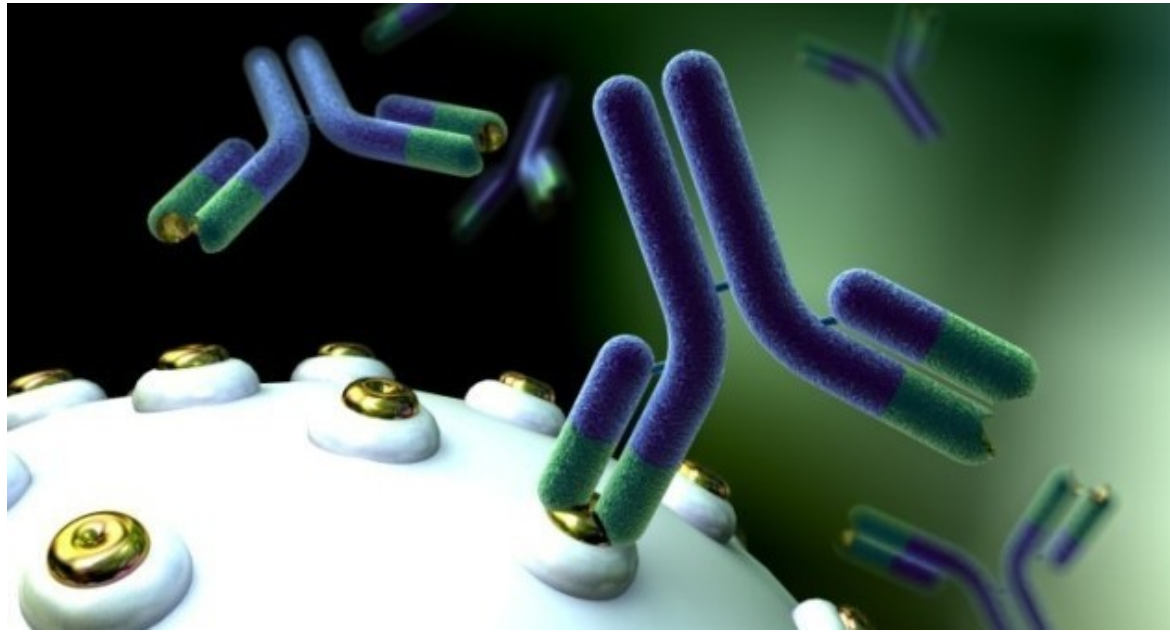


Antibody structure & function



Objectives

You should be able to:

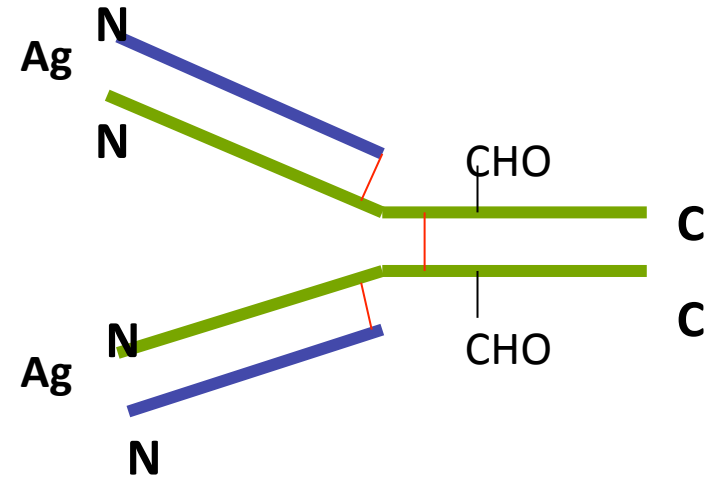
- ✓ Define antibody
- ✓ Describe antibody structure
- ✓ Compare between different types or classes of antibody and their function

Antibodies = Immunoglobulin

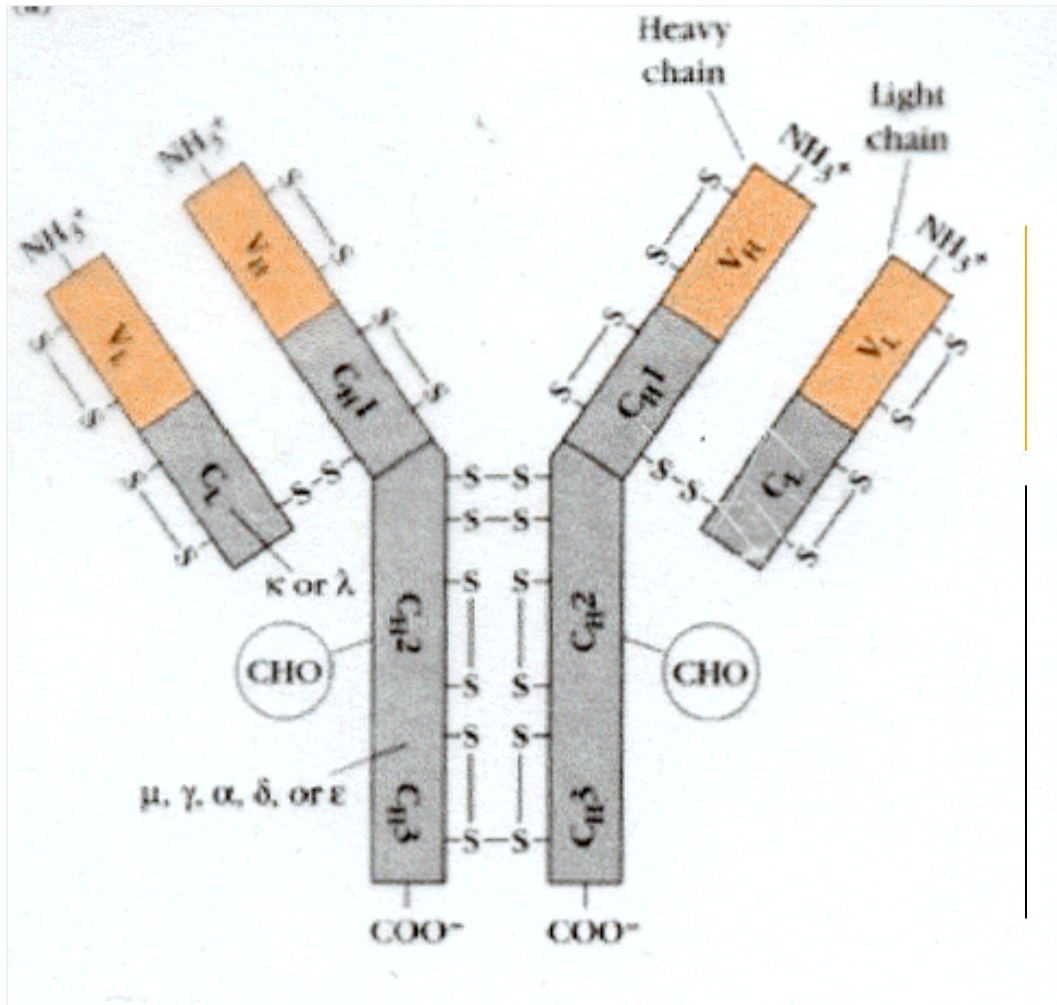
- **Glycoproteins** found in serum and tissue fluids which are produced in response to contact with immunogenic foreign molecules . They bind specifically to the antigen that induced their formation.
- A major component of humoral immunity.
- **Five Classes IgM, IgG, IgA, IgD and IgE.**
- **All have the same basic antibody structure.**

