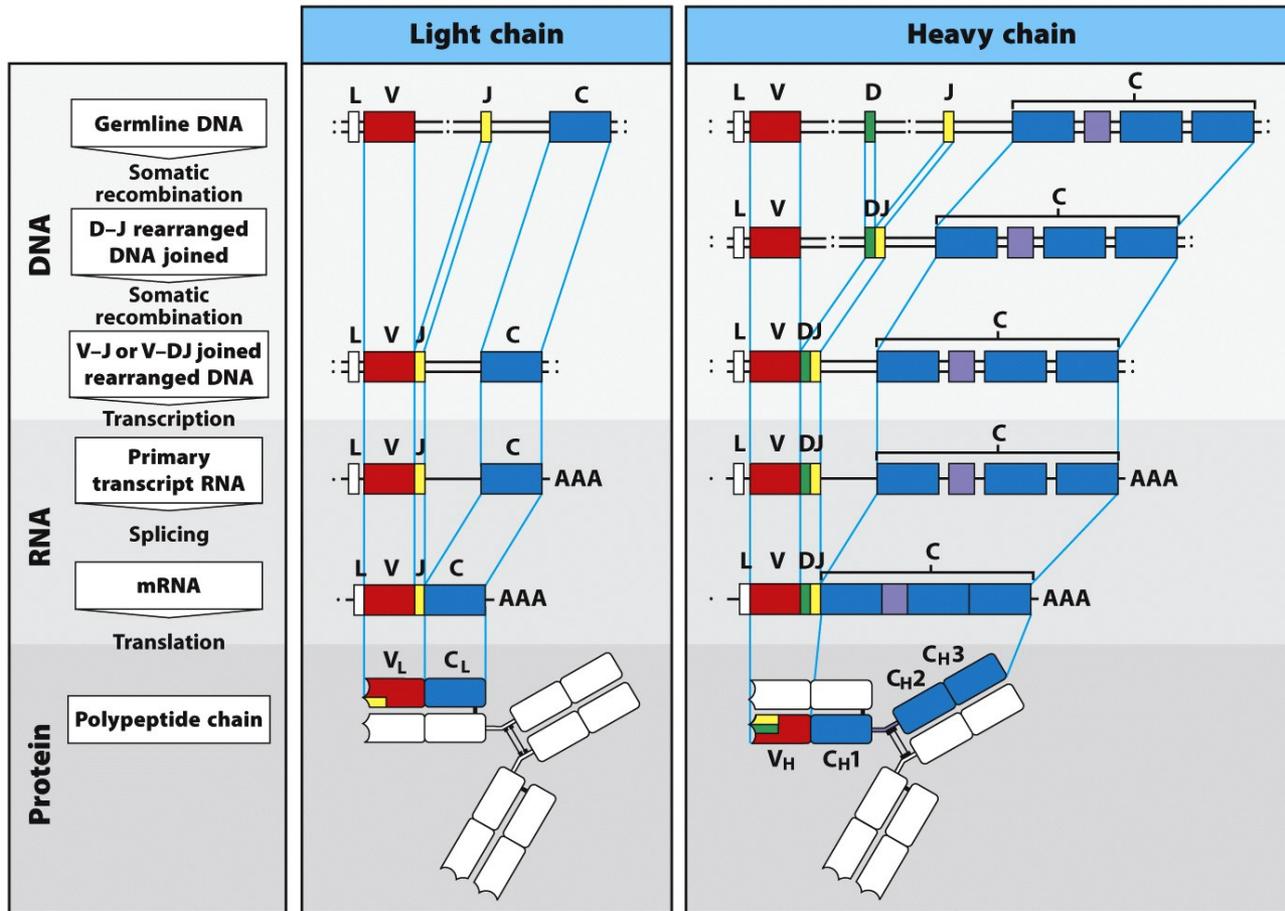


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BCR Rearrangement

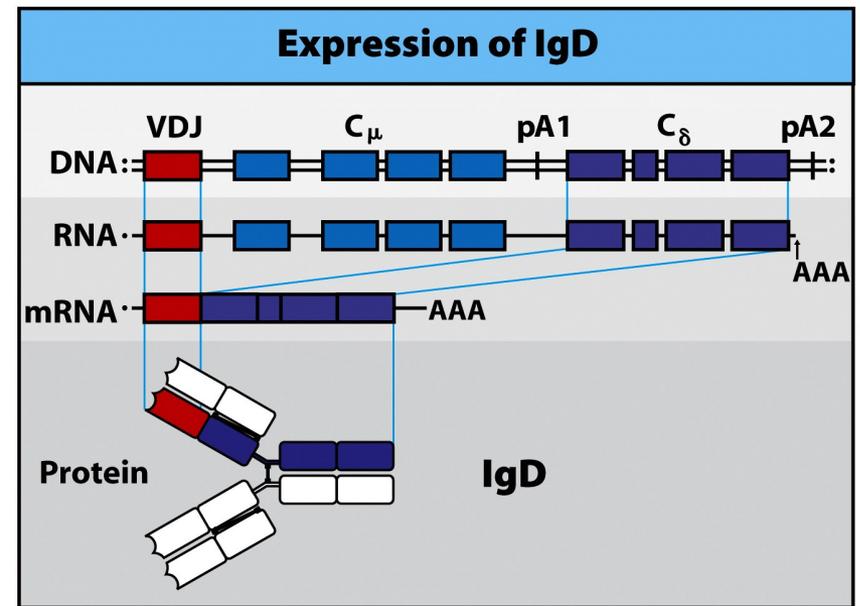
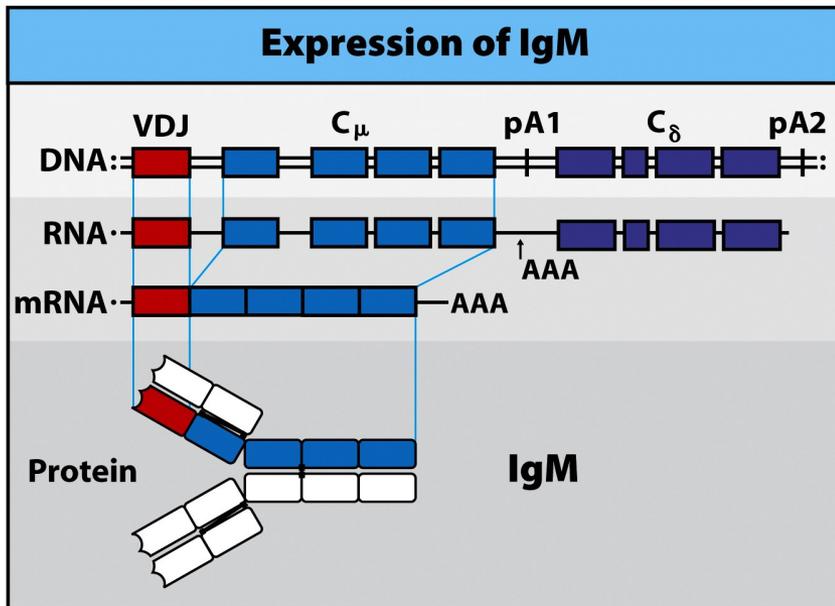


