



Centurion
UNIVERSITY
*Shaping Lives...
Empowering Communities...*

STRUCTURE OF IMMUNOGLOBULINS



Centurion
UNIVERSITY

Suman Kumar Mekap
Asst. Professor (Pharmacology)
School of Pharmacy and Life Sciences
Centurion University, Bhubaneswar



Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

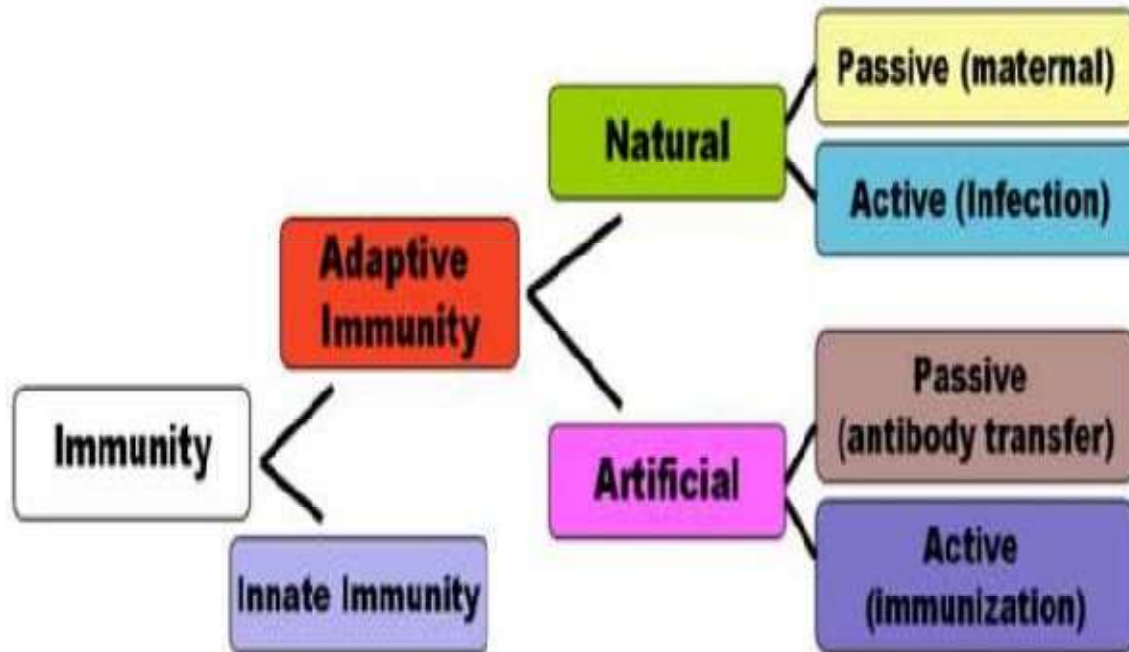
- **Immunology** = study of structure and function of the immune system
- **Immune system** = cells, tissues, and molecules that mediate resistance to infections
- **Latin Word *immunis*** = “exempt”
- **Immunity** = resistance of a host to pathogens and their toxic effects



