

Natural Defense Mechanisms

Immunology Unit
Dept. of Pathology
College of Medicine
KSU

Reference
Kuby Immunology 7th Edition
2013
Chapter 4 Pages 105-110
Chapter 5 Pages 141-176
Chapter 6 Pages 187-200 & page 213

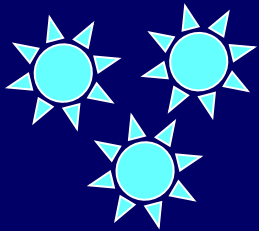
Objectives

- + To know First (non-specific immunity) and second (adaptive immunity) lines of defense
- + To understand the Complement system, its activation and how it involves in pathogen killing.
- + To recognize the importance of accumulation of inflammatory cells for clearance of infection
- + To know the role of cytokines as mediators which regulate inflammation

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

Viruses e.g.

Influenza
Polio



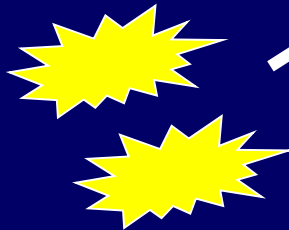
Parasites e.g.

Tapeworms
Malaria



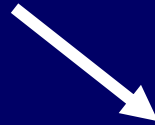
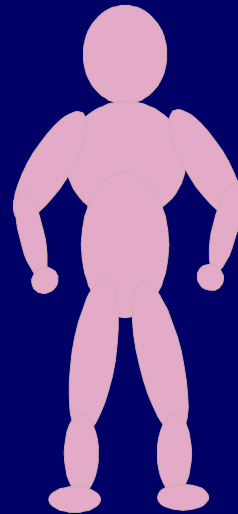
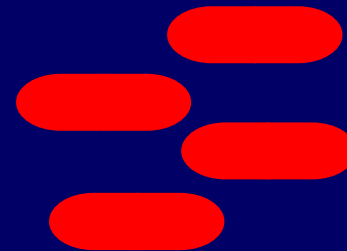
Fungi e.g.

Candida albicans



Bacteria e.g.

Tubercule 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

- Skin
- Mucous membranes
- Secretions of skin and mucous membranes

- Phagocytic white blood cells
- Antimicrobial proteins
- The inflammatory response

- Lymphocytes
- Antibodies

First line of defense :

- **Natural (Innate) Immunity**
- **Physical** (skin/ mucous membranes)
- **Mechanical** (Coughing, sneezing, vomiting, action of cilia in trachea)
- **Biochemical barriers** (antimicrobial peptides, lung secretions, mucus, saliva, tears)

Physical and mechanical barriers

- Skin, impermeable to microbes.
- Mucous membranes lining the gastrointestinal, genitourinary and respiratory tracts.
- Other protective mechanisms:
 - Shedding of outer skin layers.
 - Coughing and sneezing.
 - Flushing of urine.
 - Vomiting.
 - Mucus and cilia in respiratory tract.

Biochemical barriers

- Body secretions contain anti-bacterial substances e.g. saliva, tears and sweat.
- Antimicrobial peptides (e.g., defensins, hepcidins)
- Normal bacterial flora.
(Compete with pathogenic bacteria for nutrients)

- **Inflammation:**
- 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)

Inflammation

□ Goals

- Prevent and limit infection and further damage
- Interact with adaptive immune system
- - For example Monocytes / Macrophages serve as a link between the adaptive and innate immunity by antigen presentation
- Prepare the area of injury for healing

The Complement system

- Consists of a group of serum proteins initially present in inactive form
- Activation occurs in cascade (one component or more activating another) after enzymatic cleavage. Once components become activated they produce important biological effects that initiate inflammation.
- This system plays an important role in linking Innate & Adaptive immunity

The complement system:

3 Pathways of activation :

* **Classical**. (Requires antigen-antibody binding)

- (C1,C4,C2,C3,C5,C6,C7,C8,C9)

* **Lectin**. (Activated by mannan binding protein binding manose groups of bacterial carbohydrates)

- (C4,C2,C3,C5,C6,C7,C8,C9)

- **Alternative**. (Activated by bacterial products)

- (C3,C5,C6,C7,C8,C9)

