4TH EDITION

IMMUNOLOGY
FOR MEDICAL STUDENTS

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ISBN 978-0-7020-8434-8

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Design: Ryan Cook
Marketing Manager: Belinda Tudin

Printed in India

Last digit is the print number: 9 8 7 6 5 4 3 2 1

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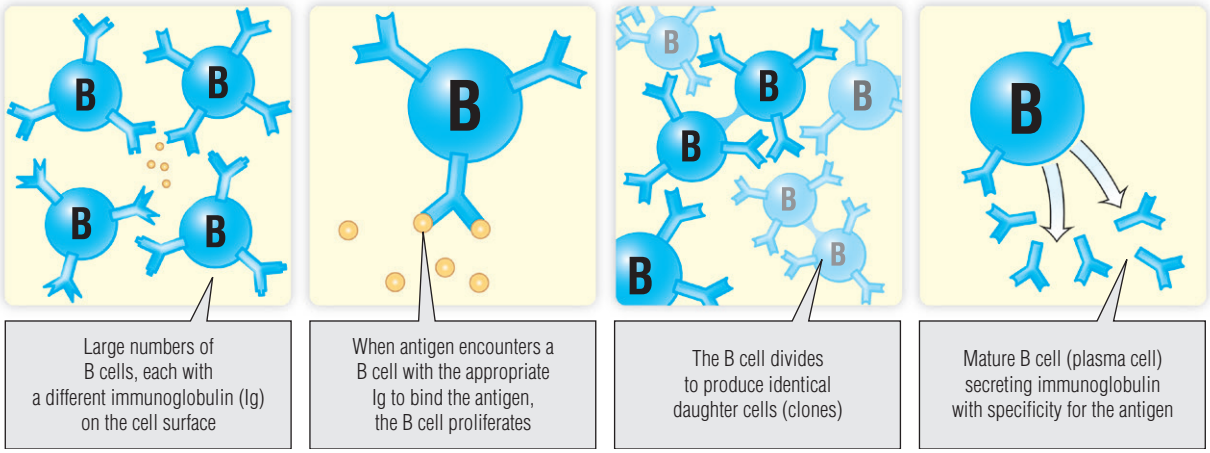

Fig. 1.2 Clonal selection of B cells.

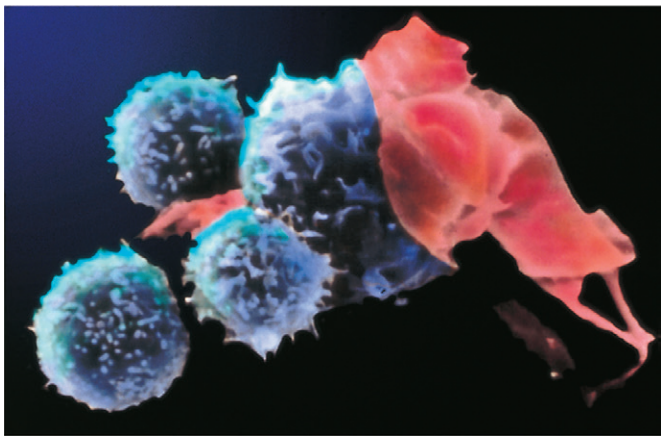

Fig. 1.3 Scanning electron micrograph of T cells (*blue*) and a tumor cell (*red*). (From BSIP Lecaque and the Science Photo Library.)

TABLE 1.1 Comparison of Some Overall Features of the Innate and Adaptive Immune Systems

	Innate	Adaptive
Characteristics	Nonspecific response Fast response (minutes) No memory	Very specific Slow response (days) Memory
Components	Natural barriers, phagocytes, and secreted molecules Few pattern-recognition molecules	Lymphocytes and secreted molecules Many antigen recognition molecules

B cells, the daughter clones produce large amounts of soluble receptor (antibody). In the case of T cells, large numbers of specific effector cells bearing the appropriate receptor on their cell surface are generated. Different types of specialist T cells, such as T-helper (TH) cells, are produced for specific situations (see Chapter 16). For example, TH1 T cells are usually produced in response to viral infections, TH2 T cells are produced in response to worms, and TH17 cells respond to fungi and extracellular bacteria.

