Antigen Presentation

K.J. Goodrum
Department of Biomedical Sciences
Ohio University
2005

T cell recognition of antigen

- T cells are needed to control intracellular pathogens and to activate B cell responses to most antigens
- T cells are specialized to recognize foreign antigens, via their TcR, as peptide fragments bound to proteins of the major histocompatibility complex (MHC)
- T cells with different functions are distinguished by CD4 and CD8 cell-surface proteins and recognize peptides bound to different classes of MHC molecule

Peptides from digested foreign proteins are bound by MHC I or MHC II proteins on antigen-presenting cells for recognition by T cells.

MHC II is a transmembrane glycoprotein (α-chain) noncovalently bound with β2-microglobulin. The folded molecule forms a peptide-binding cleft.

Figure 3 (part 2 of 2) from: Immunobiology, 4th ed. Garland Science (2008)
MHC I is a transmembrane glycoprotein (noncovalently linked $\alpha$ and $\beta$ glycoprotein chains). The folded molecule forms a peptide-binding cleft.

The MHC class I and class II molecules deliver peptides to the cell surface from two distinct intracellular compartments.

<table>
<thead>
<tr>
<th>Tissues</th>
<th>MHC class I</th>
<th>MHC class II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid tissues</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>T cells</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>B cells</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Macrophages</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Other antigen-presenting cells (e.g., Langerhans' cells)</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Epithelial cells of the thymus</td>
<td>+</td>
<td>+ + +</td>
</tr>
</tbody>
</table>

MHC I is expressed on all nucleated cells (including APC).

MHC II is expressed only on antigen-presenting cells (APC, usually immune cells).
Peptides that bind to MHC class II molecules are generated in acidified endocytic vesicles

- Extracellularly-derived peptides or peptides from intravesicular pathogens are loaded onto MHC II and the MHC II-peptide complex is transported to the APC cell surface.

T Cell Receptor for Antigen

- T cells express a co-receptor (CD4 or CD8) which binds to the MHC portion of the composite MHC:peptide ligand.
- Regulatory CD4-T helper cells recognize peptides complexed with Class II MHC on specialized antigen presenting cells.
- Cytotoxic CD8-T cells recognize peptides complexed with Class I MHC on any nucleated cell.

CD4 and CD8 proteins act as co-receptors to restrict T cell interactions with MHII or MHCI and are used to identify functional T-helper (CD4+) vs. cytotoxic T cells (CD8+).
### Major Histocompatibility Complex

- Individuals inherit 2 complete sets of MHC genes (1 paternal + 1 maternal “haplotype”)
- Both inherited alleles at each MHC gene locus are co-dominantly expressed.
  - An APC could thus express 6 different types of MHC I molecules and 6 different inherited types of MHC II molecules on its cell membrane.
Major Histocompatibility Complex-2

- Different MHC bind different peptides
- The polymorphic amino acid residues that distinguish MHC alleles determine the peptide-binding properties of different MHC molecules
- A single MHC may bind many different peptides which share “sequence motifs”

MHC Restriction

- TcR recognizes a complex of antigenic peptide and MHC
- A T cell specific for peptide x and a particular MHC allele (MHC\textsuperscript{a}) will not recognize the complex of peptide x with a different MHC allele (MHC\textsuperscript{b})

Major Histocompatibility Complex-3

- MHC genes = immune response genes (Ir)
- Immune responsiveness to any single peptide depends on inheritance of an MHC molecule which can bind that peptide.

MHC restriction

- T cell
  - TCR
  - MHC\textsuperscript{a}
  - X
  - Recognition
  - antigen-presenting cell
- T cell
  - TCR
  - MHC\textsuperscript{b}
  - X
  - No recognition
  - antigen-presenting cell
- T cell
  - TCR
  - MHC\textsuperscript{c}
  - Y
  - No recognition
  - antigen-presenting cell
Summary Points

• Processed peptides from intracellular (cytosolic) proteins form complexes with MHC I for presentation to CD8(+) Tc that destroy the self cell presenting foreign cytosolic proteins.
• Processed peptides from acidic endocytic or phagocytic vesicles form complexes with MHC II for presentation to CD4(+) T helper cells that release cytokines to activate macrophage killing of intravesicular pathogens or to activate B cell antibody production for elimination of extracellular microbes.

Summary Points-2

• Virus-infected cells or tumor cells can be engulfed and processed by APC for activation of CD4(+) T-help needed by Tc activation.
• Extracellular antigens are cross-presented by APC to both Th (via MHC II) and to Tc (via MHC I)