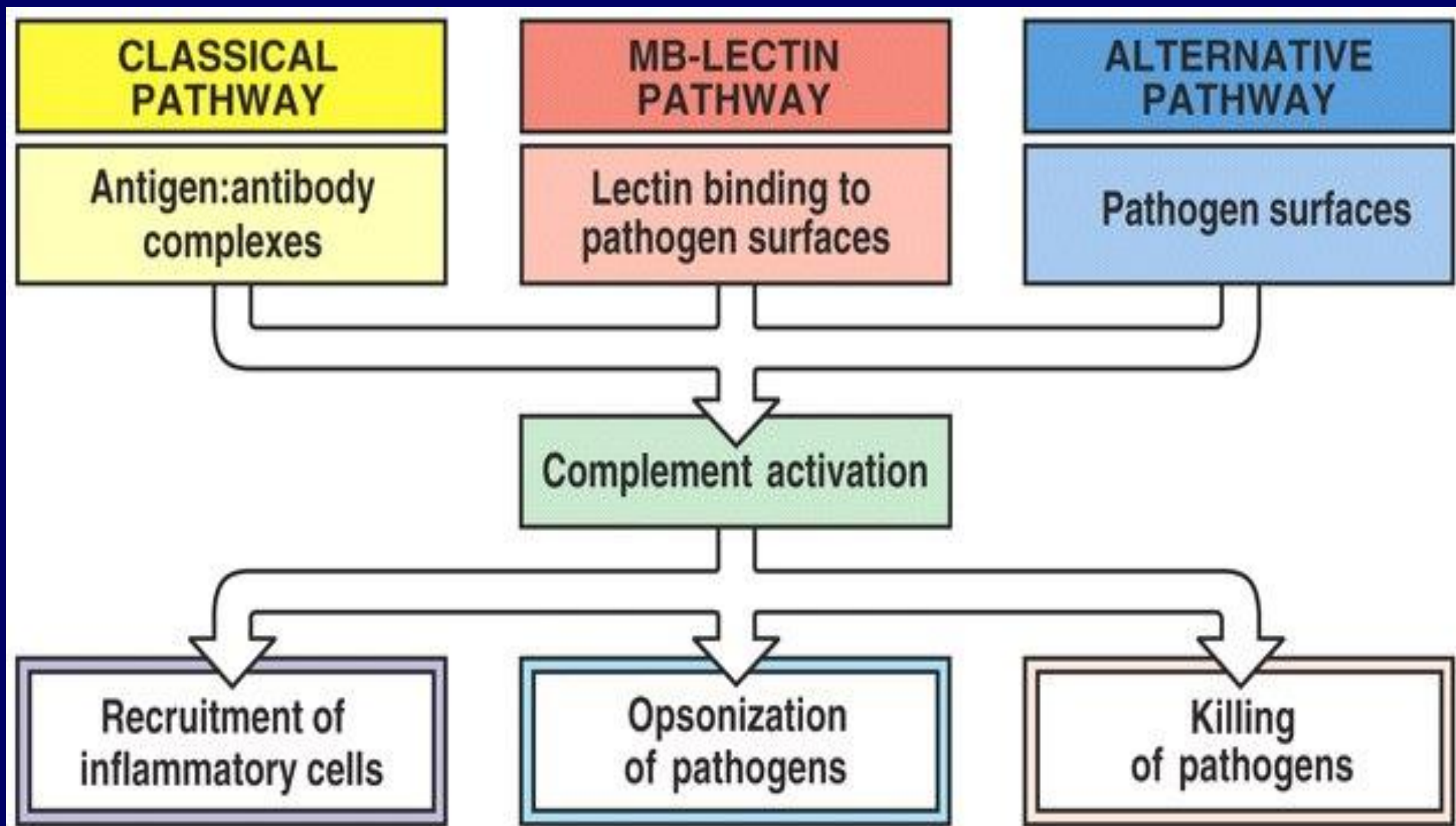
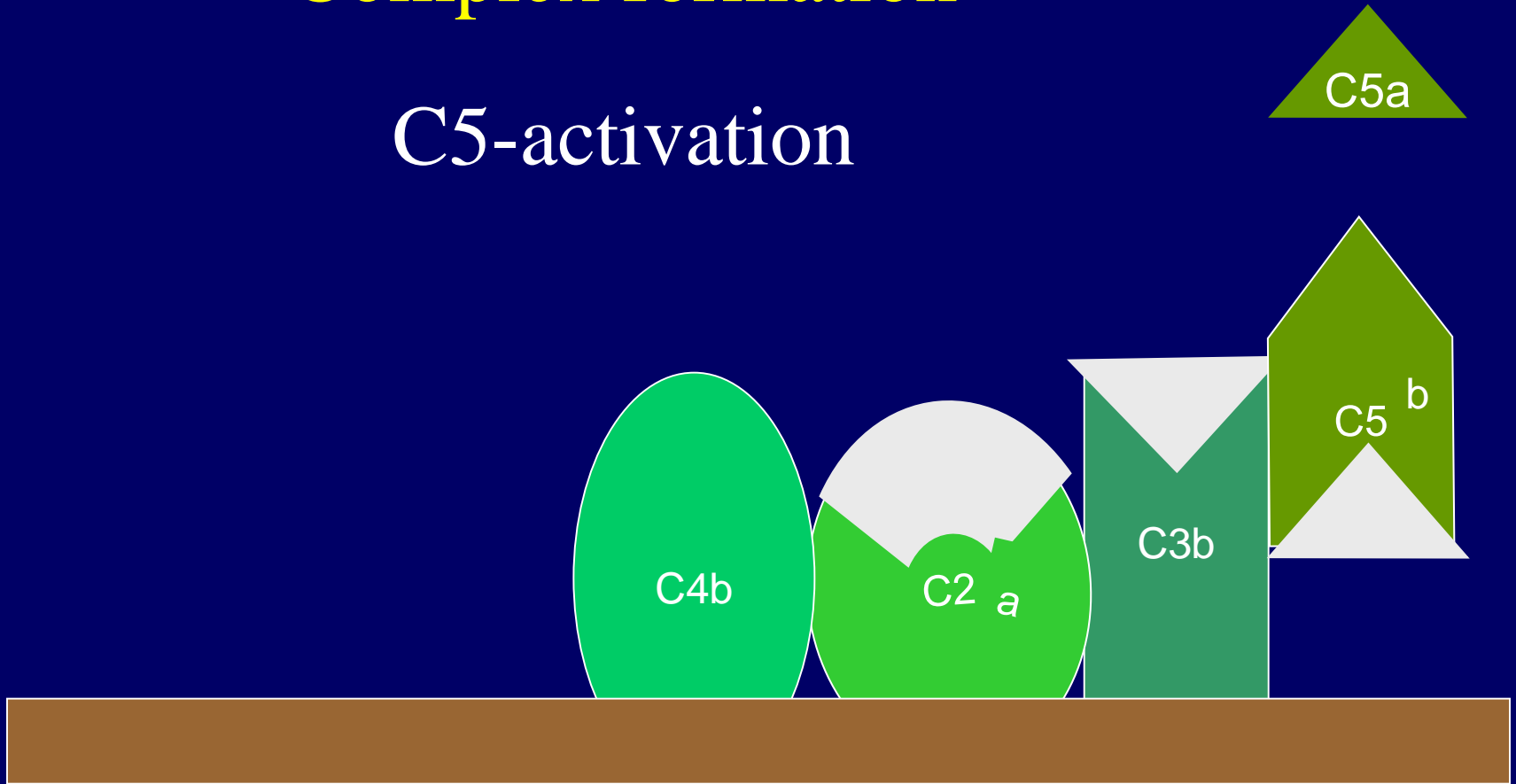


