Immune system and Cancer
Overview

1. Innate (nonspecific) defense system
   a. surface barriers
   b. internal defenses

2. Adaptive (specific) defense systems
   a. humoral immunity
   b. cellular immunity

3. Cancer
Innate (nonspecific) defense

Surface Barriers

Skin

- keratin - resists weak acids and bases, bacterial enzymes and toxins
- pH 3-5: inhibits bacterial growth
- lipids in sebum are toxic to bacteria
- dermcidin in sweat - toxic to bacteria
Innate (nonspecific) defense
Surface Barriers

Mucous membranes
- Saliva and tears: lysozyme - enzyme that destroys bacteria
- mucus in digestive and respiratory tracts capture bacteria
- stomach acidity and enzymes kill bacteria
- vaginal secretion acidity inhibits bacterial growth
Innate (nonspecific) defense

Internal defenses

- phagocytes
- NK cells
- inflammation
- antimicrobial proteins
- fever
Innate (nonspecific) defense

Internal defenses - phagocytes

- macrophages (WBCs)
- neutrophils (WBCs)
- microglia (brain)
Innate (nonspecific) defense
Internal defenses - NK cells

Natural Killer Cells
- in blood and lymph
- lyse cancer cells and virus infected cells
- secrete perforins and granzymes
Innate (nonspecific) defense

Internal defenses - inflammation

- triggered by disruption of body tissue
- prevents spread of damage
- disposes of cell debris and pathogens
- preps for repair
Innate (nonspecific) defense
Internal defenses - inflammation

• The cardinal signs
  • Calor (heat)
  • Rubor (redness)
  • Tumor (swelling)
  • Dolor (pain)
Innate (nonspecific) defense

Internal defenses - inflammation

1. Tissue injury; release of chemical signals such as histamine
2. Dilation and increased leakiness of local blood vessels; migration of phagocytes to the area
3. Phagocytes (macrophages and neutrophils) consume bacteria and cell debris; tissue heals
pus = dead WBCs (neutrophils) + dead tissue cells + pathogens (live and dead)
abcess = walled off infection (by collagen fibers)
Innate (nonspecific) defense
Internal defenses - antimicrobial proteins

1) Interferons
2) complement
Innate (nonspecific) defense
Internal defenses - antimicrobial proteins - interferon

- Virus infects cell
- Signal sent to host cell nucleus
- Viral replication activates host cell gene for interferon
- Interferon gene
- Interferon is synthesized and released
- Interferon binds to surface of neighboring cell
- Signal to nucleus
- Cell is stimulated to produce antiviral protein (AVP)
- Antiviral proteins block viral replication

AVP gene
Innate (nonspecific) defense

Internal defenses - antimicrobial proteins - complement

- 20+ different complement proteins
- 2 pathways (classic and alternative)
- cascade of events leads to amplification of inflammation, promotes phagocytosis, and causes cell lysis
Innate (nonspecific) defense
Internal defenses - fever

- systemic response
- Hypothalamus in the brain regulates body temperature
- Pyrogens resets the temperature higher
  - secreted by macrophages and leukocytes exposed to foreign matter
Adaptive (specific) defense

components
- specific
- systemic
- memory

2 categories (both triggered by antigens)
- humoral (antibody mediated) immunity
- cellular (cell mediated) immunity
Adaptive (specific) defense - antigens

- large complex molecules not normally in the body - "non-self"
- self-antigens - protein molecules on your cells that mark them as "yours"; these are antigens to other people
- MHC (major histocompatibility proteins)
Adaptive (specific) defense - types of cells

- B lymphocytes (cells): humoral immunity; mature in bone marrow
- T lymphocytes (cells): cell mediated immunity; mature in thymus
  (both lymphocytes are immunocompetent and self tolerant)
Adaptive (specific) defense - types of cells

Of the lymphocytes produced, only a few bear membrane proteins that bind to the antigen.

