Immune / Lymphatic System

Fighting the Enemy Within!

lymphocytes attacking cancer cell

phagocytic leukocyte

lymph system
Avenues of attack

- **Points of entry**
  - digestive system
  - respiratory system
  - urogenital tract
  - break in skin

- **Routes of attack**
  - circulatory system
  - lymph system
Why an immune system?

- **Attack from outside**
  - lots of organisms want you for lunch!
  - animals are a tasty nutrient- & vitamin-packed meal
    - cells are packages of macromolecules
  - animals must defend themselves against invaders *(pathogens)*
    - viruses
      - HIV, flu, cold, measles, chicken pox
    - bacteria
      - pneumonia, meningitis, tuberculosis
        - Lyme disease
    - fungi
      - yeast ("Athlete’s foot"…)
    - protists
      - amoeba, malaria

- **Attack from inside**
  - cancers = abnormal body cells

Mmmmm, What’s in your lunchbox?
Lymph system
Production & transport of leukocytes
Traps foreign invaders

lymph vessels
(intertwined amongst blood vessels)
Development of Red & White blood cells

Pluripotent stem cells (in bone marrow)

- Lymphoid stem cells
- Myeloid stem cells

Red blood cells

- Lymphocytes
  - B cells
  - T cells

Erythrocytes

- Platelets
- Leukocytes
  - Monocytes develop into macrophages
  - Neutrophils short-lived phagocytes 60-70% WBC
  - Basophils
    - inflammatory response
  - Eosinophils
    - fight parasites

- Macrophages
Lines of defense

- **1st line:** Non-specific barriers
  - broad, external defense
    - “walls & moats”
  - skin & mucous membranes
- **2nd line:** Non-specific patrols
  - broad, internal defense
    - “patrolling soldiers”
  - leukocytes = phagocytic WBC
- **3rd line:** True immune system
  - specific, acquired immunity
    - “elite trained units”
  - lymphocytes & antibodies
    - B cells & T cells

Bacteria & insects inherit resistance. Vertebrates acquire immunity.
**Non-specific External defense**

- **Barrier**
  - skin

- **Traps**
  - mucous membranes, cilia, hair, earwax

- **Elimination**
  - coughing, sneezing, urination, diarrhea

- **Unfavorable pH**
  - stomach acid, sweat, saliva, urine

- **Lysozyme enzyme**
  - digests bacterial cell walls
  - tears, sweat
Non-specific patrolling cells

- Patrolling cells & proteins
  - Attack pathogens, but don’t “remember” for next time
    - **leukocytes**
      - Phagocytic white blood cells
      - Macrophages, neutrophils, natural killer cells
    - **complement system**
      - Proteins that destroy cells
    - **inflammatory response**
      - Increase in body temp.
      - Increase capillary permeability
      - Attract macrophages
Leukocytes: Phagocytic WBCs

- Attracted by chemical signals released by damaged cells
  - ingest pathogens
  - digest in lysosomes
- **Neutrophils**
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- **Macrophages**
  - “big eater”, long-lived
- **Natural Killer Cells**
  - destroy virus-infected cells & cancer cells
Natural Killer Cells perforate cells

- release **perforin** protein
- insert into membrane of target cell
- forms pore allowing fluid to flow in & out of cell
- cell ruptures (lysis)

- **apoptosis**
Anti-microbial proteins

- **Complement system**
  - ~20 proteins circulating in blood plasma
  - attack bacterial & fungal cells
    - form a **membrane attack complex**
    - perforate target cell
    - **apoptosis**
      - cell lysis

![Diagram showing complement proteins forming a cellular lesion and attacking a bacterial cell]
Inflammatory response

- Damage to tissue triggers local non-specific inflammatory response
  - release chemical signals
    - histamines & prostaglandins
  - capillaries dilate, become more permeable (leaky)
    - delivers macrophages, RBCs, platelets, clotting factors
      - fight pathogens
      - clot formation
  - increases temperature
    - decrease bacterial growth
    - stimulates phagocytosis
    - speeds up repair of tissues
Fever

