Immunoglobulins

A GUIDE TO IMMUNOGLOBULINS STRUCTURE AND FUNCTION

Structure and function of Immunoglobulins

Immunoglobulins form one branch of the adaptive immune system, recognizing pathogens or foreign material and initiating an immune response. Several known antibodies, immunoglobulins are a group of glycoproteins present in the tissue and body fluids of all eukaryotes, based on the surface of all cells in the body's immune system. There is a number of immunoglobulin classes, which differ in size, charge, amino acid composition, and range of glycosylation. Each immunoglobulin structure is distinct. The Fc region is responsible for antigen binding, and the Fab region for binding valence receptors, catalyzing the effector function. The structure of all immunoglobulins consists of four chains, two identical light chains and two identical heavy chains, making up the recognizable Y shape of the antibody. The Fab region consists of a variable and a constant domain. Each light chain consists of a variable (V) and a constant domain, while the heavy chains are divided into variable (VH) and constant (CH) domains.

Immunoglobulin classes and types

Table 1: Structural and functional characteristics of the human immunoglobulins.

<table>
<thead>
<tr>
<th>Isotype</th>
<th>Total MW (kDa)</th>
<th>Distribution</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM</td>
<td>480</td>
<td>Intra- and extravascular</td>
<td>Primarily mediates antibody-dependent cellular cytotoxicity (ADCC), activates complement, and neutralizes bacterial toxins</td>
</tr>
<tr>
<td>IgG</td>
<td>150</td>
<td>Intravascular</td>
<td>Mediates humoral immunity, opsonization, and neutralization of antigens</td>
</tr>
<tr>
<td>IgA</td>
<td>225</td>
<td>Intravascular</td>
<td>Mediates immune adherence, opsonization, and neutralization of antigens</td>
</tr>
<tr>
<td>IgD</td>
<td>150</td>
<td>Extravascular</td>
<td>Mediates cellular immunity and antibody-dependent cellular cytotoxicity (ADCC)</td>
</tr>
<tr>
<td>IgE</td>
<td>150</td>
<td>Extravascular</td>
<td>Mediates allergic reactions and parasitic infections</td>
</tr>
</tbody>
</table>

Key

1. Variable domain (V)
2. Constant domain (C)
3. Disulfide bond
4. O-glycosylation site
5. Fc fragment
6. F(ab')2 fragment
7. Fab fragment
8. Fragment that binds to specific cell receptors

Fab fragment

Dissociation of the Fab region components exposes the epitope of the antigen, allowing the Fab fragment to exhibit its antigen-binding activity. The epitope is a region on the antigen that is recognized by the Fab fragment of an antibody. The Fab fragment is the smallest active fragment of an antibody that contains both the variable and constant domains.

F(ab')2 fragment

The F(ab')2 fragment is obtained by cleaving the antibody with pepsin, resulting in two Fab fragments linked together by a disulfide bond. This fragment retains both the antigen-binding and effector functions of the intact antibody.

Fc fragment

The Fc fragment is obtained by proteolytic digestion of an antibody, resulting in a fragment that contains the constant domains of the heavy chains. The Fc fragment lacks antigen-binding activity but retains the effector functions of the antibody.

Antibody specificity

Antibody specificity is the specificity of an antibody for a particular antigen. Antibodies are highly specific, meaning that they can distinguish between very subtle differences in the structure of different antigens. This specificity is achieved through the antigen-binding site (AB site) of the antibody, which is composed of hypervariable regions (HVR). The AB site is located within the variable (V) domains of the light and heavy chains.

Immunoglobulin isotypes

IgM

IgM is the first antibody to be produced in response to an immune challenge. It is a pentamer consisting of five single chains, each made up of a heavy chain and a light chain. IgM antibodies are the first to be produced in a primary immune response and are responsible for the initial immune response to a new antigen.

IgG

IgG is the most abundant immunoglobulin in serum and is involved in the humoral immune response. It is a dimer consisting of two heavy chains and two light chains. IgG antibodies are responsible for opsonization, neutralization, and clearance of antigens.

IgA

IgA is found in secretions such as saliva, tears, and milk. It is critical in the immune defense of mucosal surfaces and is responsible for the antibody response to antigens that enter the body through mucosal surfaces.

IgD

IgD is a monomer and is the only immunoglobulin that is present on the surface of B cells. It plays a role in the activation of B cells and in the regulation of the immune response.

IgE

IgE is involved in allergic responses and is responsible for the allergic reaction. It is a monomer with a high affinity for mast cells and basophils, allowing rapid activation of these cells in response to allergens.

IgY

IgY is a unique immunoglobulin found in birds, particularly in the egg, and is used for diagnostic and research purposes. It shares structural similarities with IgG but has a higher affinity for antigen.

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