

# Monoclonal Antibodies (I)

Dr. Aws Alshamsan  
Department of Pharmaceutics  
Office: AA87  
Tel: 4677363  
[aalshamsan@ksu.edu.sa](mailto:aalshamsan@ksu.edu.sa)

# Objectives of this lecture

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

1. Define terms such as monoclonal, polyclonal, isotype, idiotype, allotype, CDR, and hybridoma
2. Compare monoclonal-antibody production methods
3. Identify different mAb types
4. List some applications of mAb in medicine

# Antibody Response

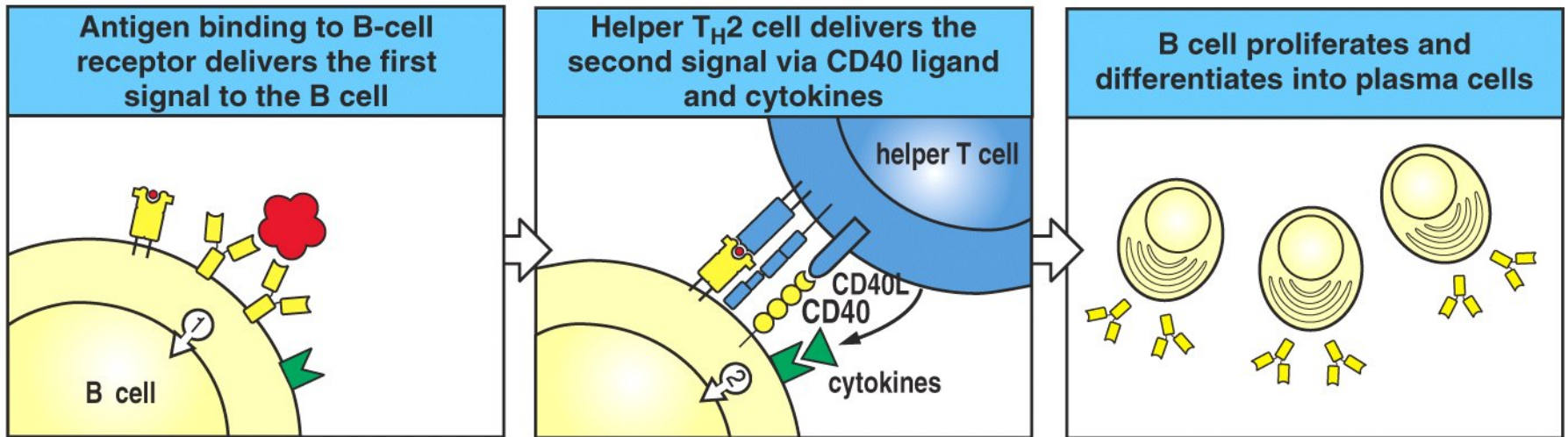


Figure 7-8 The Immune System, 2/e (© Garland Science 2005)

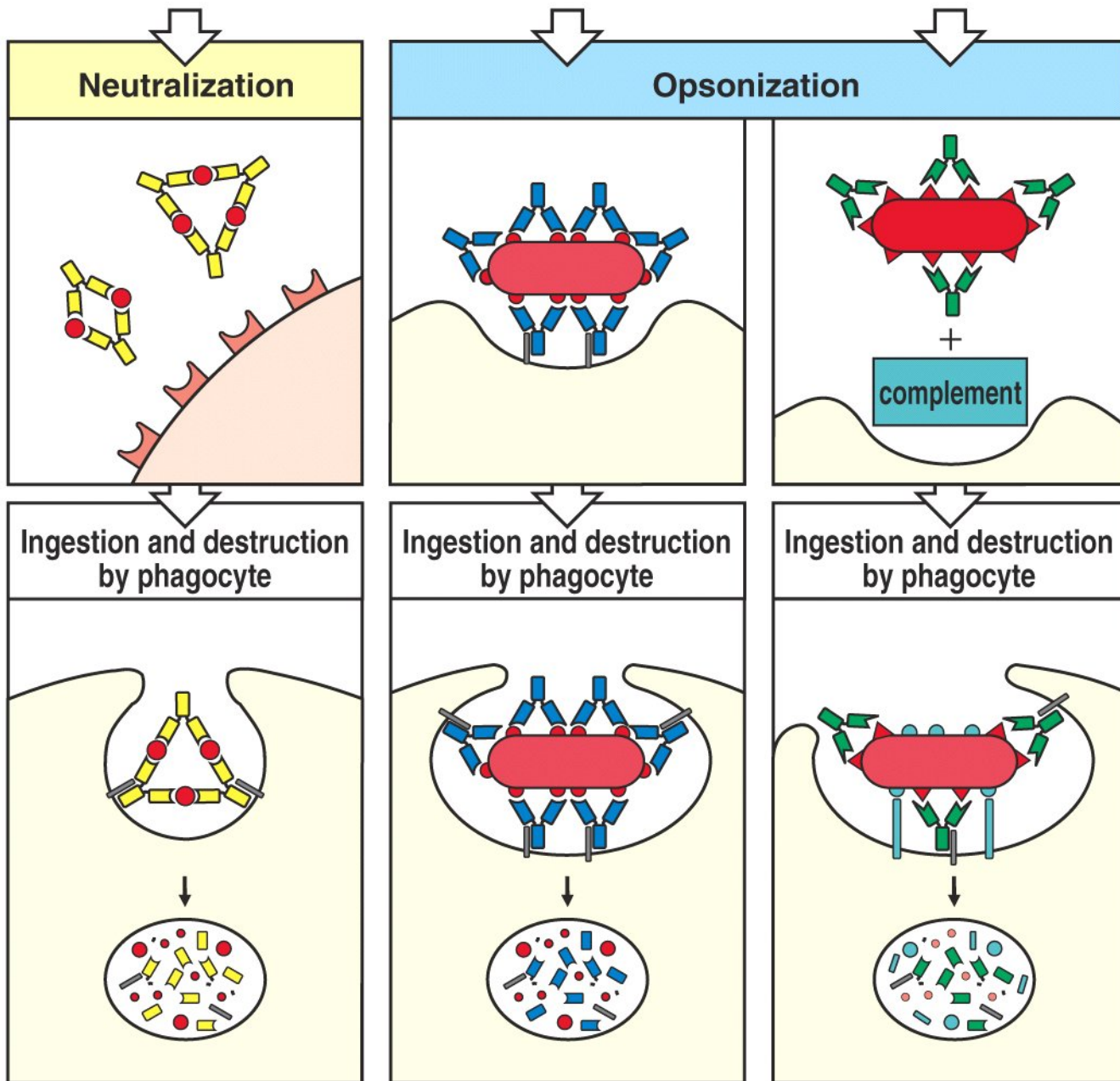
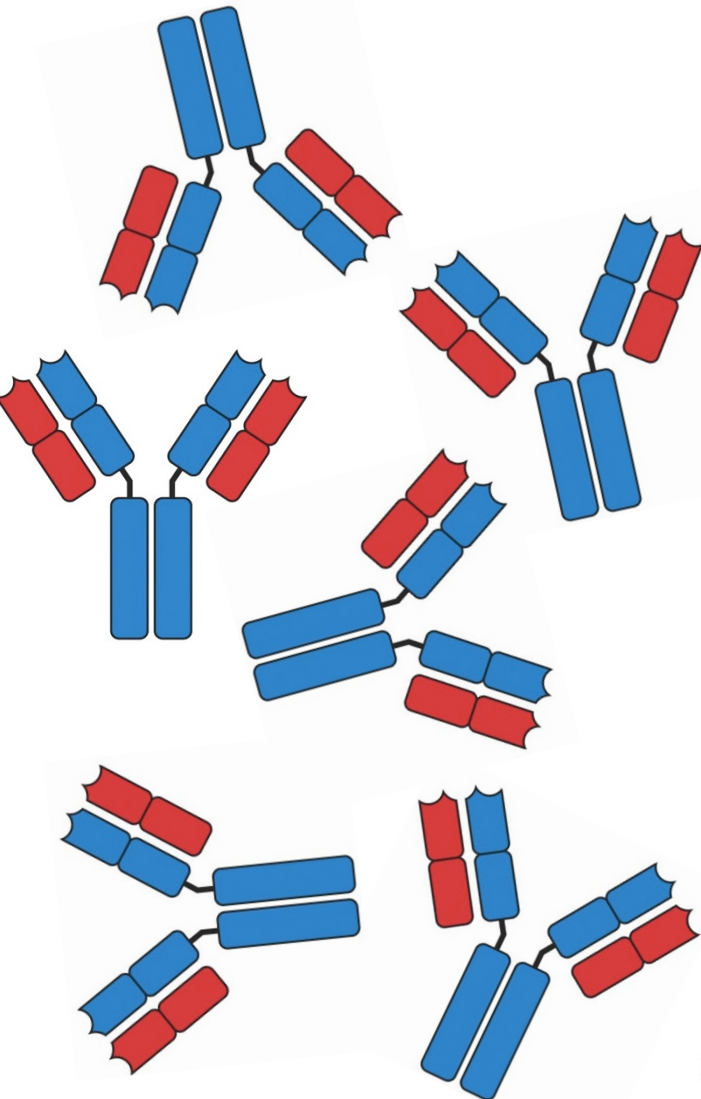


