Lecture 7: Introduction to Acquired Immunity
Overview of Innate and Acquired System

Types of Acquired Immunity:
- **Humoral Immunity:**
  - Antibody (Ab)
  - B cell → plasma → secrete Ab
- **Cellular Immunity:**
  - Tc → TCTL

External Antigens:
1. Antigens captured by proAPCs (professional antigen-presenting cells)

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Location</th>
<th>Receptor for Endocytosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophage</td>
<td>tissue</td>
<td>C3bR, FcR</td>
</tr>
<tr>
<td>Dendritic Cell</td>
<td>tissue → lymph node</td>
<td></td>
</tr>
<tr>
<td>B-cell</td>
<td>lymph node</td>
<td>B cell Receptor (BCR) Can't body</td>
</tr>
</tbody>
</table>

2. Antigen processed by enzymes in primary & secondary granules, lysosome.
3. Peptides from antigen presented on class II MHC (DC also on class I)
4. Specific interaction with T-cell receptor (TCR) on T\(_{H}\) cells.
5. Activation of T\(_{H}\) cells, followed by response of presenting cell.

Internal Antigens (all cells)
1. Presentation of internally synthesized peptides on class I MHC.
2. Activation of T\(_{C}\) cells.
3. Development into T\(_{CTL}\) (cytotoxic T lymphocytes)
Development and Properties of B-cells:

i) Mature in the bone marrow.

ii) B-cell receptor binds foreign material (e.g. proteins, carbohydrates) via antibody component. Highly specific interaction. Contains signaling chains.

iii) All B-cell receptors are identical on a single B-cell, but diversity is on the order of $10^6$ different B-cells within an individual. Genetic diversity in population is low.

iv) Antibody component of the BCR receptor is originally IgM.

v) Self-reactive B-cells are eliminated.

vi) Activation leads to expansion of specific B-cell population and generation of plasma and memory cells. This is the basis of the clonal selection theory.

vii) Memory B-cells & plasma cells often produce a different type of antibody (but same specificity).

Overview of Acquired B-cell Response → Ab production & Memory Cells

i) Antigen binds to B-cell receptor (membrane bound antibody).

ii) Antigen internalized, digested, peptides from antigen displayed (presented) on class II MHC.

iii) MHC-peptide recognized by $T_H$ cells

iv) Population of B-cells expanded (clonal selection)

v) Activated $T_H$ cells activate B-cells → Plasma cells (Ab secreting)

vi) Memory T and B cells formed, which will produce a faster and more intense secondary response due to the higher number of cells that recognize a particular antigen.
**Major Histocompatibility Complex (MHC):**

Heterodimeric and membrane bound.

- i. Bind peptides with low specificity, length from 8-9 (MHC I) or longer (MHC II).
- ii. Many different MHCs on one cell.
- iii. Individuals have same MHCs on all cells.
- iv. Population is highly polymorphic with many, many alleles – “immunological self”
- v. Both foreign and self-peptides are presented indiscriminately.
- vi. Only **foreign** peptides presented by self-MHC elicit an immune response (normally).

<table>
<thead>
<tr>
<th>Found on:</th>
<th>Class I - MHC</th>
<th>Class II - MHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptides</td>
<td>All cells</td>
<td>“Professional” Antigen-presenting cells (macrophage, dendritic, B-cell)</td>
</tr>
<tr>
<td>Presented:</td>
<td>Internally synthesized (except for dendritic cells)</td>
<td>Outside of cell, via phagocytosis or receptor mediated endocytosis.</td>
</tr>
<tr>
<td>Recognized by:</td>
<td>T&lt;sub&gt;C&lt;/sub&gt; Activation → T&lt;sub&gt;CTL&lt;/sub&gt;</td>
<td>T&lt;sub&gt;H&lt;/sub&gt;</td>
</tr>
</tbody>
</table>

**Antigen presenting Cells (APC):**

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Source of Antigen</th>
<th>MHC Class</th>
<th>Typical “Infectious” Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophage</td>
<td>External antigen</td>
<td>I&lt;sub&gt;(I)&lt;/sub&gt;</td>
<td></td>
</tr>
<tr>
<td>Dendritic Cell</td>
<td>I</td>
<td>I&lt;sub&gt;(II)&lt;/sub&gt;</td>
<td>bacteria,</td>
</tr>
<tr>
<td>B-Cell</td>
<td>I</td>
<td>I&lt;sub&gt;(II)&lt;/sub&gt;</td>
<td>virus.</td>
</tr>
<tr>
<td>All cells</td>
<td>Internal (ribosome)</td>
<td>I</td>
<td>virus, cancer antigens</td>
</tr>
</tbody>
</table>
Antigen Presentation Pathways (Left – all cells. Right – proAPCs)

Important players:
- Ribosome
- Proteasome (LMP)
- Tap1&2 (transporter)
- Invariant chain
- Clp protease

Cross presentation (DC & to a minor extent macrophage): Presentation of extracellular antigens on class I MHC.