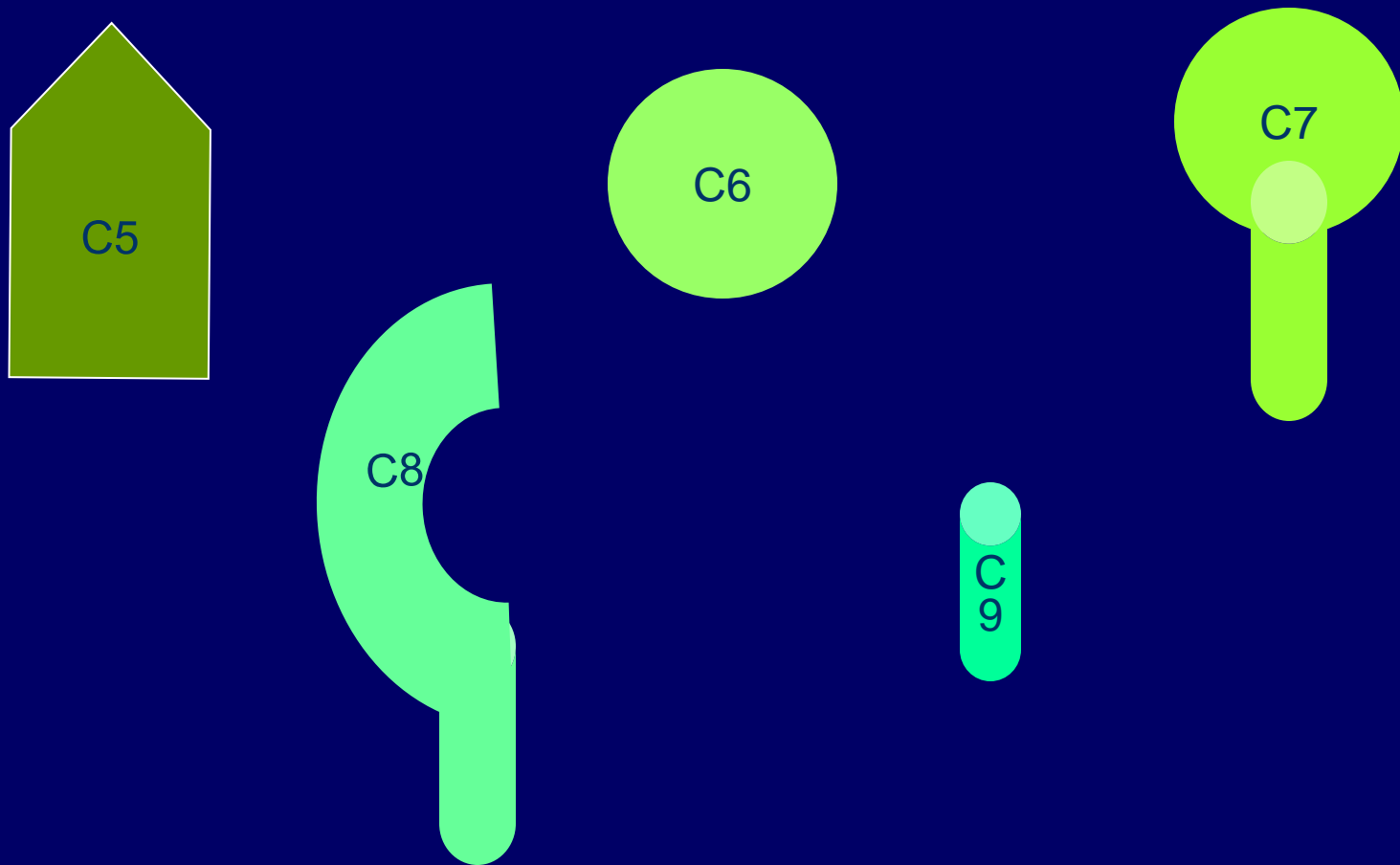
Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)

