

The background features several large, overlapping, semi-transparent swirls in shades of light green, light purple, and light blue. Interspersed among these swirls are numerous small, yellow, starburst-like shapes, some pointing towards the center and others pointing outwards, creating a dynamic and energetic feel.

# **Antibodies**

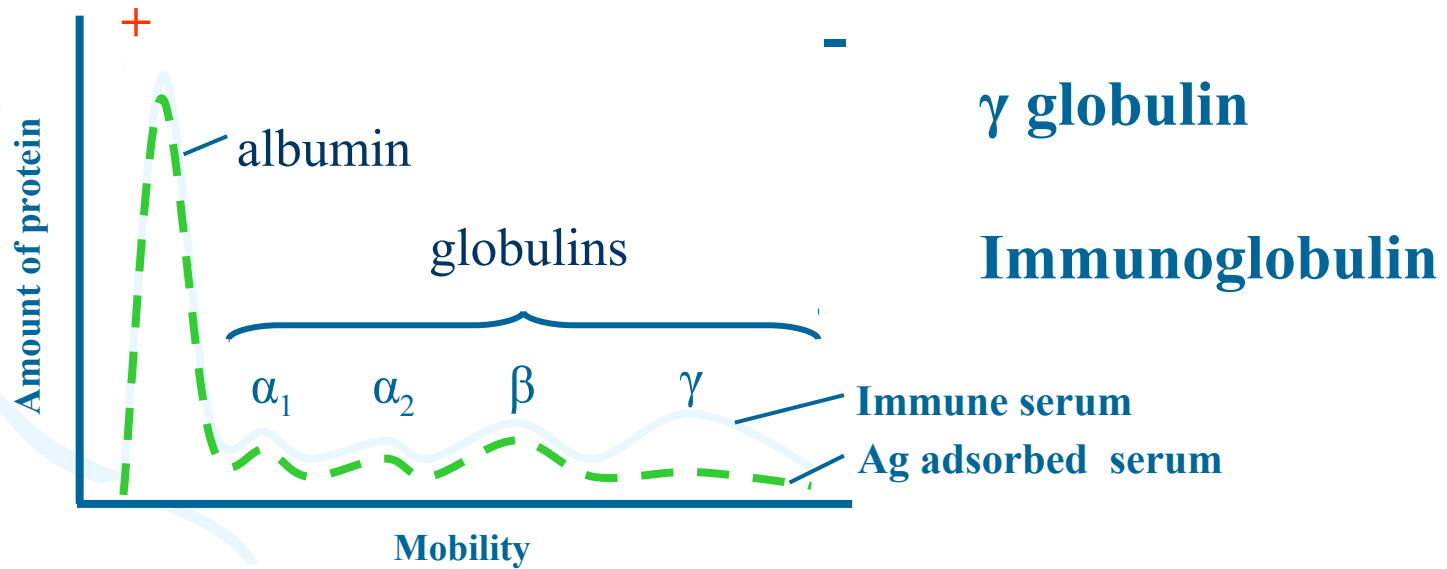
## **Structure and Function**



# objectives

- General features of Antibodies
- Structure
- Antibody and Antigen binding
- Class and subclasses of Antibodies
- Functions

- Definition: Protein molecules that are produced by B and plasma cells in response to an antigen



Electrophoresis

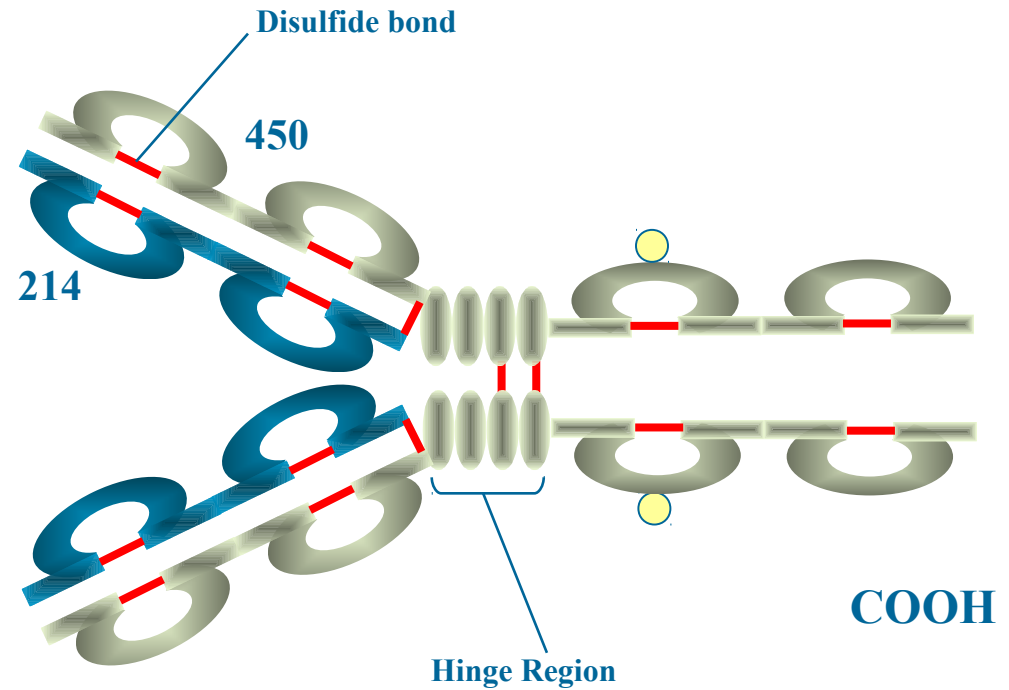


# General Functions of Immunoglobulins

- Ag binding
  - Can result in protection
- Effector functions (Usually require Ag binding)
  - Fixation of complement
  - Binding to various cells

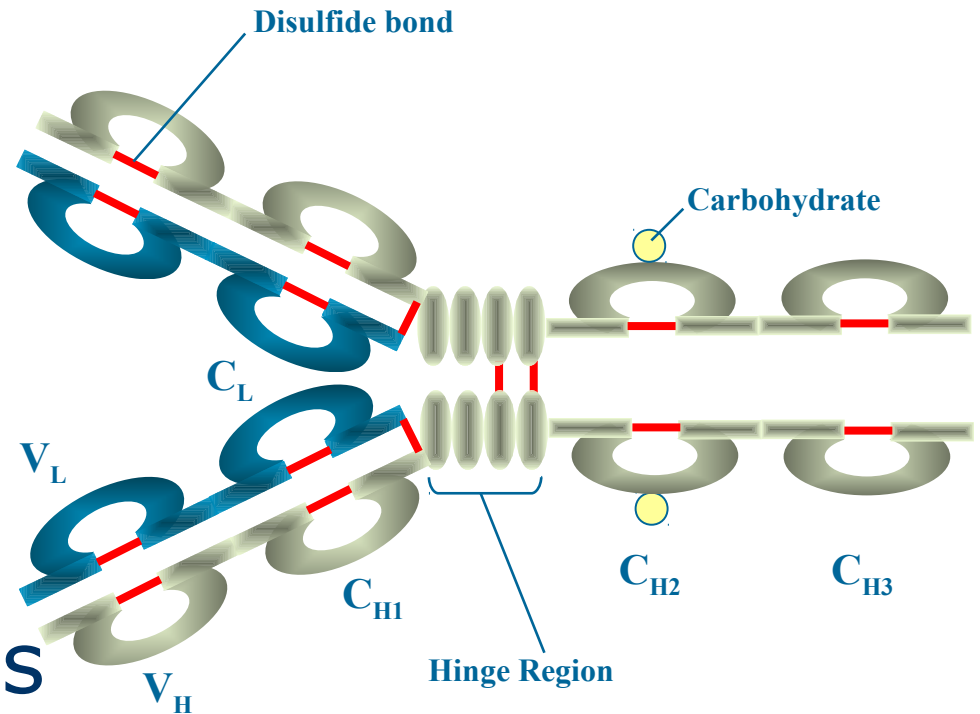
# Immunoglobulin Structure

- Heavy & Light Chains
- Disulfide bonds
  - Inter-chain
  - Intra-chain
  - Domain



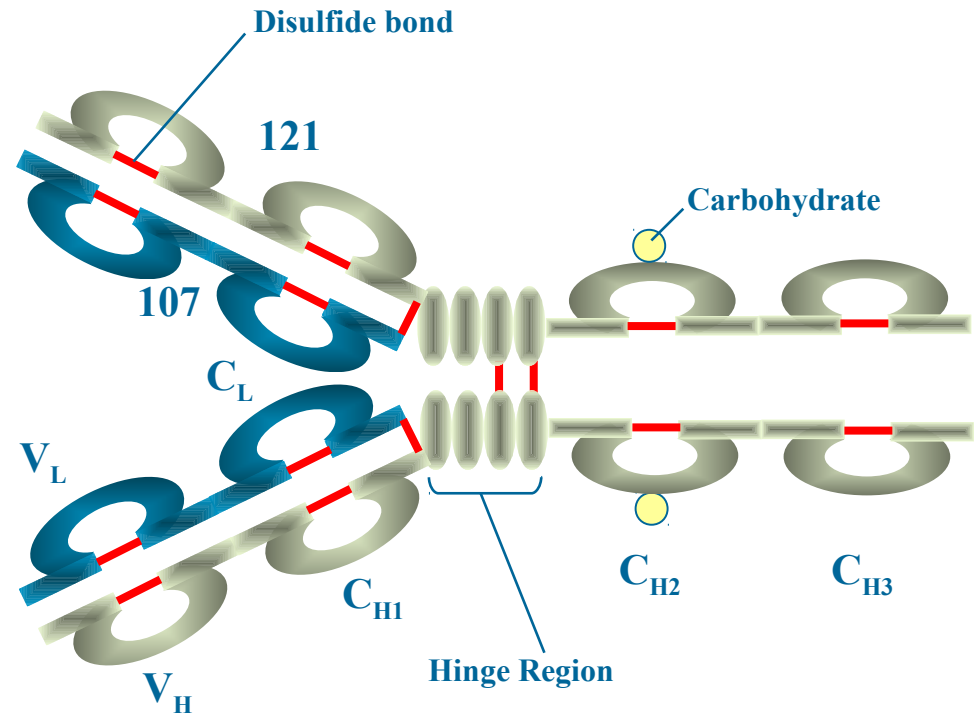
# Immunoglobulin Structure

- Domains
  - Heavy chains (4-5 Domains)
  - Light chains (2 Domains)
- Oligosaccharides (10%)



# Immunoglobulin Structure

- **Variable & Constant Regions**
  - $V_L$  &  $C_L$
  - $V_H$  &  $C_H$
- **Hinge Region**  
(10-60 aa)



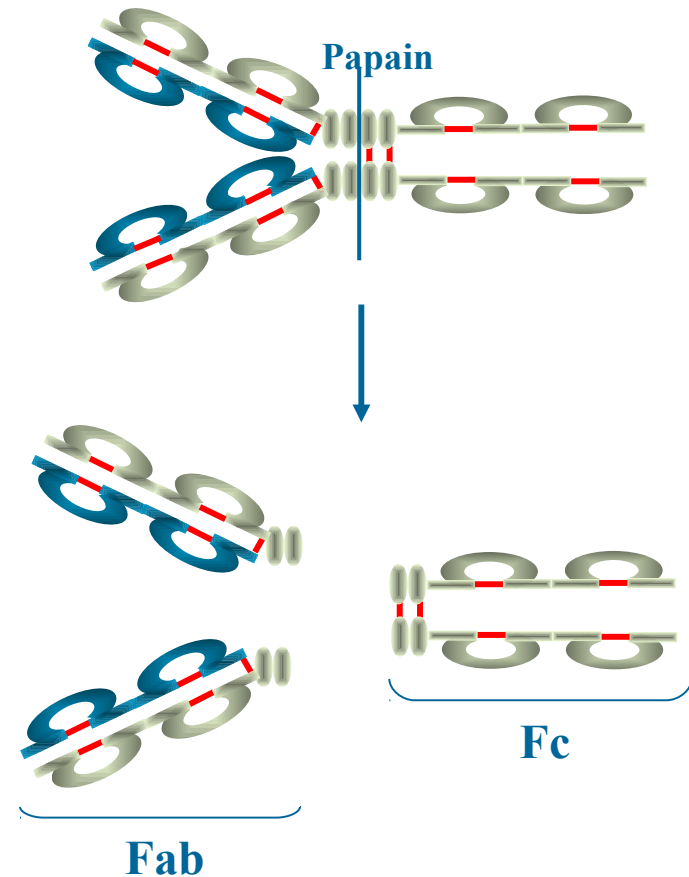
- Fab Fragment Ag binding
- Fc Fragment cristalizable

