Naturel Defense

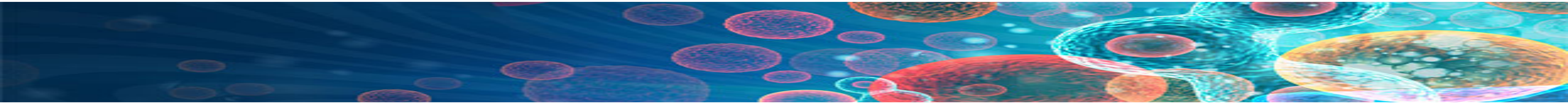
Objectives

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

2-Complement activation provides protection by killing pathogens

3-Accumulation of inflammatory cells important for clearance of infection

4-Cytokines as mediators regulate inflammation

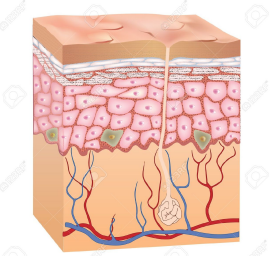


The main function of the immune system is to protect us from getting infected.

NONSPECIFIC DEFENSE MECHANISMS		SPECIFIC DEFENSE MECHANISMS (IMMUNE SYSTEM)
First line of defense	Second line of defense	Third 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 e.g.(skin/ mucous membranes).



- Mechanical e.g.(Coughing, sneezing, vomiting, action of cilia in trachea).

- Biochemical barriers e.g.(antimicrobial peptides, lung secretions, mucus, saliva, tears).

Physical

- Skin: impermeable to microbes.
- Mucous membranes lining the GIT, genitourinary and respiratory tracts.

Mechanical :

- Shedding of outer skin layers.
- Coughing and sneezing.
- Flushing (to dispose) of urine.
- Vomiting.
- Cilia in respiratory tract.

Biochemical barriers

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

INFLAMMATION

Inflammation is the first response of the immune system when there is an infection or irritation.

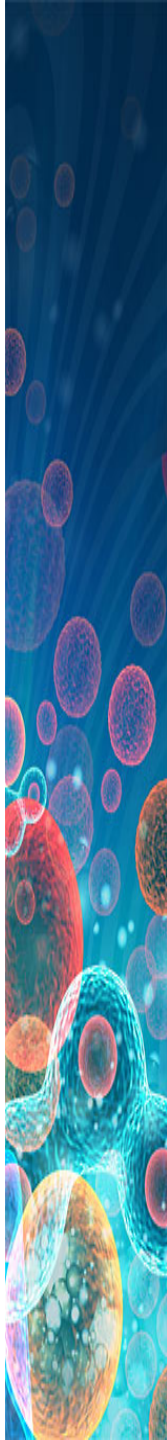
It consist of a series of vascular & cellular changes that occur in response to various stimuli.

e.g. infections, injury, radiation etc.

Microbial infections initiate inflammation.

Because bacteria have pro-inflammatory molecules like:

Lipopolysaccharides (LPS).



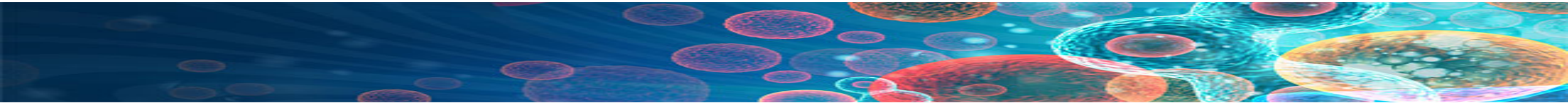
INFLAMMATION

The purpose of inflammation:

- To prevent and limit infections from causing further damage.
- To interact with adaptive immune system.

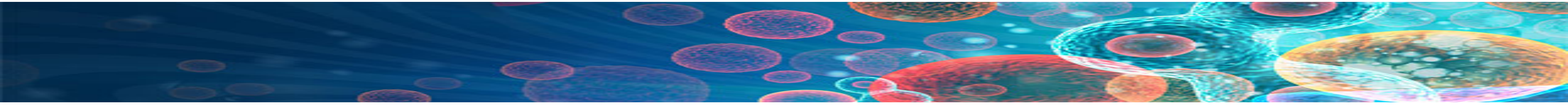
e.g. Monocytes / Macrophages serve as a link between the adaptive and innate immunity by antigen presenting cells .

- To prepare the area of injury for healing.