Membrane Attack Complex formation

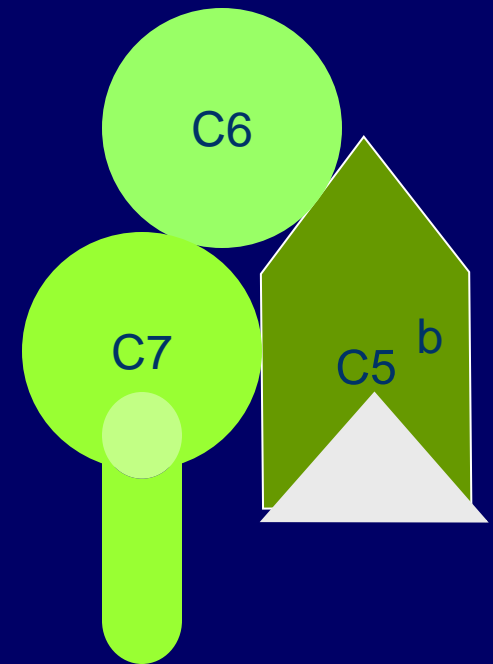
C5-activation



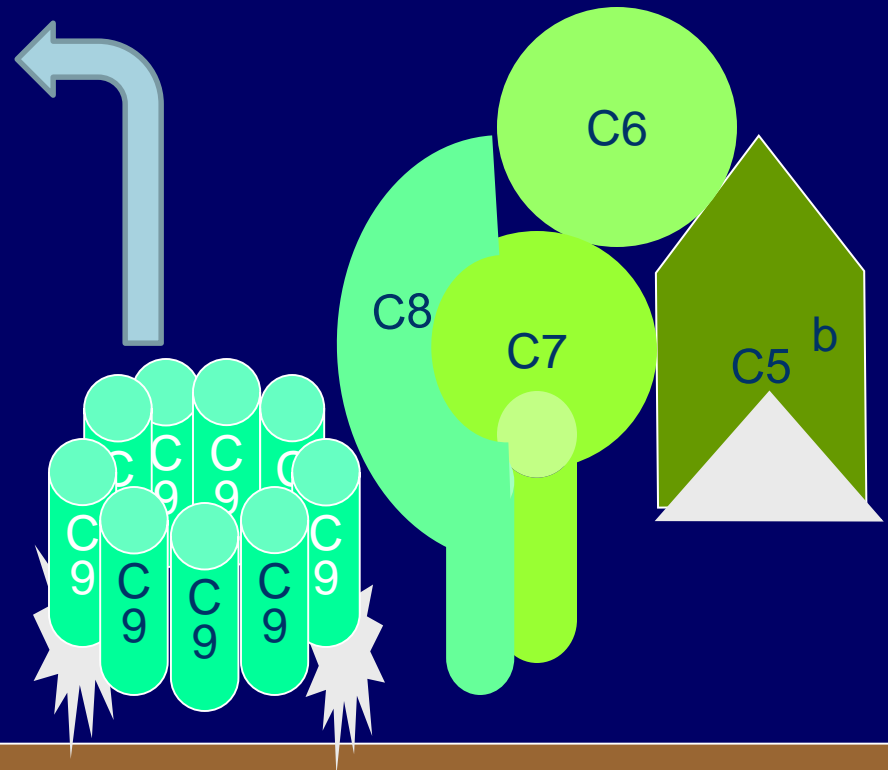
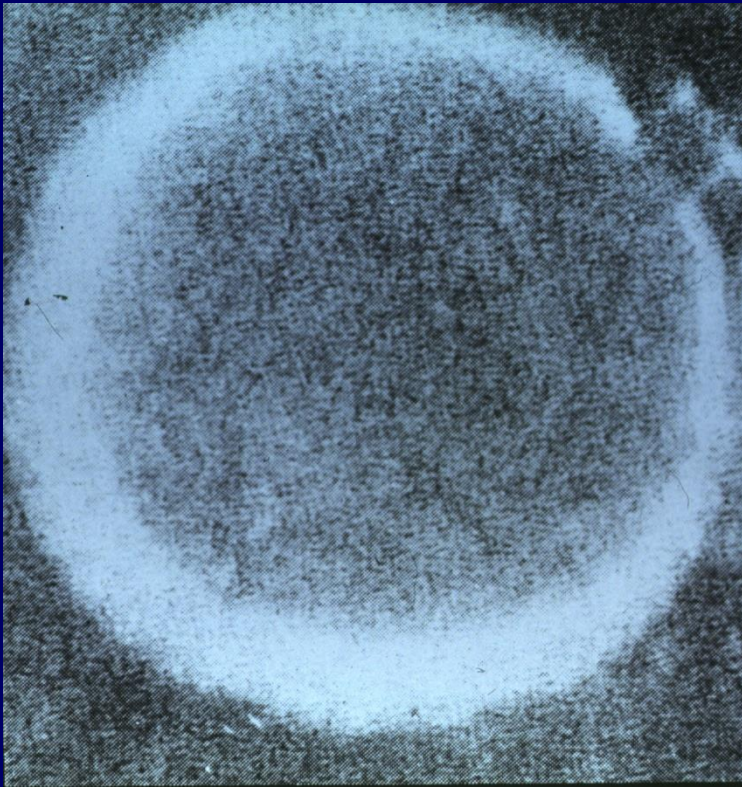
Components of the Membrane Attack Complex



