

# STRUCTURE OF IMMUNOGLOBULINS

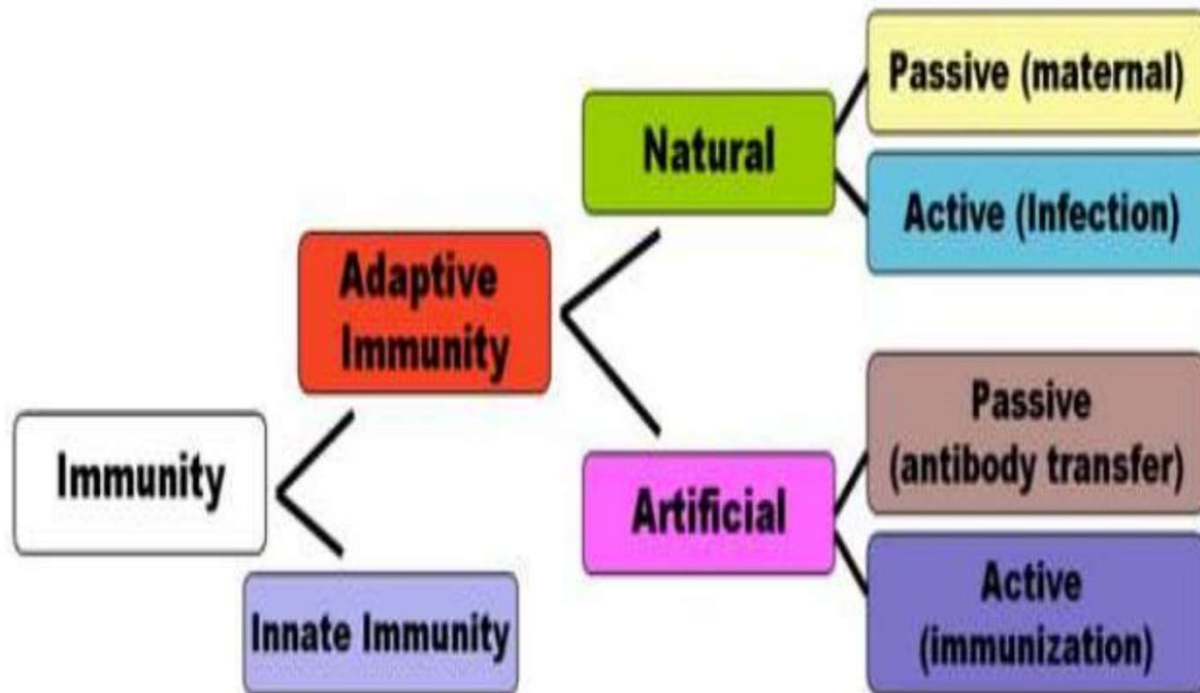
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- **Immunology** = study of structure and function of the immune system
- **Immune system** = cells, tissues, and molecules that mediate resistance to infections
- **Latin Word *immunis*** = “exempt”
- **Immunity** = resistance of a host to pathogens and their toxic effects

