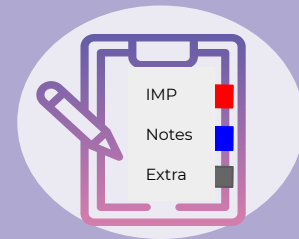


Natural Defense Mechanisms

Revised & Approved
by:
Shayma Abdullah Alghazwan
Yusuf Mohammad Alrabiah



Objectives

01

First (non-specific immunity) and second (adaptive immunity) lines of defense

02

Complement activation provides protection by killing pathogens

03

Accumulation of inflammatory cells important for clearance of infection

04

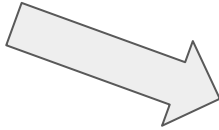
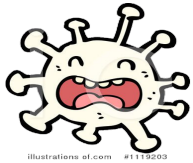
Cytokines as mediators regulate inflammation

helpful video to understand the concept of innate immunity in general:

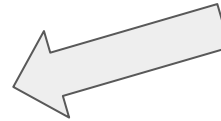


The main function of the immune system is to protect from infections:

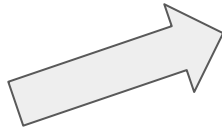
Viruses e.g:Influenza Polio



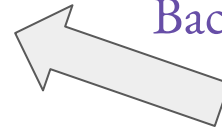
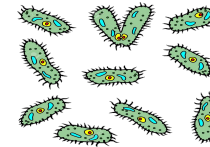
Parasites e.g:Tapeworms Malaria



Fungi e.g:Candida albicans



Bacteria e.g:Tubercle bacillus,Staphylococci



First and the second lines of defense:

NONSPECIFIC DEFENSE MECHANISMS

SPECIFIC DEFENSE MECHANISMS (IMMUNE SYSTEM)

First Line of Defense

Second Line of Defense

Natural (innate) immunity

- Phagocytes white blood cells.
- the inflammatory response.
- Antimicrobial proteins

Physical and mechanical barriers

- **Physical:** -Skin, impermeable to microbes.
- Mucous membranes lining the gastrointestinal, genitourinary and respiratory tracts.
- -Secretions of skin and mucous membranes.
- **Mechanical:** coughing, sneezing, vomiting, action of cilia in trachea
- *Urine is washed Continuously To prevent infections.
- Other protective mechanisms:
 - Shedding of outer skin layers.
 - Flushing of urine.
 - Mucus and cilia in respiratory tract.

Biochemical barriers

- -Body secretions contain anti-bacterial substances :
(e.g. saliva, tears and sweat, mucus, lung secretion)
- -Antimicrobial peptides/proteins:
(e.g., defensins, hepcidins)
- -Normal bacterial flora. (Compete with pathogenic bacteria for nutrients)
- In HIV, the problem is not the HIV Virus itself, The problem is that it Attacks The immune System And it takes Away the immune Response And All those organisms that Are within The body will be Able to make us ill.

- Lymphocytes
- Antibodies

Inflammation

- **Definition:** Inflammation is the first response of the immune system to infection or irritation.
- **It consist of** a series of **vascular & cellular** changes that occur in response to various stimuli
e.g. infections, injury, radiation etc.

- **Microbial infections initiate inflammation**
As bacteria possess an array of pro-inflammatory molecules:
e.g. Lipopolysaccharides (LPS)




In surface of microorganism and our immune system know if as something should defense against

- **Goals of inflammation:**
 1. Prevent and limit infection and further damage.
 2. Interact with adaptive immune system
For example: Monocytes / Macrophages serve as a link between the adaptive and innate immunity by antigen presentation *this point will explain later*
 3. Prepare the area of injury for healing

The Complement system

- Consist of a group of serum proteins circulate in inactive form once they become activated they produce important biological effects that initiate inflammation.
- Complement system plays an important role in linking Innate & Adaptive immunity.

