

Antibody Structure

Antibodies are glycoproteins. The basic functional unit of each antibody is an immunoglobulin (Ig) monomer (containing only one Ig unit); secreted antibodies can also be dimeric with two Ig units as with IgA, tetrameric with four Ig units like teleost fish IgM, or pentameric with five Ig units, like mammalian IgM.

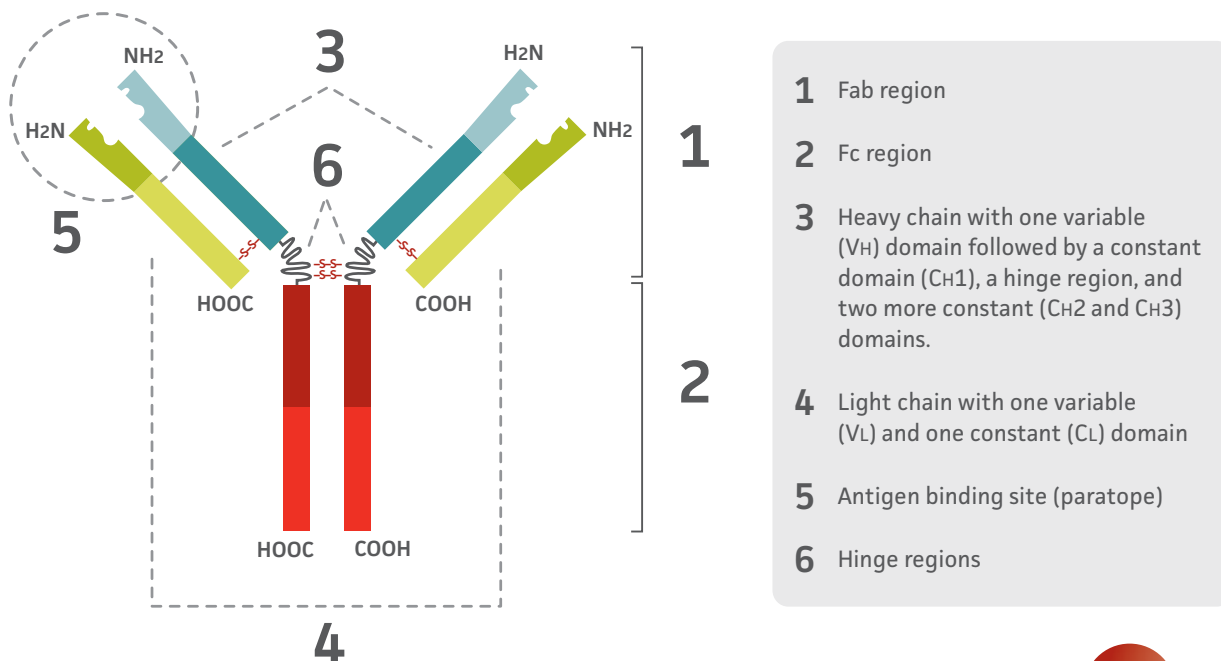
Several immunoglobulin domains make up the two heavy chains and the two light chains of an antibody. The immunoglobulin domains are composed of between 7 (for constant domains) and 9 (for variable domains) β -strands. Note: The variable parts of an antibody are its V regions, and the constant part is its C region.

Immunoglobulin domains

The Ig monomer is a “Y”-shaped molecule that consists of four polypeptide chains; two identical heavy chains and two identical light chains connected by disulfide bonds. Each chain is composed of structural domains called immunoglobulin domains. These domains contain about 70-110 amino acids and are classified into different categories (for example, variable or IgV, and constant or IgC) according to their size and function. They have a characteristic immunoglobulin fold in which two beta sheets create a “sandwich” shape, held together by interactions between conserved cysteines and other charged amino acids.

Heavy chain

There are five types of mammalian Ig heavy chain denoted by the Greek letters: α , δ , ϵ , γ , and μ . The type of heavy chain present defines the class of antibody; these chains are found in IgA, IgD, IgE, IgG, and IgM antibodies, respectively. Distinct heavy chains differ in size and composition; α and γ contain approximately 450 amino acids, while μ and ϵ have approximately 550 amino acids.



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Heavy chain (cont.)

Each heavy chain has two regions, the constant region and the variable region. The constant region is identical in all antibodies of the same isotype, but differs in antibodies of different isotypes. Heavy chains γ , α and δ have a constant region composed of three tandem (in a line) Ig domains, and a hinge region for added flexibility; heavy chains μ and ϵ have a constant region composed of four immunoglobulin domains. The variable region of the heavy chain differs in antibodies produced by different B cells, but is the same for all antibodies produced by a single B cell or B cell clone. The variable region of each heavy chain is approximately 110 amino acids long and is composed of a single Ig domain.

Light chain

For more details on this topic, see Immunoglobulin light chain. In mammals there are two types of immunoglobulin light chain, which are called lambda (λ) and kappa (κ). A light chain has two successive domains: one constant domain and one variable domain. The approximate length of a light chain is 211 to 217 amino acids. Each antibody contains two light chains that are always identical; only one type of light chain, κ or λ , is present per antibody in mammals. Other types of light chains, such as the iota (ι) chain, are found in lower vertebrates like Chondrichthyes and Teleostei.