The particular lymphocyte that binds to the antigen proliferates to form more lymphocytes bearing identically shaped membrane proteins.
Adaptive (specific) defense - types of cells

- APCs (antigen-presenting cells) examples include:
  a. dendritic cells (connective tissue and epidermis)
  b. macrophages
  c. B lymphocytes

spleen: lymphocytes and APCs protect against blood borne pathogens

tonsils: lymphocytes and APCs protect oral and nasal cavities
Adaptive (specific) defense - humoral immunity
Adaptive (specific) defense - humoral immunity
Adaptive (specific) defense - humoral immunity

Basic structure of an Antibody

Light chain

Variable region

Heavy chain

Constant region

antigen binding

Fab

Fc

disulphide bond
<table>
<thead>
<tr>
<th>CLASS</th>
<th>GENERAL STRUCTURE</th>
<th>LOCATION</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>Monomer</td>
<td>Free in blood plasma; about 80 percent of circulating antibodies</td>
<td>Most abundant antibody in primary and secondary immune responses; crosses placenta and provides passive immunization to fetus</td>
</tr>
<tr>
<td>IgM</td>
<td>Pentamer</td>
<td>Surface of B cell; free in blood plasma</td>
<td>Antigen receptor on B cell membrane; first class of antibodies released by B cells during primary response</td>
</tr>
<tr>
<td>IgD</td>
<td>Monomer</td>
<td>Surface of B cell</td>
<td>Cell surface receptor of mature B cell; important in B cell activation</td>
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<tr>
<td>IgA</td>
<td>Dimer</td>
<td>Saliva, tears, milk, and other body secretions</td>
<td>Protects mucosal surfaces; prevents attachment of pathogens to epithelial cells</td>
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<tr>
<td>IgE</td>
<td>Monomer</td>
<td>Secreted by plasma cells in skin and tissues lining gastrointestinal and respiratory tracts</td>
<td>When bound to antigens, binds to mast cells and basophils to trigger release of histamine that contributes to inflammation and some allergic responses</td>
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mechanisms of antibody action

- **Example:** IgA  Bacterial toxins  Neutralization  Ingestion by macrophage

  - Cell with receptors for toxin

- **Example:** IgG  Bacteria in extracellular space  Opsonization  Ingestion by macrophage

  - Macrophage

- **Example:** IgM  Bacteria in plasma  Immune complexes  Lysis and ingestion

  - Complement
mechanisms of antibody action

Activated complement proteins attach to pathogen’s membrane in step-by-step sequence, forming a membrane attack complex (a MAC attack). MAC pores in the membrane cause cell lysis.
Adaptive (specific) defense - immunological memory
Adaptive (specific) defense - cell mediated immunity

- T cells interact directly with antigen presenting cells (APCs)
- T cells DO NOT MAKE ANTIBODIES!
- T cells clear the body of cells that have been invaded by viruses (or other pathogens)
- T cells reject tumor cells, transplants
- T cells are responsible for some allergies
Adaptive (specific) defense - cell mediated immunity

T cell

dendritic cell
Adaptive (specific) defense - cell mediated immunity
Adaptive (specific) defense - cell mediated immunity
Adaptive (specific) defense - cell mediated immunity
Immune imbalances

- immunodeficiencies - when immune cells (any) behave abnormally
  (AIDS - cripples helper T cells)
- autoimmune diseases - body cannot distinguish self
- hypersensitivities (allergies) - immune system is overly sensitive to perceived threats (pollen, dander)
Cancer

characterized by cells that
- divide indefinitely
  - lack a response to stop growing
- can recruit a blood supply
- can migrate
- lack normal interactions with other cells
Cancer

- multiple mutations, multiple genes
- proto-oncogenes - promote normal cell division
  - mutate to oncogenes
- tumor suppressor genes - control normal cell division
  - mutate to become non-functioning
Cancer

a. In situ cancer
b. Invasion of the tumour border
c. Lymphatic spread
d. Intravasation of the circulatory system
  Survival, transport
e. Arrest extravasation
f. Solitary dormant cells
  Occult micrometastases
g. Progressive colonization
  Angiogenesis