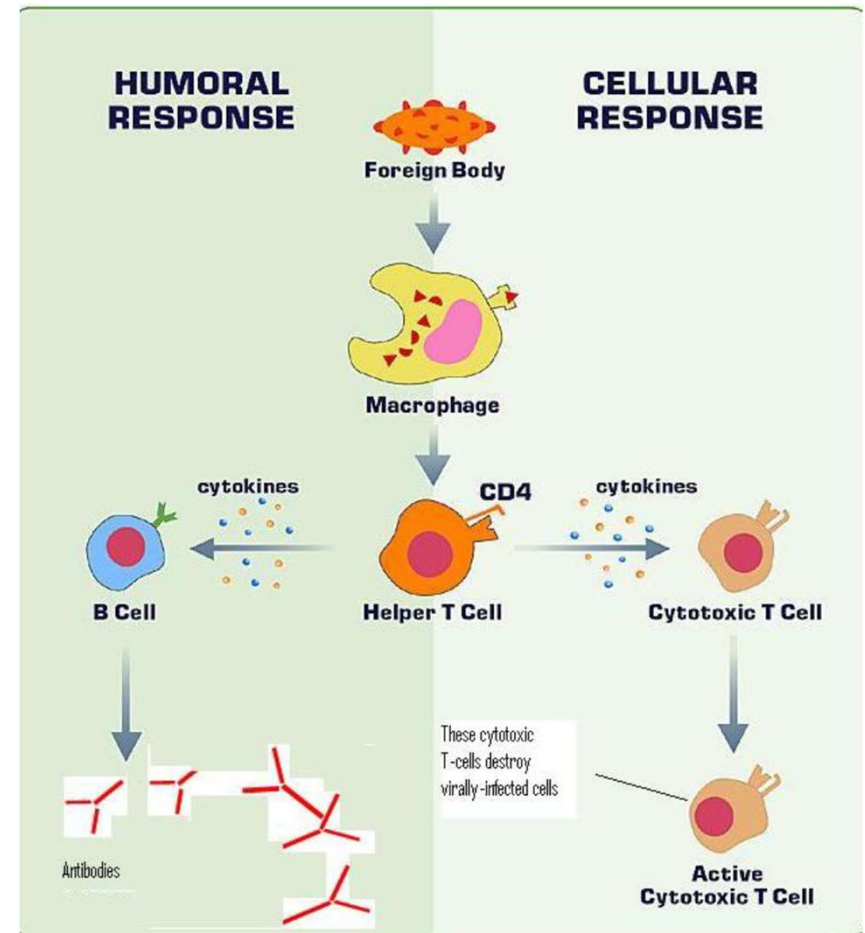


# Types of immunity



# Immune response

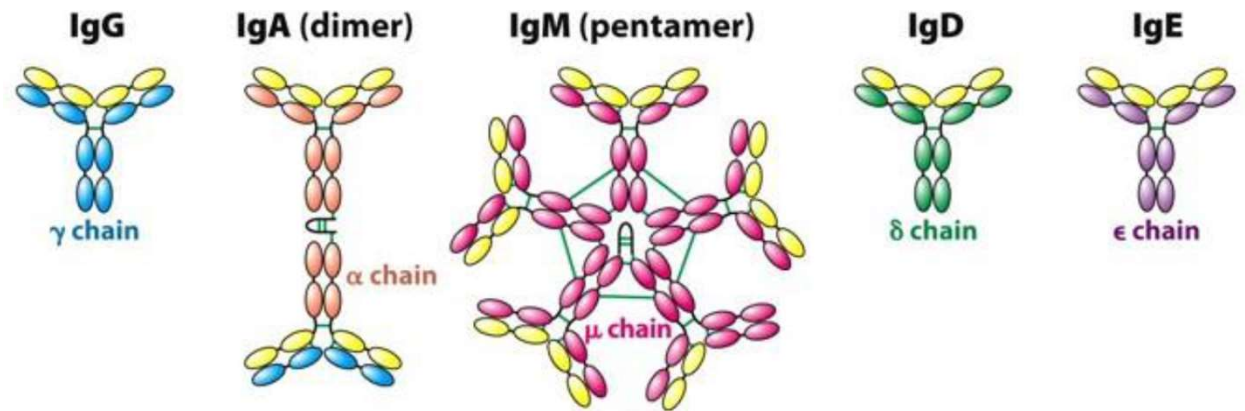
Collective and coordinated response to the introduction of foreign substances in an individual mediated by the cells and molecules of the immune system



# Immunoglobulins

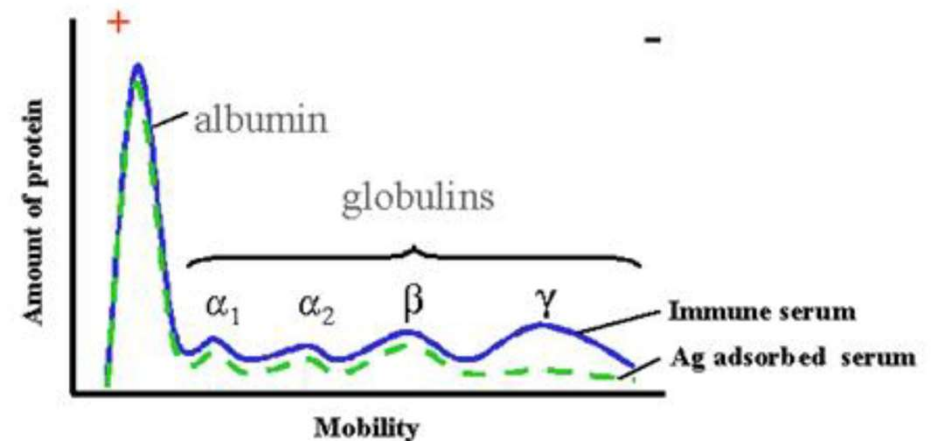
Immunoglobulins are:

- glycoprotein molecules
- function as antibodies
- produced by plasma cells
- In response to an immunogen.



# Immunoglobulins

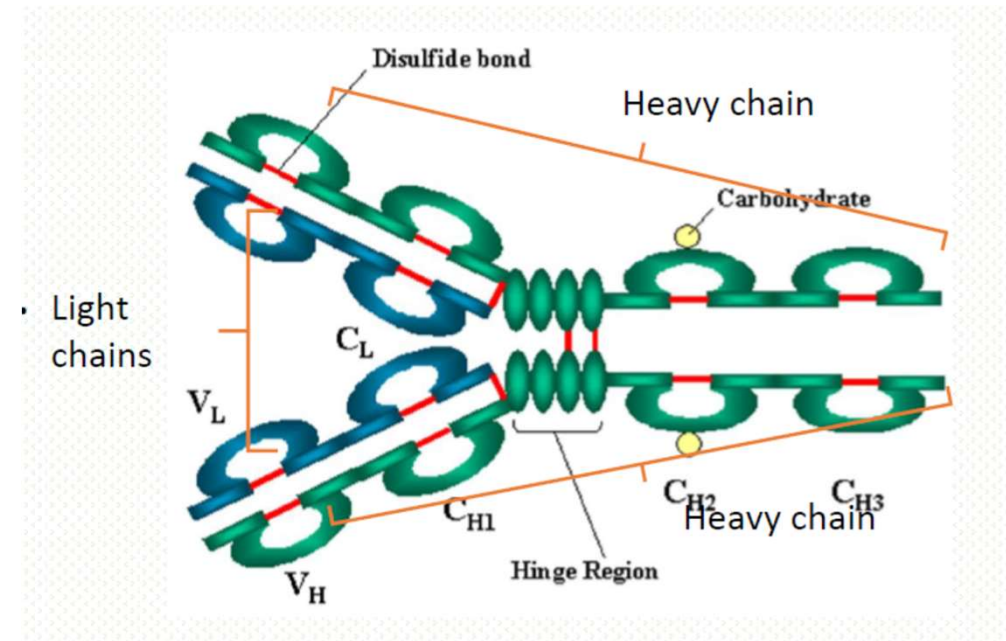
- The immunoglobulins derive their name from the finding that they migrate in the region of globulins when antibody-containing serum is placed in an electrical field.



