



Tikrit University
College of Veterinary Medicine

Lecture 2: Principal Components of Innate Immunity

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Lecturer name:

Assist.Prof.Dr. Agharid Ali Hussein

Prof.Dr.Bashar Sadeq Noomi

Academic Email:

agharidalrasheed@tu.edu.iq

vetbashae@tu.edu.iq



Lecturers link

Lecture 2: Principal Components of Innate Immunity

By Asssit. Prof. Dr. Agharid Ali Hussein

1. Types of Immunity

There are two major types of immunity:

1. Innate (Natural or Nonspecific) Immunity

This type of immunity is inherited from the parents and protects the organism from birth throughout life. It provides resistance to a broad range of microorganisms and foreign materials and lacks immunological memory.

2. Acquired (Adaptive or Specific) Immunity

This form of immunity develops after birth. It is specific, mediated by antibodies or lymphocytes, and capable of recognizing and remembering particular antigens.

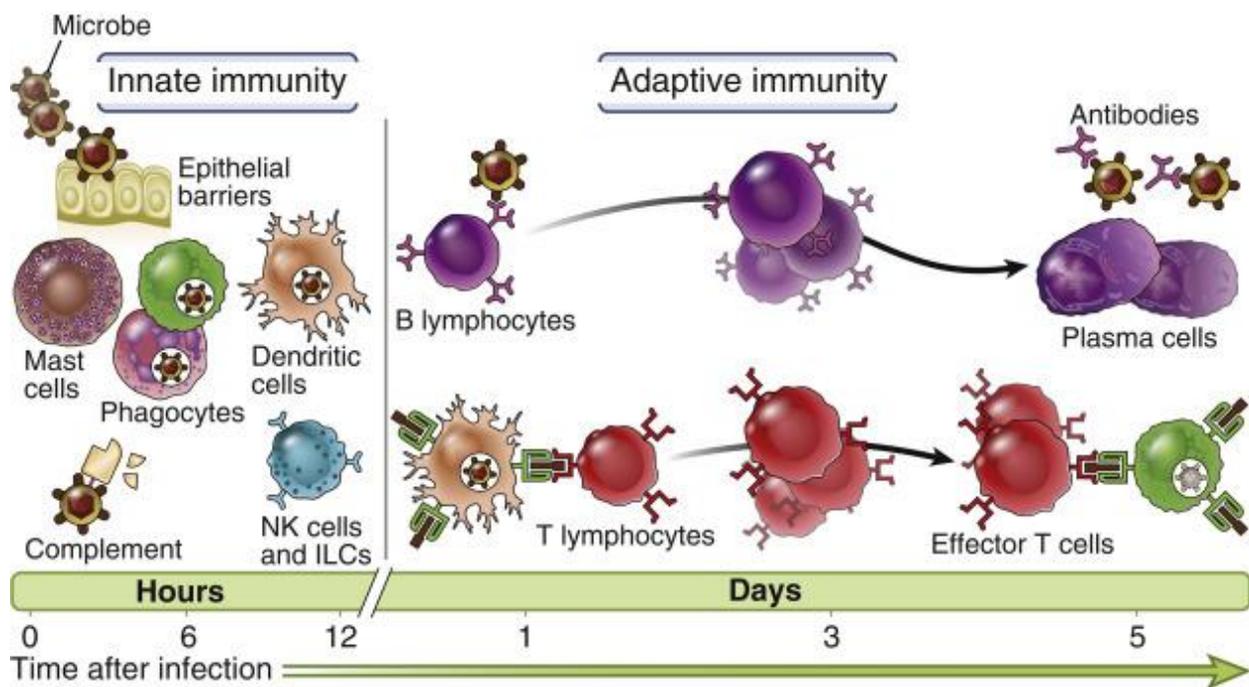


Figure: Coordination Between Innate and Adaptive Immunity Over Time

2. Innate Immunity Overview

Innate immunity has evolved across all multicellular organisms as a primary defense mechanism. It provides the first line of defense against infections and responds rapidly to pathogens. It can be influenced by factors such as age, sex, nutrition, hormones, and lifestyle.

