

# Natural Defense Mechanisms

Immunology Unit  
Dept. of Pathology  
College of Medicine  
KSU

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

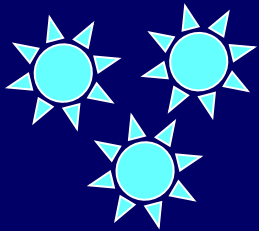
# Objectives

- + 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*



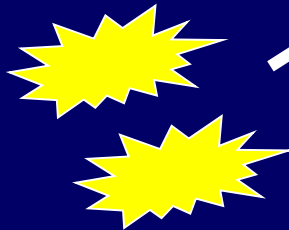
## Parasites e.g.

Tapeworms  
Malaria



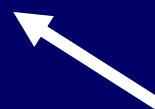
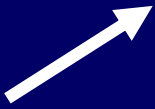
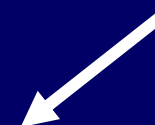
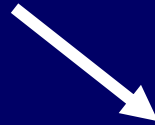
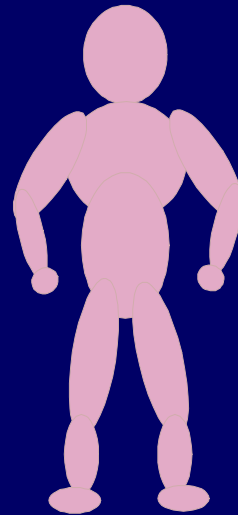
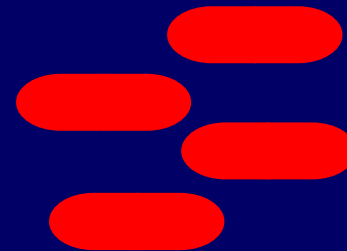
## Fungi e.g.

*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 activating another) after enzymatic clivage. 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**)



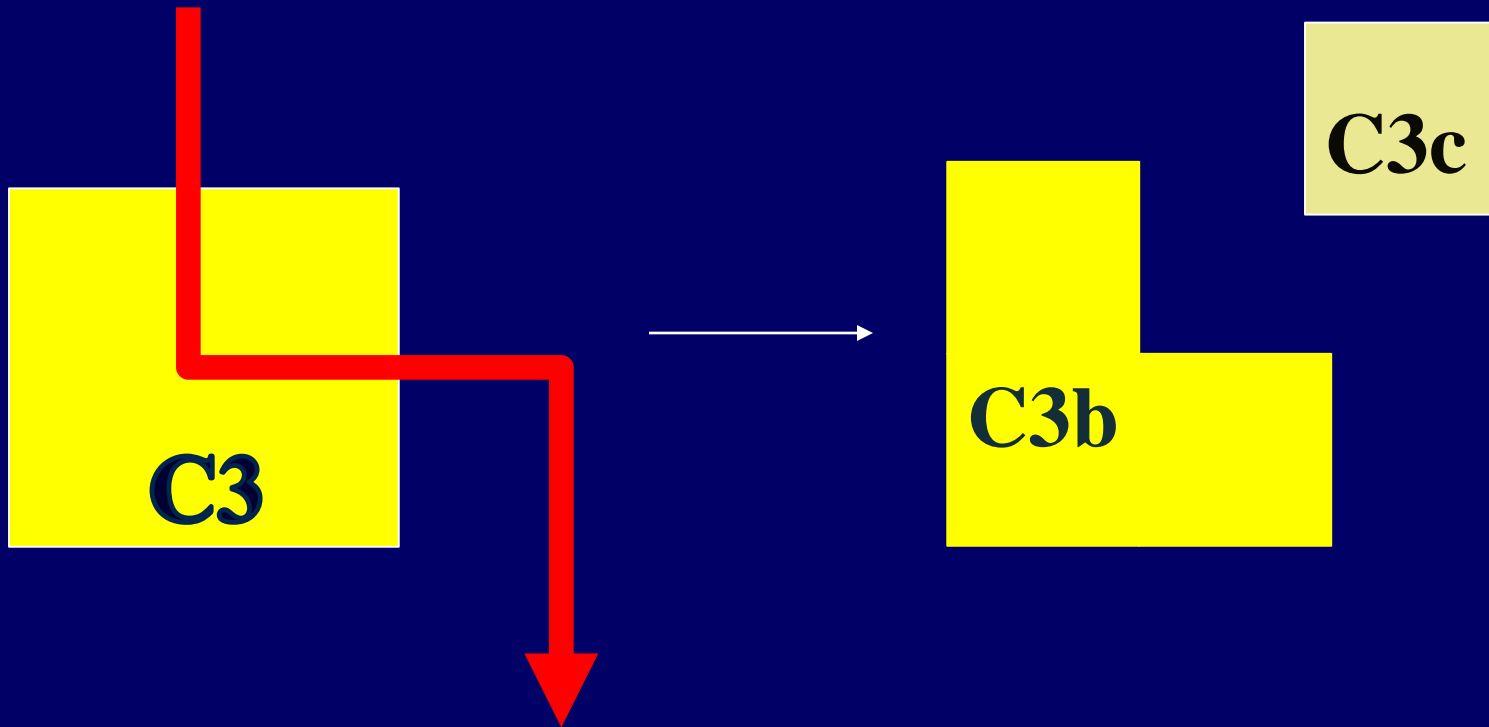
\* **Lectin.** (Activated by mannan binding proteins binding mannose groups of bacterial carbohydrates)