Figure 4-18 part 1 of 2 Immunobiology, 7ed. (© Garland Science 2008)

Figure 4-18 part 2 of 2 Immunobiology, 7ed. (© Garland Science 2008)

Antibodies

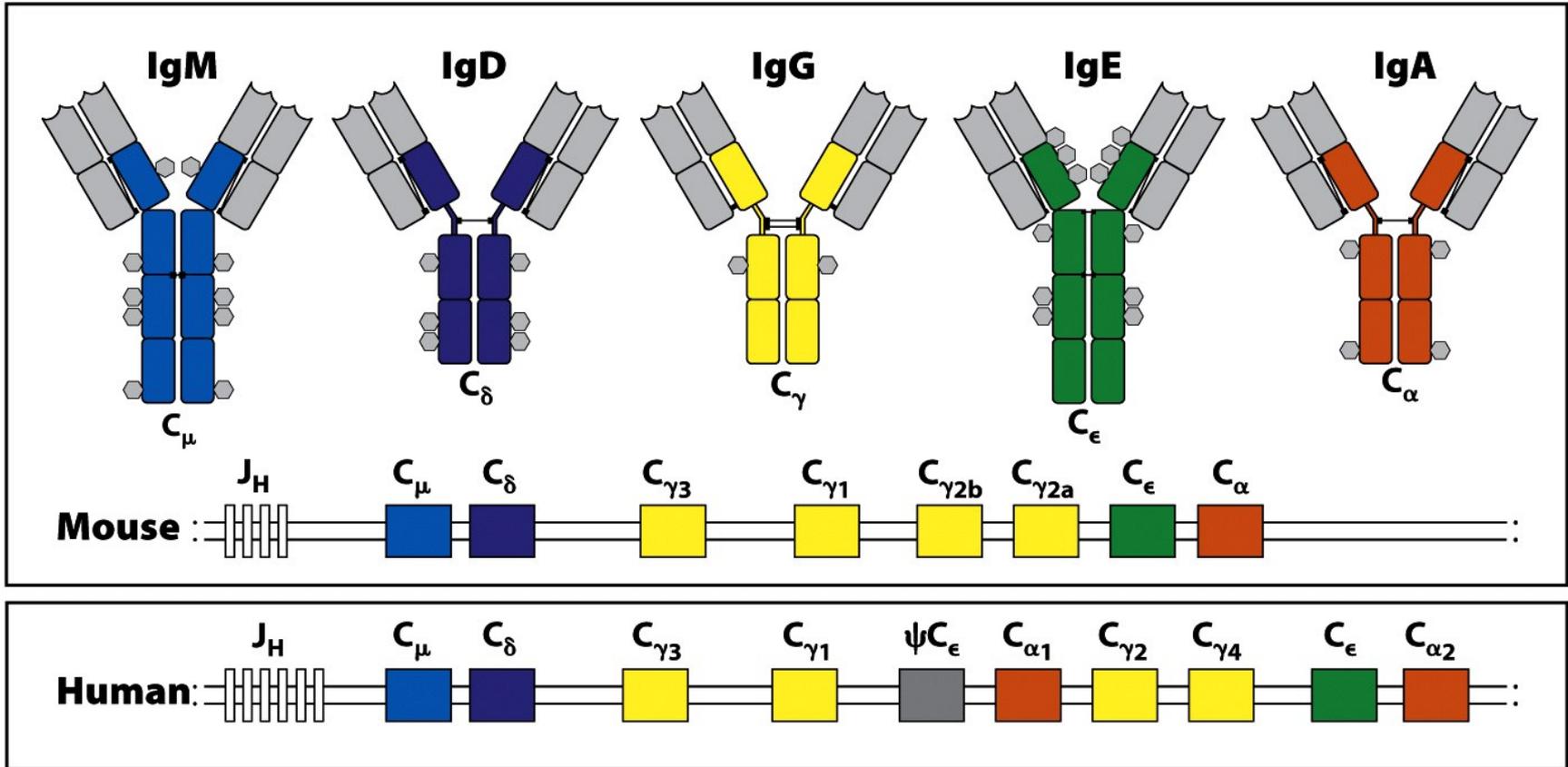
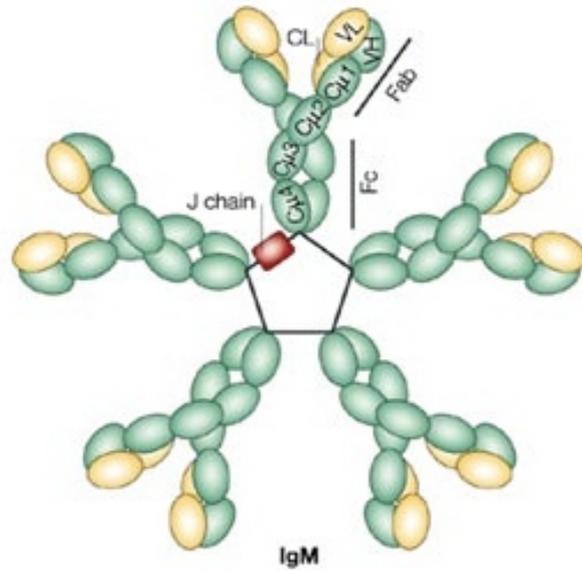
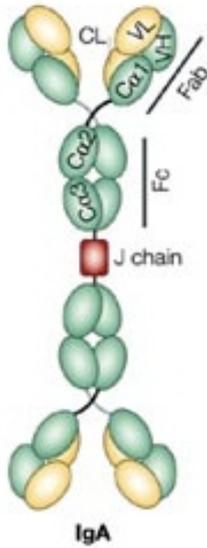
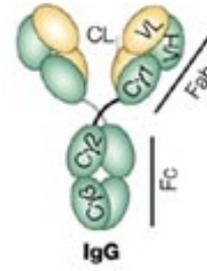
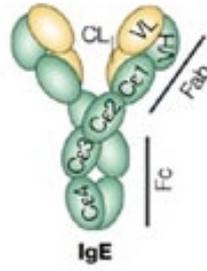
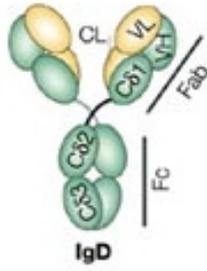
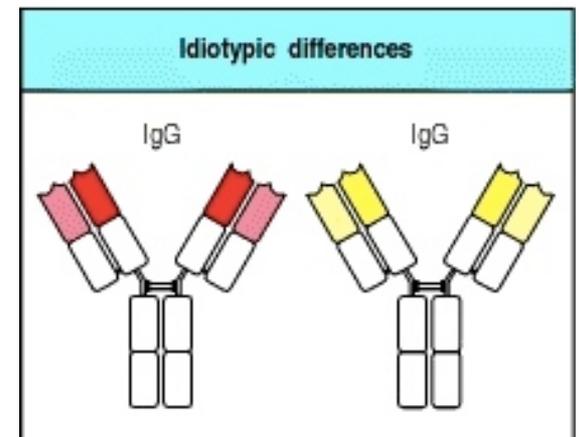
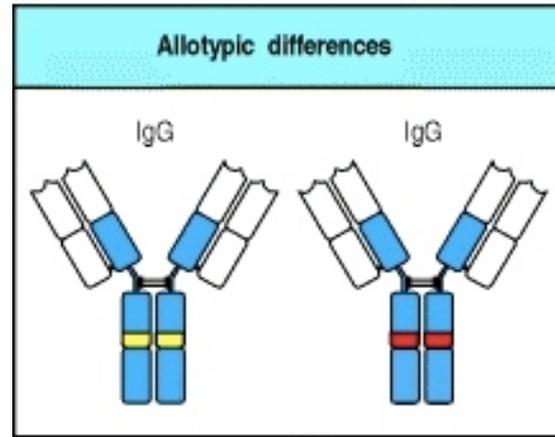
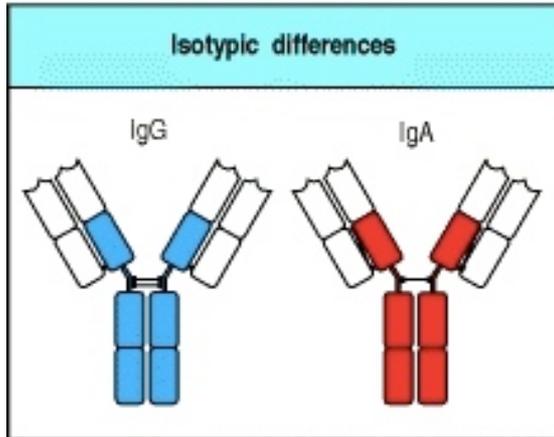
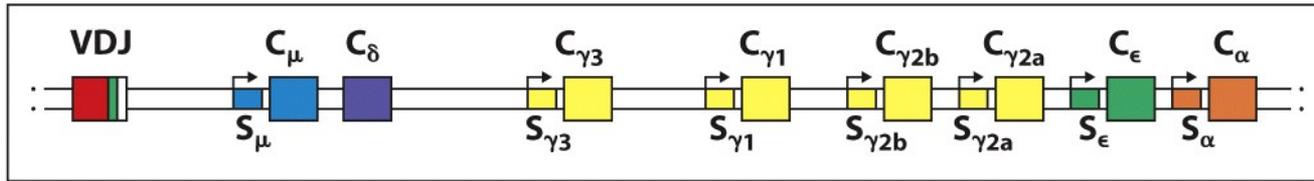


