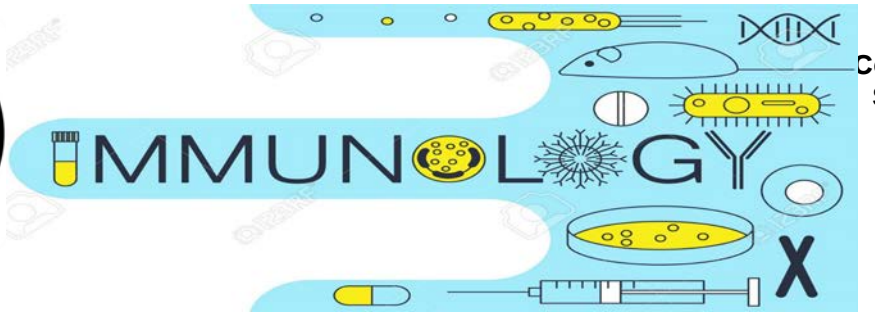
University of Baghdad

College of Education for Pure Sciences (Ibn Al-Haitham)

Department of Biology
Fourth stage

2018/2019



Proff. Dr. Anwar Idrees Sulaiman

Assist. Prof Dr. Hazima Mousa Khaleel

Assist. Prof. Dr. Sahar Saadi Karieb

Lecture 1

Introduction

- **Immunity**:- is a biological term that describes a state of having sufficient biological defenses to avoid infection, disease, or other unwanted biological invasion
- Immunology is the study of the organs, cells, and chemical components of the immune system that implicated in the mechanism of body defense against invaders or foreign antigens.
- The immune system creates both innate and adaptive immune responses.
- The innate response exists in many lower species, all the way up the evolutionary ladder to human, and it acts against large classes of pathogens bacteria, viruses, fungi and parasites like protozoa & worms.
- The adaptive response is unique to vertebrates, reacting to foreign invaders with specificity and selectivity. On the other words the immune system is the Human Battle against the Microbe World.

- The immune system must maintain a delicate balance, with potent defensive responses capable of destroying large numbers of foreign cells and viruses and maintain host's body.
- When the immune system cannot mount a sufficient defense of the host, there is an immune deficiency; this is seen in (Human Immuno Deficiency Virus (HIV) infection. If, on the other hand, the immune system acts too vigorously and begins to attack the host, we have autoimmunity.This is a defiance of the integral immune system property of self/non-self recognition. That is, the immune system begins attacking or forming antibodies against the host's own body tissues. Examples of autoimmune diseases include Graves' disease, Hashimoto's thyroiditis, myasthenia gravis and type I diabetes mellitus.

Essential differences between the innate and adaptive immune systems

Innate immune system	Adaptive immune system
1- It is referred to as immediate (rapid) immune response immune (it takes minutes to hours to activate).	1- It takes time to develop improve
2- It is nonspecific and includes barriers to infectious agents—eg, skin and mucous membranes, phagocytic cells, inflammatory mediators.	2- It is specific for each different antigen and is mediated by either antibody or lymphoid cells. It can be passive or active
3- This types of response dos not improve with repeated exposure	3- Initial exposure to an antigen leaves memory cells so that a specific response will be initiated (quick) soon after entry of the same pathogen in future

Lecture 2

Cellular components of immune system

Cells of immune system play an important role in the defense of body against foreign bodies; cells move in blood stream and lymph and can reside inside tissues. There is high heterogeneity in the cells of immune system, most of which originate from hematopoietic stem cells originated in bone marrow and then differentiate into several types of cells including lymphocytes, red blood cells, platelets and phagocytic cells. Hematopoietic stem cells can differentiate into the following two major cells: (Figure 1)

A - Lymphoid progenitor (generate non- granulated cells)

- T-lymphocyte (70% of total lymphocytes) (adaptive immune response)
- B-lymphocyte (20% of total lymphocytes) (adaptive immune response)
- Natural killer (NK) cells (10% of total lymphocytes)

B- Myeloid progenitor (Myeloblast)

1- Granulocyte-Monocyte progenitor

- Neutrophil (polymorph nuclear neutrophils (PMNs)
- Eosinophil progenitor (generate eosinophil)
- Basophil progenitor (generate basophil)
- Monocyte (Macrophage)

2- Megakaryocytes: generates blood platelet (blood clotting and inflammations)

3- Erythroid progenitor: forms red blood cells (RBCs)