The **principal components of innate immunity** include: - Physical and chemical barriers (skin, epithelial cells, tears, mucus, etc.) - Plasma protein mediators (acute-phase proteins, complement, cytokines) - Genetic factors - Inflammation - Temperature-dependent defenses - Cellular barriers (phagocytes, NK cells)

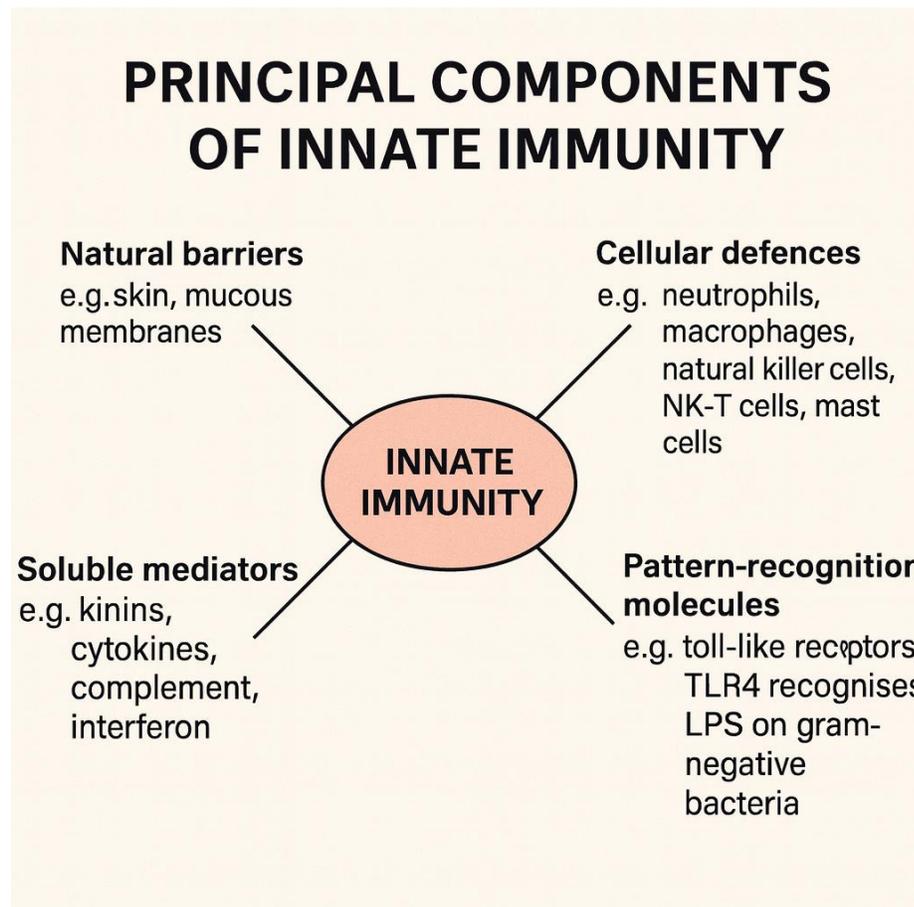


Figure 2: Principal Components of Innate Immunity

A. Physical and Chemical Barriers

These barriers prevent the attachment and entry of pathogens into the body.

- **Skin:** The stratum corneum and intercellular lipids form a tough barrier. Breaks in the skin allow pathogen entry.
- **Mucus and Cilia:** Trap and remove microbes in the respiratory tract.
- **Secretions:** Saliva, tears, urine, and gastric acid contain antimicrobial substances like lysozyme and acid.
- **Normal Flora:** Resident bacteria in the gut inhibit pathogenic microbes.

- **pH and Enzymes:** Stomach acid, bile salts, and ear wax create inhospitable environments for pathogens.

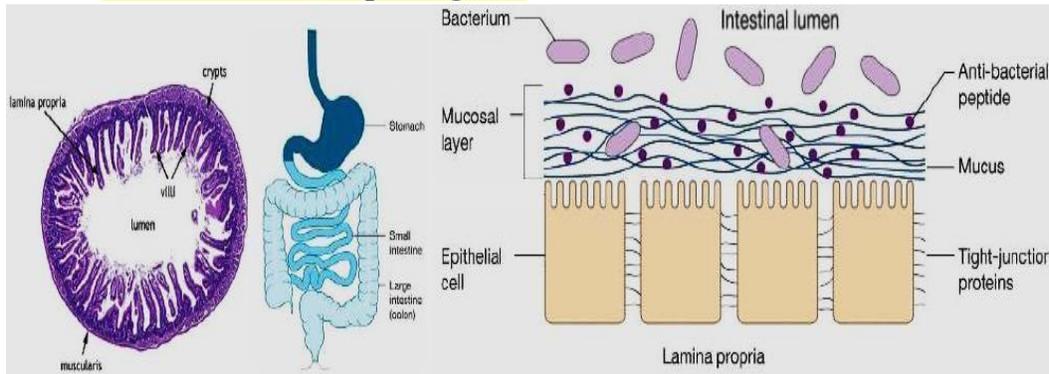


Figure 3: Structure and Innate Immune Defense of the Intestinal Mucosa

Organized by body system:

1. **Gastro-intestinal tract:**

The gastro-intestinal tract contains residential bacteria which not only help in digestion of certain polysaccharides (such as cellulose in herbivores) but also play an important role in the control of potential pathogens. The gastric pH may be sufficiently low to have an antimicrobial effect. In addition to antimicrobial peptides, lysozyme is synthesized in the gastric mucosa and in macrophages within the intestinal mucosa.

