

# Antibody structure and isotypes

Heavy chains, light chains, F(ab)/Fc regions  
and isotypes

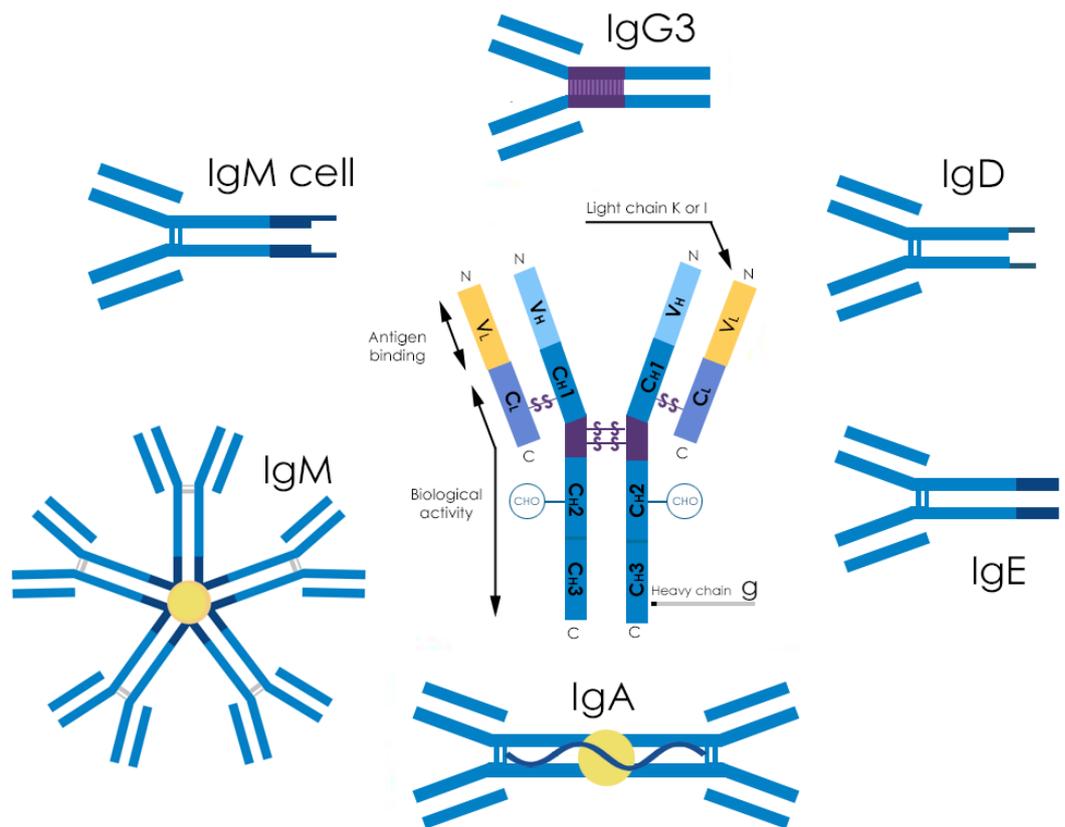
# Introduction

Antibodies are glycoproteins that bind specific antigens.

They are produced in response to invasion by foreign molecules in the body. Antibodies exist as one or more copies of a Y-shaped unit, composed of four polypeptide chains. Each Y contains two identical copies of a heavy chain, and two identical copies of a light chain, which are different in their sequence and length. The top of the Y shape contains the variable region, which binds tightly and specifically to an epitope on the antigen.

The light chains of an antibody can be classified as either kappa ( $\kappa$ ) or lambda ( $\lambda$ ) type based on small differences in polypeptide sequence. The heavy chain makeup determines the overall class of each antibody (Figure 1).

Figure 1. Antibody structure and isotypes.



## Antibody isotypes

In mammals, antibodies are divided into five isotypes: IgG, IgM, IgA, IgD and IgE, based on the number of Y units and the type of heavy chain. The isotypes differ in their biological properties, functional locations and ability to deal with different antigens:

Isotype	Heavy chain	Light chain	MW (kDa)	Structure	Function
IgA1 IgA2	α1 α2	λ or κ	150–600	Monomer - tetramer	Most produced Ig. Found in mucosal areas, such as the gut, respiratory and urogenital tract, and prevents their colonization by pathogens. Resistant to digestion and is secreted in milk.
IgD	δ	λ or κ	150	Monomer	Function unclear. Works with IgM in B cell development; mostly B cell bound.
IgE	ε	λ or κ	190	Monomer	Binds to allergens and triggers histamine release from mast cells and is involved in allergy. Also protects against parasitic worms.
IgG1 IgG2a IgG2b IgG3 IgG4	γ1, γ2, γ3, γ4	λ or κ	150	Monomer	Major Ig in serum. Provides the majority antibody based in immunity against invading pathogens. Moderate complement fixer. IgG3 can cross placenta.
IgM	μ	λ or κ	900	Pentamer	First response antibody. Expressed on the surface of B cells and in a secreted form with very high avidity. Eliminates pathogens in the early stages of B cell mediated immunity before there is sufficient IgG.

## Heavy chains

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

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  $\gamma$ ,  $\alpha$  and  $\delta$  have a constant region composed of three tandem Ig domains and a hinge region for added flexibility, heavy chains  $\mu$  and  $\epsilon$  have a constant region composed of four immunoglobulin domains. The variable region of the heavy chain differs depending on the B cell that produced it, 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 chains

In mammals there are only two types of light chain,  $\lambda$  and  $\kappa$ . A light chain has two successive domains: one constant domain and one variable domain. The approximate length of a light chain is 211–217 amino acids. Each antibody contains two light chains that are always identical. Other types of light chains, such as the iota ( $\text{I}$ ) chain, are found in lower vertebrates like Chondrichthyes and Teleostei.

## F(ab) and Fc regions

The Y-shape of an antibody can be divided into three sections: two F(ab) regions and an Fc region. The F(ab) regions contain the variable domain that binds to cognate antigens. The Fc fragment provides a binding site for endogenous Fc receptors on the surface of lymphocytes, and is also the site of binding for secondary antibodies. In addition, dye and enzymes can be covalently linked to antibodies on the Fc portion of the antibody for experimental visualization.

These three regions can be cleaved into two F(ab) and one Fc fragments by the proteolytic enzyme pepsin. Antibody fragments have distinct advantages in certain immunochemical techniques. Fragmenting IgG antibodies is sometimes useful because F(ab) fragments (1) will not precipitate the antigen and (2) will not be bound by immune cells in live studies because of the lack of an Fc region. Often, because of their smaller size and lack of crosslinking (due to loss of the Fc region), F(ab) fragments are radiolabeled for use in functional studies. Fc fragments are often used as Fc receptor blocking agents in immunohistochemical staining.