

Antibody Structure

An antibody molecule is a Y-shaped structure that comprises four polypeptide chains, two identical light chains (L) of 25000 Da (approx-214 amino acids) and two identical heavy chains (H) of 50000 Da (approx-450 amino acids). One light chain is attached to each heavy chain and the two heavy chains are attached to each other to form a Y-shaped structure.

The first 110 or so amino acids of amino terminal of light or heavy chains have a variable sequence and composition among antibodies of different specificities. These segments of the highly variable sequence are called variable (V) region of light (V_L) or heavy (V_H) chain. The regions beyond the variable region (from 110-214 amino acids in L or 110-450 amino acids in H chain) have the same composition and a relatively constant sequence in different antibodies. This segment is referred to as constant (C) region of light (C_L) or heavy (C_H) chain. A typical antibody molecule has two intrachain disulphide bonds in the light chain – one in the variable region and one in the constant region. There are an average of four covalent disulphide bonds linking the heavy chains.

Both the light and heavy chains have several repeating homologous units, each of about 110 amino acid residues in length, which form an independent common globular motif called as immunoglobulin domain.

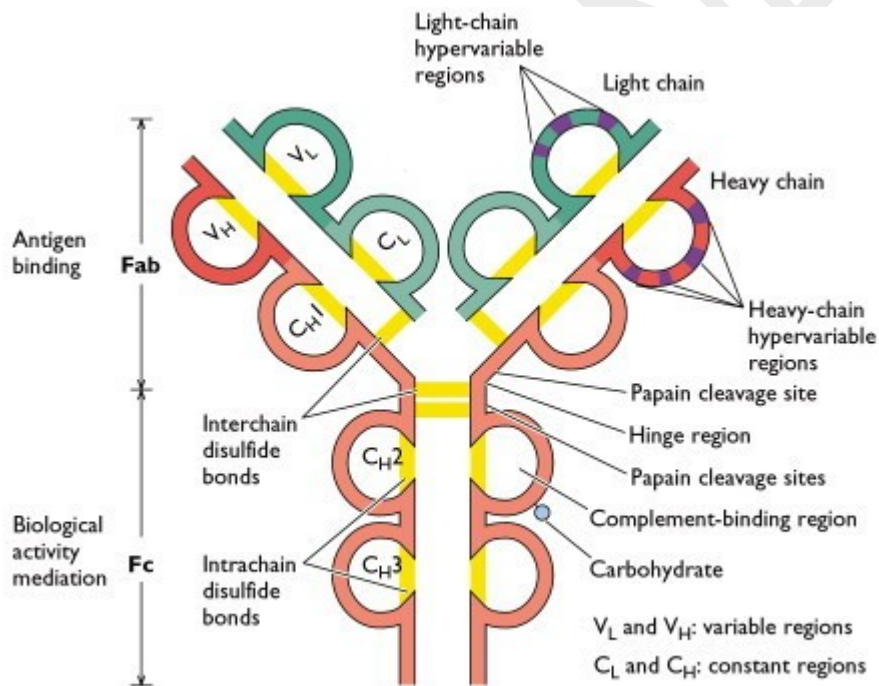


Fig. no.-1 : Structure of Antibody

Within each domain, there is an intra-chain disulphide linkage which forms a loop of about 60-70 amino acids. Light chains contain one variable domain (V_L) and one constant domain (C_L). Heavy chains contain one variable domain (V_H) and three or four constant domains (C_{H1} , C_{H2} , C_{H3} , and C_{H4}) depending on class of antibody.

Within the region of both heavy and light chains, some short of polypeptide sequences show exceptional variability. These are termed hypervariable regions and are located near amino acids 25-35, 50-55 and 95-100. These hypervariable regions are called as complementarity-determining regions (CDRs).

HINGE REGION : The region of the immunoglobulin heavy chain located between the C_{H1} (First domain on constant region of heavy chain) and C_{H2} domain is called the hinge region. It is an open rod-like helical structure or an extended peptide sequence with a flexible conformation.