The Complement system

- Consist of a group of serum proteins that circulate in the blood and tissue fluids in an inactive form. Once they become activated they produce important biological effects that initiate inflammation.
- It plays an important role in linking Innate & Adaptive immunity.
- More than 20 proteins make up the complement system.
- Many are pro-enzymes or (pro-proteins).
- Initially inactive. They are sequentially activated in a cascade.
- (C3) is a Key protein, which is activated by C3 convertase.



Classical pathway: Requires antigen-antibody binding.

(C1,C4,C2,C3,C5,C6,C7,C8,C9) ← the sequence is based on the function's order.

FOR ILLUSTRATION:

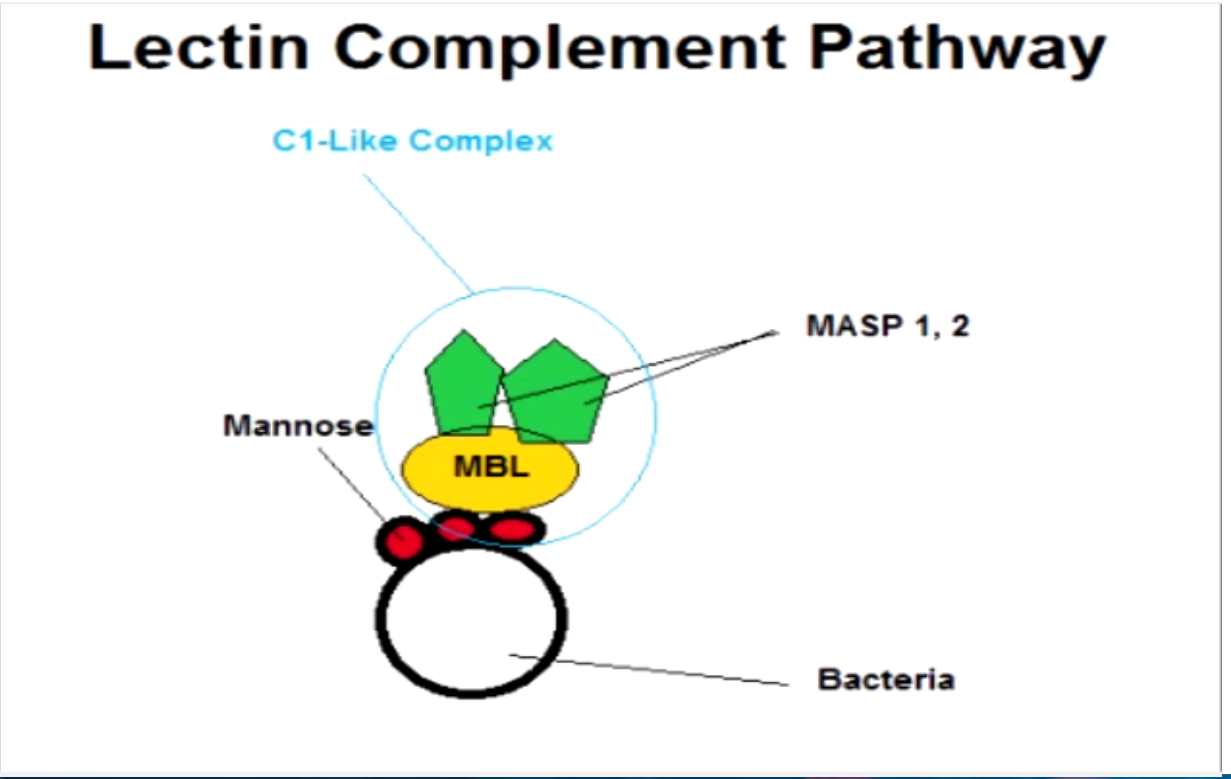
C1 binds to Antigen-Antibody complex → C4,C2 are cleaved by C1 → C4b,C2a binds together forming C3 convertase → C3 is cleaved by C3 convertase → C3b binds to C4bC2a forming C3/C5 convertase → C5 is cleaved by C3/C5 convertase → C5b binds with C6,C7,C8 forming the (membrane attack complex)→ C9 binds to membrane attack complex forming cylindrical pores in the bacterial membrane which disrupt both the ionic and osmotic balance across the membrane causing cell death.

* classical pathway video:
https://www.youtube.com/watch?v=tJJAyPWQ3fk

Lectin pathway: activated by mannan binding protein , binding mannose groups of bacterial carbohydrates.