Figure 4-17 Immunobiology, 7ed. (© Garland Science 2008)

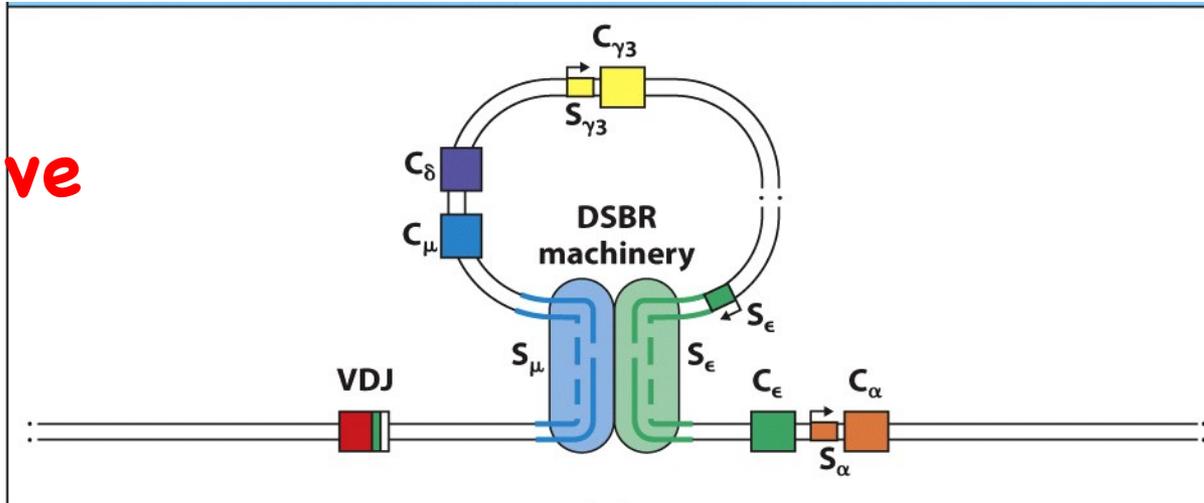


Antibodies Differences

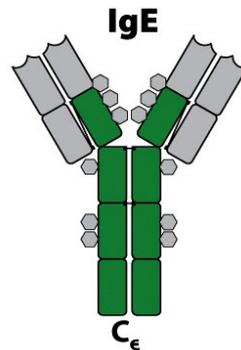
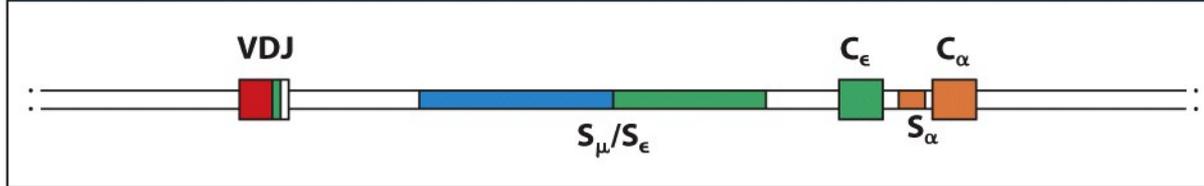




