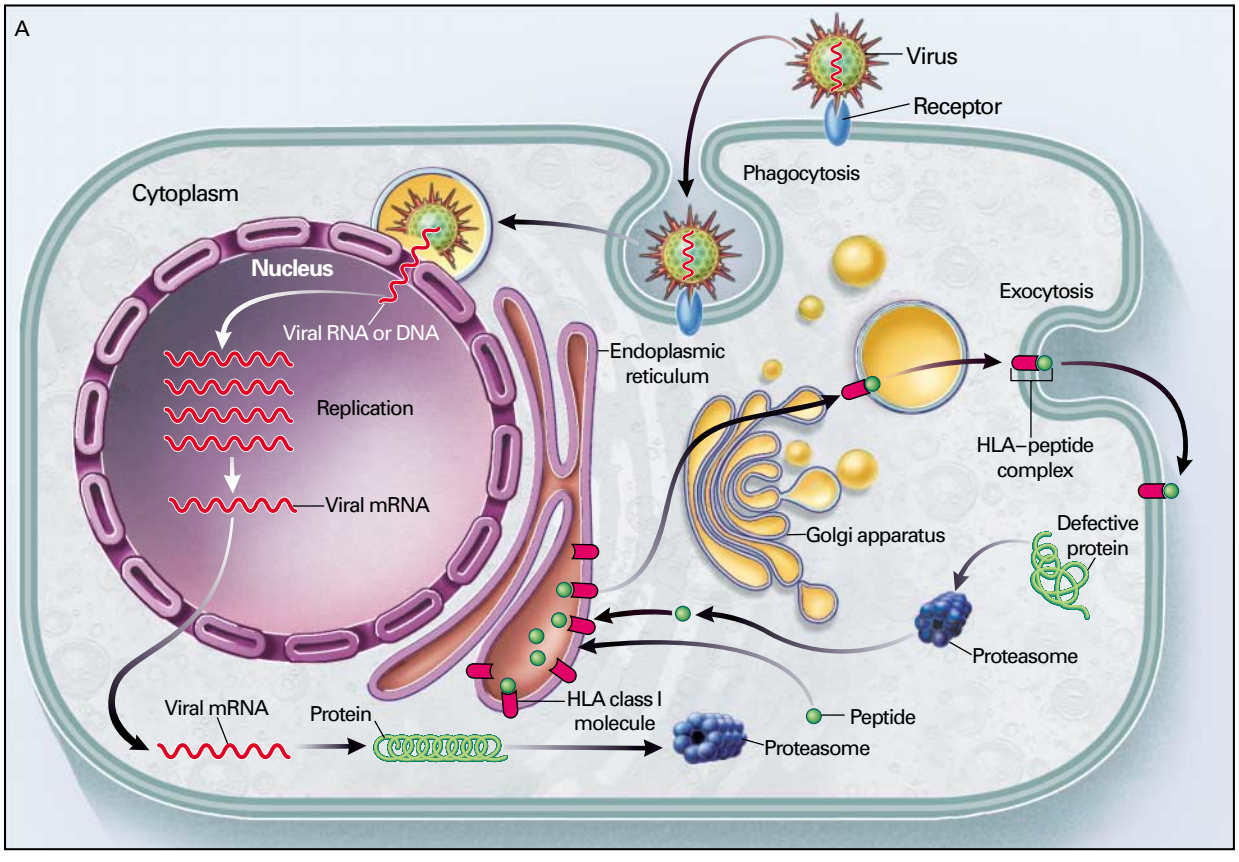
A
Virus
Receptor
Phagocytosis
Cytoplasm
Nucleus
Viral RNA or DNA
Replication
Viral mRNA
Endoplasmic reticulum
Exocytosis
HLA–peptide complex
Golgi apparatus
Defective protein
Proteasome
HLA class I molecule
Peptide
Viral mRNA
Protein
Proteasome