**Centurion
UNIVERSITY**

*Shaping Lives...
Empowering Communities...*

Types of immunity

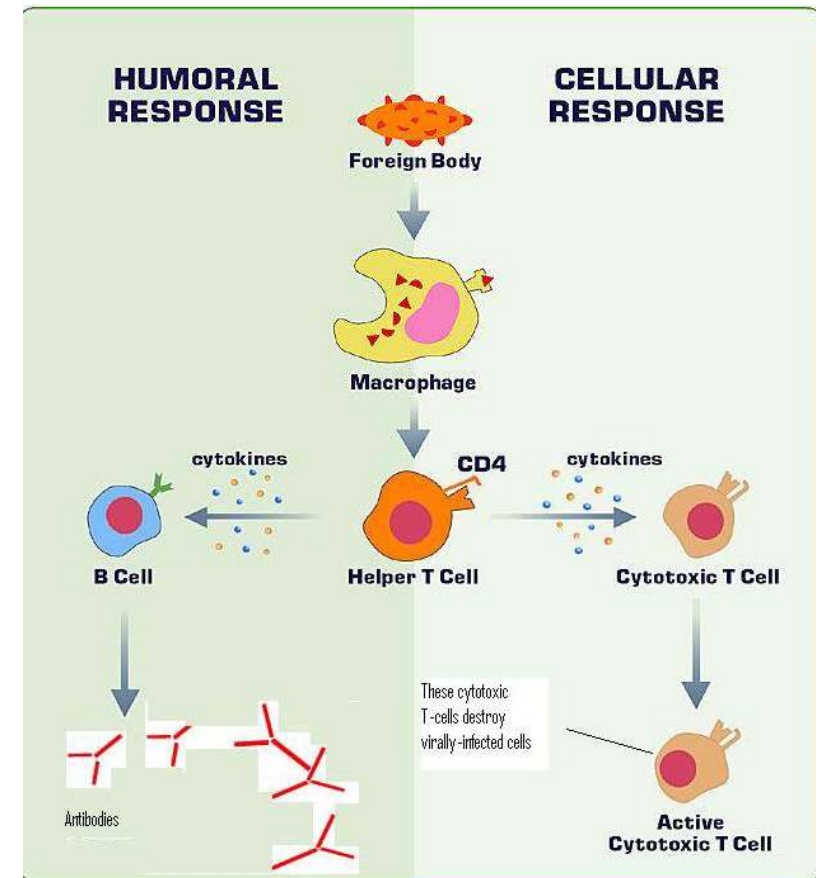




Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities

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



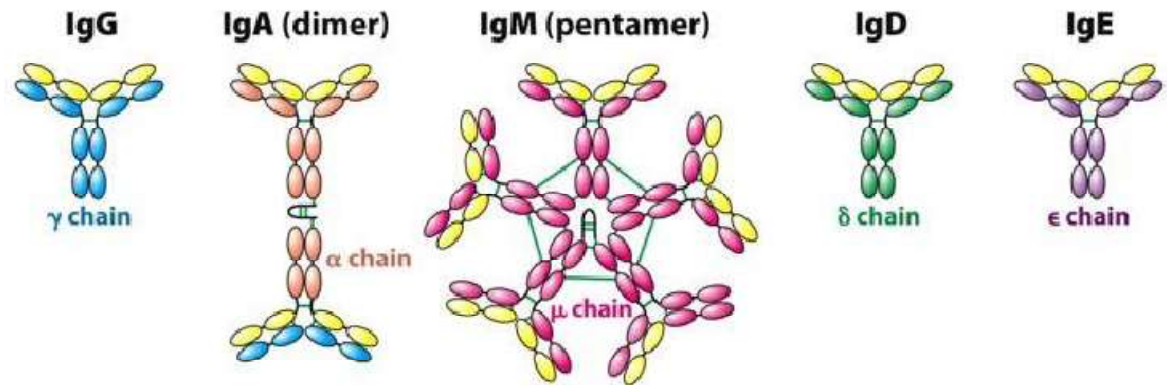


**Centurion
UNIVERSITY**
*Shaping Lives...
Empowering Communities...*

Immunoglobulins

Immunoglobulins are:

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

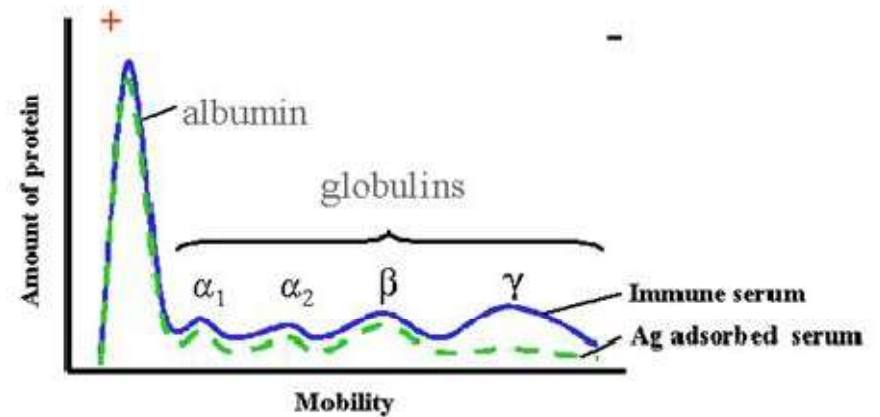




Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

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.



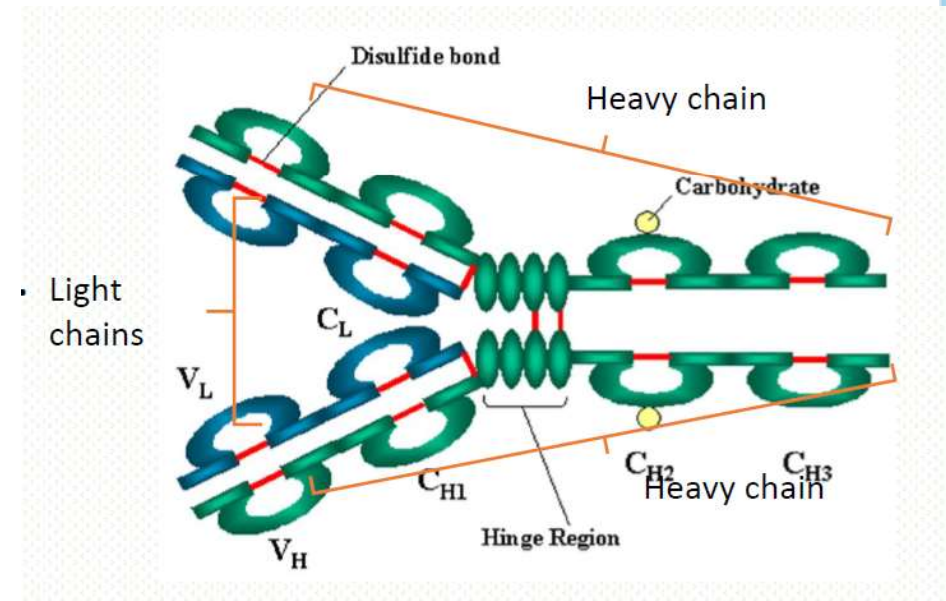


Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

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)