Alternative Splicing



The selected constant region is now located adjacent to the VDJ region



Antibody Diversity

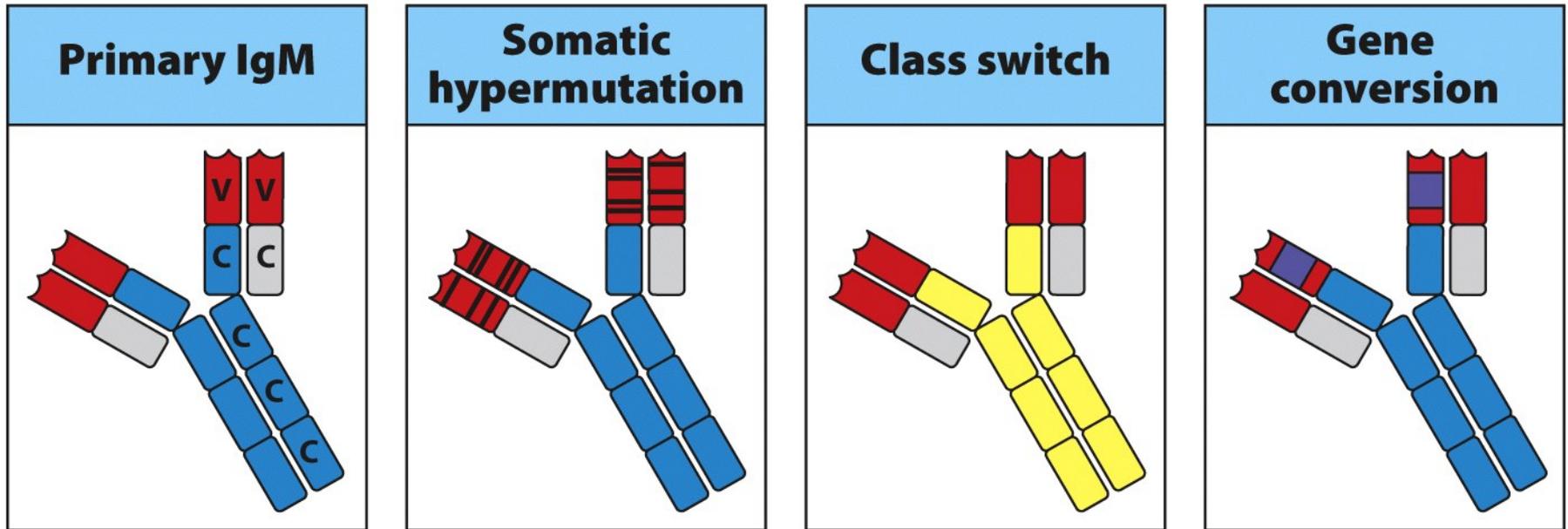


Figure 5.20 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Antibody Diversity

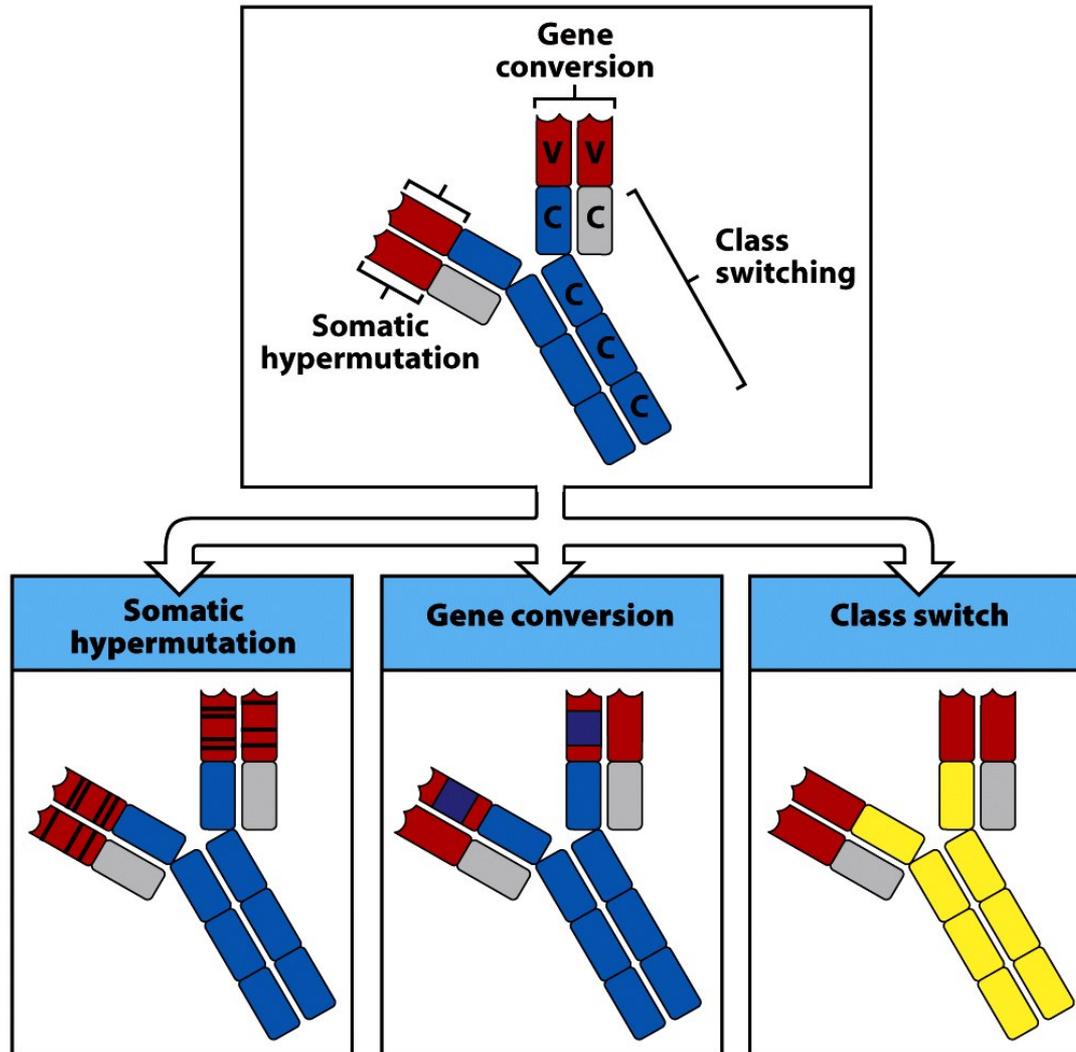
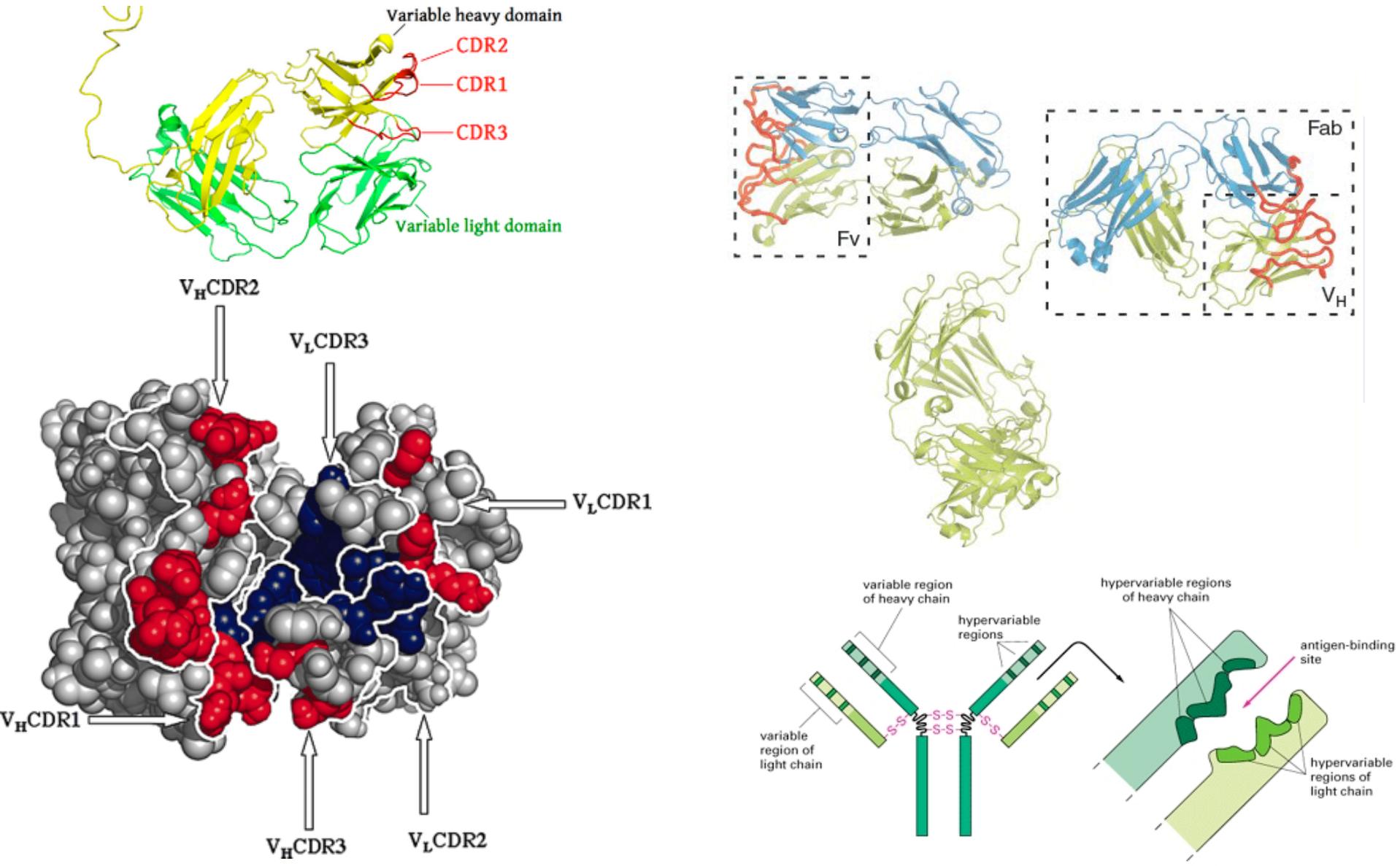