 *The main function of the complement system is to make a hole in the bacterial cell wall (Lysis of bacterial cell wall) .

complement system is a part of innate system.

if C 3 and C 4 levels Are:

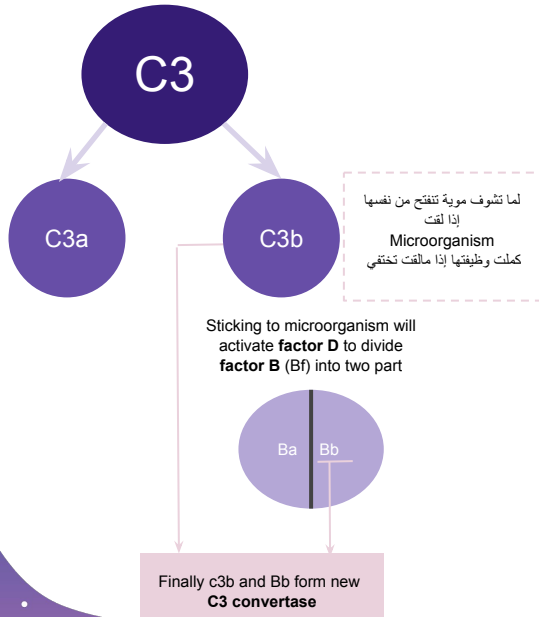
1) Normal: No Activation of complement system 2) low: Classical 3) High C4 and low C3 levels: Alternative Activation



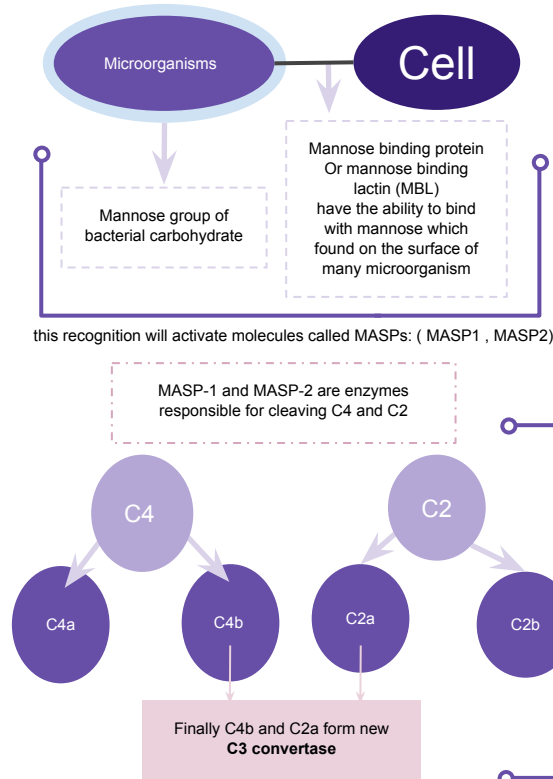
- the complement system is a System composed 20 different proteins. We will discuss the main 9 Proteins of them.
- These Proteins Are Normally in a proenzyme form. (The Enzyme is Originally in inactive form That is called "Pro enzyme")
- The Pro enzyme means that the complement System is in Shut State (Not doing Anything).
- Once the pro enzyme is Activated (Against Microbes) Complement System Starts.
- When the proenzyme is Activated Against Normal Cells, An autoimmune disease develops.
- Proenzymes Are produced in the liver, people with a chronic liver disease will have a problem with their Complement system

