Lecture 21 & 22 - Chapter 15

**Third line of Defense**
Specific immunity is a complex system of immune cells interacting against antigens

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**Adaptive immunity**
Immune Response (IR) (mediated by B- & T-lymphocytes)

- Specificity
- Tolerance
- Memory

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**Lymphocyte Receptors**

- Present on B and T cells
  - Have Variable & Constant regions
  - Functional as dimers
- **B cell receptors**: Immunoglobulins
  - Light chain & Heavy chain form hetero-dimers
  - Secreted immunoglobulins (Igs) are called antibodies
- **T cell receptors**: only homo-dimers of one chain

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**Major Histocompatibility Complex (MHC)**

- Host cell surface proteins (Glycoproteins)
- “Human leukocyte antigen” (HLA) is an old term for the MHC
- 3 Classes of MHC (I, II, III)
Classes of MHC

- Each individual has a unique MHC profile because of the expression of a particular combination of MHC genes

- **Class I** — all nucleated host cells

- **Class II** — only antigen-presenting cells (*macrophages, dendritic cells, B-cells*)

Antigen presenting cells (APC)

- *Macrophages, dendritic cells* and B-cells
  - process and present antigen in association with MHC (class) II
  - Interact with T-cell receptor (TCR)/CD4 co-receptor complex, which recognizes MHC II and antigen/MHC II complex

Antigens

- Foreign material
- Alloantigens
- Superantigens

Antibody (soluble B-cell receptor, Immunoglobulin)

- Activated B cells (plasma cell) produce Immunoglobulin (Ig) or antibody

- **Structure**
  - Four polypeptides
  - Connected by disulfide bonds
  - Antigen binding Fragment (Fab)
  - Crystallizable Fragment (Fc)

- **Classes**

Fab (function: antigen-binding)

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

Fc (function: constant)

- Constant (C-terminal of heavy chain)
- Recognized by macrophage receptors
- Anchors membrane-bound Ig to lymphocyte
- Held together by disulfide bonds
- Responsible for class identification
5 Classes of Igs

- based on the Fc fragment of Ig
  - IgM
  - IgG
  - IgD
  - IgA
  - IgE

IgM - first circulatory Ig

- Receptor for antigens on B cells
- **First to be synthesized** during primary immune response
- Circulates in the blood
- **Five monomers**, held together by a J-chain
- Associated with complement fixation and opsonization

IgG - major circulatory Ig

- Monomer
- **Primary response** antibody
- **Memory cell response**
- **Most prevalent** in tissue fluid and blood

IgD - minor circulatory Ig

- **Receptor** for antigens on B cells
- Monomer
- **Small amounts** in the serum

Table 15.2 Characteristics of the immunoglobulin classes.
IgA - secreted Ig

- 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

IgE - “allergic” Ig

- Allergies
- Parasite infections
- Fc portion binds to basophils and mast cells
  - release of chemical mediators that aid in inflammation

Antibody-antigen interactions

- Opsonization
- Agglutination
- Neutralization
- Complement fixation

Opsonization

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

Agglutination

- Antibodies cross-link cells or particles into clumps
- Renders microbes immobile
- Enhances phagocytosis
- Principle for certain immune tests (RBC typing)
- Reason for some symptoms of disease
Neutralization

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

Complement fixation

- Interaction of antibodies with complement proteins (-> classical pathway) thereby delivering the compliment to antigen.
- Usually followed by lysis of microbial cell facilitated by MAC

The different functions of antibodies.

Fig. 15.13 Summary of antibody functions

Clonal selection

- The synthesis of varied receptor types
  - Approximately 500 genes can undergo rearrangement
  - Not all individuals have all possible antigen-specificities (~10¹⁴) at any given time (but throughout life span)
  - Eventually one clone recognizes an antigen and expands (proliferates) or it dies
- 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

T-cell development

- Occurs in Thymus gland (later in bone marrow)
- 2 steps of selection:
  - Positive selection: Specificity (TCR-CD4/8 and MHC I/II)
  - Negative selection: Tolerance (TCR - self-MHC)
- Mature tolerant T-cells released into blood and lymph systems
B-cell development

- Have Igs as B-cell receptors (IgM, IgD)
  - Specificity
- Need to be activated by receptor-antigen interaction (equal to antibody-antigen interaction) to:
  - produce soluble Igs
  - establish Memory

B-cell clones

- Process of activation is selection and propagation of a single B-cell (then called a clone) to develop into a mature Plasma Cell for the synthesis of antibodies. If only one B-cell is selected, monoclonal antibodies are produced.
- A monoclonal antibody possess only one single specificity for a given antigen

B-cell Activation

- B-cell encounters and binds antigen
- B-cell processes antigen, presents it with MHC I & II
- MHC II interacts with TCR + CD4, followed by instruction by chemical mediators (interleukins)
- Transmission of signal to the nucleus
- B cell changes into an active cell called plasma cell (lots of ribosomes, enhanced cell division)
- Clonal expansion and memory cell formation
- Antibody production and secretion

Fig. 15.10 Events in B-cell activation and antibody synthesis.

Responses to antigens

We distinguish 2 responses to antigens
- Primary
- Secondary

Primary Response

- First exposure to antigen
  - Latent period
    - Lack of antibody synthesis
  - Synthesis of antibodies
    - Level of antibodies (titer)
    - IgM first
    - Followed by IgG, and some IgA and IgM, very little IgD
Secondary Response

- Re-exposure to the same antigen (Anamnestic response)
- Antibody synthesis, titer, and length of antibody persistence is rapid and amplified
  - Primarily due to memory cells

If used for medical purposes, what is this called?

Cell-mediated immunity

- Subset of T cells have unique CD receptors (CD4, CD8)
- Direct involvement of T cells
- Produce and react to cytokines
- Activated simultaneously with B cell activation

T cell clones

- Activation
- Types

Activation

- Activated T cells prepare for mitosis
- Effector cells or types ($T_H$, $T_C$) are being produced
- Memory cells are produced
- After interaction with other cells, armed effector cells are produced

Types

- Helper T cells ($T_H$)
- Cytotoxic T cells ($T_C$)
Specific Acquired Immunities

- Active
- Passive
- Natural
- Artificial
- Vaccines

Active

- Can be natural or artificial
- Adaptive Immunity
  - Specificity, Tolerance, Memory
- Long-term protection
Passive
• Can be natural or artificial
• Receive antibodies from another individual or animal
• No memory cells
• No antibody production
• Short-term protection (extended 2nd line of defense)

Natural
• Immunity produced by normal biological experiences, no medical intervention
  – Natural active
    • Example: Infection
  – Natural passive
    • Example: Mother to child

Artificial
• Immune protection through medical procedures or intervention
  – Artificial active
    • Example: vaccination
  – Artificial passive
    • Example: immunotherapy

Vaccines
• Types
  – Killed whole cell or inactivated viruses
  – Live, attenuated cells or viruses
  – Antigenic molecules from bacteria or viruses (large enough to elicit and IR)
  – Genetically engineered microbes or microbial antigens

Benefits of vaccinations
• Long-lasting immunity
• Herd immunity
  – Indirect protection of non-immune
  – Prevents epidemics