CHAPTER 11

THE IMMUNE RESPONSE

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Steps of adaptive immune responses

- *Antigen processing and presentation*
- *Immune recognition*
- *Activation of Helper T lymphocytes*
- *Activation of B cells*
- *Activation of Cytotoxic T cells and*
- *Elimination of antigen*
- *Contraction*
- *Memory*

Antigen processing and presentation

- Two different classes of MHC proteins - recognized by two major subsets of T cells
- Class I MHC - CD8; **Cytosolic Pathway**
- Class II MHC - CD4 by TCR **Endocytic Pathway**

HELPER T LYMPHOCYTES ACTIVATION

- **Antigen processing and presentation**

- **T cells recognize *only* polypeptide antigens that** are presented in association with MHC proteins.

- Helper T cells : recognize antigen in association with class II MHC proteins,
- cytotoxic T cells: recognize antigen in association with class I MHC proteins.
- This is called **MHC restriction.**

HELPER T LYMPHOCYTES ACTIVATION

- **Antigen processing and presentation**

- Class I MHC proteins present **endogenously synthesized** antigens (e.g., viral proteins),

- class II MHC proteins present the antigens of **extracellular** microorganisms that have been phagocytized (e.g., bacterial proteins).

- **1. The endogenously synthesized proteins**

- (e.g., viral proteins)
- are cleaved by a proteasome, and
- the peptide fragments
- associate with a "TAP transporter" that
- transports the fragment into the rough endoplasmic reticulum,
- where it associates with the class I MHC protein.
- The complex of peptide fragment and class I MHC protein then migrates via the Golgi apparatus to the cell surface.