Pathways activate the complement system

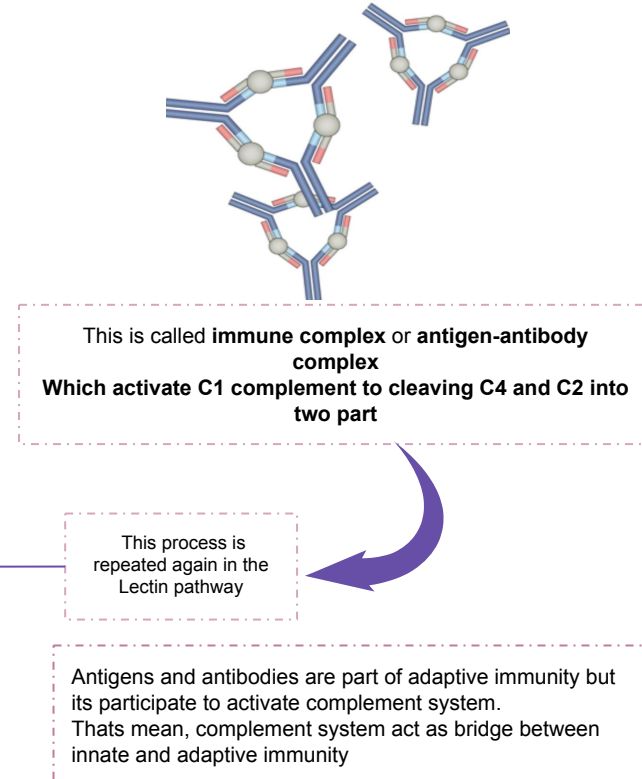
Third pathway Alternative pathway



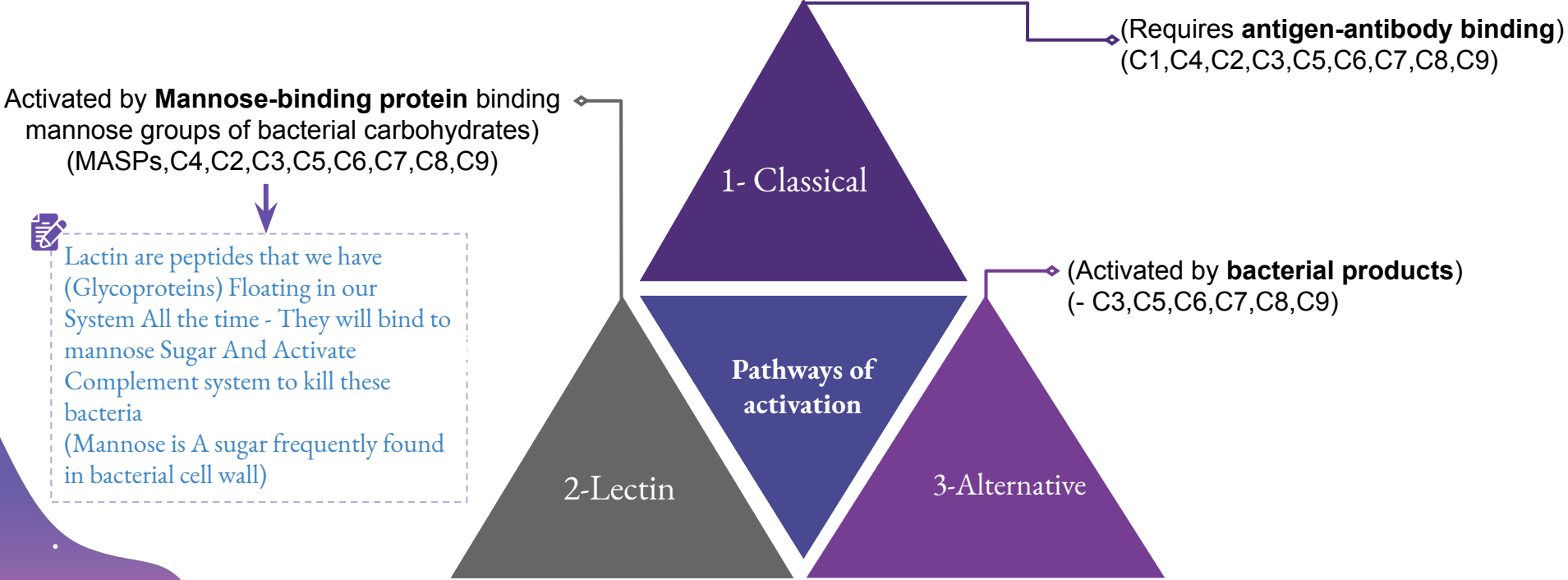
Second pathway Lectin pathway



First pathway Classical pathway



More details about activation pathways



Biological Effect of Complement Activation (start after pathway get activated)

Anaphylatoxin functions (C3a, C4a, C5a)

- 1) Trigger **degranulation** (release of substances) of granular leukocytes
- 2) Induce **histamine** release from (**mast cells**) causing **smooth muscle contraction** and Increase **vascular permeability**
- 3) Attract additional **inflammatory cells**
*That means they also mediate chemotaxis

Opsonization (Mainly C3b,C4b to lesser extent)

Coating of bacteria **enhances phagocytosis**

The (b) component attaches to the bacterial cell wall and “prepare” it for phagocytosis to occur.