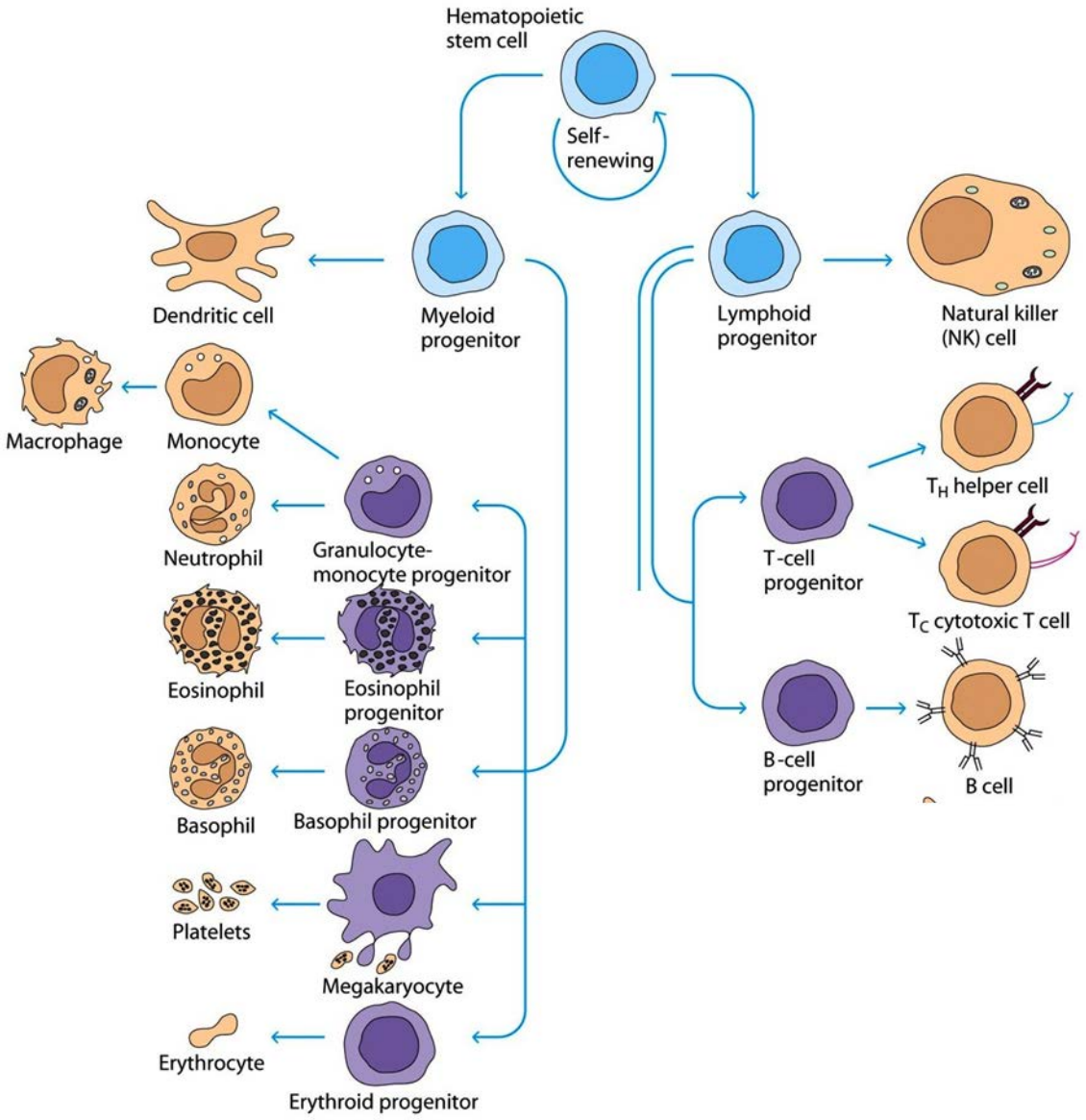


Figure 1: Hematopoietic stem cells differentiation. All lymphoid cells differentiated from lymphoid progenitor cells while all cells of myeloid lineage generates from myeloid progenitors.

Lecture 3

Lymphoid System

- Tissues and organs of the immune system have been found to play an important role in the Immune response, maturation and development of lymphocytes as well as control the response to invaders.
- Specialized organs and collections of tissue where lymphocytes interact with non-lymphoid cells, which are important either to their maturation or to the initiation of adaptive immune responses.
- Lymphatic tissues are characterized by having numerous lymphocytes and significant numbers of reticular fibers.
- Lymphoid organs and tissues are either primary or secondary.

