Topic 8
Specific Immunity (adaptive)
(Ch 15_16)

Topics
- 3rd of Defense
- B cells
- T cells
- Specific Immunities

Third line of Defense

• Specific immunity is a complex interaction of immune cells (leukocytes) reacting against antigens
  – Stages
  – Self and non-self
  – Clonal selection
  – Antigens

So – What is adaptive immunity?

• Ability to recognize and defend (distinct invaders and their products)
• Has 5 Five attributes:
  1) Specificity
  2) Inducibility
  3) Clonality
  4) Unresponsiveness to self
  5) Memory
What does it involve?

- Lymphocyte Activities
  - 2 main cell types:
    - B lymphocytes (B cells - bone marrow)
    - T lymphocytes (T cells – thymus)
  - Two types of immune responses:
    - Humoral
    - Cell-mediated (CMI)
  - Surveillance by Tissues and Organs

What do lymphocytes look like?

Specific Immunity Stages

1. Dual lymphocyte development and differentiation
2. Presentation of antigens
3. Challenge of B and T lymphocytes by antigens
4. Production of antibodies by B cells (plasma cell)
5. T lymphocyte responses
Overview:
Lymphocyte development and function stages

Self vs. non-self
how do we know?

• Markers
  – Glycoproteins, located on the cell surface
• Specificity
  – Host cells receptors (ex. MHC) confer specificity and identity
• Role – detection, recognition, and communication
• Lymphocyte cells recognize the host cell receptors as “self”
• Lymphocyte cells recognize microbe receptors as “non-self”

Lymphatic System Tissues and Organs

– Lymphatic vessels
  • One-way system (from tissues, returns to circulatory system.
  • Lymph - from fluid leaked from blood vessels into surrounding tissues
– Lymphoid organs
  • Primary: Red bone marrow, Thymus
  • Secondary: Lymph nodes, Spleen, Tonsils, Mucosa-associated lymphatic tissue (MALT)
Major histocompatibility complex (MHC)

- Self receptor, each individual has a unique MHC profile
- Glycoprotein
- Found on all nucleated cells
- In humans – Human leukocyte antigen (HLA) is equivalent to the MHC
- Classes of MHC:
  - Class I – all nucleated cells
  - Class II – macrophages, dendritic cells, B cells

Human major histocompatibility complex

Class I and II MHC for humans are surface receptors consisting of glycoproteins.

Clonal selection

- The synthesis of varied receptor types
  - approximately 500 genes undergo rearrangement
  - eventually one clone recognizes an antigen and expands (proliferates)
- Clone
  - each mature lymphocyte possesses a single combination or receptor specificity
- Expansion
  - a single cell is stimulated by antigen recognition
- Clonal deletion
  - cells that recognize self are removed
The clonal selection theory describes lymphocyte development and diversity.

B cell clone

- Application of immunology
- Propagate a single clone to synthesize monoclonal antibodies that possess a single specificity for an antigen.
Major stages in the development of B and T cells

Mature T and B cells migrate to the lymphoid tissue, where they encounter antigens.

Receptors

- Present on B and T cells
  - Immunoglobulin molecule
    - Light chain
    - Heavy chain
    - Variable region
    - Constant region
  - B cell receptors are secreted as antibodies
B Lymphocyte (B Cell) and Antibodies

Specificity of the B cell receptor (BCR):

- Each B lymphocyte has multiple copies of the B cell receptor
- Each B cell generates a single BCR
- Two variable regions of the BCR form the antigen-binding sites
- Each BCR recognizes only one epitope
- The entire repertoire of an individual’s BCRs is capable of recognizing millions of different epitopes

Generalized soluble antibody structure (B cell receptor)

The B cell receptor – in place
Antigens – what are they?

- Foreign material
- Size and shape
- Alloantigens
- Superantigens

Foreign material

- Proteins and polypeptides
  - enzymes, cell surface structures, hormones, exotoxins
- Lipids
  - cell membranes
- Glycoproteins
  - blood cell markers
- Nucleoproteins
  - DNA complexed to proteins
- Polysaccharides
  - capsules, LPS
Antigenic size and shape

- **Immunogen**
  - Less than 1000 daltons – no immune recognition
  - Greater than 1000 daltons – immune recognition
  - Proteins are better immunogens than polysaccharides
- **Epitope**
  - Portion of the antigen (ex. Amino acids) recognized by lymphocyte receptor
- **Haptens**
  - Antigens that are too small to elicit an immune response by themselves

How to make a hapten antigenic?