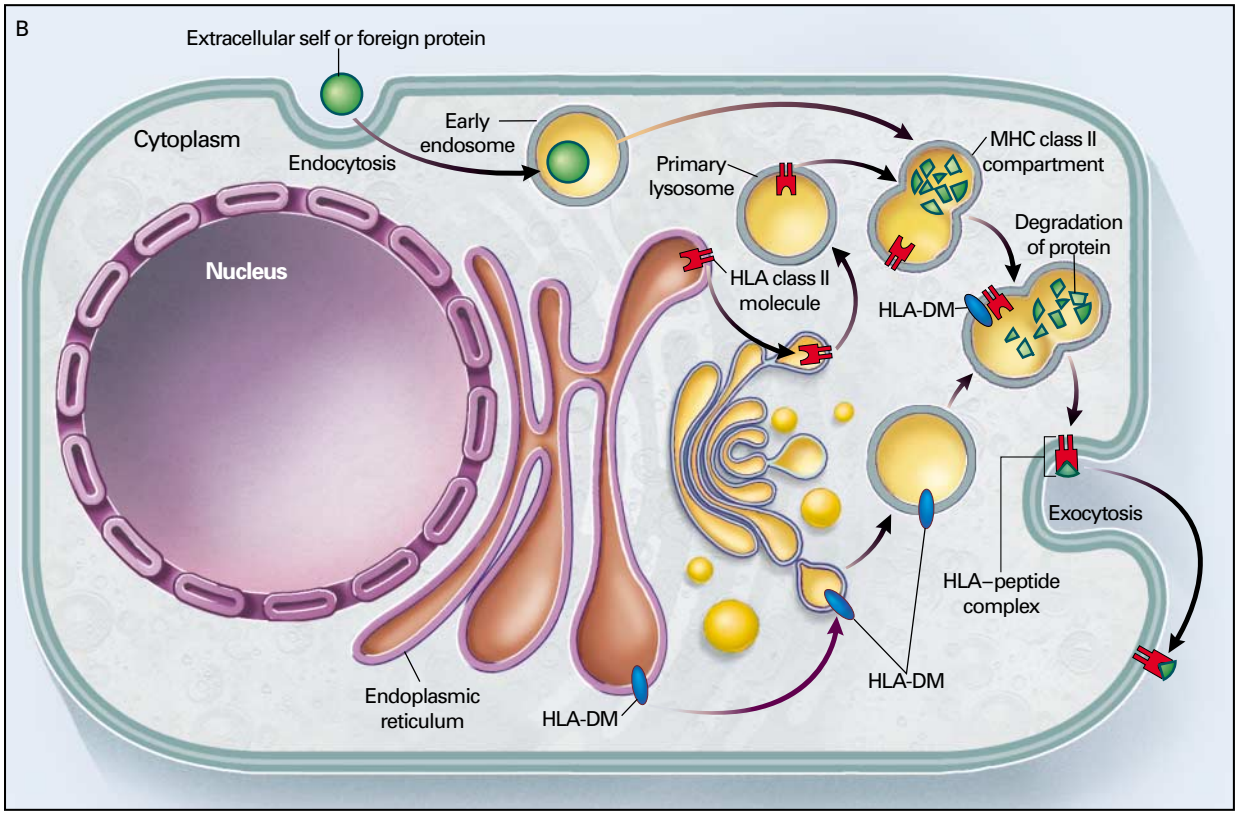
B
Extracellular self or foreign protein
Cytoplasm
Endocytosis
Early endosome
Primary lysosome
MHC class II compartment
Degradation of protein
Nucleus
HLA class II molecule
HLA-DM
Exocytosis
HLA–peptide complex
HLA-DM
Endoplasmic reticulum
HLA-DM

Figure 3 (facing page). Antigen Processing.

Panel A shows the principal pathways of generating peptides for loading onto HLA class I molecules. Worn-out or defective proteins in the cytosol are degraded into peptides in proteasomes. Selected peptides are then transported into the endoplasmic reticulum, where they are loaded onto newly synthesized class I molecules. The HLA–peptide complexes are exported by way of the Golgi apparatus to the surface of the cell. In tissues infected with a virus, viral particles are taken up by cells and uncoated. The viral DNA or RNA enters the nucleus and replicates within it. The viral messenger RNA (mRNA) then enters the cytosol and is transcribed into proteins. Some of the proteins are subsequently degraded in proteasomes, and the peptides are delivered into the endoplasmic reticulum, where they are loaded onto class I molecules for export to the surface of the cell. Panel B shows the processing of extracellular proteins. Self or foreign proteins are taken up by endocytosis (or phagocytosis) and sequestered into endosomes. Class II molecules synthesized in the endoplasmic reticulum are delivered by way of the Golgi apparatus into primary lysosomes, which fuse with the early endosomes to form the major-histocompatibility-complex (MHC) class II compartment. Enzymes brought into this compartment by the lysosomes degrade the engulfed proteins into peptides. HLA-DM molecules synthesized in the endoplasmic reticulum and delivered into the MHC class II compartment by transport vesicles help load the peptides onto the class II molecules. The HLA–peptide complexes are then exported to the surface of the cell.