(C4,C2,C3,C5,C6,C7,C8,C9) < same as classical but without C1 >

* No need for antigen-antibody complex. (like alternative)
* lectin pathway video https://www.youtube.com/watch?v=mgGgeaF-2co



Mannan = Mannose group

Mannose: sugar found on the microbial service. (acts like antigen).

MBL: Mannon Binding Lectin (protein) , a protein available in plasma.

MASP 1,2: mannose-binding lectin associated with serine protase, which helps in the cleavage of C4.

C1-like complex: it is the combination of MASP,MBL and Mannose, it has the same function as C1 in classical pathway but without the need of Antigen-Antibody complex.

Alternative pathway: Activated by bacterial products.

(C3,C5,C6,C7,C8,C9) ← the sequence is based on the function's order.

FOR ILLUSTRATION:

- It is the spontaneous cleavage of C3 in the plasma.
- The C3b combined with factor Bb forming anther type of C3 convertase .
- C3 is cleaved to C3b and C3a, C3b then combined with C3 convertase which consist of two (C3b)s and factor Bb to form C5 convertase and the sequence continue same as classic and lectin pathways.

Alternative pathway video:

https://www.youtube.com/watch?v=qga3Wn76d9w

Complement

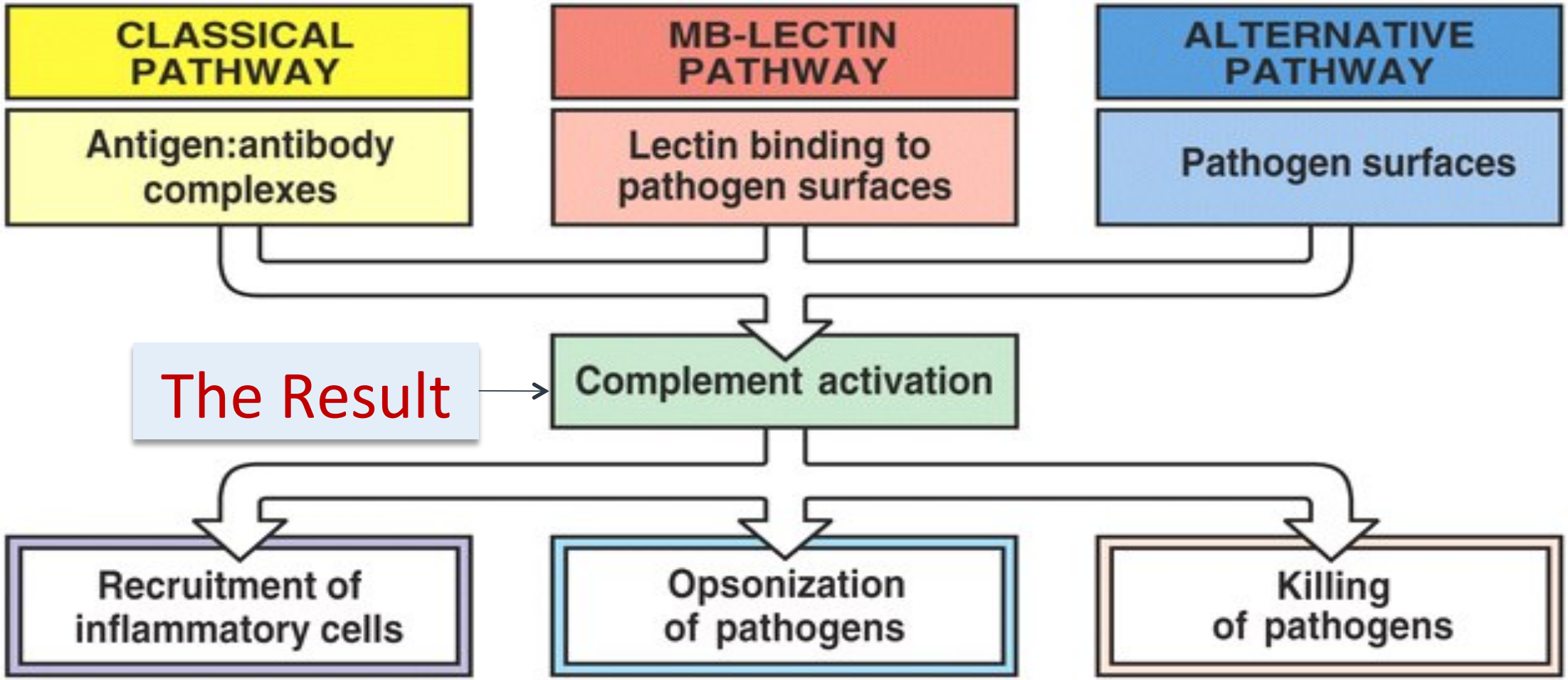
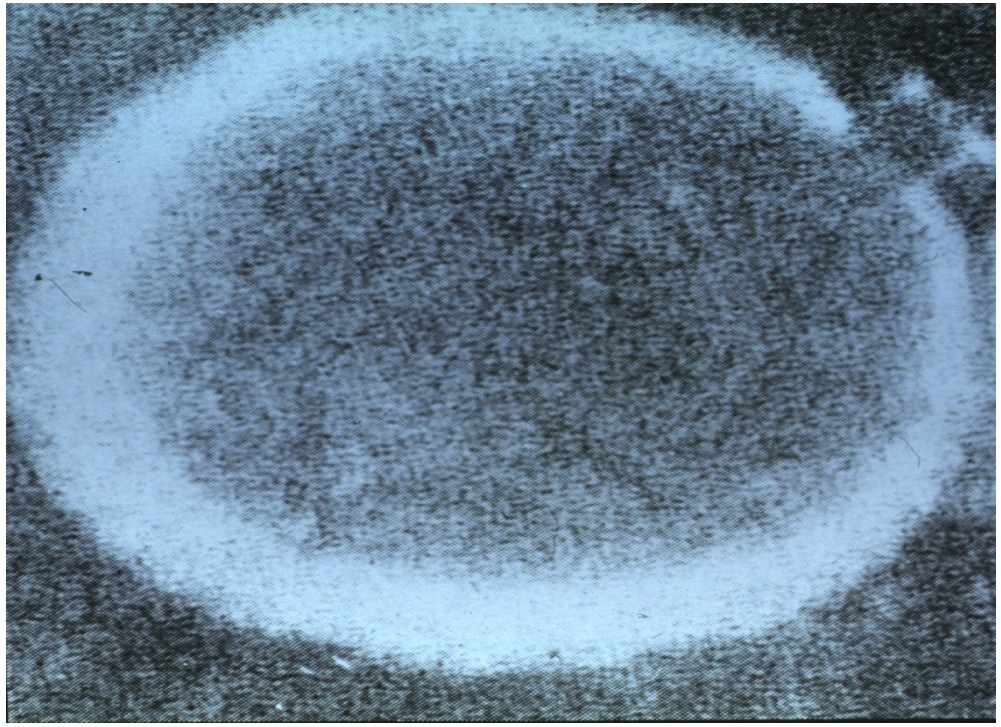
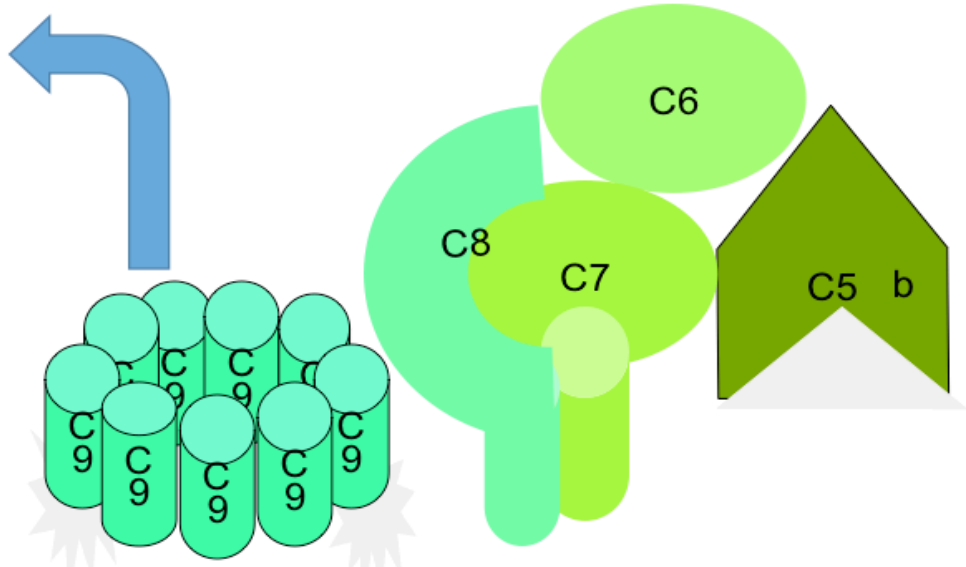