The hinge contains from 10 to about 60 amino acid residues. Although the greatest differences between the constant regions of the heavy chains are concentrated in the hinge region (In $I_g G$ subclasses), this region is rich in proline, cysteine, lysine and aspartic acid which promotes the exposure of this region without tight folding. Among the subclasses of $I_g G$, $I_g G3$ is unique in having a long hinge region (about four times as compared to $I_g G1$) having about 62 amino acids. The relatively open structure of the hinge region makes it particularly susceptible to proteolytic cleavage. It is this region that is cleaved by proteases such as papain and pepsin. The flexibility is important in allowing the two antigen-binding sites to bind epitopes placed at varying angles. The presence of the hinge region allows the F_{ab} arms to twist and align to tightly bind the displayed epitopes.

J CHAIN : These are small proteins that connect two or more basic units (That is, Y-shaped molecules) in polymeric immunoglobulin. They are named as J (joining) chains. The J-chain is a glycopeptide of a molecular weight of approx 15KDa and is disulphide-bonded to the carboxyl terminal portion of α and μ heavy chains.

DISULPHIDE BONDS : Disulphide (-s-s-) bonds that hold together the four polypeptides are of two types - inter-chain bonds and intra-chain bonds. Inter-chain bonds occur between heavy chains (H-H) and between heavy and light chains (H-L). The H-H bonds vary from 1-15 depending on class and subclass of immunoglobulin. H-H bonds occur primarily in the hinge region of the antibody molecules. H-L chains are connected by only one disulphide bond. $I_g A2$ lacks the H-L bond. Disulphide bonds between light chains are rare and usually found under pathological condition. Intra-chain bonds occur within an individual polypeptide, as follows :

- Light chains have two.
- Human γ , α and δ heavy chains have four
- Human μ and ϵ heavy chains have five.

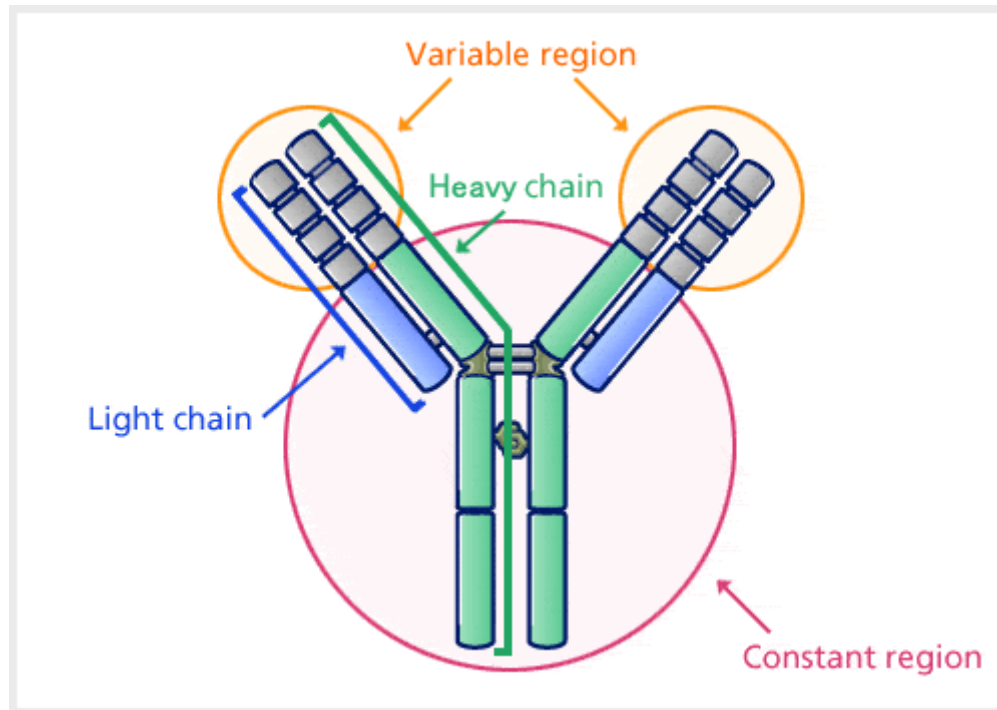


Fig. no. - 2 : Structure of Antibody.

Ref. Book : F.H. Khan.