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

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

- (**C3, B, D**, **C5, C6, C7, C8, C9**)

# Enzymatic cleavage



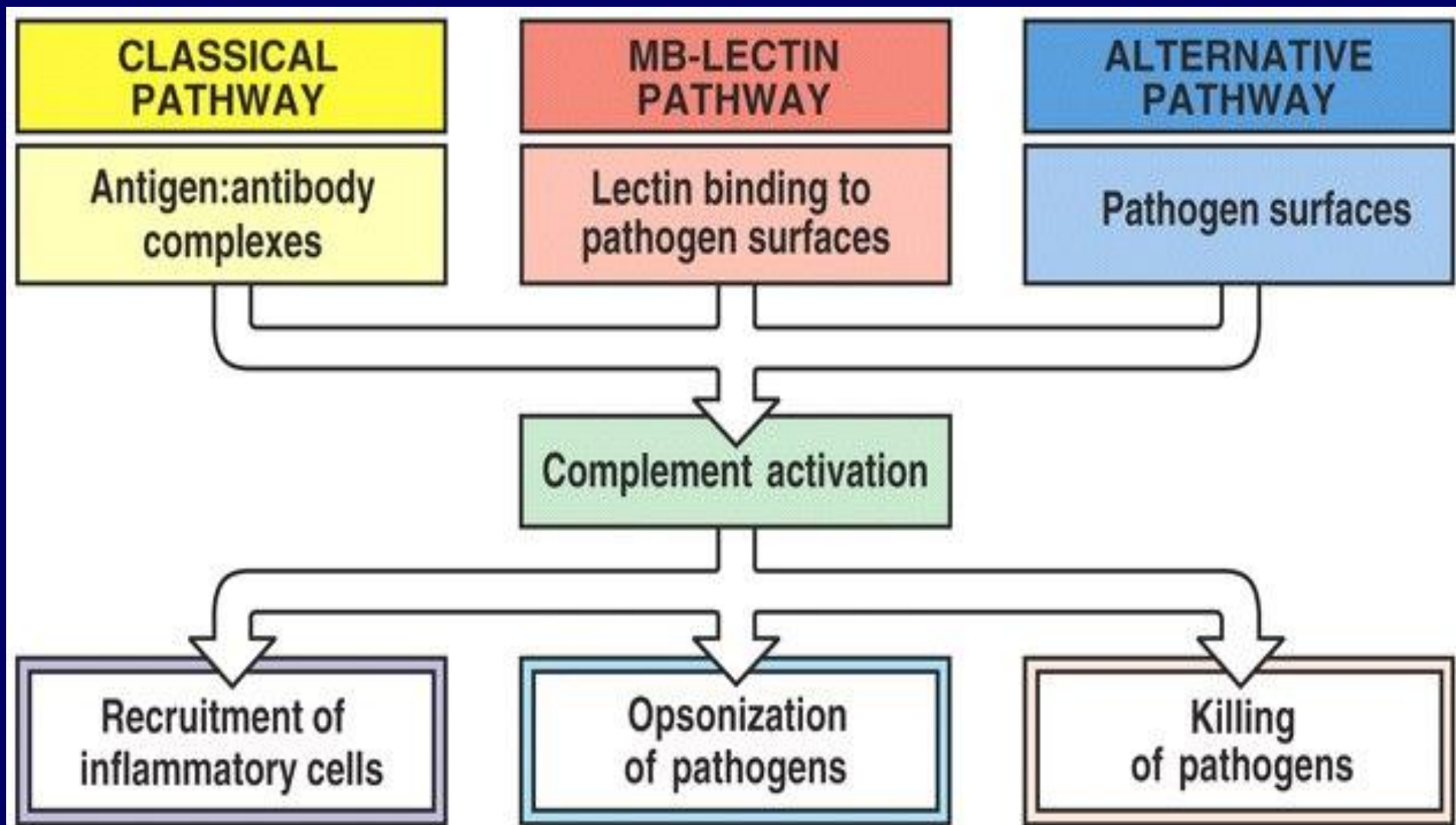
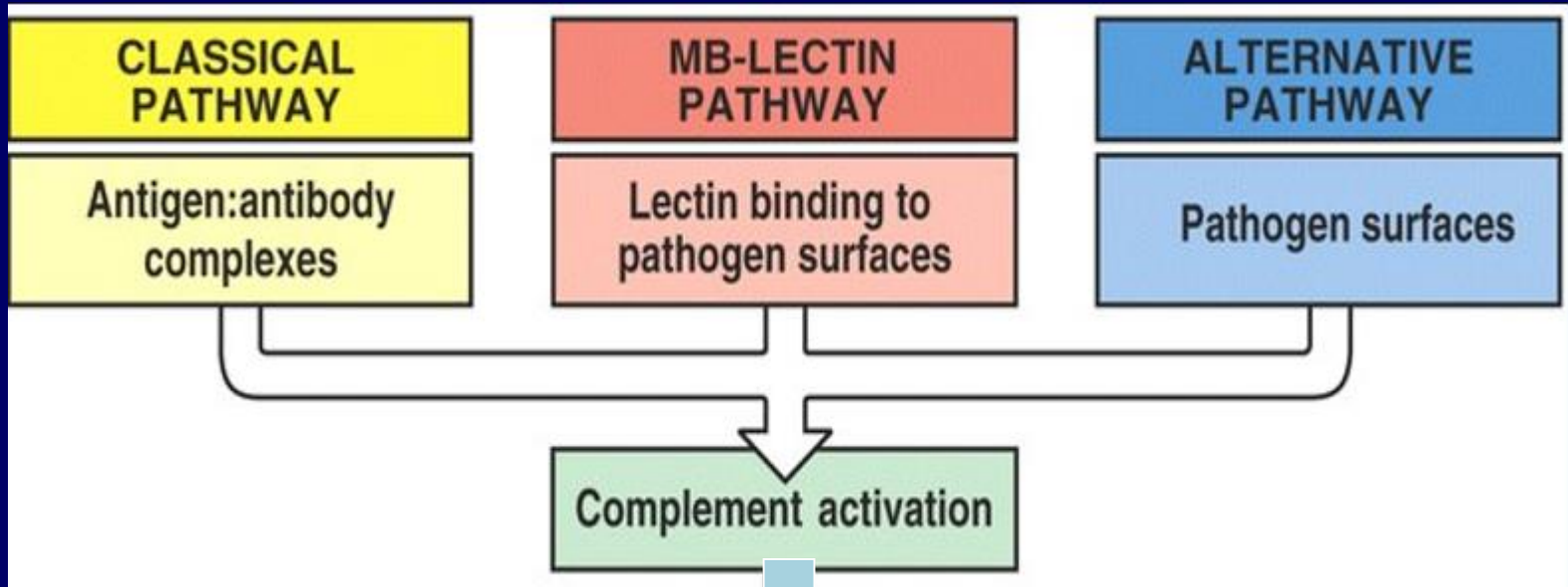


Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)



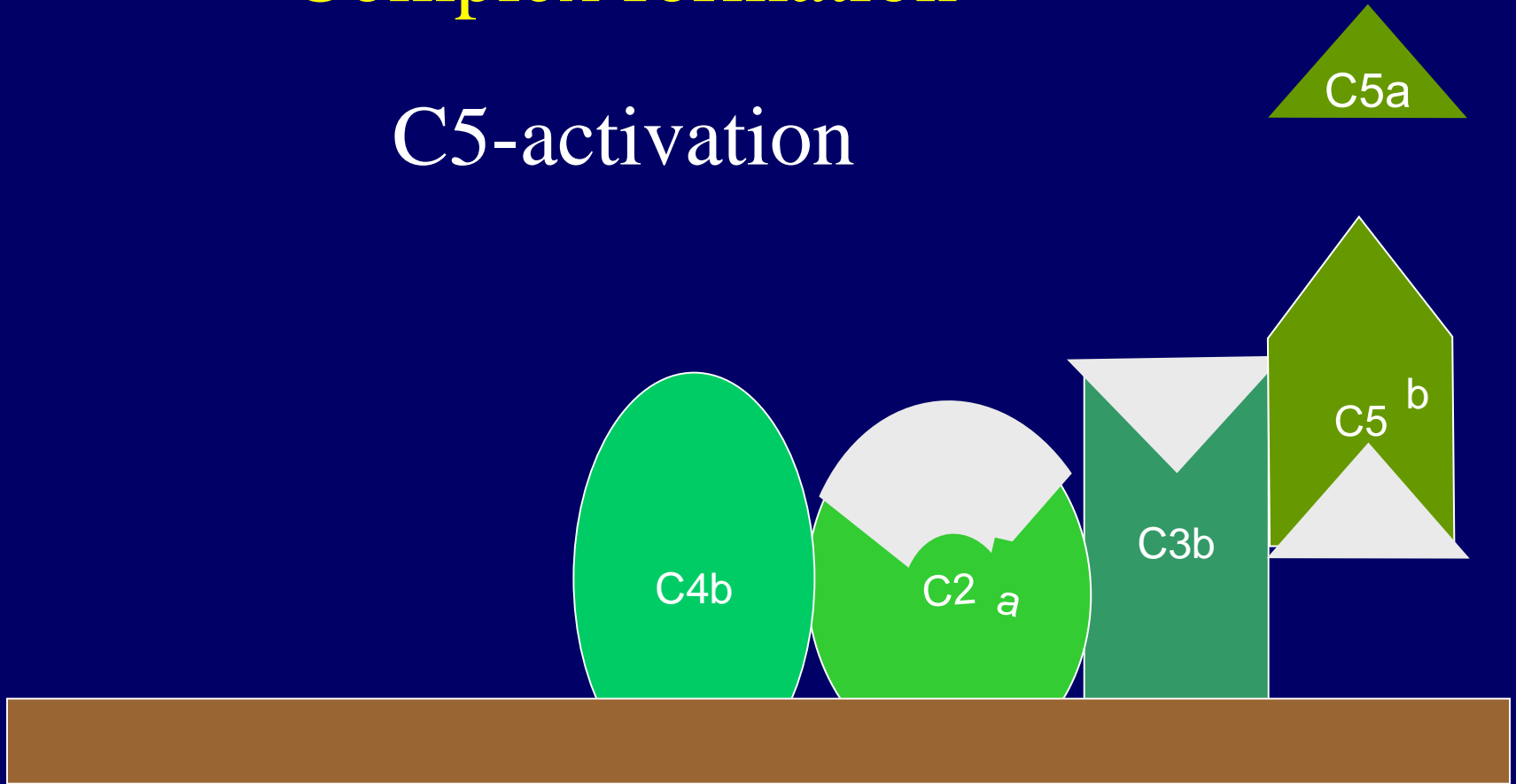
C5 convertases

C5  $\longrightarrow$  C5a + C5b

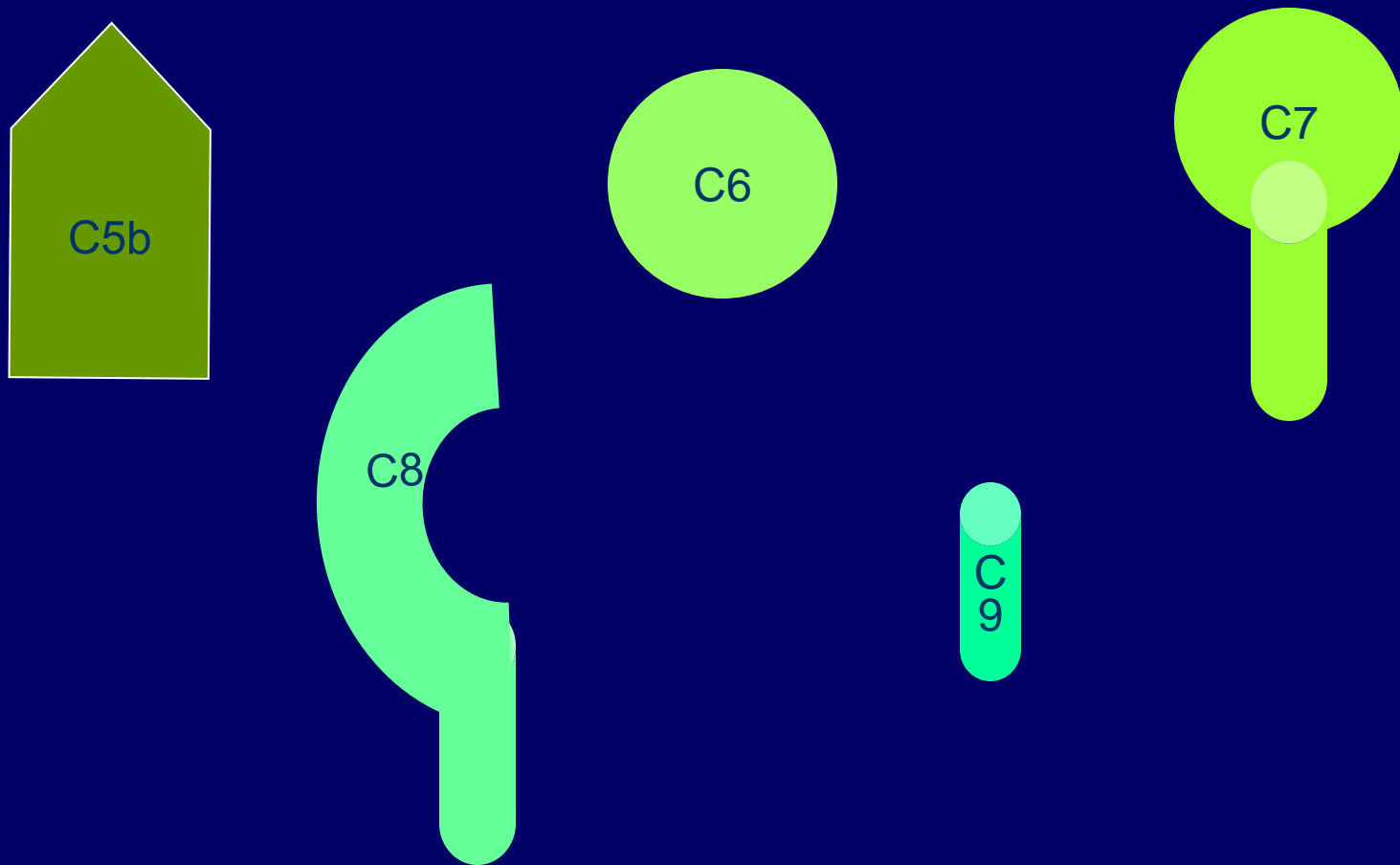


# Membrane Attack Complex formation

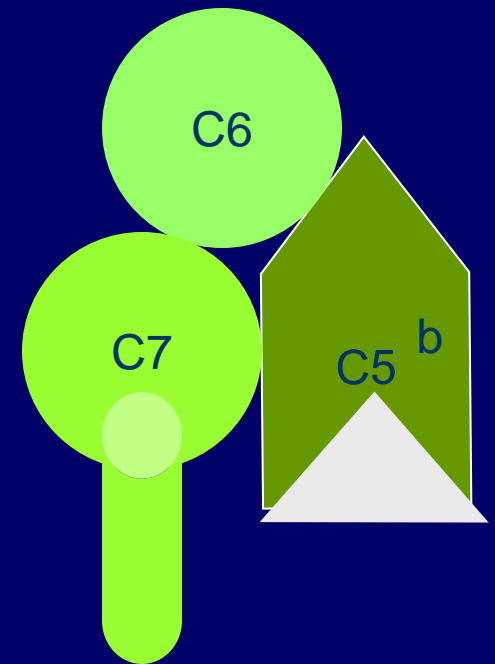
C5-activation



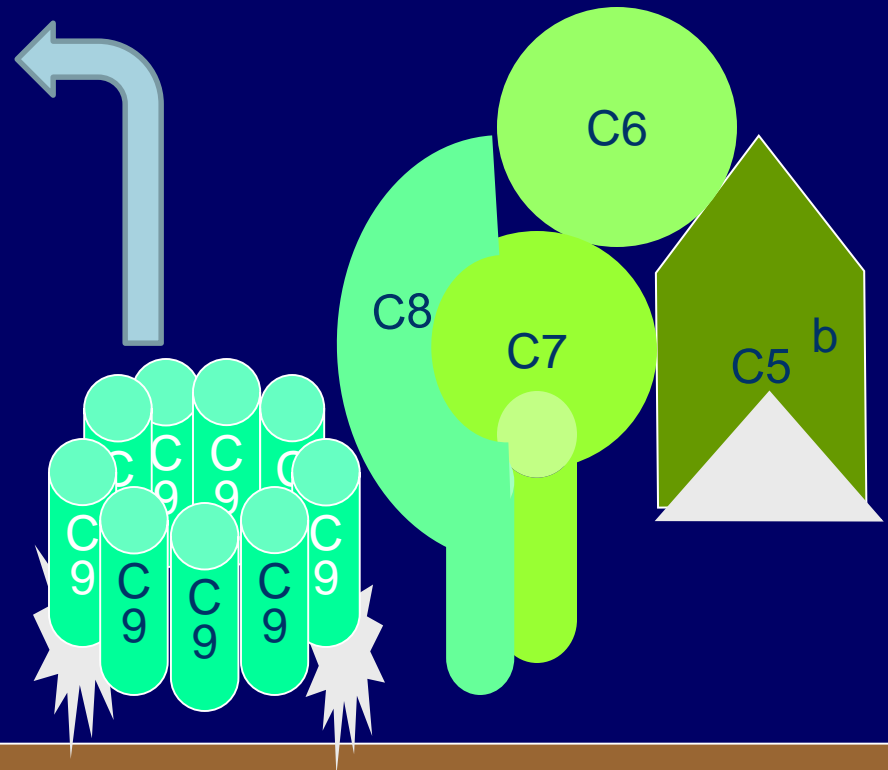
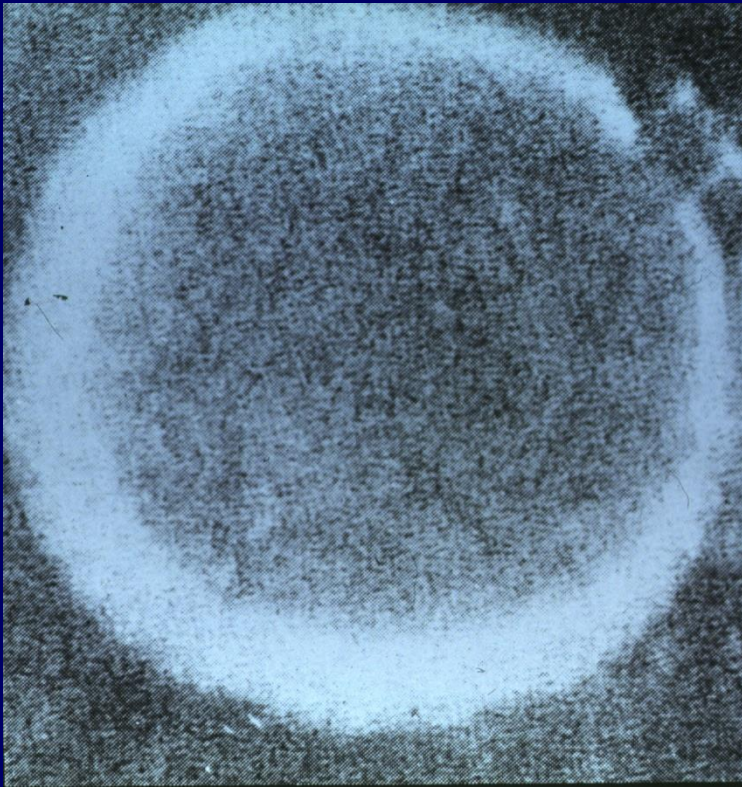