B-cell and T-cell antigen receptors differ in one very important way: B-cell antigen receptors can interact directly with antigen, whereas T-cell antigen receptors recognize an antigen only when it is presented to them on the surface of another cell by MHC molecules (see Chapters 2, 7, and 8).

In addition to recognizing nonself antigens, the cells of the immune system also recognize alterations of self that result from certain disease processes—for example, modified self-antigens found on tumor cells—and may eliminate the tumor cell once it has been recognized (Fig. 1.3; see Chapter 35). The ability to recognize unaltered self-antigen can, if unregulated, lead to autoimmune disease, such as with some forms of diabetes mellitus (see Chapter 28). Fortunately, the adaptive immune system contains a number of mechanisms to ensure that unaltered self-antigens are tolerated, which prevents autoimmune disease in most people (see Chapter 18.)

A critically important feature of the adaptive immune response is that it displays memory of a previous encounter with a microbe (or antigen). This is the basis of protection from disease by vaccination with an attenuated form of the pathogen (Box 1.2; see also Box 2.1), but it is also the way in which the body is protected from reinfection. For example, we are regularly exposed to coronaviruses (Box 1.3). If we reencounter the same antigenic form of coronavirus, or even an antigenically similar (i.e., cross-reactive) form, the response is faster and greater in magnitude, and infection is limited or prevented. Unfortunately, because coronaviruses are one of a class of infectious agents capable of radically changing their genetic structure (and antigenic makeup), new viruses are always around to cause new infections. The most obvious example of this is from the SARS-CoV-2 or COVID-19 pandemic. Several overall characteristics of the innate and adaptive immune systems are summarized in Table 1.1.

The medical successes associated with advances in knowledge about the host defense system include improvements in public health that have arisen from vaccination against communicable diseases (see Box 1.2 and Chapter 25); success with organ transplantation, such as with kidneys and hearts (see Box 1.4 and

GLOSSARY

Activation phase. Phase of the immune response when a lymphocyte divides to give many more of the same cell (clonal expansion).

Active immunity. Protective immunity that develops after exposure to infection or vaccination.

Acute-phase response. A systemic reaction to infection or inflammation, mediated by cytokine production and characterized by fever and production of acute-phase proteins.

Adaptive (acquired) immune system response. Part of the immune system in which genetic recombination is used to recognize specific molecules. Slow to respond, but produces lasting memory.

Adjuvant. Substance that increases the immunogenicity of a vaccine, usually by activating the innate immune system.

Affinity. Strength of binding between antigen and antibody or T- or B-cell receptor.

Affinity maturation. Process by which B cells undergo somatic hypermutation and increase the affinity of the B-cell receptor.

Allele. Normal genetic variants that occur in more than 1% of the population. For example, eye color or different human leukocyte antigen types.

Allelic exclusion. Any one B cell expresses only immunoglobulin of one allotype in a heterozygous individual.

Allergen. An environmental substance capable of eliciting an immediate hypersensitivity reaction.

Allergy. Immediate hypersensitivity reaction to an otherwise harmless environmental substance, mediated by immunoglobulin E.

Allogeneic. Immune reactions to a genetically different member of the same species.

Allogeneic transplant. Transplant between genetically different members of the same species.

Allotype. Genetic polymorphisms (different alleles) of both heavy and light chain immunoglobulin genes that can be detected by antibodies.

Alternative pathway. Activation of the complement cascade by exposure to a solid surface lacking complement inhibitors.

Anaphylatoxin. Low-molecular-weight product of complement activation that increases capillary permeability and attracts leukocytes.

Anergy. State of dormancy induced by exposure to antigen in certain circumstances.

Antibody. Protein produced in response to and capable of binding specifically with an antigen. Antibodies have an immunoglobulin structure.

Antigen. Molecules specifically recognized by receptors of the adaptive immune system.