# Structural characteristics

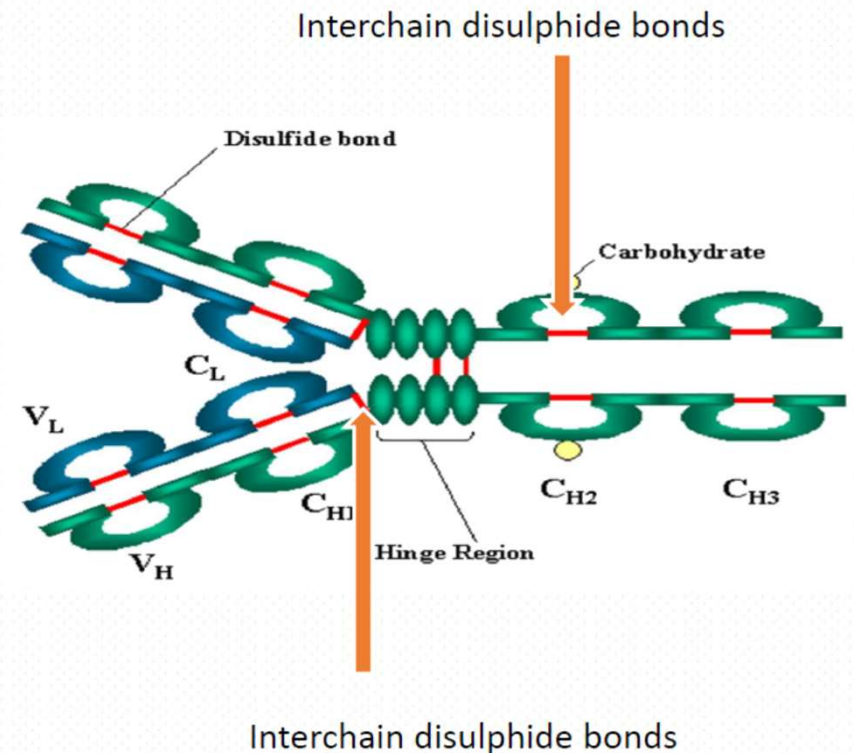
## A. Heavy and Light Chains

- All immunoglobulins have a four chain structure as their basic unit.
- They are composed of two identical light chains (23kD) and two identical heavy chains (50-70kD)



## B. Disulfide bonds

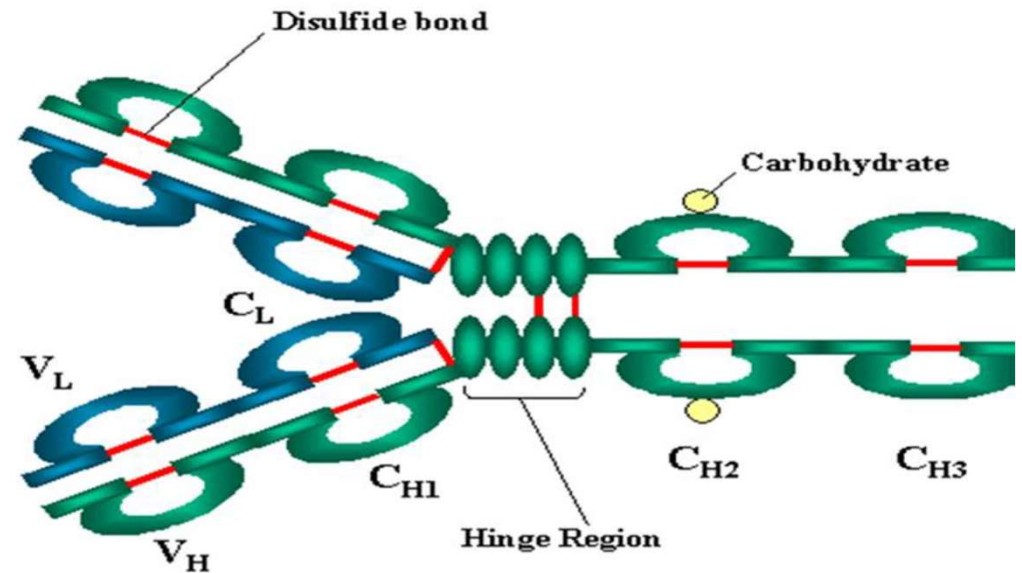
- **Inter-chain disulfide bonds** -The heavy and light chains and the two heavy chains are held together by inter-chain disulfide bonds and by non-covalent interactions.
- The number of inter-chain disulfide bonds varies among different immunoglobulin molecules.
- **Intra-chain disulfide binds** -Within each of the polypeptide chains there are also intra-chain disulfide bonds.





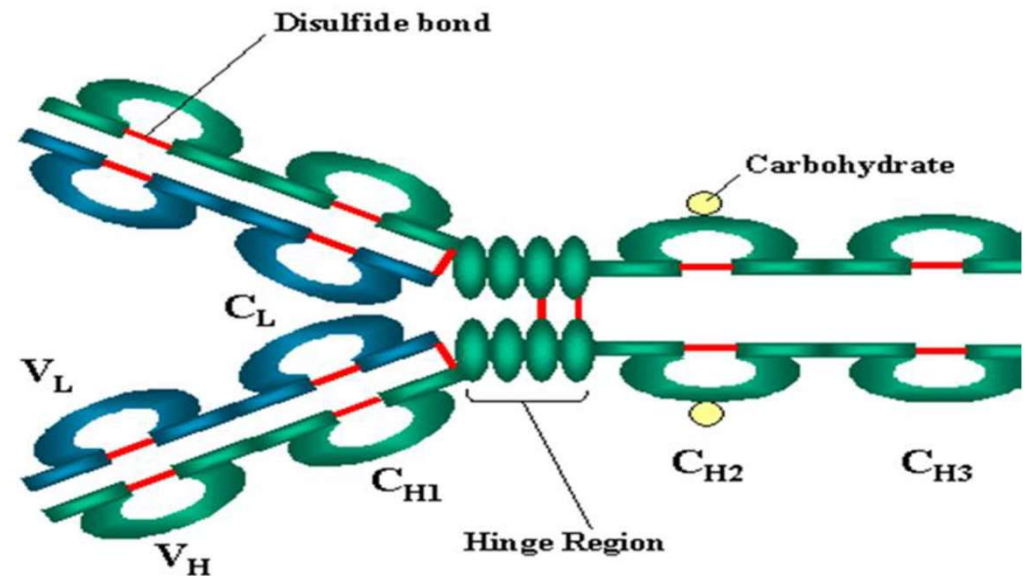
## C. Variable (V) and Constant (C) Regions

- Both the heavy and light chain can be divided into two regions based on variability in the amino acid sequences. These are the
  - Light Chain -VL(110 amino acids) and CL(110 amino acids)
  - Heavy Chain -VH(110 amino acids) and CH(330-440 amino acids)



## D. Hinge Region

- This is the region at which the arms of the antibody molecule form a Y.
- It is called the hinge region because there is some flexibility in the molecule at this point.

