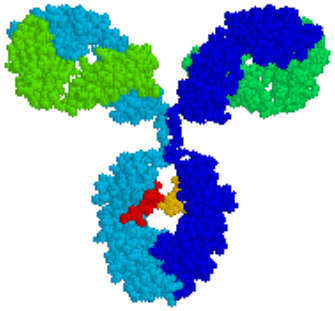
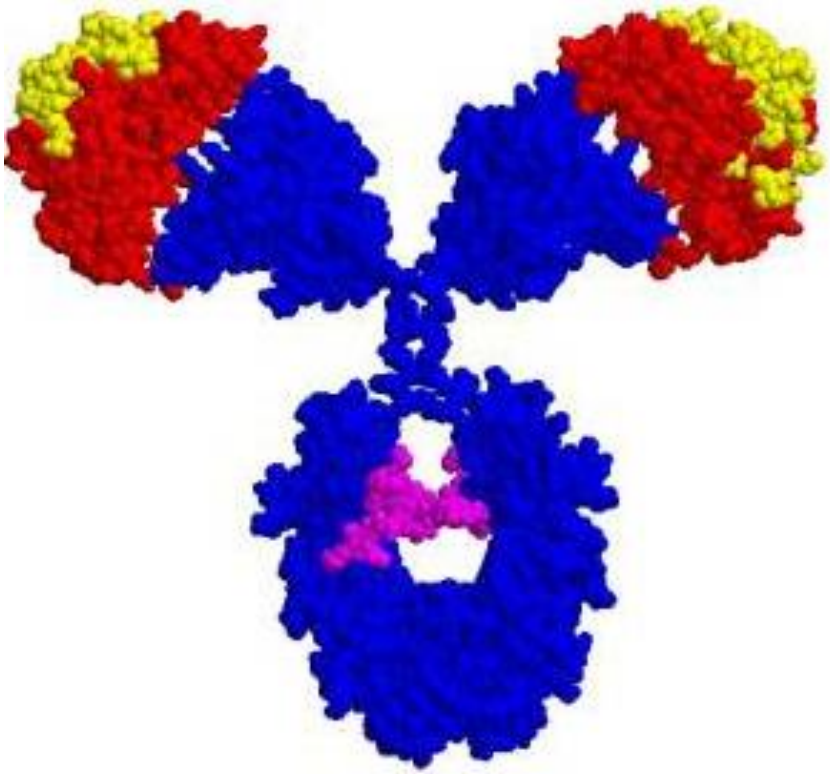
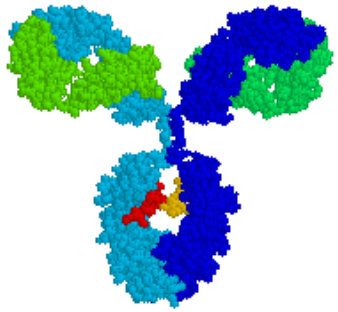


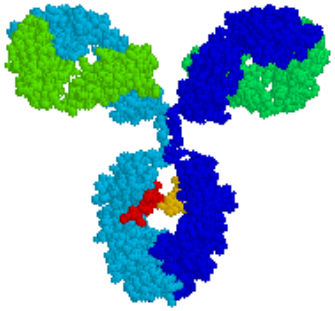
Antibodies

Immunoglobulins(Ig)





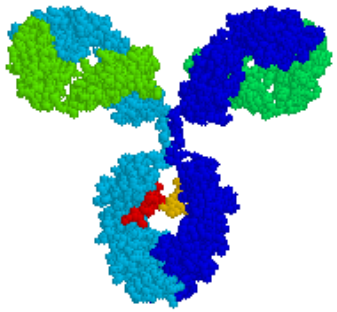
Antibodies



Antibodies

BY

Prof. Dr. Rafal Khaleel Farhan



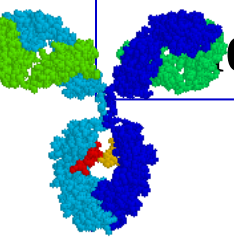
Antibodies

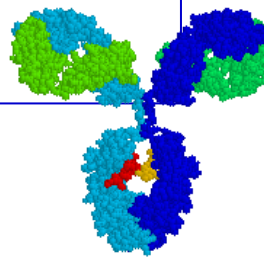
Antibody or immunoglobulin

- Both the terms, immunoglobulin (Ig) and antibody are used interchangeably; representing the physiological &functional properties of same molecule respectively.
- Immunoglobulin (Ig) constitutes 20-25 per cent of total serum proteins.
- There are five classes (or isotypes) of immunoglobulins recognised-IgG, IgA, IgM, IgD and IgE.