Figure 1-29 part 2 of 2 The Immune System, 2/e (© Garland Science 2005)

# Antibody Structure



## Surface immunoglobulin

antigen-binding site

site

light chain

heavy chain

transmembrane region

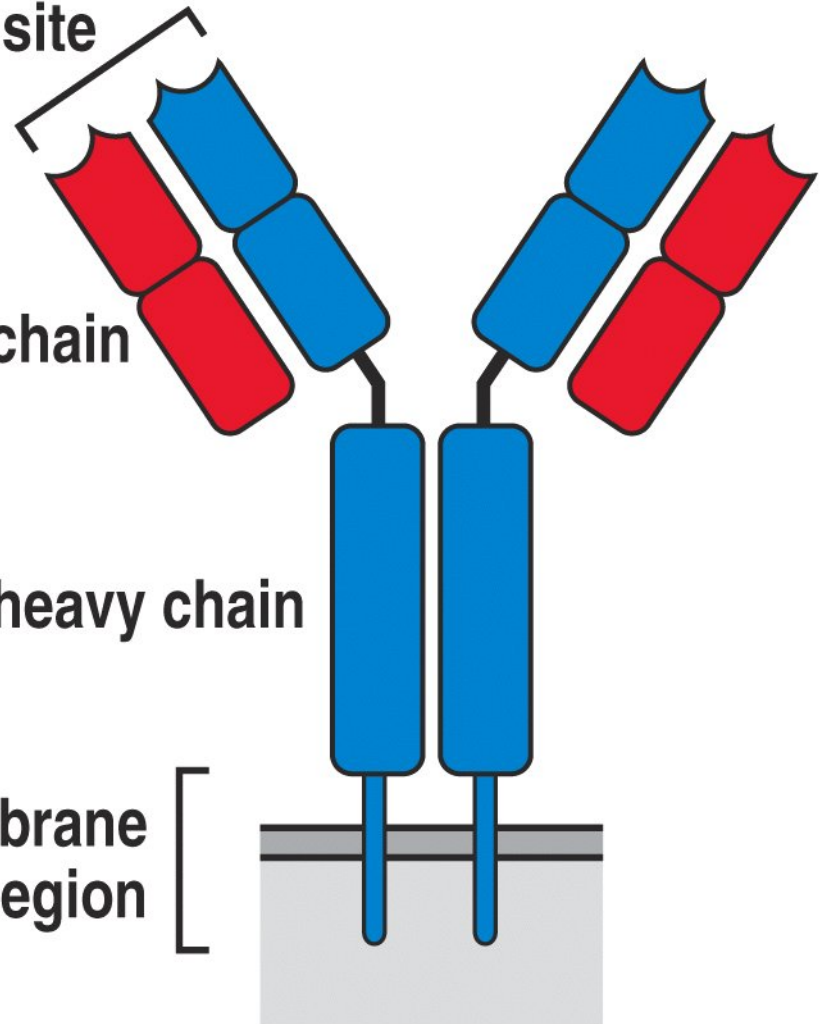
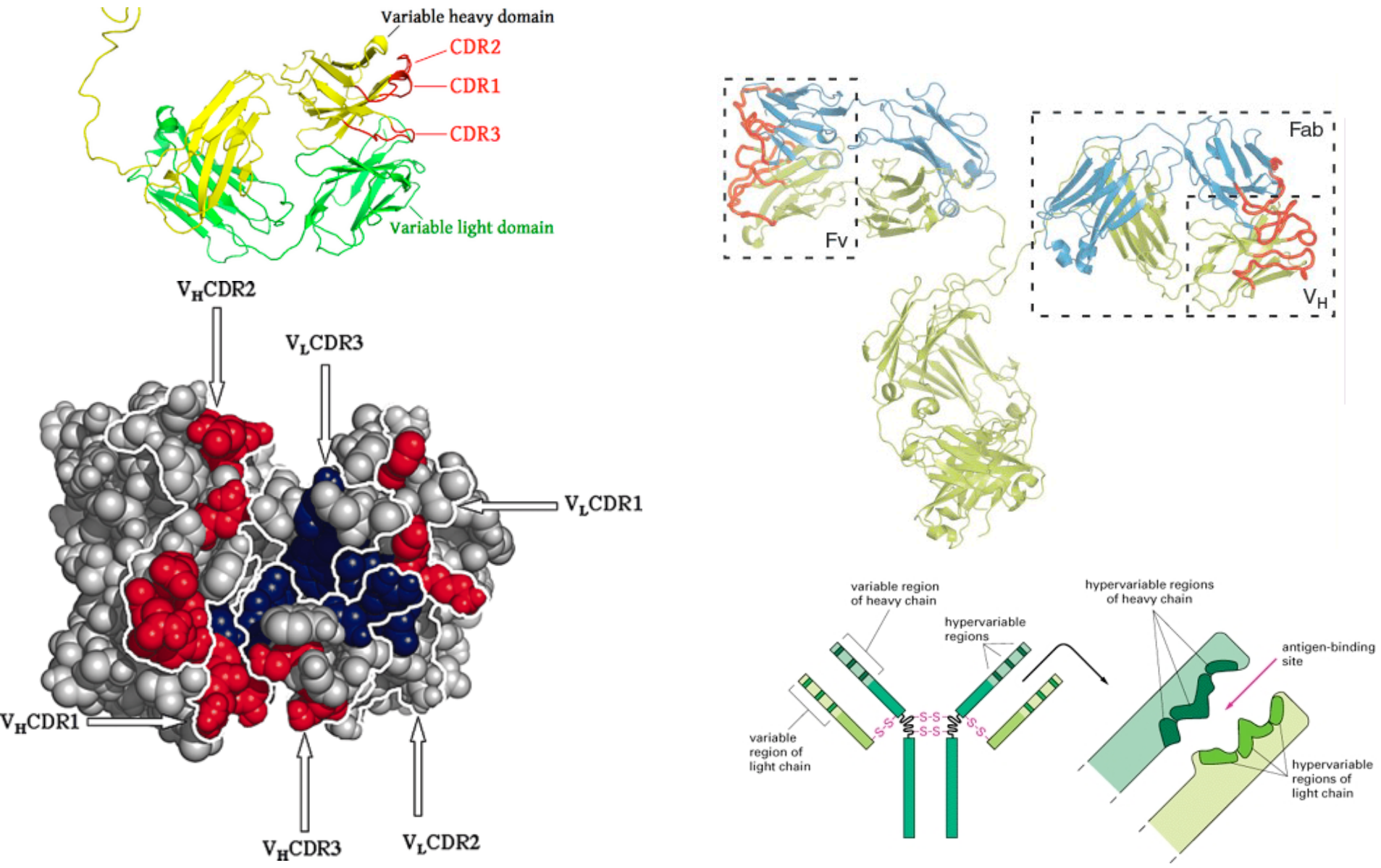