# Components of the Membrane Attack Complex



# Membrane Attack Complex components Assembly



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



# Biological effects of complement activation

1. Anaphylatoxin (C3a, C5a) (recruit more cells to help out !!!)

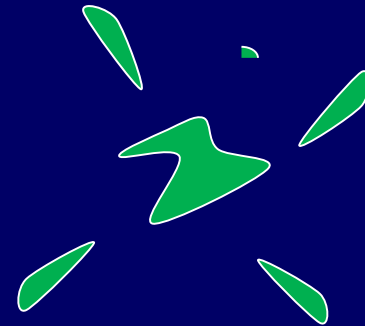
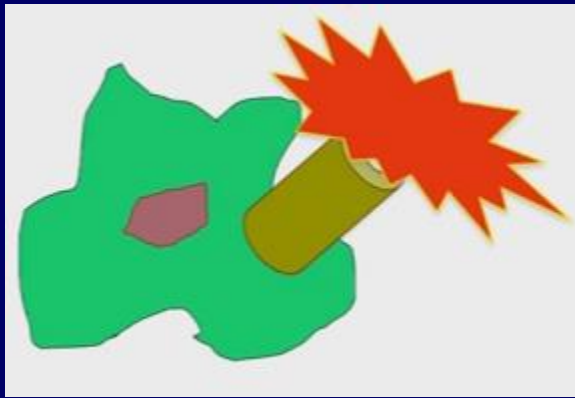
- Induce histamine and cytokines release from mast cells
- blood supply by binding to endothelial cells
- Attraction of additional inflammatory cell to the site of activation

2. Opsonization: (opsonin, C3b and C4b ) ( helps to eat microbes !!!!)

- Coating of bacteria enhances phagocytosis

### 3. Cause direct cell lysis

- Destruction of bacteria. (blasts holes in bacteria making them leak so die !!!)