Membrane Attack Complex components Assembly



Membrane Attack Complex formation : insertion of lytic complex into cell membrane



Biological effects of complement activation

1. Anaphylatoxin functions (e.g. C3a, C5a):

- Trigger degranulation (release of substances) of endothelial cells, mast cells or phagocytes.
- Induce smooth muscle contraction and increased vascular permeability.
- Attract additional inflammatory cells to the site of activation.

2. Opsonization: C3b is the main opsonin and to a lesser extent C4b.

- Coating of bacteria enhances phagocytosis

3. Direct cell lysis:

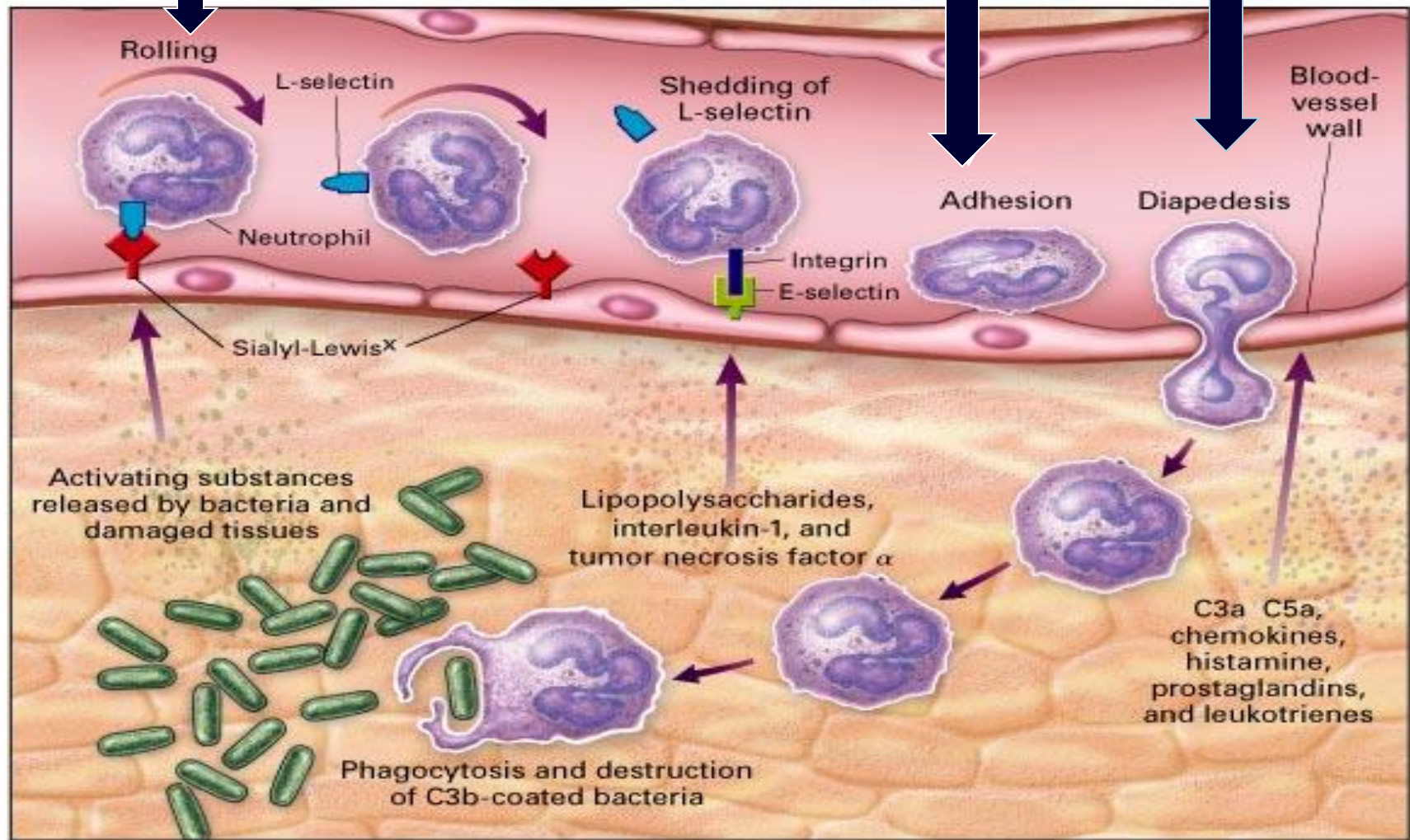
- Destruction of bacteria.