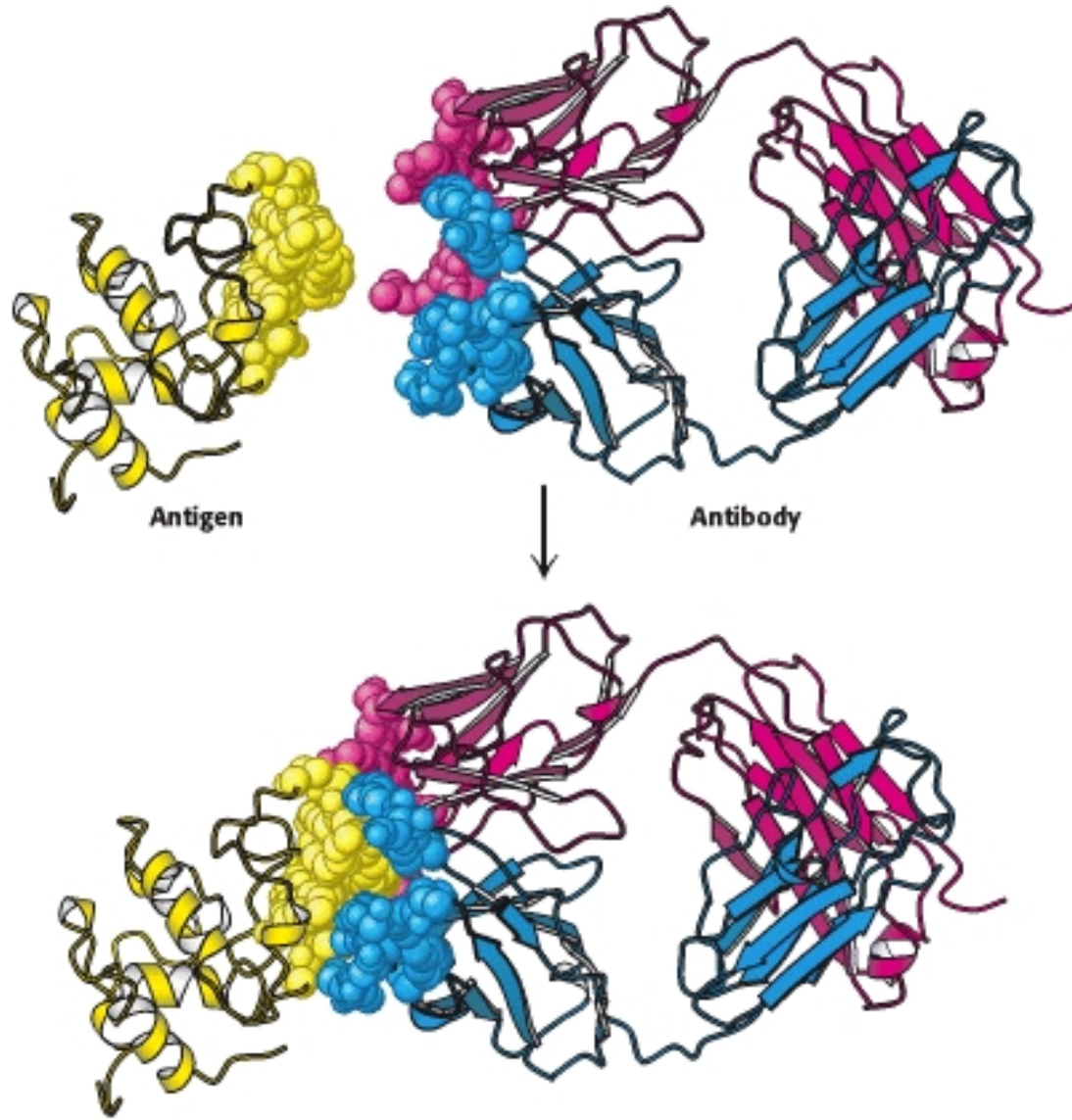
Figure 1-21 part 1 of 2 The Immune System, 2/e (© Garland Science 2005)