Figure 2-18 Immunobiology, 6/e. (© Garland Science 2005)

Membrane Attack Complex formation :

Insertion of lytic complex into cell membrane

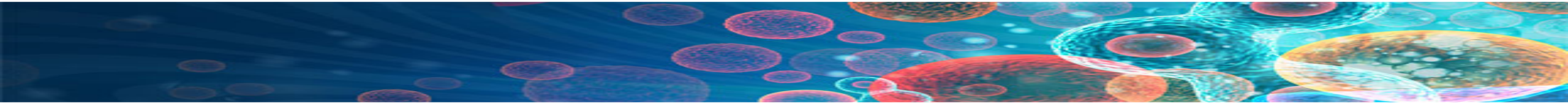




https://www.youtube.com/watch?v=E_fdPaBBPic

Biological effects of complement activation:

Anaphylatoxin (C3a, C5a)	Opsonization (opsonin, C3b)	Cause direct cell lysis
• Induce histamine release from mast cells. • Release chemotactic agents.	• Coating of bacteria enhances phagocytosis	• Destruction of bacteria



Bacterial recognition by complement

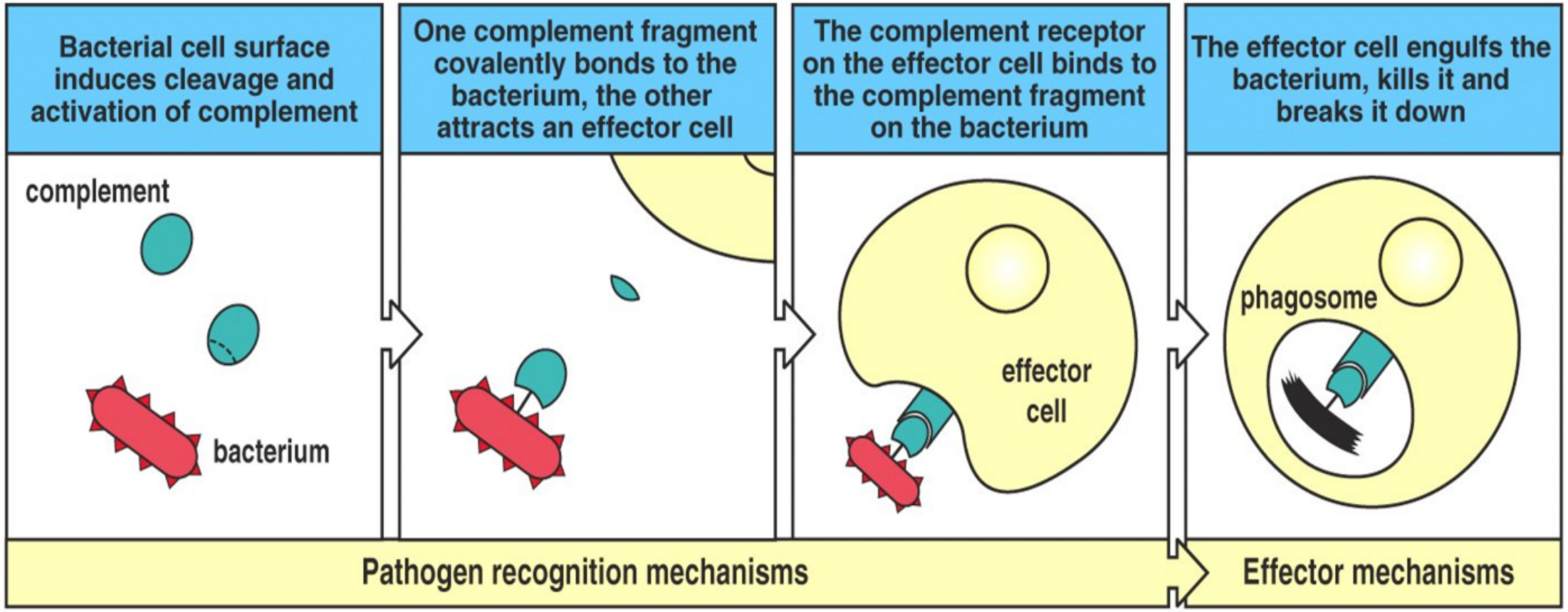
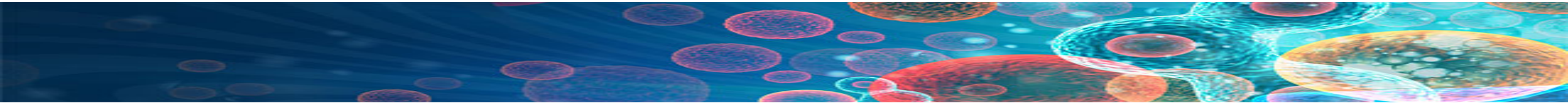


