

Antibody

Introduction

- Antibody or immunoglobulin is a specialized glycoprotein, produced from activated B cells (plasma cells) in response to an antigen, and is capable of combining with the antigen that triggered its production
- Located in Y- globulin fraction
- Both the terms, immunoglobulin (Ig) and antibody are used interchangeably, representing physiological and functional properties of same molecule respectively.
- Constitutes 20% to 25% of the serum protein

Structure of antibody

- An antibody molecule is a 'Y-shaped' heterodimer, composed of four polypeptide chains
- **Two identical light (L) chains**, of molecular weight 25,000 Da each
- **Two identical heavy(H) chains** each having molecular weight 50,000 Da or more

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.

- The five classes of immunoglobulins (IgG, IgA, IgM, IgD and IgE) are classified based on the amino acid sequences of the heavy chains (Table 11.1).

TABLE. 11.1: Type of heavy chain in each immunoglobulin class

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

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

- In humans, 60% of the light chains are kappa and 40% are lambda type (ratio 3:2).
- Both the light chains of an antibody molecule should be of same type, either κ or λ , but never both.

Variable and Constant Regions

Each H and L chain comprises of two regions—variable and constant region, depending upon whether the amino acid sequences of the regions show variable or uniform pattern among different antibodies.

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- The actual region of variable region that makes actual contact with antigen is called paratope

Constant region: it constitutes the remaining portion of antibody

H and L Chain Domains

Heavy and light chains are further folded into domains, each containing about 110 amino acid residues. Within the domain, a loop like structure of 60 amino acids is present which is formed due to an intrachain disulfide bond. The number of domains in each chain varies:

- Light chain contains one variable domain (V_L) and one constant domain (C_L).
- Heavy chains possess one variable domain (V_H) and 3 or 4 numbers of constant domain (C_H):