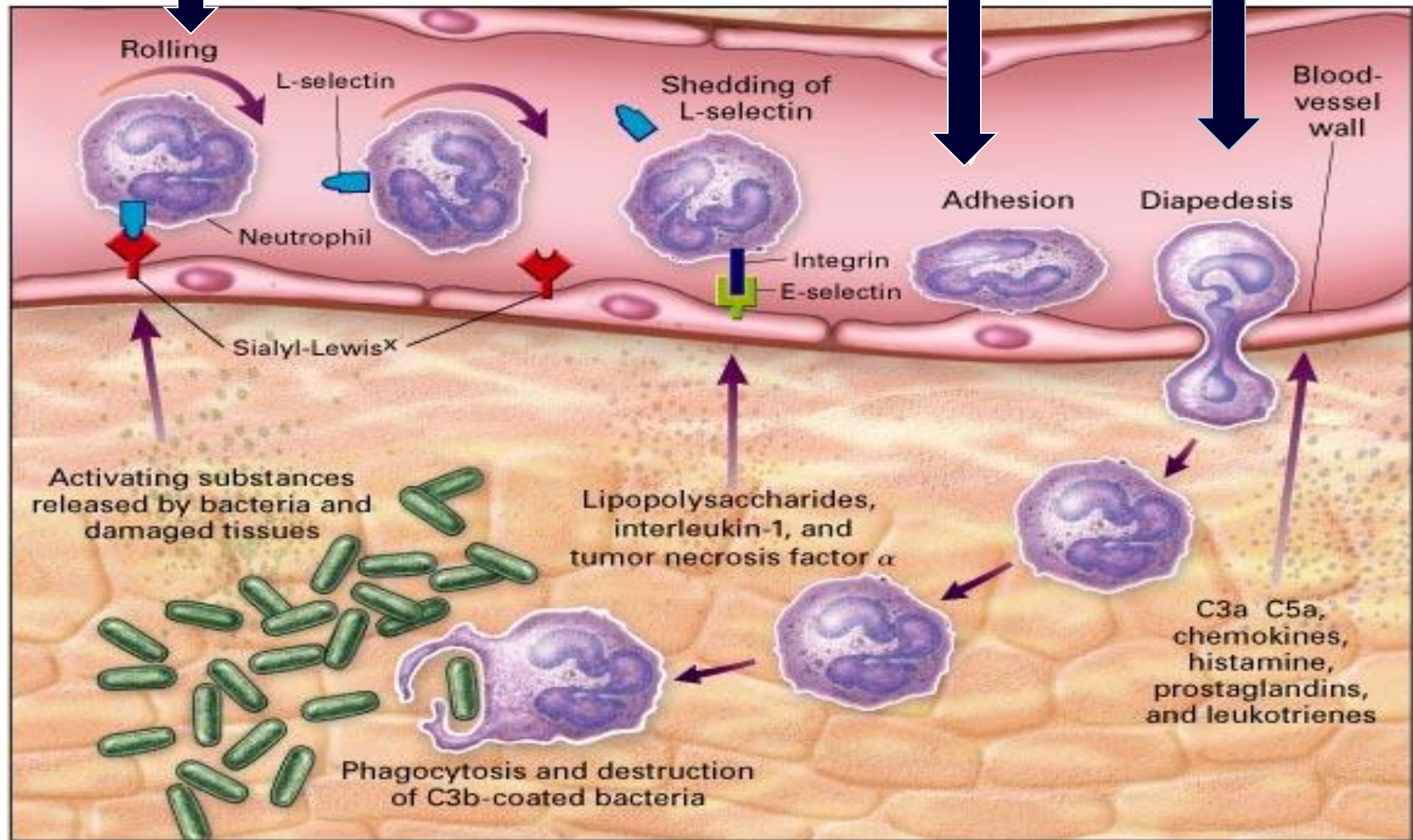


# Process of chemotaxis:

Rolling on vessel wall.

Adhesion (attach)

Pass through.