Antigen recognition molecules (ARMs). The ARMs are the B- and T-cell receptor molecules and the proteins encoded by the major histocompatibility complex.

Antigen-binding site. The portion of the antibody that makes contact with antigen.

Antigenemia. High levels of antigen circulating in the bloodstream.

Antigenic drift. Gradual change in an organism's antigens consequent to acquisition of mutations.

Antigen-presenting cells (APCs). Cells that can process antigen and present antigen to T cells.

Apoptosis. Deliberate, programmed cell death.

Asthma. Transient airflow limitation due to bronchial smooth muscle constriction and mucus secretion.

Atopy. Genetic predisposition to allergy.

Attenuated vaccine. Vaccine produced by genetically modifying a pathogenic organism.

Autoantibody. Antibody produced against self antigen.

Autoimmune disease. Disease caused by hypersensitivity reactions that occur as exaggerated autoimmunity.

Autoimmunity. Recognition of normal components of the body by the adaptive immune system. Occurs in healthy individuals but can also cause autoimmune disease.

Autologous transplant. Tissue returning to the same individual after a period outside the body, usually in a frozen state.

B-cell receptor (BCR). The cell surface–located receptor for antigen on B cells.

B lymphocytes. Subset of white blood cells that can secrete antibody molecules.

Bence Jones protein. Monoclonal light chain present in the urine in myeloma.

Biopharmaceutical (biologic). Medication, usually proteins, produced by living cells.

Biosimilar. Two biopharmaceuticals with identical amino acid sequences but produced by different manufacturers. Cannot be assumed to be identical.

Blasts. Immature, rapidly proliferating cells.

Bone marrow. The major hematopoietic organ in humans. Particularly important in B-cell generation, but all the blood cell types—except mature T cells—are generated in the bone marrow.

Caspase. Proteolytic enzymes involved in triggering apoptosis.

CD. Cluster of differentiation nomenclature system for cell surface molecules (and thus for cell subsets).

CD4 count. Number of circulating $CD4^+$ T cells; used to monitor HIV infection.

Cell-mediated immunity. Refers to the function of T cells as opposed to humoral or antibody-mediated immunity.

Central tolerance. Tolerance induced in immature T or B cells in the thymus and bone marrow, respectively.

Chemokines. Chemotactic cytokines; these attract cells to the site of infection.

Chemotaxis. Directed movement of cells, often to the site of infection.

Chimeric monoclonal antibody. Monoclonal antibody using mouse immunoglobulin variable regions and human immunoglobulin constant regions.

Class switching. The process by which an individual B cell can, during maturation, switch immunoglobulin heavy chain usage while retaining the same variable genes and antigen specificity.

Classical pathway. Activation of the complement cascade by exposure to aggregated immunoglobulin.

Clonal selection theory. The idea that each lymphocyte expresses a unique antigen receptor and that this preexisting cell divides on exposure to antigen and gives rise to many daughter cells (clones).

Clone. In immunology, a series of genetically identical lymphocytes, all derived from one B cell or T cell after receptor recombination.

Cognate antigen. The precise antigen that a given antigen receptor has specificity for.

Cognitive phase. Phase of an active immune response during which antigen is recognized by a cell bearing a receptor specific for the antigen.

Collectin. Molecules forming part of the innate immune system, containing lectin (carbohydrate-binding) domains and collagen-like domains.

Colony-stimulating factor (CSF). Growth factors that induce differentiation of specific cell lineages during hematopoiesis.

Combinatorial diversity. Refers to immunoglobulin or T-cell receptor variable region gene segments recombining in multiple combinations (e.g., 30 $V\kappa \times 5\ J\kappa = 150$ different variable regions).

Complement. Cascade of serum enzymes activated by the presence of pathogens.

C-reactive protein (CRP). Acute-phase protein produced at high levels during inflammation.

Cross-reactivity. Occasionally, an antigen recognition molecule is specific for a particular antigen, but a different antigen fits well enough for stable binding to occur.

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