Lecture six **Dr. wurood &Dr. Zaid**

Antibody: definition, structures, classes

Antibodies, or immunoglobulins, are Y-shaped glycoproteins produced by differentiated B-cells called plasma cells. They are present in bodily fluids, secretions and on the surface of B-cells. Antibodies recognise and bind to unique **epitopes**, which are molecular structures on the surface of their cognate antigens.

Structure

Heavy and light chains

Antibody molecules consist of two identical **heavy chains** and two identical **light chains**, which consequently give the antibody two **antigen-binding sites**. Disulphide bonds bind the heavy chains to each other and to the light chains (Figure 1). In addition, the heavy and light chains consist of several amino-acid sequences; each corresponding to a protein domain. Proteins domains are the functional units of the antibody and correspond to a discrete, folded region of protein structure.

There are five heavy chain types: μ (**M**u), γ (**G**amma), α (**A**lpha), ε **(E**psilon) and δ (**D**elta), which classify IgM, IgG, IgA, IgE and IgD respectively.

There are two light chain types: κ (kappa) and λ (lambda). Each antibody can have either two **κ** or two **λ** chains but not one of each. The ratio of κ and λ is 2:1. However, there are no functional differences between the types.

Fc and Fab regions

Each antibody contains two **variable regions** and one **constant region**

The Fc region (fragment crystallisable) consists of the remaining constant domains from the two **heavy chains**. The Fc region interacts with different immune cells and mediates various functions. For example, opsonisation (see below).

The constant region involves the constant domains from both the Fab and Fc parts. The **heavy chain** constant domains determine antibody class and are the **same** for all antibodies of the same class.