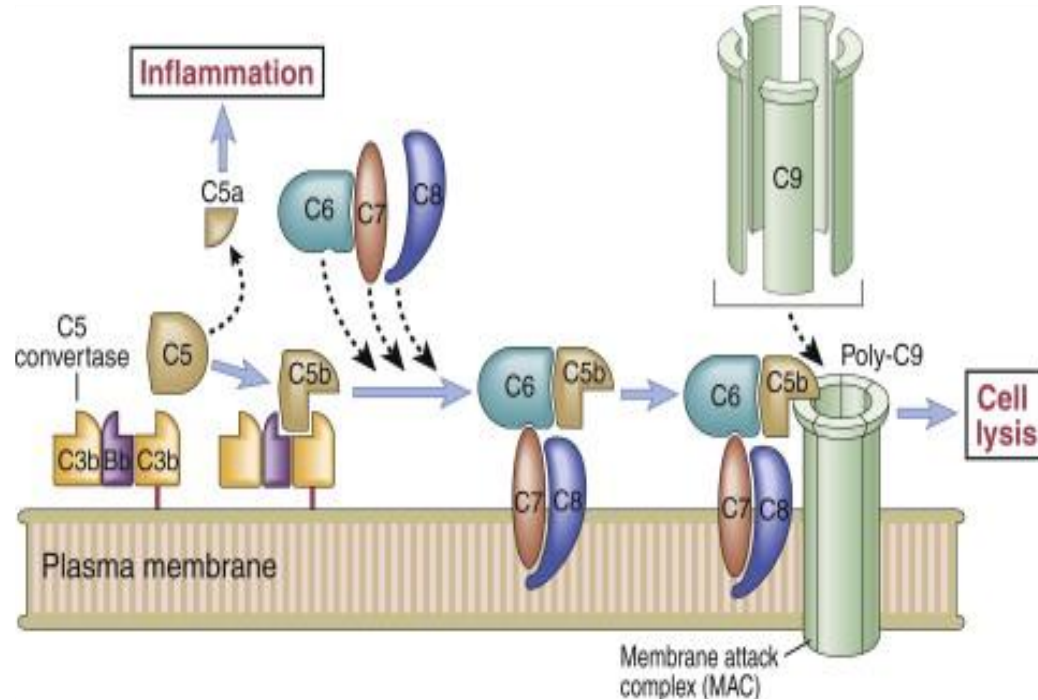
Killing of pathogens (Cell Lysis)

Destruction of bacteria by blasting holes in the bacteria making them leak to death.

Membrane Attack Complex:
C5b, C6, C7, C8, C9
*(explained in the next slide)

The Complement System

Membrane Attack Complex formation (MAC)