Immunoglobulin

- Immunoglobulins (Ig), are proteins produced by the immune system to identify and neutralize harmful invaders like bacteria, viruses, and toxins. They play a critical role in both immediate defense mechanisms and long-term immunity.
- Antibodies are part of the adaptive immune response.
- They specifically recognize antigens (foreign substances) and help the immune system neutralize them.
- Antibodies are secreted by **B cells**(specifically plasma cells) and play a key role in recognizing and neutralizing pathogens.



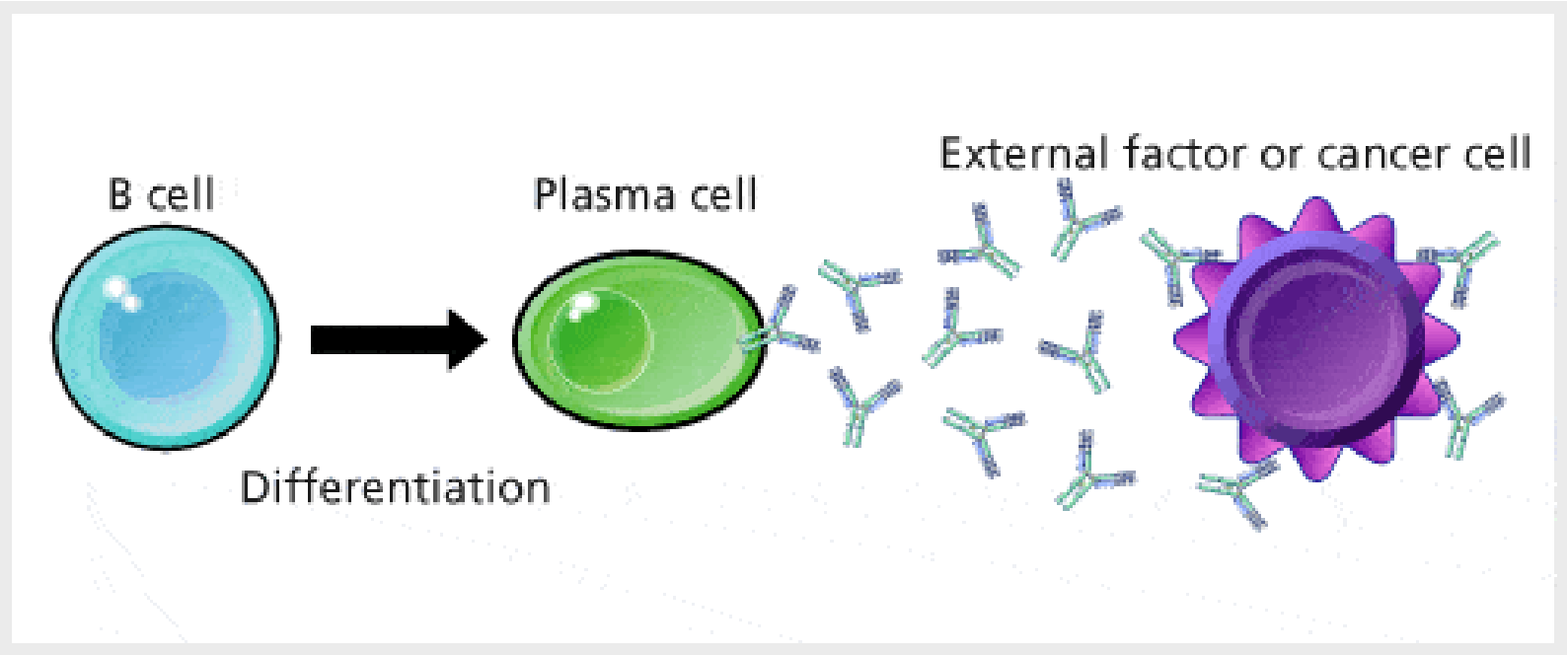


Antibodies help the immune system by:

- **Neutralizing** pathogens directly by binding to them.
- **Opsonizing** pathogens (marking them for phagocytosis by immune cells).
- **Activating the complement system**, which leads to the destruction of the pathogen.

