BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024,

Tamil Nadu, India

Programme: M.Sc., Biomedical Science

Course Code: BM35C6

Course Title: Immunology

Unit-III

Antigens

Dr. R. POORNIMA

Guest Faculty

Department of Biomedical Science

Unit III:

Antigens – Factors influence immunogenicity, Epitopes, haptens – Effector molecules of innate system -Acute phase proteins, complements- classical & alternative pathways of complement system. Effector molecules of cell-mediated and humoral immune responses - cytokines - Properties, receptors and antibodies / Immunoglobulins – Structure, antigenic determinants, immunoglobulin classes and functional significances.

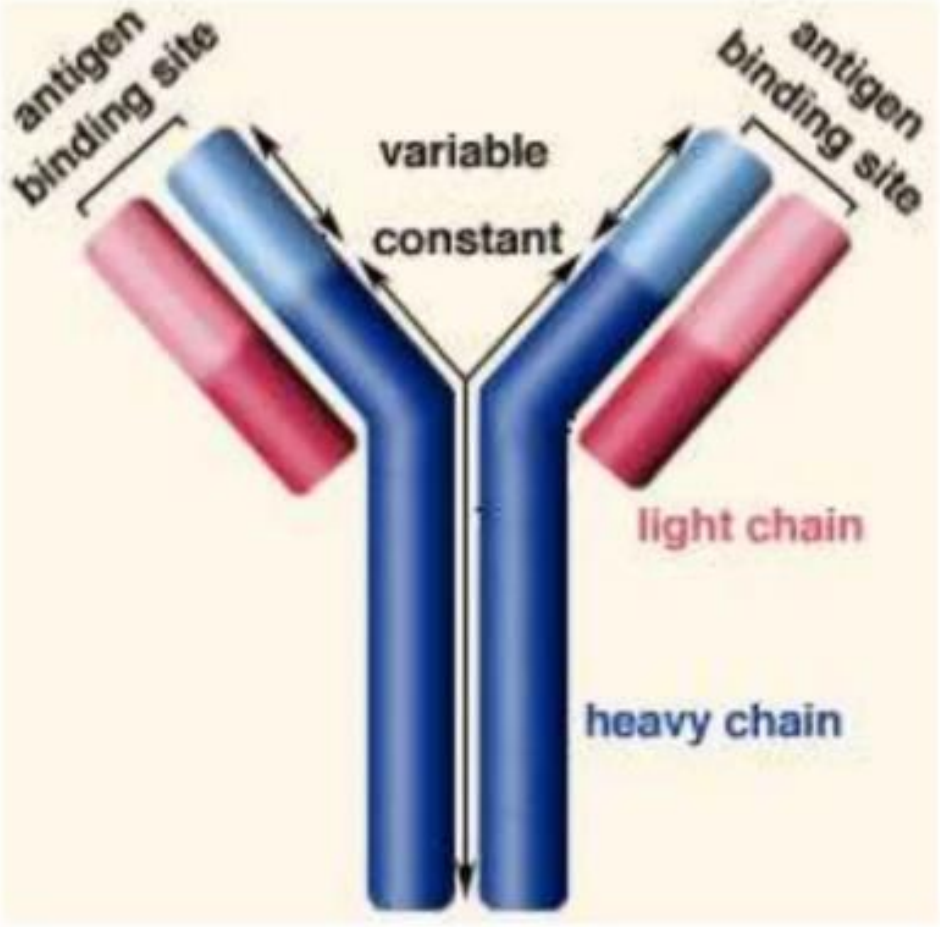
PRESENTATION: 3

Immunoglobulins- structure, antigenic determinants

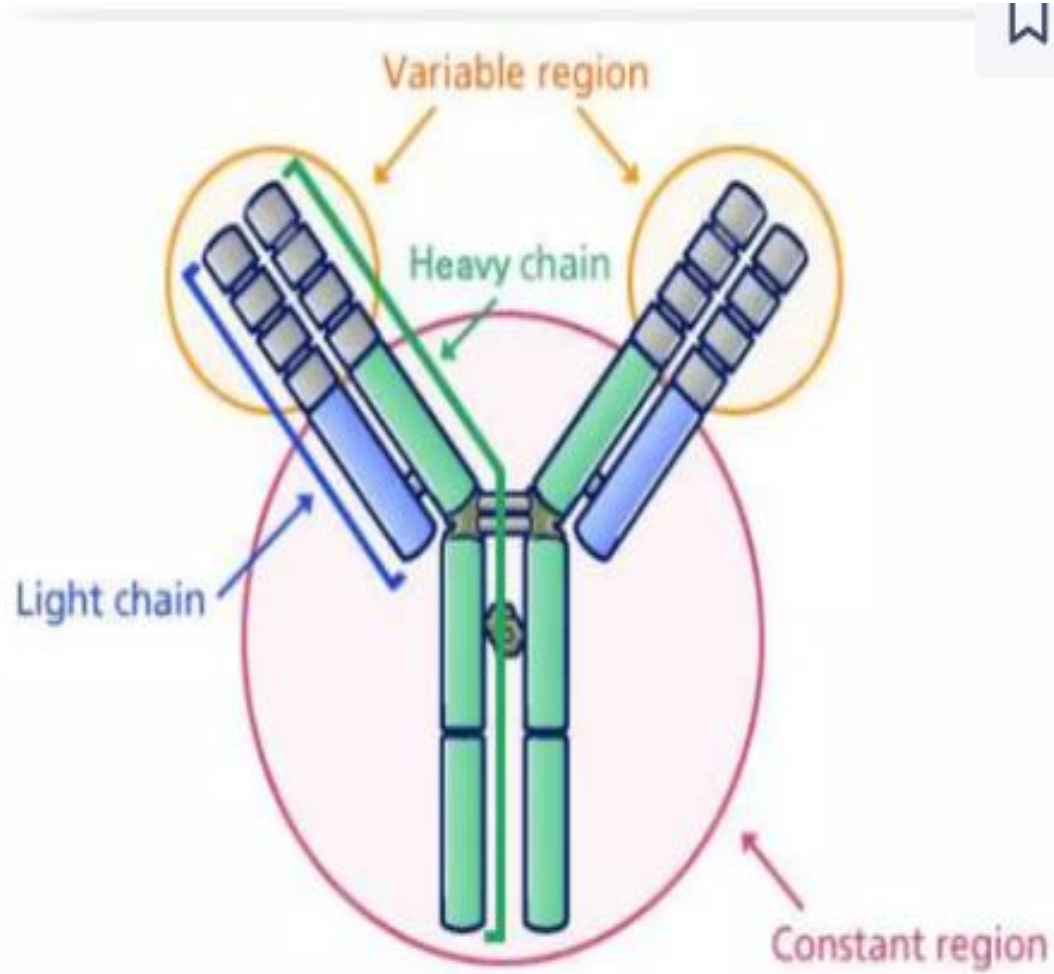
- The humoral immunity is mediated by a special group of antigen binding proteins called Immunoglobulins or antibodies, produced by B-lymphocytes.
- This Y-shaped proteins detect and bind to harmful specific substances like antigens - bacteria and other foreign substances.
- Since the majority of the antibody types are found in this globulin fraction, the antibodies are also called as Immunoglobulins.
- In 1931, Tiselius and Kabat identified and isolated the **antibodies** from the blood plasma by electrophoretic mobility assay.
- WHO officially coined the term **Immunoglobulin (Ig)** for antibodies in 1964.
- The production of antibodies are carried out by B lymphocyte.
- Immunoglobulins can either be membrane-bound (B-cell receptor) or secreted (antibody).