Process of chemotaxis:

Rolling on vessel wall.

Adhesion (attach)

Pass through.



Types of Cells attracted to the site of infection that mediate inflammation :

Monocytes :

- Become Macrophages when they leave the blood and enter the tissues.

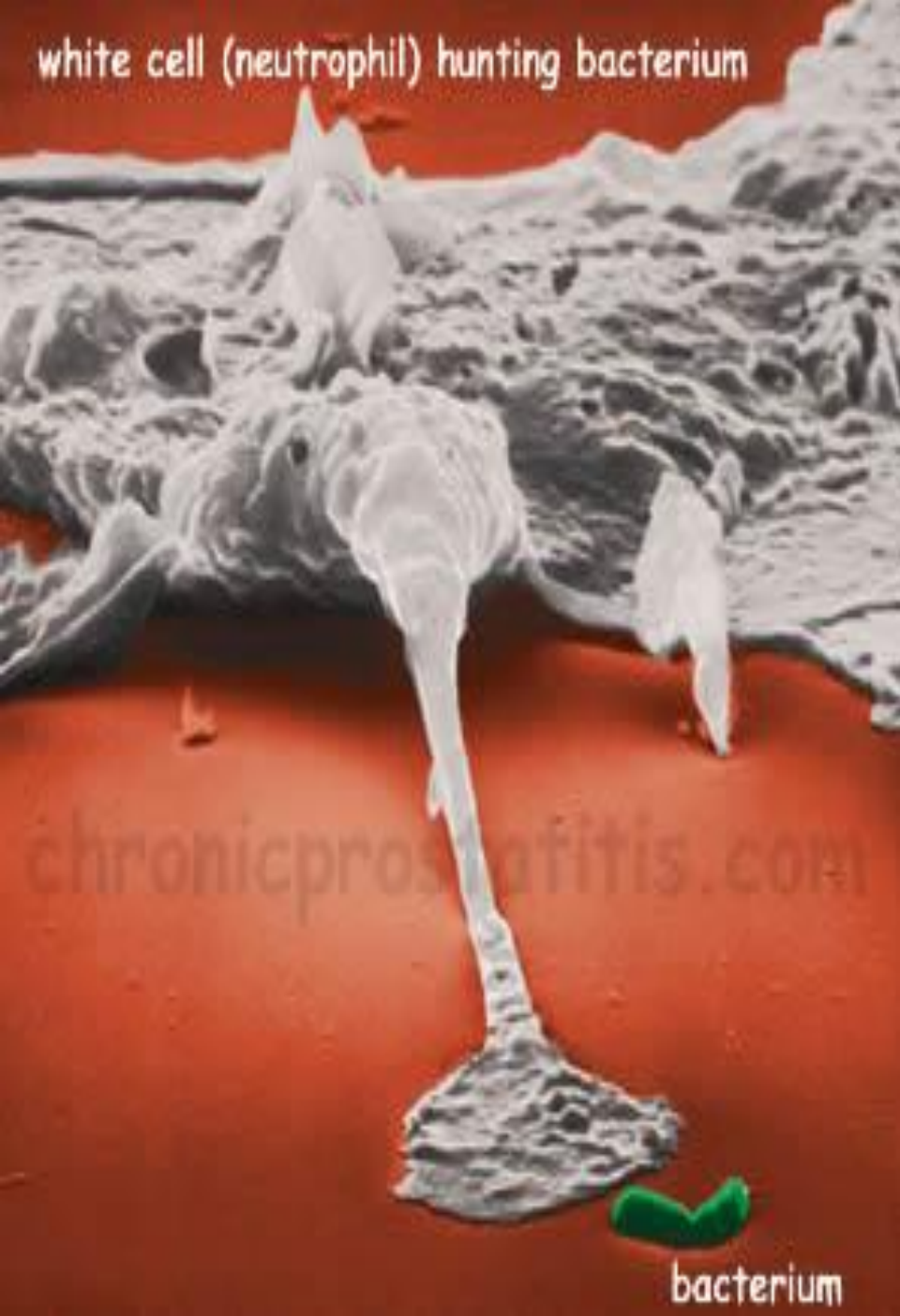
Neutrophils: (Phagocytic cells)