Janeway, C. A., et al. (2001). *Immunobiology: The Immune System in Health and Disease* (5th ed.). Garland Science.

- The production of antibodies is a major function of the immune system and is carried out by a type of white blood cell called a B cell (B lymphocyte), differentiated B cells called plasma cells. The produced antibodies bind to specific antigens express in external factors and cancer cells.



History of Antibodies

Year	Scientist(s)	Discovery/Contribution
Late 1800s	Louis Pasteur & Robert Koch	**Germ Theory of Disease: Provided the foundation for understanding how the body fights infections.**
1890	Emil von Behring & Shibasaburo Kitasato	**Discovery of Antitoxins: Demonstrated that blood serum from animals exposed to diphtheria or tetanus could neutralize toxins.**
1901	Paul Ehrlich	**Proposed the "Side-Chain Theory": Suggested that cells have receptors that bind to pathogens, forming the basis for antibody theory.**
1930s	Michael Heidelberger & Oswald Avery	**Demonstrated that antibodies are proteins and can precipitate antigens (proof of antibody-protein nature).**
1940s	Linus Pauling	**Explained that antibody-antigen reactions are based on structural complementarity (how antibodies and antigens fit together).**

1959	**Gerald M. Edelman & Rodney R. Porter**	**Structure of Antibodies: Discovered the structure of antibodies, revealing that they are composed of two light chains and two heavy chains. This work earned them the Nobel Prize in 1972.**
1975	César Milstein & Georges Köhler	**Developed the Hybridoma Technique for producing monoclonal antibodies, leading to the development of highly specific antibodies for research, diagnostics, and treatment. They were awarded the Nobel Prize in 1984.**
1980s-2000s	Various	**Advances in genetic engineering led to the creation of recombinant antibodies, making it possible to engineer antibodies for specific therapeutic uses, including cancer treatment and autoimmune diseases.**