- Fab

- Ag binding
- Valence = 1
- Specificity

- Fc

- Effector functions





# Immunoglobulin Fragments:

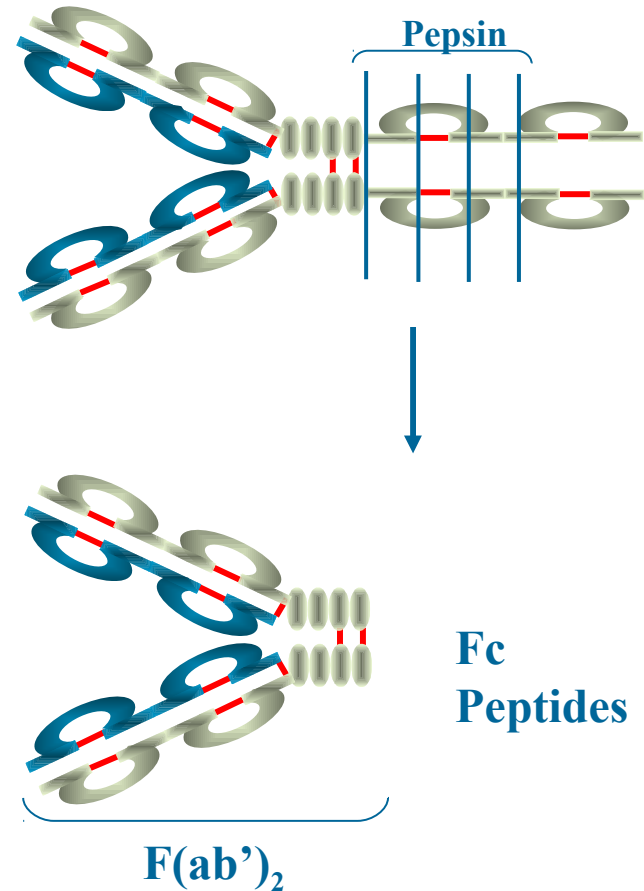
- Fab

- Ag binding

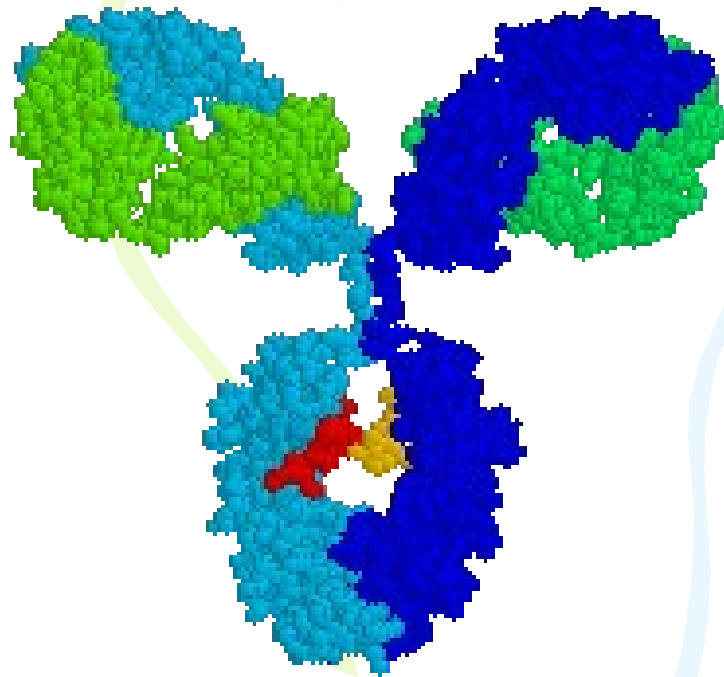
- Fc

- Effector functions

- $F(ab')_2$

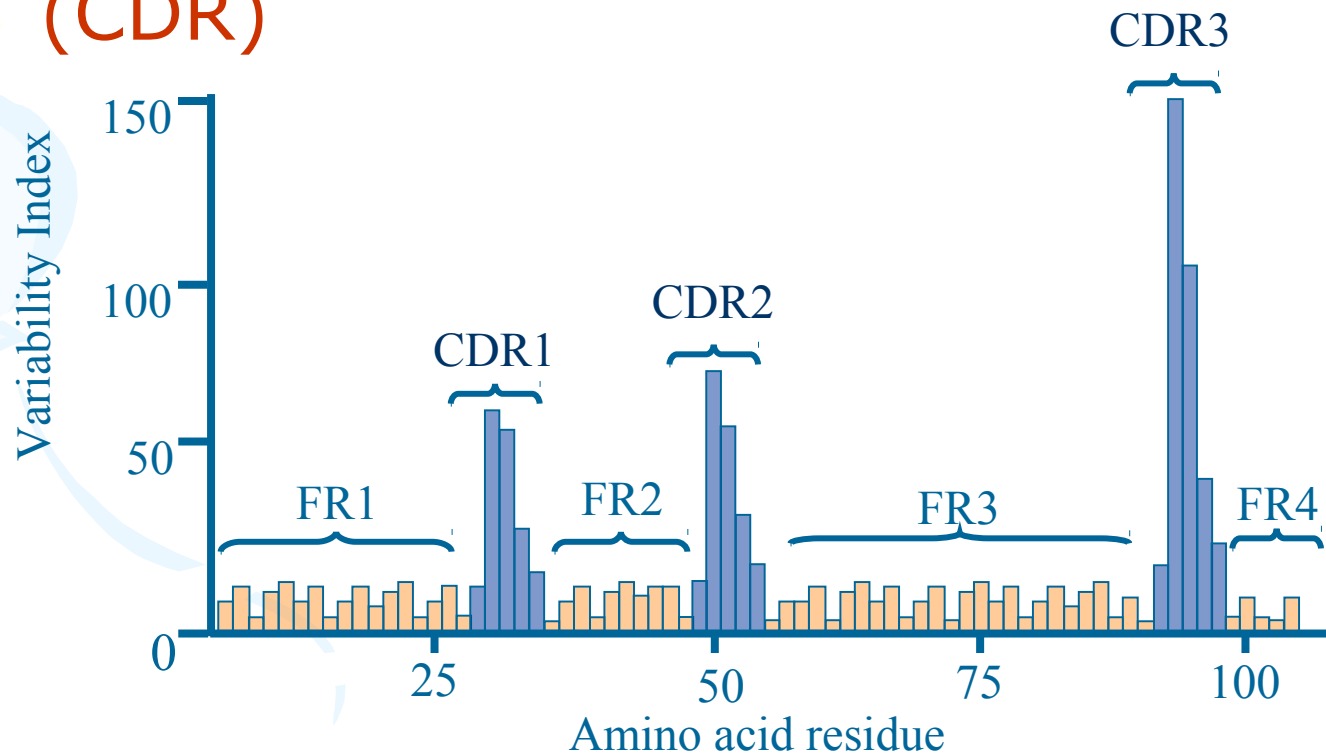


# Antibody molecule

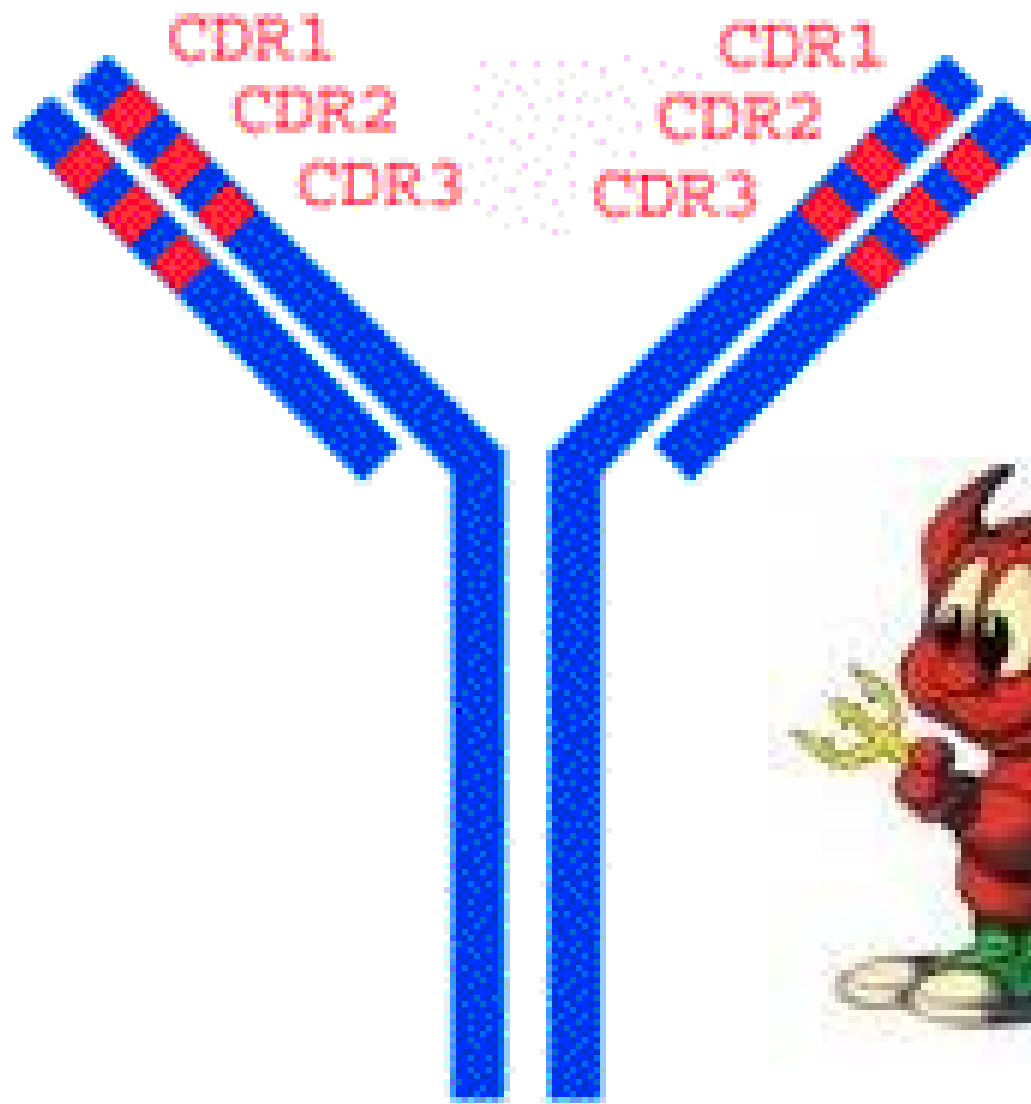


# Structure of the Variable Region

- **Hypervariable (HVR)** or **complimentarity determining regions (CDR)**



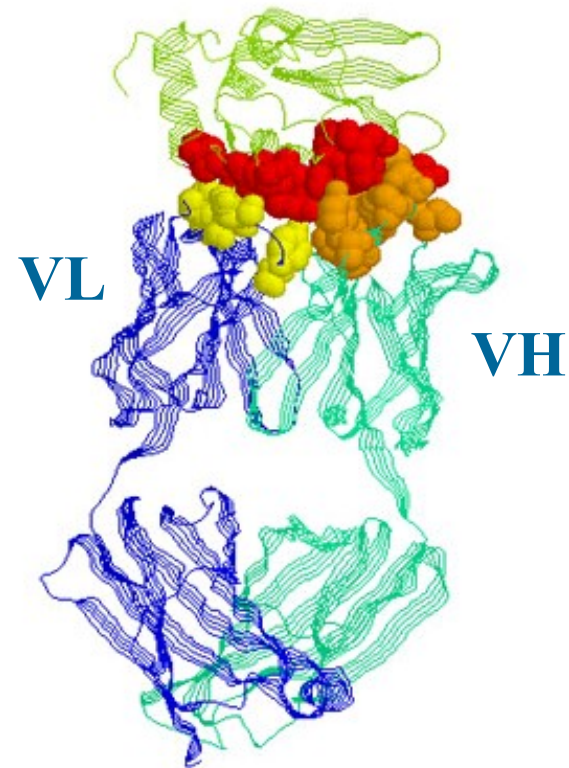
- **Framework regions**



# Nature of Ag/Ab Reactions

- Non-covalent Bonds

- Hydrogen bonds
- Electrostatic bonds
- Van der Waals forces
- Hydrophobic bonds