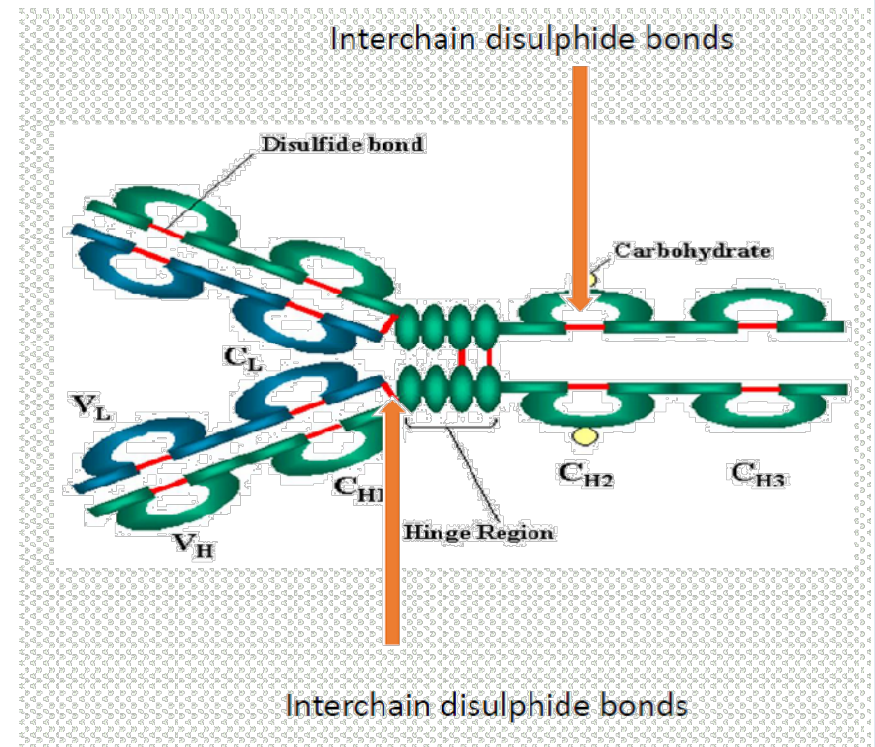
Centurion
UNIVERSITY
*Shaping Lives...
Empowering Communities...*

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.

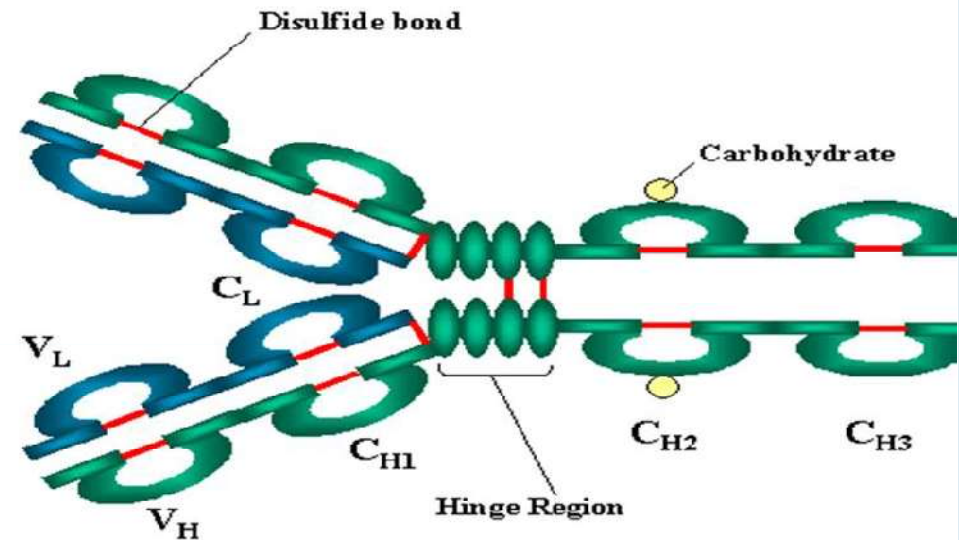




Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

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)





