CHRISTIAN EMINENT COLLEGE, INDORE

(Academy of Management, Professional Education and Research)

An Autonomous Institution Accredited with 'A' Grade by NAAC

E-Content

On

"IMMUNOGLOBULINS: STRUCTURE, TYPES AND THEIR IMPORTANCE"

19th October 2019

Prepared By: Prof. Ekta Rawat

Department of Biosciences

CONTENT

1. Introduction

Immunoglobulins (Igs) are glycoprotein molecules also called antibodies(Abs) , that are produced in response to foreign substances entering the living body-antigens or immunogens (viruses, bacteria, or toxins etc), binding to them and forming antigen-antibody complexes resulting in Ag elimination and protection of the body of the host.

2. Basic structure of Immunoglobulin

All Igs have the same basic structural units of 2 identical light chains and 2 identical heavy chains, the heavy and light chains are joined together by inter chain disulphide bonds and non-covalent interactions. The number of inter chain disulphide bonds varies among different Igs. Within the polypeptide chains i.e. the heavy and light chains there are also present intra-chain disulphide bonds. Amino acid sequence of both heavy and light chains of an Ig characterizes two distinct regions of the chains based on variability of the amino acid sequence, known as VARIABLE (V) and CONSTANT (C) regions. Light and heavy chains are composed of both a variable and constant region designated VL and CL (light chains) and VH and CH(heavy chains).The amino acid sequence of the variable region form the N-terminal ends of the chains and determine antigenic specificity of the Igs. Constant regions are the same for each specific class of Ig and carry the effector sites.

Light chain

VL-about 100-110amino acids, CL-100-110 amino acids. There are two types of light chains, kappa and lambda,(κand λ)the κ are twice as much as λ. There are also four classes of the λ chains. These chains weigh about 23KDa. Differences in the type of light chains also form a

basis for grouping of Igs into various types. The variable region makes up half of the entire light chain and the constant region the remaining half.

Heavy chains

V_H-110 amino acids, C_H-330-440 amino acids. There are 5 types of heavy chains which defines the class of Igs, namely, Alpha, Gamma, Miu, Delta and Epsilon (α, γ,μ,δ,ε).the heavy chains are between 53-75KDa.the variable region makes up a quarter of the entire heavy chain while ¾ of the remaining chain is the constant region.

The hinge region is the area of the Ig where the arms of the Abs form a 'Y', it is a flexible region. Igs also have domains formed from folds of the globular region containing the intrachain disulphide bonds and they are V_L and C_L (light chain domains) and V_H and C_H (heavy chain domains), seen in the three dimensional images of the Ig. The constant region of light chain and the appropriate heavy chain form globular constant domains while the variable regions of light chain 1 and corresponding heavy chain interact to form globular variable domain. Ig s also have attached to their C_H oligosaccharides and in other cases these carbohydrates are attached to other areas.

The variable regions of an Ig are also further divided into hyper variable or complementarity determining regions (CDRs) which distinguishes Abs with different specificities and is found on both light and heavy chains and the frame work regions lie between the CDRs. There are about 3 hypervariable regions on the V_L and 4 on the $V_{H,}$ and these contribute to uniqueness of each antibody.

Proteolytic digestion of Igs have produced fragments which have been found useful in elucidating the structure-function relationship of the Ig.

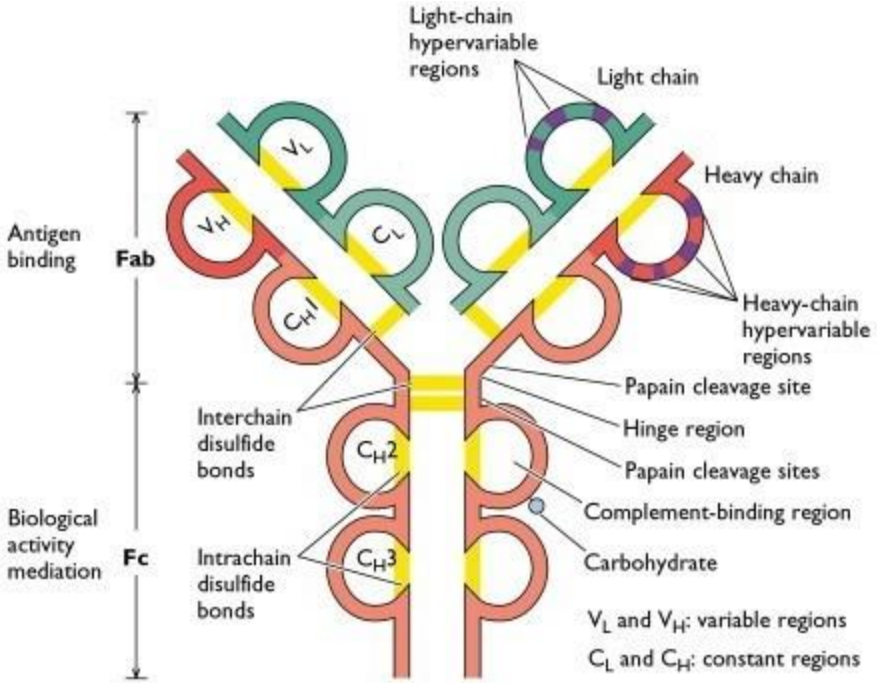
Fab- also referred to as the antigen binding fragment, is gotten upon digestion of Ig with papain and its cleavage at the hinge region. It contains the antigen binding site synonymous to V_H and V_L which is particular to the kind of antigenic determinant the Ab will bind.