# Complementarity Determining Regions

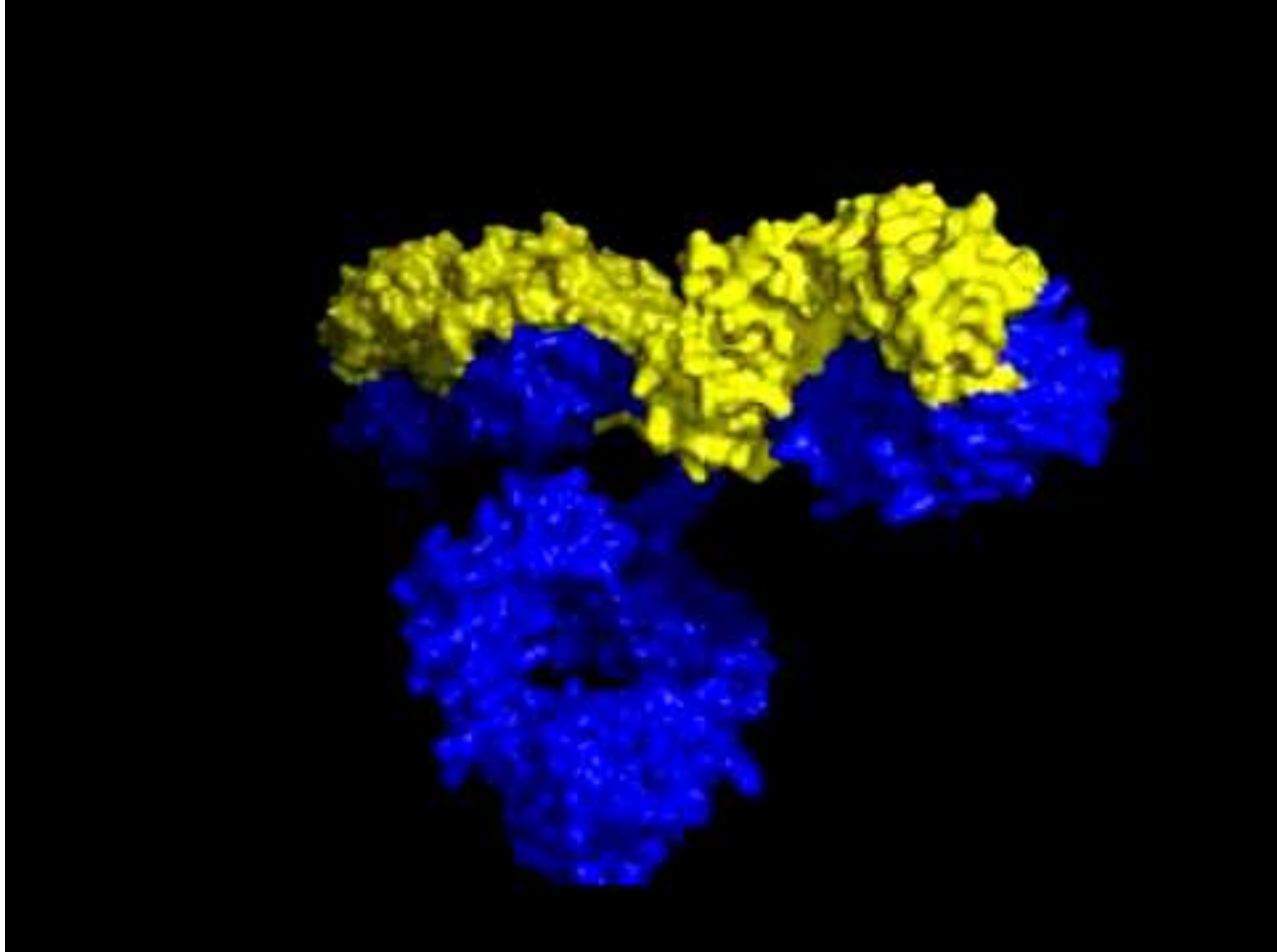




# Antigen Antibody Interaction

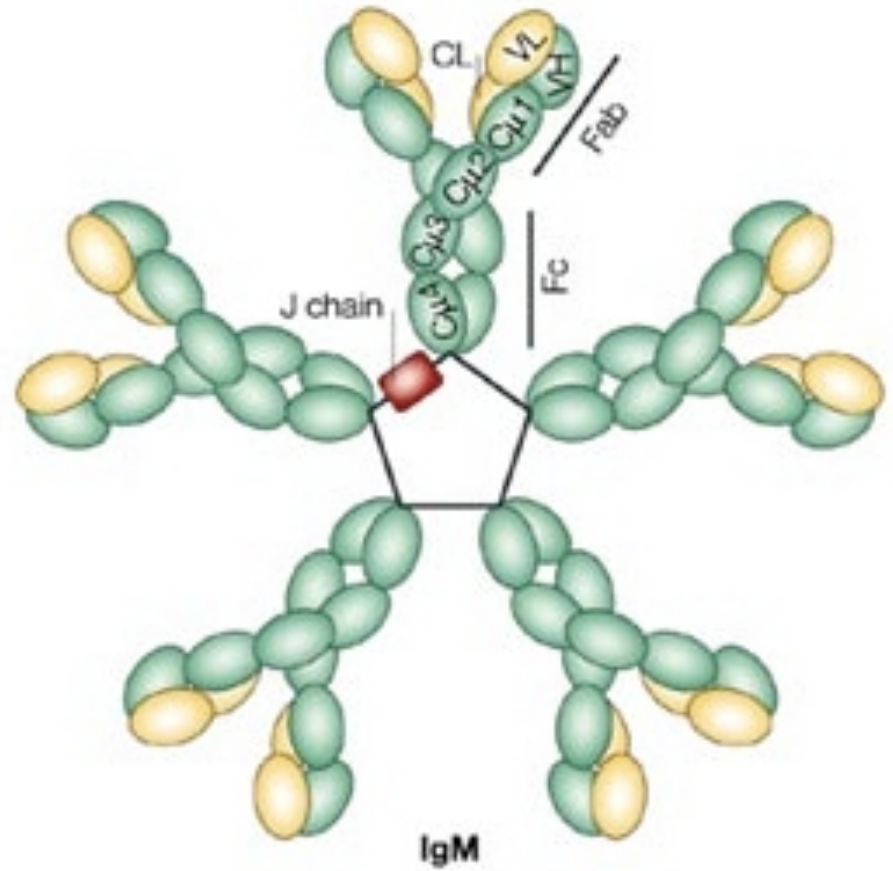
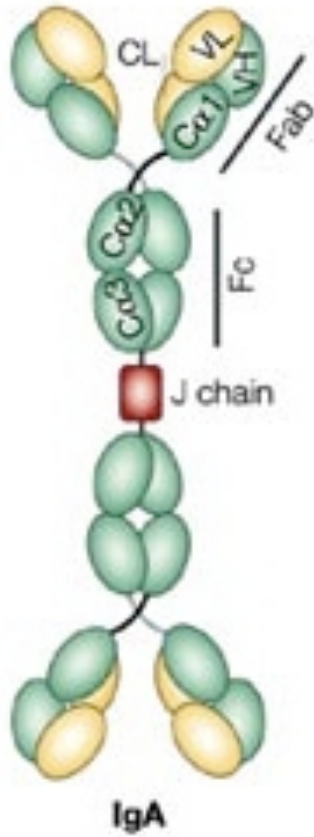
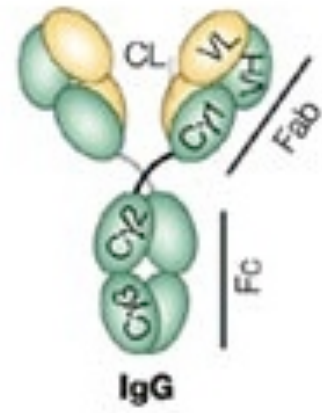
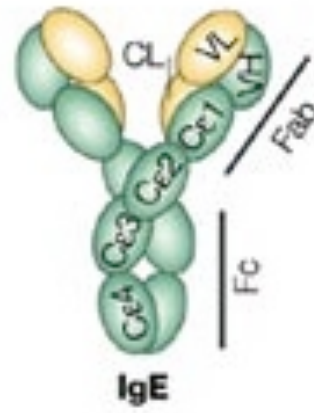
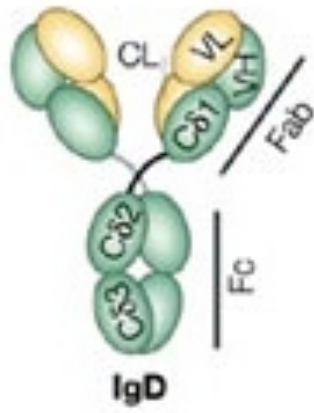


# Antigen Antibody Interaction



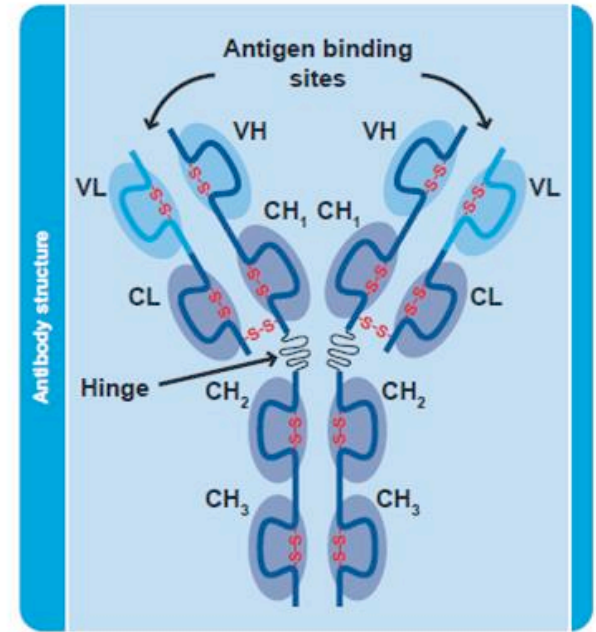


# Ab Isotypes

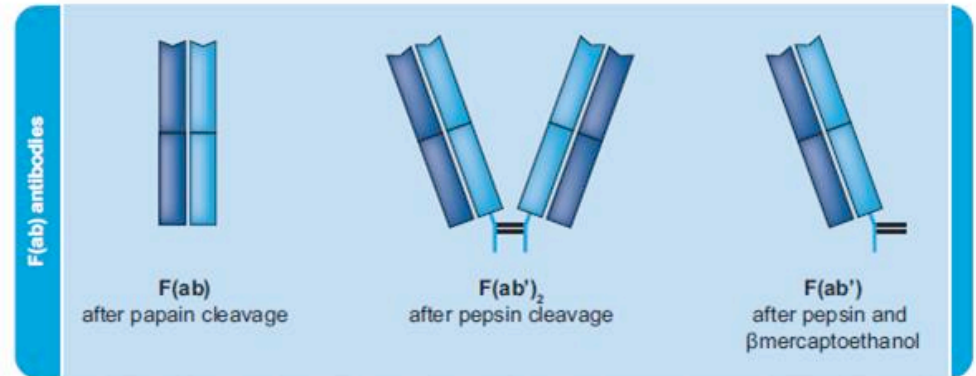
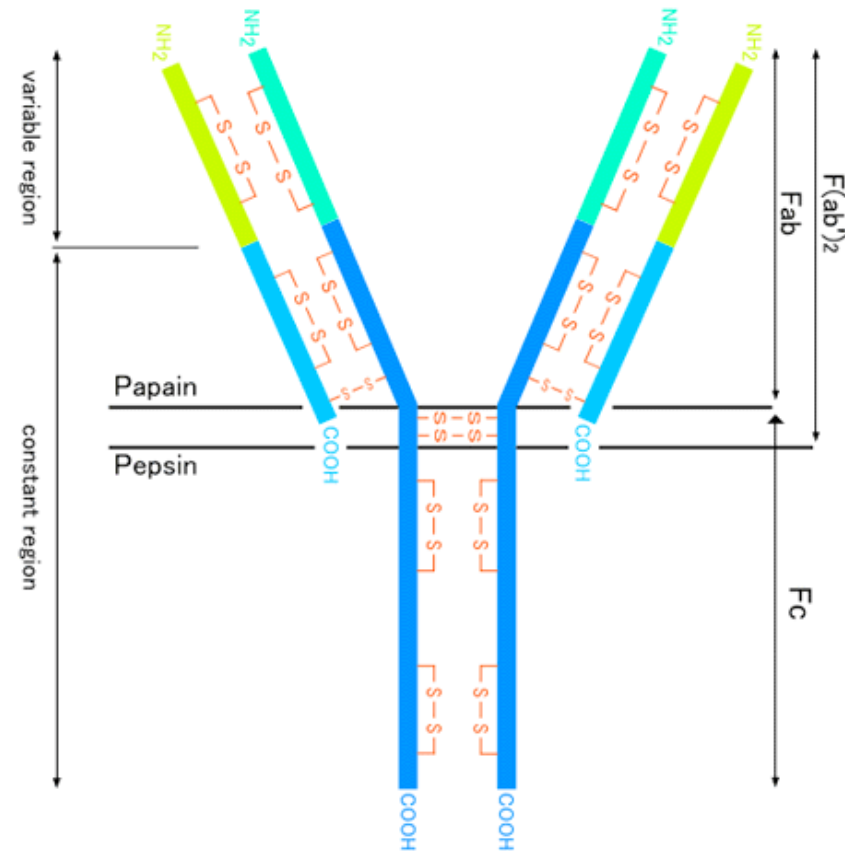


