SECTION 1 THE IMMUNE SYSTEM IN HEALTH AND DISEASE

372e Introduction to the Immune System

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DEFINITIONS

- *Adaptive immune system*—recently evolved system of immune responses mediated by T and B lymphocytes. Immune responses by these cells are based on specific antigen recognition by clonotypic receptors that are products of genes that rearrange during development and throughout the life of the organism. Additional cells of the adaptive immune system include various types of antigen-presenting cells.
- *Antibody*—B cell–produced molecules encoded by genes that rearrange during B cell development consisting of immunoglobulin heavy and light chains that together form the central component of the B cell receptor for antigen. Antibody can exist as B cell–surface antigen-recognition molecules or as secreted molecules in plasma and other body fluids.
- *Antigens*—foreign or self-molecules that are recognized by the adaptive and innate immune systems resulting in immune cell triggering, T cell activation, and/or B cell antibody production.
- *Antimicrobial peptides*—small peptides <100 amino acids in length that are produced by cells of the innate immune system and have anti-infectious agent activity.
- *Apoptosis*—the process of *programmed cell death* whereby signaling through various "death receptors" on the surface of cells (e.g., tumor necrosis factor [TNF] receptors, CD95) leads to a signaling cascade that involves activation of the caspase family of molecules and leads to DNA cleavage and cell death. Apoptosis, which does not lead to induction of inordinate inflammation, is to be contrasted with *cell necrosis*, which does lead to induction of inflammatory responses.
- *Autoimmune diseases*—diseases such as systemic lupus erythematosus and rheumatoid arthritis in which cells of the adaptive immune system such as autoreactive T and B cells become overreactive and produce self-reactive T cell and antibody responses.
- *Autoinflammatory diseases*—hereditary disorders such as hereditary periodic fevers (HPFs) characterized by recurrent episodes of severe inflammation and fever due to mutations in controls of the innate inflammatory response, i.e., the inflammasome (see below and Table 372e-6). Patients with HPFs also have rashes and serosal and joint inflammation, and some can have neurologic symptoms. Autoinflammatory diseases are different from autoimmune diseases in that evidence for activation of adaptive immune cells such as autoreactive B cells is not present.
- *B cell receptor for antigen*—complex of surface molecules that rearrange during postnatal B cell development, made up of surface immunoglobulin (Ig) and associated Ig αβ chain molecules that recognize nominal antigen via Ig heavy- and light-chain variable regions, and signal the B cell to terminally differentiate to make antigen-specific antibody.
- *B lymphocytes*—bone marrow-derived or bursal-equivalent lymphocytes that express surface immunoglobulin (the B cell receptor for antigen) and secrete specific antibody after interaction with antigen.
- *CD classification of human lymphocyte differentiation antigens*—the development of monoclonal antibody technology led to the discovery of a large number of new leukocyte surface molecules. In 1982, the First International Workshop on Leukocyte Differentiation Antigens was held to establish a nomenclature for cell-surface molecules of human leukocytes. From this and subsequent leukocyte differentiation workshops has come the *cluster of differentiation* (CD) classification of leukocyte antigens.
- *Chemokines*—soluble molecules that direct and determine immune cell movement and circulation pathways.
- *Complement*—cascading series of plasma enzymes and effector proteins whose function is to lyse pathogens and/or target them to be phagocytized by neutrophils and monocyte/macrophage lineage cells of the reticuloendothelial system.
- *Co-stimulatory molecules*—molecules of antigen-presenting cells (such as B7-1 and B7-2 or CD40) that lead to T cell activation when bound by ligands on activated T cells (such as CD28 or CD40 ligand).
- *Cytokines*—soluble proteins that interact with specific cellular receptors that are involved in the regulation of the growth and activation of immune cells and mediate normal and pathologic inflammatory and immune responses.
- *Dendritic cells*—myeloid and/or lymphoid lineage antigen-presenting cells of the adaptive immune system. Immature dendritic cells, or dendritic cell precursors, are key components of the innate immune system by responding to infections with production of high levels of cytokines. Dendritic cells are key initiators both of innate immune responses via cytokine production and of adaptive immune responses via presentation of antigen to T lymphocytes.
- *Ig Fc receptors*—receptors found on the surface of certain cells including B cells, natural killer cells, macrophages, neutrophils, and mast cells. Fc receptors bind to antibodies that have attached to invading pathogen-infected cells. They stimulate cytotoxic cells to destroy microbe-infected cells through a mechanism known as antibody-dependent cell-mediated cytotoxicity (ADCC). Examples of important Fc receptors include CD16 (FcγRIIIa), CD23 (FcεR), CD32 (FcγRII), CD64 (FcγRI), and CD89 (FcαR).
- *Inflammasome*—large cytoplasmic complexes of intracellular proteins that link the sensing of microbial products and cellular stress to the proteolytic activation of interleukin (IL)-1β and IL-18 inflammatory cytokines. Activation of molecules in the inflammasome is a key step in the response of the innate immune system for intracellular recognition of microbial and other danger signals in both health and pathologic states.
- *Innate immune system*—ancient immune recognition system of host cells bearing germline-encoded pattern recognition receptors that recognize pathogens and trigger a variety of mechanisms of pathogen elimination. Cells of the innate immune system include natural killer cell lymphocytes, monocytes/macrophages, dendritic cells, neutrophils, basophils, eosinophils, tissue mast cells, and epithelial cells.
- *Large granular lymphocytes*—lymphocytes of the innate immune system with azurophilic cytotoxic granules that have natural killer cell activity capable of killing foreign and host cells with few or no self-major histocompatibility complex (MHC) class I molecules.
- *Natural killer (NK) cells*—large granular lymphocytes that kill target cells expressing few or no human leukocyte antigen (HLA) class I molecules, such as malignantly transformed cells and virally infected cells. NK cells express receptors that inhibit killer cell function when self-MHC class I is present.