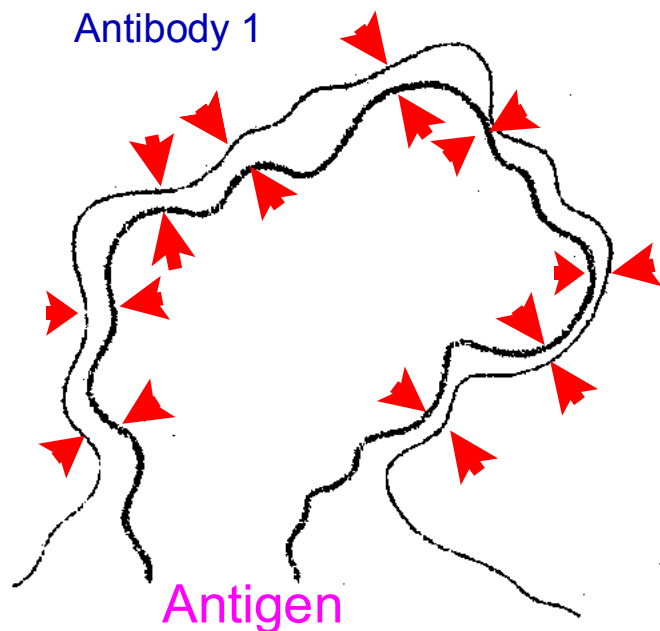
**Fab**

# Nature of Ag/Ab Reactions

- Lock and Key Concept

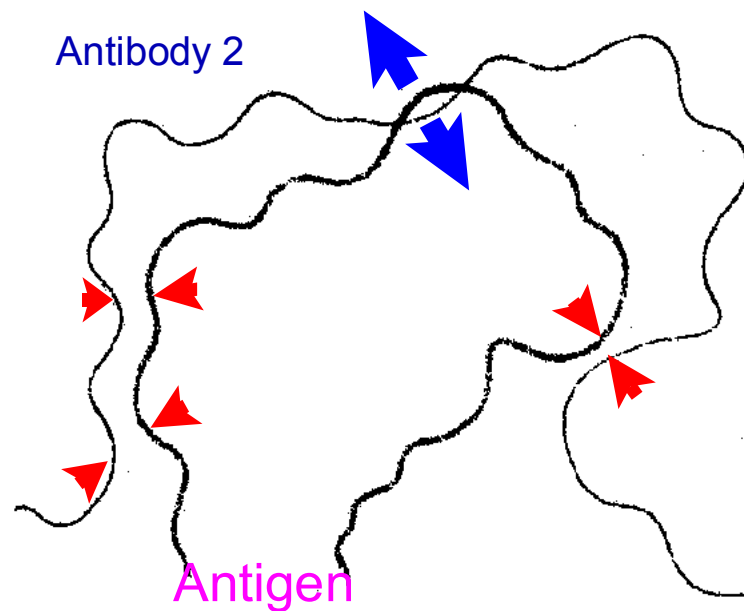


Good Fit



High Affinity

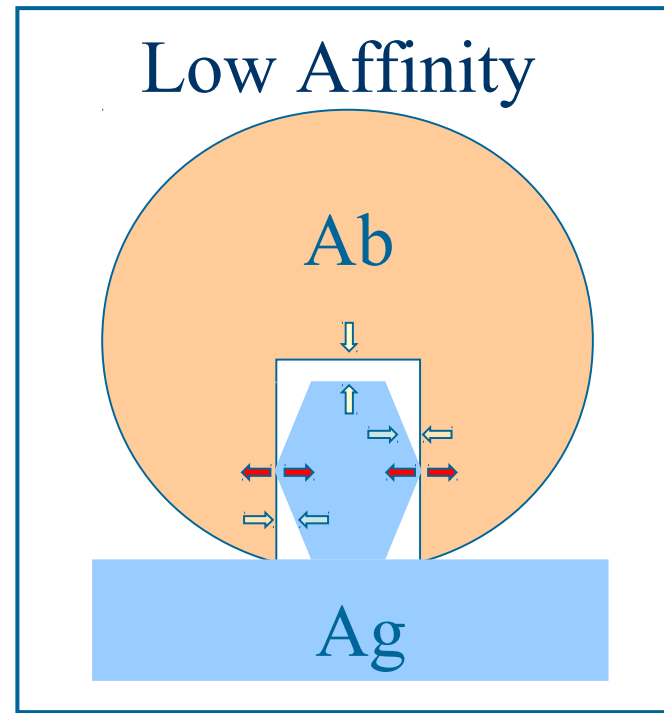
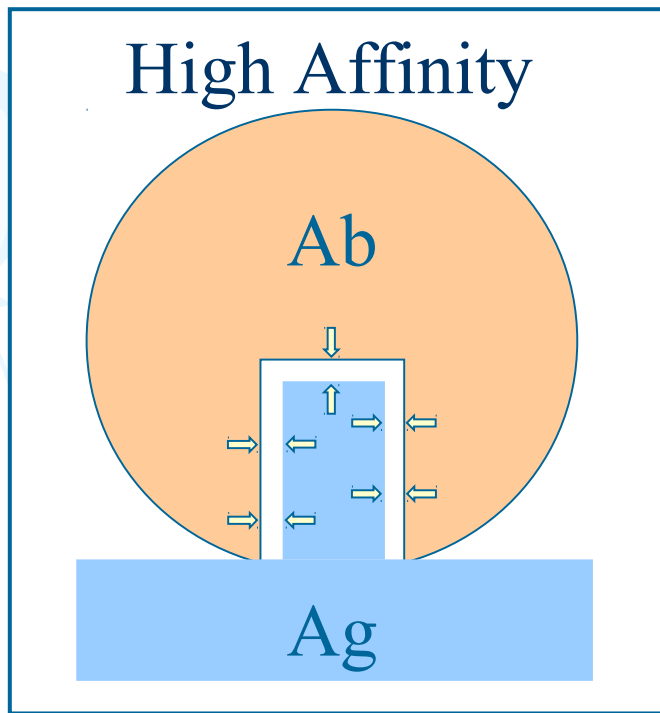
Poor Fit



Low Affinity

# Affinity

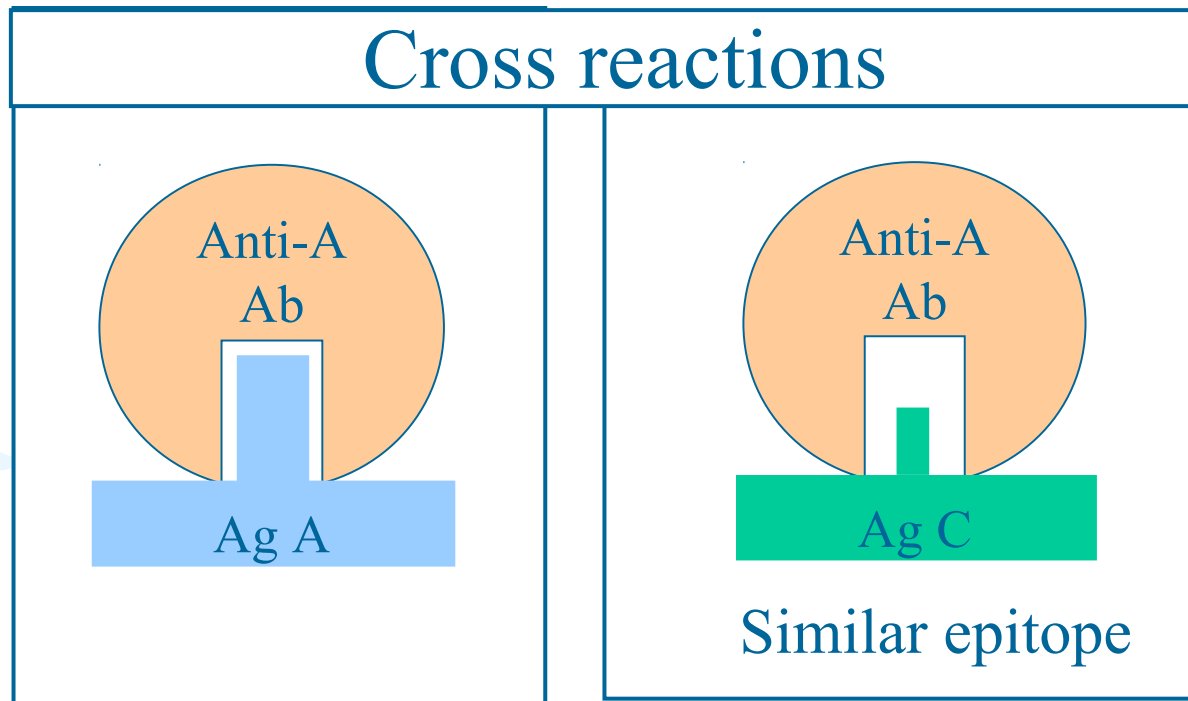
- Strength of the reaction between an epitope and a paratope





# Cross Reactivity

- The ability of an Ab to react with more than one epitope



The background features several large, overlapping, semi-transparent swirls in shades of purple, green, and blue. Scattered throughout are numerous small, yellow, triangular shapes, some pointing towards the center and others pointing outwards, creating a dynamic and celebratory feel.

**Immunoglobulin:**

**Isotypes,**

**Allotypes**

**idotypes**

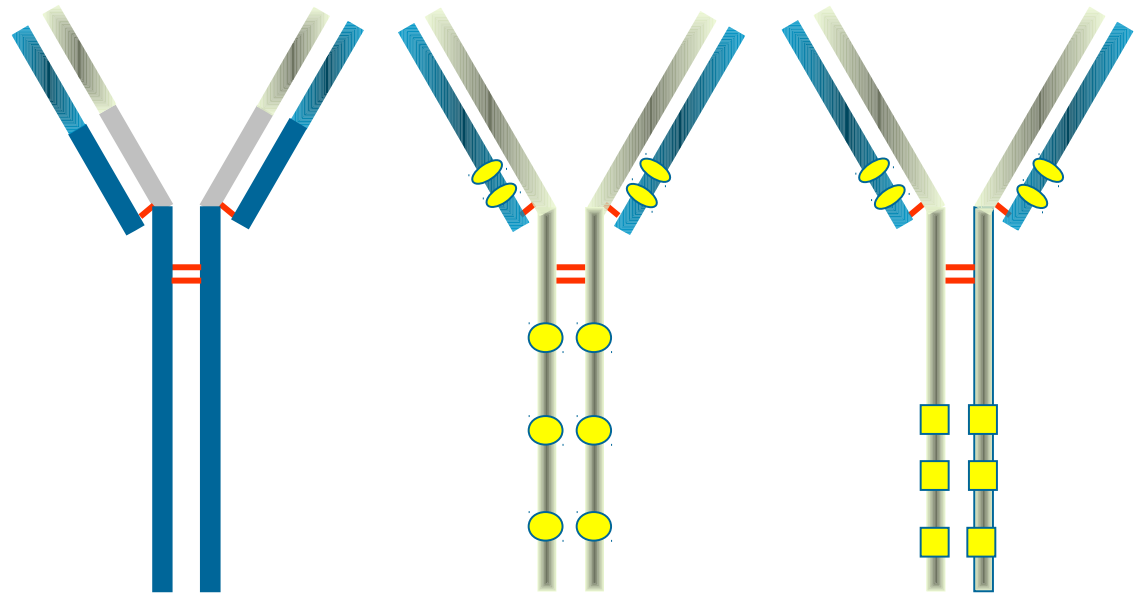


# Immunoglobulin Isotypes

- Definition - Antigenic determinants at **CL and CH** that characterize the classes and subclasses of heavy chains and **types and subtypes of light chains**

# Immunoglobulin Isotypes

- Location



IgG1 (kappa)

IgM (kappa)



# Human Immunoglobulin Classes

- IgG - Gamma ( $\gamma$ ) heavy chains
- IgM - Mu ( $\mu$ ) heavy chains
- IgA - Alpha ( $\alpha$ ) heavy chains
- IgD - Delta ( $\delta$ ) heavy chains
- IgE - Epsilon ( $\epsilon$ ) heavy chains



# Human Immunoglobulin Subclasses

- IgG Subclasses

- IgG1 - Gamma 1 ( $\gamma$ 1) heavy chains
- IgG2 - Gamma 2 ( $\gamma$ 2) heavy chains
- IgG3 - Gamma 3 ( $\gamma$ 3) heavy chains
- IgG4 - Gamma 4 ( $\gamma$  4) heavy chains

- IgA subclasses

- IgA1 - Alpha 1 ( $\alpha$ 1) heavy chains
- IgA2 - Alpha 2 ( $\alpha$  2) heavy chains

A decorative graphic on the left side of the slide features three balloons: a light green one at the top, a light blue one in the middle, and a light purple one at the bottom. Each balloon is attached to a thin, wavy string and has several small, yellow, triangular shapes around it, resembling streamers or confetti.

# Human Immunoglobulin Light Chain Types

- Kappa ( $\kappa$ )
- Lambda ( $\lambda$ )



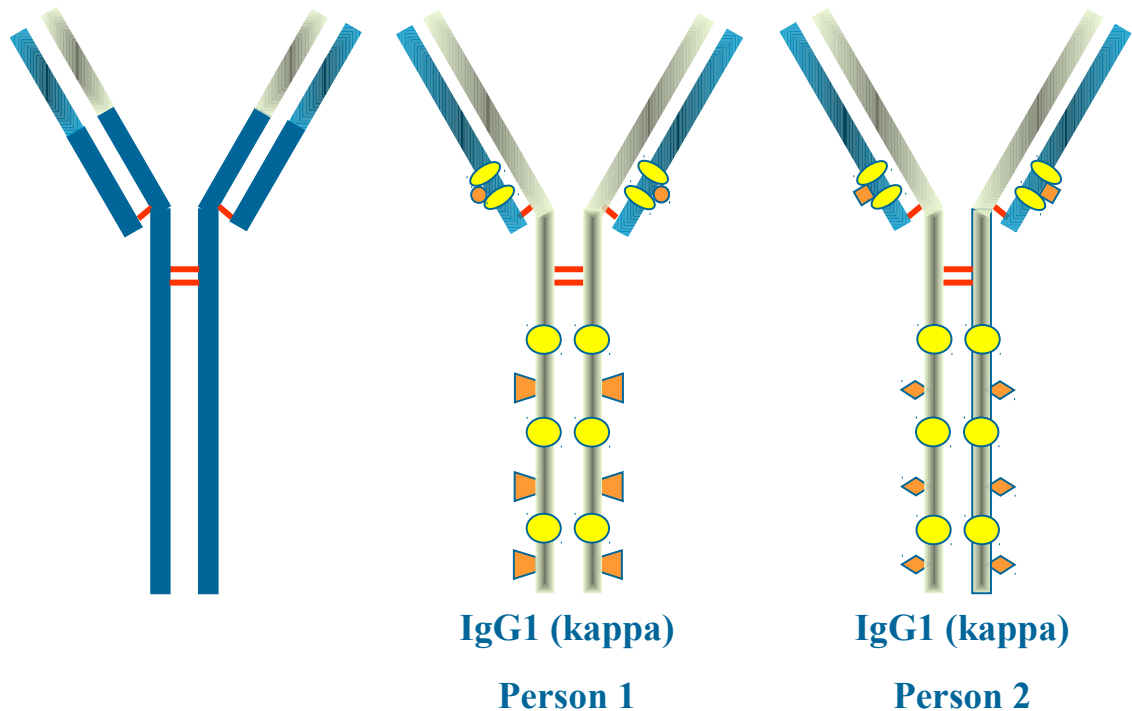
# Human Immunoglobulin Light Chain Subtypes

