Introduction to Immunology

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Objectives

You should know:

• Differences between innate and adaptive immunity.
• How the innate immune system gets rid of microbes.
Why do we have an immune system?

Cancers

Infection
Key players

Front line defence
(Innate immunity)

Special task force
(Adaptive immunity)

Immune regulatory mechanisms
The immune response

<table>
<thead>
<tr>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
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<td>Initial defense</td>
<td>Develops later.</td>
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<td>React only to microbes and products of injured cells</td>
<td>Has the ability to ‘remember’</td>
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<td>React in the same way to repeated infections</td>
<td>Can react to a larger number of antigens</td>
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<td>Can distinguish against different, even closely related microbes and molecules.</td>
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Components of the innate immune system

- Barriers: skin, mucosal membranes
- Flushing mechanisms
- Antimicrobial peptides: defensins and cathelidins
- Circulating and tissue resident effector cells: phagocytes, innate like lymphoid cells, mast cells, eosinophils, basophils, dendritic cells
- Circulating effector proteins: acute phase proteins, complement
- Cytokines: interferons
Innate and adaptive immunity

**Innate immunity**
- rapid response
  - eosinophil
  - basophil
  - neutrophil
  - mast cell
  - natural killer cell
  - dendritic cell
  - macrophage

**Adaptive immunity**
- slow response
  - CD4⁺ T cell
  - natural killer T cell
  - CD8⁺ T cell
  - B cell

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Main functions of the innate immune system

1. Initial response to microbes: Prevents controls and eliminates infection. All invertebrates only have an innate immune system.

2. Eliminate of damaged cells and initiate tissue repair.

3. Stimulates the adaptive immune system and influences the type of adaptive immune response that develops in response to infection and damage.
What is meant by specificity?

- Dengue
- Measles
- Candida
- Streptococcus pyogenes
- Tetanus
- Cockroach
- Collagen IV
- House dust mite
Specificity and memory of adaptive immune response

- Antigen X
- Antigen X + Antigen Y

Serum antibody titer

- Activated B cells
- Memory B cells
- Naive B cells

Primary anti-X response
Primary anti-Y response
Secondary anti-X response

Weeks

© Elsevier. Abbas et al: Cellular and Molecular Immunology 6e - www.studentconsult.com
Cells of the innate immune system

Phagocytes: neutrophils, macrophages,
Granulocytes: eosinophils, basophils, neutrophil
Others: dendritic cells

Lymphocytes
Natural killer cells
Natural killer T cells
Innate lymphoid cells

Platelets
Phagocytes

The main phagocytes are neutrophils and macrophages.

Neutrophils circulate in the blood and the macrophages reside in tissues.

There are many other types of phagocytic cells in the liver, brain etc...
Dendritic cells

- the most important antigen presenting cells
- play a major role in presenting antigen to T cells and activating them
- They are the main link between the innate and the adaptive immune system
- are widely distributed in lymphoid tissue, mucosal epithelium and in organs.
Eosinophils

Host defence
- Pathogens: bacteria, viruses, fungi, parasites
  - Granules, Mitochondrial DNA traps

Cell activation
- Mast cell
- T cell
- Epithelial cell
  - Granules, Cytokines

Metabolic homeostasis
- AAMs
  - AAM differentiation, Glucose metabolism
- Adipose tissue

Immune response regulation
- Production of mediators, Antigen presentation

Tissue remodelling and repair
- Fibrosis, Cell death
  - Cardiac muscle, Epithelium in oesophagus and airway

Humoral immunity
- Plasma cell
  - High-affinity antibodies
Mast cells

Are found adjacent to small blood vessels in tissues.

Have receptors with high affinity for IgE antibodies.

Become activated when antigen binds to surface IgE.

Can also be activated directly by certain chemicals.

Play a major role in allergic responses.
Natural killer cells

Are a subset of lymphocytes that can kill target cells without prior activation.

They represent 5-12% of the circulating lymphocytes.

Important for defense against viruses, intracellular microorganisms and tumors.
Natural killer cells

Have activating and inhibitor receptors. When receptors are engaged the NK cells are not activated because the signals are balanced.

If the inhibitory signals are missing (down regulation of MHC class I molecules) or if there is an over expression of activating signals the NK cells are activated.
What happens during initial encounter with the enemy?
Steps of the Inflammatory Response

The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?

1. Damaged tissues release histamines, increasing blood flow to the area.

2. Histamines cause capillaries to leak, releasing phagocytes and clotting factors into the wound.

3. Phagocytes engulf bacteria, dead cells, and cellular debris.

4. Platelets move out of the capillary to seal the wounded area.
Diapedesis

Chemotaxis Migration

Phagocytosis Microbicidal mechanisms

Phagocytosis of apoptotic neutrophils

Kantari et al. 2008 Contrib Microbiol
Chemotactic factors

- Complement
- Chemicals released by injured cells
- Chemokines (chemicals released by leucocytes)
How does a neutrophil know that there is a bacterial invasion?
Pattern recognition receptors
Toll-like receptors (TLRs) - discovery lead to Nobel prize!
Pattern recognition receptors

- Toll-like receptors
- C-type lectins
- Scavenger receptors
- Nod like receptors
Initial cellular responses to stress by innate immune cells

Certain PRRs (NOD like receptors) form signaling complexes inside cells called inflammasomes.

The inflammasomes produce IL-1β and IL-18 in response to microbes and cellular stress.

Many environmental and microbe factors activate the inflammasome

Persistent activation leads to many disease processes
Effects of chronic Inflammasome activation

- Microbial Attack: PAMPs
- Sterile Attack: DAMPs

Inflammasomes:
- Lung: Asbestosis, COPD, Asthma
- Skin: Psoriasis, Allergy
- Brain: Alzheimer's Disease, Parkinson, Multiple Sclerosis, Prion
- Joints: Rheumatoid Arthritis, Gout
- Intestine: Inflammatory Bowel Disease
- Heart: Hypertension
- Metabolism: Artherosclerosis, Type II Diabetes
- Cancer: Mesothelioma, Hepatomas
Atherosclerosis and the inflammasome
Inflammasome and type 2 diabetes

IL1-β has profound cytotoxic effects on the beta cells of the pancreas and inhibitory functions on the islets. High glucose or free fatty acid found in type 2 diabetes can directly activate the inflammasome.
Summary

• The immune system plays a huge role in protecting against infection and cancers

• The cells of the innate immune system recognize pathogens by PRRs

• They are also activated by DAMPs

• The inflammasome is made up by a group of PRRs called the NOD like receptors

• They produce IL-1β and IL-18 which are potent mediators of inflammation and are responsible for the occurrence of many metabolic diseases