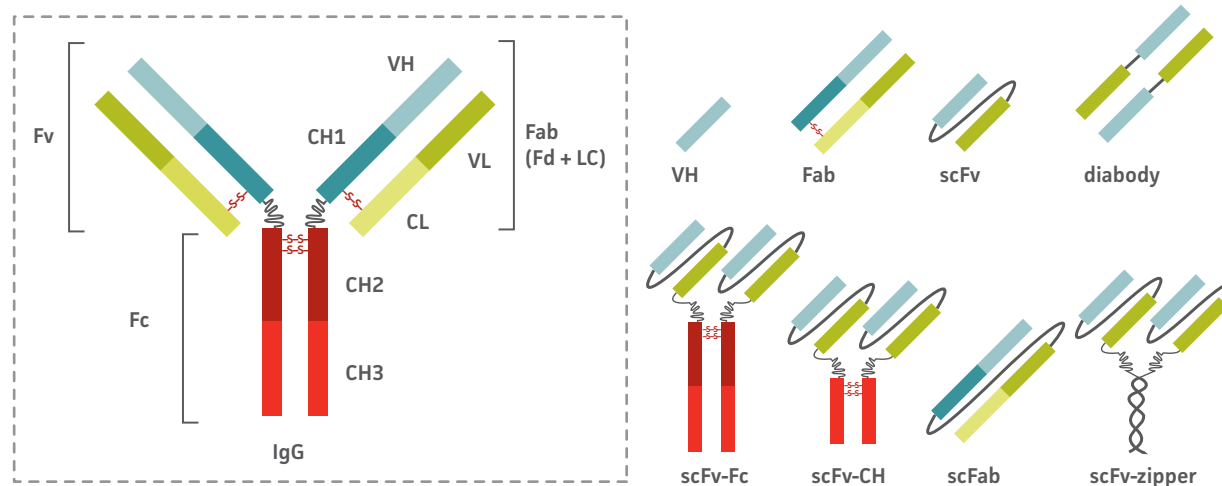
CDRs, Fv, Fab and Fc Regions

Some parts of an antibody have unique functions. The arms of the Y, for example, contain the sites that can bind two antigens (in general identical) and, therefore, recognize specific foreign objects. This region of the antibody is called the Fab (fragment, antigen binding) region. It is composed of one constant and one variable domain from each heavy and light chain of the antibody. The paratope is shaped at the amino terminal end of the antibody monomer by the variable domains from the heavy and light chains. The variable domain is also referred to as the FV region and is the most important region for binding to antigens. More specifically variable loops, three each on the light (VL) and heavy (VH) chains are responsible for binding to the antigen. These loops are referred to as the complementarity determining regions (CDRs). In the framework of the immune network theory, CDRs are also called idiotypes. According to immune network theory, the adaptive immune system is regulated by interactions between idiotypes.

The base of the Y plays a role in modulating immune cell activity. This region is called the Fc (Fragment, crystallizable) region, and is composed of two heavy chains that contribute two or three constant domains depending on the class of the antibody. By binding to specific proteins the Fc region ensures that each antibody generates an appropriate immune response for a given antigen. The Fc region also binds to various cell receptors, such as Fc receptors, and other immune molecules, such as complement proteins. By doing this, it mediates different physiological effects including opsonization, cell lysis, and degranulation of mast cells, basophils and eosinophils.

[CDRs, Fv, Fab and Fc Regions Diagram >](#)

Antibody Structure



A **single-chain variable fragment (scFv)** is a fusion protein of the variable regions of the heavy (VH) and light chains (VL) of immunoglobulins, connected with a short linker peptide of ten to about 25 amino acids. The linker is usually rich in glycine for flexibility, as well as serine or threonine for solubility, and can either connect the N-terminus of the VH with the C-terminus of the VL, or vice versa. This protein retains the specificity of the original immunoglobulin, despite removal of the constant regions and the introduction of the linker.

These molecules were created to facilitate phage display, where it is highly convenient to express the antigen-binding domain as a single peptide. As an alternative, scFv can be created directly from subcloned heavy and light chains derived from a hybridoma. ScFvs have many uses, e.g., flow cytometry, immunohistochemistry, and as antigen-binding domains of artificial T cell receptors.

Unlike monoclonal antibodies, which are often produced in mammalian cell cultures, scFvs are more often produced in bacteria cell cultures such as *E. coli*.

The **fragment antigen-binding (Fab fragment)** is a region on an antibody that binds to antigens. It is composed of one constant and one variable domain of each of the heavy and the light chain. These domains shape the paratope — the antigen-binding site — at the amino terminal end of the monomer. The two variable domains bind the epitope on their specific antigens.

In an experimental setting, Fc and Fab fragments can be generated in the laboratory. The enzyme papain can be used to cleave an immunoglobulin monomer into two Fab fragments and an Fc fragment. The enzyme pepsin cleaves below hinge region, so a $F(ab')_2$ fragment and a pFc' fragment is formed. The $F(ab')_2$ fragment can be split into two **Fab'** fragments by mild reduction.

The variable regions of the heavy and light chains can be fused together to form a single-chain variable fragment (scFv), which is only half the size of the Fab fragment, yet retains the original specificity of the parent immunoglobulin.

A **diabody** is two scFvs with connected with linker peptides that are too short for the two variable regions to fold together (about five amino acids), forcing the scFvs to dimerize. Diabodies have been shown to have dissociation constants up to 40-fold lower than corresponding scFvs, meaning that they have a much higher affinity to their target.

Two scFv's (which bind to the same or different antigens) may also be connected with longer linkers such as leucine zippers.

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