Figure 1-5 The Immune System, 2/e (© Garland Science 2005)

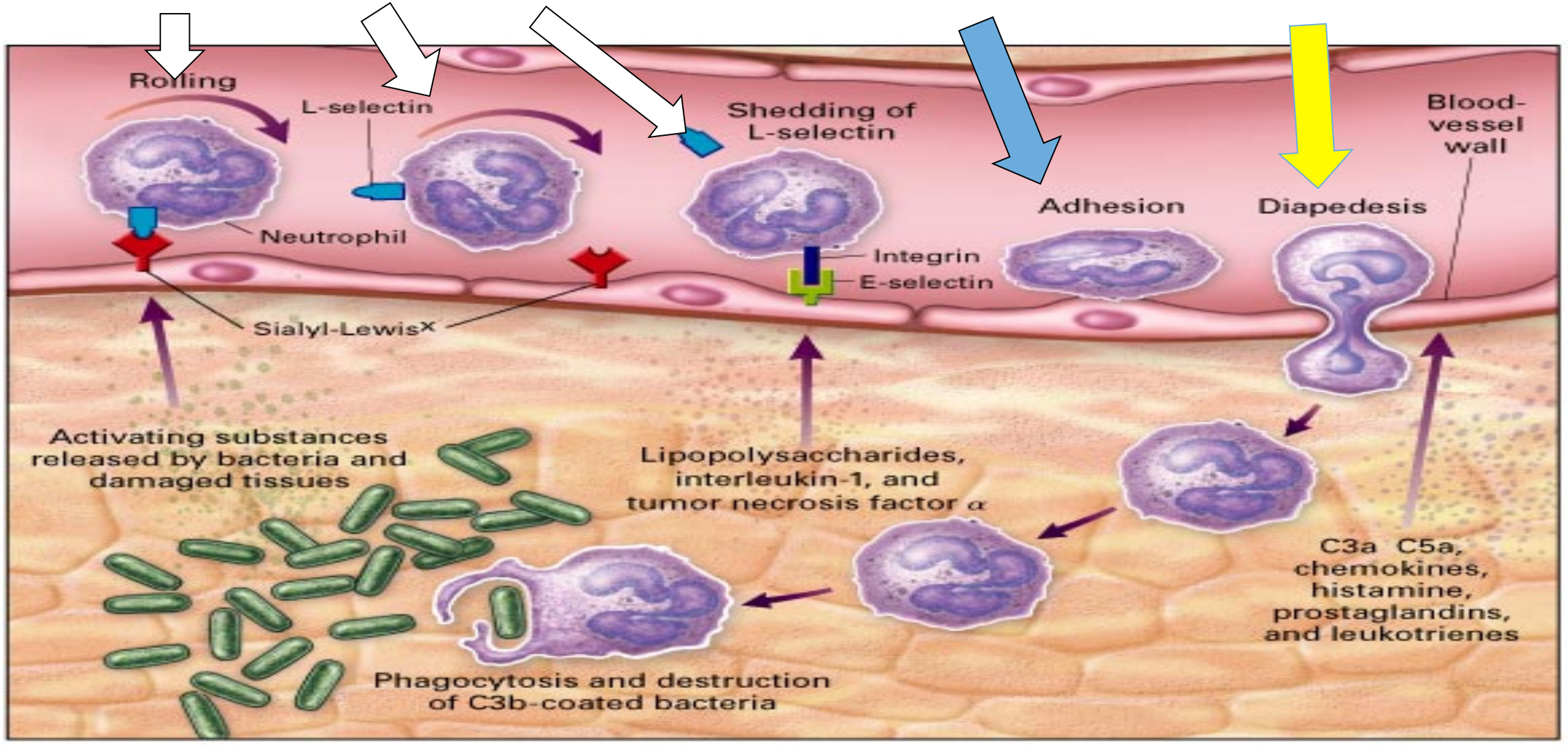
Types of Cells attracted to site of infection that mediate inflammation