2. **Respiratory tract:**

A blanket of mucus gel produced by goblet cells lines the upper respiratory tract. The mucus contains soluble host defense molecules such as lysozyme, lactoferrin, surfactant proteins, and cationic peptides such as defensins and cathelicidins. Most microorganisms that enter the mucus layer are likely to be killed rapidly.

3. **Urogenital tract:**

The flow of urine and low pH provides the lumen of the urogenital tract with sufficient protection. The anaerobic degradation of glycogen upon the epithelial surface of genital organs by lactobacilli results in the production of lactic acid, which acts as a deterrent to pathogenic infection.

4. **Mammary glands:**

Milk contains bacterial inhibitors called lactenin. Lactenin includes complement, lysozyme, and iron-binding proteins such as lactoferrin and the lactoperoxidase enzyme.

B. Plasma Protein Mediators and Immune Molecules

I. Protein Mediators

These proteins circulate in the plasma and perform various immune functions.

1. Cytokines

Small proteins that mediate communication between immune cells as chemical messengers. They can act: - Autocrine (on the same cell) - Paracrine (on nearby cells) - Endocrine (on distant cells). Cytokine is a general name; other names include lymphokine (cytokines made by lymphocytes), monokine (cytokines made by monocytes), chemokine (cytokines with chemotactic activities that attract immune cells to infection sites), and interleukin (cytokines made by one leukocyte and acting on other leukocytes).

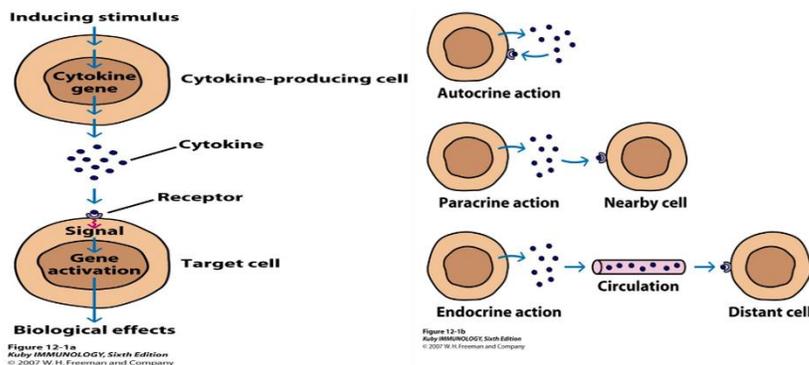


Figure 4: Cytokine Production and Modes of Action in Immune Signaling

2. Acute-Phase Proteins (APPs)

Produced mainly by the liver in response to cytokines like IL-1, IL-6, and TNF- α . Examples include: - **Positive APPs**: C-reactive protein, serum amyloid A, complement factors. - **Negative APPs**: Albumin and transferrin (decrease during inflammation).

3. Antimicrobial peptides (AMPs)

Antimicrobial peptides (AMPs) are important effector molecules in the innate immune response and are secreted mainly by innate and epithelial cells, including keratinocytes. Their antimicrobial activity is broad, acting against fungi, bacteria, and viruses. **Cathelicidin (LL-37)**: Released by neutrophils and epithelial cells, LL-37 disrupts microbial membranes and modulates immune responses. **Defensins**: Include α - and β -defensins. α -defensins (α D-1, -2, -3, -4) are stored in the azurophil granules of neutrophils, while α D-5

cationic proteins, and major basic protein. Once formed, these structures can bind and kill microbial pathogens by trapping them in a web-like structure that prevents dissemination and facilitates destruction.

