Lecture 1: Introduction to Immunology

Key Points:

- **Innate Immunity**
- **Acquired Immunity**
- **Endocytosis**
- **Phagocytosis**
- **Antigen Presentation**
- **Apotosis**
- **Inflammatory Response**
- **Cytokines**
- **Leukocytes (white blood cells)**
- **Lymphocytes (acquired immunity)**
- **NK-cells**
- **Class I MHC**

The defense of a host towards foreign bodies can be divided into Innate Immunity and Acquired Immunity.

Innate immunity is present continuously, it is a defense mechanism that is present from birth.

Acquired immunity is induced by the presence of foreign material and is usually quite specific. The fundamental properties of acquired immunity are:

1. Specificity
2. Adaptiveness
3. Discrimination between self and non-self
4. Memory

1. Innate Immunity:

1.1 Physical Barriers:

- skin acts as a physical barrier
- mucous membranes in the respiratory, gastrointestinal, urogenital tract trap bacteria which are subsequently removed by ciliated cells.

1.2 Physiological Barriers:

- acid pH on skin, in stomach, and in the urogenital tract inhibit bacterial growth
- detergent-like activity on skin (fatty acids from sebaceous glands), bile (small intestine) inhibit bacterial growth
- hydrolytic activity of lysozyme in saliva, tears, vaginal secretions destroys bacterial cell walls
- Interferons and complement are proteins that can be activated by infected/damage cells that participate in cell killing. Complement kills by forming pores in membranes.

1.3 Cellular Barriers:

- Ingestion of foreign material by cells leads to its destruction (primary outcome) *and* to the development of acquired immunity (secondary outcome). Phagocytes include leukocytes, macrophages, and dendritic cells.
- Modes of ingestion are:
  - *Pinocytosis*: ingestion of fluid surrounding cells
  - *Receptor-mediated endocytosis*: Molecules bound to membrane receptors is internalized.
  - *Phagocytosis*: Intact particles (e.g. bacteria) are internalized whole.
- *Receptor-mediated endocytosis & phagocytosis are an important step in the generation of acquired immunity.*
- *These processes are also facilitated by opsonination (e.g. coating of bacteria or virus with antibodies or other proteins (C-reactive Protein, see below)*

Cellular Fate of Ingested Material:

- In the case of pinocytosis and receptor-mediated endocytosis the ingested membrane vesicles first fuse with endosomes. The endosomes fuse with lysosomes to give secondary lysosomes.
- In the case of phagocytosis, the phagosome, containing the particle, fuses with lysosomes to give a phagolysosome.
- Killing occurs because the secondary lysozomes/phagolysosome contain hydrolytic enzymes, reactive oxygen species (e.g. superoxide anion, hydrogen peroxide), reactive nitrogen species (nitrous acid).
- Digested material is exocytosed out of the cell.
- A small number of peptides from the foreign substance bind to surface receptors. These **antigens** are *presented* on the surface of the cell by macrophages and dentritic cells.

1.4 Direct Cellular Killing: Natural-killer (NK) cells are lymphocytes that can recognize and destroy viral or cancerous cells. NK cells contact other cells. If the other cell appears to be abnormal (i.e. virally infected or cancerous) then the NK cell releases cytotoxic molecules that cause the abnormal cell to undergo apoptosis. NK cells respond to levels of **class I MHC** (major histocompatibility antigen) molecules on cell surface. Reduced levels in viral and cancerous cells result in killing.

- The target cell is made permeable by a pore-forming protein called perforin
- Apoptosis may be initiated by TNF-α (tumor necrosis factor α)

Apoptosis-programmed cell death without release of cellular contents.

- DNA degradation
- Cell fragments into apoptotic bodies that enclose intercellular contents
- Apoptotic bodies are rapidly removed by macrophages.

1.5 Inflammatory Response: This is an important response to cellular injury or infection. It has both a rapid innate phase as well as a prolonged phase that is an important component of acquired immunity.

Immediately after injury or infection a number of proteins are released. These lead to the physiological characteristics of inflammation: swelling, redness, heat, and last but not least, pain.

Acute phase proteins that are released are:

kinins	• cause contraction of muscles distal to the site, causing blood to back-up at the affected site, • cause vascular cells to contract and to express endothelial adhesion molecules. These allow cells in the blood stream to first attach to the capillaries and then enter the affected site, • simulate nerves, leading to pain.
Cytokines	• induce adhesion molecules, • increase vascular permeability, • attract leukocytes.
C-reactive protein	• Primes certain bacteria for destruction by the complement system.

The three major cytokines released from tissue macrophages are IL-1 (interleukin 1), TNF-α, IL-6. The roles of these proteins in the inflammatory response are listed below (from Kuby):

Effect		**IL-1**	**TNF-α**	**IL-6**
• Increased vascular permeability		+	+	+
• Increased adhesion molecules on endothelium		+	+	-
Acute-phase response				
• Platelet production		+	-	+
• Induce fever via hypothalamus		+	+	+
• Induce production of acute phase proteins:	C-reactive protein, fibrinogen (blood clotting)	+	+	+
• T and B cell activation		+	+	+
• Increased immunoglobulin synthesis		-	-	+

If the response persists for more than a few hours then macrophages and lymphocytes are recruited to the site. These cells aid in phagocytotic activity. Macrophages also are involved in presentation of foreign peptides to cells of the acquired immunity system, initiating the formation of antibodies against the infectious agent.