Monocytes :	**become macrophages when they leave the blood and enter the tissues**
Neutrophils:	**(Phagocytic cells).**
Eosinophils:	**(Allergy and Parasitic infections).**
Natural Killer cells NK:	**(Kill tumor cells and virus infected cells).**



Process of chemotaxis :

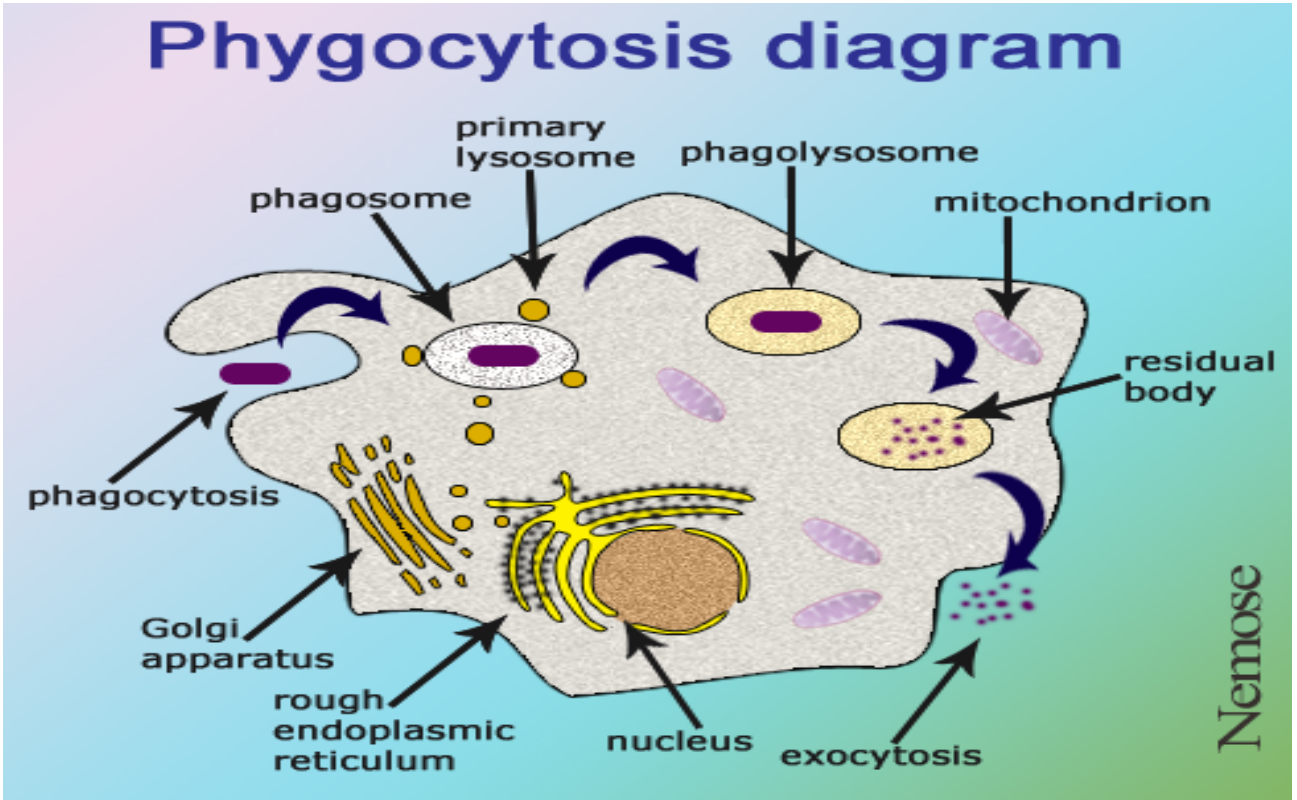
1-Rolling on vessel wall. 2-Adhesion (attachment). 3-Pass through.



