

β barrels in separate domain regions, each about 110 amino acids long, which are found in two identical light chains (LC with two domains) and two identical heavy chains (HC with four domains) (Furtado et al., 2004). These domains interact with each other and fold into three lobes linked by a flexible hinge region (Figure 1.2(b)) forming the overall Y shape of the molecule.

The basic primary structure of antibodies consists of two regions: a variable (V) region and a constant (C) region connected by the flexible hinge region (Figure 1.2(c)). The V region is contained in two identical structures that are at the top of the Y structure called Fabs and contains the target-binding (antigen) region. The C region is essentially the stem of the Y structure and consists of regions that interact with cellular receptors and molecules that modulate the immune system, often referred to as “cell effector function.” These chains are linked by noncovalent as well as several covalent disulfide bonds. There are four intrachain disulfide bonds in the H and L chain domains of each Fab arm, which stabilize those domains, as well as two intrachain disulfide bonds in each of the heavy chains that make up the Fc regions. Four interchain disulfide bonds link the heavy chains to the LC (Figure 1.2(c)).

The immunoglobulins can be classified as five different classes: IgA, IgD, IgE, IgM, and IgG, which are based on the composition of their C regions which can contain one of five heavy-chain classes designated as α , δ , ϵ , μ , and γ (Wang et al., 2007). Although most immunoglobulins are monomeric, IgA and IgM are dimers and pentamers, respectively. Commercially the most used class of immunoglobulin is the IgG class which has a molecular mass of ~150 kDa and will be the focus of all further discussions.

The IgGs are further classified into subclasses, IgG1, IgG2, and IgG4 consisting of different heavy chains designated as γ 1, γ 2, γ 3, and γ 4, respectively. The number and location of the interchain disulfide bonds are different in these subtypes. The LC are of two types, λ and κ . Approximately, the first 110 amino acid residues of both the heavy and light chains make up the antigen-binding site of the Fab regions, whereas the remaining sequences are constant regions that form the Fc region.

The variable regions in an IgG consist of three hypervariable sequences also called complementarity-determining regions (CDRs) (HV1, HV2, and HV3) on both heavy and light chains which are flanked by sequences termed framework regions. These framework residues form β sheets with the hypervariable regions displayed as three loops at the end of a β barrel. The C regions can also be subdivided into three domains termed CH₁, CH₂, and CH₃. The interactions with immune cells appear to reside mainly in the CH₂ region in the Fc (Tao & Morrison, 1989).

The IgG molecules also have a flexible hinge region that connects the two arms of the Fabs to the Fc region. This hinge region, which imparts flexibility to these molecules, varies in length as well as flexibility (Oda, 2004) between the subtypes. It has also been suggested that the flexibility of the hinge region may impact stability as shown by increased fragmentation around the hinge region during storage (Cordoba, Shyong, Breen, & Harris, 2005).

mAbs are also glycosylated proteins where for IgGs one N-linked oligosaccharide chain is attached to the conserved Asn-297 in each of the CH₂ Fc domains. These carbohydrate chains of the IgG are sequestered in the interior between the CH₂ domains