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

## Monocytes :

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

**Neutrophils:** (Phagocytic cells)

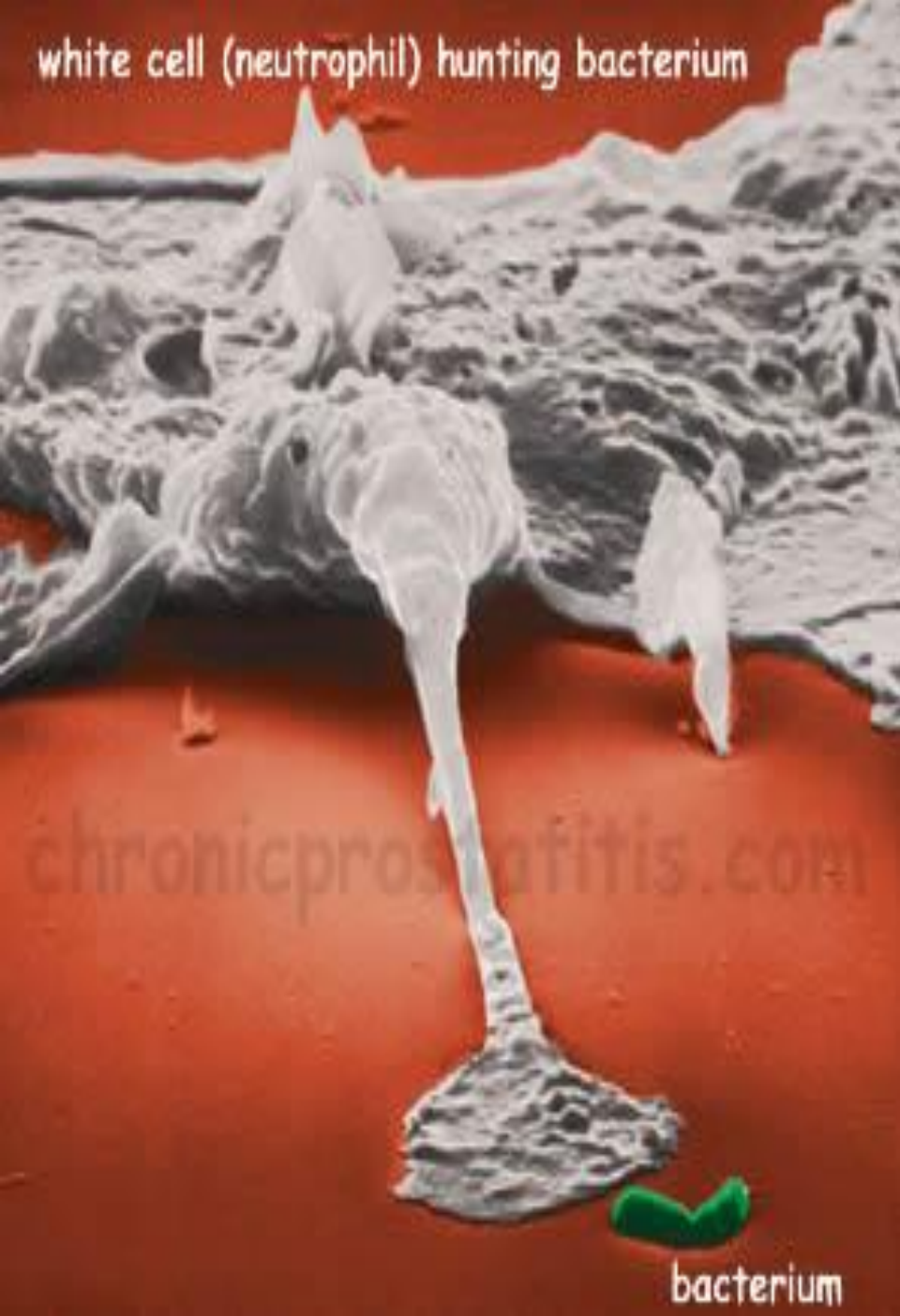
**Eosinophils:** (Allergy and Parasitic infections)

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



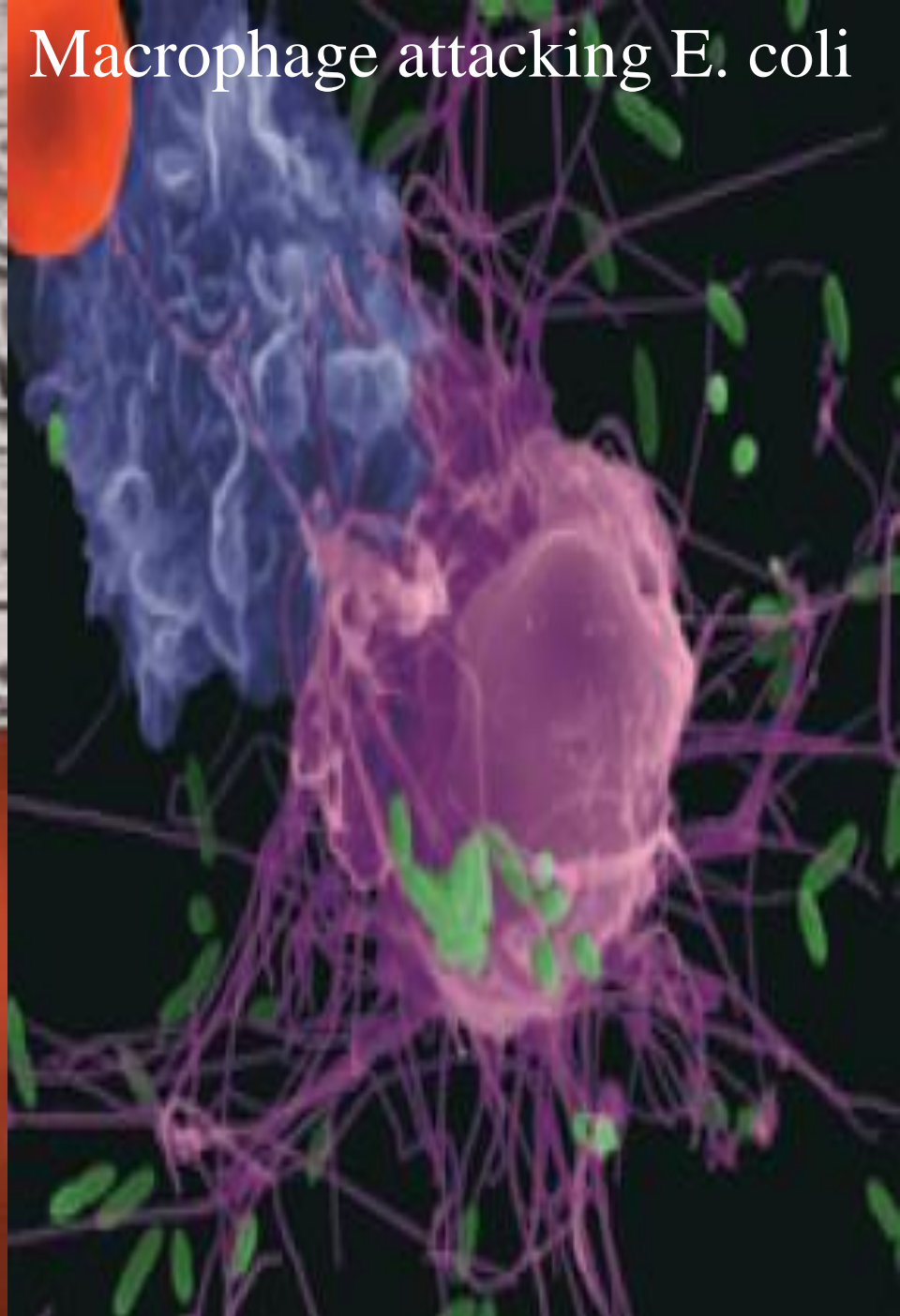
Phagocytic cells (neutrophils & macrophages) at site of infection start the process of **phagocytosis** which is the process by which a cell **engulf** a solid particle such as bacteria to form **internal vesicle** known as **phagosome**

