

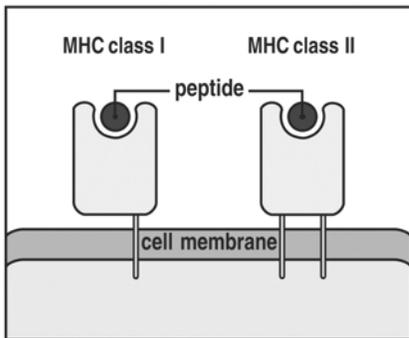
Antigen Presentation

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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 MHCII proteins on antigen-presenting cells for recognition by T cells.



MHC II is a transmembrane glycoprotein (α -chain) noncovalently bound with β_2 -microglobulin. The folded molecule forms a peptide-binding cleft.

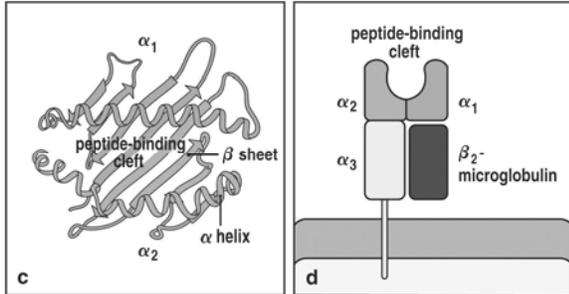


Figure 3-20 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

MHC I is a transmembrane glycoprotein (noncovalently linked α and β glycoprotein chains). The folded molecule forms a peptide-binding cleft.

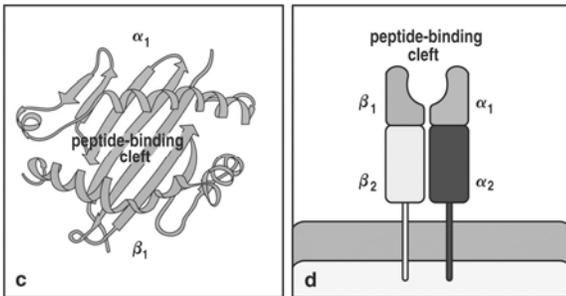


Figure 3-21 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)

Tissue	MHC class I	MHC class II
Lymphoid tissues		
T cells	+++	+
B cells	+++	+++
Macrophages	+++	++
Other antigen-presenting cells (eg Langerhans' cells)	+++	+++
Epithelial cells of the thymus	+	+++
Other nucleated cells		
Neutrophils	+++	-
Hepatocytes	+	-
Kidney	+	-
Brain	+	-†
Non-nucleated cells		
Red blood cells	-	-

Figure 3-19 Immunobiology, 6/e. (© Garland Science 2005)

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

MHC II is expressed only on antigen presenting cells (APC; usually immune cells).

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

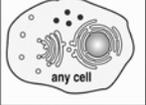
	Cytosolic pathogens	Intravesicular pathogens	Extracellular pathogens and toxins
			
Degraded in	Cytosol	Endocytic vesicles (low pH)	Endocytic vesicles (low pH)
Peptides bind to	MHC class I	MHC class II	MHC class II
Presented to	CD8 T cells	CD4 T cells	CD4 T cells
Effect on presenting cell	Cell death	Activation to kill intravesicular bacteria and parasites	Activation of B cells to secrete Ig to eliminate extracellular bacteria/toxins

Figure 5-3 Immunobiology, 6/e. (© Garland Science 2005)

Peptides that bind to MHC I molecules are actively transported from the cytosol to the endoplasmic reticulum. Cytosol-derived peptides are loaded onto MHC I and MHC I-peptide complexes transported to the cell surface.

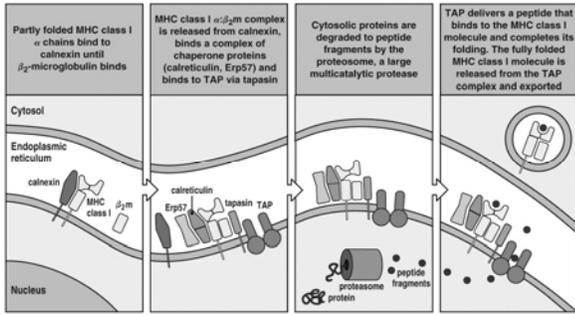


Figure 5-6 Immunobiology, 6/e. (© Garland Science 2005)

Peptides that bind to MHC class II molecules are generated in acidified endocytic vesicles