- Lambda light chains
  - Lambda 1 ( $\lambda 1$ )
  - Lambda 2 ( $\lambda 2$ )
  - Lambda 3 ( $\lambda 3$ )
  - Lambda 4 ( $\lambda 4$ )



# Immunoglobulin Allotypes

- Definition - Antigenic determinants at **CL** and **CH** specified by allelic forms of the Ig genes



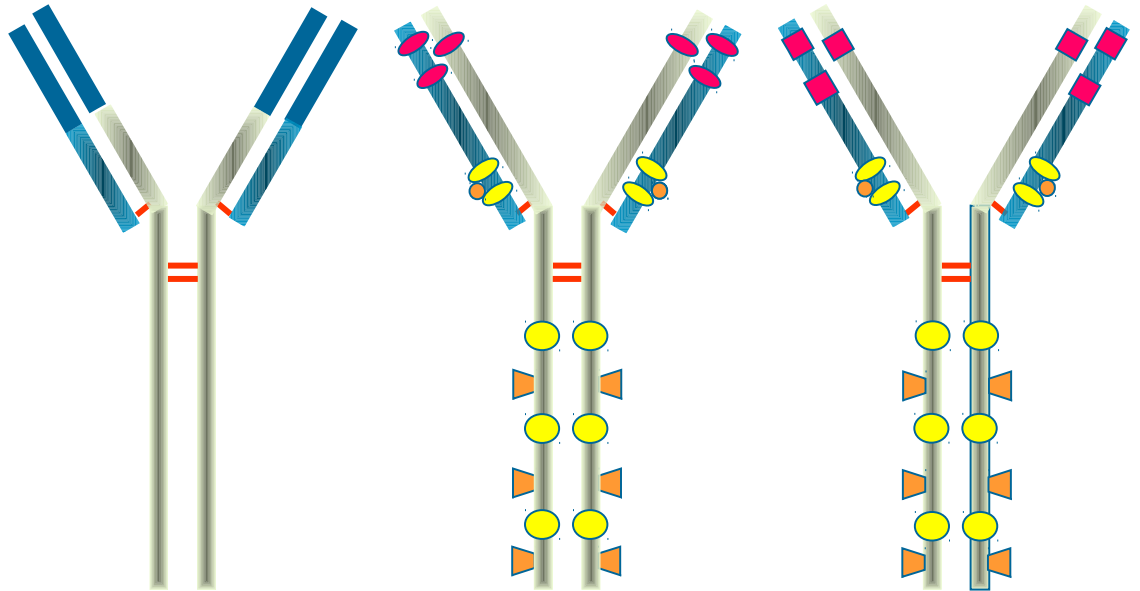


# Immunoglobulin Idiotypes

- Definition - Unique antigenic determinants present on individual antibody molecules at variable region

# Immunoglobulin Idiotypes

- Definition
- Location



IgG1 (kappa)

Person 1

anti-A

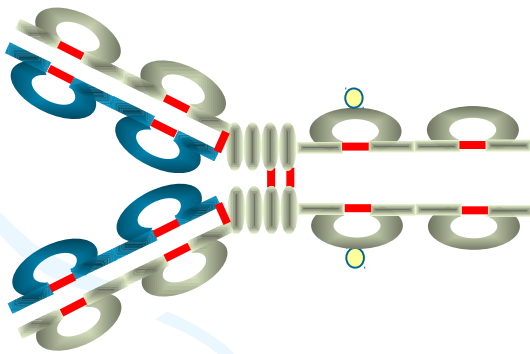
IgG1 (kappa)

Person 1

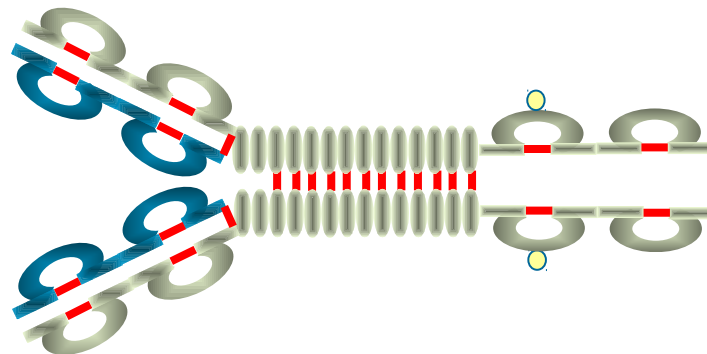
anti-B

# IgG

- Structure
  - Monomer (7S)



IgG1, IgG2 and IgG4



IgG3

**IgG1, 60-70%; IgG2, 20%; IgG3, 4-8%, IgG4; 2-6%**

# IgG

## Structure

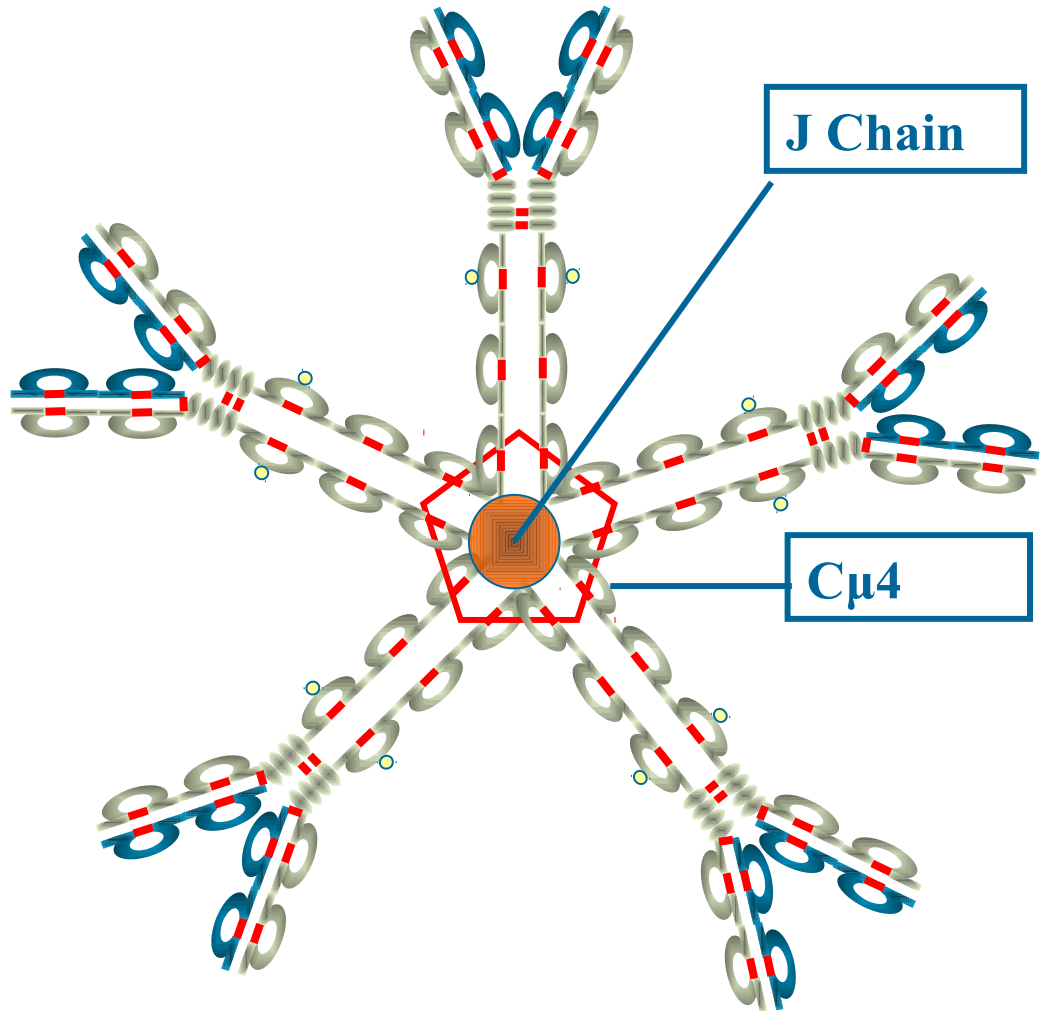
### • Properties

- Major serum Ig (75%) (13.5 mg/ml)
- Major Ig in extravascular spaces
- Placental transfer – Does not require Ag binding (□ IgG2)
- Fixes complement (□ IgG4),
- Binds to Fc receptors (□ IgG2, IgG4)
- Secondary response

# IgM

- Structure

- Pentamer (19S)
- Extra domain ( $C_{H4}$ )
- J chain



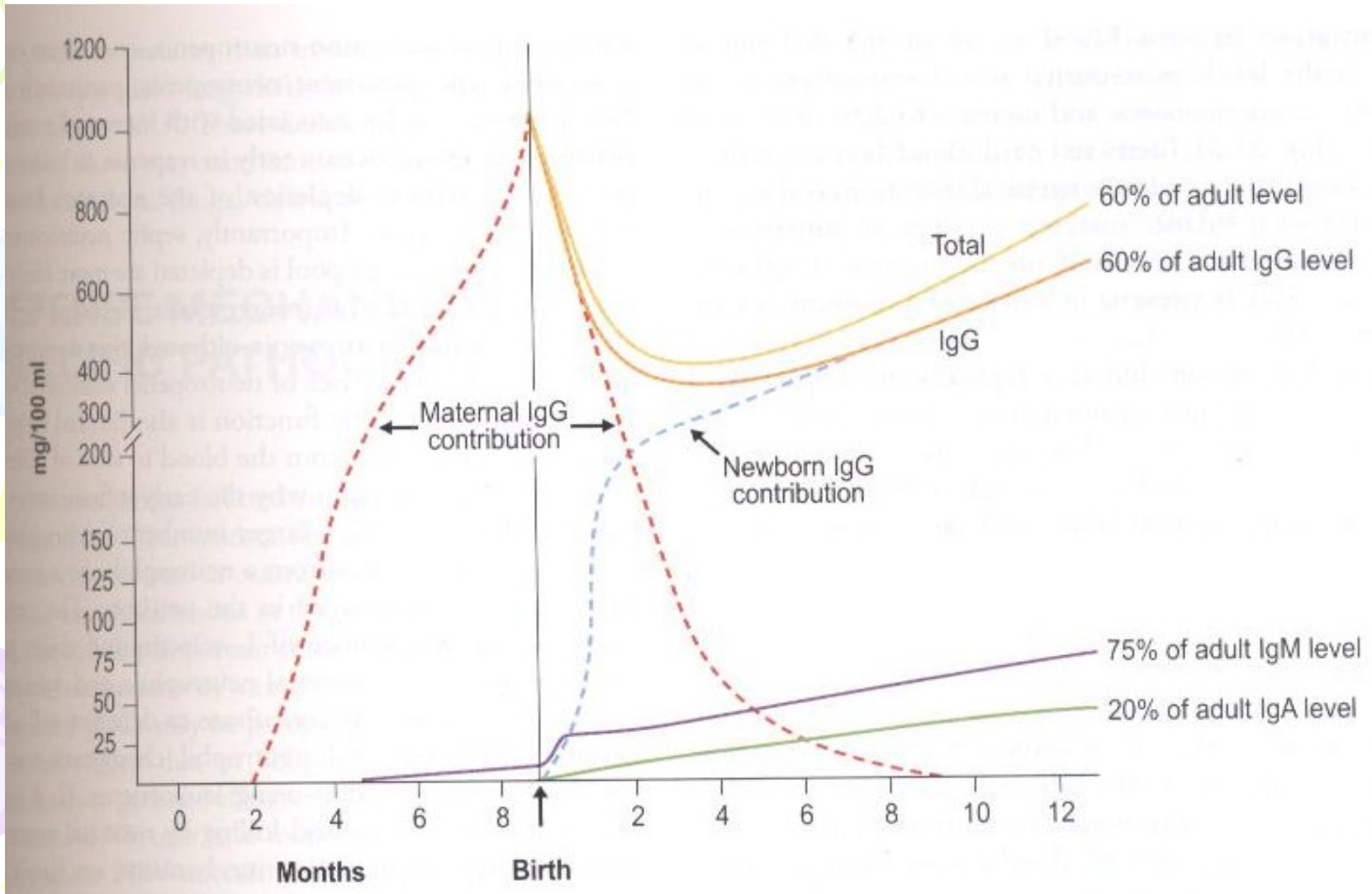
# IgM

## Structure

- Properties

- 3rd highest serum Ig (10%), 1.5 mg/ml
- First Ig made by fetus and B cells
- Fixes complement