# Ab Fragments

## Antibody structure and F(ab) antibodies

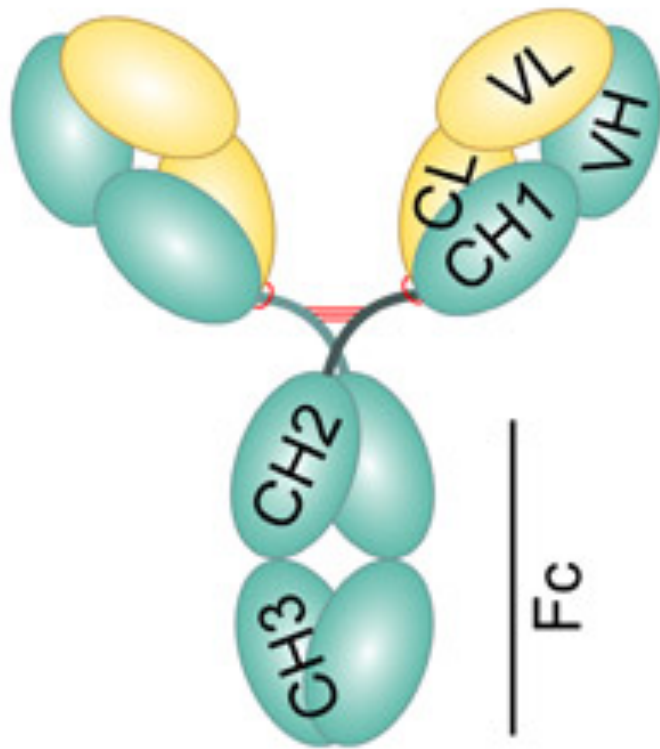


The light chain (LH) folds into a variable domain (VL) and a constant domain (CL) whereas the heavy chain is composed of one variable domain (VH) and three (IgG and IgA) or four constant domains (IgE).

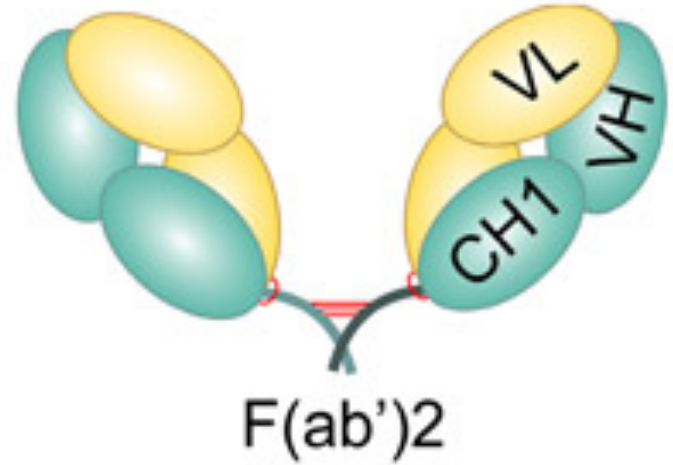


The **F(ab)** fragment is an antibody structure that still binds to antigens but is monovalent with no Fc portion. An antibody digested by the enzyme papain yields two F(ab) fragments of about 50 kDa each and an Fc fragment. In contrast, **F(ab')<sub>2</sub>** fragment antibodies are generated by pepsin digestion of whole IgG antibodies to remove most of the Fc region while leaving intact some of the hinge region. F(ab')<sub>2</sub> fragments have two antigen-binding F(ab) portions linked together by disulfide bonds, and therefore are divalent with a molecular weight of about 110 kDa.

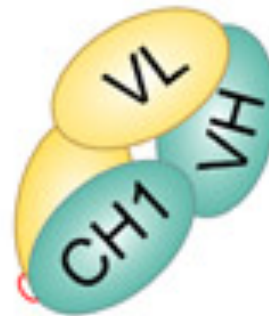
# Ab Fragments



IgG



F(ab')<sub>2</sub>



Fab



scFv



NDC 0281-0365-10

*Digoxin Immune  
Fab (Ovine)  
DigiFab®*

Package contains one vial of  
DigiFab® for intravenous injection.  
Diluent not included.

To be reconstituted with  
4 mL Sterile Water for Injection USP  
by gentle mixing.

Use immediately after reconstitution.  
Store at 2° to 8°C (36° to 46°F).  
Do not freeze.

*Rx* only



NDC 0281-0365-10

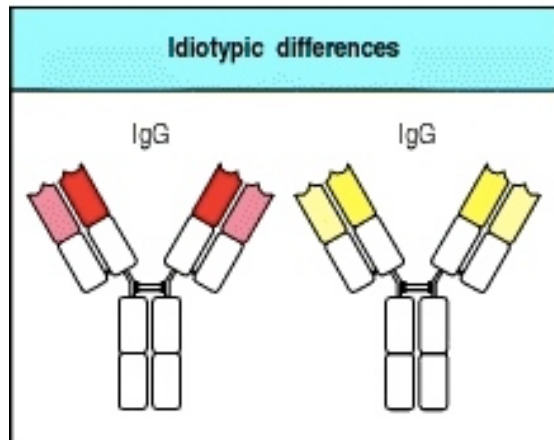
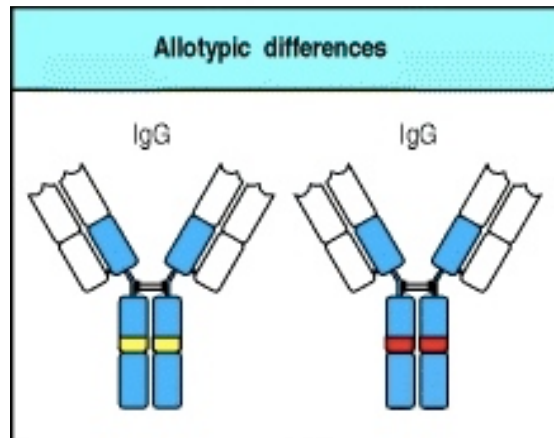
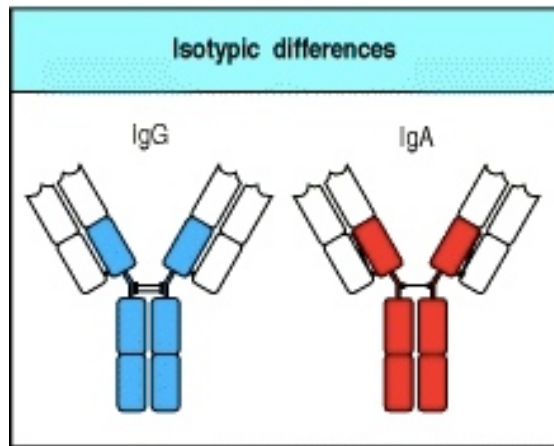
*Digoxin Immune Fab (Ovine)  
DigiFab®*