Lymph and Lymphoid Tissues

- The flow of lymph from the tissues into the lymphatic collecting system. Lymph is formed from the tissue fluid that fills the interstitial spaces of the body. It is collected into lymph capillaries, which carry the lymph to the larger lymph vessels. It is then transported through larger lymphatic vessels to lymph nodes, where it is cleaned by lymphocytes.
- Lymph fluid is similar to plasma but with less proteins, no RBCs but contains WBCs and lymphocytes.
- Lymph may pick up bacteria and bring them to lymph nodes, where they are destroyed. Metastatic cancer cells can also be transported via lymph. Lymph also transports fats from the digestive system to the blood.
- Lymphoid tissues are associated with the lymphatic system is concerned with immune functions in defending the body against the infections. It

consists of connective tissue with various types of white blood cells, most numerous being lymphocytes.

- Lymphocytes constantly circulate between blood, lymph and tissues.
- The resting lymphoid tissue consists of three areas:

1. The cortex which contains B lymphocytes.
2. The paracortex contains T lymphocytes.
3. The medulla contains the connective tissue.

Organs of Immune System

Development of cells in organs of immune system include acquire specific molecules (lineage markers) that are important for their function and also to detect self and non-self-antigens. Lymphoid organs are composed of lymphoid cells and tissues.

They are classified as follows:

1- Primary (central) lymphoid organs

- Thymus
- Bone marrow

2- Secondary (peripheral) lymphoid organs

- Lymph node
- Spleen
- Mucosa-associated lymphoid tissue (MALT)

Lecture 4

Antigens and Immunogens

Antigen (Ag.)

Antigen is a substance/molecule has the ability to react with the products of immune response after activation such as the production of the antibodies by the immune system.

Immunogen

Immunogen is a specific type of antigen; it is capable to induce an immune response and binds to the products of the immune response, while an antigen is able to combine with the products of the immune response once they are made.

The foreign substances that induce an immune response possess two properties:-

1- Immunogenicity is the ability of a substance (immunogen) to induce a specific immune response, resulting in the formation of antibodies or cell-mediated immune response.

2- Antigenicity is the property of a substance **(antigen)** that causes it to react specifically with the final products of the immune response (i.e. secreted antibodies and/or surface receptors on T-cells).

- Although, All immunogens are antigens but not all antigens are immunogens because all immunogens can stimulate and binds to the components of immune system but not all antigens can induce the immune response.

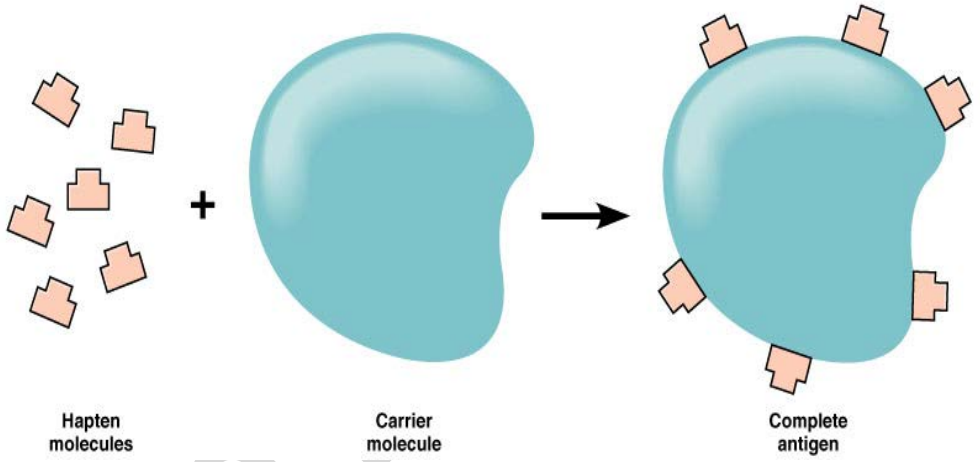
- All molecules that have the property of immunogenicity also have the property of antigenicity.

Hapten (Incomplete antigen)

- Hapten is a molecule or substance with low molecular weight (Non-immunogenic) that cannot induce an immune response on its own.
- However, if a hapten is combined with larger macromolecules (usually proteins) which serve as **carriers** then a response can be induced.