Complex it with a larger carrier protein to make it bigger and stimulate an immune response...

Alloantigens

- Cell surface markers that occur in some members of the same species
  - Blood typing (transfusion)
  - MHC profile (organ grafting)
Superantigen

- Bacterial toxins
- T cell activation much greater than normal antigens
- Large release of cytokines
- Rapid, extensive and dangerous rise in fever
- Results in toxic shock syndrome and some autoimmune diseases

Example antigens and their characteristics

How B cells work…

1. Activation
2. Antibody
3. Antibody-antigen interaction
4. Response
1- Activation

- Clonal selection and binding of antigen
- Instruction by chemical mediators
- Transmission of signal to the nucleus
- B cell changes into a plasma cells and begins mitosis
- Clonal expansion and memory cell formation
- Antibody production and secretion

B-cell activation and antibody synthesis stages

Antibody structure

(more specific)

- Product of B cell (plasma cell) activation
  - Immunoglobulin (Ig) or antibody
- General structure
  - Four polypeptides
  - Connected by disulfide bonds
  - Antigen binding fragment (Fab)
  - Crystallizable fragment (Fc)
- 5 Classes – IgA, IgD, IgE, IgG, IgM
Fab

- Variable (N-terminal of the heavy and light chains)
- Binds to antigenic determinant
- Swiveling enables more efficiency
- Held together by disulfide bonds

F_C portion

- Constant (C-terminal of heavy chain)
- Binds to macrophages
- Anchors Ig to lymphocyte
- Held together by disulfide bonds
- Responsible for class identification

IgG antibody structure.
Ig Classes

- Isotypes – based on the Fc fragment
- Immunoglobulin (Ig)
  - IgG
  - IgA
  - IgM
  - IgD
  - IgE

IgG

- Monomer
- Primary response
- Memory cell response
- Most prevalent in tissue fluid and blood
- Good opsonin
- Fixes complement

IgA

- Monomer or dimer (secretory IgA)
- Dimer – held together by a J chain
- Secretory IgA (mucous and serous secretions)
  - Local immunity
  - Salivary glands, intestine, nasal membrane, breast, lung, genitourinary tract
- Protection for newborns
- Normally does NOT fix complement
IgM

- Five monomers
- Held together by a J chain
- First to be synthesized during primary immune response, 3rd most common
- Associated with complement fixation
- Receptor for antigens on B cells
- Circulates in the blood
- Fixes complement well.

IgD

- Monomer
- Small amounts in the serum, role uncertain
- Receptor for antigens on B cells
- Does NOT bind complement

IgE

- Least common
- Allergies
- Parasite infections
- Fc portion binds to mast cells and basophils
  - release chemical mediators that aid inflammation
- Does NOT fix complement
Immunoglobulin class characteristics

**Table 15.1** Characteristics of the Immunoglobulin (Ig) Classes

<table>
<thead>
<tr>
<th>Ig Class</th>
<th>α</th>
<th>β</th>
<th>γ</th>
<th>δ</th>
<th>ε</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of heavy chains</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>150,000</td>
<td>150,000</td>
<td>150,000</td>
<td>250,000</td>
<td>150,000</td>
</tr>
<tr>
<td>Percent of total antibody in Circles</td>
<td>84%</td>
<td>11%</td>
<td>4%</td>
<td>1%</td>
<td>0.01%</td>
</tr>
</tbody>
</table>
| Average Age of Plasma Cell | 25 | 4 | 3 | 3 | 2
| Other Characteristics | Yes | No | No | No | Yes |
| In vivo to In vitro | Yes | No | No | No | Yes |
| Biological function | Long-range immunity | Memory antibodies | Secretory antibody or mucosal antibodies | Produces Ig that induces cell-mediated immune response | Secretory or T-fucose

Antibody-antigen interactions

- Opsonization
- Agglutination
- Neutralization
- Complement fixation
- Killing w/ oxidation
- Antibody-dependent cellular cytotoxicity (ADCC)

Antibody-Antigen binding

A complementary fit between an antibody and antigen involves hydrogen bonds and electrostatic attractions.