40 mg

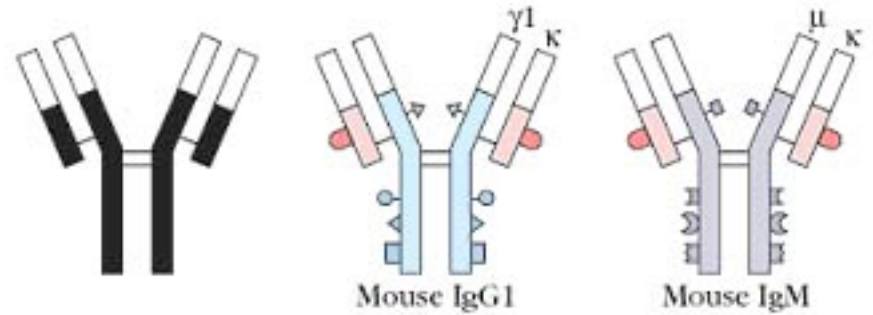


(01)00302810365100

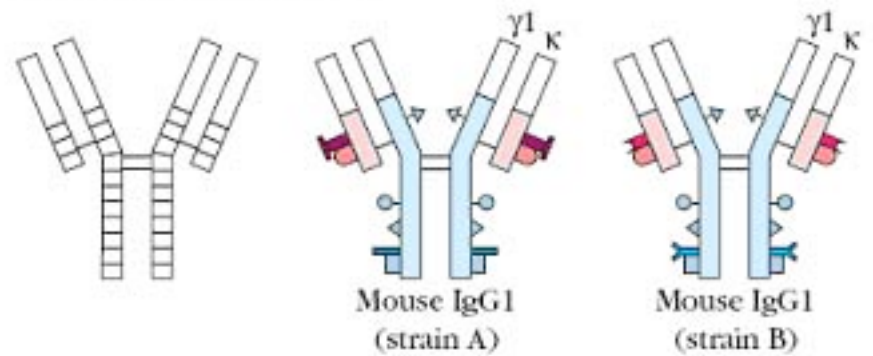
# Ab types differences



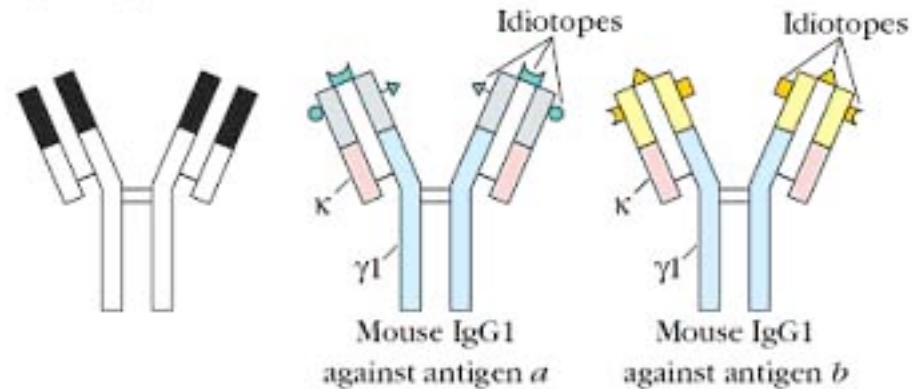
(a) Isotypic determinants



(b) Allotypic determinants

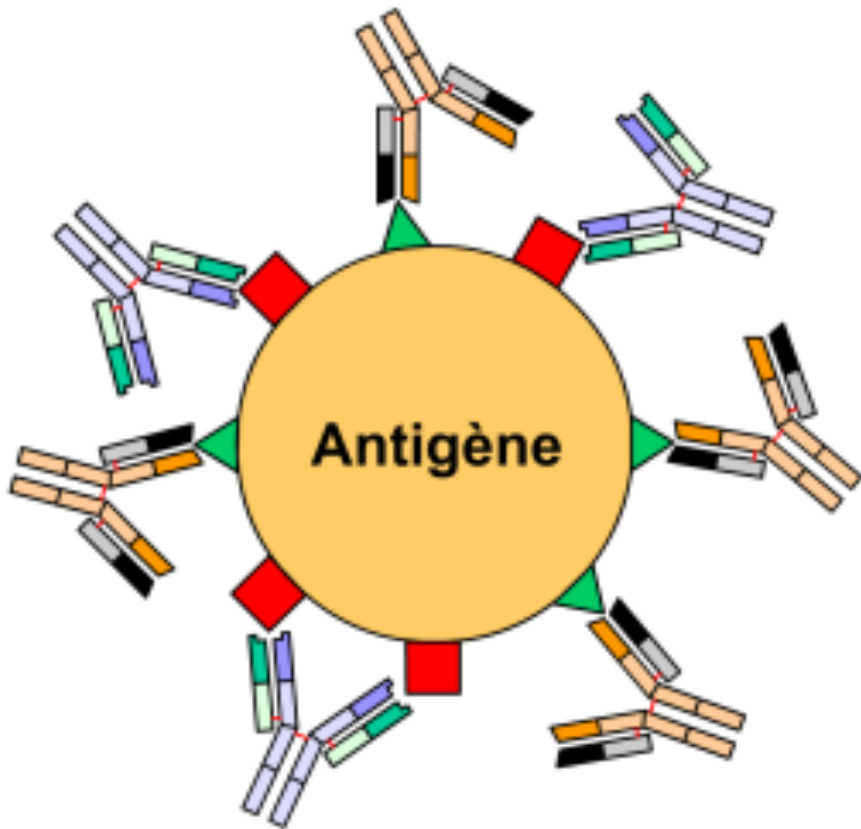


(c) Idiotypic determinants

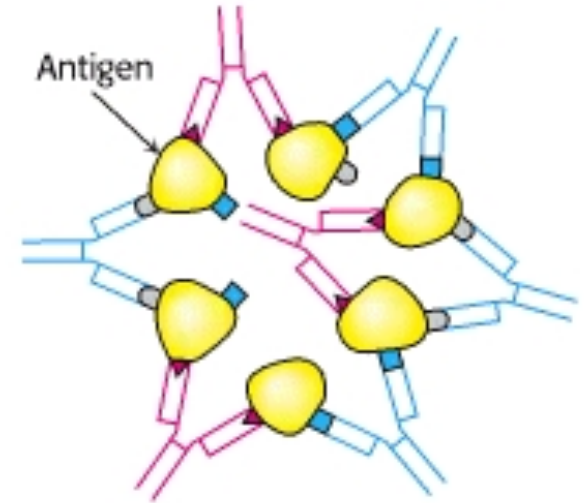




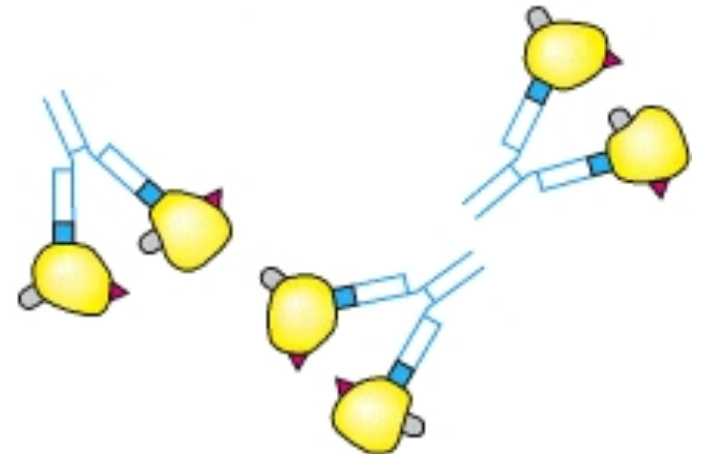
# Polyclonal v.s. Monoclonal



**Polyclonal Antibodies**



**Monoclonal Antibodies**



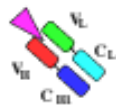
# Affinity and Avidity

**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.

# Affinity and avidity

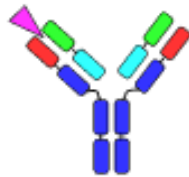
**Fab**



1

1

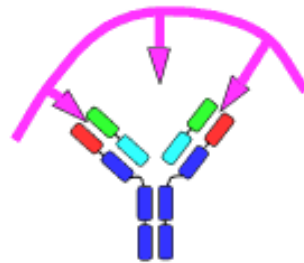
**IgG**



1

1

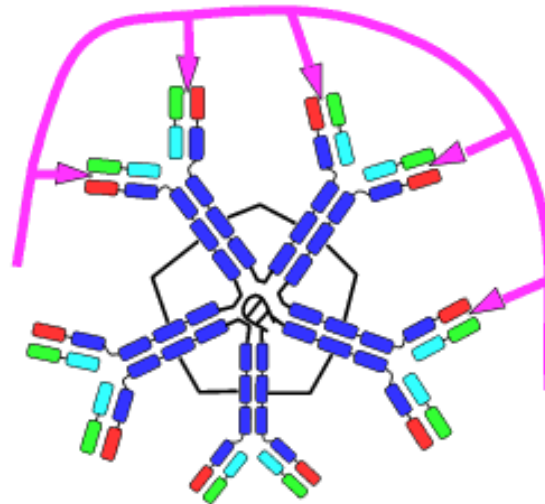
**IgG**



2

100

**IgM**



5

$10^4 - 10^5$

effective valence