Hapten + carrier ⟶ complete antigen (immunogen)

- Examples of haptens are antibiotics, analgesics, penicillin and other low-molecular weight compounds
- The carrier molecules may be albumins, globulins, or synthetic polypeptides.



Epitopes (antigenic determinants)

- Epitopes (also called **determinant groups or antigenic determinants**) are the sites either on or within the antigen with which antibodies react.

- Antibodies are specific for epitopes.
- A particular antigen molecule may have many different epitopes or determinant, each of which can be a target for antibody binding.
- The epitopes on an antigen can be linear or conformational (Figure 1).

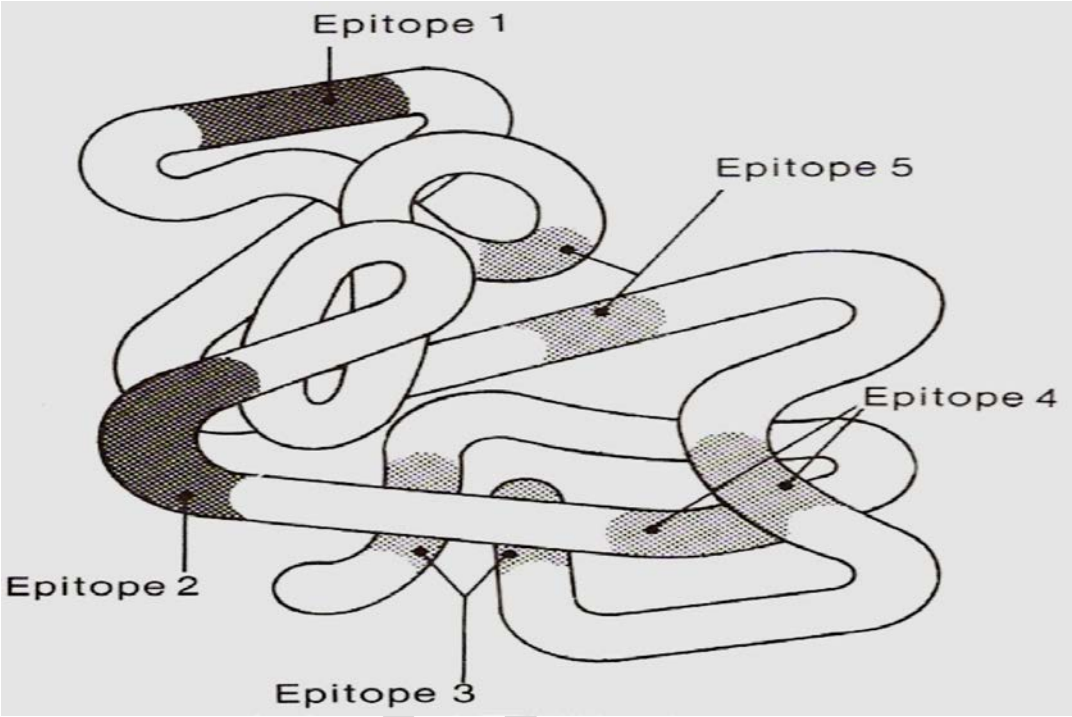


Figure 1. Model of epitopes on lysozyme, the shaded areas is the specific epitopes. They are composed of chain segments that are either linear (epitopes 1 and 2) or conformational (epitopes 3-5).

Lecture 5

Immunoglobulines (Ig.) or Antibodies (Abs)

- Immunoglobulins are glycoprotein molecules that are produce by B-cells in response to an immunogen. B-lymphocytes are differentiate into plasma cells that secretes Abs
- Antibodies are important in adaptive immune response especially in humoral immune response
- Antibodies found in the serum and tissue fluids, thus antibodies can be found in two forms: membrane-bound and secreted antibodies
- Antibodies can differentiate into several classes as fallowing: IgG, IgM,IgA, IgE and IgD
- IgM is the main antibody in the primary immune response while IgG is the main Antibody in secondary immune response
- **There are two main properties of antibodies**

1. Specificity
2. Biological activity

Functions of immunoglobulines

1. Neutralization of microbes and toxins
2. Activation of complement system.
3. Opsonization: Fc portion of the antibody binds to an Fc receptor on Phagocytic cells, eosinophil, mast cells, and basophils facilitating phagocytosis. The efficiency of this process is markedly enhanced if the phagocyte can bind the particle with high affinity. This binding can activate the cells to perform some function
4. Agglutination with microbes and foreign bodies

5. Immobilization of microorganisms
6. Precipitation: Interaction of antibody with a soluble antigen forms a precipitate which phagocytoses and destroys by phagocytes.
7. Placental transfer: immunoglobuline (only IgG) has the ability to cross the placenta from mother to fetus.

