جامعة الانبار
كلية العلوم
قسم التقنيات الأحيائية

اسم المادة: المناعة
عنوان المحاضرة :Immunoglobulins
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IMMUNOGLOBULINS

Immunoglobulin (Ig)

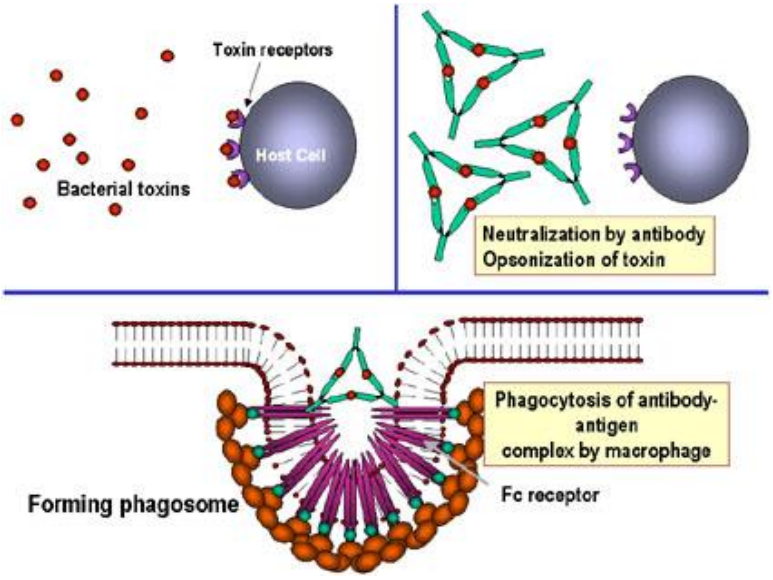
Immunoglobulins are glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies.

GENERAL FUNCTIONS OF IMMUNOGLOBULINS

Antibodies are the primary defense against extracellular pathogens and they function in four major ways:

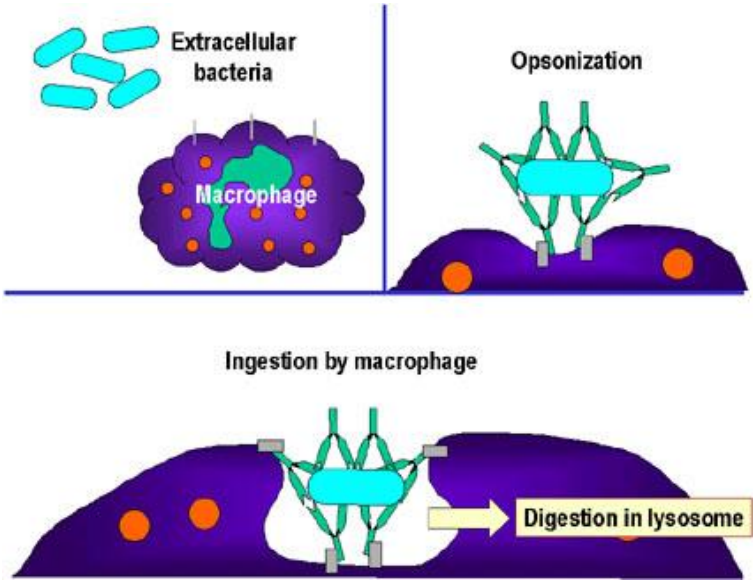
1. **Neutralization**

   By binding to the pathogen or foreign substance antibodies can block the association of the pathogen with their targets. For example, antibodies to bacterial toxins can prevent the binding of the toxin to host cells thereby rendering the toxin ineffective. Similarly, antibody binding to a virus or bacterial pathogen can block the attachment of the pathogen to its target cell thereby preventing infection or colonization.



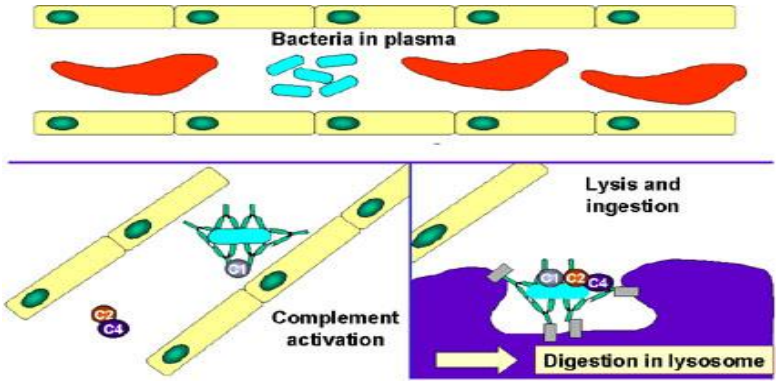
2. Opsonization

Antibody binding to a pathogen or foreign substance can opsonize the material and facilitate its uptake and destruction by phagocytic cells. The Fc region of the antibody interacts with Fc receptors on phagocytic cells rendering the pathogen more readily phagocytosed.