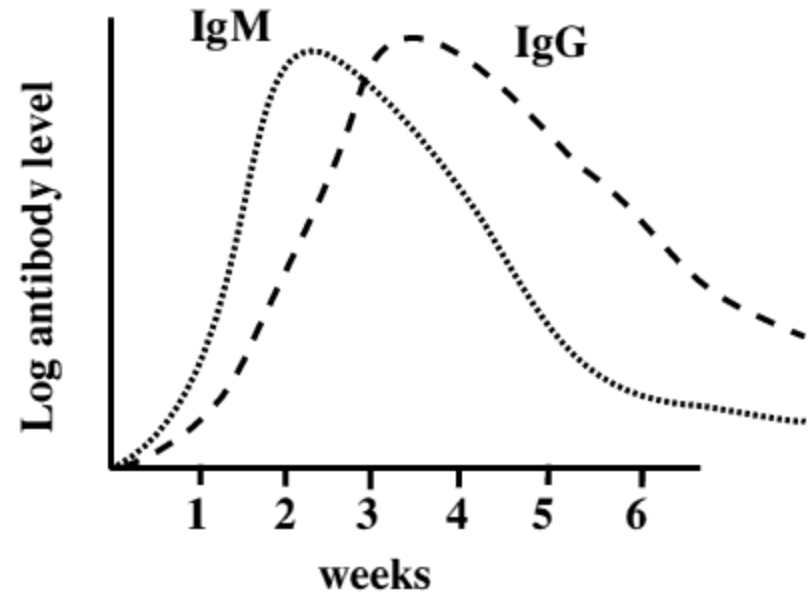
relative equilibrium constant

**monovalent affinity**

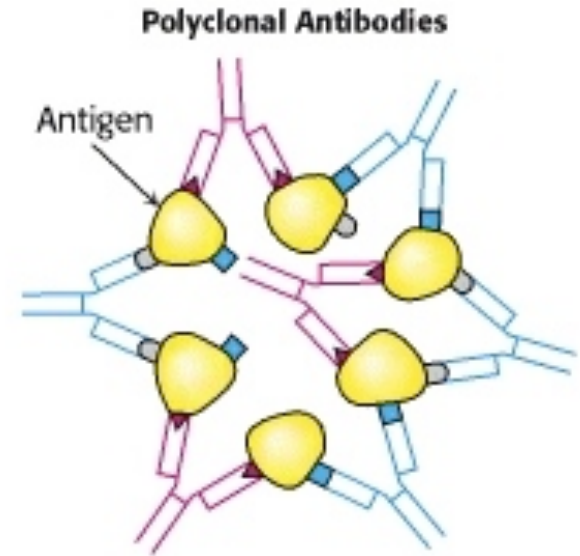
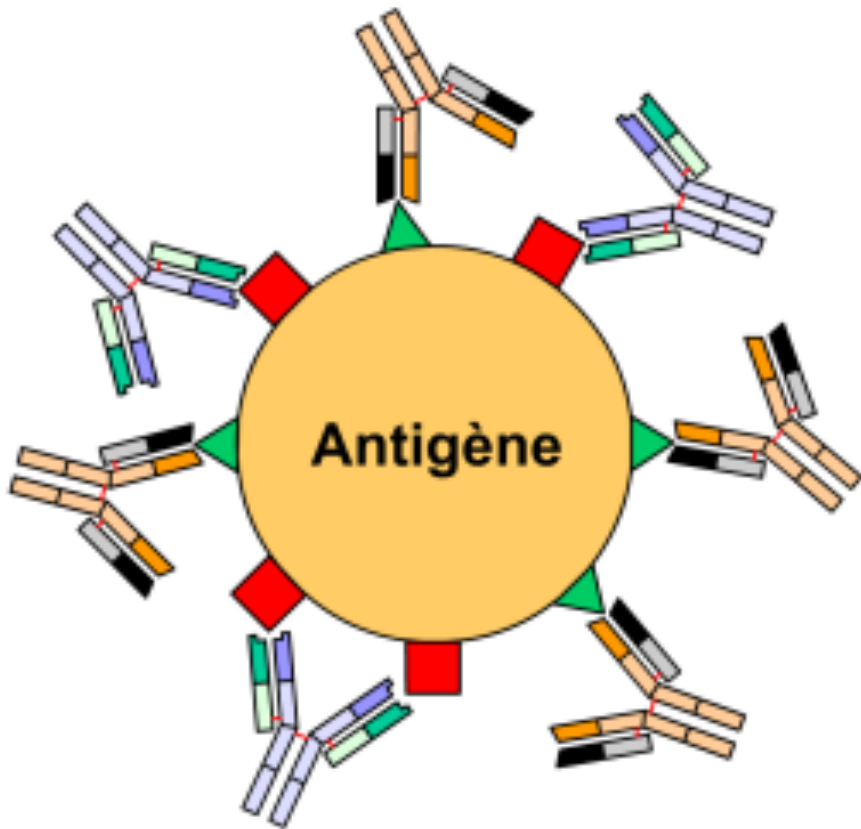
**multivalent avidity**

# Affinity and Avidity, continued

IgM is produced early in an immune response when the affinity for antigen often is low; as an immune response continues, antibody affinity is improved, this is combined by “class switching” to the use of smaller molecules (IgG, IgE and IgA). The increased affinity compensates for the decrease in number of binding sites in maintaining the overall avidity for antigen.



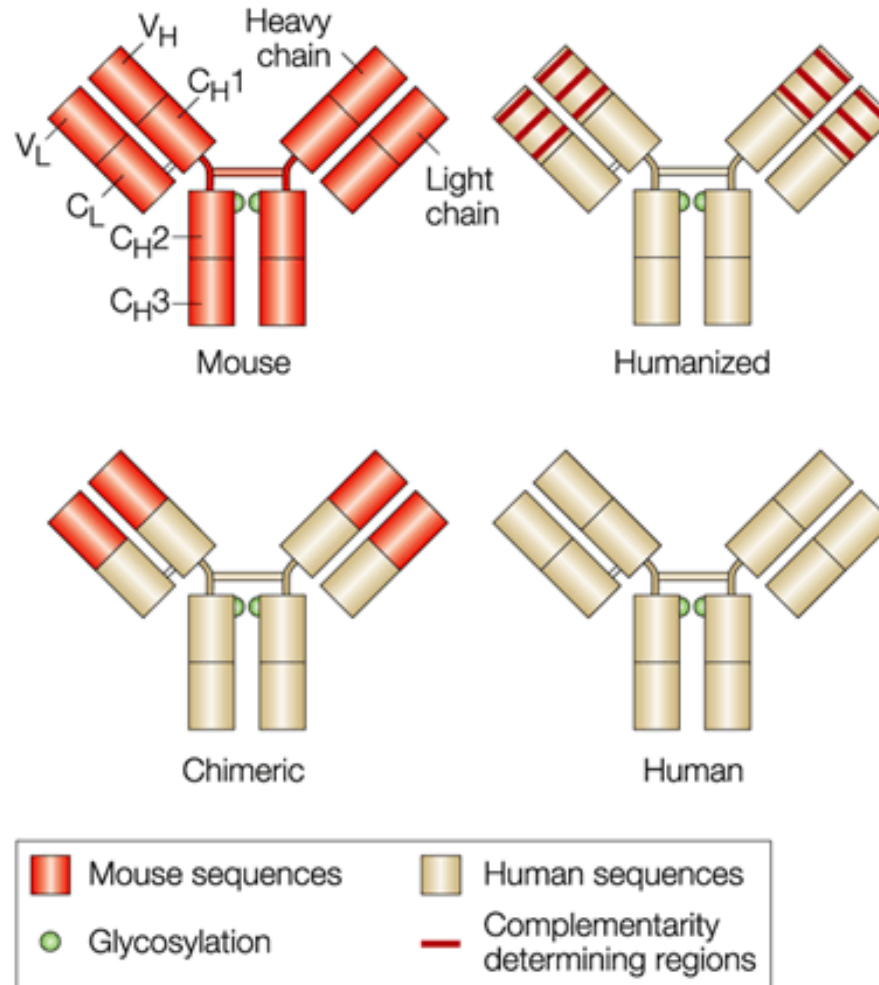
# Polyclonal Response





- Polyclonal antibody
  - Antigens possess multiple epitopes
  - Serum antibodies are heterogeneous,
    - To increase immune protection in vivo
    - 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 Types