Structure of Antibodies

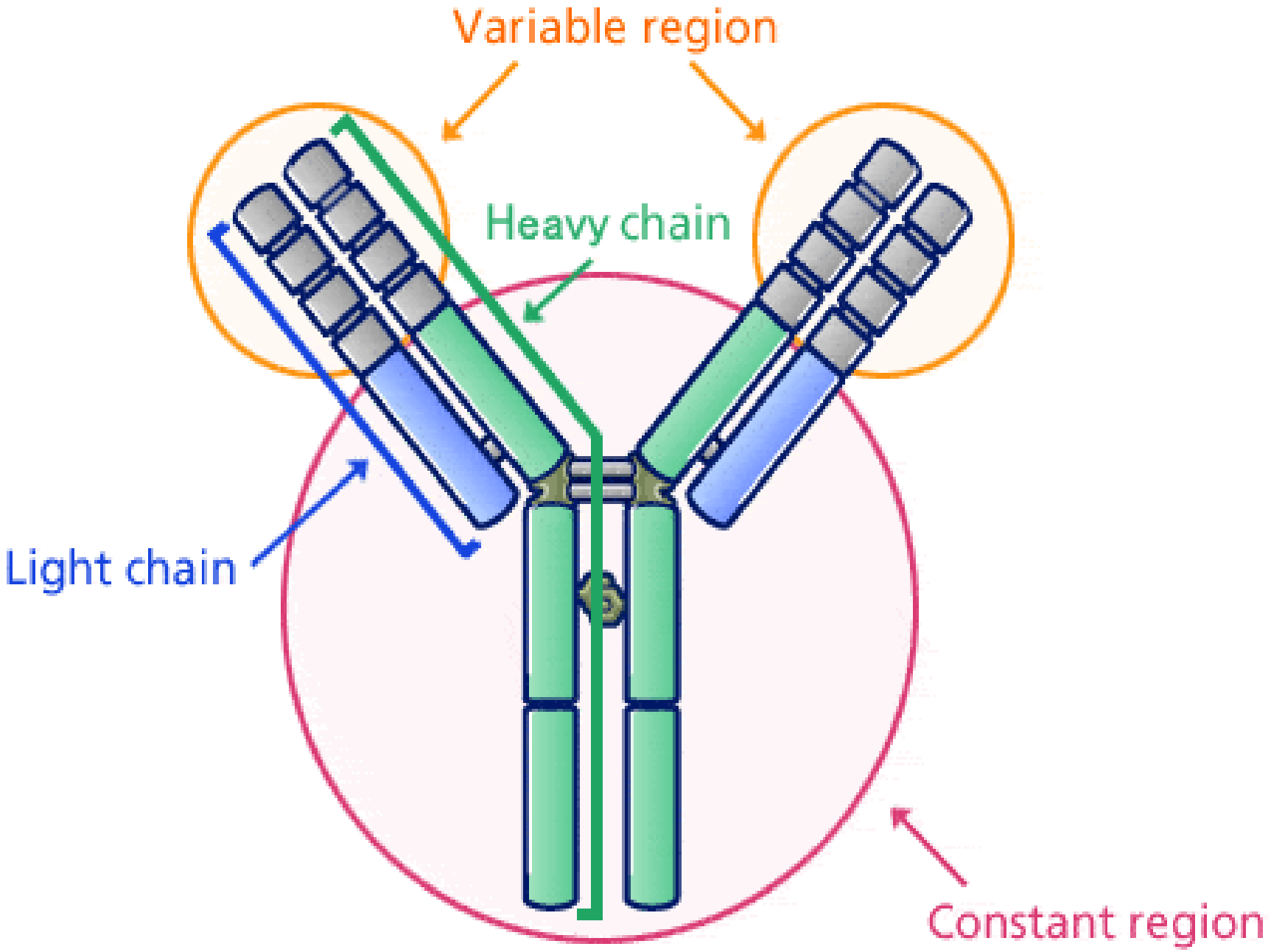
Y-shaped structure:

Variable (Fab) region:

Constant (Fc) region .

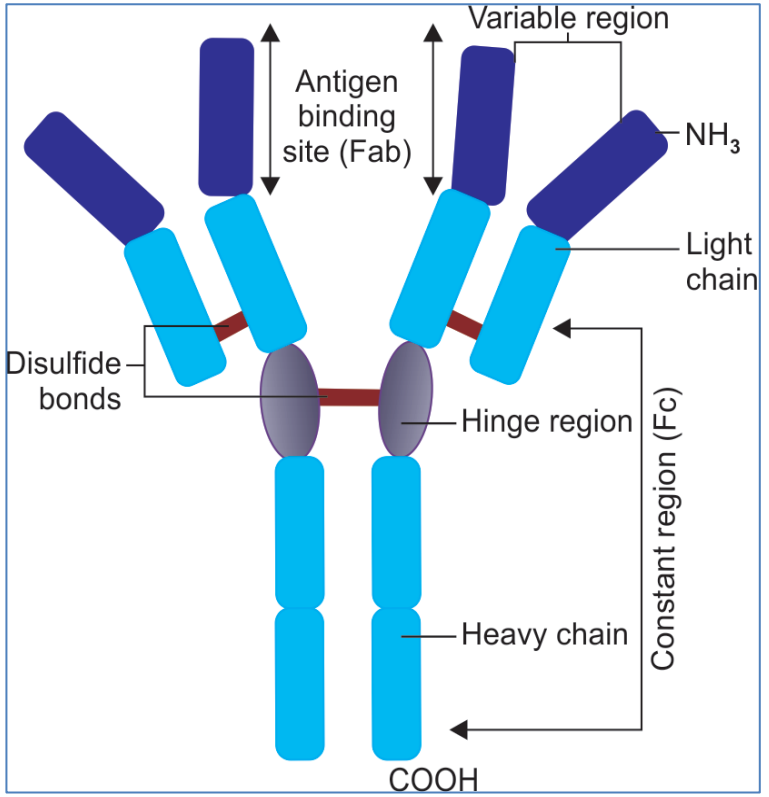
Antigen-Binding Sites

Fc Region:


Variable region
Heavy chain
Light chain
Constant region

Overall Shape:

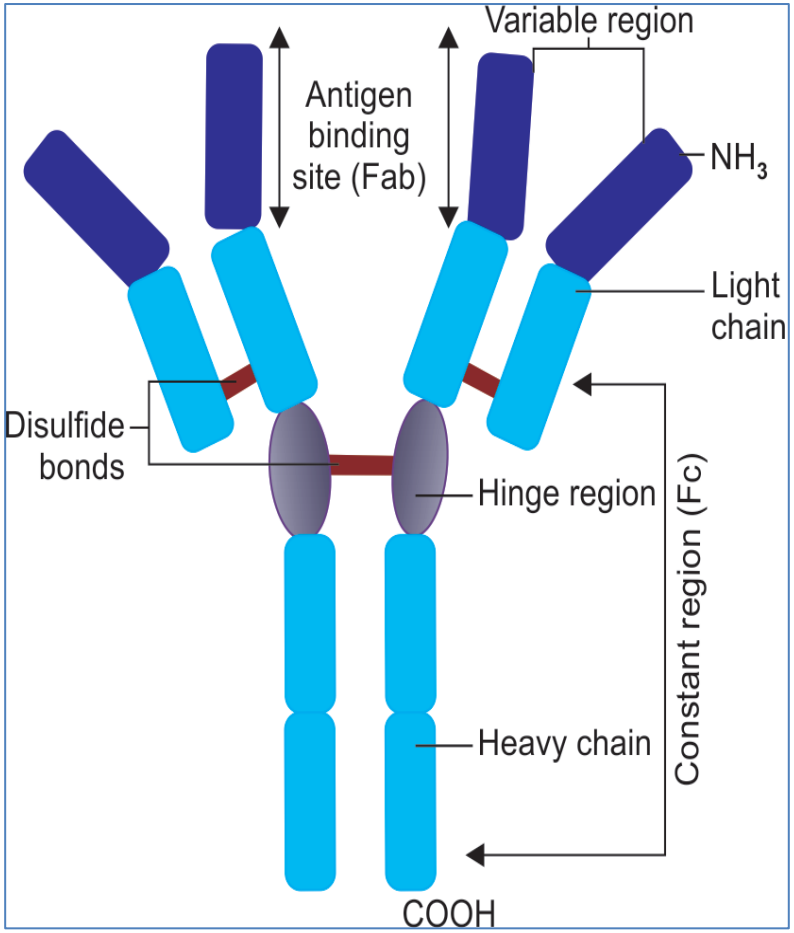
- The antibody has a **Y-shaped structure** heterodimer; composed of four polypeptide chains.
- Two identical heavy (H)(longer) chains each having molecular weight 50,000 Da or more.
- Two identical light (L)(shorter). , of molecular weight 25,000 Da each



H and L chain:

All four H and L chains are bound to each other by *disulfide bonds*, and by noncovalent interactions such as salt linkages, hydrogen bonds, and hydrophobic bonds.

All the chains have two ends- an amino terminal end (NH_3) and a carboxyl terminal end (COOH).



Variable (Fab) region

- Binds specifically to antigens.
- At the tips of the "**Y**" are the **variable regions**, one on each arm of the antibody. These regions are responsible for binding specifically to antigens(Foreign Substances).
- The structure here is highly specific and varies between different antibodies.

Constant Region:

- The base and part of the arms of the "Y" are made up of the **constant region**. This portion is less variable and interacts with other immune system components, such as cells or proteins, to help clear pathogens.
- Responsible for immune system signaling.