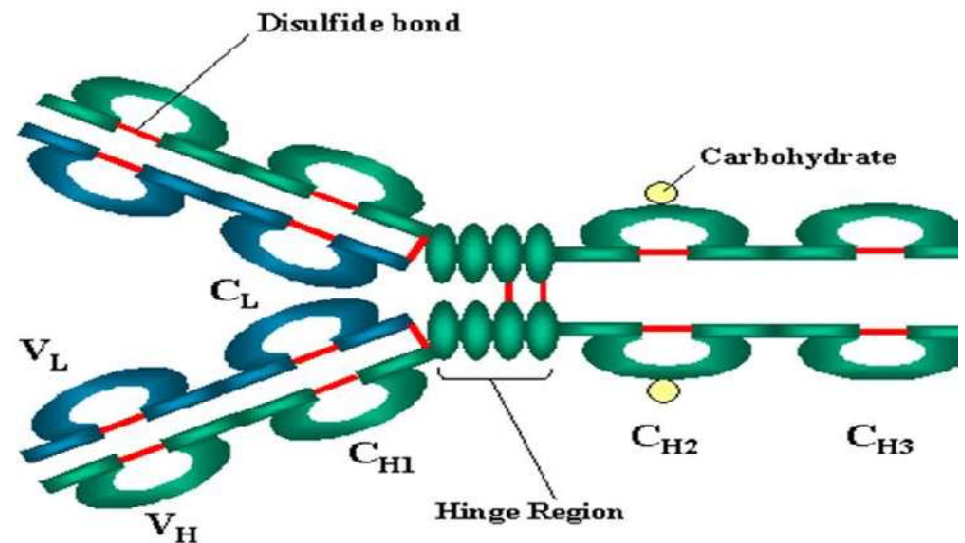
D. Hinge Region

Centurion
UNIVERSITY

Shaping Lives...
Empowering Society...

- 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.



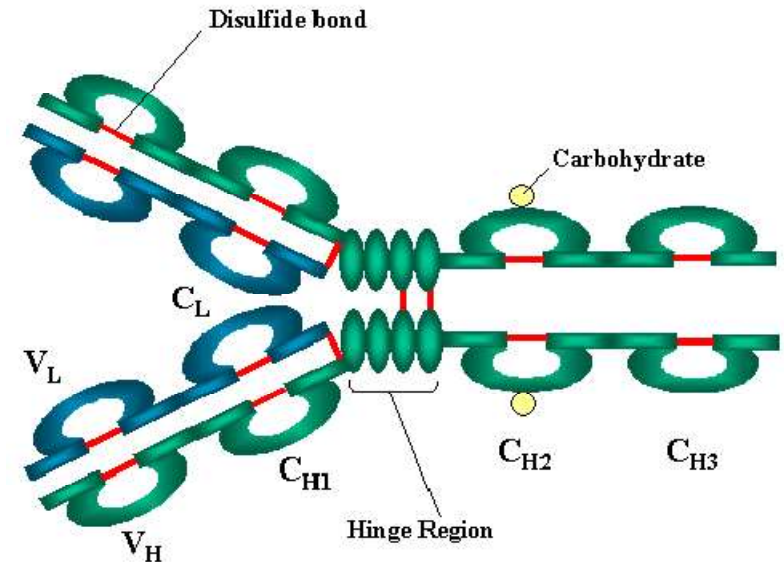


E. Domains

- 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 –VL and CL
2. Heavy Chain Domains –VH,
CH1,CH2,CH3(or CH4)

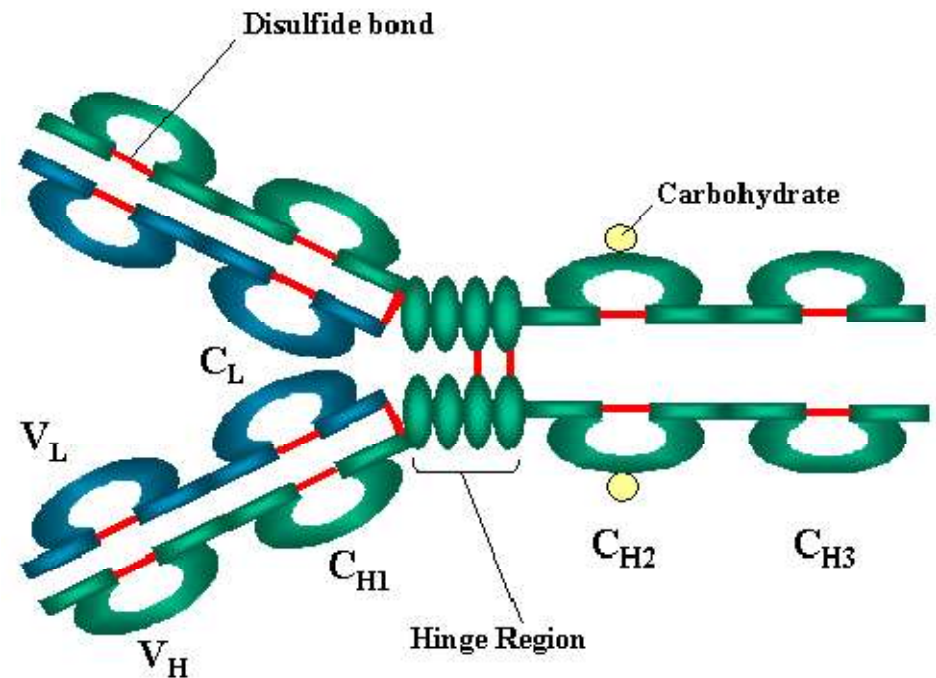




**Centurion
UNIVERSITY**
*Shaping Lives...
Empowering Communities...*

F. Oligosaccharides

- Carbohydrates are attached to the CH₂ domain in most immunoglobulins.
- However, in some cases carbohydrates may also be attached at other locations.