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

NDC 50242-053-0

# **Rituximab** **RITUXAN™**

**500 mg**

**Jointly Manufactured by:**

**IDEC Pharmaceuticals Corp.** Genentech, Inc.  
11011 Torreyana Road 1 DNA Way  
San Diego, CA 92121 South San Francisco, CA 94080-4990

**US License No.**

# **Rituximab** **RITUXAN™**

**500 mg**

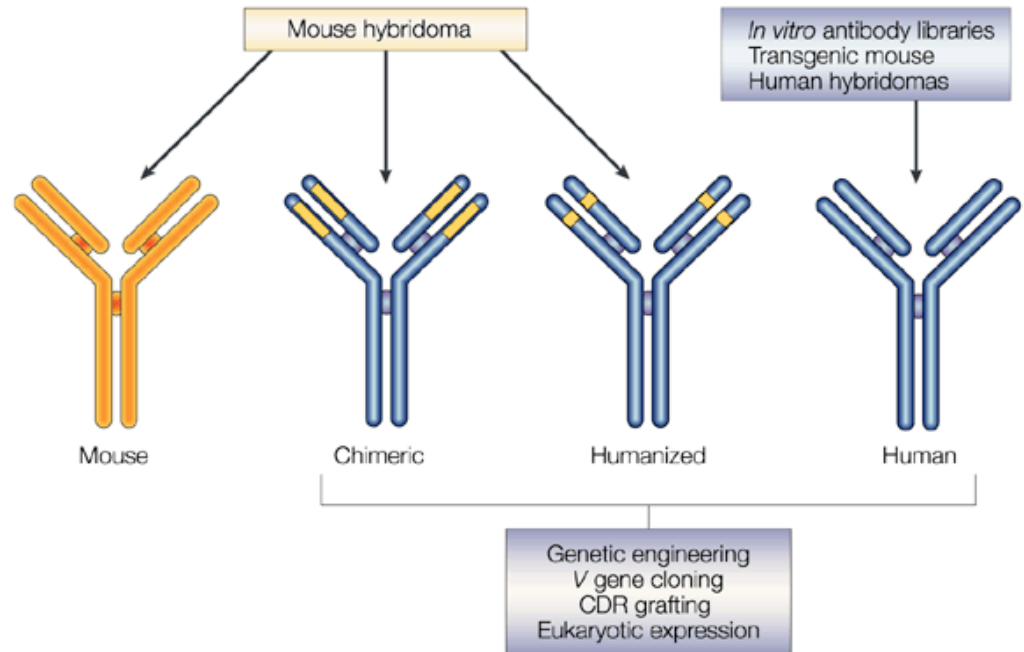
**Dosage and Administration:** For IV administration only. See package insert for full prescribing information. Infusion solutions are stable at 2-8°C/36-46°F for 24 hours and at room temperature for 24 hours.  
**Storage:** 2-8°C/36-46°F. Protect vials from direct sunlight.  
**Caution:** Federal (USA)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

**Jointly Manufactured by:**  
**IDEC Pharmaceuticals Corp.,** San Diego, CA 92121  
**Genentech, Inc.,** South San Francisco, CA 94080-4990



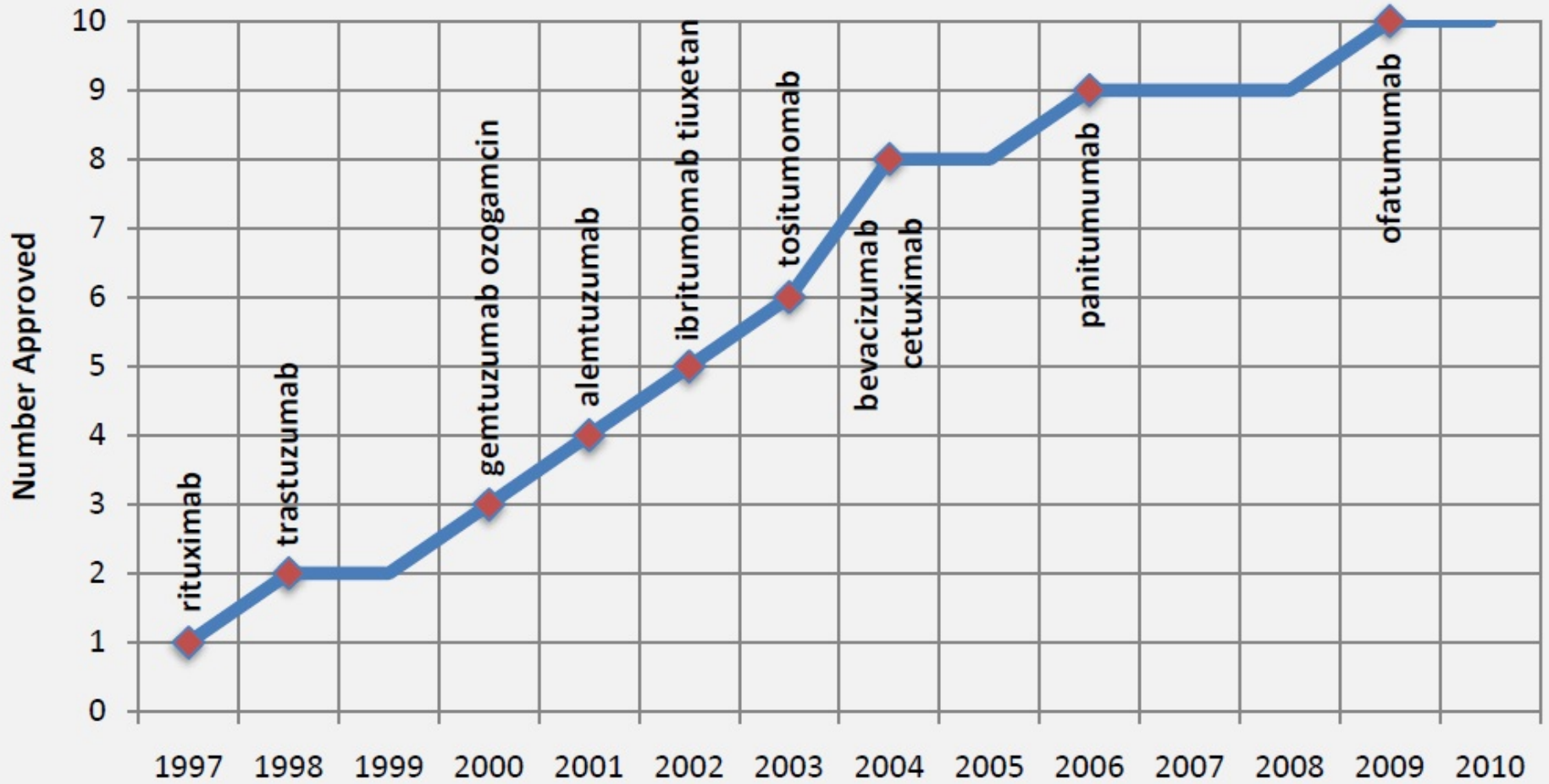
# mAb nomenclature

Source stem	Suffix
o	mAb
xi	mAb
zu	mAb
u	mAb





# FDA Approved mAbs for Cancer Therapy



## **You are now able to:**

- ✓ Define terms such as monoclonal, polyclonal, isotype, idiotype, allotype, CDR, and hybridoma
- ✓ Compare monoclonal-antibody production methods
- ✓ Identify different mAb types
- ✓ List some applications of mAb in medicine