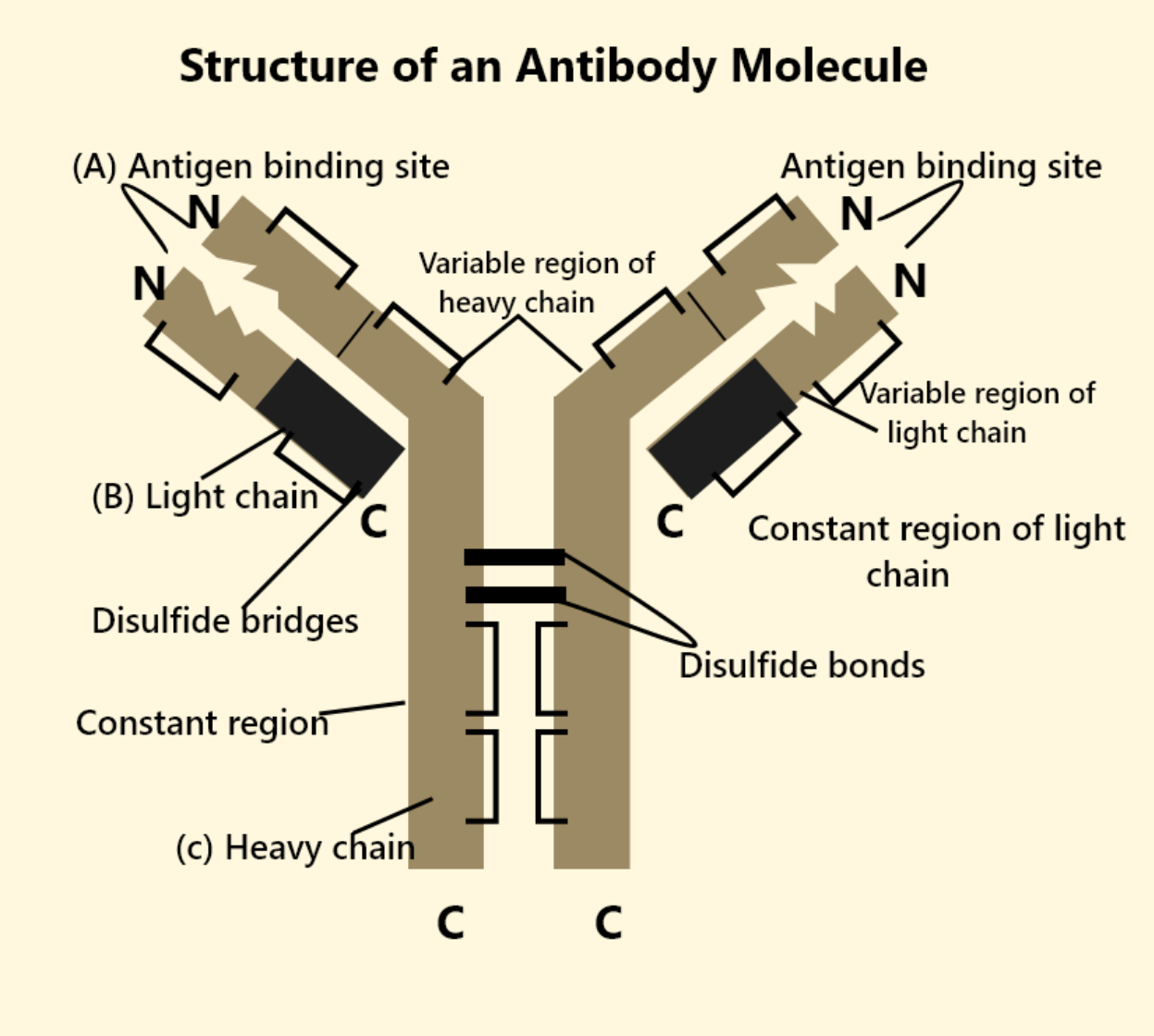

Figure (1) structure of antibody

Classification

Antibodies are classified according to **heavy chain** type, which is encoded by a gene on chromosome 14. The different classes are IgG, IgA, IgM, IgD and IgE; in **descending** order of abundance in serum.

Immunoglobulin classes

The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a given class will have very similar heavy chain constant regions. These differences can be detected by sequence studies or more commonly by serological means (*i.e.* by the use of antibodies directed to these differences).

1. IgG - Gamma heavy chains
2. IgM - Mu heavy chains
3. IgA - Alpha heavy chains
4. IgD - Delta heavy chains
5. IgE - Epsilon heavy chains

Immunoglobulin Subclasses……

The classes of immunoglobulins can de divided into subclasses based on small differences in the amino acid sequences in the constant region of the heavy chains. All immunoglobulins within a subclass will have very similar heavy chain constant

region amino acid sequences. Again these differences are most commonly detected by serological means.

1. IgG Subclasses

a) IgG1 - Gamma 1 heavy chains

b) IgG2 - Gamma 2 heavy chains

c) IgG3 - Gamma 3 heavy chains

d) IgG4 - Gamma 4 heavy chains

2. IgA Subclasses

a) IgA1 - Alpha 1 heavy chains

b) IgA2 - Alpha 2 heavy chains

Immunoglobulin Types

Immunoglobulins can also be classified by the type of light chain that they have. Light chain types are based on differences in the amino acid sequence in the constant region of the light chain. These differences are detected by serological means.

Kappa light chains

Lambda light chains

Immunoglobulin Subtypes

The light chains can also be divided into subtypes based on differences in the amino acid sequences in the constant region of the light chain.

Lambda subtypes

a) Lambda 1

b) Lambda 2

c) Lambda 3

d) Lambda 4

IgG

Structure

The structures of the IgG subclasses are presented in figure 7. All IgG's are monomers (7S immunoglobulin). The subclasses differ in the number of disulfide bonds and length of the hinge region.

Properties

IgG is the most versatile immunoglobulin because it is capable of carrying out all of the functions of immunoglobulin molecules.

a) IgG is the major Ig in serum - 75% of serum Ig is IgG

b) IgG is the major Ig in extra vascular spaces

c) Placental transfer - IgG is the only class of Ig that crosses the placenta. Transfer is mediated by a receptor on placental cells for the Fc region of IgG. Not all subclasses cross equally well; IgG2 does not cross well.

d) Fixes complement - Not all subclasses fix equally well; IgG4 does not fix complement

e) Binding to cells - Macrophages, monocytes, PMNs and some lymphocytes have Fc receptors for the Fc region of IgG.

IgM

Structure

The structure of IgM is presented in figure 8. IgM normally exists as a pentamer (19S immunoglobulin) but it can also exist as a monomer.

Properties

a) IgM is the third most common serum Ig.

b) IgM is the first Ig to be made by the fetus and the first Ig to be made by a virgin B cells when it is stimulated by antigen.

c) As a consequence of its pentameric structure, IgM is a good complement fixing Ig. Thus, IgM antibodies are very efficient in leading to the lysis of microorganisms.

d) As a consequence of its structure, IgM is also a good agglutinating Ig . Thus, IgM antibodies are very good in clumping microorganisms for eventual elimination from the body.

e) IgM binds to some cells via Fc receptors.