Centurion
UNIVERSITY
*Shaping Lives...
Empowering Communities...*

Immunoglobulin fragments: structure/function relationships

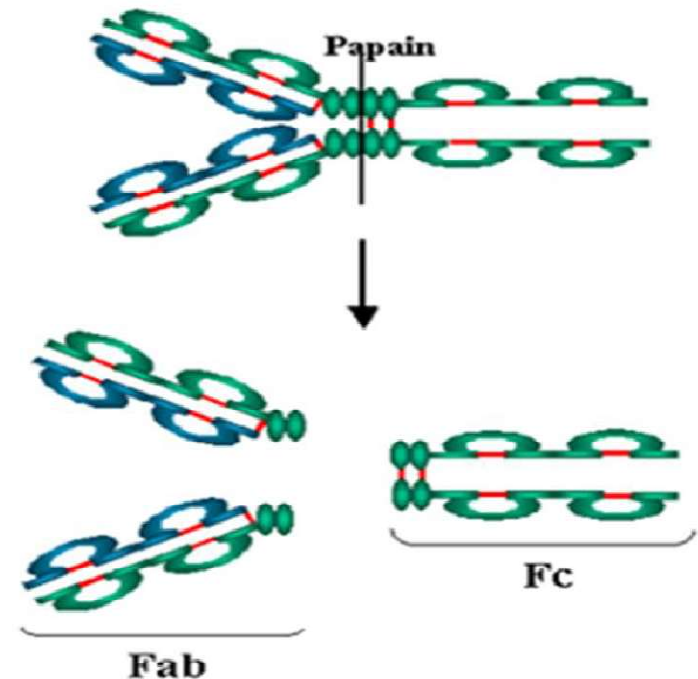
- Immunoglobulin fragments produced by proteolytic digestion –
- **A. Fab** Digestion with papain breaks the immunoglobulin molecule in the hinge region before the H-H inter-chain disulfide bond.
- This results in the formation of two identical fragments that contain the light chain and the VH and CH₁ domains of the heavy chain.



Centurion
UNIVERSITY
Shaping Lives
Empowering Communities...

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 V_H and V_L .





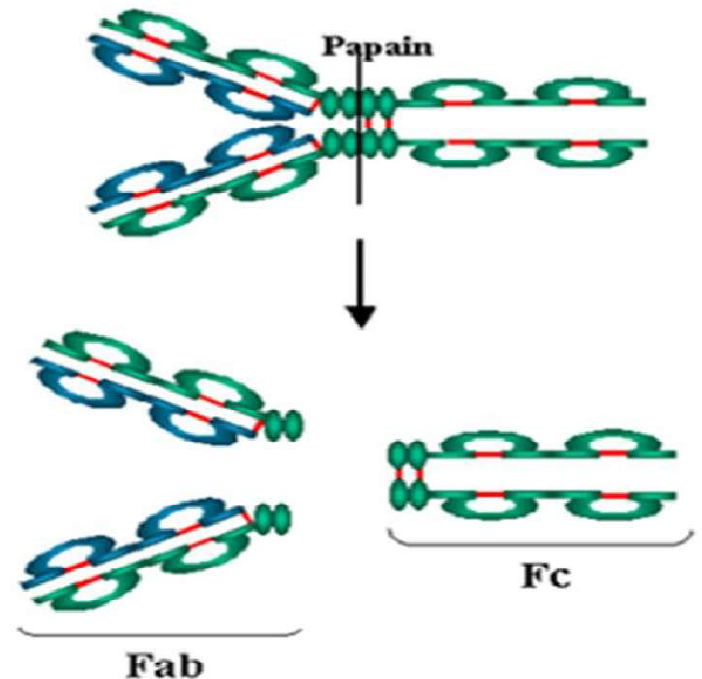
Centurion
UNIVERSITY

Shaping Lives...
Empowering Communities

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 CH₂ and CH₃ domain.

- This fragment was called Fc because it was easily crystallized.





Centurion
UNIVERSITY

Shaping Lives...
Empowering Communities...

Structure-function relationship

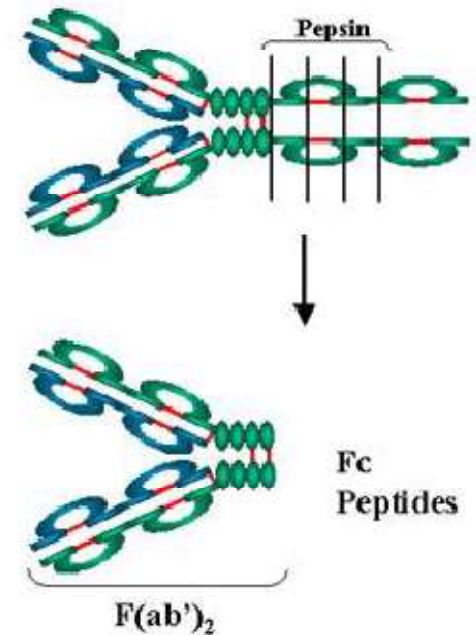
- **Antigen binding function of Immunoglobulins is carried out by Fab part,**
- **Effector functions** -The effector functions are mediated by Fc part of the molecule.
- Different functions are mediated by the different domains in this fragment.



Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

Immunoglobulin fragments by Pepsin

- **F(ab')₂**-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')₂ because it is divalent.
- **The Fc region** of the molecule is digested into small peptides by pepsin. The F(ab')₂ binds antigen but it does not mediate the effector functions of antibodies.



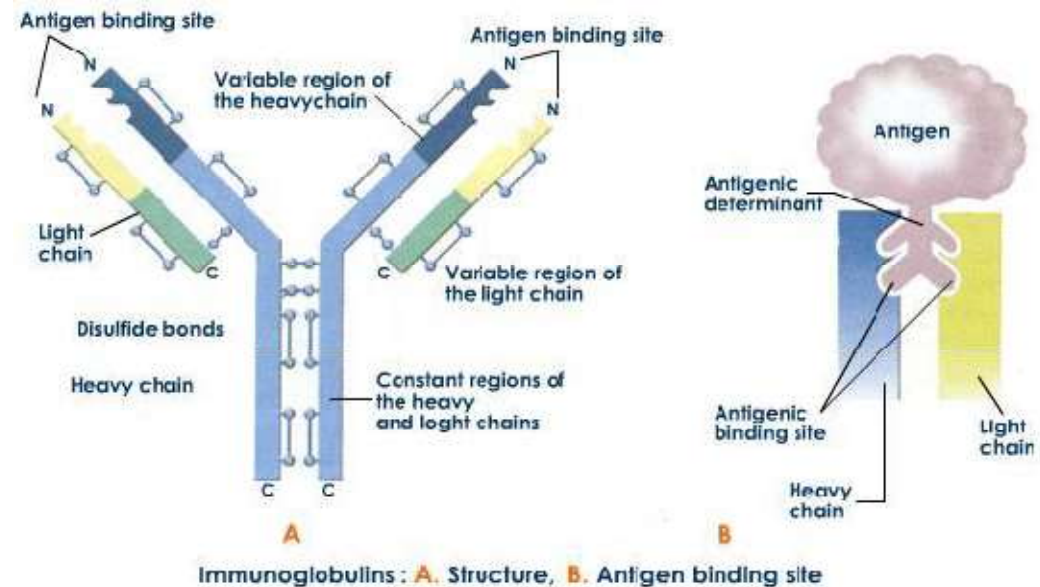


**Centurion
UNIVERSITY**
*Shaping Lives...
Empowering Communities...*

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.

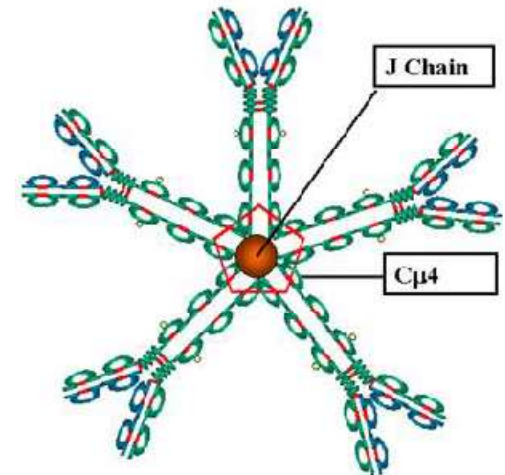
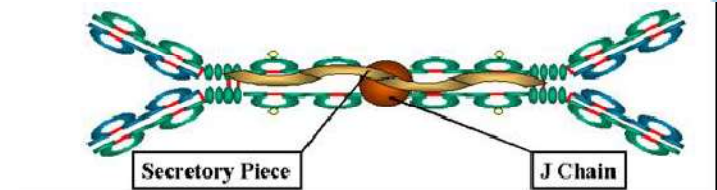
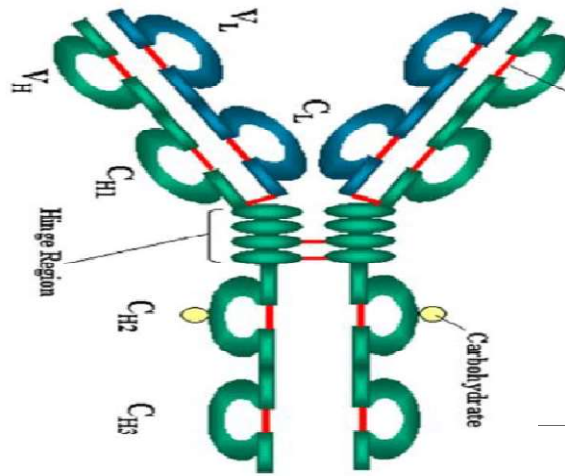




Centurion
UNIVERSITY
Shaping Lives
Empowering Communities...

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.