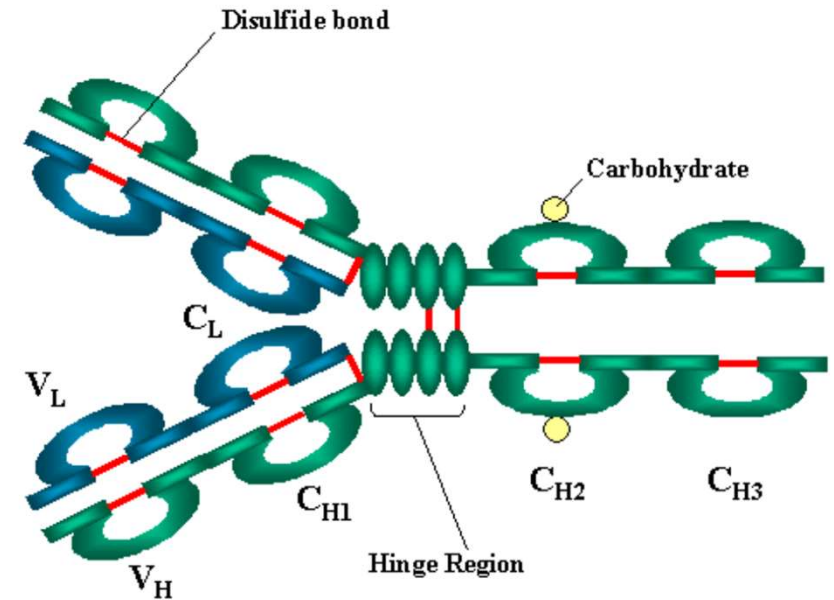


## E. Domains

• Three dimensional images of the immunoglobulin molecule show that it is not a straight molecule rather, it is folded into globular regions each of which contains an intra-chain disulfide bond .

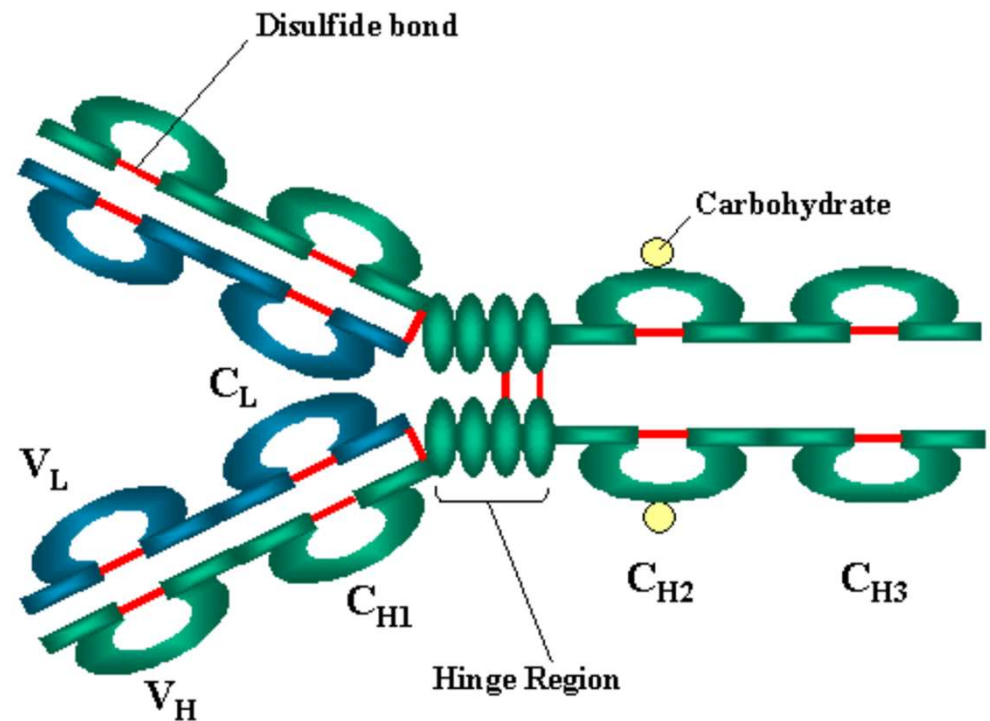
• These regions are called **domains**.

1. Light Chain Domains -V<sub>L</sub> and C<sub>L</sub>
2. Heavy Chain Domains -V<sub>H</sub>, C<sub>H1</sub>, C<sub>H2</sub>, C<sub>H3</sub>(or C<sub>H4</sub>)



## F. Oligosaccharides

- Carbohydrates are attached to the CH<sub>2</sub> domain in most immunoglobulins.
- However, in some cases carbohydrates may also be attached at other locations.