- When a local response is not enough
  - system-wide response to infection
  - activated macrophages release **interleukin-1**
    - triggers **hypothalamus in brain** to readjust body thermostat to raise body temperature
  - higher temperature helps defense
    - inhibits bacterial growth
    - stimulates phagocytosis
    - speeds up repair of tissues
    - causes liver & spleen to store iron, reducing blood iron levels
      - bacteria need large amounts of iron to grow
3rd line: Acquired (active) Immunity

- Specific defense with memory
  - lymphocytes
    - B cells
    - T cells
  - antibodies
    - immunoglobulins

- Responds to...
  - antigens
    - cellular name tags
      - specific pathogens
      - specific toxins
      - abnormal body cells (cancer)
How are invaders recognized?

- **Antigens**
  - cellular name tag proteins
    - “self” antigens
      - no response from WBCs
    - “foreign” antigens
      - response from WBCs
      - pathogens: viruses, bacteria, protozoa, parasitic worms, fungi, toxins
      - non-pathogens: cancer cells, transplanted tissue, pollen
Lymphocytes

- **B cells**
  - mature in **bone marrow**
  - **humoral response system**
    - “humors” = body fluids
    - attack pathogens still circulating in blood & lymph
  - produce antibodies

- **T cells**
  - mature in **thymus**
  - **cellular response system**
    - attack invaded cells

- **“Maturation”**
  - learn to distinguish “self” from “non-self” antigens
    - if react to “self” antigens, cells are destroyed during maturation
B cells

- Attack, learn & remember pathogens circulating in blood & lymph
- Produce specific **antibodies** against specific **antigen**
- Types of B cells
  - **plasma cells**
    - immediate production of antibodies
    - rapid response, short term release
  - **memory cells**
    - continued circulation in body
    - long term immunity
Antibodies

- **Proteins that bind to a specific antigen**
  - multi-chain proteins
  - binding region matches molecular shape of antigens
  - each antibody is unique & specific
    - millions of antibodies respond to millions of foreign antigens
  - tagging “handcuffs”
    - “this is foreign...gotcha!”

Each B cell has ~50,000 antibodies.
Structure of antibodies

- **Light chains**
- **Heavy chains**
- **Antigen-binding site**
- **Variable region**

B cell membrane
What do antibodies do to invaders?

- **Neutralize**: Neutralization (blocks viral binding sites; coats bacteria and/or opsonization)
- **Capture**: Agglutination of antigen-bearing particles, such as microbes
- **Precipitate**: Precipitation of soluble antigens
- **Apoptosis**: Complement fixation (activation of complement)

**Invading pathogens** tagged with antibodies lead to enhanced phagocytosis by macrophages, which results in cell lysis.

*Diagram shows visual representations of virus, bacterium, phagocytosis, and apoptosis.*
Classes of antibodies

- **Immunoglobulins**
  - **IgM**
    - 1st immune response
    - activate complement proteins
  - **IgG**
    - 2nd response, major antibody circulating in plasma
    - promote phagocytosis by macrophages
  - **IgA**
    - in external secretions, sweat & mother’s milk
  - **IgE**
    - promote release of histamine & lots of bodily fluids
    - evolved as reaction to parasites
    - triggers allergic reaction
  - **IgD**
    - receptors of B cells???
B cell immune response

invader (foreign antigen)

memory cells “reserves”

captured invaders

macrophage

plasma cells release antibodies

tested by B cells (in blood & lymph)

B cells + antibodies

recognition

clones 1000s of clone cells

10 to 17 days for full response

B cell immune response"
Vaccinations

- Immune system exposed to harmless version of pathogen
  - stimulates B cell system to produce antibodies to pathogen
    - “active immunity”
  - rapid response on future exposure
  - creates immunity without getting disease!
- Most successful against viruses
Jonas Salk