BASIC ANTIBODY STRUCTURE

- Two identical **light chains** λ or κ , 220AA (25 KDa).
- Two identical **Heavy chains**, 450AA (50 KDa).
- **Covalent** and non-covalent forces.
- Two identical antigen binding sites.
- Carbohydrate (CHO).
- Each light chain bound to heavy chain by **disulfide bond** (L-H) and also (H-H)
- Hinge region



Variable & Constant Regions



Variable regions

Constant regions

Immunoglobulin Domain Structure

1. Domains

a) V_L & C_L

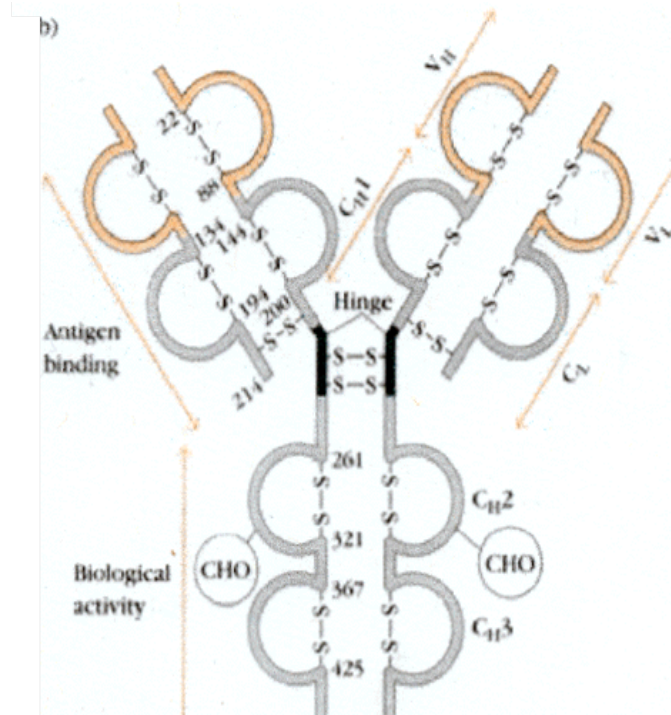
b) V_H & $C_{H1} - C_{H3}$ (or C_{H4})

2. Oligosaccharides

3. Complementarity

Determining Regions (CDR)