Antigen-Binding Sites

- Each antibody has two **antigen-binding sites** located at the tips of the "Y." These sites allow the antibody to bind to specific antigens on the surface of a pathogen, like a virus or bacterium.

Fc Region:

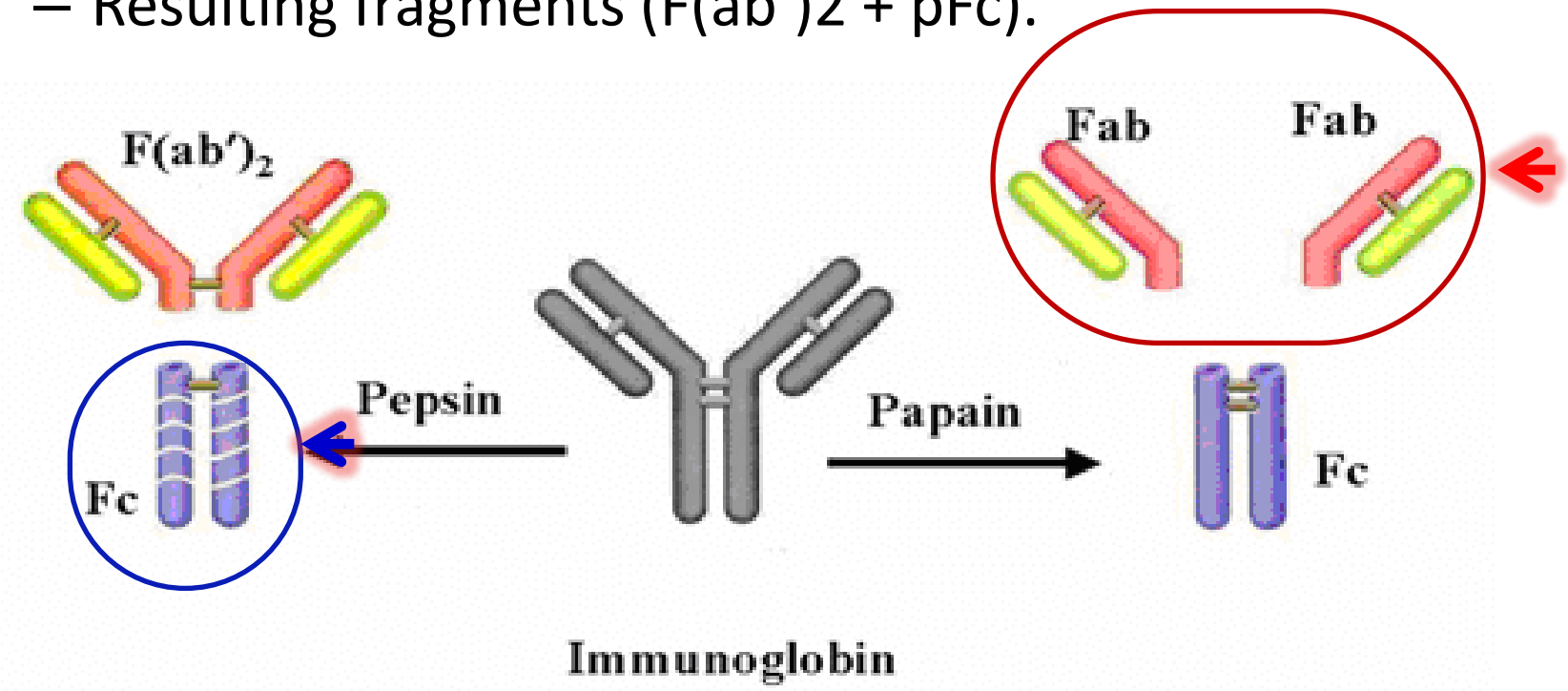
- The base of the "Y" is called the **Fc (fragment crystallizable)region**. This region does not bind antigens but instead interacts with immune cells (e.g., macrophages, neutrophils) and proteins (e.g., complement system) to trigger immune responses.

