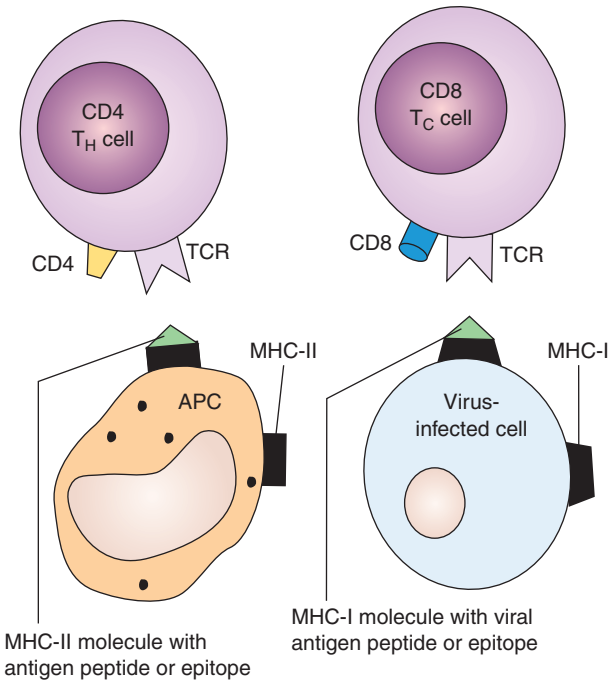

FIGURE 17-7 • Recognition by a T-cell receptor (TCR) on a $CD4^+$ helper T (T_H) cell of an epitope associated with a class II major histocompatibility complex (MHC) molecule on an antigen-presenting cell (APC); and by a TCR on a $CD8^+$ cytotoxic T (T_C) cell of an epitope associated with a class I MHC molecule on a virus-infected cell.

antigen peptide associated with the class I MHC molecule. During a typical viral infection of a cell, small peptides from degraded viral proteins associate with MHC-I molecules and are then transported to the infected cell membrane. This complex communicates to the T-cytotoxic cell that the cell must be destroyed for the overall survival of the host. *Class II MHC* (MHC-II) molecules, which are found primarily on antigen-presenting cells such as macrophages, dendritic cells, and B lymphocytes, communicate with the antigen receptor and CD4 molecule on T-helper lymphocytes.

Class II MHC molecules also have a groove or cleft that binds a fragment of antigen from pathogens that have been engulfed and digested during the process of phagocytosis. The engulfed pathogen is degraded into peptide in cytoplasmic vesicles and then complexed with MHC-II molecules. T-helper cells recognize these complexes on the surface of antigen-presenting cells and become activated. These triggered T-helper cells multiply quickly and direct other immune cells to respond to the invading pathogen through the secretion of cytokines. A third group of genes located on the same chromosome near the class I and II MHC genes encode other proteins with diverse functions. Some complement and cytokines important for signaling an immune response are examples of class III MHC molecules. These secreted molecules are structurally and functionally unrelated to the class I and II MHC molecules.

Each individual has a unique collection of MHC proteins, and a variety of MHC molecules can exist in a population. Thus, MHC molecules are both polygenic and polymorphic. The MHC genes are the most polymorphic genes known. MHC alleles affect immune responses as well as susceptibility to a number of diseases. Because of the number of MHC genes and the possibility of several alleles for each gene, it is almost impossible for any two individuals to have an identical MHC profile, unless they are identical twins. In contrast to the receptors on T and B lymphocytes that bind a unique antigen molecule, each MHC protein can bind a broad spectrum of antigen peptides.

Human MHC proteins are called *human leukocyte antigens* (HLA) because they were first detected on white blood cells. Because these molecules play a role in transplant rejection and are detected by immunologic tests, they are commonly called *antigens.* More recently, analysis of the genes for the HLA molecules has ensured a more complete identification of the potential antigens present in an individual. The classic human MHC-I molecules are divided into types called HLA-A, HLA-B, and HLA-C, and the MHC-II molecules are identified as HLA-DR, HLA-DP, and HLA-DQ (Table 17-3). Additional, less well-studied, nonclassic MHC genes have been described and shown to influence other immune interactions. Each of the gene loci that describe HLA molecules can be occupied by multiple alleles or alternative genes. For example, there are more than 350 possible alleles for the A locus, 650 alleles for the B locus, and 180 alleles for the C locus. The genes and their expressed molecules are designated by a letter and numbers (*i.e.,* HLA-B27).

Because the class I and II MHC genes are closely linked on one chromosome, the combination of HLA genes usually is inherited as a unit, called a *haplotype.* Each person inherits a chromosome from each parent and therefore has two HLA

TABLE 17-3 Properties of Class I and II MHC Molecules

PROPERTIES	HLA ANTIGENS	DISTRIBUTION	FUNCTIONS
Class I MHC	HLA-A, HLA-B, HLA-C	Virtually all nucleated cells	Present processed antigen to cytotoxic $CD8^+$ T cells; restrict cytolysis to virus-infected cells, tumor cells, and transplanted cells
Class II MHC	HLA-DR, HLA-DP, HLA-DQ	Immune cells, antigen-presenting cells, B cells, and macrophages	Present processed antigenic fragments to $CD4^+$ T cells; necessary for effective interaction among immune cells

HLA, human leukocyte antigen; MHC, major histocompatibility complex.