f) B cell surface Ig……
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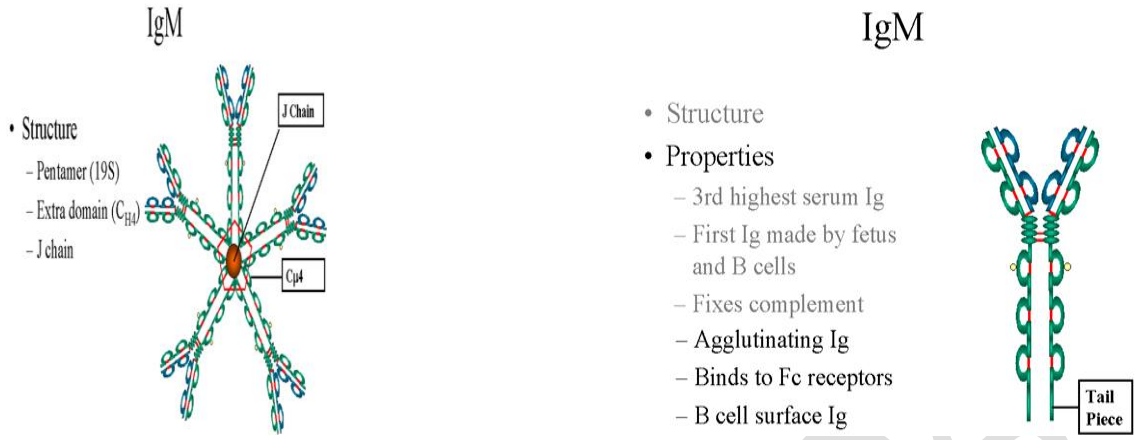


IgM structure

IgA

Structure

Serum IgA is a monomer but IgA found in secretions is a dimer as presented in Figure 11. When IgA exits as a dimer, a J chain is associated with it.When IgA is found in secretions is also has another protein associated with it called the secretory piece or T piece; sIgA is sometimes referred to as 11S immunoglobulin. Unlike the remainder of the IgA which is made in the plasma cell, the secretory piece is made in epithelial cells and is added to the IgA as it passes into the secretions .The secretory piece helps IgA to be transported across mucosa and also protects it from degradation in the secretions.

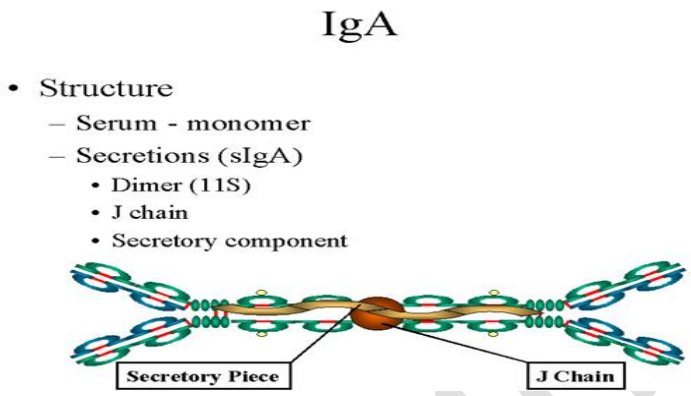
Properties

a) IgA is the 2nd most common serum Ig.

b) IgA is the major class of Ig in secretions - tears, saliva, colostrum, mucus. Since it is found in secretions secretory IgA is important in local (mucosal) immunity.

c) Normally IgA does not fix complement, unless aggregated.

d) IgA can binding to some cells - PMN's and some lymphocytes



IgD

Structure

The structure of IgD is presented in the Figure 13. IgD exists only as a monomer.

Properties

a) IgD is found in low levels in serum; its role in serum uncertain.

b) IgD is primarily found on B cell surfaces where it functions as a receptor for antigen. IgD on the surface of B cells has extra amino acids at C-terminal end for anchoring to the membrane. It also associates with the Ig-alpha and Ig-beta chains.

c) IgD does not bind complement.

IgE

Structure

The structure of IgE is presented in Figure 14. IgE exists as a monomer and has an extra domain in the constant region.

Properties

a) IgE is the least common serum Ig since it binds very tightly to Fc receptors on basophils and mast cells even before interacting with antigen.

b) Involved in allergic reactions - As a consequence of its binding to basophils an mast cells, IgE is involved in allergic reactions. Binding of the allergen to the IgE on the cells results in the release of various pharmacological mediators that result in allergic symptoms.

c) IgE also plays a role in parasitic helminth diseases. Since serum IgE levels rise in parasitic diseases, measuring IgE levels is helpful in diagnosing parasitic infections. Eosinophils have Fc receptors for IgE and binding of eosinophils to IgE-coated helminths results in killing of the parasite.

d) IgE does not fix complement.

IgE

- Structure
  - Monomer
  - Extra domain (C_{H4})