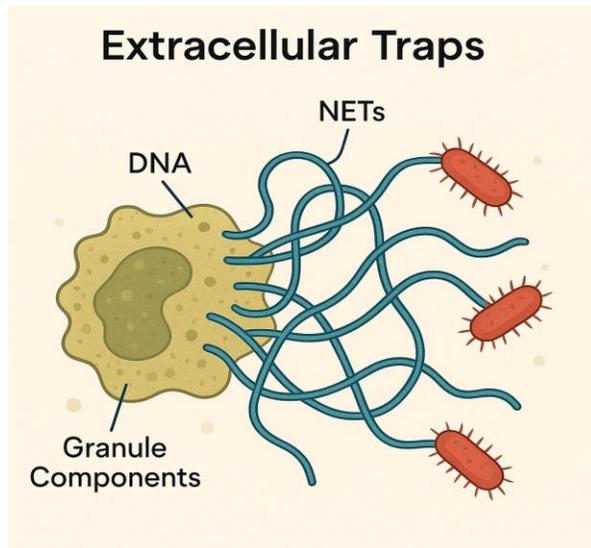


Figure 5. illustration of Extracellular Traps showing NETs capturing bacteria using DNA and granule components

C. Inflammation

Inflammation is the body's immediate protective response to injury or infection. It involves: - Increased blood flow and vascular permeability. - Migration of white blood cells (extravasation and diapedesis). - Release of cytokines, prostaglandins, and leukotrienes.

Cardinal signs of inflammation: - Redness (Rubor) - Heat (Calor) - Pain (Dolor) - Swelling (Tumor) - Loss of Function

Stages of Inflammation: 1. **Vasodilation:** Blood vessels expand, increasing flow to the affected area. 2. **Increased Permeability:** Plasma proteins and leukocytes exit the bloodstream. 3. **Leukocyte Migration:** White blood cells adhere to vessel walls (margination) and move into tissues (diapedesis). 4. **Phagocytosis:** Macrophages and neutrophils engulf and destroy pathogens. 5. **Resolution:** Anti-inflammatory cytokines (e.g., IL-10) downregulate the response to prevent tissue damage.

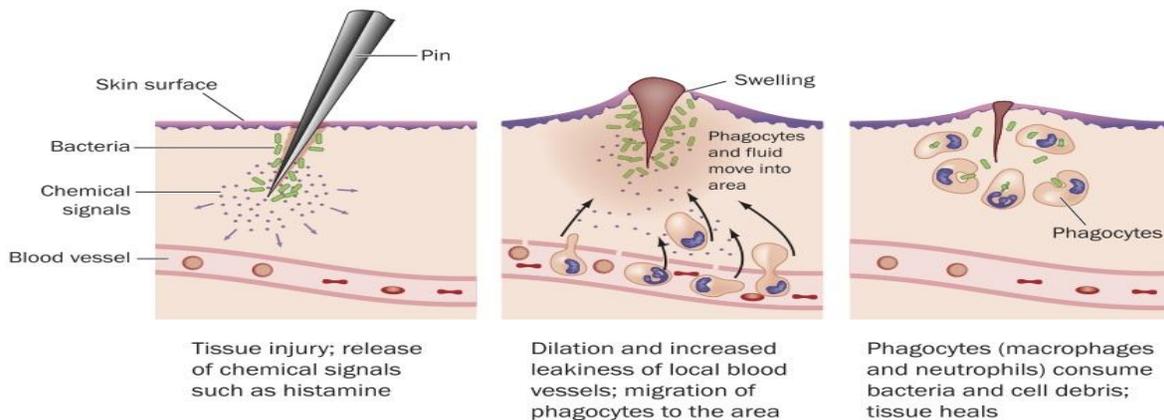


Figure 7: Diagram of Inflammation Process showing vasodilation, leukocyte migration, and phagocytosis.

Uncontrolled inflammation may result in chronic conditions, scarring, and tissue necrosis. Therefore, regulation by cytokines and immune checkpoints is vital.

D. Temperature-Dependent Innate Defense

Fever is a systemic response to infection that enhances immune activity. It results from: 1. **Exogenous pyrogens** (e.g., bacterial endotoxins) 2. **Endogenous pyrogens** (e.g., IL-1) acting on the hypothalamus.

Benefits of Fever: - Inhibits microbial growth. - Enhances immune cell activity. - Stimulates interferon production.

E. Recognition of Pathogens and Infected Cells

1. Pathogen Recognition

Cells detect **Pathogen-Associated Molecular Patterns (PAMPs)** using **Pattern Recognition Receptors (PRRs)** like Toll-like receptors (TLRs). This triggers cytokine release and immune activation.

2. Recognition of Infected Cells

Natural Killer (NK) cells detect cells that lack **MHC class I** molecules, a common sign of viral infection or cancer. NK cells then release **perforin** and **granzyme**, causing cell lysis.