# Ab levels in fetus and infants in the first year of life





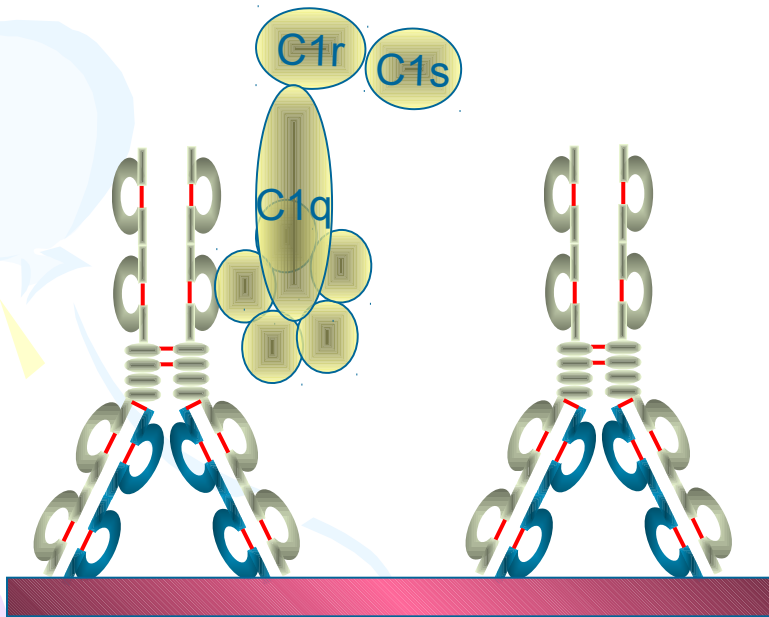
# IgM

## Structure

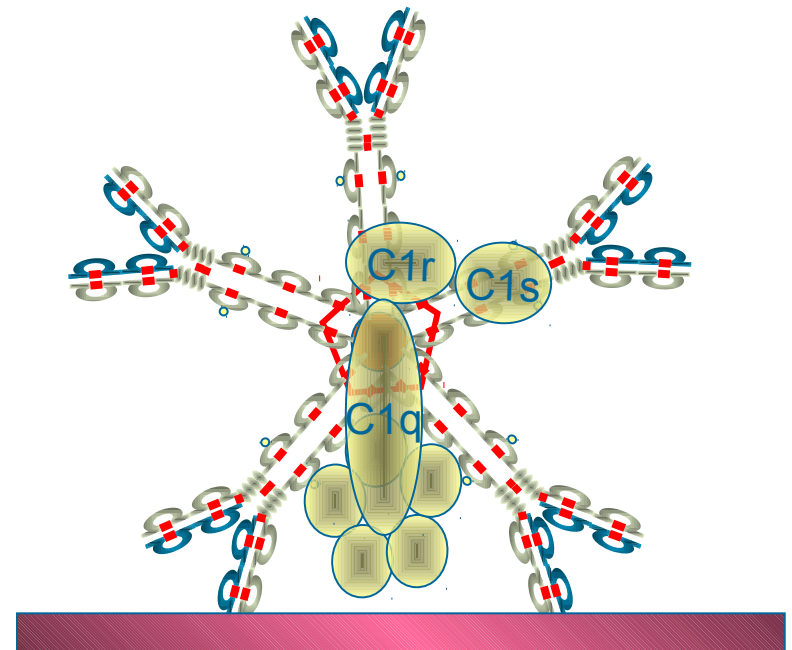
- Properties

- 3rd highest serum Ig (10%), 1.5 mg/ml
- First Ig made by fetus and B cells
- **Fixes complement**

# Fixation of C1 by IgG and IgM Abs



**No activation**

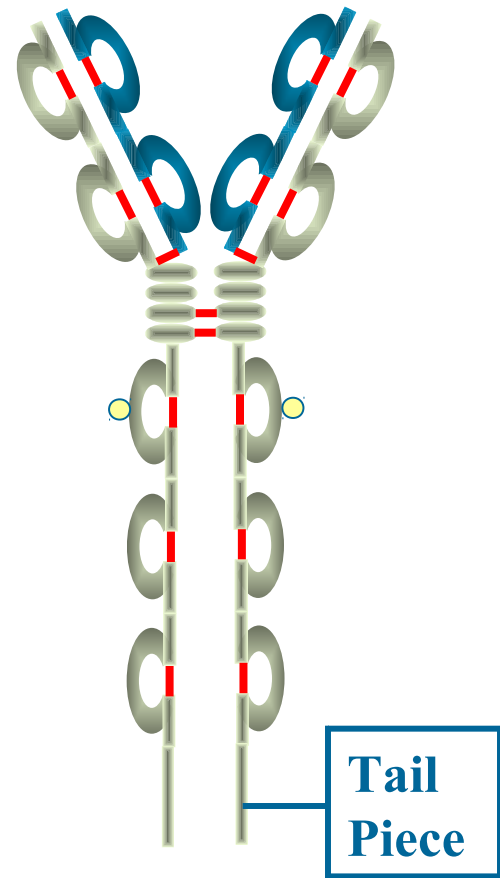


**Activation**

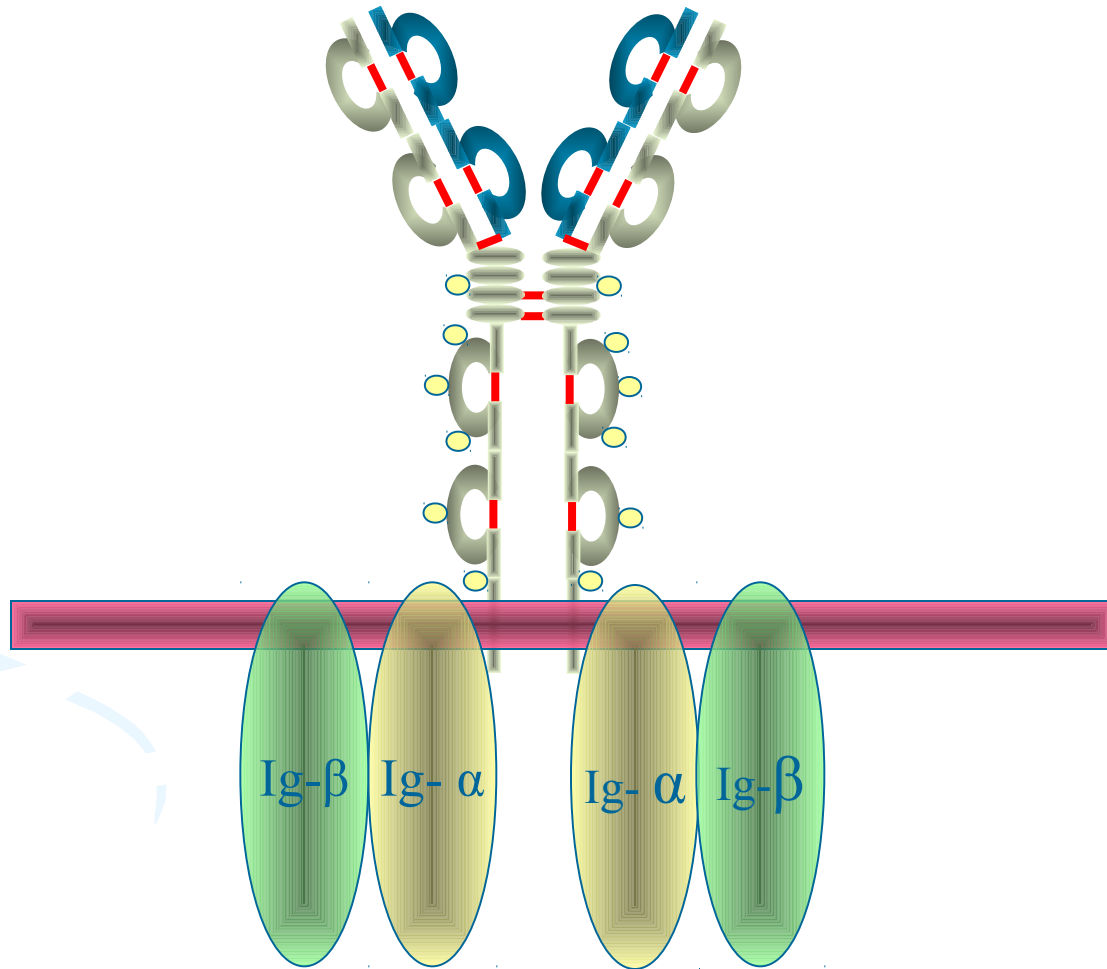
# IgM

- Structure
- Properties

- Agglutinating Ig
- B cell surface Ig



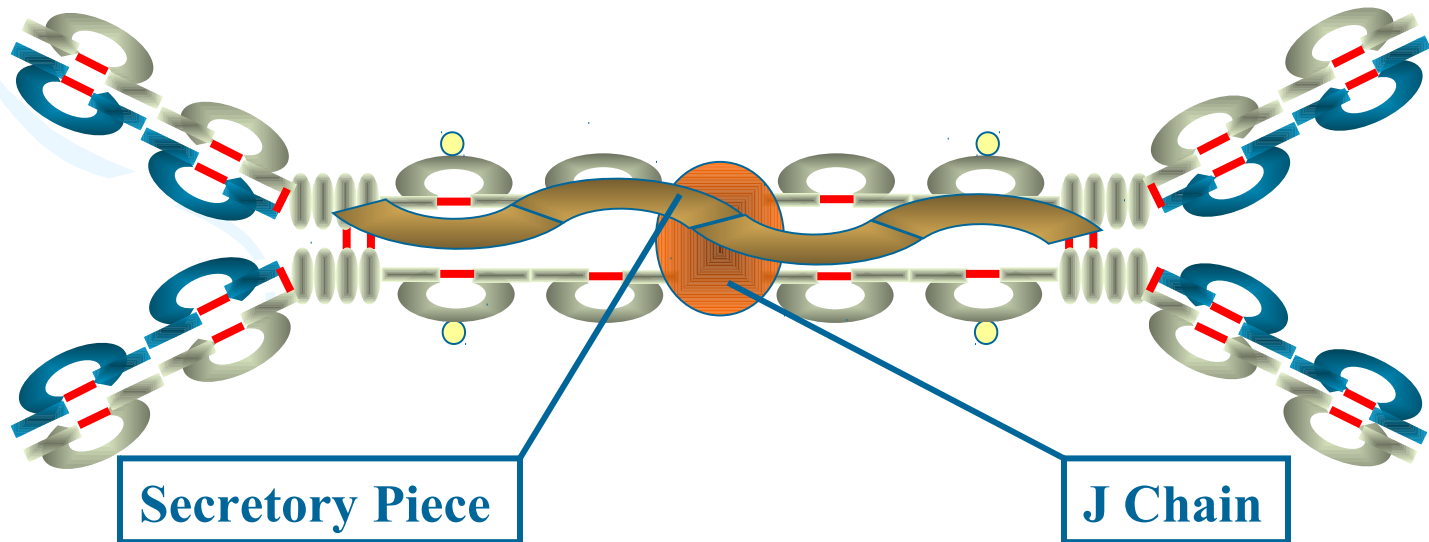
# B Cell Antigen Receptor (BCR)



# IgA

- Structure

- Serum - monomer
- Secretions (sIgA)
  - Dimer (11S),
  - J chain
  - Secretory component



# IgA

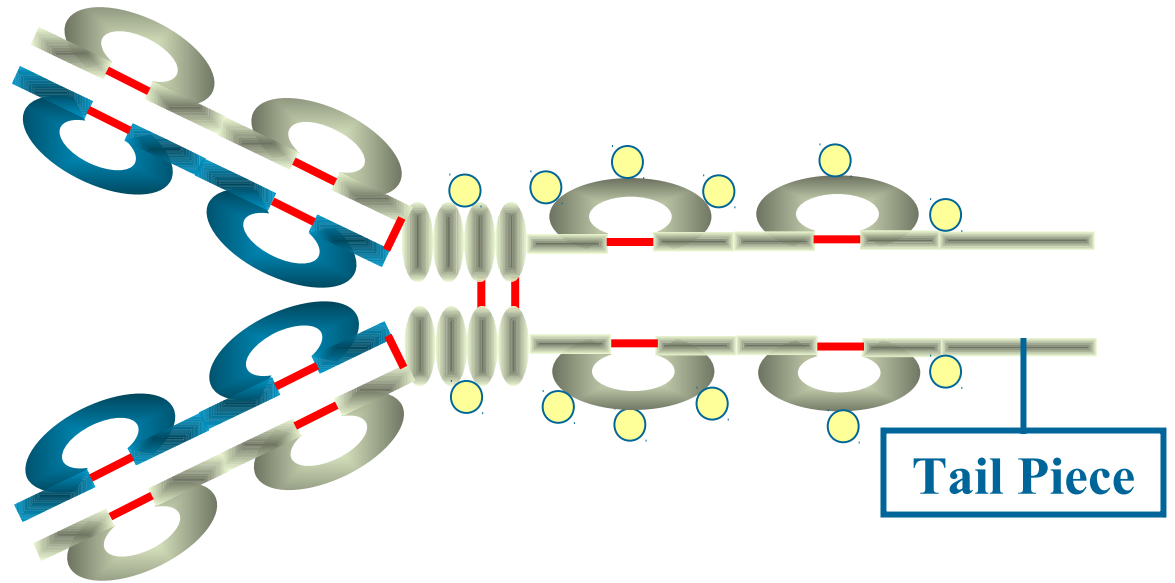
- Structure

- Properties

- 2nd highest serum Ig (15%) ; 3.5 mg/ml
- Major secretory Ig (Mucosal Immunity)
  - Tears, saliva, gastric and pulmonary secretions
- Does not fix complement (unless aggregated)