Centurion
UNIVERSITY
*Shaping Lives...
Empowering Communities...*

B. Effector Functions

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

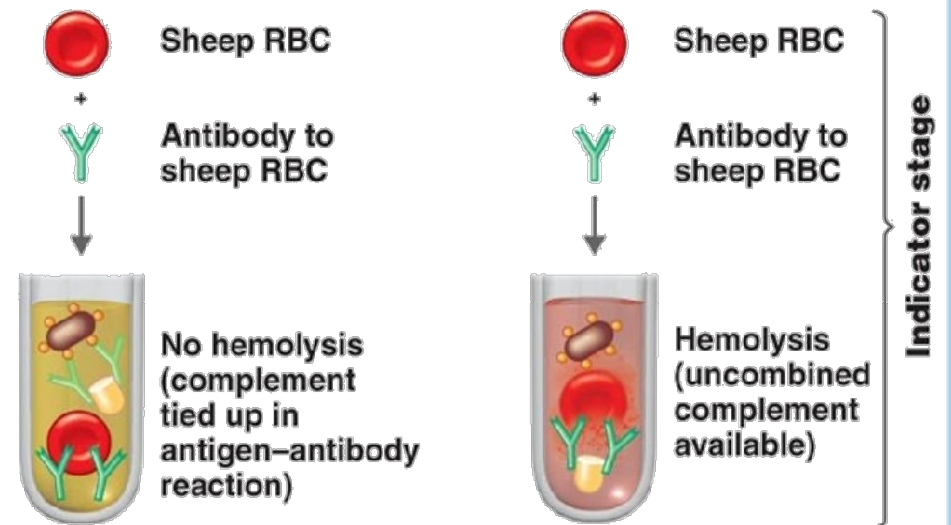


Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

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



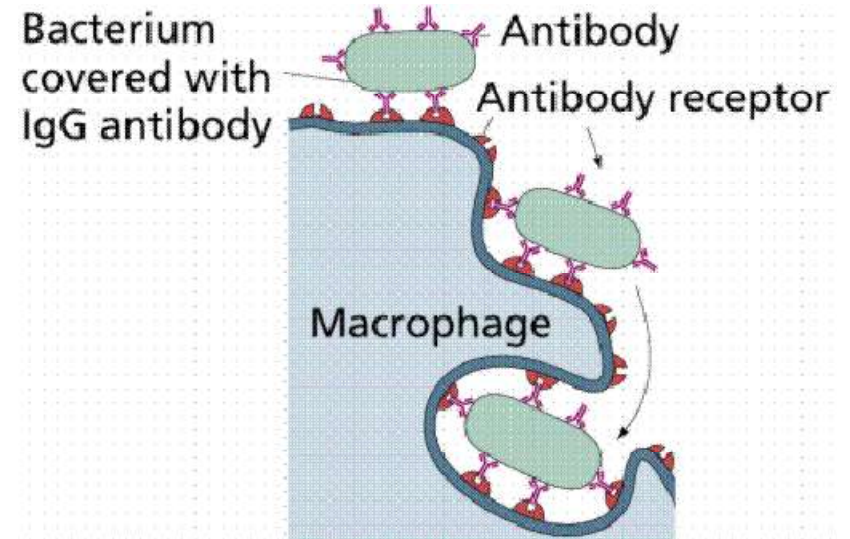


Centurion
UNIVERSITY

Shaping Lives...
Empowering Tomorrow...

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.

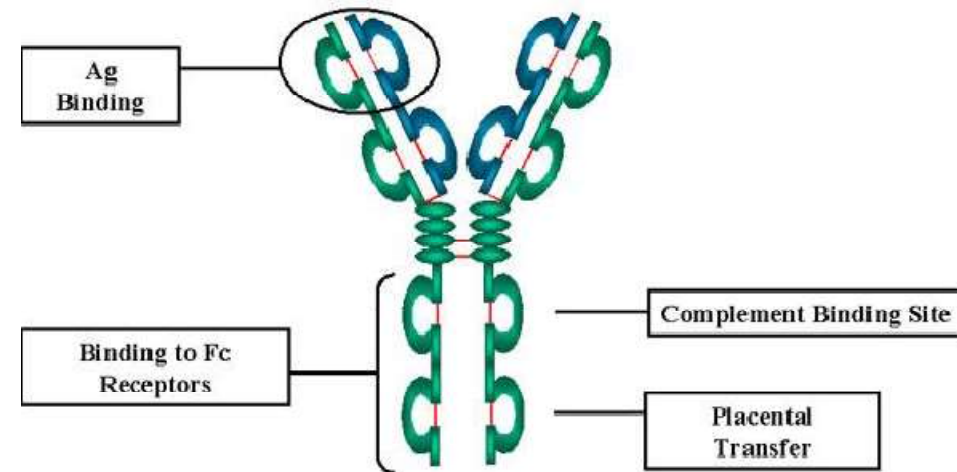




Centurion
UNIVERSITY
*Shaping the Future...
Empowering Communities...*

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.