Figure 4-21 Immunobiology, 7ed. (© Garland Science 2008)

Complementarity Determining Regions



CDRs of Antibodies

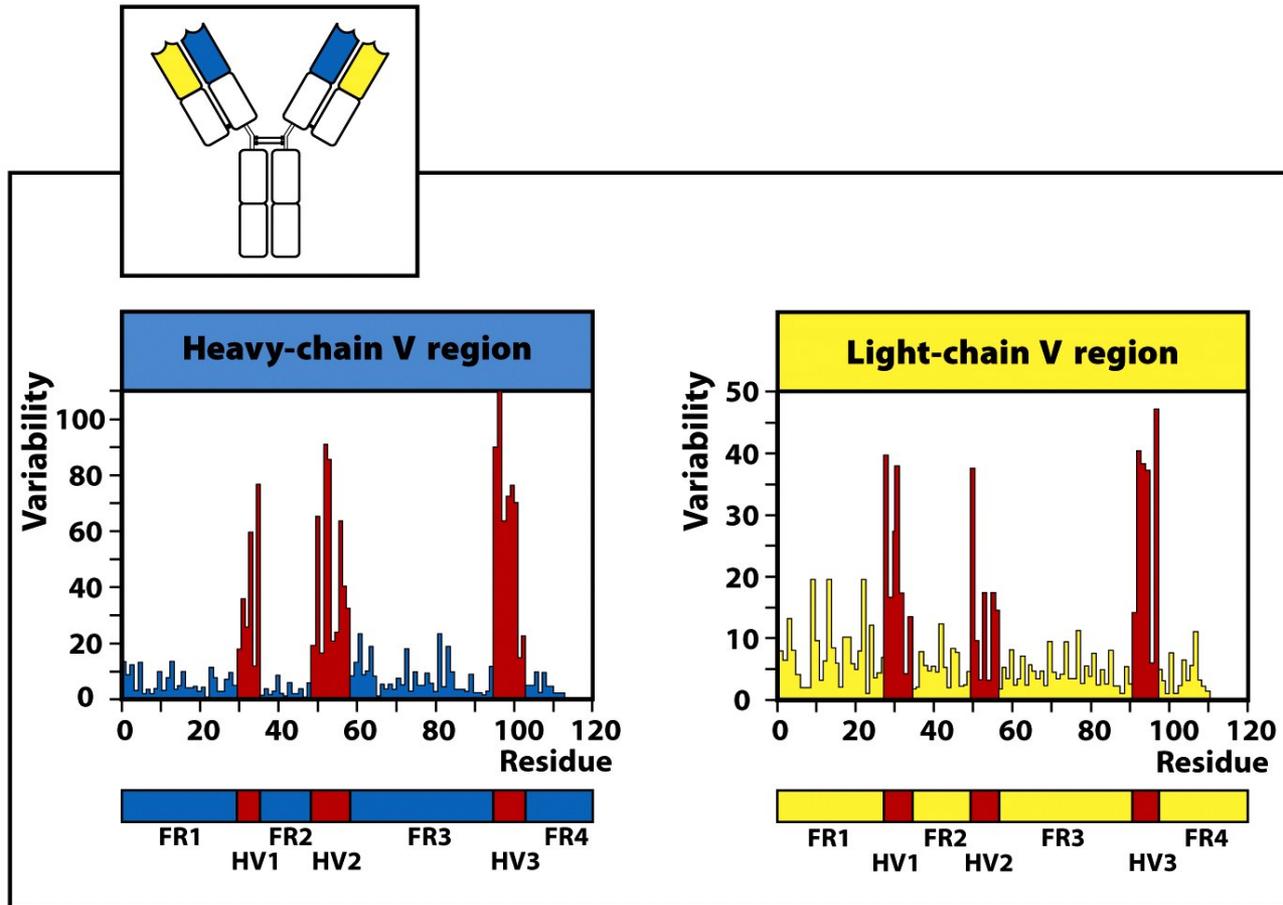


Figure 3-6 Immunobiology, 7ed. (© Garland Science 2008)