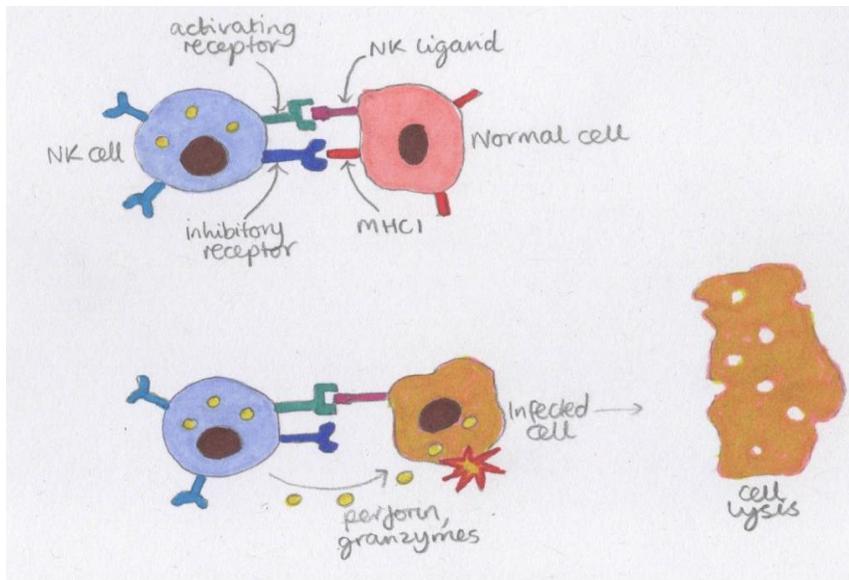


Figure 8: NK Cell Recognition Process showing inhibitory and activating receptors binding to healthy and infected cells.

F. Phagocytosis

Phagocytosis is the ingestion of pathogens by specialized immune cells such as macrophages and neutrophils. It bridges innate and adaptive immunity by displaying antigens on MHC class II molecules.

Steps of Phagocytosis:

- 1. Chemotaxis:** Phagocytes are attracted to infection sites by cytokines.
- 2. Adherence:** The phagocyte binds to the pathogen via pattern recognition receptors.
- 3. Ingestion:** The cell membrane engulfs the pathogen, forming a **phagosome**.
- 4. Digestion:** Lysosomes fuse with the phagosome, forming a **phagolysosome** where enzymes and reactive oxygen species digest the microbe.
- 5. Exocytosis & Antigen Presentation:** Debris is expelled, and antigen fragments are displayed on the phagocyte's surface (via MHC II) to activate T cells.

Mechanisms of Killing:

- **Oxygen-dependent:** Involves reactive oxygen and nitrogen intermediates (superoxide radicals, nitric oxide).
- **Oxygen-independent:** Involves lysosomal enzymes and antimicrobial peptides such as defensins.

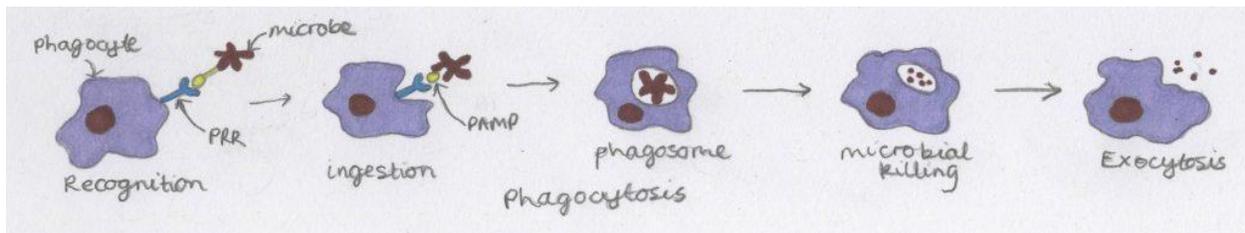


Figure9: Diagram of Phagocytosis showing stages from chemotaxis to antigen presentation.)

Phagocytosis not only clears pathogens but also activates adaptive immunity, making it a crucial bridge between the two systems.

Summary

The innate immune response is the body's rapid and non-specific defense system against pathogens. It acts through physical barriers, chemical mediators, inflammation, and immune cells such as macrophages and NK cells. Although it lacks memory, innate immunity is essential for survival and provides the foundation upon which adaptive immunity builds. Proper regulation ensures protection without harming the body's own tissues.