STRUCTURE

- All the immunoglobulin (Ig) molecules basically consist of
  - Two identical heavy (H) chains (Molecular Weight 53,000 to 75,000 each) and
  - Two identical light (L) chains (mol. wt. 23,000 each) held together by disulfide linkages and non-covalent interactions.
- Each heavy chain contains approximately, 450 amino acids
- Each light chain has 212 amino acids.
- There are five types of Ig heavy chain (in mammal) denoted by the Greek letters: α, δ, ε, γ, and μ.
- There are two types of Ig light chain (in mammal), which are called lambda (λ) and kappa (κ).
- The heavy chains of Ig are linked to carbohydrates, hence immunoglobulins are glycoproteins



- Both types of chains (heavy and light) are comprised of two regions:
  - Variable region and Constant region.
  - The region that changes to various structures depending on differences in antigens is called the **variable region.**
  - The region that has a constant structure is called the **constant region**.



Hinge Region:

•Located between the first and second constant domains (CH1 and CH2) of the heavy chain in IgG, IgA, and IgD antibodies.

•Provides flexibility to the antibody molecule, allowing it to adjust the distance between its two antigen-binding sites and bind to different epitopes simultaneously.

Fab and Fc Fragments:

Fab (Fragment, antigen-binding):

•The portion of the antibody that contains the variable regions of both the heavy and light chains and is responsible for binding to the antigen. There are two Fab fragments in each antibody.