CDRs of Antibodies

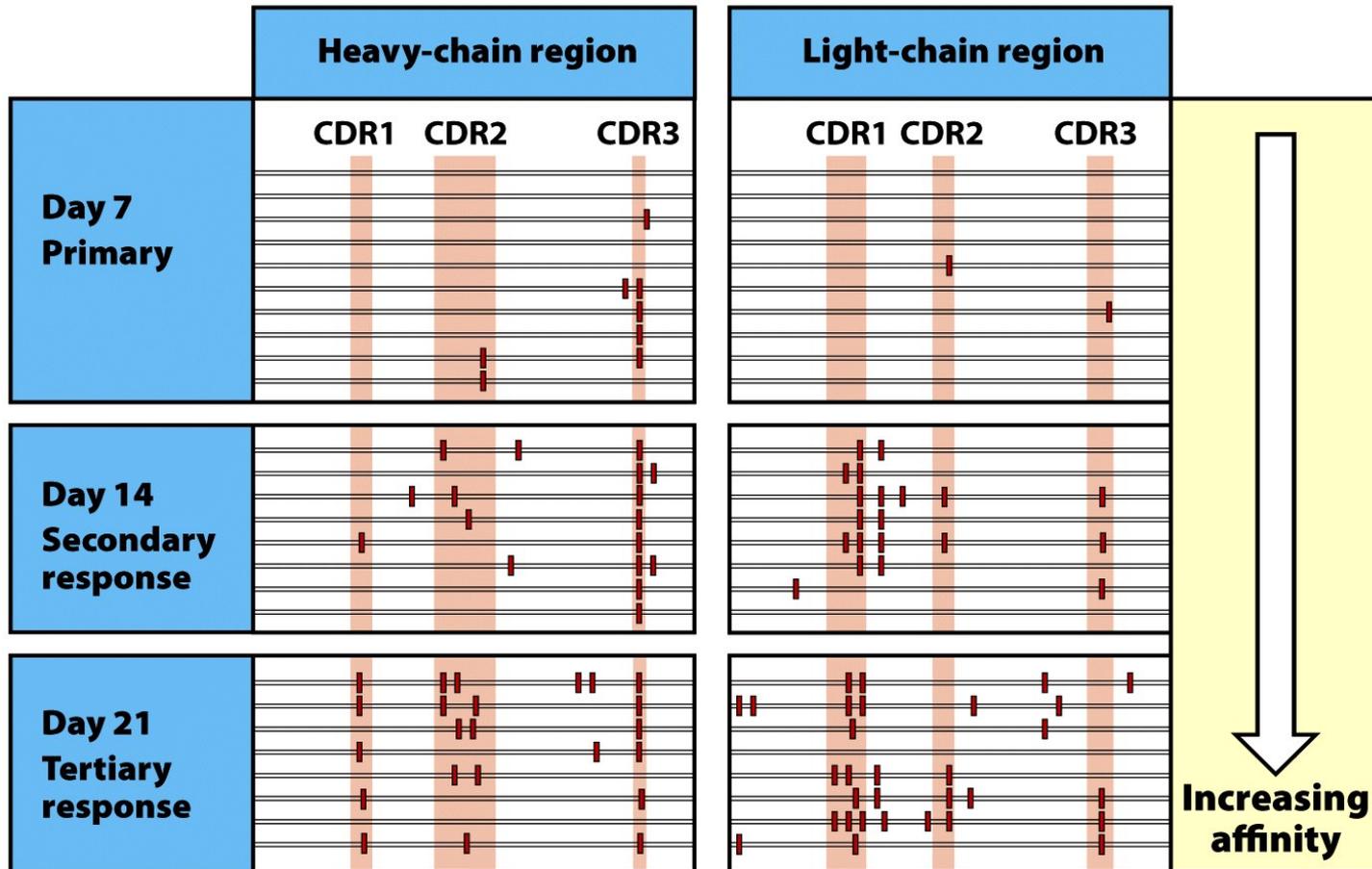


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Light-chain V region

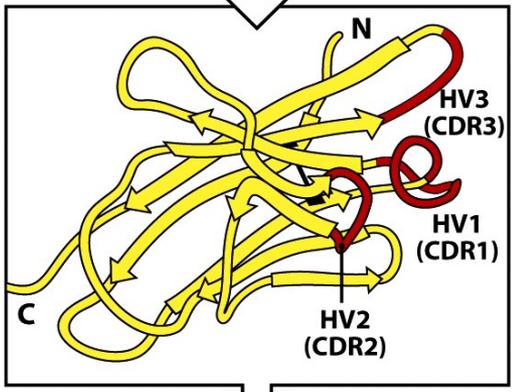
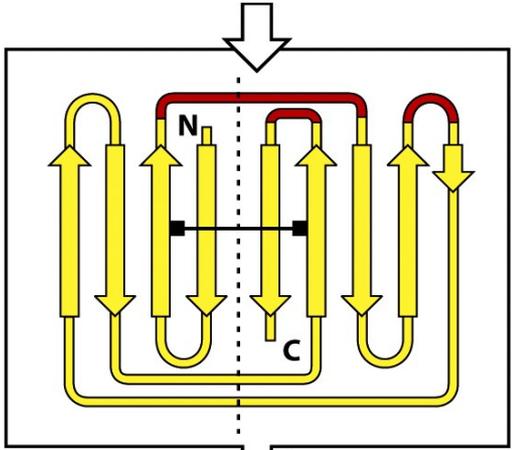
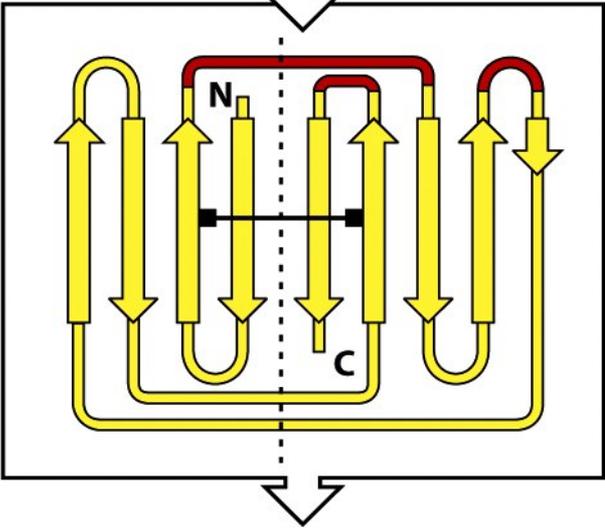
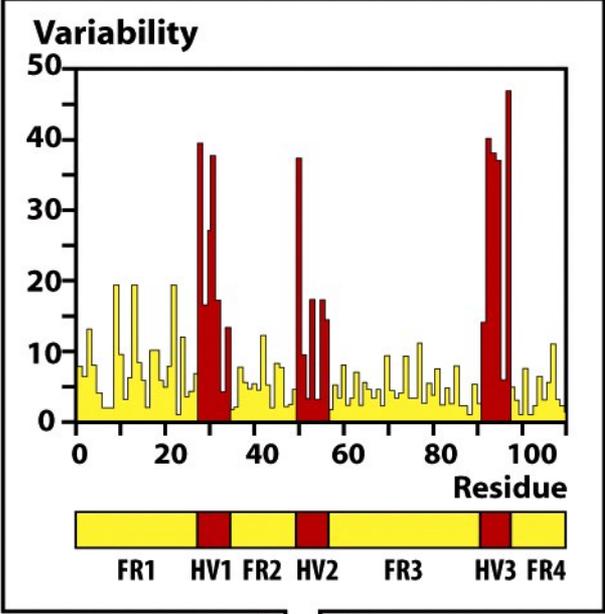


Figure 3-7 part 2 of 3 Immunobiology, 7ed. (© Garland Science 2008)

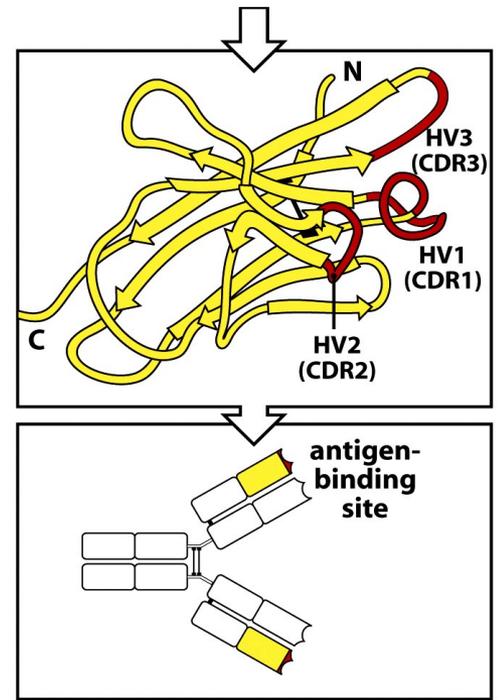


Figure 3-7 part 3 of 3 Immunobiology, 7ed. (© Garland Science 2008)