Enzymatic digestion of antibodies

- **Common Enzymes Used for Digestion**
- **Papain**:
  - Cuts above the hinge region.
  - Produces two Fab fragments and one Fc fragment.
- **Pepsin**:
  - Cuts below the hinge region.
  - Produces a single F(ab')2 fragment and a smaller Fc fragment.
- **Other Enzymes**: Briefly mention others like trypsin and ficin.

Mechanism of Action

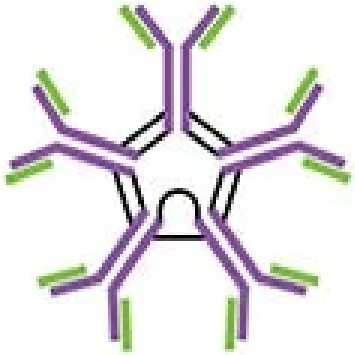
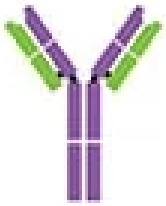
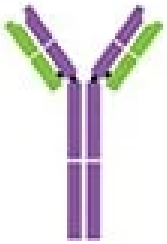
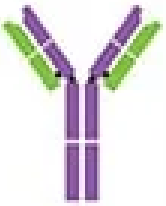
- **Papain Digestion**:
  - Diagram showing the cleavage points.
  - Resulting fragments (2 Fab + Fc).
- **Pepsin Digestion**:
  - Diagram showing cleavage below the hinge region.
  - Resulting fragments (F(ab')2 + pFc).



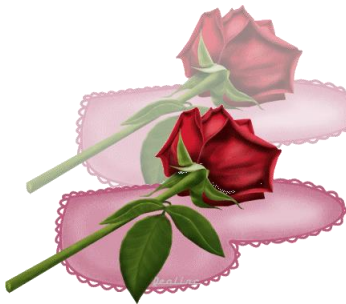
Classes/Types of Antibody

- Serum containing antigen-specific antibodies is called antiserum,
- The 5 types – IgG, IgM, IgA, IgD, IgE – (isotypes) are classified according to the type of heavy chain constant region, and are distributed and function differently in the body.

Immunoglobulin class	**Heavy chain type**
IgG	γ(gamma)
IgA	α (alpha)
IgM	μ(mu)
IgD	δ(delta)
IgE	ε(epsilon)

The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Heavy chains	μ	γ	α	ε	δ

L chains are of two types- kappa (κ) and lambda (λ), named after Korngold and Lapari who originally described them.



Classes/Types of Antibody

- **Immunoglobulins (Ig)**, are divided into five main types based on their structure and function. Each type has a specific role in the immune system. Here's a summary of the five types of antibodies:

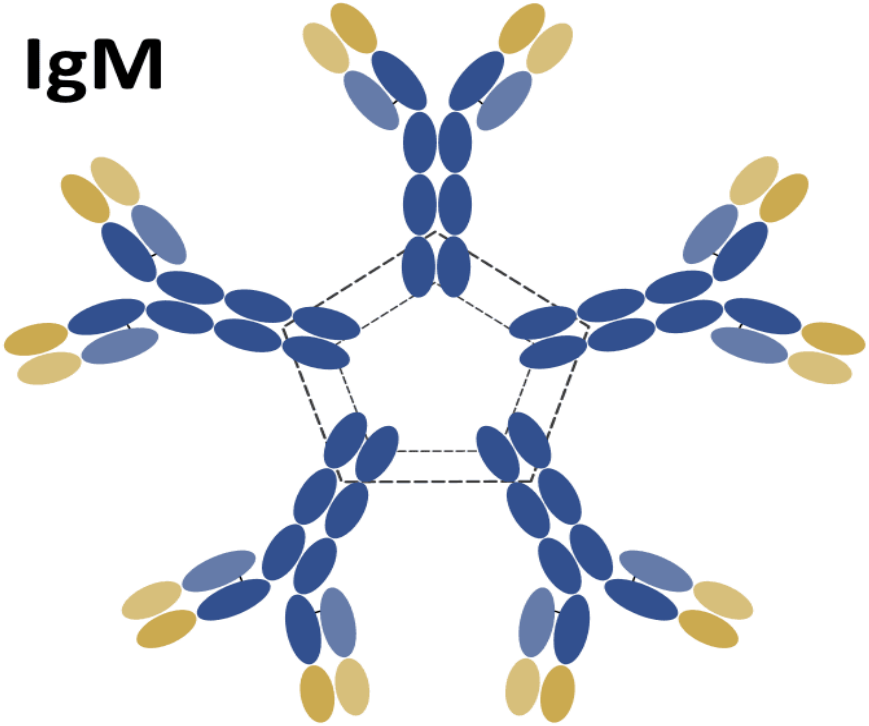
IgG (Immunoglobulin G)