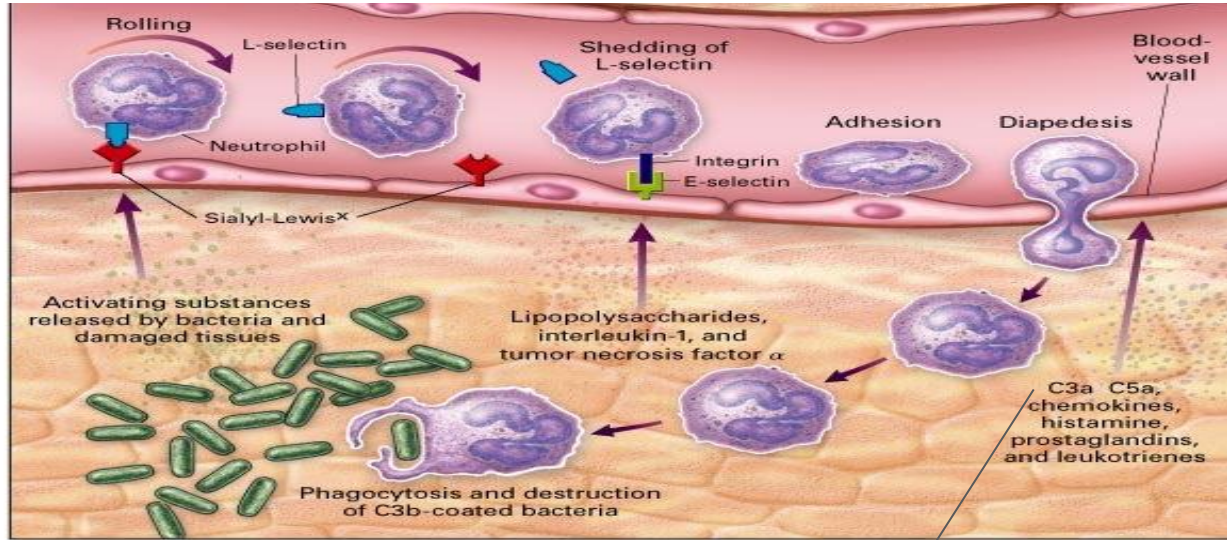


MAC : is a structure formed at the pathogen's **cell membrane** after the activation of the host's complement system. It forms a channel that disrupts the cell membrane leading to **cell lysis and death**.

اثناء الشرح ماتم توضيح المراحل بين
C3 convertase > C5 convertase

* C5 convertase will cause the activation of C5 to split into two components C5a and C5b. C5a will get involved in the process of chemotaxis. While C5b will bind with (C6,C7,C8) which will create C5bC6C7C8 complex therefore leading to the polymerization of C9 and creating the membrane attack complex (C5bC6C7C8C9). At the end resulting in cell lysis.

Process of Chemotaxis: is the movement of the responsible cells to a **specific place of injury** in response to a chemoattractant.



C3a, C5a increase vascular permeability
(Anaphylatoxin functions)

1

Rolling: the **slowing down** of the neutrophils in the blood vessels. *(margination)

2

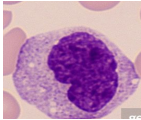
Adhesion: the **attachment** of the neutrophil to the endothelial cells

3

Diapedesis: the neutrophil **leaves** the blood vessel

Cells Attracted to The Site of Infection that Mediate Inflammation:

Monocytes :



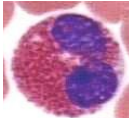
They become macrophages when they leave the blood and enter the tissue

Naturalized killer (NK) cells:



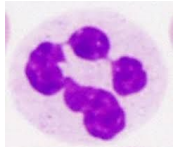
Kill tumor cells and virus infected cell

Eosinophils:

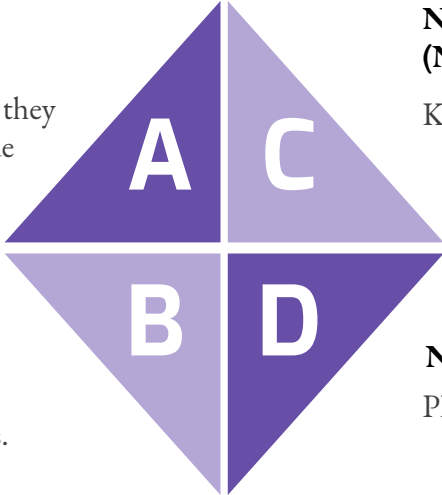


Allergy and parasitic infections.

