In antigen-presenting cells (APCs), such as dendritic cells (DCs) and B cells, heterogeneous intracellular pathways and mechanisms are responsible for generating complexes of MHC class I and class II molecules with peptide antigens, and complexes of CD1 molecules with lipid antigens, for presentation to T cells. This process — referred to as antigen processing and presentation — allows T cells to continuously assess the intracellular and extracellular milieu for signs of infection or abnormal cell growth. Although MHC class I molecules typically bind peptides derived from endogenous proteins and MHC class II molecules typically bind peptides derived from proteins that are endocytosed or phagocytosed by APCs, this simple division is not strictly enforced. Indeed, exogenous proteins internalized by DCs can generate peptide-MHC class I complexes that are recognized by CD8+ T cells, a phenomenon referred to as cross-presentation. Similarly, endogenous and viral proteins can generate peptide-MHC class II complexes that are recognized by CD4+ T cells in a process involving autophagy. Understanding the processes and mechanisms by which antigens are captured, processed and loaded onto MHC molecules for presentation to T cells provides us with crucial insights that are necessary for the design of vaccines and therapeutic strategies to bolster T-cell responses.

**The MHC class I pathway**

All nucleated cells express MHC class I molecules and present exogenous peptide antigens to CD8+ T cells, but some DC subsets can also present exogenous peptides to CD8+ T cells through cross-presentation. Cell-surface expression of MHC class I molecules is monitored by natural killer (NK) cells, which express receptors that trigger signals on T cells when the expression of MHC class I is downregulated, such as occurs during viral infections or cell transformation. Endogenous peptides for MHC class I presentation are generated in the cytosol from a variety of sources by the proteasome and cytosolic proteases. These enzymes and proteases are then transported through the trans-Golgi network (TGN) and loaded onto MHC class I molecules in the ER. MHC class I molecules are then transported to the cell surface for presentation to CD8+ T cells.

**The MHC class II pathway**

MHC class II molecules are assembled within the endoplasmic reticulum (ER) as a nonameric complex with the invariant chain (Ii), which protects against premature peptide or protein interactions in pre-biosomal compartments. This complex traffics to the lysosome, where it is subjected to sequential proteolytic degradation. The final cleavage product, a peptide known as class II-associated invariant chain peptide (CIAP), encounters the peptide-binding groove and must be released prior to loading with high-affinity peptides, an event that typically results in the inhibition of MHC class II molecules. Following reduction of disulphide bonds by interferon-γ (IFN-γ), peptide-MHC class II complexes are generated following reduction of disulphide bonds by interferon-γ (IFN-γ). MHC class II molecules are delivered to the cell surface, and the CIAP peptide is released. MHC class II molecules are present on CD4+ T cells, B cells, and some subsets of cells. 

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**The CD1d pathway**

The CD1d pathway is a unique antigen-presenting pathway—only molecules that are generated by phagocytosis following degradation of the Golgi stack and the endosomal or MIIC compartments (MIIC), where Ii is subjected to sequential proteolysis. The CD1d pathway presents lipid antigens to NKT cells. — just load your samples and reagents, and return to separated cells.

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