**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
  - no cell wall
  - traded mobility for susceptibility
  - animals must defend themselves against invaders
    - viruses
    - HIV, flu, cold, measles, chicken pox, SARS
    - bacteria
    - pneumonia, meningitis, tuberculosis
    - fungi
    - yeast (“Athlete’s foot…”)
    - protists
    - amoeba, Lyme disease, malaria
- **Attack from inside**
  - defend against abnormal body cells = cancers

**Lymph system**
- **Production & transport of leukocytes**
- **Traps foreign invaders**
- **Development of Red & White blood cells**
  - **Lymphoid stem cells**
  - **Pluripotent stem cells (in bone marrow)**
  - **Myeloid stem cells**
  - **Erythrocytes**
  - **Monocytes**
  - **Neutrophils**
  - **B cells**
  - **T cells**
  - **Thrombocytes**
  - **Inflammatory response**
  - **Infected body**
- **Lines of defense**
  - **1st line: Barriers**
    - broad, **external** defense
    - skin & mucus membranes
  - **2nd line: Non-specific patrol**
    - broad, **internal** defense
    - “patrolling soldiers”
    - leukocytes = phagocytic WBC
    - macrophages
  - **3rd line: Immune system**
    - specific, **acquired immunity**
    - “elite trained units”
    - lymphocytes & antibodies
      - B cells & T cells
1st line: External defense
- Physical & chemical defenses
  - non-specific defense
- External barrier
  - epithelial cells & mucus membranes
    - skin
    - respiratory system
    - digestive system
    - uro-genital tract

Lining of trachea: ciliated cells & mucus secreting cells

1st line: Chemical barriers on epithelium
- Skin & mucous membrane secretions
  - sweat
    - pH 3-5
  - tears
    - washing action
  - mucus
    - traps microbes
  - saliva
    - anti-bacterial = "lick your wounds"
  - stomach acid
    - pH 2
  - anti-microbial proteins
    - lysozyme enzyme
      - digests bacterial cell walls

2nd line: Internal, broad range patrol
- Innate, general defense
  - rapid response
- Patrolling cells & proteins
  - attack invaders that penetrate body’s outer barriers
    - leukocytes
      - phagocytic white blood cells
    - complement system
    - anti-microbial proteins
    - inflammatory response

Leukocytes: Phagocytic WBCs
- Attracted by chemical signals released by damaged cells
  - enter infected tissue, engulf & ingest microbes
    - **Lysosomes** digest pathogens once engulfed
- **Neutrophils**
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- **Macrophages**
  - “big eater”, long-lived
- **Natural Killer Cells**
  - destroy virus-infected cells & cancer cells

Phagocytes
- Macrophage
- Yeast

Destroying cells gone bad!
- Natural Killer Cells perforate cells
  - release **perforin** protein
  - insert into membrane of target cell
  - forms pore allowing fluid to flow into 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
    - complement proteins form cellular lesion
    - extracellular fluid
    - plasma membrane of invading microbe
    - bacterial cell

Inflammatory response

- Damage to tissue triggers local non-specific inflammatory response
  - release histamines & prostaglandins
  - capillaries dilate, more permeable (leaky)
    - increase blood supply
    - delivers WBC, RBC, platelets, clotting factors
    - fight pathogens
    - clot formation
    - accounts for swelling, redness & heat of inflammation & infection

Inflammatory response

- Reaction to tissue damage
  - Pin or splinter
  - Bacteria
  - Chemical alarm signals
  - Blood vessel
  - Blood clot
  - Swelling
  - Phagocytes

Fever

- When a local response is not enough
  - systemic 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
  - lymphocytes
    - B lymphocytes (B cells)
    - T lymphocytes (T cells)
  - antibodies
    - immunoglobulins
- Responds to...
  - antigens
    - Surface glycoproteins
    - specific pathogens
    - specific toxins
    - abnormal body cells (cancer)

How are invaders recognized: antigens

- Antigens
  - proteins that serve as cellular name tags
    - foreign antigens cause response from WBCs
      - viruses, bacteria, protozoa, parasitic worms, fungi, toxins
      - non-pathogens: pollen & transplanted tissue
  - B cells & T cells respond to different antigens
    - an “immune response”
      - B cells recognize intact antigens
        - pathogens in blood & lymph
      - T cells recognize antigen fragments
        - pathogens which have already infected cells
  - “self”
  - “foreign”
**Lymphocytes**