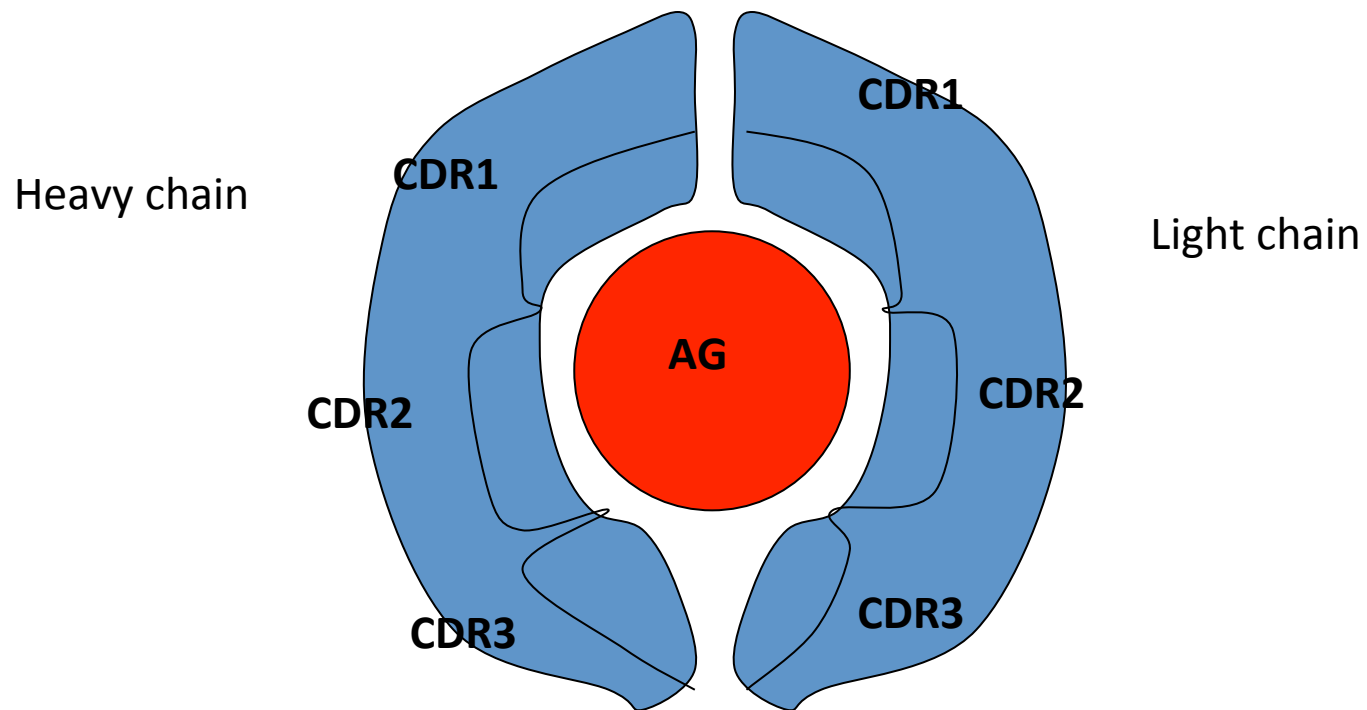
المناطق المحددة التكميلية



Ag binding

Effector
function

A Basic antibody binding site



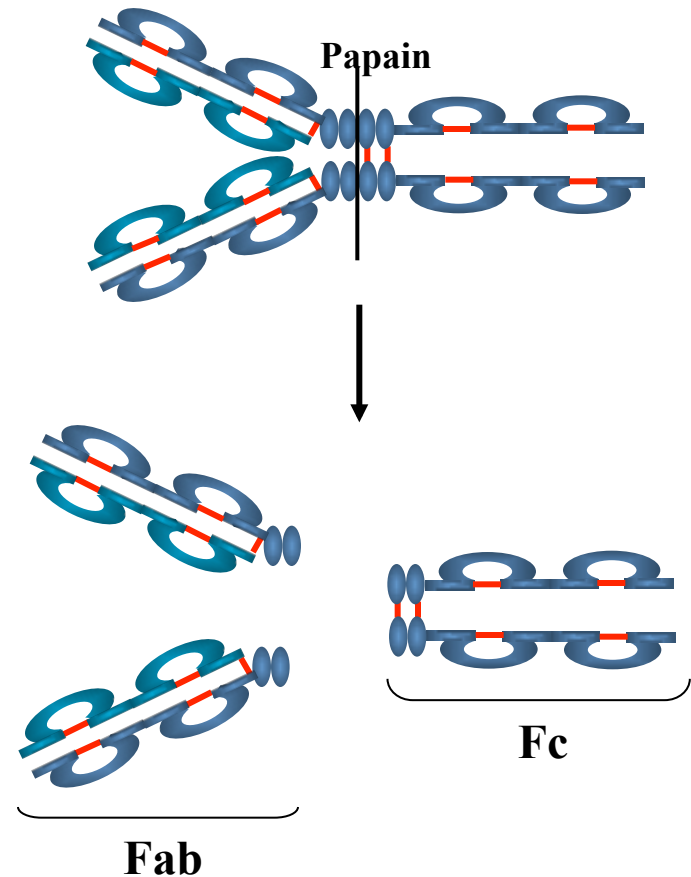
Immunoglobulin Fragments

1- Fab

- Ag binding
- Valence = 1
- Specificity determined by V_H and V_L

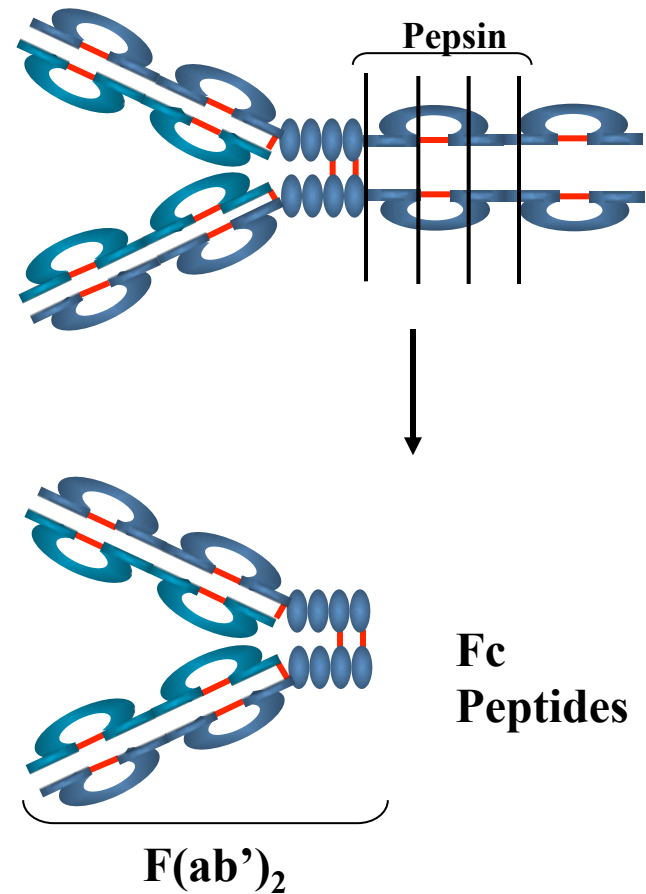
2- Fc

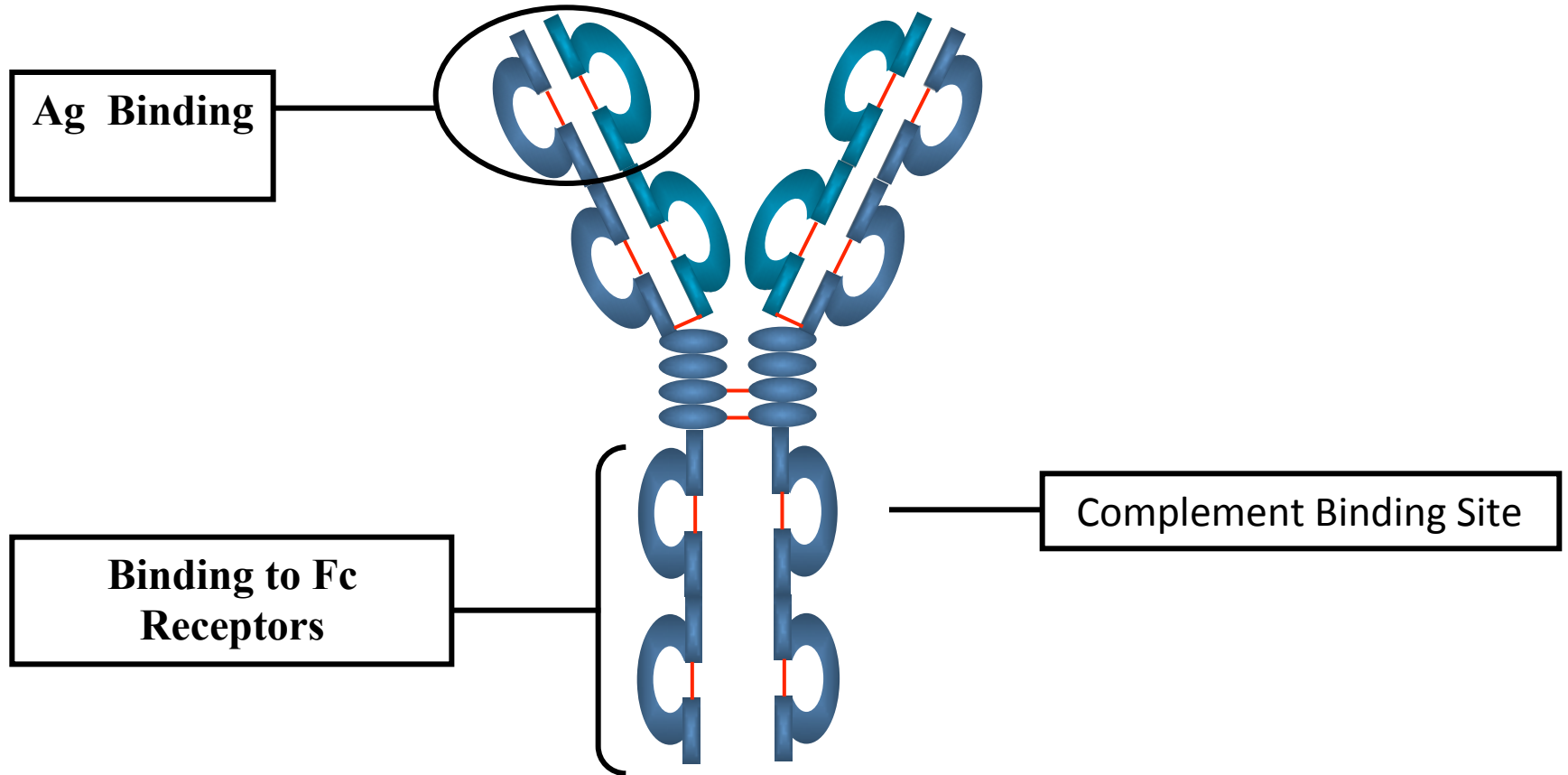
- Effector functions



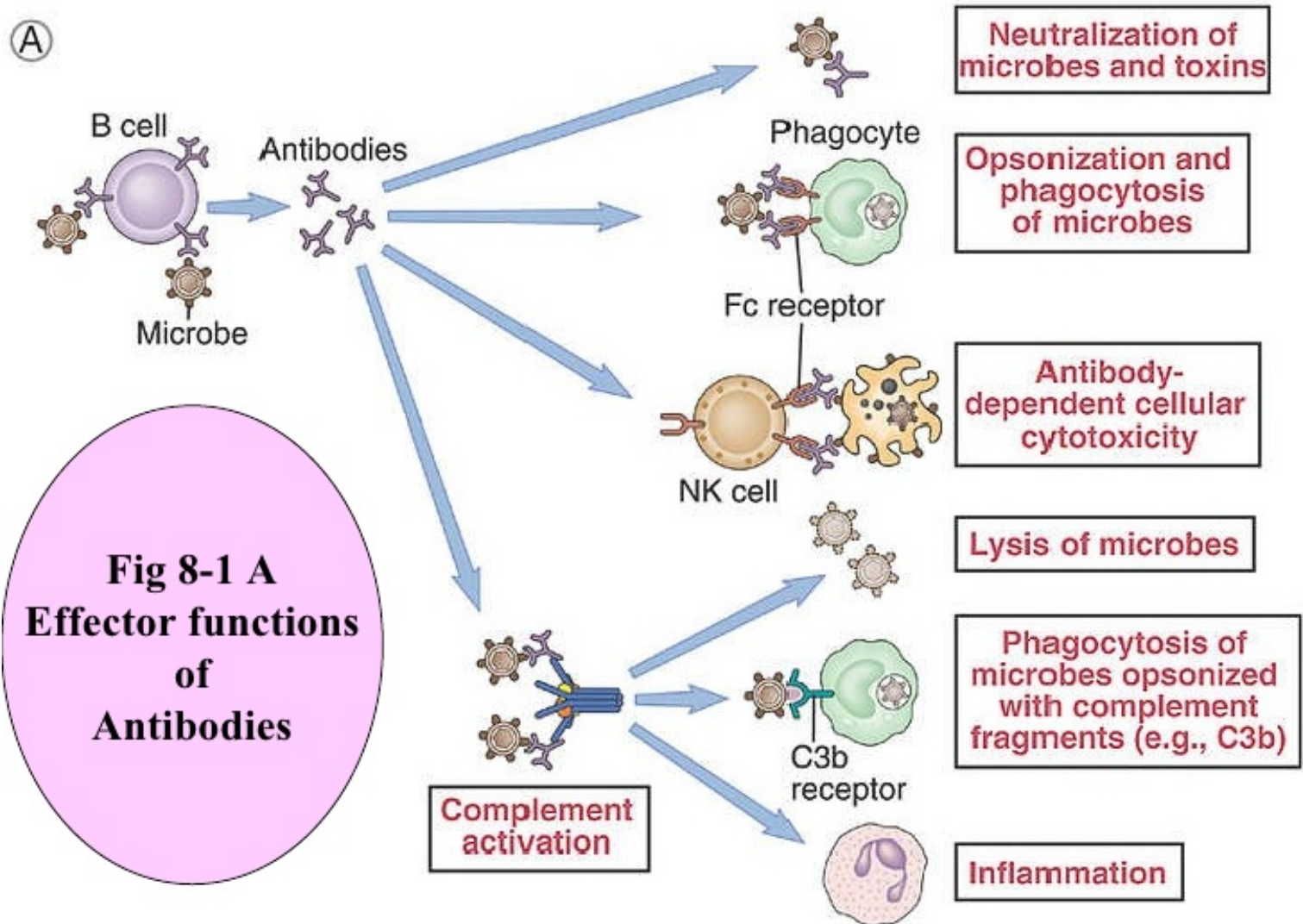
Immunoglobulin Fragments

3- $F(ab')_2$





Antibody Functions



Classes of immunoglobulin

Differences:

- Number of basic subunits which form the Ab
- The polypeptide sequence in the heavy chain constant regions are different, giving different functional characteristics

Classes of immunoglobulin.

1. IgM - Mu (μ) heavy chains
2. IgG - Gamma (γ) heavy chains
3. IgA - Alpha (α) heavy chains
4. IgD - Delta (δ) heavy chains
5. IgE - Epsilon (ϵ) heavy chains

Subclasses of immunoglobulin.