# IgD

- Structure
  - Monomer
  - Tail piece



# IgD

- Structure

- Properties

- serum Ig (trace)

- B cell surface Ig

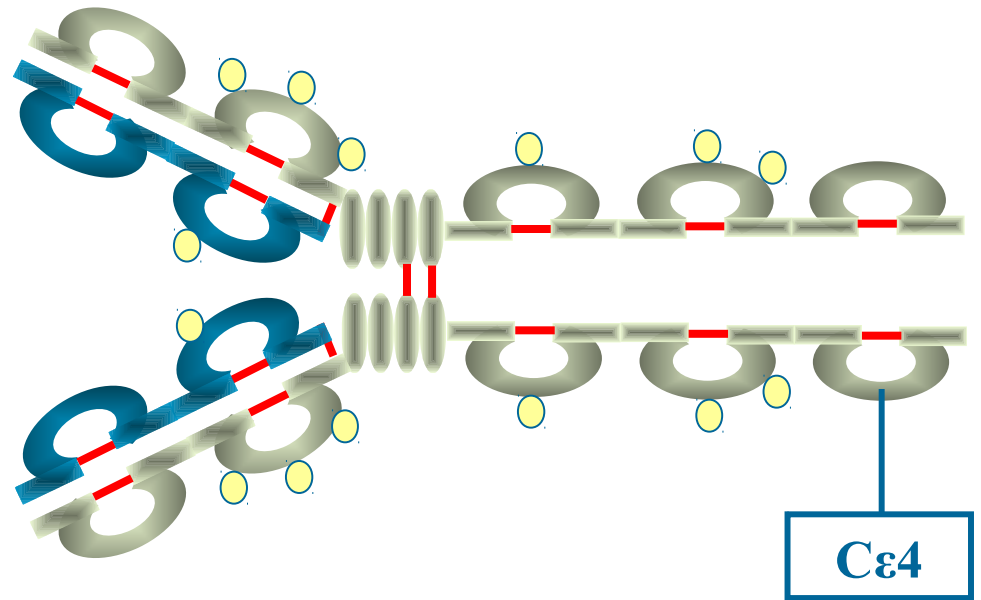
- Does not bind complement

- Susceptible to proteolysis



# IgE

- Structure
  - Monomer
  - Extra domain ( $C_{H4}$ )





# IgE

- Structure

- Properties

- Least common serum Ig (0.05 mg/ml)
  - Binds to basophils and mast cells (Does not require Ag binding)
- Allergic reactions
- Parasitic infections (Helminths)
  - Binds to Fc receptor on eosinophils
- Does not fix complement
- Plasma cells located at RT & GI

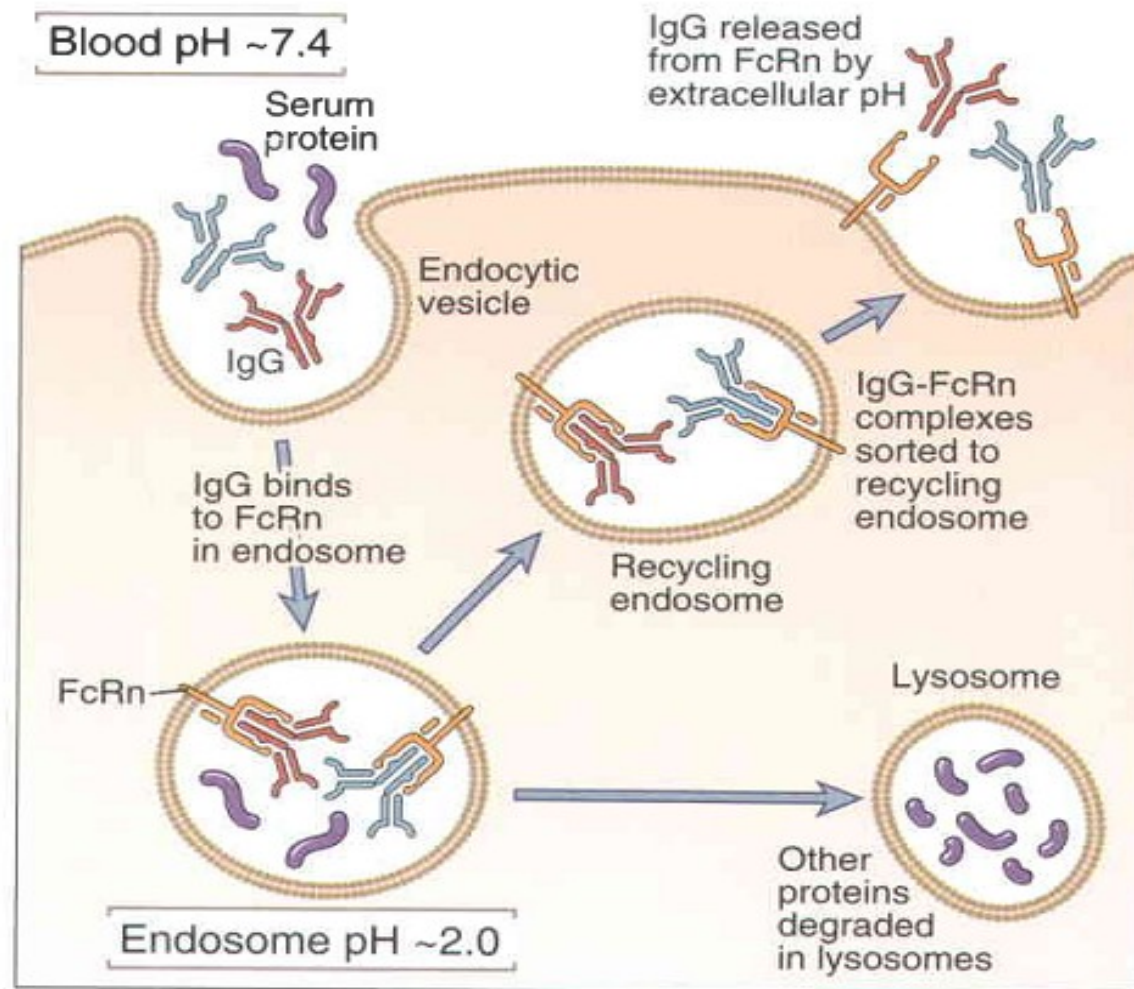
Immunoglobulin									
	IgG1	IgG2	IgG3	IgG4	IgM	IgA1	IgA2	IgD	IgE
Heavy chain	$\gamma_1$	$\gamma_2$	$\gamma_3$	$\gamma_4$	$\mu$	$\alpha_1$	$\alpha_2$	$\delta$	$\epsilon$
Molecular weight (kDa)	146	146	165	146	970	160	160	184	188
Serum level (mean adult mg ml <sup>-1</sup> )	9	3	1	0.5	1.5	3.0	0.5	0.03	$5 \times 10^{-5}$
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)