1. The endogenously synthesized proteins

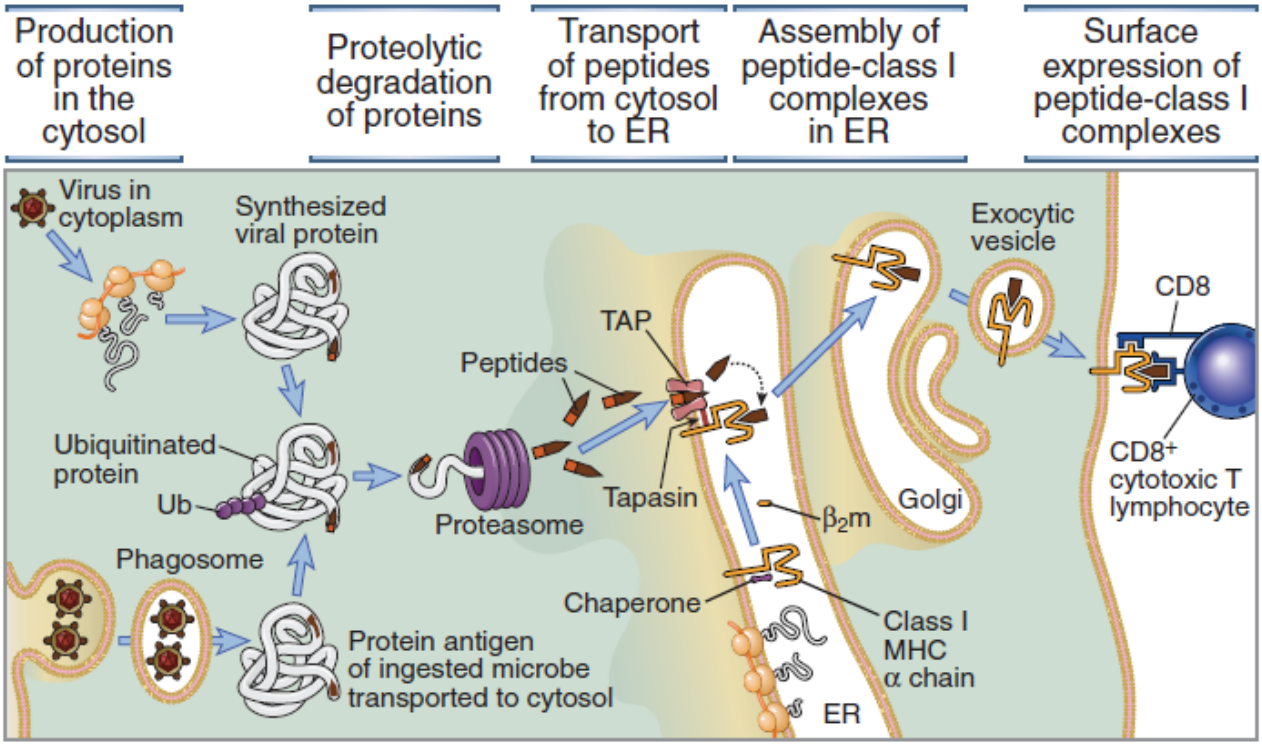


FIGURE 3–15 Class I major histocompatibility complex pathway of processing of cytosolic antigens. Proteins enter the cytoplasm of cells either from phagocytosed microbes or from endogenous synthesis by microbes, such as viruses, that reside in the cytoplasm of infected cells. Cytoplasmic proteins are unfolded, ubiquitinated, and degraded in proteasomes (Ub, ubiquitin).