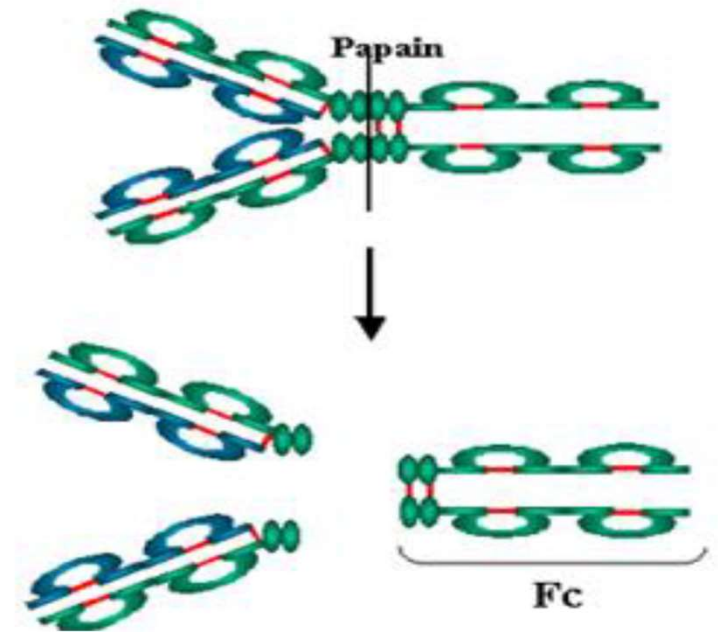
# Immunoglobulin fragments: structure/function relationships

- Immunoglobulin fragments produced by proteolytic digestion –
- **A. Fab** Digestion with papain breaks the immunoglobulin molecule in the hinge region before the H-H inter-chain disulfide bond.
- This results in the formation of two identical fragments that contain the light chain and the VH and CH<sub>1</sub> domains of the heavy chain.



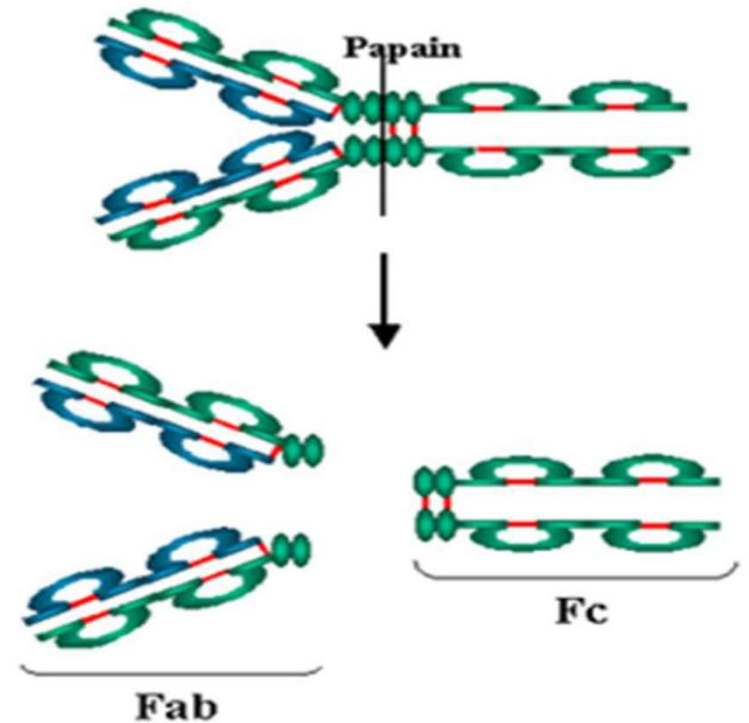
# Immunoglobulin fragments by Papain

- **Fab**-These fragments are called the Fab fragments because they contained the **antigen binding** sites of the antibody.
- Each Fab fragment is monovalent whereas the original molecule was divalent.
- The combining site of the antibody is created by both VHand VL.



# Immunoglobulin fragments by Papain

- **B. Fc Digestion** with papain also produces a fragment that contains the remainder of the two heavy chains each containing a CH<sub>2</sub> and CH<sub>3</sub> domain.
- This fragment was called Fc because it was easily crystallized.



# Structure-function relationship

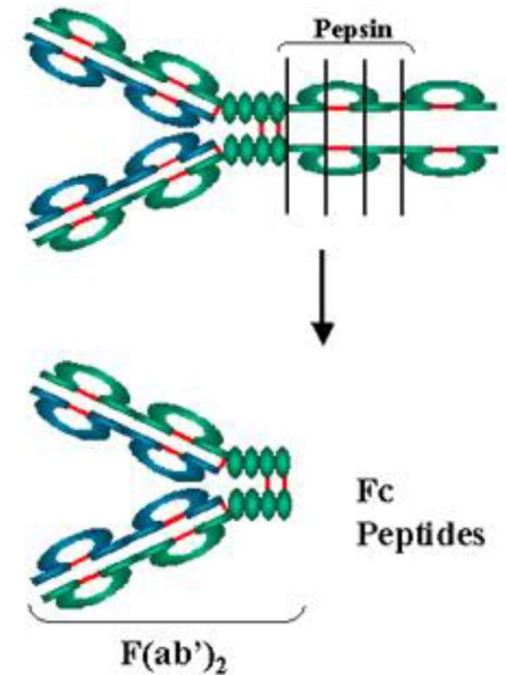
- **Antigen binding function of Immunoglobulins is carried out by Fab part,**
- **Effector functions** -The effector functions are mediated by Fc part of the molecule.
- Different functions are mediated by the different domains in this fragment.