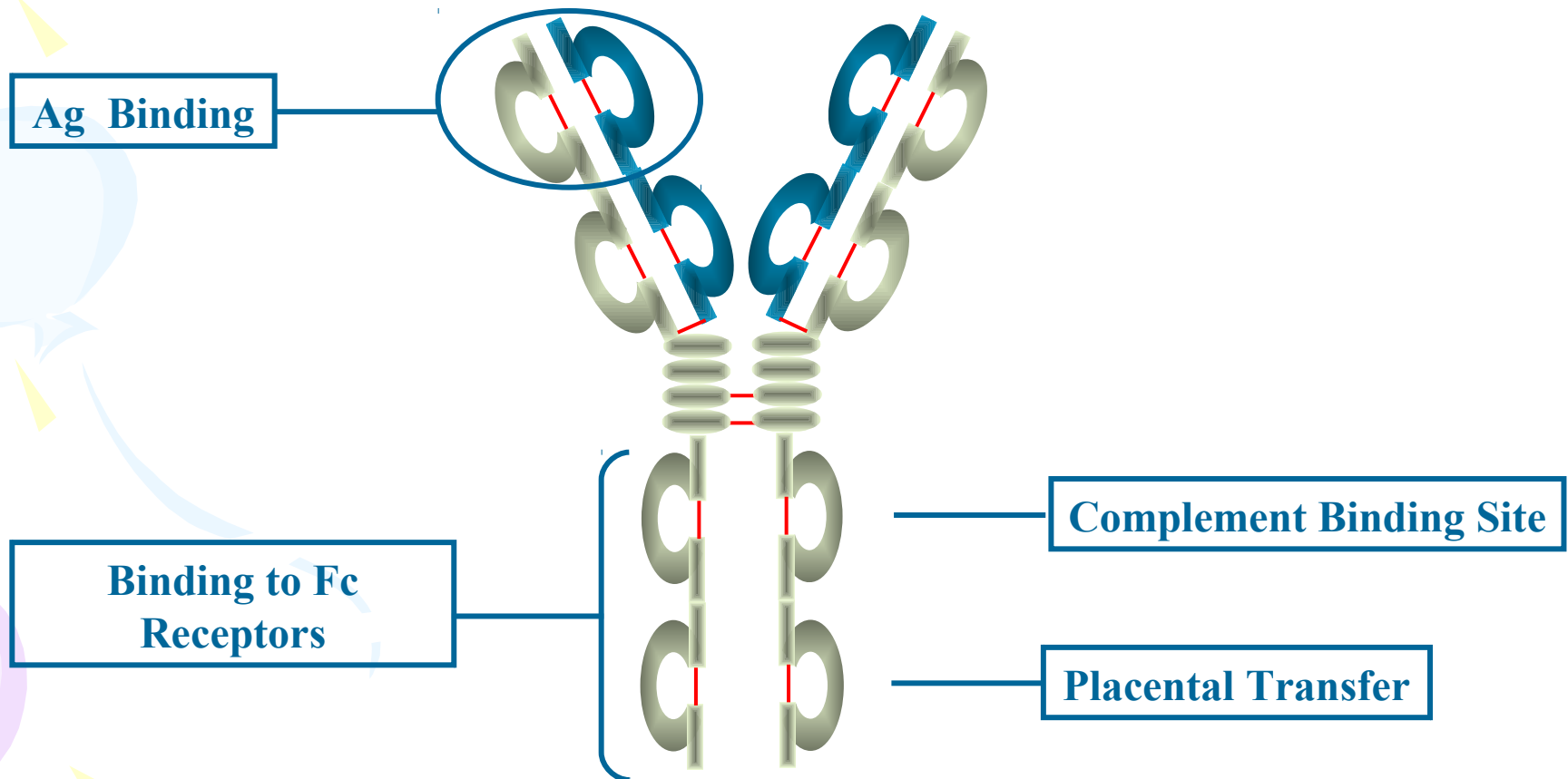
## FcRn: Fc receptor neonatal

On the surface of endothelial cells ,  
and placenta

# FcRn contributes to the long half-life of IgG molecules.



# Immunoglobulin Function



# Neutralization of Toxins by IgG Antibodies Protects Cells From Their Damaging Action

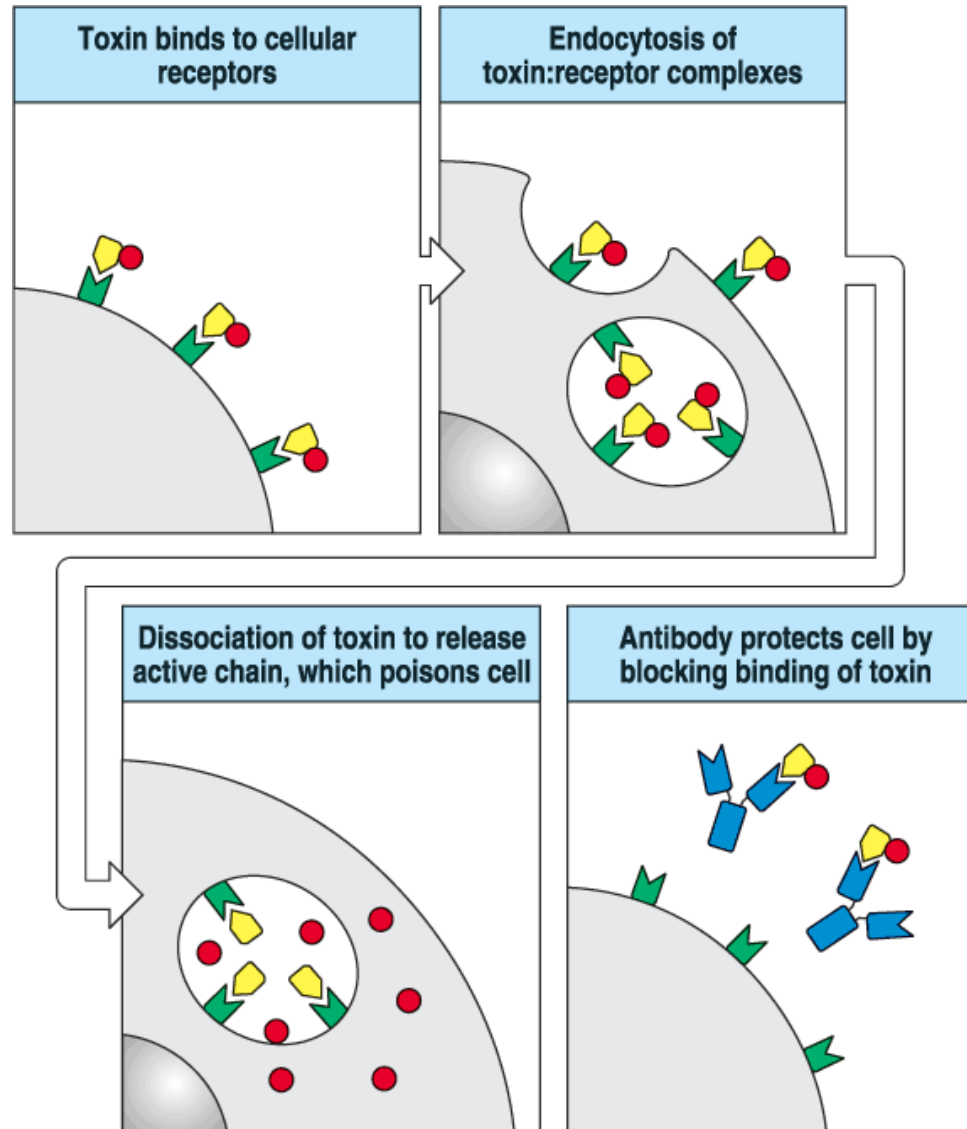


Fig 9.24 © 2001 Garland Science

# Viral Infection of Cells Can Be Blocked by Neutralizing Antibodies

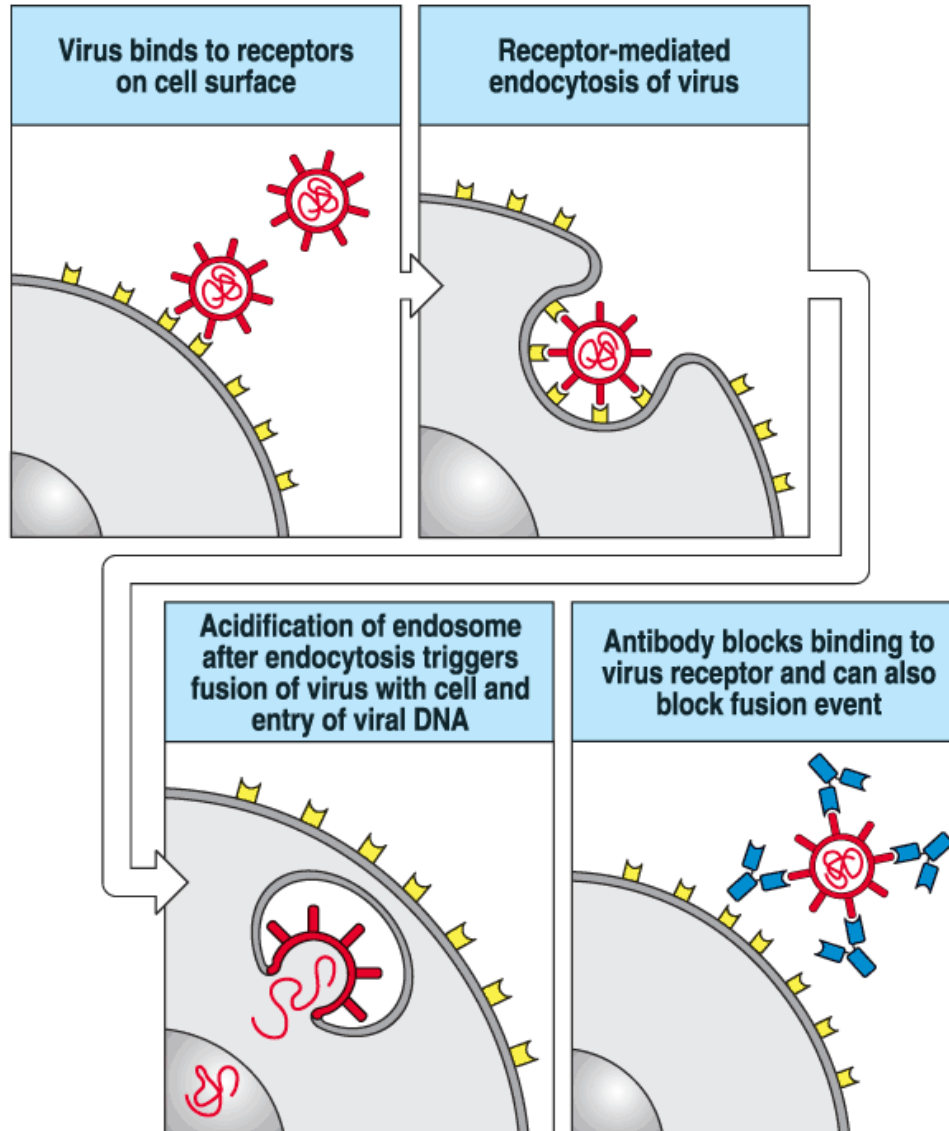


Fig 9.25 © 2001 Garland Science

# Antibodies Can Prevent Attachment of Bacteria to Cell Surfaces

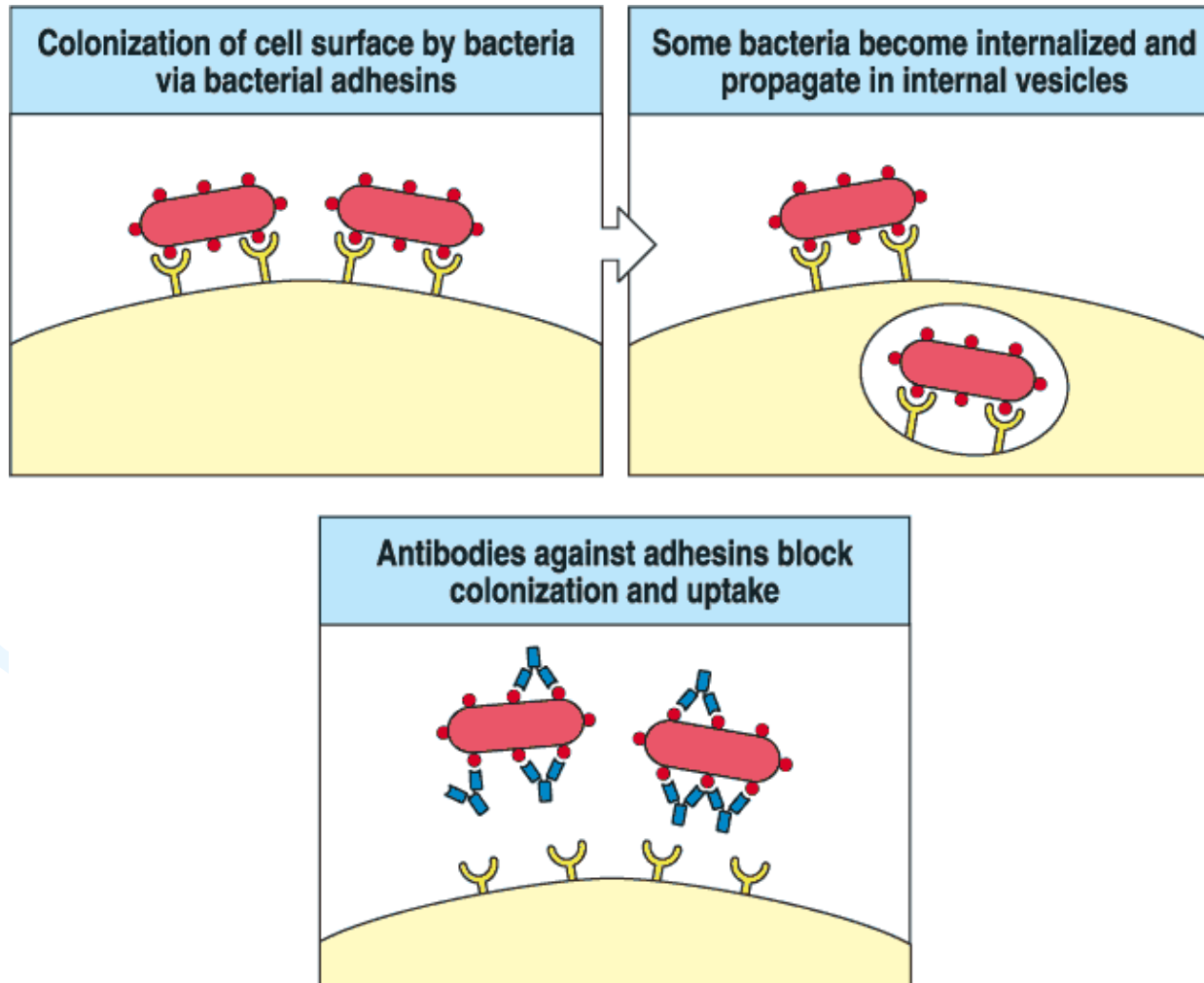
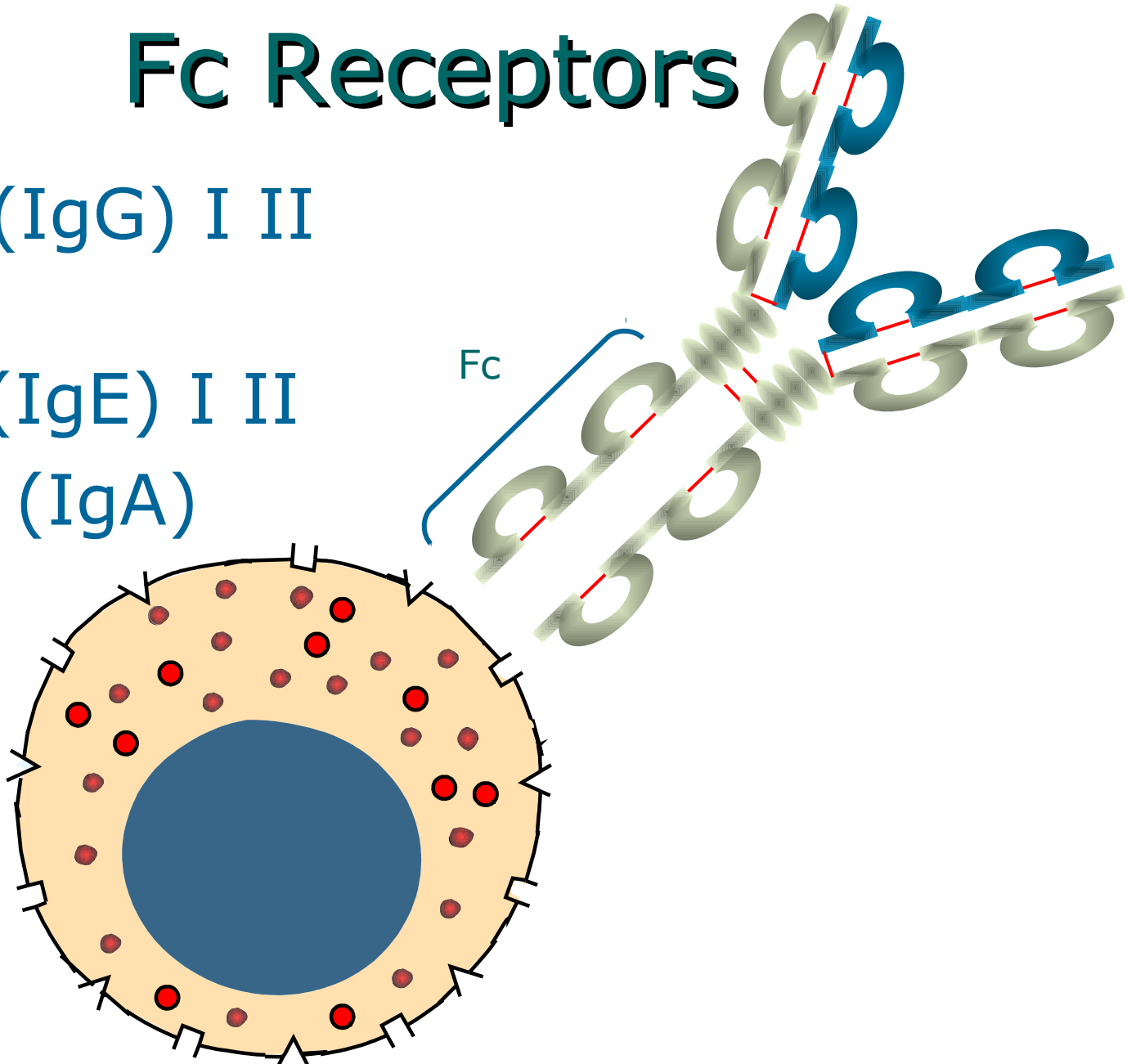


Fig 9.26 © 2001 Garland Science



# Fc Receptors

- Fc $\gamma$ R (IgG) I II III
- Fc $\epsilon$ R (IgE) I II
- Fc $\alpha$ R (IgA)



FcR	Affinity for immunoglobulin	Cell distribution	Function
FcγRI (CD64)	High ( $K_d \sim 10^{-9}$ M); binds IgG1 and IgG3, can bind monomeric IgG	Macrophages, neutrophils; also eosinophils	Phagocytosis; activation of phagocytes
FcγRIIA (CD32)	Low ( $K_d > 10^{-7}$ M)	Macrophages, neutrophils; eosinophils, platelets	Phagocytosis; cell activation (inefficient)
FcγRIIB (CD32)	Low ( $K_d > 10^{-7}$ M)	B lymphocytes	Feedback inhibition of B cells
FcγRIIIA (CD16)	Low ( $K_d > 10^{-6}$ M)	NK cells	Antibody-dependent cell-mediated cytotoxicity
FcγRIIIB (CD16)	Low ( $K_d > 10^{-6}$ M); GPI-linked protein	Neutrophils, other cells	Phagocytosis (inefficient)
FcεRI	High ( $K_d > 10^{-10}$ M); binds monomeric IgE	Mast cells, basophils, eosinophils	Cell activation (degranulation)
FcεRII (CD23)	Low ( $K_d > 10^{-7}$ M)	B lymphocytes, eosinophils, Langerhans cells	Unknown
FcαR (CD89)	Low ( $K_d > 10^{-6}$ M)	Neutrophils, eosinophils, monocytes	Cell activation?



