Short Course on Immunology

Adaptive Immune System

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Immune System

- Innate Immunity: (Present before infection)
- Adaptive Immunity: (Develops in response to infection)
Adaptive Immunity

“Immunity that an organism develops and adapts to recognize, eliminate and remember specific pathogens (antigen)”

What is an antigen?

An antigen is any substance that elicits an immune response.
<table>
<thead>
<tr>
<th>Attribute</th>
<th>Innate immunity</th>
<th>Adaptive immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response time</td>
<td>Minutes/hours</td>
<td>Days</td>
</tr>
<tr>
<td>Specificity</td>
<td>Broad recognition: less-specific</td>
<td>Highly specific</td>
</tr>
<tr>
<td>Diversity</td>
<td>Limited number of germ line-encoded receptors</td>
<td>Highly diverse; Adaptive: G.O.D</td>
</tr>
<tr>
<td>Memory response</td>
<td>None</td>
<td>Present</td>
</tr>
<tr>
<td>Self/non-self discrimination</td>
<td>Perfect</td>
<td>Very good</td>
</tr>
<tr>
<td>Major cell types</td>
<td>Phagocytes, natural killer cells, dendritic cells</td>
<td>T cells, B cells, antigen-presenting cells (APC)</td>
</tr>
</tbody>
</table>

*Source: Kuby Immunology, Sixth Edition*
Players and their effector functions
Duality of Adaptive Immune System

- Humoral (Antibody-Mediated) Immunity
  - (Extra cellular pathogens)
- Cell Mediated Immunity
  - (Intra cellular pathogens)
Humoral (Antibody-Mediated) Immunity

- Involves production of antibodies against foreign antigens.
- Antibodies (membrane bound and soluble) are produced by a subset of lymphocytes called B cells. (Bone marrow)
- Antibodies can recognize free antigen on their own.

B cell differentiation (T cells help)

- Plasma cells: Secrete antibodies
- Memory B cells: Secondary response

Detect and prevent the entry of extracellular pathogens
Antibody structure

Antigen-binding site

Variable region (Fab)

Disulfide bonds

Light chain

Heavy chain

Plasma membrane

Constant region (Fc): effector functions

Surface antibody

Soluble antibody

Five classes of antibodies: IgG, IgA, IgM, IgD, and IgE. Each have a different function.
Production of antibodies

B cell binds pathogen

Peptides from the pathogen are presented (MHC II) to the T cell resulting in the activation of the B cell

Pathogen is internalized and degraded

B cells differentiate into antibody-secreting plasma cells

Produce antibodies against pathogen

Production of antibodies

Pathogen (virus or bacteria)

MHC II

B cell

T\textsubscript{H}2

cytokine

Plasma cells

B cell proliferation
Cell Mediated Immunity

**Involves specialized set of lymphocytes called T cells (Thymus)** with membrane bound T cell receptor (TCR).

Two main types:
1. CD4+ (TH1 and TH2): Stimulate other immune cells.
2. CD8+ Cytotoxic T cells (T\(_{\text{C}}\)): Kill intracellularly-infected cells.

**Recognition of processed Ag in the context of Major Histocompatability complex (MHC)**

**T cells detect presence of intracellular pathogens**

And T cells, the cells that “help”, are the “brains” of the immune system.
Antigen Presentation to T cells: MHC Restriction

**Target cell**

Class I MHC

- CD8
- TCR complex
- (endogenous antigen) 8-10 amino acid peptide
- CD8+ T cell

**Antigen presenting cell**

Class II MHC

- CD4
- TCR complex
- (exogenous antigen) 13aa or more peptide
- CD4+ T cell

MHC I: on most of the cells

MHC II: Dendritic cells, macrophages and B cells
Cells that link the innate and adaptive immune systems: Antigen Presenting Cells (APCs)

1. Dendritic cells
2. Macrophages
3. B lymphocytes

- Ag is internalized
- Stimulates T-helper cells
- They provide co-stimulatory signals
Cytokines

- Cytokines are soluble protein factors that can activate many cells

  Ex. Cytokines secreted by $T_H$ can affect B-cells, CTLs, $\text{M}\Phi$, NK: IL-4, IL-5 etc.
Cytokine functions

(a) PLEIOTROPY
Activated TH cells → IL-4 → B cell
- Activation, Proliferation, Differentiation

(b) REDUNDANCY
Activated TH cells → IL-2, IL-4, IL-5 → B cell
- Proliferation

(c) SYNERGY
Activated TH cells → IL-4 + IL-5 → B cell
- Induces class switch to IgE

(d) ANTAGONISM
Activated TH cells → IL-4 → IFN-γ → B cell
- Blocks class switch to IgE induced by IL-4

(b) CASCADE INDUCTION
Activated TH cells → IFN-γ → Macrophage
- Activated TH cells

Macrophage
- IFN-γ, TNF, IL-2, and other cytokines
- IL-12
- Proliferation
Antigen Recognition by T-cells