# Immunoglobulin fragments by Pepsin

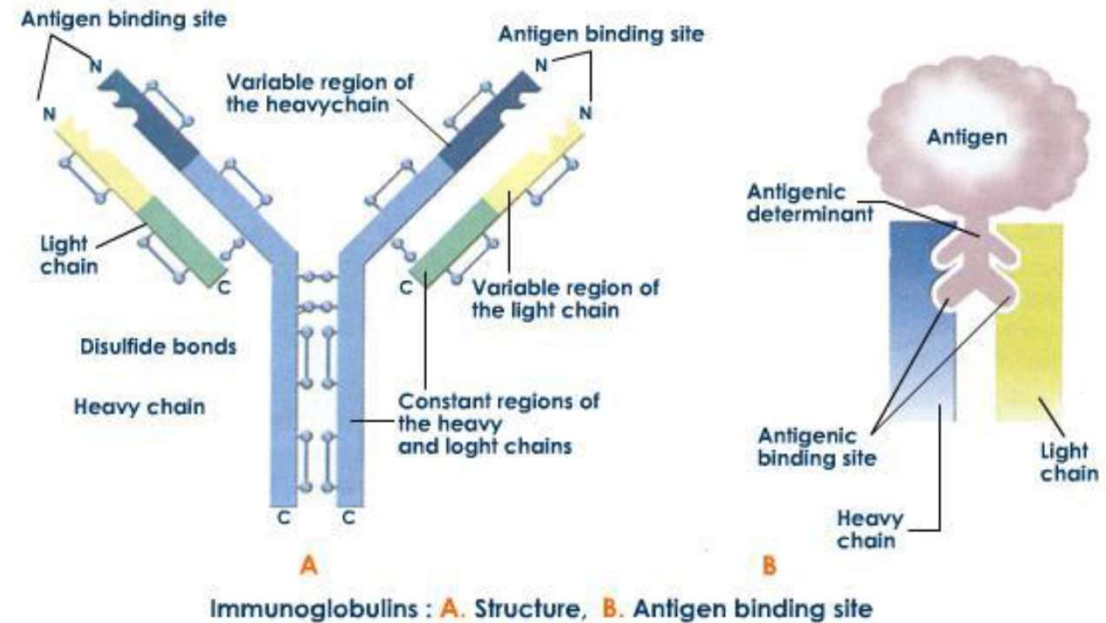
- **F(ab')<sub>2</sub>**-Treatment of immunoglobulins with pepsin results in cleavage of the heavy chain after the H-H inter-chain disulfide bonds resulting in a fragment that contains both antigen binding sites . This fragment is called F(ab')<sub>2</sub> because it is divalent.
- **The Fc region** of the molecule is digested into small peptides by pepsin. The F(ab')<sub>2</sub> binds antigen but it does not mediate the effector functions of antibodies.



# General functions of immunoglobulins

## A. Antigen binding

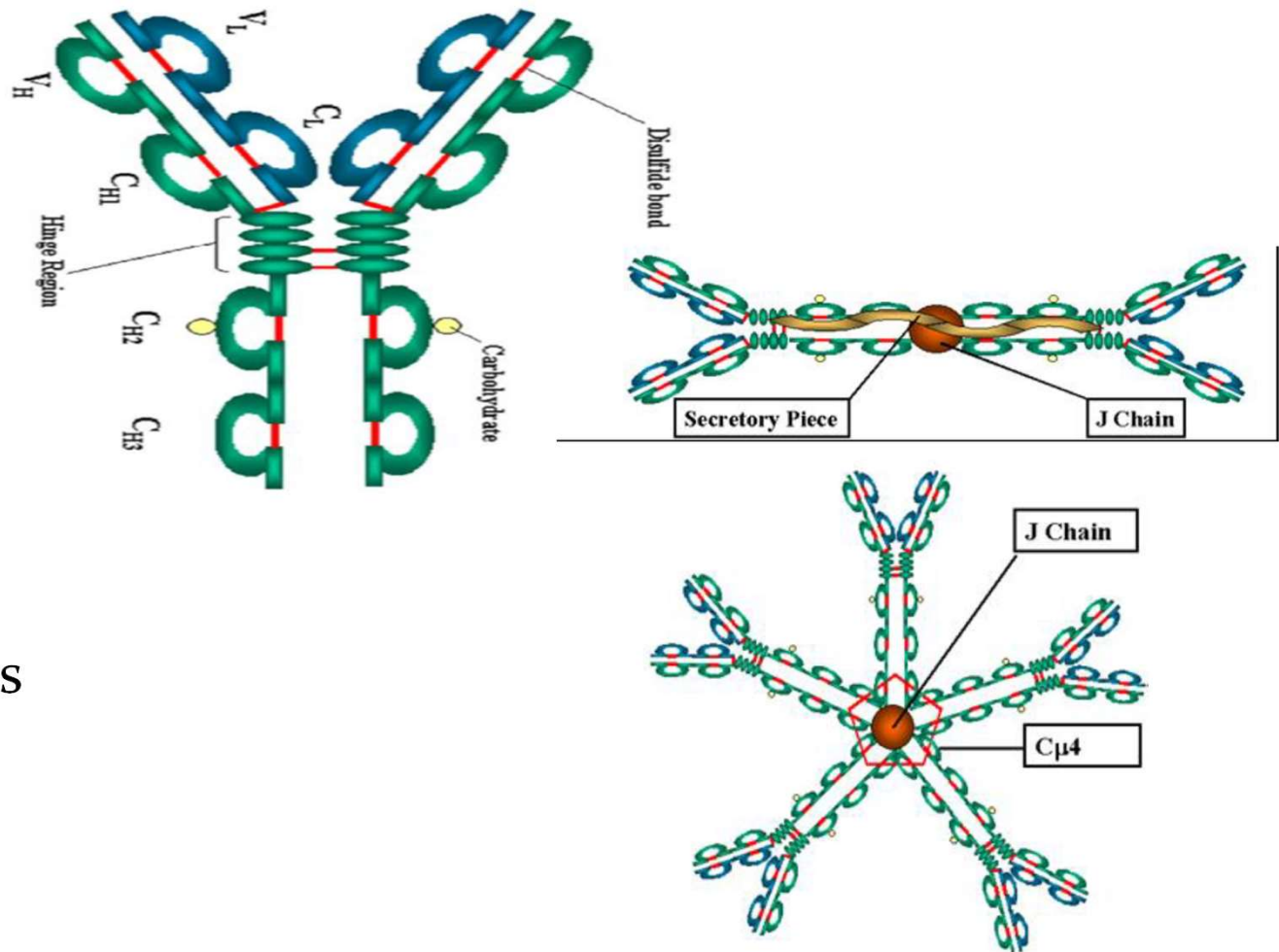
- Antigen binding by antibodies is the primary function of antibodies and can result in protection of the host.
- Each immunoglobulin binds to a specific antigenic determinant.



# Valency of antibody

- The valency of antibody refers to the number of antigenic determinants that an individual antibody molecule can bind.

- The valency of all antibodies is at least two and in some instances more.