Structure of Immunoglobulin

The structure of immunoglobuline is illustrated in (**Figure 1**):

- The Ig monomer is a "Y"-shaped molecule that consists of four polypeptide chains linked covalently by disulfate bonds, 2 identical light **(L)** chains (22kDa) and 2 identical heavy **(H)** chains (55kDa)
- Each heavy chain is consist of 440 amino acid, while the light chain included 220 amino acid
- The light chain found with two forms: **kappa (K) and Lambda (λ)**. Each type of antibody contain one type of light chain either kappa or lambda
- Each light chain covalently attached to one heavy chain via disulfide bridge

The light and heavy chain are divided into two regions (Figure 1)

1- Variable region (V)

- In the light chain (VL) and (Vh) in the heavy chain
- The site of binding to specific Ag. finished with amine group ($NH3^{+}$) due to containing complementary-determining region **(CDR)** that binds to epitopes.

2- Constant region (C)

- In the light chain (CL) and (Ch) in the heavy chain
- The light chain contain (1) constant region while the heavy chain contain (3-4) regions.

- Finished with carboxyl group (COO^-)
- There are five different constant regions, each constituting an class of antibody: gamma (IgG), meo (IgM), alpha (IgA), epsilon (IgE), delta (IgD)
- Antibody molecule act as **bifunctional molecule** due to its ability to combine with antigen (by amino terminal) and also combine with other immune cells, phagocytes and complement system (by carboxyle terminal).