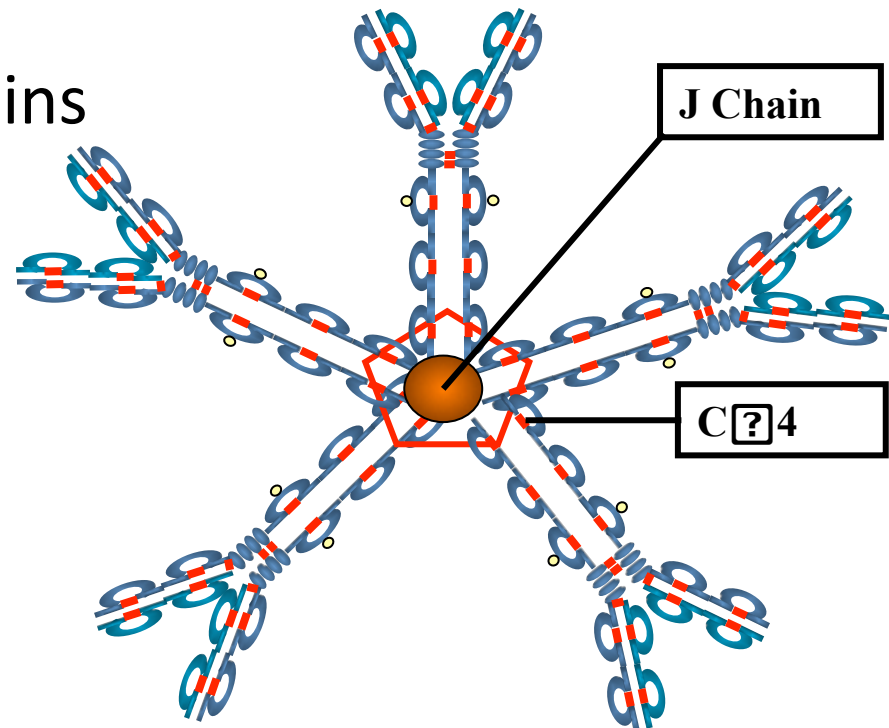
- IgG Subclasses: IgG1, IgG2, IgG3 and IgG4
- IgA subclasses: IgA1 and IgA2
- No subclasses of IgM, IgD, and IgE

Immunoglobulin Light Chain Types

1. Kappa (κ)	60%	Human
2. Lambda (λ)	40%	
• Kappa	95%	Mouse
• Lambda	5%	

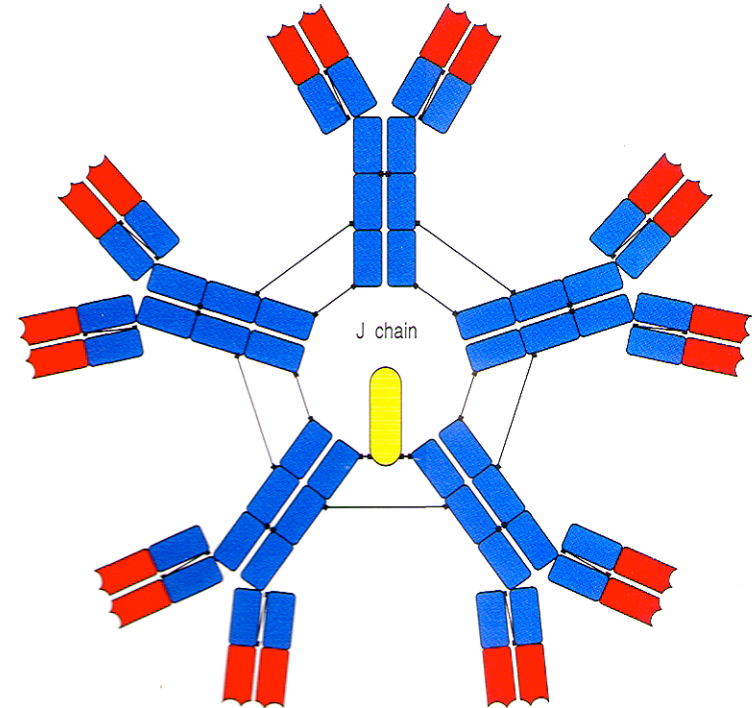
IgM

- 10% of normal serum Ig (1.8mg/ml)
- Pentamer composed of 5 basic Ig monomers
- 10 antigen binding sites
- Heavy chain has five domains



Pentameric IgM

- 10 light chains
- 10 heavy chains
- 10 identical antigen binding sites
- 1 J chain

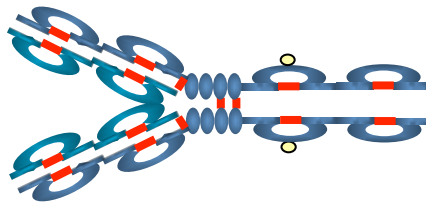


IgM

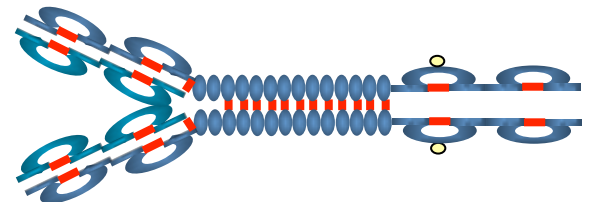
- Predominant Ab of primary immune response
- Most efficient complement fixing antibody
- Half life 10 days
- Not found extravascularly
- Good at Opsonisation
- Found at B lymphocyte cell surface as a membrane bound monomer. Here it acts as a cell surface receptor in antigen recognition.

IgG

- IgG: 4 subclasses $\gamma 1$ - $\gamma 4$ heavy chains
- 75% of normal serum Ig (12mg/ml)
- Basic monomer structure
- 4 subclasses IgG1, IgG2, IgG3, IgG4, which are 70%, 20%, 8% and 2% of the normal serum IgG in humans
- In mouse these are IgG1, IgG2a, IgG2b, IgG3
- Life span: 21 days



