Immune System

- Immunity – the ability to resist disease
Innate Immunity

• Recognizes and destroys foreign stuff.
• Response does not require previous exposure.
• Barriers
• Cells and chemicals
Adaptive Immunity

- Recognizes and destroys foreign stuff

- Exhibits:
  - Specificity
  - Memory
  - Improvement
Barriers – Skin

- Awesome
- Stratified
- Keratinized
- Sweat
- Sebum
- Normal flora.
Barriers – Body Fluids
Barriers – Body Fluids – Lysozyme
Barriers – Mucosae

- Line the tracts
- Potential entrances
- Mucus
- Acid
- Lysozyme
- Normal flora.
Specific Example → Respiratory Mucosa

- Mucociliary escalator

- Other respiratory events
Nonspecific Cellular Defense – Neutrophils

• Small phagocytes.

• Kill bacteria

• First on the scene
Nonspecific Cellular Defense – Eosinophils

Eosinophils: Parasite-destroying cells

Cytotoxic chemicals

Parasitic worm

Eosinophil
Nonspecific Cellular Defense – Macrophages

- Large
- Derived from monocyes
- “Free” vs. “Fixed”
Phagocytosis

1. Phagocyte adheres to pathogens or debris.
2. Phagocyte forms pseudopods that eventually engulf the particles forming a phagosome.
3. Lysosome fuses with the phagocytic vesicle, forming a phagolysosome.
4. Lysosomal enzymes digest the particles, leaving a residual body.
5. Exocytosis of the vesicle removes indigestible and residual material.
• Phagocytosis is more likely if the microbe is tagged.
Natural Killer Cells

• Specialized type of lymphocyte.

• Attack and kill infected cell/tumor cells…

• How do they know?
Interferons

- Synthesizes enzymes that interfere with viral replication
- Normal cell
- Infected cell
- NK cell (causes apoptosis)
- IFN
- Macrophage (phagocytizes infected cell)
- Perforin
- Granzymes
- Apoptosis
Complement System

- Plasma proteins.
- Made by...
- Activated by...
Complement: Chemotaxis & Opsonization

- Macrophage
- Pathogen
- Complement
- C
Activated Complement Proteins → Bind to → Releasing...

Local resistance will...

Local blood flow will...

Causes local vaso...

Causes capillary permeability to...

Inflammation
Complement: Lysis

Pathogen

Pore of membrane attack complex

Complement proteins

Water and ions enter cell

H₂O and ions

Cell swells and lyses
Inflammation

• Occurs whenever…

• Benefits:
  – Prevents…
  – Disposes...
  – Sets the stage...

• 4 classic signs
What body cells release inflammatory chemicals?
Inflammatory chemicals cause:

- Vessel diameter
- Capillary permeability to...
- Pain

Capillary blood flow and fluid loss to:

- Heat
- Redness
- Access to damaged area for cells, chemicals
- Swelling
- Loss of function

Access to damaged area for cells, chemicals:
Fever

• Systemic
• Body T°...

• When is it good?
• When is it bad?
Adaptive Immune System

- Specific
- Systemic
- Memory
- Improvement
Antigen-Presenting Cells

Macrophages, dendritic cells, and B lymphocytes
Formation and docking of MHC class II molecules in an APC (e.g., dendritic cell, macrophage, B-lymphocytes): Cells that engulf microbes through phagocytosis:

1. MHC class II molecules are synthesized by the RER of the APC.
2. MHC class II molecules are shipped by the endomembrane system through the Golgi apparatus to the plasma membrane.
3. During the process of phagocytosis and destruction of an exogenous antigen, vesicles containing digested peptide fragments merge with vesicles containing MHC class II molecules; the foreign antigen binds with MHC class II molecules within the vesicles.
4. MHC class II molecules and foreign antigen are displayed within the plasma membrane.
Primary lymphatic structure responsible for maturation of T-lymphocytes

Primary lymphatic structure responsible for production of lymphocytes

Red bone marrow

Pre-T-lymphocytes

Thymus

Naive immunocompetent B-lymphocytes

Naive immunocompetent T-lymphocytes (both helper and cytotoxic T-lymphocytes)
T Lymphocytes

- Immunocompetence
- Response
- Self-Tolerance
T-lymphocytes: Cells of cell-mediated immunity

Each cell has approximately 100,000 receptors.

- Helper T-lymphocyte
- Cytotoxic T-lymphocyte

- CD4 protein
- CD8 protein
- TCR
B Lymphocytes

- Immunocompetence
- Self-Tolerance
- Response
Lymphocytes

• More than a million different varieties.

• Where do newly immunocompetent cells migrate?
2 Components of Adaptive Immunity

• Antibody-mediated immunity.
  • Deals with extracellular pathogens.
  • A.k.a. humoral immunity
  • B lymphocytes and plasma cells

• Cell-mediated immunity.
  • Deals with intracellular pathogens.
  • Killer T cells (Cytotoxic T cells)
Helper T Cells “Control” Adaptive Immunity

• *Where were helper T cells born?*

• *Where did they mature?*

• *What is on their surface?*
Activating Helper T Cells

First stimulation:
- CD4 binds with MHC class II molecule of APC; TCR interacts with antigen within MHC class II molecule.

