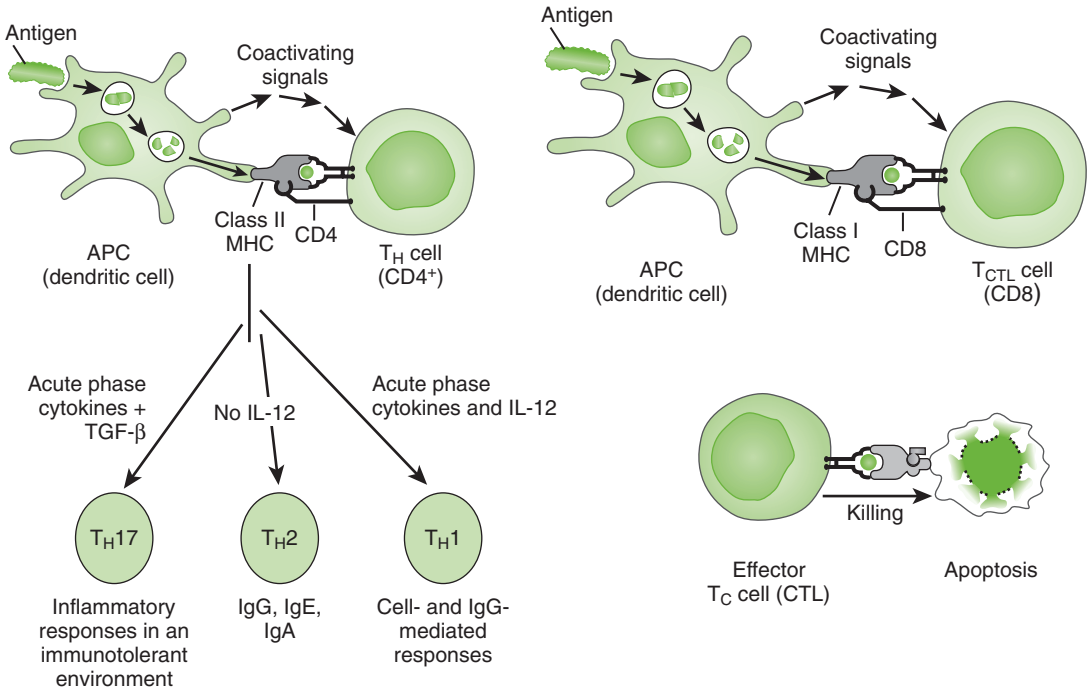

FIGURE 86-3 Overview of T-cell activation. The dendritic cell (DC) initiates the interaction with a $CD4^+$ or $CD8^+$ T cell through a major histocompatibility complex (MHC)–peptide interaction with the T cell receptor. The DC provides an 11-amino-acid peptide on the class II MHC, B7 coreceptor, and cytokines to activate $CD4^+$ T cells. The $CD8^+$ T cell is activated through the class I MHC and 8- to 9-amino-acid peptide plus the B7 coreceptor and cytokines. Presentation of antigen to CD4 T cells and cross-presentation to $CD8^+$ T cells is shown. The cytokines produced by the DCs determine the type of helper T (T_H) cell. Activated $CD8^+$ T cells can interact with and lyse target cells through T-cell receptor recognition of peptide in class I MHC molecules on target cells. APC, Antigen-presenting cell; CTL, cytotoxic T lymphocyte; Ig, immunoglobulin; TGF-β, transforming growth factor-β. (From Rosenthal KS, Tan MJ, editors: Rapid review microbiology and immunology, ed 3, Philadelphia, 2011, Mosby.)

Alternatively, $CD4^+$ T cells can become T_H2 cells that drive processes such as antiparasitic activity. T_H2 cells stimulate B cells to produce antibodies against extracellular pathogens through the production of IL-4, and they stimulate proliferation of eosinophils for activity against parasites (e.g., worms) through the production of IL-5.

T_H17 cells are stimulated by IL-23 and produce IL-17, which plays an important role in amplifying the inflammatory response by attracting neutrophils to sites of infection caused by extracellular bacteria and possibly fungi. The complexity of these $CD4^+$ T-cell subsets is still being explored.

$CD8^+$ T cells respond to pathogens that initially enter phagocytic cells directly, such as viruses. Upon intracellular replication, viral proteins are marked for destruction by covalent binding to the protein ubiquitin. The tagged molecules are then degraded by a proteasome, which is a cytoplasmic enzyme complex. Resulting peptide chains of 6 to 24 amino acids then associate with MHC class 1 molecules in a complex intracellular process in the APC and are presented on the surface of the APC. Naïve $CD8^+$ cells that are specific for the presented antigen adhere to the presented MHC class I/antigen complex and express IL-2 receptors. $CD4^+$ T_H1 antigen-specific cells also interact with the APC, which stimulates the production of IL-2 by the $CD4^+$ cell and increases CD80/86 expression by the APC. CD28 on the $CD8^+$ T cell interacts with the CD80/86 on the APC to stimulate the $CD8^+$ T cell to proliferate and differentiate into cytotoxic T lymphocytes. The cytotoxic T cells can lyse target cells expressing the appropriate MHC class I/antigen complex. Several signals, including MHC class I/antigen recognition, IL-2 stimulation, and CD28 and CD80/86 adherence, combine to optimally initiate $CD8^+$ cytotoxic T cells to attack virus-infected cells.

$CD4^+$ and $CD8^+$ T cells help to regulate the immune response. $CD4^+$ regulatory T cells (Tregs) express CD4 and CD25 and help to regulate immune responses, particularly those related to autoimmune diseases but also some infectious diseases. $CD8^+$ suppressor T cells inhibit some autoimmune inflammatory processes.

HOST DEFENSE RESPONSE TO PATHOGENS

Humans are constantly threatened by microbial pathogens. Organisms such as *S. pneumoniae*, group A streptococci, and respiratory viruses colonize the respiratory tract. *S. aureus*, fungi, and many other organisms live on the skin. Every type of pathogen lives in the gastrointestinal tract; some are benign, and some are dangerous.

Host defenses need to react continuously and appropriately to breaches in nonimmunologic host defenses as described earlier. For example, if a person suffers a cut on the hand, the skin barrier is breached, and pathogens may be inoculated into the subcutaneous tissues. This stimulates an immediate nonimmunologic host defense response that includes phagocytosis by cells such as macrophages, which produce cytokines such as IL-1 and TNF-α. Cytokines stimulate the expression of adhesion molecules on vascular endothelium. Neutrophils then bind to the endothelium, move into tissues, and are attracted by a chemokine gradient to the site of invasion.