Cytotoxic T cells (CD8) recognize antigen presented by MHC I and kills the cell

$T_H^1$ cells (CD4) recognize antigen presented by MHC II and activates macrophages

$T_H^2$ cells (CD4) recognize antigen presented by MHC II and activates B cells

- Cytotoxic T cell
  - Kills
  - Virus-infected cell
  - Apoptotic cell

- $T_H^1$ cells
  - Activates
  - Macrophage
  - Dead intracellular bacteria

- $T_H^2$ cells
  - Activates
  - B cell
  - Anti-toxin antibodies
Characteristics of Adaptive Immune System

• Antigenic Specificity
• Diversity
• Memory response
• Self/non-self discrimination
Antigenic specificity

Is due to the CLONAL EXPANSION of only those lymphocytes with antigen specific receptors.

- B lymphocytes – BCR/Antibody
- T lymphocytes - T Cell Receptor

Each lymphocyte expresses only a SINGLE SPECIFICITY RECEPTOR
Diversity

- Human genome has ~30,000 protein encoding genes
- Exposure to unlimited number of antigens
- Humans have such a large immune repertoire. How?

by

G.O.D
### Generation of Diversity (G.O.D): BCR and TCR

<table>
<thead>
<tr>
<th>Multiple germ-line gene segments (Inherited diversity)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Combinatorial V-(D)-J joining</td>
<td></td>
</tr>
<tr>
<td>Junctional flexibility</td>
<td></td>
</tr>
<tr>
<td>Combinatorial association of light and heavy chains</td>
<td></td>
</tr>
<tr>
<td>Somatic hypermutation</td>
<td></td>
</tr>
<tr>
<td>Class-switch recombination</td>
<td></td>
</tr>
</tbody>
</table>

- **BCR**
- **TCR**
Combinatorial antibody diversity in humans

| Multiple germ-line segments | Heavy chain | LIGHT CHAINS | | | |
|----------------------------|-------------|-------------|---|---|
|                            |             | κ           | λ  |
| ESTIMATED NUMBER OF SEGMENTS IN HUMANS* |             |             |   |   |
| V                           | 48          | 41          | 34 |
| D                           | 23          | 0           | 0  |
| J                           | 6           | 5           | 5  |
| Combinatorial V-D-J and V-J joining (possible number of combinations) | 48 × 23 × 6 = 6624 | 41 × 5 = 205 | 34 × 5 = 170 |

Possible combinatorial associations of heavy and light chains†

\[6624 \times (205 + 170) = 2.48 \times 10^6 + \]

*These numbers have been determined from studies of single subjects; slight differences may be seen among different individuals. In the cases of both human and mouse, only the functional gene segments have been listed. The genome contains additional segments that are incapable of rearrangement or contain stop codons or both.

†Because of the diversity contributed by junctional flexibility, P-region nucleotide addition, N-region nucleotide addition, and somatic mutation, the actual potential exceeds these estimates by several orders of magnitude.

Table 5-2
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The potential number of immune receptors is around \( \sim 10^{12} \)
Self/non-self discrimination: The Clonal selection
The attribute of the adaptive immune system mediated by MEMORY CELLS where by second encounter with same antigen results in heightened state of immune reactivity
Phases of adaptive immune responses.

- Recognition phase
- Activation phase
- Effector phase
- Decline (homeostasis)
- Memory

- Antibody-producing cell
- Effector T lymphocyte
- Elimination of antigens
- Humoral immunity
- Apoptosis
- Surviving memory cells

- Clonal expansion
- Differentiation
- Time after antigen exposure

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Innate immunity and Adaptive immunity collaborate to protect the body.

**Tissues**
- Dendritic cells gather antigen.
- Free antigen.
- Plasma cells produce antibody; depending on site of infection and duration of exposure, the class may be IgM, IgG, IgA, or IgE.
- Th1 cells activate macrophages that present antigen via MHC class II molecules; also produce cytokines that orchestrate other responses.
- Effector T-cytotoxic cells destroy cells that presented antigen via MHC class I molecules; also produce cytokines that allow neighboring cells to become more vigilant against intracellular pathogen.

**Secondary lymphoid organs**
- Antigen presented by MHC Class I molecules in the presence of co-stimulatory molecules activates naive T-cytotoxic cells.
- Antigen presented by MHC Class II molecules in the presence of co-stimulatory molecules activates naive T-helper cells.
- Naive T-cytotoxic (CD8) cells.
- Naive T-helper (CD4) cells.
- Activates B cells that present antigen.
- Activation, proliferation, development of effector T cell functions.
- Activation, proliferation, development of effector T cell functions.
- Th2 and Th1.
- Memory cells.
- Activation, proliferation, class switching, affinity maturation.
- Memory T-cytotoxic cells.
- Effector T-cytotoxic cells.
- Memory T-helper cells.
- Effector T-helper cells.
Adaptive Immune System

• Antigenic Specificity

• Diversity

• Memory response

• Self/non-self discrimination
Thank You