# Functions

- Opsonization (Intracellular killing)
- Antibody dependent cellular cytotoxicity (ADCC)  
(Extracellular killing)
- Inhibition of Ab production

# OPSONIZATION AND PHAGOCYTOSIS

FcR

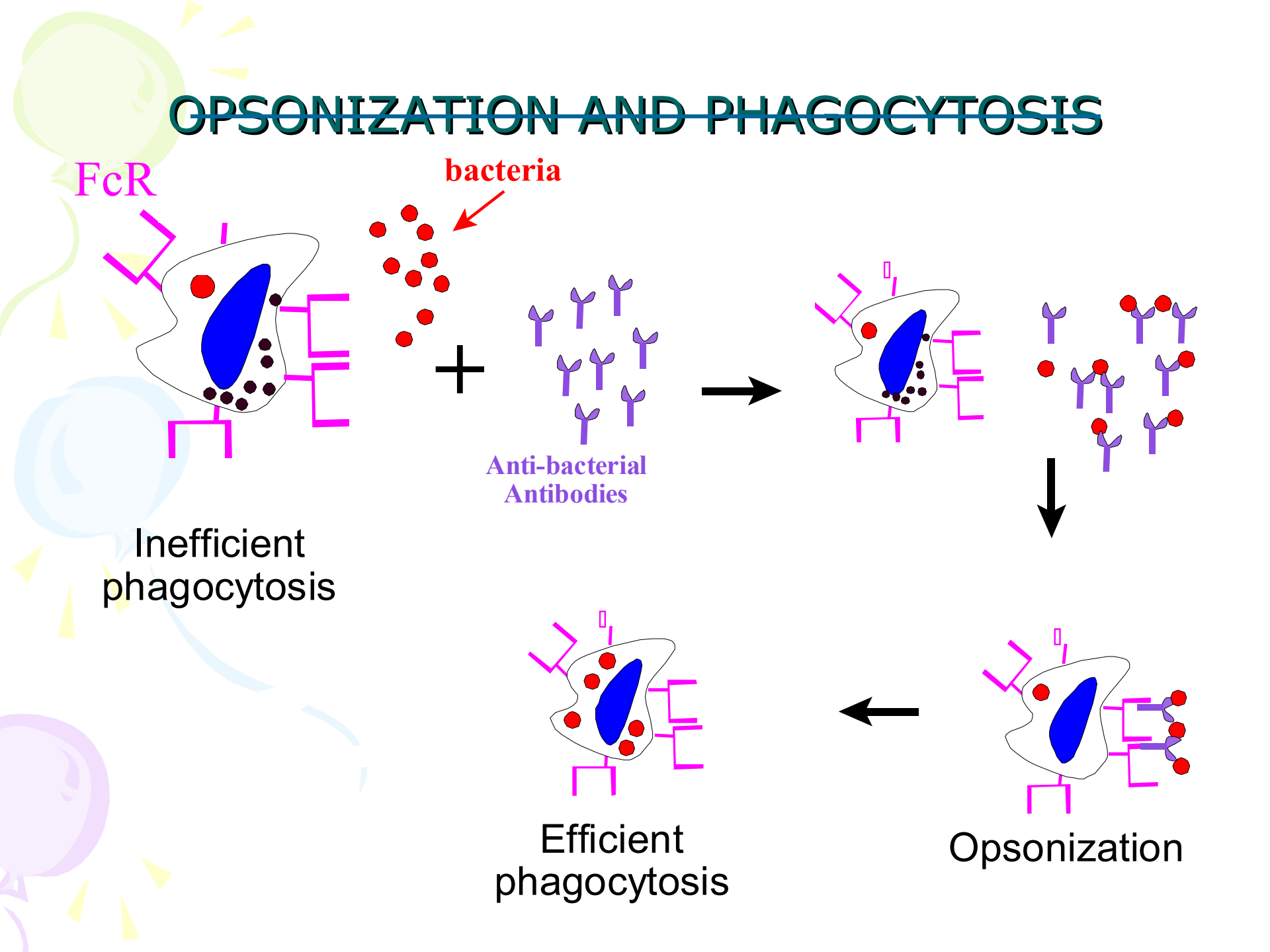
bacteria

Anti-bacterial  
Antibodies

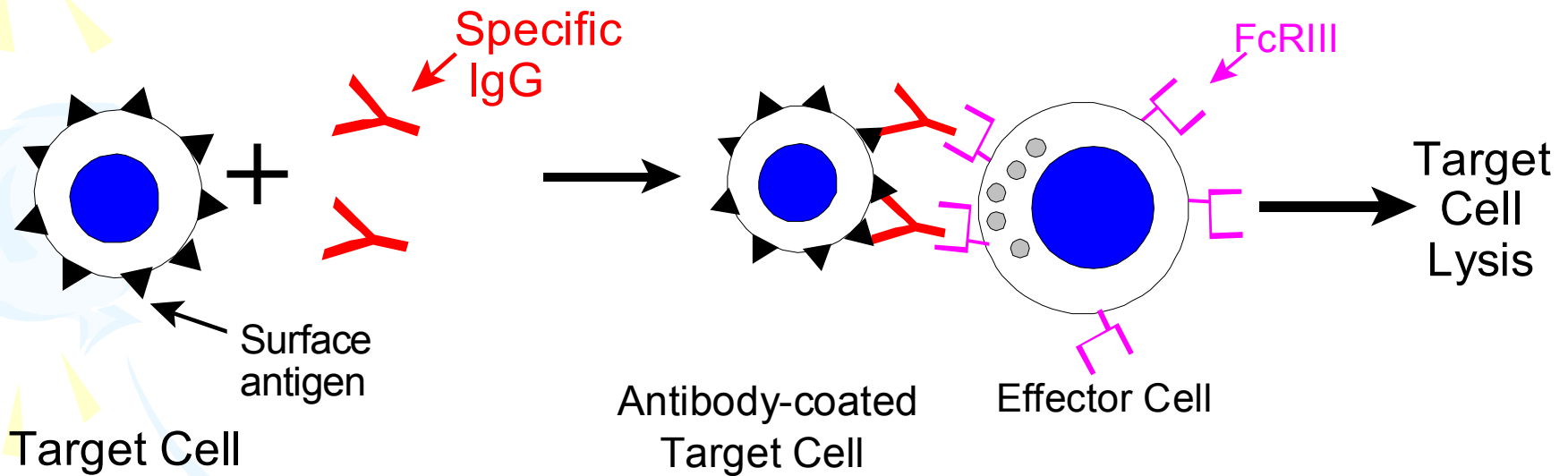
Inefficient  
phagocytosis

Efficient  
phagocytosis

Opsonization

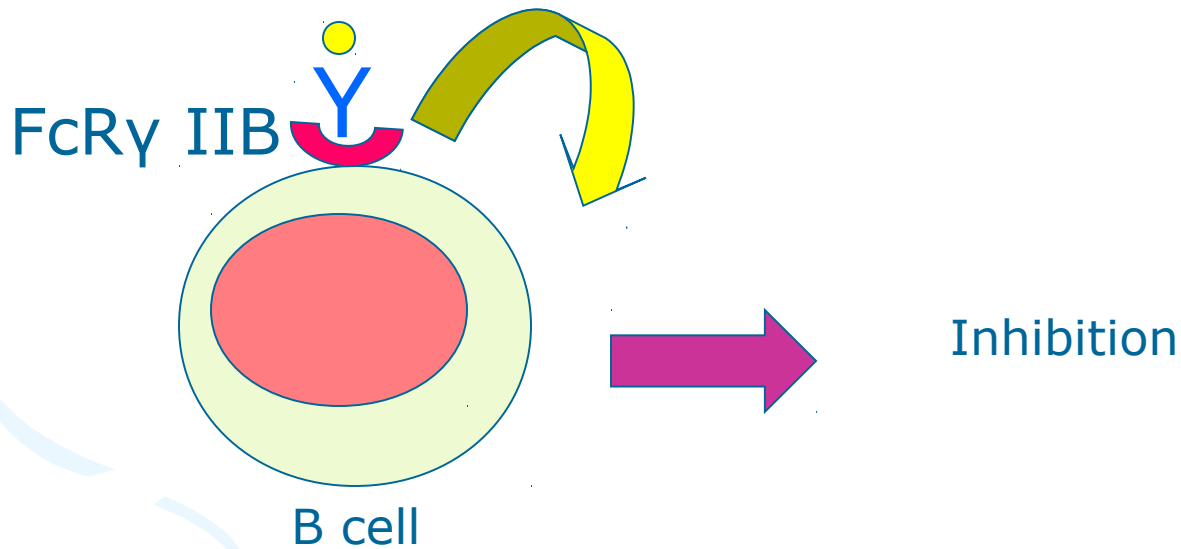


# Antibody-Dependent Cellular Cytotoxicity ADCC

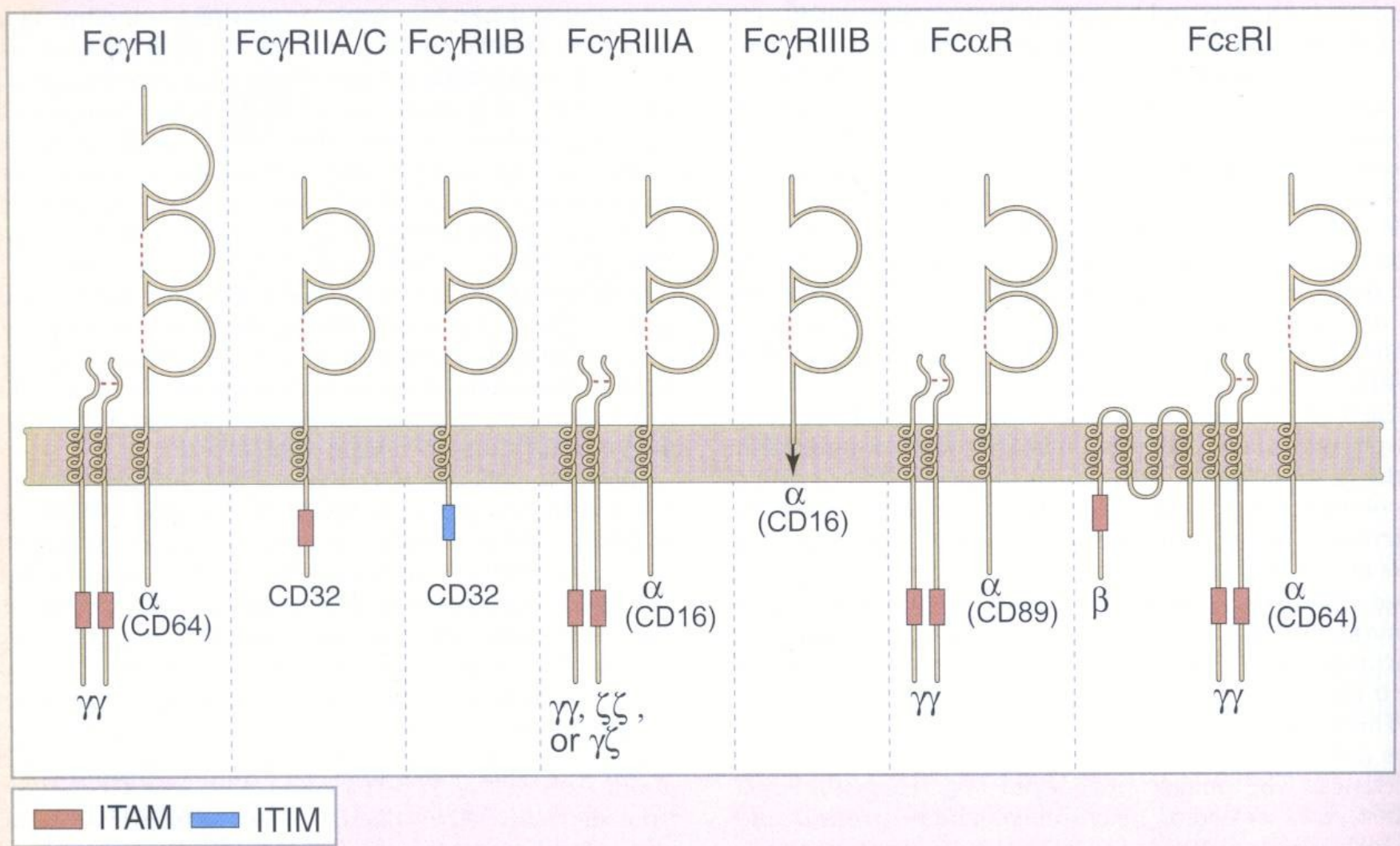


Perforin/Granzyme/Caspase/Apoptosis

# Feedback Inhibition of Immune response



# Fc receptors



Immunoreceptor tyrosine-based activation (inhibitory) motif