IgG1, IgG2 and IgG4

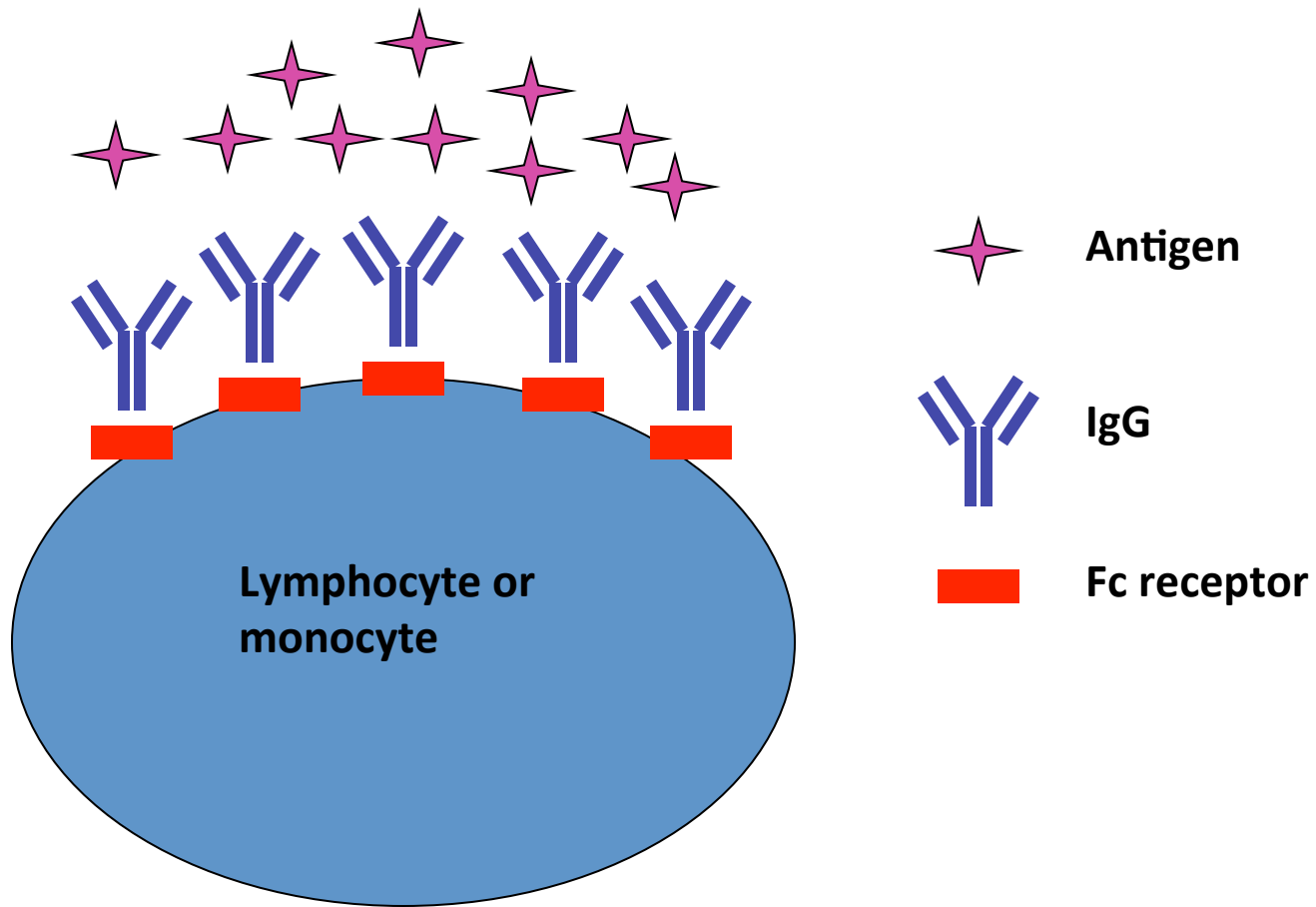


IgG3

IgG

- Predominant Ab of a secondary immune response
- Extravascular
- Fixes complement $\text{IgG3} > \text{IgG1} > \text{IgG2} > \text{IgG4}$
- Opsonisation
- Placental transfer IgG1, 3 and 4

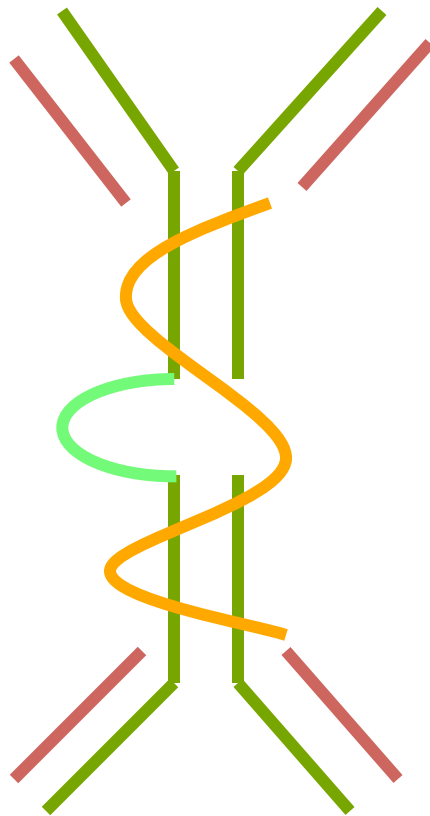
IgG Binds to cell surface Fc receptors on lymphocytes and monocytes



IgA

- IgA 2 subclasses $\alpha 1$, $\alpha 2$ heavy chains
- 10-15% of normal serum Ig
- In human serum mainly monomeric (above 80%)
- Subclasses IgA1 and IgA2
- Predominant Ig in secretions eg. saliva and colostrum and in the gut where it is present as a dimer of two Ig monomers one J chain and one secretory component polypeptide.
- Life span: 6 days