The extracellularly acquired protein

- are cleaved to peptide fragments within an endosome, where the fragment associates with class II MHC proteins. This complex then migrates to the cell surface.

- Macrophages can readily capture particulate immunogens by phagocytosis

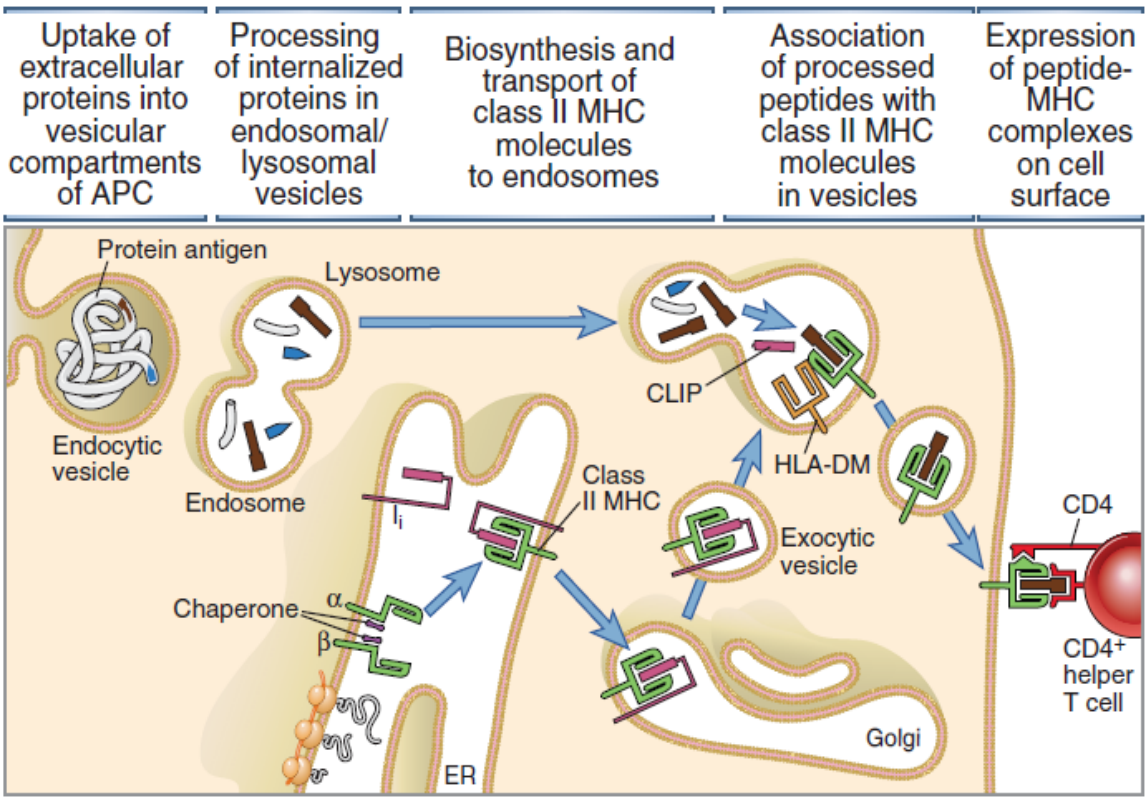
- Other types of APCs: B lymphocytes and dendritic cells capture Ag by pinocytosis or receptor mediated endocytosis