- **Structure**: Monomer (single Y-shaped unit).
- **Location**: Blood, extracellular fluids, and can cross the placenta.
- **Function**:
- Provides long-term immunity after an infection or vaccination.
- Can cross the placenta to provide passive immunity to the fetus.
- Major antibody in secondary immune responses.
- **Subclasses**: IgG1, IgG2, IgG3, IgG4 (vary slightly in function and prevalence)
- **Lifespan**: **21-23 days** (longest half-life among antibodies).
- This long lifespan contributes to its role in lasting immunity.
- **Special Feature**: Crosses the placenta to provide passive immunity to the fetus.

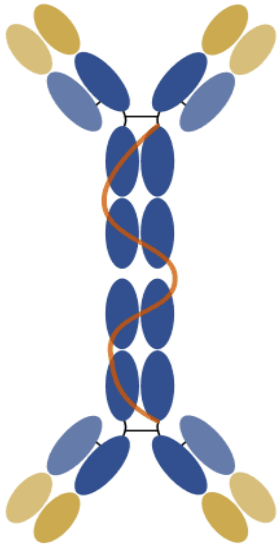
Antibody Type	Location	Structure	Main Function	Lifespan
IgG	Monomer	Blood, extracellular fluids, placenta	Long-term immunity, neutralization, opsonization	**21-23days**
IgA	Dimer	Mucosal areas, secretions	Mucosal immunity, protection in respiratory and GI tracts	**5-6 days**
IgM	Pentamer	Blood, lymph	First response to infection, activates complement	**5 days**
IgE	Monomer	Blood (low), tissues (mast cells)	Allergic responses, defense against parasites infection	**2-3 days**
IgD	Monomer	B cell surfaces, low in blood	B cell activation	**2-3 days**

IgG

IgM



IgA



IgD

IgE

Roles of antibodies against infection:

antibody Function	Mechanism	Result/Outcome	Key Antibody Types Involved
Neutralization of Pathogens	Antibodies bind directly to pathogens or toxins, blocking their interaction with host cells.	Pathogens are unable to enter cells, preventing infection or toxin damage.	IgG, IgA
Opsonization (Tagging for Phagocytosis)	Antibodies coat pathogens, making them easier to recognize by immune cells (macrophages, neutrophils).	Pathogens are engulfed and destroyed by phagocytic cells.	IgG, IgM
Activation of the Complement System	Antibodies bind to pathogens, triggering the complement cascade.	Complement system causes pathogen lysis and enhances phagocytosis.	IgM, IgG

Antibody-Dependent Cellular Cytotoxicity (ADCC)	Antibodies bind to infected or abnormal cells. Immune cells (e.g., NK cells) recognize these cells and kill them.	Infected or abnormal cells are destroyed.	IgG
Agglutination (Clumping of Pathogens)	Antibodies bind to multiple pathogens, causing them to clump together.	Pathogens are immobilized and more easily phagocytosed by immune cells.	IgM, IgA
Prevention of Pathogen Adherence	Antibodies bind to structures on pathogens used for attachment to host cells.	Pathogens cannot adhere to or invade host tissues.	IgA, IgG
Neutralization of Toxins	Antibodies bind to toxins, blocking their harmful effects on host cells.	Toxins are neutralized and cannot cause damage.	IgG, IgA
Maternal Antibody Protection (Passive Immunity)	Antibodies are transferred from mother to fetus through the placenta (IgG) or via breast milk (IgA).	Provides newborns with temporary immunity against infections.	IgG (placenta), IgA (breast milk)

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