Figure 3-7 part 1 of 3 Immunobiology, 7ed. (© Garland Science 2008)

B Cell Response

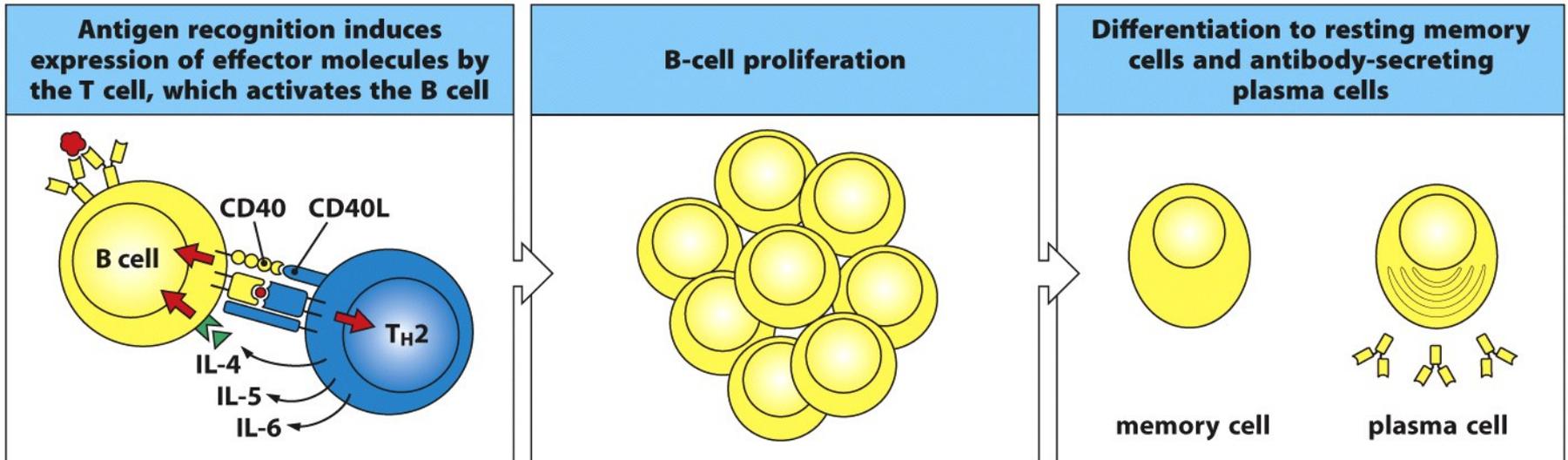


Figure 10.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

B Cell Polyclonal Response

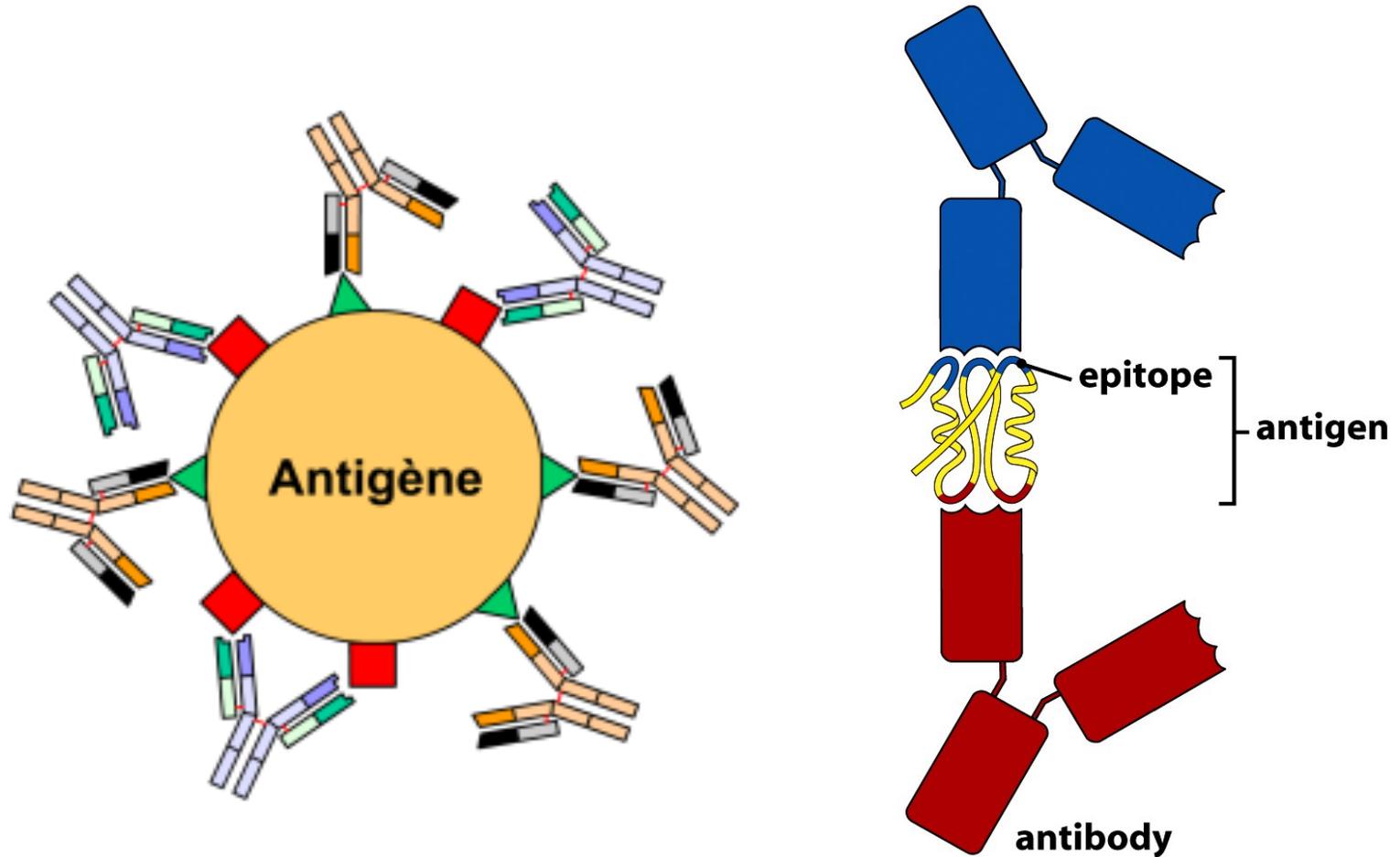


Figure 1-15 Immunobiology, 7ed. (© Garland Science 2008)

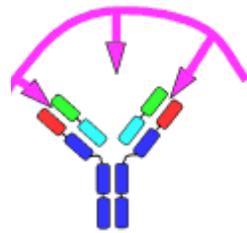
Affinity vs. Avidity

Affinity: the strength of binding between a single binding site and a single ligand.