- **B cells**
  - mature in bone marrow
  - **humoral** response system
    - “humors” = body fluids, concentrated in lymph nodes and spleen after maturing
    - produce antibodies

- **T cells**
  - mature in thymus
  - **cellular** response system
  - Learn to distinguish “self” from “non-self” antigens during maturation
    - if they react to “self” antigens, they are destroyed during maturation

**Antibodies**

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

**Structure of antibodies**

- Each B cell has ~100,000 antigen receptors

**How antibodies work**

- Binding of antibodies to antigens inactivates antigens by:
  - Neutrophils
  - Phagocytosis
  - Complement

**Classes of antibodies**

- **Immunoglobulins**
  - IgM
    - 1st immune response
    - activate complement proteins
  - IgG
    - 2nd response, major antibody circulating in plasma
    - promote phagocytosis by macrophages
    - Most common, can pass placental barrier
  - 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?? Function unclear—found in blood
B cell immune response

- Tested by B cells (in blood & lymph) + antibodies
- Memory cells reserve response
- Captured invaders
- Plasma cells release antibodies in clones

1° vs 2° response to disease

- Memory B cells allow a rapid, amplified response with future exposure to pathogen

How do vertebrates produce millions of antibody proteins, if they only have a few hundred genes coding for those proteins?

By DNA rearrangement & somatic mutation, vertebrates can produce millions of B & T cells

Immune system exposed to harmless or weakened version of pathogen
- Triggers artificial active immunity
- Stimulates immune system to produce antibodies to invader
- Rapid response if future exposure

Most successful against viral diseases

The Polio Vaccine

- Developed first mass-administered vaccine in USA
- Against polio
- Attacks motor neurons

1914 – 1995

- April 12, 1955

Jonas Salk

The Polio Vaccine

- 1962

oral vaccine

Hilary Koprowski

1950–1954

vaccine

Albert Sabin

1994

oral vaccine

Polio epidemics

- 1979: last domestic outbreak
- 1994: America is 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 some of your cells?
You need trained assassins to kill off these infected cells!

T cells
- Cell-mediated response
  - Immune response to infected cells
    - Viruses, bacteria & parasites (pathogens) within cells
    - Defense against “non-self” cells
      - Cancer & transplant cells
- Types of T cells
  - Helper T cells
    - Alerts immune system
  - Killer (cytotoxic) T cells
    - Attack infected body cells

How are cells tagged with antigens
- Major histocompatibility (MHC) proteins
  - Antigen glycoproteins
  - MHC proteins 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”
    - “Antigen presentation”

How do T cells know a cell is infected
- Infected cells digest pathogens & MHC proteins bind & carry pieces to cell surface
  - Antigen presenting cells (APC)
  - Alerts helper T cells

T cell response
- Infected cell
- Helper T cell
  - Interleukin 1
  - Activates macrophage
- Helper T cell
  - Interleukin 2
  - Activates killer T cells
- Killer T cell
  - Interleukin 2
  - Activates B cells & antibodies
  - Stimulates B cells
**Attack of the Killer T cells**

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

**Blood type**

<table>
<thead>
<tr>
<th>Blood type</th>
<th>Antigen on RBC</th>
<th>Antibodies in blood</th>
<th>Donation status</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>AB</td>
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<tr>
<td>O</td>
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<td></td>
</tr>
</tbody>
</table>

Matching compatible blood groups is critical for blood transfusions. A person produces antibodies against foreign blood antigens.

**Blood donation**

<table>
<thead>
<tr>
<th>Blood group</th>
<th>Genotype</th>
<th>Antigen present in blood serum</th>
<th>Results from adding red blood cells from groups below to serum from groups at left</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>p^a p^a  or p^A p^A</td>
<td>Anti-B</td>
<td><img src="image" alt="Blood donations" /></td>
</tr>
<tr>
<td>B</td>
<td>p^b p^b  or p^B p^B</td>
<td>Anti-A</td>
<td><img src="image" alt="Blood donations" /></td>
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<td></td>
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<td>O</td>
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