Eosinophils: (Allergy and Parasitic infections)

Natural Killer (NK) cells: (Kill tumor cells and virus infected cells)

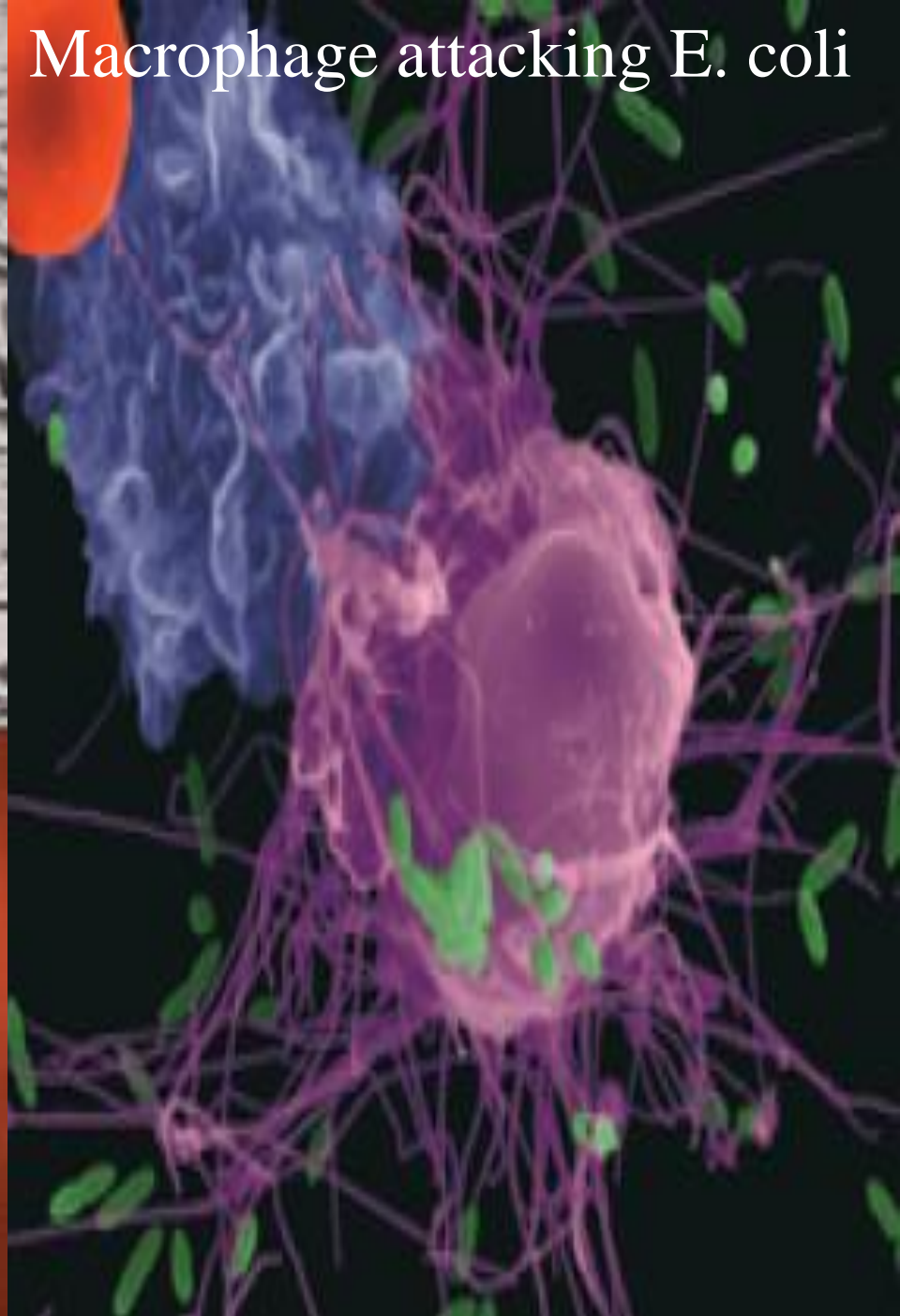
Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis** which is the process by which a cell **engulf** a solid particle such as bacteria to form **internal vesicle** known as **phagosome**