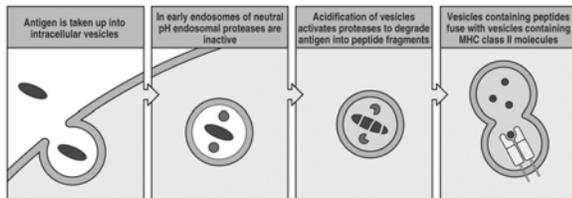
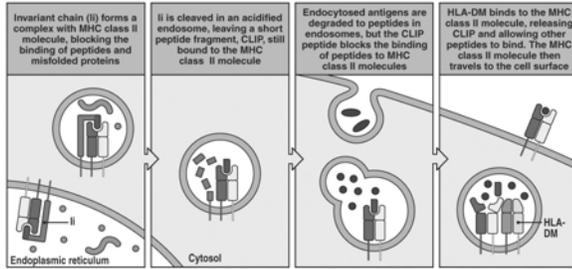


Figure 5-7 Immunobiology, 6/e. (© Garland Science 2005)

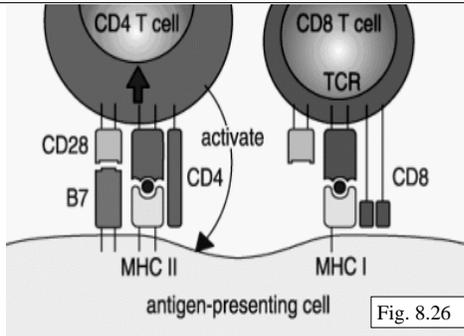
Extracellularly-derived peptides or peptides from intravesicular pathogens are loaded onto MHC II and the MHC II-peptide complex is transported to the APC cell surface.



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 MHC I or MHC II and are used to identify functional T-helper (CD4+) vs. cytotoxic T cells (CD8+).



Cytotoxic T cell recognizes complex of viral peptide with MHC class I and kills infected cell

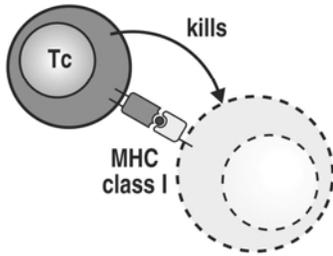


Figure 1-30 Immunobiology, 6/e. (© Garland Science 2005)

T_H1 cell recognizes complex of bacterial peptide with MHC class II and activates macrophage

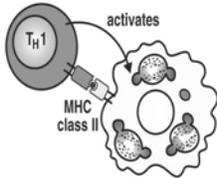
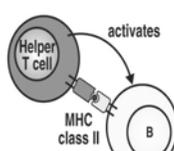


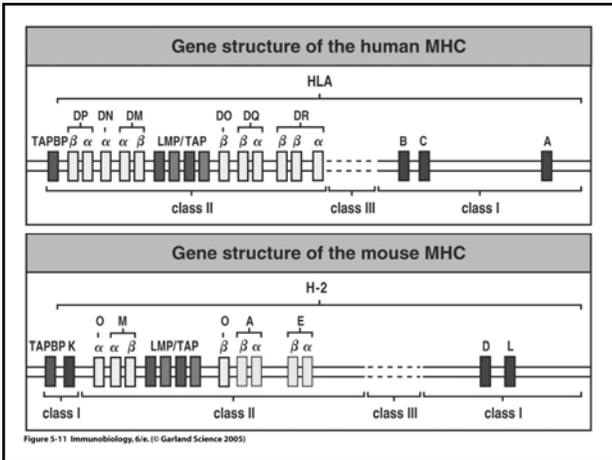
Figure 1-31 Immunobiology, 6/e. (© Garland Science 2005)

Helper T cell recognizes complex of antigenic peptide with MHC class II and activates B cell



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

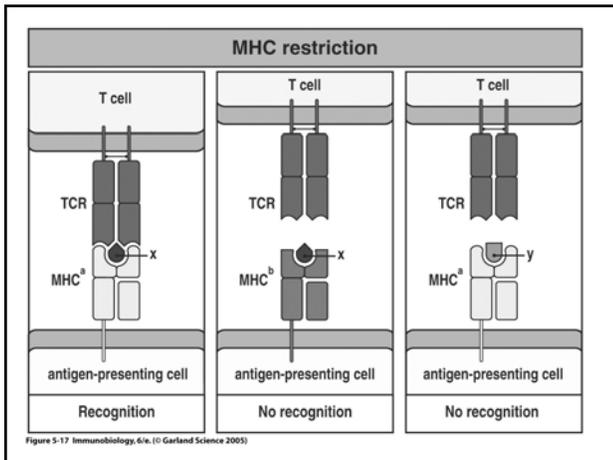
- Different MHC bind different peptides
- The polymorphic amino acid residues that distinguish MHC alleles determine the peptide-binding properties of different MHC molecules
- A single MHC may bind many different peptides which share "sequence motifs"

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

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



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)