Fc- this is also called fragment crystallizable because it is readily crystallized and it contains the remainder of the two heavy chains. It contains different domains ands which mediate effector functions of an Ig. Variations in the Fc determines the different classes of Igs.

The hinge region is between the Fab and the Fc portion and controls interactions between these portions.

F $(ab)_2$- treatment of Igs with pepsin results in cleavage of the heavy chain, resulting in a fragment that contains both antigen binding sites, it is

called F(ab)$_2$ because it is divalent.



Structure of Immunoglobulins

3. Types of Immunoglobulin and their functions

The Igs can be divided into five different classes in humans namely, IgA, IgD, IgE, IgG and IgM. Among these IgA, IgD, IgE and IgG occur as monomers with the basic structure H_2L_2 i.e. two heavy and two light polypeptide chains. Serum IgA can polymerize to the dimeric $(H_2L_2)_2$ and the oligomeric $(H_2L_2)_n$ forms.

- **Immunoglobulin G** is the main immunoglobulin present in the blood and represents 70% to 75% of the total immunoglobulin pool. Several forms (subclasses) of IgG cross the placental barrier and are responsible for defense against infection in the first few months of a baby's life.
- **Immunoglobulin A** provides localized antibody protection on mucosal surfaces. It is found in mucosal secretions such as saliva, tears, sweat, nasal fluids, fluids of the lung and colostrum, genito-urinary tract, and gastro-intestinal tract. It is a primary defense against microorganisms attacking exposed mucosal surfaces. IgA functions by preventing the microorganism from adhering to, and penetrating, the mucosal epithelial lining.
- **Immunoglobulin M** is the major immunoglobulin present on the surface of immature B cells and is effective against microbes by binding with complement and causing agglutination and bacteriolysis. It is the first immunoglobulin to take part in the immune response and plays an important role in controlling bacteria that find their way into the blood stream (bacteremia).
- **Immunoglobulin E** is found in very low concentration in human serum, but it increases during allergic reactions and some parasitic infections. IgE is bound to high affinity membrane receptors (FceRI) on mast cells in the tissue and basophils in the blood. Cross-linking of cell bound IgE by an allergen elicits the release of inflammatory mediators like histamine and several cytokines. IgE is also the main immunoglobulin responding to infection caused by certain parasites.
- **Immunoglobulin D** is a trace antibody in the serum and is present on the surface of B cells. It may be involved in stimulating and suppressing these antibody producing cells in the manufacture of antibodies.

4. Biomedical importance of Immunoglobulins

IgG- Increases occur in: - chronic granulomatous infections and infections of all types, hyperimmnunization, liver disease, severe malnutrition, dysproteinemia, rheumatoid arthritis etc.

Decreases occur in: - aggammaglobulinemia, lymphoid aplasia, selective IgG, IgA deficiency, IgA myeloma and chronic lymphoblastic leukemia.

IgM. Increases occur in: - Waldenstrom's macroglobulinemia, Trypanosomosis, Actinomycosis, Bartonellosis, Malaria, Lupus erythromatosis, Rheumatoid arthritis, Dysgammaglobulinemia etc.
Decreases occur in: - Aggammaglobulinemia, lymphoproliferative disorders, lymphoid aplasia, IgG and IgA myeloma and chronic lymphoblastic leukemia.

IgA Increases occur in: - Wiskott-Aldrich syndrome, cirrhosis of the liver, IgA myeloma, autoimmune disorders, rheumatoid arthritis, lupus erythromatosis etc.
Decreases occur in: - hereditary ataxia Telangectasia, Ig deficiency states, malabsorbtion syndromes, lymphoid aplasia, IgG myeloma, chronic lymphoblasticleukemia etc.

IgD Increases occur in: - chronic infections, IgD myelomas

IgE Increases occur in: - atopic skin diseases e.g. eczema, hay fever, asthma, anaphylactic shock and IgE myelomas.
Decreases occur in: - congenital Aggammaglobulinemia, Hypogammaglobinemia etc.