Second stimulation:
- Helper T-lymphocyte releases IL-2, which stimulates the helper T-lymphocyte.

Activated helper T-lymphocyte proliferates and differentiates to form a clone of activated and memory helper T-lymphocytes.
Infection

Effector response of helper T-lymphocytes

Activated helper T-lymphocyte

Cytokines (e.g., IL-2)

Synthesis and release of various cytokines (e.g., IL-2) regulate the cells of the immune system (both adaptive and innate).
B Cell Primary Response

1. First stimulation: Free antigen binds to BCR; B-lymphocyte engulfs and presents antigen to activated helper T-lymphocyte.

2. Second stimulation: IL-4 released from activated helper T-lymphocyte stimulates B-lymphocyte.

Activated helper T-lymphocyte

- CD4
- TCR

Activated B-lymphocyte proliferates and differentiates to form a clone of plasma cells and memory B-lymphocytes.

Memory B-lymphocytes

Activated B-lymphocyte

- MHC II with antigen

Antigen is presented with MHC class II molecules.

Plasma cells produce antibodies.

Antibodies

Naive B-lymphocyte

Antigen

BCR

Antigen cross-links BCRs

First stimulation:
Free antigen binds to BCR; B-lymphocyte engulfs and presents antigen to activated helper T-lymphocyte.
Antibodies

- Specific immune proteins.
- Released by plasma cells
- A.k.a. immunoglobulins, gamma globulins, or Ig’s.
### Antibody Action

**Neutralization**
- Antibody covers biologically active portion of microbe or toxin.

**Agglutination**
- Antibody cross-links cells (e.g., bacteria), forming a "clump."

**Precipitation**
- Antibody cross-links circulating particles (e.g., toxins), forming an insoluble antigen-antibody complex.

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Exposed Fc portion following antigen binding by antibody promotes:

- Complement fixation
  - Fc region of antibody binds complement proteins; complement is activated.

- Opsonization
  - Fc region of antibody binds to receptors of phagocytic cells, triggering phagocytosis.

- Activation of NK cells
  - Fc region of antibody binds to an NK cell, triggering release of cytotoxic chemicals.

[Diagram showing the interactions of antibody with various cells and molecules, including Bacterium, Antigen, Complement, Fc region of antibody, and Phagocyte.]
Primary vs. Secondary B Cell Response

- **Primary response**
  - Lag phase
  - Serum antibody titer vs. Days from first exposure to antigen
  - IgM and IgG peaks

- **Secondary response**
  - Serum antibody titer vs. Days from reexposure to same antigen
  - IgG peak
  - IgM peak
B Cell Immunity

• Natural or Artificial.

• Active or Passive.
B Cell Immunity

- Natural or Artificial.

- Active or Passive.
Smallpox and Variolation
Autism

No Correlation

Vaccines
Cell-Mediated Immunity

• What is the big limitation of antibodies?

• Cell-mediated immunity will deal with intracellular pathogens (as well as cancerous cells).

• Killer T cells
MHC class I molecules are synthesized by the RER. During production, peptide fragments of the cell (self-antigens) bind with the MHC class I molecules.

Transport vesicles are produced from the RER that contain MHC class I molecules with bound self-antigen. They are shipped by the endomembrane system through the Golgi apparatus to the plasma membrane.

MHC class I molecules with bound self-antigen are displayed within the plasma membrane following fusion of the secretory vesicles with the plasma membrane.
**Infected Cells and MHC I Proteins**

Formation and docking of MHC molecules in an unhealthy cell (e.g., viral-infected cell)

1. Proteasome digests protein of viral particles.
2. Peptide fragments of viral particles attach to MHC class I molecules.
3. Transport vesicles contain MHC class I molecules with foreign antigen.

MHC class I molecules with bound foreign antigen are displayed within the plasma membrane following fusion of the secretory vesicles with the plasma membrane.

Proteins of viral particles (or other microbes) are digested by proteasomes into peptide fragments; peptide fragments are taken up into the RER.

1. As MHC class I molecules are synthesized by the RER, peptide fragments of the viral particle (foreign antigen) become attached to MHC class I molecules.
2. Transport vesicles are produced from the RER that contain MHC class I molecules with viral peptide fragments. They are shipped by the endomembrane system through the Golgi apparatus to the plasma membrane.
3. MHC class I molecules with bound foreign antigen are displayed within the plasma membrane following fusion of the secretory vesicles with the plasma membrane.
Activating Killer T Lymphocytes

1. First stimulation: CD8 binds with MHC class I molecule of infected cell; TCR interacts with antigen within MHC class I molecule.

2. Second stimulation: IL-2 released from activated helper T-lymphocyte stimulates the cytotoxic T-lymphocyte.

Activated cytotoxic T-lymphocyte proliferates and differentiates to form a clone of activated and memory cytotoxic T-lymphocytes.
Killer T Cell Killing

Activated cytotoxic T-lymphocyte

Perforin and granzymes

Perforin

Granzymes

Abnormal cell (e.g., infected cell, tumor cell, transplanted cell)

Apoptosis of abnormal cell

Release of cytotoxic chemicals induces apoptosis of abnormal cells.
Regulatory T Cells

• Release cytokines that…

• What could happen if they weren’t around?