Neutrophils:



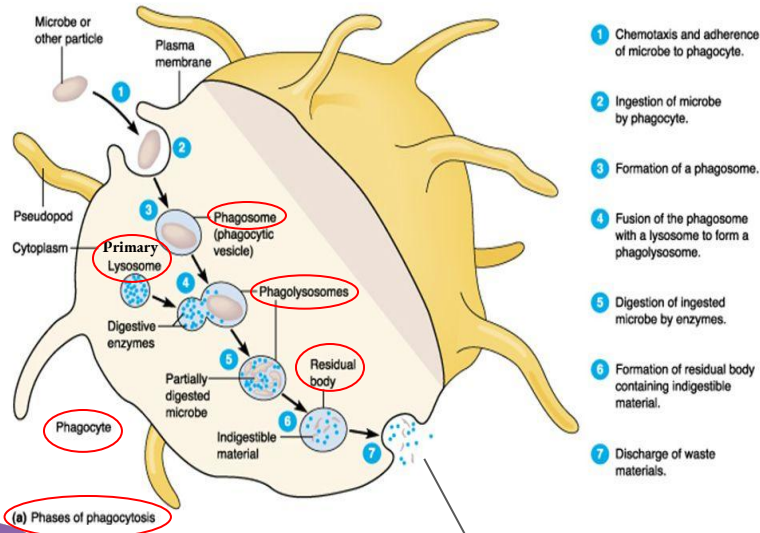
Phagocytic cell



438:
*Are weak phagocytes

Phagocytosis

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis** which is the process by which a cell **engulf** a solid particle such as bacteria to form **internal vesicle** known as **phagosome**.



- 1 Chemotaxis and adherence of microbe to phagocyte.
- 2 Ingestion of microbe by phagocyte.
- 3 Formation of a phagosome.
- 4 Fusion of the phagosome with a lysosome to form a phagolysosome.
- 5 Digestion of ingested microbe by enzymes.
- 6 Formation of residual body containing indigestible material.
- 7 Discharge of waste materials.

Exocytosis


Cytokines

Soluble molecules, produced by **different cells**, that control cell functions e.g. **differentiation, proliferation, activation or inhibition**.

Interleukins

Produced primarily by **macrophages and lymphocytes** in response to a pathogen.
Examples:
IL-1, IL-2, IL-3.....

Interferons

Protects against viral infections (Antiviral agents)
Produced and released by **virally infected** cells in response to viral infections.
 * **Virally infected cells release (interferons)** to warn other non affected cells.

Tumor Necrosis Factor

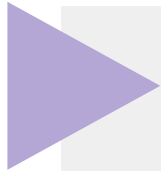
Secreted by **macrophages**.
- Induces **fever** by acting as an **endogenous pyrogen** (a substance released from inside the body that produces fever)

- **Increases** synthesis of **inflammatory** serum proteins
- **Increase** expression of **adhesion** molecules on endothelial cells and vascular permeability

Take Home Messages :



Non-specific (innate immunity) acts as a first line of defense against invading pathogens



Innate immunity is an important initial step for generation of adaptive immune response



Inflammation is vital for controlling infection and limiting tissue damage

 Quiz

Question 1: which of the following plays an important role in linking Innate & Adaptive immunity?

- A -immune system B- Complement system C- Inflammation D- Phagocytosis

Question 2: which of the following is a part of Pathways of activation?

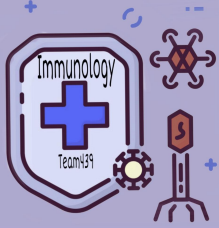
- A - Classical B- Lectin C- Alternative D- all the above

Question 3:What is the most important component involved in opsonization?

- A - C5a B- C4b C- C3b D- C3a

Question 4: What is the cytokine that protects us from viral infections ?

- A - Tumor Necrosis factor B-Interferon C-LPS D-Interleukin



team leaders

Hessah Fahad Alalyan

Faisal alotaibi



- Asma Alamri
- Fatimah Almeather
- Nourah Almasaad
- Renad AlOsaimi
- Sara Alrashidi
- Sarah Alqahtani
- Shatha Aldhohair
- Yara Alzahrani



- Abdulaziz alamri
- Abdulaziz arabiah
- Hamad Almousa
- Homoud Algadheb
- Mohammed albabtain
- Saleh Algarni
- Osama Mobeirek



Immunologyteam439@gmail.com

editing file
click [here](#)