Secretory IgA

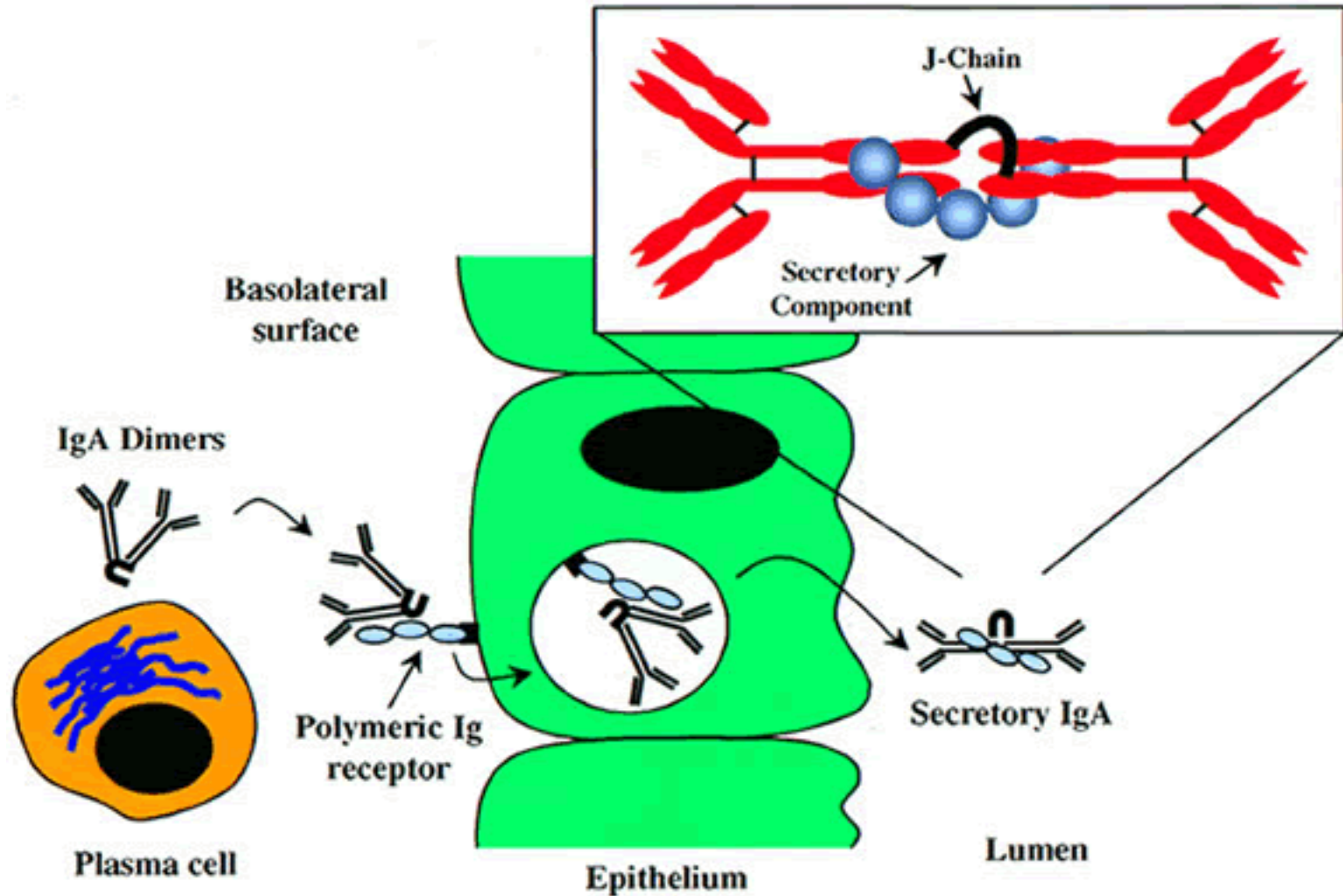


— Secretory component produced by epithelial cells. Protection from cleavage.

— J Chain

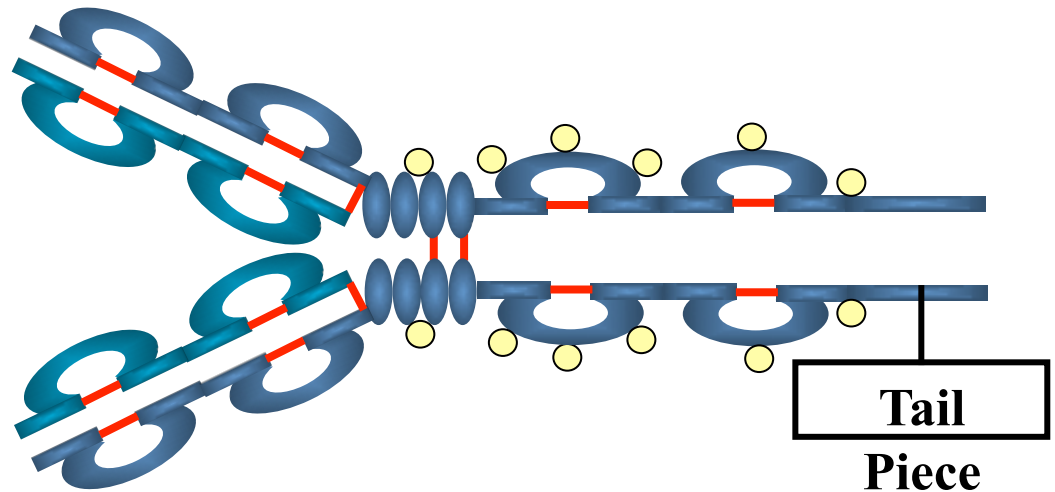
Specialised for transport to areas in which Ab producing B cells are absent eg. gut and via colostrum to the newborn

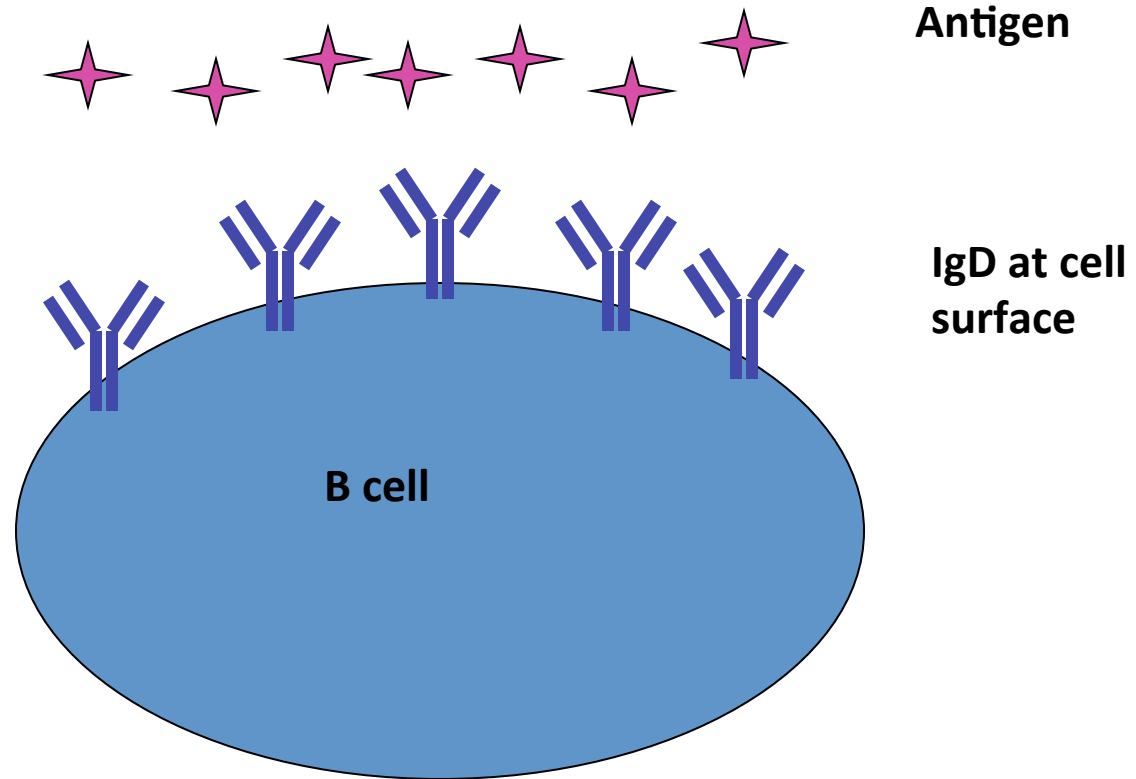
Origin of Secretory Component of sIgA



IgD


- Very low levels in serum at least 1000 fold lower than IgG (<1%)
- Basic monomer structure.
- Found on the surface of circulating B lymphocytes often co-expressed with IgM.
- Life span: 3 days