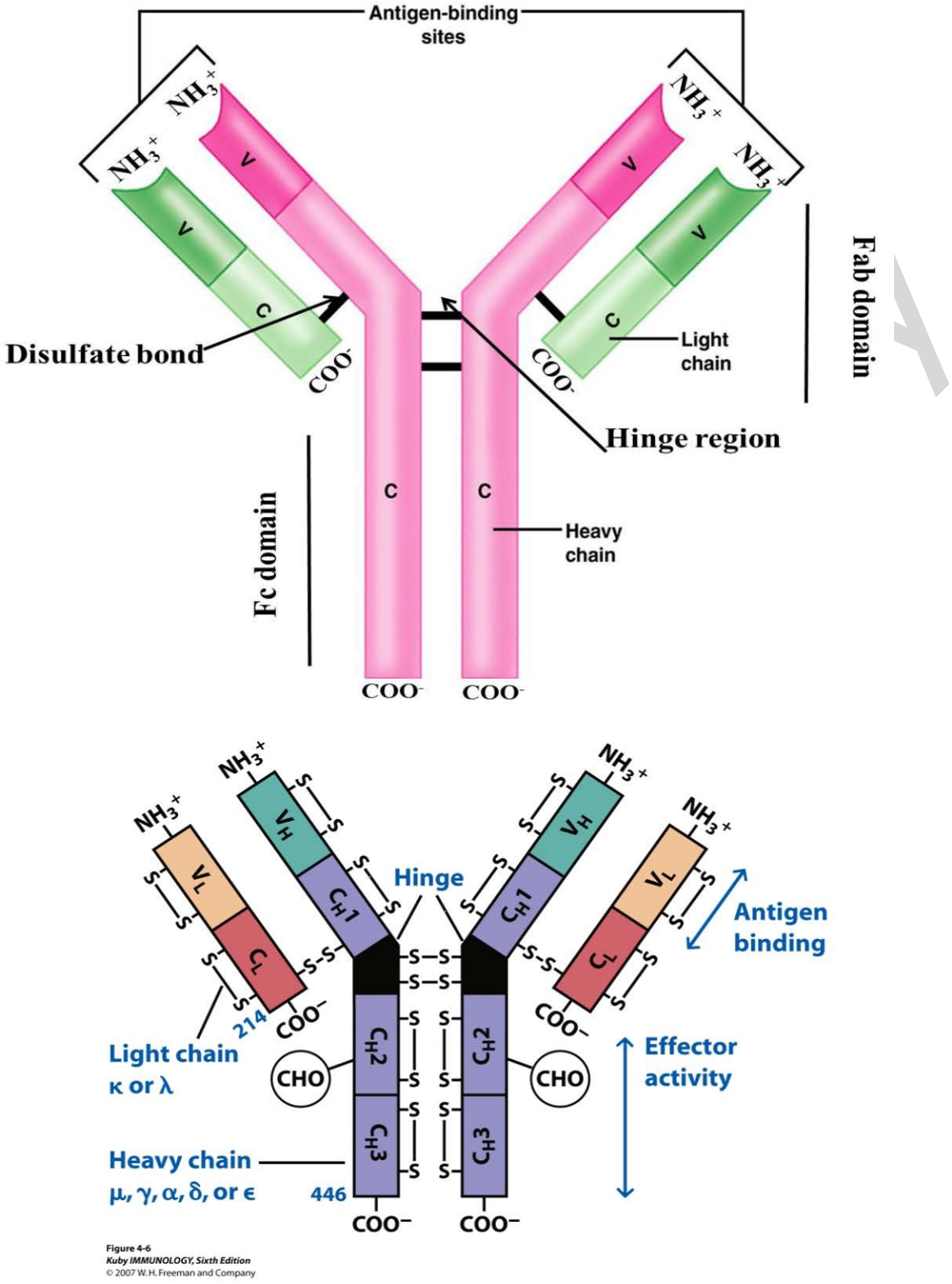


Figure 1: The basic structure of immunoglobuline molecule derived from amino acid sequencing studies.

- By using enzymes, the basic antibody structure discovered by **Edelman and porter** which are awarded Nobel Prize **(1959)** for this. They are noticed that these enzymes cleavage rabbit IgG into different parts as fallowing **(Figure 2)**:

A- Papain enzyme cleavage antibody molecule into three fragments:

1- Doubled fragments of Fab: included one antigen-binding site

2- Single fragment of fragment crystallizable

B- Pepsin enzyme separated antibody molecule into two fragmants:

1- Fragment antigen binding (Fab)2 : consist of two parts of Fab coupled by disulfate bound including two of antigen binding site.

2- Single fragment of Fragment crystallizable (Fc)

Lecture 6

Innate and Acquired Immune System

- There are two types of immunity in human body:

1- Innate or natural (non-specific).

2- Acquired or adaptive (specific

Lecture 7

The complement system

➢ The **complement system** or "complements" helps the ability of antibodies and phagocytic cells to clear pathogens from an organism. It is a part of innate and adaptive immune system.

➢ The term "complement" was introduced by Bordet and Paul Ehrlich in the late 1890s, as part of his larger theory of the immune system. Ehrlich named this heat-labile component "complement," because it is something in the blood that "complements" the cells of the immune system. Bordet also believed that there is only one type of complement.

➢ The complement system consists of a number of small proteins (Over 25 proteins and protein fragments, make up the complement system) found in the blood.

➢ The proteins and glycoproteins that constitute the complement system are synthesized by hepatocytes. But significant amounts are also produced by tissue macrophages, blood monocytes, and epithelial cells of the genitourinal tract and

gastrointestinal tract; however the complement proteins are synthesized by the liver.

➢ Normally the complement proteins circulating as inactive state (pro-proteins) and after stimulation by one of several triggers, proteases in the system cleave specific proteins and initiate an amplifying cascade of further cleavages. The end-result of this activation cascade is massive amplification of the response and activation of the cell-killing membrane attack complex (MAC).

➢ Three biochemical pathways activate the complement system: the classical complement pathway, the alternative complement pathway, and the lectin pathway.

➢ The classical complement pathway typically requires antigen-antibody complexes for activation (specific immune response), whereas the alternative and mannose-binding lectin pathways can be activated by C3 hydrolysis or antigens without the presence of antibodies (non-specific immune response).

➢ The following are the basic functions of complement:

1- **Opsonization** - enhancing phagocytosis of antigens.

2-Chemotaxis - attracting macrophages and neutrophils.

3- **Clearance of immune complexes.**

4-Clumping of antigen-bearing agents.

5- Cell Lysis - rupturing membranes of foreign cells.

Lecture 8

Cytokines

Lecture 9 Phagocytosis

Lecture 10 Inflammation

Lecture 11 Major histocompatibity complex

Lecture 12 Primary & Secondary Immune Response

Lecture 13 The Immune Response, Humoral and Cell Mediated Immunity

Lecture 14 Immune Tolerance

Lecture 15 Autoimmune Diseases

Lecture 16 Hyper Sensitivity Reactions