Phagocytosis:

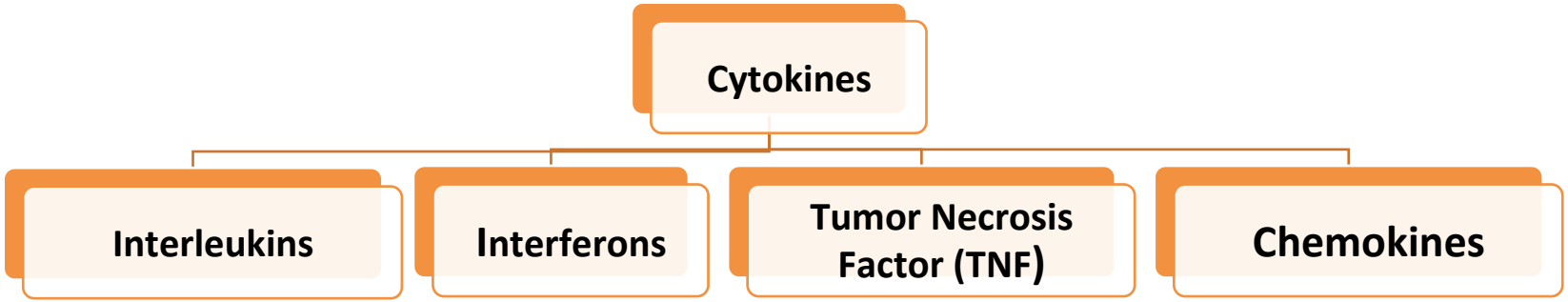
It is the process by which a cell ingests and destroys foreign material.

Phagocytic cells (neutrophils & macrophages) at site of infection start the process of phagocytosis



Cytokines:

- They are soluble molecules, produced by different cells, that control cell functions.
- Small Proteins (20-25 kD) that are released by cells and induce their effects by binding to specific receptors.



Interleukins:

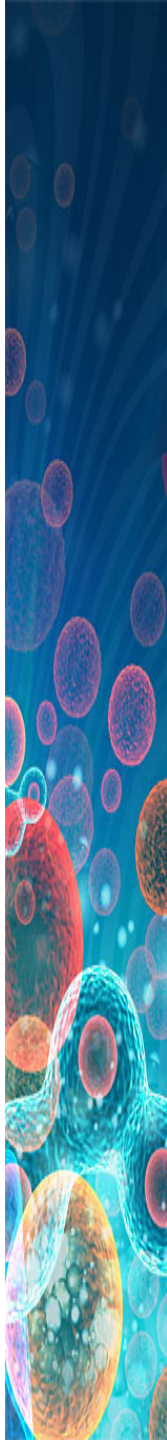
Produced in response to a pathogen primarily by macrophages and lymphocytes

Types of Interleukins :

- IL-1, IL-2, IL-3 .
- IL-1 inflammation :

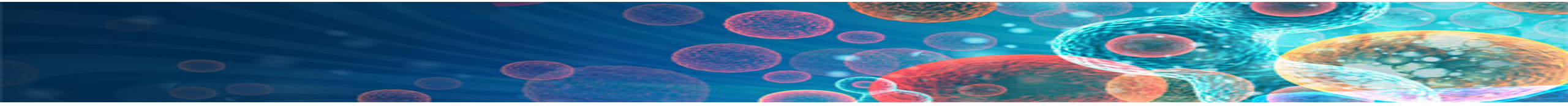
1) Inflammation (Increases vascular permeability).
2) Fever.
3) Production of IL-6.
4) Local tissue destruction.

- IL-6 induces fever, acute phase proteins.
- IL-12 activates NK cells, CD4 T cells .



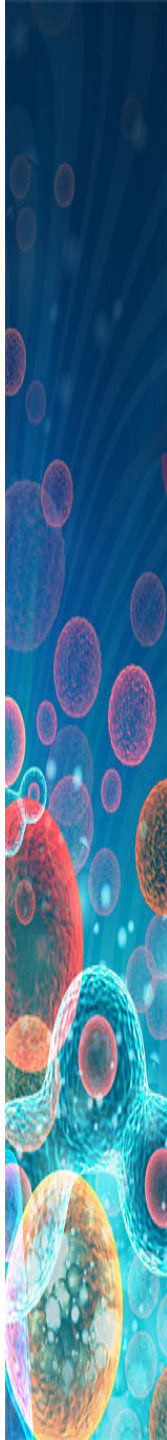
Cytokines

Interferons	• Protects against viral infections . • Produced and released by virally infected cells in response to viral infections.
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
Chemokines	• Class of cytokines with chemoattractant properties • Recruit cells to sites of infection • Interact with specific receptors • Related in amino acid structure • Example: CXC and CC



Summary

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



Thank you!

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