- Captured Ag become enclosed within membrane-lined vesicles in its cytoplasm (Phagosome/ endosome) and undergo denaturation and partial proteolytic digestion , cleaved into short peptides - **(antigen processing).**

- A limited number of the resulting peptides then associate non-covalently with class II MHC proteins and are transported to the APC surface ,
- and recognized by T cells with TCR. process is called –

- **-antigen presentation.**

1. The endogenously synthesized proteins



APC

- APC has little or no antigen specificity.
- APC present several different antigens simultaneously,
- one on each of its many surface MHC proteins.

MHC II and MHC I
Exogenous and Endogenous pathway

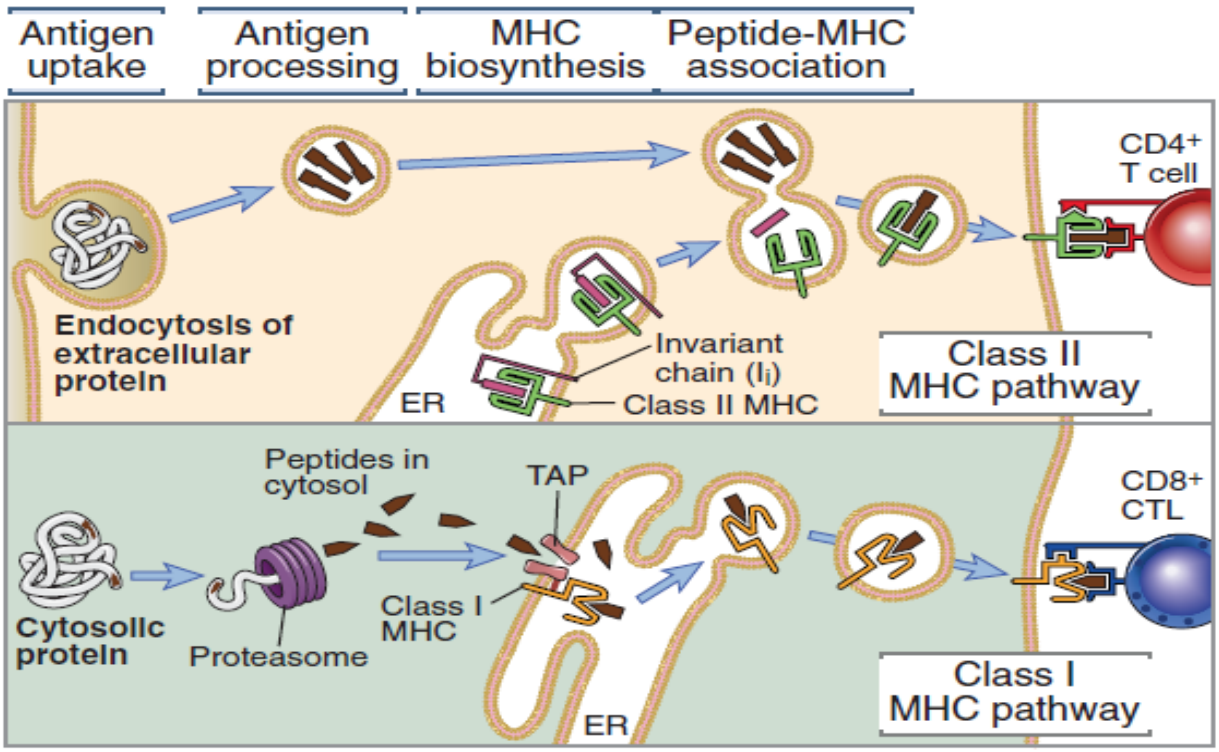


FIGURE 3–12 Pathways of intracellular processing of protein antigens. The class II MHC pathway converts protein

Antigen Processing Pathway

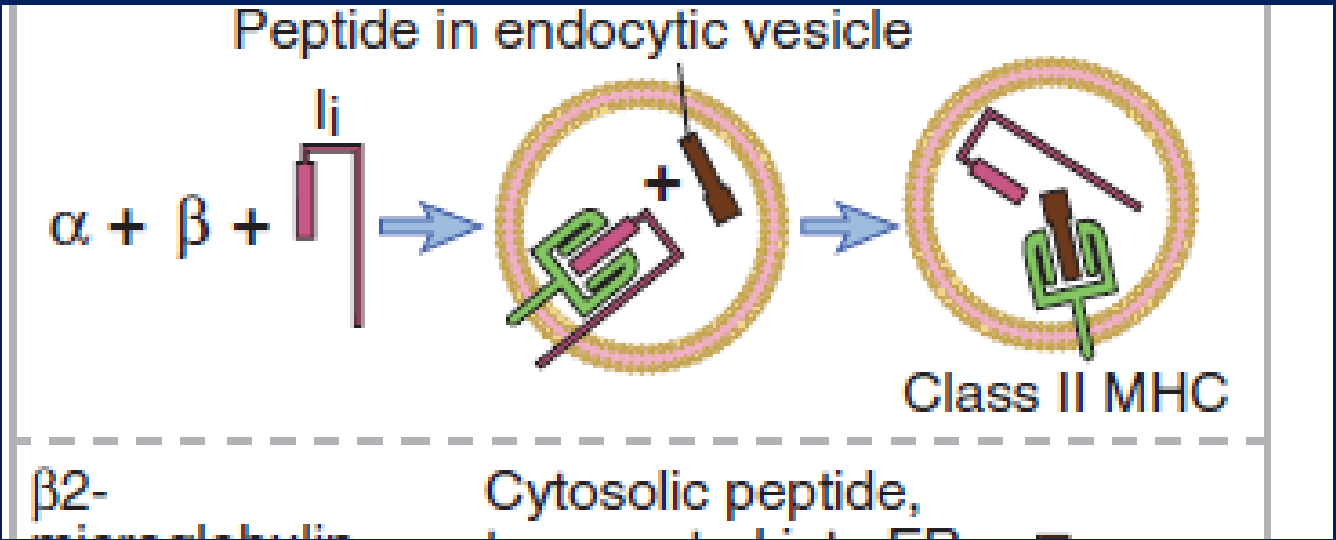
Endocytic	Cytosolic
- extracellular proteins - lysosomal enzyme - professional APC - Endocytic vesicles - Class II - CD4 (helper T cells)	- intracellular pathogens - proteosomes - all nucleated cells - rough ER - Class I - CD8 (cytotoxic T cells)