Fc (Fragment, crystallizable):

•The tail region of the antibody that contains the constant domains of the heavy chains. The Fc region determines the antibody's isotype and mediates effector functions, such as binding to Fc receptors on immune cells, complement activation, and opsonization.

J Chain and Secretory Component:

•In dimeric IgA and pentameric IgM, a **J (joining) chain** links the monomers, allowing their polymerization.

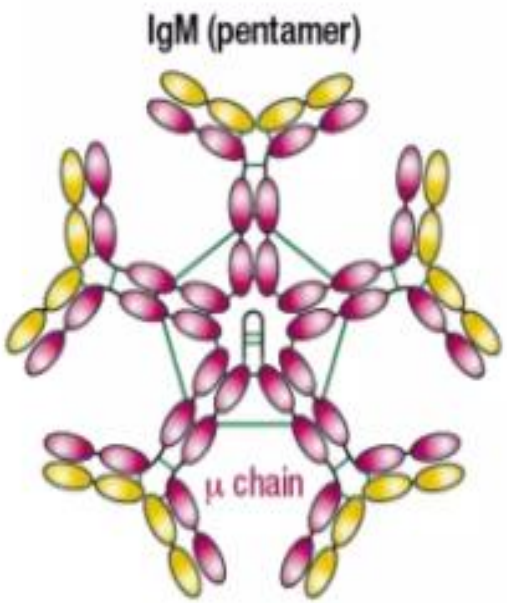
- **Secretory IgA (sIgA)** has an additional component called the **secretory component**, which facilitates transport across mucosal surfaces and protects the antibody from proteolytic degradation.

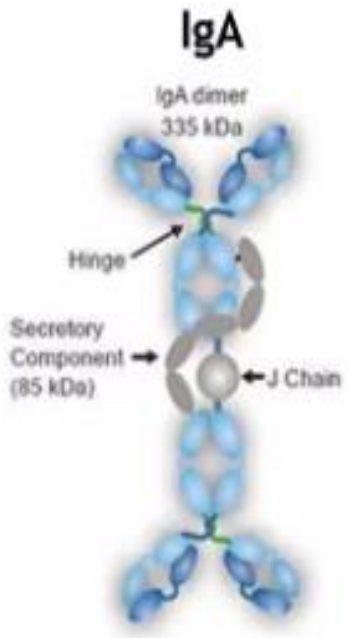
Antigenic Determinants of Immunoglobulins:

- Antigenic determinants, also known as **epitopes**, are specific parts of an antigen recognized and bound by antibodies.
- However, when discussing **immunoglobulins themselves**, antigenic determinants refer to regions of the antibody molecule that can be recognized by other antibodies or immune receptors.

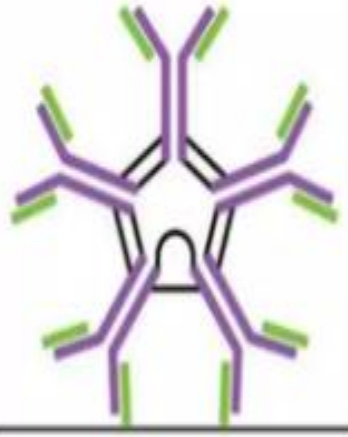
CLASSES

- There are five classes of Immunoglobulin : IgM, IgG, IgM, IgA, IgE and IgD





TYPES

The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor
Percentage of total antibody in serum	6%	80%	13%	0.002%	1%

Properties of Immunoglobulins

The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	

Functional significances:

1. Antigen Recognition and Neutralization:

- The primary function of antibodies is to recognize and bind specific antigens (foreign molecules such as pathogens, toxins, and allergens) with high specificity and affinity.
- The variable regions of the antibody (Fab regions) contain hypervariable regions that determine the antigen-binding site, allowing them to neutralize pathogens by preventing their attachment and entry into host cells.

- **Neutralization** is particularly important for viruses, bacteria, and toxins. For example, antibodies can bind to viral particles, preventing their entry into host cells or neutralizing bacterial toxins by blocking their receptor-binding sites.

2. Opsonization:

- **Opsonization** is the process by which antibodies coat the surface of pathogens or foreign particles, tagging them for phagocytosis by immune cells like macrophages and neutrophils.
- The Fc region of the antibody binds to Fc receptors on the surface of phagocytic cells, enhancing the ability of these cells to engulf and destroy the pathogen.
- This function is essential in clearing encapsulated bacteria and other pathogens that are resistant to direct recognition by phagocytes.