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Opsonization

- Microbes or particles coated with antibodies
- Enables macrophages to recognize and phagocytize microbe

Agglutination

- Homologous antibodies cross-link cells or particles into clumps
- Renders microbes immobile
- Enhances phagocytosis
- Principle for certain immune tests (RBC typing)

Neutralization

- Antibody binds to
  - The microbe or virus receptor
  - Antigenic site of a molecule (e.g. Exotoxin)
- Prevents further binding of microbe or toxin
Complement fixation

• Antibodies interaction with complement proteins (e.g. Classical pathway)
• Lysis of microbial cell

Overview - antibody functions

Responses

• Primary (first response):
  – Latent period - lack of antibodies synthesis
  – Synthesis of antibodies
    • Level of synthesis (titer)
    • IgM first
    • Followed by IgG, and some IgA and IgM
• Secondary (Re-exposure to same immunogen, called Anamnestic response)
  – No latent period, primarily due to memory cells
  – Antibody synthesis, titer, and length of antibody persistence is rapid and amplified
Primary vs. secondary response to antigens

T cell

- Activation
- Types

Activation

- Cell-mediated immunity
- Antigen presenting cells
- Transformation
Cell-mediated immunity (CMI)

- Direct involvement of T cells
- Produce and react to cytokines
- Activated simultaneously with B cell activation
- Subset of T cells have unique CD receptors (CD4, CD8)
Antigen presenting cells (APC)
- Macrophages and dendritic cells
  - Process and present antigen in association with MHC II
  - T cell CD receptor recognize antigen/MHC II

Transformation
- Activated T cells prepare for mitosis
- Effector cells or types ($T_H$, $T_C$) are produced
- Memory cells are produced

T-cell types
- Helper T cells ($T_H$)
- Cytotoxic T cells ($T_C$)
TH

- Regulate immune reactions to antigens by releasing cytokines
- CD4 receptor
- Type of cytokine will determine subset of TH
  - TH1 (activate other T cells, delayed type hypersensitivity)
  - TH2 (B cell differentiation)
- Cytokines also activate macrophages
- Most prevalent in the blood

TC

- Binds and lyses cells (apoptosis)
  - microbe, viral infected cells, foreign cells, cancer cells
- CD8 receptor
- Perforins – punch holes in the membrane
- Granzymes – degrade proteins
- Natural killer (NK) cells
  - related to TC
  - attack virus infected cells and cancer cells

Example helper and cytotoxic T cell activation and differentiation
Characteristics of T cell subsets

<table>
<thead>
<tr>
<th>Types</th>
<th>Primary Receptors on T Cell</th>
<th>Functions/Important Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>T helper cell 1 (Th1)</td>
<td>CD4</td>
<td>Activates the cell-mediated immunity pathway, secretes interleukin-2, interferon-gamma, and tumor necrosis factor (TNF)</td>
</tr>
<tr>
<td>T helper cell 2 (Th2)</td>
<td>CD4</td>
<td>Produces interleukin-4 (IL-4), IL-5, IL-6, IL-9, IL-10, and IL-13, and activates B cells.</td>
</tr>
<tr>
<td>T regulatory cell (Treg)</td>
<td>CD25</td>
<td>Suppresses excessive immune responses, particularly autoimmune reactions.</td>
</tr>
</tbody>
</table>

Specific Immunities

- Active
- Passive
- Natural
- Artificial
- Vaccines
Active

- Natural or artificial
- Antigen activates B and T cells
- Memory cells
- Long-term protection

Passive

- Natural or artificial
- Receive antibodies from another individual or animal
- No memory cells
- No antibody production
- Short-term protection

Natural

- Immunity produced by normal biological experiences, no medical intervention
  - Natural active
    - For example, Infection
  - Natural passive
    - Mother to child
Artificial

- Immune protection through medical procedures or intervention
  - Artificial active
    - Vaccination
  - Artificial passive
    - Immunotherapy

Summary: Acquired immunities