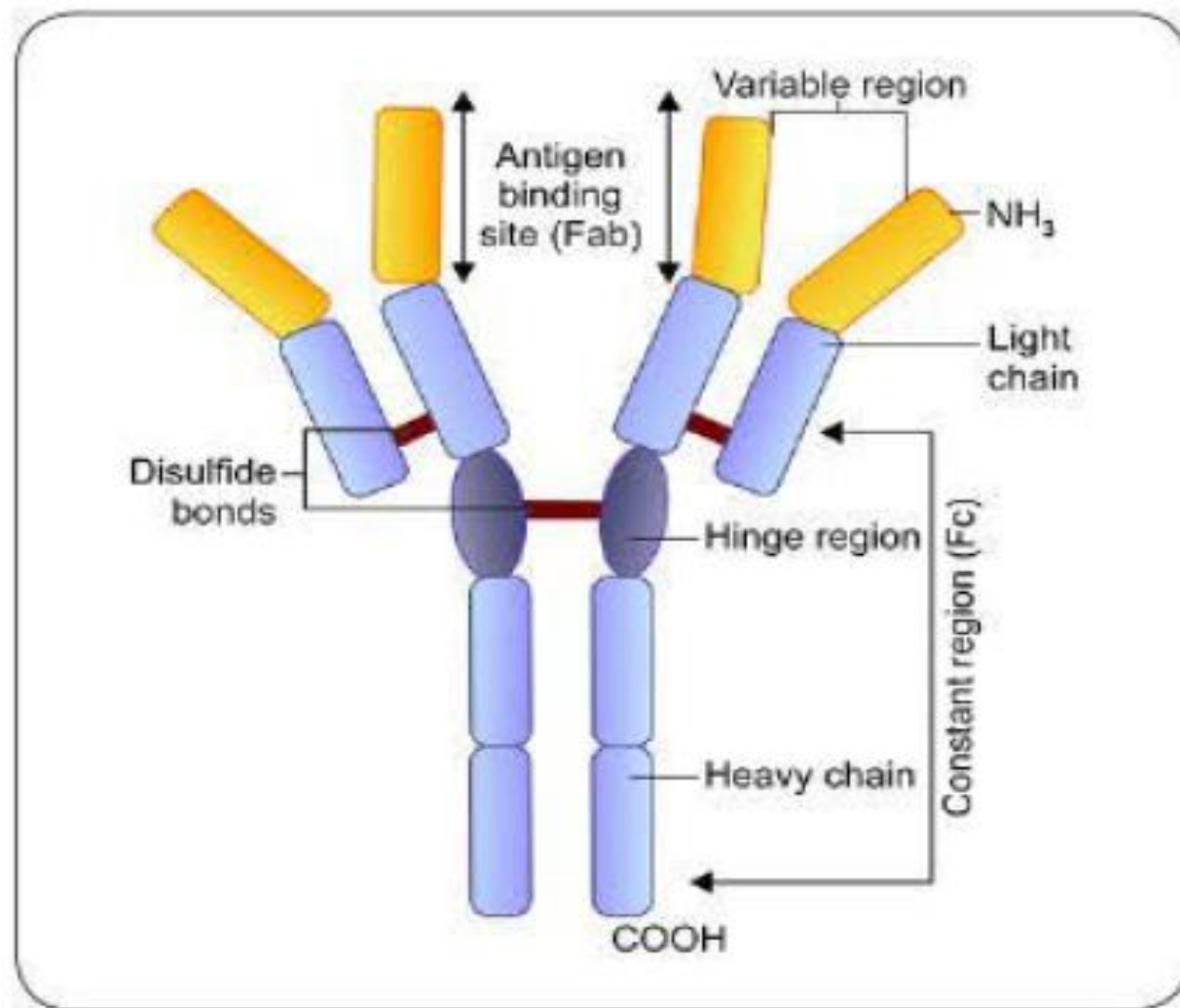


Fig. 11.2: General structure of antibody

Antigenic determinants of immunoglobulin

Isotypes

The five classes of Ig (IgG, IgA, IgM, IgD and IgE) and their subclasses are called as isotypes; they vary from each other in the amino acid sequences of the constant region of their heavy chains. Such variation is called as isotypic variation.

- Isotypes that are present in all members of a given species are similar in nature.
- Hence, antibody against isotypes can be produced by injecting the Ig from one species into another.

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Idiotypes

The unique amino acid sequence present in paratope region (in V_H and V_L regions) of one member of a species acts as antigenic determinant to other members of the same species.

- Such antigenic determinants are called as idiotopes and the sum total of idiotopes on an Ig molecule constitutes its idiotypes.

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Allotypes

The antigenic determinants present in the isotype genes in the constant region of H and L chains, encoded by multiple alleles are called as allotypes.

- Although all members of a species inherit the same set of isotype genes, multiple alleles exist for some of the allele genes.
- Hence, allotypes are present in the constant region of Ig molecules of the same class, in some, but not all, members of a species.

Function of antibody

FUNCTIONS OF IMMUNOGLOBULINS

Antigen Binding (by Fab Region)

Binding to the antigen is the primary function of an antibody which can result in protection of the host.

Effector functions by Fc region are as follows:

1) Fixation of complement:

➤ Antibody coating the target cell binds to complement through its Fc receptor leading to complement mediated lysis of target cell

2) Binding to various cell types:

Phagocytes, mast cells, NK cell, eosinophils bear Fc receptors (FcR) that bind to Fc region of immunoglobulins.

This binding can activate cells to perform biological functions

IgG

- Constitutes about 70-80% of total Ig in human body
- Four subclasses(Ig1,Ig2,Ig3 and Ig4) based on differences in amino acid sequence in the constant region of heavy chain
- Functions:
 - Ability to cross placenta, provides protection to fetus and new born
 - Activates the classical complement pathway
 - Opsonization
 - Major role in neutralization of toxin
- IgG is raised *after* long time following infection and represents chronic or past infection (recovery).

IgM

- Present only in intravascular compartment, not in body fluids or secretions
- Exists in monomeric form(membrane bound on Bcell) and pentameric form(secreted from)
- Functions:
 - First antibody to form following infection. Hence, represents acute or recent infection
 - Most potent activator of classical complement pathway
 - More potent than IgG in opsonization
 - Present on B cells and acts as antigen binding site
 - First antibody to be produced in fetal life
 - Responsible for protection of blood by microbes

IgA

- Second most abundant after IgG (10-20% of total ab in serum)
- Exists in monomeric and dimeric form
- Serum IgA is mostly monomeric
- Secretory IgA(found in tears, saliva, milk) are dimeric
- Serum IgA can initiate function like antibody dependent cell mediated cytotoxicity(ADCC)
- Secretory IgA provides local or mucosal immunity
- IgA in milk provides protection to infant

IgE

- Have the lowest serum concentration among all Ig
- Only heat labile antibody(inactivated at 56°C in 1 hour)
- Mostly extravascular in distribution
- Functions:
 - Mediate type I hypersensitivity reaction by binding to mast cells leading to degranulation
 - Helps to eliminate helminthes by antibody dependent cell mediated cytotoxicity(ADCC)

Immunoglobulin D

Immunoglobulin D (IgD)

IgD is found as membrane Ig on the surface of B cells and acts as a B cell receptor along with IgM. It has the highest carbohydrate content among all the immunoglobulin. No other function is known for IgD so far.

Abnormal Immunoglobulins

- Bence Jones Proteins:
 - Useful in diagnosis of myeloma
- Cryoglobulins:
 - precipitates at temperatures below 37°C and dissolves on re-warming
 - Seen in multiple myeloma

Monoclonal antibody

- Antibodies derived from a single clone of plasma cells
- Produced by hybridoma technique
- Types of monoclonal antibody(mAb)
 - Mouse mAb
 - Chimeric mAb
 - Humanized mAb
 - Human mAb

Application of monoclonal antibody

- Diagnostic reagents: detection of infections, tumor detection
- Passive immunity: post-exposure prophylaxis, immune-compromised patients
- Isolation and purification of molecules