3. **“invariant chain”**

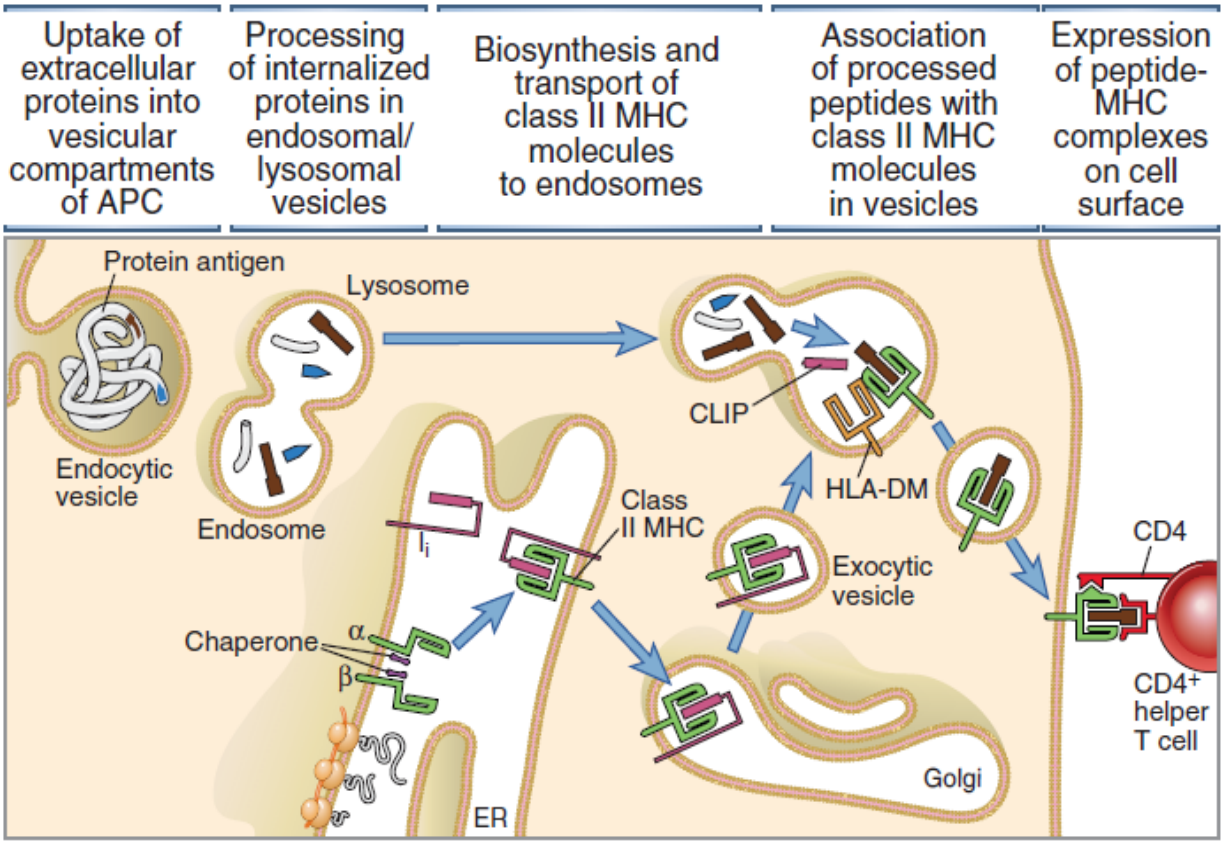
- An “invariant chain” is attached to the class II MHC proteins and prevents endogenously synthesized proteins from associating with class II MHC proteins when these proteins are outside of the endosome.

- The invariant chain is degraded by proteases within the endosome, allowing the peptide fragment to attach to the class II MHC proteins only within that compartment.

Invariant chain



“invariant chain”



B cells/ CD I MHC

- B cells can then present the antigen, after internalization and processing, to helper T cells in association with class II MHC proteins located on the surface of the B cells.

- **CD1 MHC molecules** have a heavy chain and a light chain (β2-microglobulin), but bind **glycolipids** rather than peptides.

- CD1 molecules are primarily expressed on DC and present antigen to the TCR on CD8T or NKT (CD4-CD8-) cells. CD1 molecules are especially important for defense against mycobacterial infections.

- T-cell antigenic peptides must be linear epitopes.