## **B. Effector Functions**

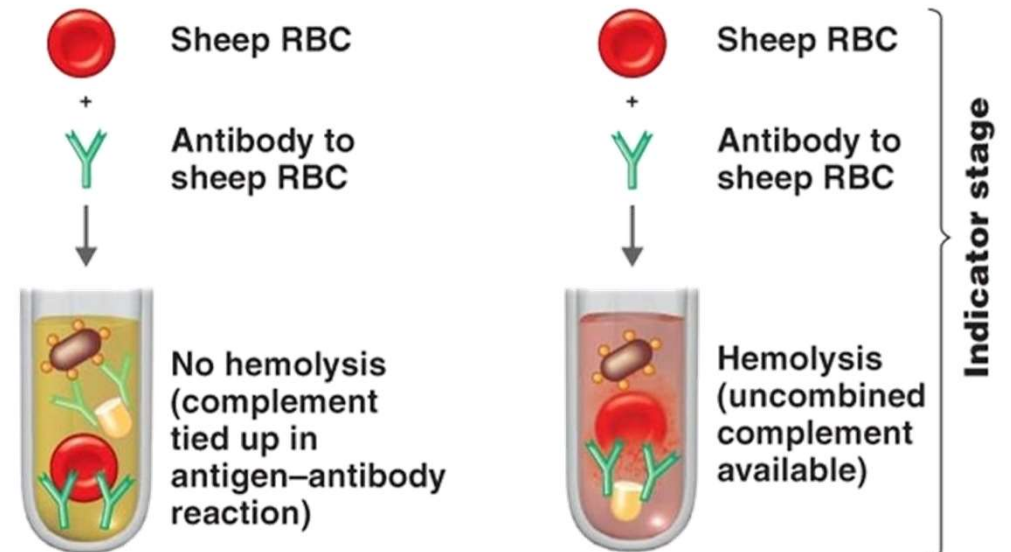
- **Complement fixation**
- **Binding to various cell types**
- **Placental transfer**
- **Opsonization**



# Complement fixation

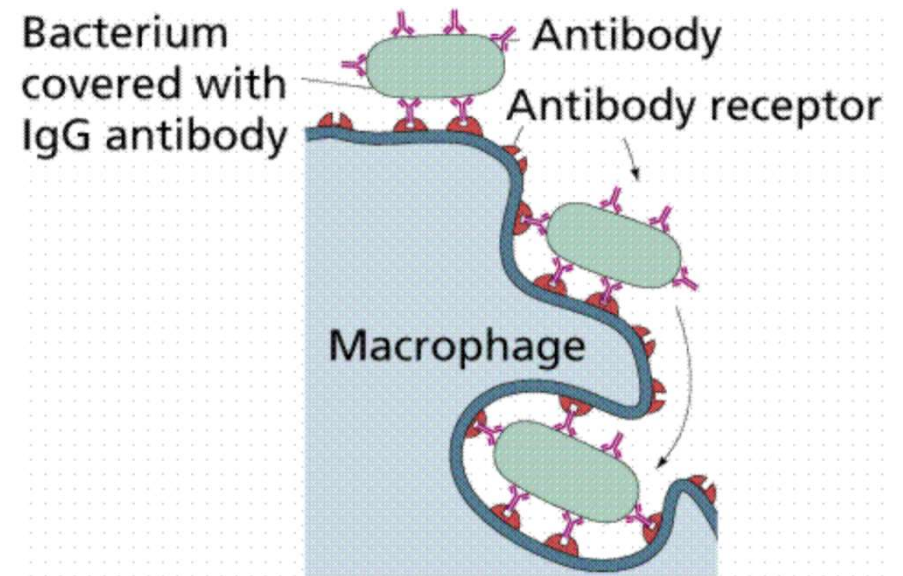
- The process of binding serum **complement** to the product formed by the union of an antibody and the antigen for which it is specific that occurs when **complement** is added to a mixture (in proper proportion) of such an antibody and antigen.

## Complement Fixation Test



# Binding to various cell types

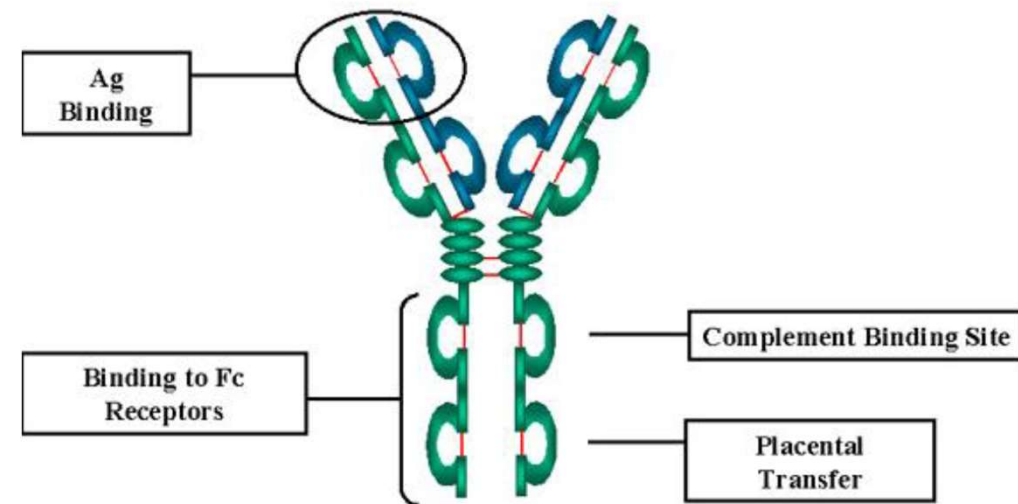
- Phagocytic cells, lymphocytes, platelets, mast cells, and basophils have receptors that bind immunoglobulins.
- This binding can activate the cells to perform some function.



# Placental transfer

- Some immunoglobulins also bind to receptors on placental trophoblasts, which results in transfer of the immunoglobulin across the placenta.