3. Activation of the Complement System:

- Certain classes of antibodies (e.g., IgM and IgG) can activate the **complement system**, a cascade of proteolytic enzymes that enhances the immune response.
- Activation of the classical complement pathway leads to the formation of the **membrane attack complex (MAC)**, which creates pores in the membranes of pathogens, leading to their lysis and death.
- Complement activation also results in the production of **opsonins (like C3b)** and **anaphylatoxins (C3a, C5a)** that promote inflammation and recruit additional immune cells to the site of infection.

4. Antibody-Dependent Cellular Cytotoxicity (ADCC):

•Antibodies (primarily IgG) can bind to infected or abnormal cells (such as virus-infected cells or tumor cells), tagging them for destruction by immune cells such as **natural killer (NK) cells**.

•NK cells recognize the Fc region of antibodies bound to target cells through their Fc receptors (FcγR), leading to the release of cytotoxic granules containing perforin and granzymes, which induce apoptosis in the target cell.

5. Mucosal Immunity:

- **IgA** plays a crucial role in mucosal immunity. It is the predominant antibody class found in mucosal surfaces, such as the respiratory, gastrointestinal, and urogenital tracts.
- Secretory IgA (sIgA) is resistant to proteolytic enzymes and helps prevent the attachment and penetration of pathogens across mucosal barriers, providing a first line of defense at entry points.
- IgA neutralizes pathogens and toxins at mucosal surfaces, preventing them from establishing infections.

6. Allergic Responses and Parasite Defense:

- **IgE** is primarily involved in allergic reactions and defense against parasitic infections.
- IgE binds to high-affinity Fc receptors (FcεRI) on mast cells and basophils. Upon exposure to an allergen or parasite, cross-linking of IgE molecules leads to degranulation of these cells and the release of inflammatory mediators like histamine.
- This response is beneficial in fighting parasitic infections but can lead to allergic reactions and anaphylaxis in response to non-pathogenic allergens (e.g., pollen, food).

7. Immune Regulation and Homeostasis:

- **IgG** antibodies, especially **IgG4**, play a role in immune regulation by blocking excessive immune responses and maintaining immune tolerance.
- Certain antibodies (e.g., **IgG**) can interact with regulatory receptors, like FcγRIIb, on B cells or other immune cells, providing negative feedback to prevent over-activation of the immune response and minimize tissue damage.

8. Immune Memory:

- Antibodies are a crucial part of the immune memory response. Following an initial infection or vaccination, memory B cells are generated that rapidly produce high-affinity antibodies upon re-exposure to the same pathogen.
- This secondary immune response is faster and more effective, providing long-lasting protection against previously encountered pathogens.

9. Transplacental Immunity:

- **IgG** is the only class of antibody that can cross the placenta from the mother to the fetus, providing passive immunity to the newborn against pathogens that the mother has encountered.
- This transplacental transfer of antibodies is critical for protecting infants during the early months of life when their own immune system is still developing.

10. Immune Complex Formation:

- Antibodies can form complexes with antigens (immune complexes), which are then cleared from the circulation by immune cells like phagocytes in the liver and spleen.
- Immune complex formation is important for eliminating soluble antigens, such as toxins, and for resolving immune responses, though excessive complex formation can contribute to autoimmune and inflammatory diseases.

Immunoglobulins and their functions

1.	**IgG:** 1. Provides the majority of antibody-mediated immunity in blood and tissues. 2. **Capable of crossing the placenta**, activating complement (except IgG4), opsonizing pathogens, and mediating ADCC. 3. Has the longest half-life among antibodies, providing long-lasting protection.
2.	**IgA:** 1. Major antibody **in mucosal secretions** (tears, saliva, breast milk, etc.). 2. Protects mucosal surfaces by neutralizing pathogens and toxins and preventing their adherence and entry.
3.	**IgM:** 1. The **first antibody produced during the initial** immune response. 2. Highly effective at agglutinating pathogens and activating the complement system. 3. Its pentameric structure allows for multiple antigen-binding sites, enhancing its ability to bind to antigens.
4.	**IgE:** 1. Plays a key role in **allergic responses and defense against parasitic infections**. 2. Binds to high-affinity Fc receptors on mast cells and basophils, triggering degranulation and the release of inflammatory mediators.
5.	**IgD:** 1. Primarily functions as a receptor on the surface of naive B cells, involved in **B cell activation and differentiation**. 2. Its exact role in immunity is less well-defined but is believed to help in initiating immune responses.

ACKNOWLEDGEMENT

- The presentation is being used for educational and non-commercial purposes.
- Thanks are due to all the original contributors and entities whose pictures were used to create this presentation.