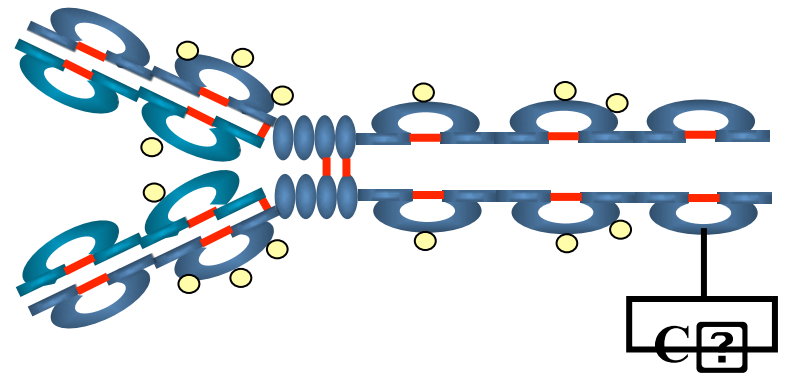




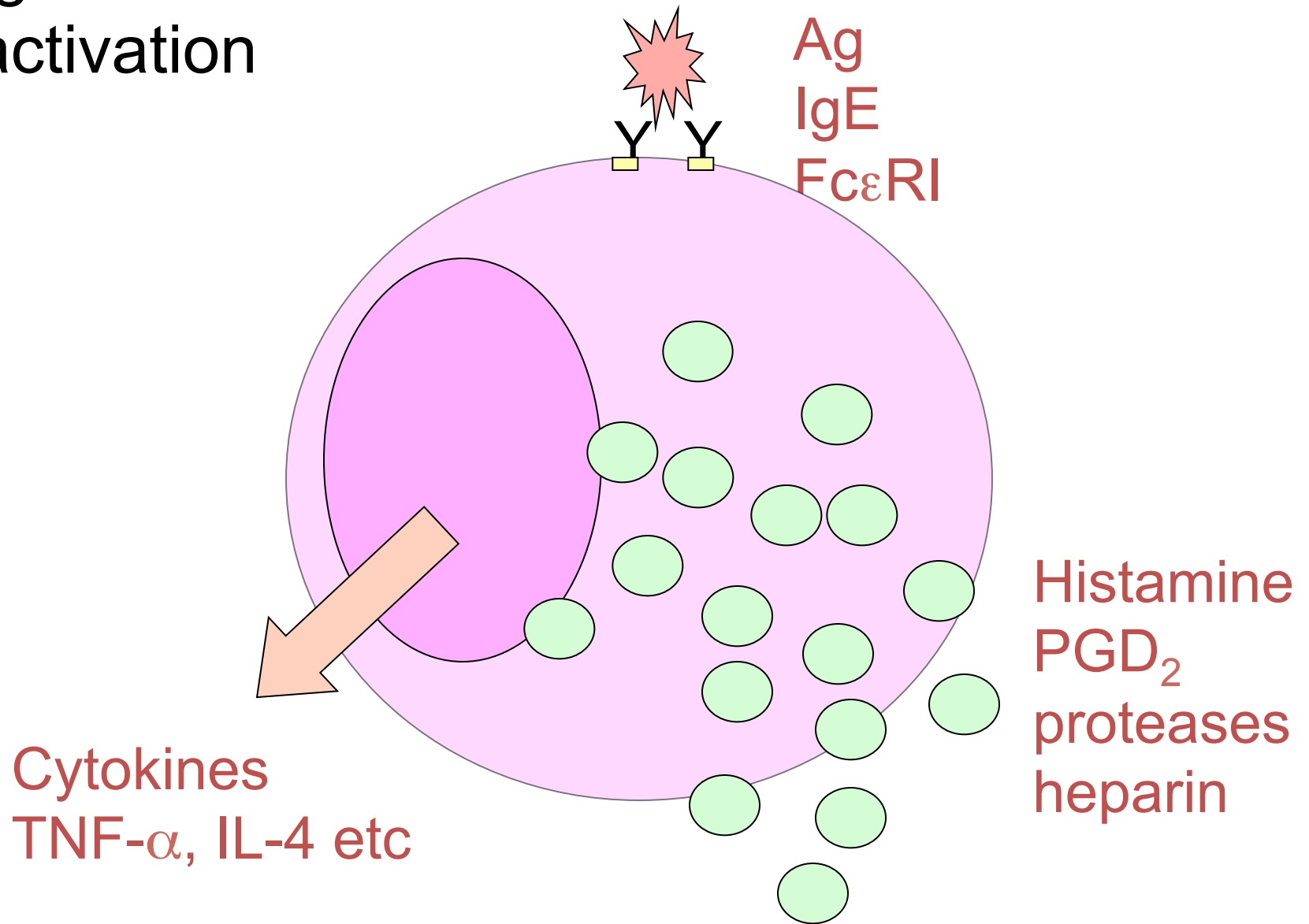
**Ig at the cell surface allows antigen binding
and triggers B cell activation**

IgE


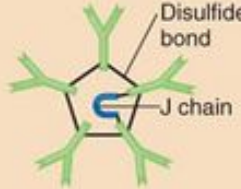
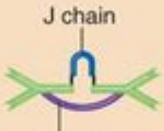


- Lowest serum concentrations 0.0003mg/ml
 - Basic monomer structure
 - Heavy chain consists of 5 domains
 - Binds to the Fc receptors of mast cells and basophils. Contact with antigens subsequently leads to the release of pro-inflammatory agents
 - Half life: 2 days
- 
- A diagram showing a mast cell, which is a large, blue, irregularly shaped cell. On its surface, there are several blue, Y-shaped structures representing IgE antibodies. These antibodies are bound to small, yellow, circular receptors on the cell surface. The diagram illustrates the interaction between the antibodies and the receptors, which is a key step in the allergic response.



IgE and mast cell - activation



Summary:

Table 17.1 A Summary of Immunoglobulin Classes					
Characteristics	IgG	IgM	IgA	IgD	IgE
					
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
Percentage of Total Serum Antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood, lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Molecular Weight	150,000	970,000	405,000	175,000	190,000
Half-Life in Serum	23 days	5 days	6 days	3 days	2 days
Complement Fixation	Yes	Yes	No [†]	No	No
Placental Transfer	Yes	No	No	No	No
Known Functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

*Percentage in serum only; if mucous membranes and body secretions are included, percentage is much higher.

[†]May be yes via alternative pathway.

By the end you will be able to answer these questions

- What is antibody?
- Draw and describe the structure of Ab?
- Compare between Ab classes?
- What are the function of Ab?