- A T-cell antigen must be a peptide of 8 to 12 amino acids.

Cross-presentation of antigen

- is used by dendritic cells to present antigen to naïve CD8 T cells to initiate the response to viruses and tumor cells.

- After picking up antigen (including debris from apoptotic cells) in the periphery, the protein is degraded or its peptides enter the cytoplasm and are then shuttled through the TAP into the ER to bind to MHC I molecules.

- The DCs present the antigenic peptide to CD8 T cells in the lymph node to initiate the response.

Cross presentation

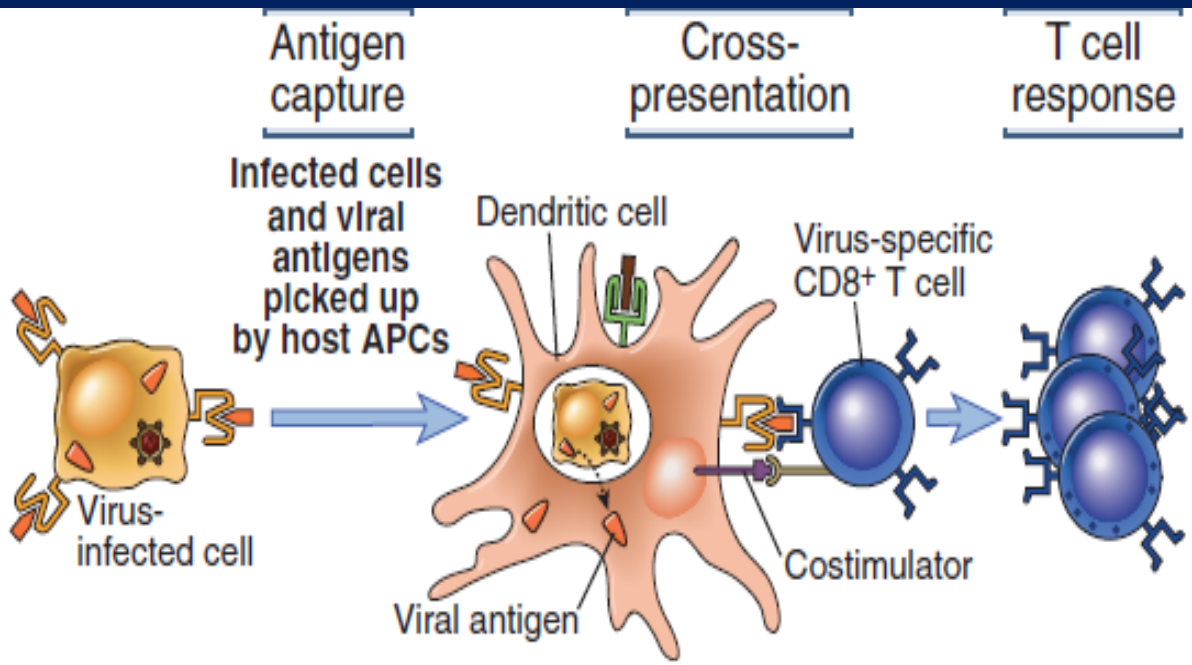


FIGURE 3–16 Cross-presentation of microbial antigens from infected cells by dendritic cells (APCs).

- There are many different alleles within the class I and class II MHC genes;
- hence there are many different MHC proteins.
- These various MHC proteins bind to different peptide fragments.
- The polymorphism of the MHC genes and the proteins they encode are a means of presenting many different antigens to the T-cell receptor.

- Class I and class II MHC proteins can *only* present peptides;
- derived from self proteins as well as from foreign proteins; therefore, whether an immune response occurs is determined by whether a T cell bearing a receptor specific for that peptide has survived the positive and negative selection processes in the thymus.

- there are multiple alleles at each gene locus.

- Each of these MHC proteins can present peptides with a different amino acid sequence. This explains, in part, our ability to respond to many different antigens.