- As a result, the transferred maternal antibodies provide immunity to the fetus and newborn.





•The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains.

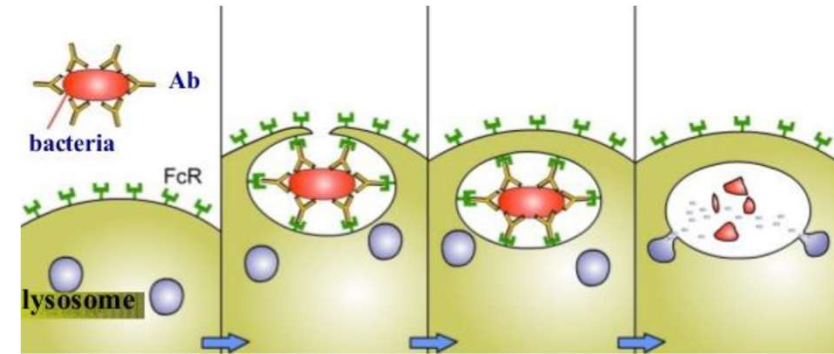
- 1. **IgG** –Gamma heavy chains
- 2. **IgM** –Mu heavy chains
- 3. **IgA** -Alpha heavy chains
- 4. **IgD** –Delta heavy chains
- 5. **IgE** –Epsilon heavy chains





# Opsonization

- The term **opsonin** is used to describe substances that enhance phagocytosis.
- IgG is a good opsonin.
- The antibody prepares the antigen for killing by the phagocytic cells.
- Macrophages, monocytes and neutrophils and some lymphocytes have Fc receptors for the Fc region of IgG.
- A consequence of binding to the Fc receptors on such cells is that the cells can now internalize the antigen better.

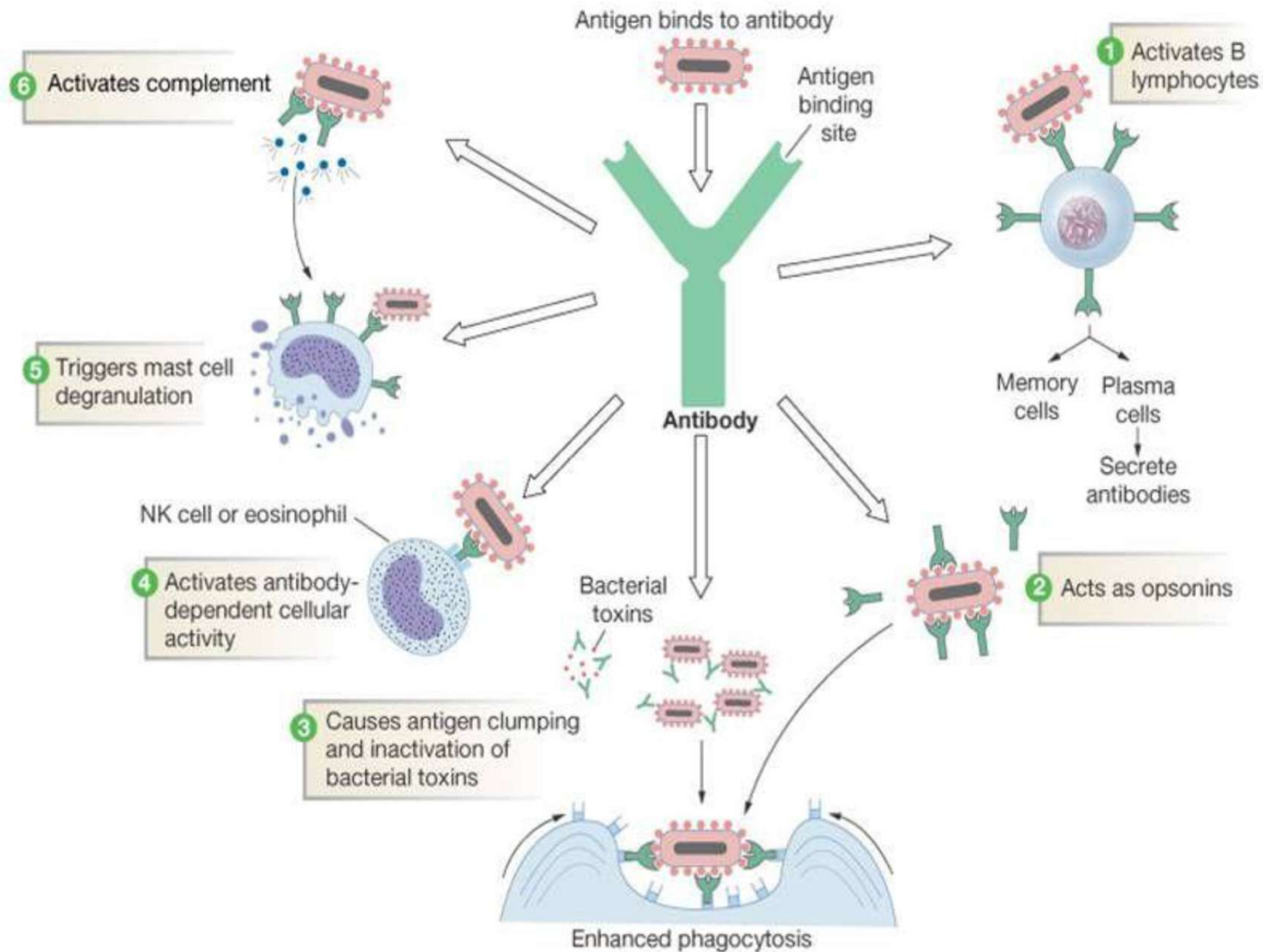


## c) Involved in allergic reactions

- As a consequence of its binding to basophils and mast cells, IgE is involved in allergic reactions.
- Binding of the allergen to the IgE on the cells results in the release of various pharmacological mediators that result in allergic symptoms.



# Functions of Immunoglobulins-an overview



**THANK YOU**