white cell (neutrophil) hunting bacterium

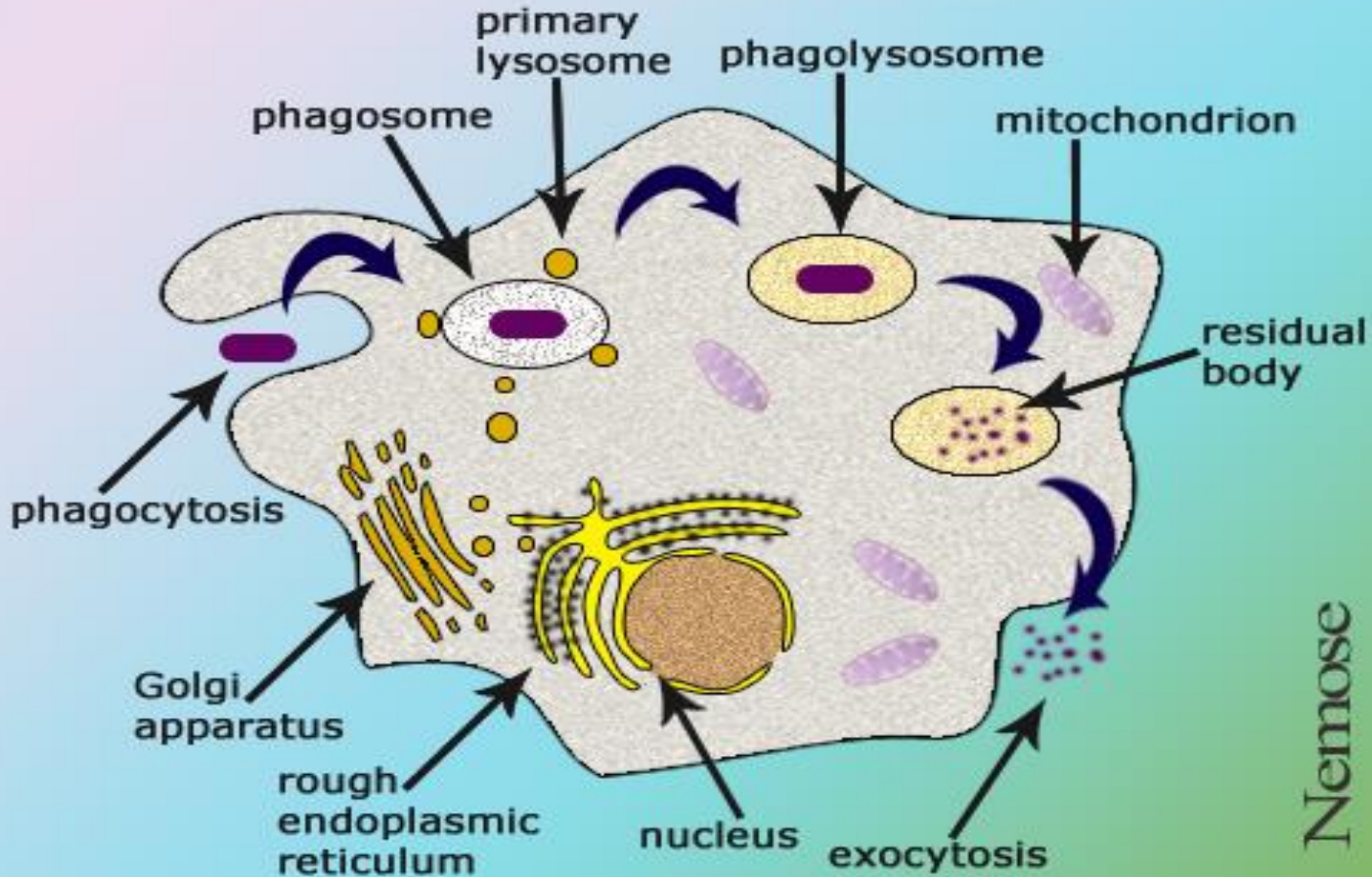


bacterium

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/ 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/ C reactive protein

- 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