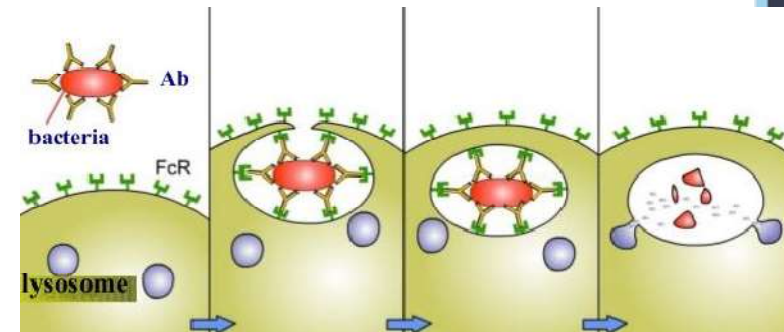
- The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains.

- 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.





Centurion
UNIVERSITY
*Shaping Lives...
Empowering Communities...*

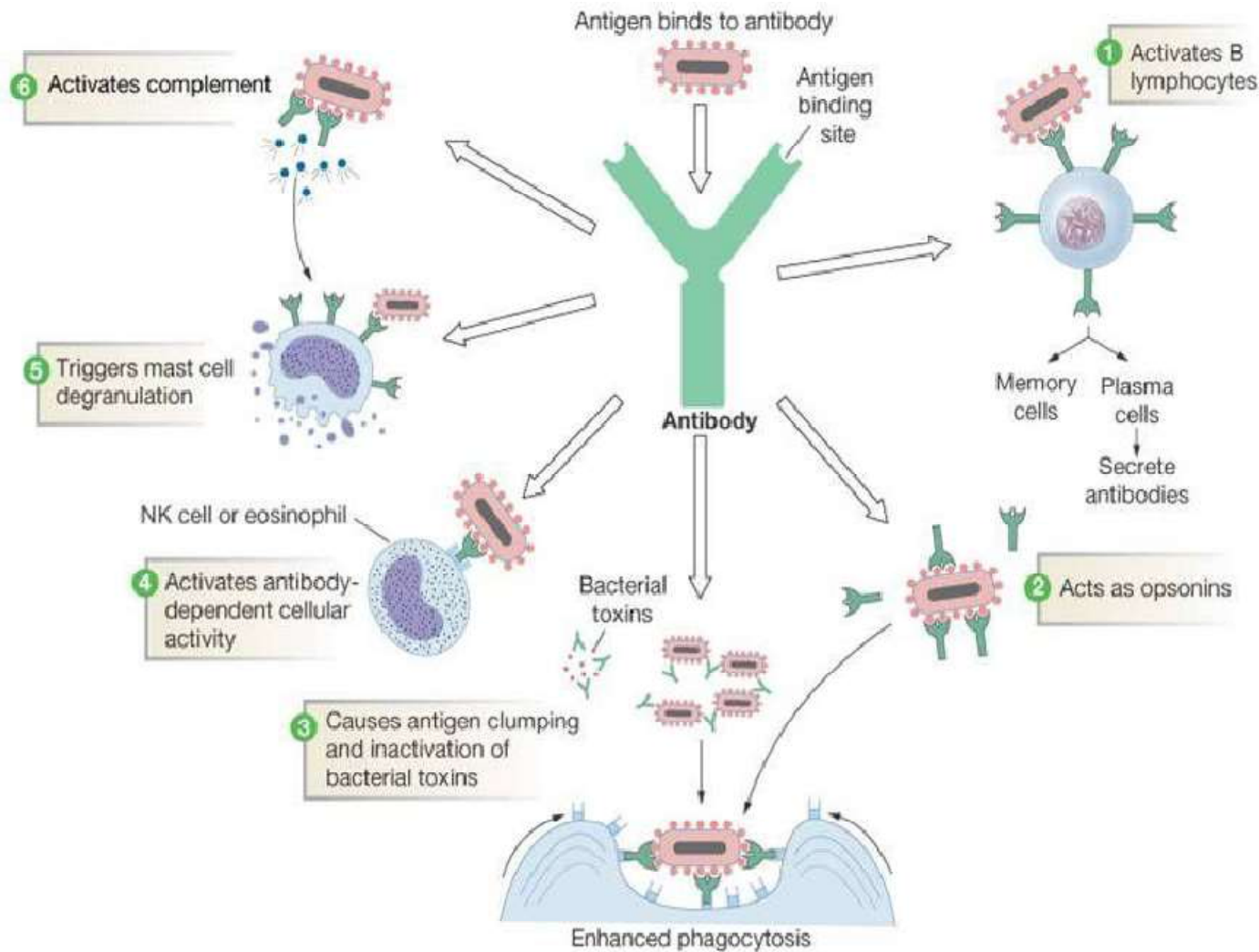
c) Involved in allergic reactions

- 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.



**Centurion
UNIVERSITY**
*Shaping Lives...
Empowering Communities...*

Functions of Immunoglobulins-an overview





Centurion
UNIVERSITY
Shaping Lives...
Empowering Communities...

THANK YOU



Centurion
UNIVERSITY

*Shaping Lives...
Empowering Communities...*

THANK YOU



Happy to Answer if you have any question.....