Avidity: the strength of binding between a molecule and a complex ligand, e.g. if there are multiple binding sites then the avidity may be increased by increasing the number of binding sites or by increasing the affinity of those binding sites.

Avidity

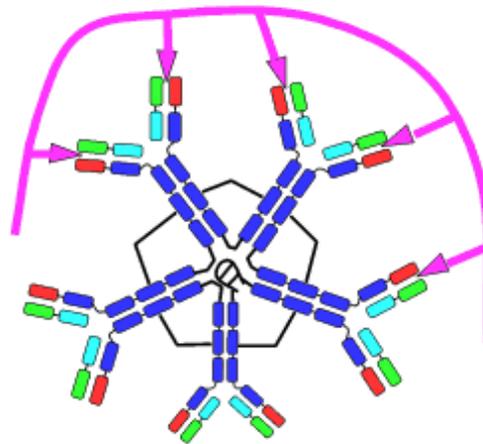
IgG



2

100

IgM



5

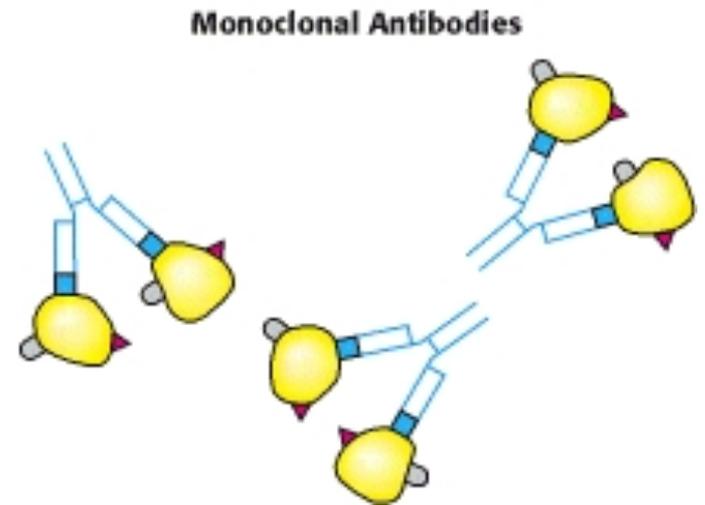
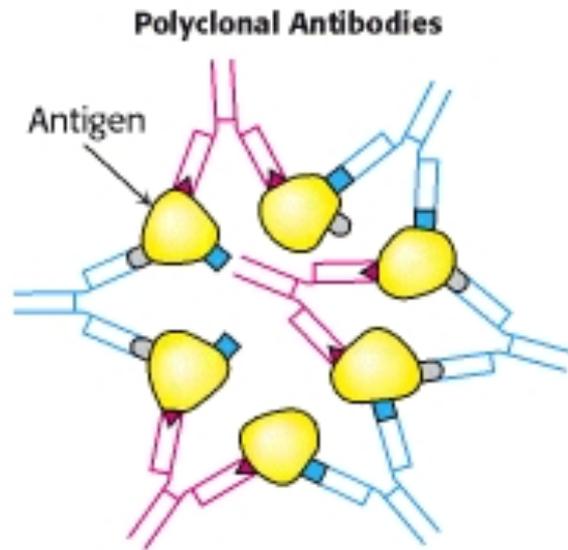
$10^4 - 10^5$

effective valence

relative equilibrium constant

multivalent avidity

Polyclonal v.s. Monoclonal



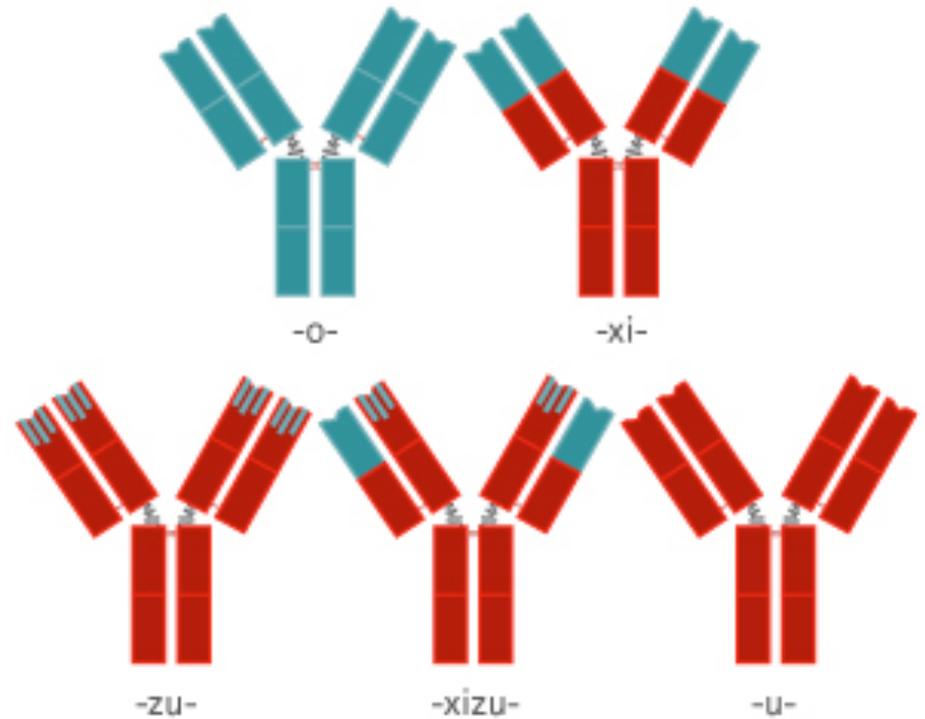
- Polyclonal antibody
 - Antigens possess multiple epitopes
 - Serum antibodies are heterogeneous,
 - To increase immune protection *in vivo* (**avidity**)
 - To reduce the efficacy of antiserum for various *in vitro* uses
 - To response facilitates the localization, phagocytosis, and complement-mediated lysis of antigen
 - To have clear advantages for the organism *in vivo*
- Monoclonal antibody
 - Derived from a single clone, **specific for a single epitope**
 - For most research, diagnostic, and therapeutic purposes

mAb nomenclature

Components

Substem for origin / source

Source subSTEMS: mouse (top left), chimeric (top right), humanized (bottom left), chimeric/humanized (bottom middle), and human (bottom right) monoclonal antibodies. Human parts are shown in red, non-human parts in blue.



One 500 mg vial
50 mL vial (10 mg/mL)

NDC 50242-053-0

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Rituximab **RITUXAN™**

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Dosage and Administration: For IV administration only. See package insert for full prescribing information. Infusion solutions are stable at 2-8°C/36-46°F for 24 hours and at room temperature for 4 hours.
Storage: 2-8°C/36-46°F. Protect vials from direct sunlight.
Caution: Federal (USA) law prohibits dispensing without a prescription.

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You are now able to:

- ✓ Describe the structure and genetics of TCR
- ✓ Describe the structure and genetics of BCR and **antibodies**
- ✓ Differentiate between **monoclonal** and **polyclonal** antibodies