- Developed first vaccine
  - against polio
    - attacks motor neurons

1914 – 1995
April 12, 1955

Albert Sabin
1962
oral vaccine
Polio epidemics

1994: Americas polio free
Passive immunity

- Obtaining antibodies from another individual
  - maternal immunity
    - antibodies pass from mother to baby across placenta or in mother’s milk
    - critical role of breastfeeding in infant health
      - mother is creating antibodies against pathogens baby is being exposed to
  - Injection
    - injection of antibodies
    - short-term immunity
What if the attacker gets past the B cells in the blood & actually infects (hides in) some of your cells?

You need trained assassins to recognize & kill off these infected cells!

Attack of the Killer T cells!

But how do T cells know someone is hiding in there?
How is any cell tagged with antigens?

- **Major histocompatibility (MHC) proteins**
  - proteins which constantly carry bits of cellular material from the cytosol to the cell surface
  - “snapshot” of what is going on inside cell
  - give the surface of cells a unique label or “fingerprint”

Who goes there? self or foreign?
How do T cells know a cell is infected?

- Infected cells digest some pathogens
  - MHC proteins carry pieces to cell surface
    - foreign antigens now on cell membrane
    - called **Antigen Presenting Cell (APC)**
      - macrophages can also serve as APC
    - tested by Helper T cells
T cells

- Attack, learn & remember pathogens hiding in infected cells
  - recognize antigen fragments
  - also defend against “non-self” body cells
    - cancer & transplant cells

- Types of T cells
  - helper T cells
    - alerts rest of immune system
  - killer (cytotoxic) T cells
    - attack infected body cells
  - memory T cells
    - long term immunity
**T cell response**

**APC:**
- infected cell

**helper T cell**
- recognition

**APC:**
- activated macrophage

**helper T cell**
- recognition

**interleukin 1**

**killer T cell**
- activate killer T cells
- stimulate B cells & antibodies

**clones**
Attack of the Killer T cells

- Destroys infected body cells
  - binds to target cell
  - secretes **perforin** protein
    - punctures cell membrane of infected cell
      - apoptosis

Killer T cell binds to infected cell

infected cell destroyed

Killer T cell

vesicle

cell membrane

cell membrane

target cell

Killer T cell

perforin

punctures cell membrane
## Immune system & Blood type

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<th>antigen on RBC</th>
<th>antibodies in blood</th>
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Matching compatible blood groups is critical for blood transfusions. A person produces antibodies against foreign blood antigens.
**Immune response**

- **Skin**
  - Pathogen invasion
  - Antigen exposure

- **Free antigens in blood**
  - Humoral response
    - B cells
      - Plasma B cells
      - Memory B cells
      - Antibodies

- **Antigens on infected cells**
  - Cellular response
    - T cells
      - Memory T cells
      - Cytotoxic T cells

- **Macrophages (APC)**
  - Alert
    - Helper T cells
HIV & AIDS

- **Human Immunodeficiency Virus**
  - virus infects **helper T cells**
    - helper T cells don’t activate rest of immune system: killer T cells & B cells
    - also destroys helper T cells

- **AIDS: Acquired ImmunoDeficiency Syndrome**
  - infections by opportunistic diseases
  - death usually from “opportunistic” infections
    - pneumonia, cancers
Immune system malfunctions

- **Auto-immune diseases**
  - immune system attacks own molecules & cells
    - lupus
      - antibodies against many molecules released by normal breakdown of cells
    - rheumatoid arthritis
      - antibodies causing damage to cartilage & bone
    - diabetes
      - beta-islet cells of pancreas attacked & destroyed
    - multiple sclerosis
      - T cells attack myelin sheath of brain & spinal cord nerves

- **Allergies**
  - over-reaction to environmental antigens
    - allergens = proteins on pollen, dust mites, in animal saliva
    - stimulates release of histamine