3. Complement activation or Fixation of complement

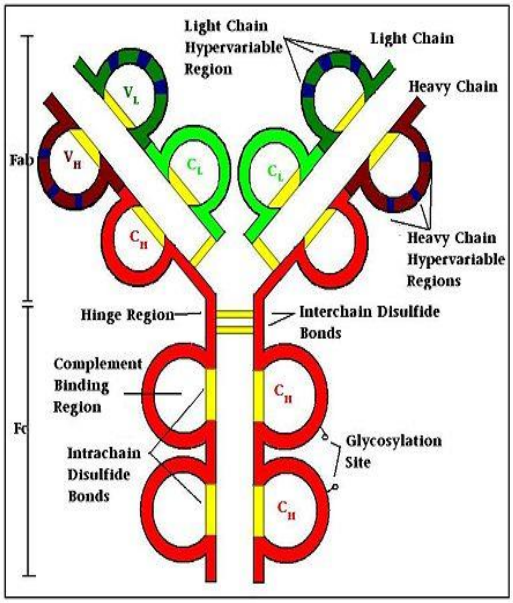
Activation of the complement cascade by antibody can result in lysis of certain bacteria and viruses. In addition, some components of the complement cascade (*e.g.* C3b) opsonize pathogens and facilitate their uptake via complement receptors on phagocytic cells.

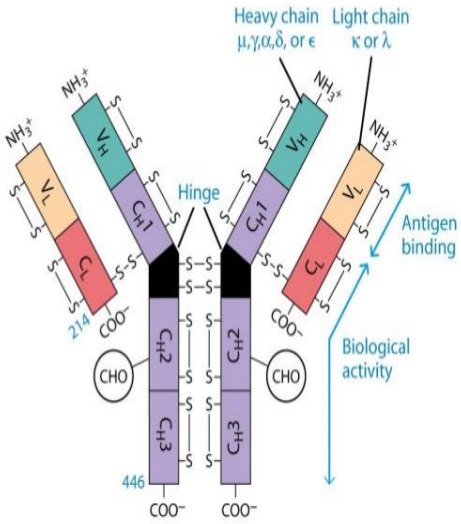


4- Binding to various cell types - Phagocytic cells, lymphocytes, platelets, mast cells, and basophils have receptors that bind immunoglobulins. This binding can activate the cells to perform some function.

BASIC STRUCTURE OF IMMUNOGLOBULINS

The basic structure of the immunoglobulin is illustrated in figure below. Although different immunoglobulins can differ structurally, they all are built from the same basic units.





Heavy and Light Chains

All immunoglobulins have a four chain structure as their basic unit. They are composed of two identical light chains (23kD) and two identical heavy chains (50-70kD)

Disulfide bonds

Inter-chain disulfide bonds

The heavy and light chains and the two heavy chains are held together by inter-chain disulfide bonds and by non-covalent interactions The number of inter-chain disulfide bonds varies among different immunoglobulin molecules.

Intra-chain disulfide binds

Within each of the polypeptide chains there are also intra-chain disulfide bonds.

Variable (V) and Constant (C) Regions

When the amino acid sequences of many different heavy chains and light chains were compared, it became clear that both the heavy and light chain could be divided into two regions based on variability in the amino acid sequences. These are the:

Light Chain - $\mathbf{V_L}$ (110 amino acids) and $\mathbf{C_L}$ (110 amino acids)

Heavy Chain - $\mathbf{V_H}$ (110 amino acids) and $\mathbf{C_H}$ (330-440 amino acids)

Hinge Region

This is the region at which the arms of the antibody molecule form a Y. It is called the hinge region because there is some flexibility in the molecule at this point.

Domains

It is folded into globular regions each of which contains an intra-chain disulfide bond. These regions are called domains.

Light Chain Domains - V_L and C_L

Heavy Chain Domains - V_H, C_{H1} - C_{H3} (or C_{H4})

Oligosaccharides

Carbohydrates are attached to the C_{H2} domain in most immunoglobulins. However, in some cases carbohydrates may also be attached at other locations.

Fab

Digestion with papain breaks the immunoglobulin molecule in the hinge region before the H-H inter-chain disulfide bond

Antigen binding - These fragments were called the Fab fragments because they contained the antigen binding sites of the antibody. The combining site of the antibody is created by both V_H and V_L .

Fc

Digestion with papain also produces a fragment that contains the remainder of the two heavy chains each containing a C_{H2} and C_{H3} domain. This fragment was called Fc because it was easily crystallized.

HUMAN IMMUNOGLOBULIN CLASSES, SUBCLASSES, TYPES AND SUBTYPES

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.

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 divided into subclasses based on small differences in the amino acid sequences in the constant region of the heavy chains.

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.

i. Kappa light chains
ii. Lambda light chains

References:-

1- Richard Coioco and Geoffery Sunshine (2014). Immunology.Seventh edition.Wiley Blackwell.