white cell (neutrophil) hunting bacterium

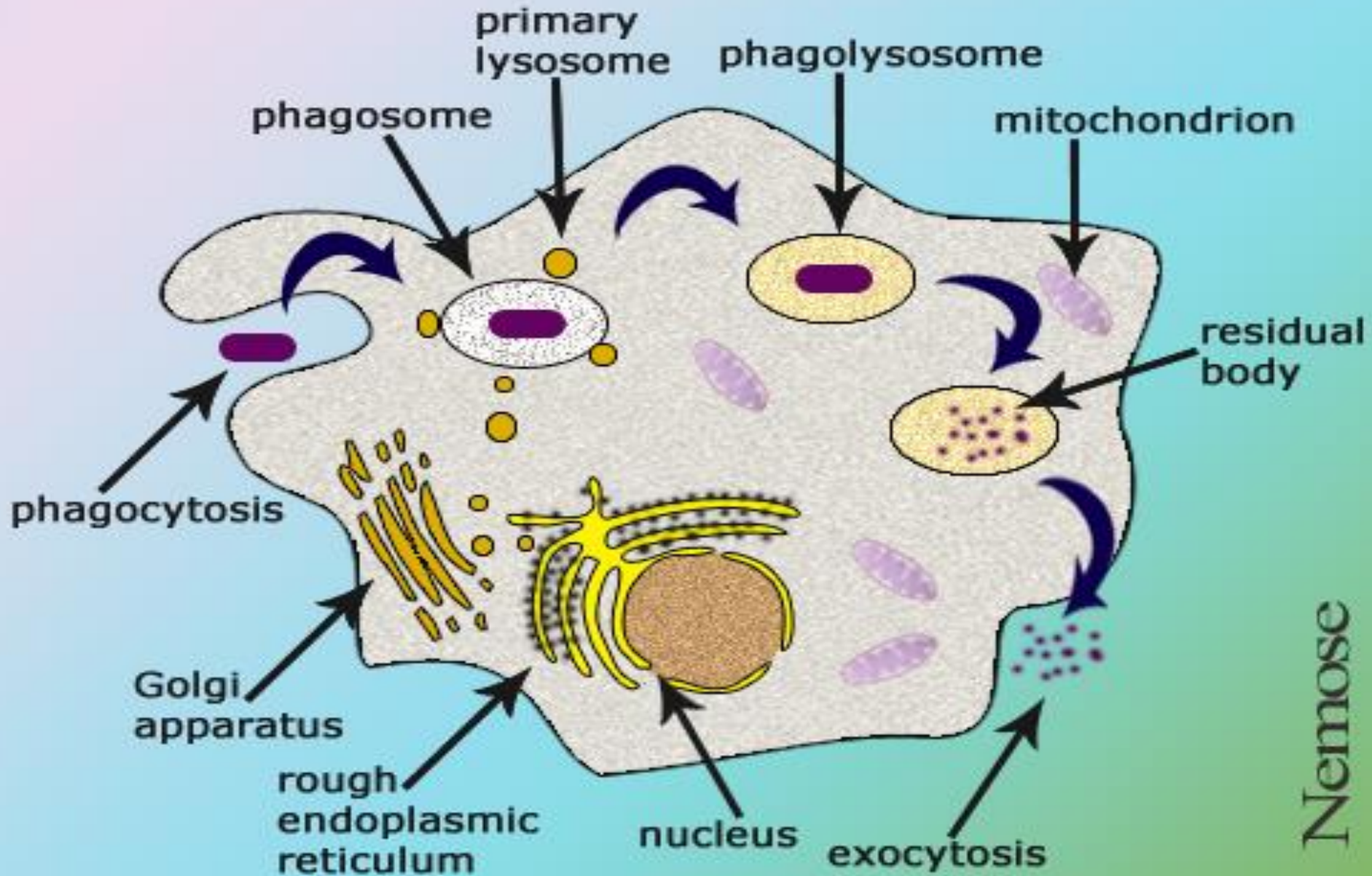


bacterium

Macrophage attacking E. coli



Phagocytosis



Cytokines

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

e.g. **Interleukins**

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

Cytokines

□ Interferons:

- Protects against viral infections
- Produced and released by virally infected cells in response to viral infections.

Cytokines

□ Tumor necrosis factor (TNF)

■ 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 message

- 1. Non-specific (innate immunity) acts as a first line of defense against invading pathogens
- 2. Innate immunity is an important initial step for generation of adaptive immune response
- 3. Inflammation is vital for controlling infection and limiting tissue damage

Thank you