

# Contents in Brief

## PREFACE

What's New in the Tenth Edition

Resources for Instructors and Students

Acknowledgments

About the Authors

## PART I AN INTRODUCTION TO IMMUNOBIOLOGY AND INNATE IMMUNITY

Chapter 1 Basic Concepts in Immunology

Chapter 2 Innate Immunity: The First Lines of Defense

Chapter 3 Cellular Mechanisms of Innate Immunity

## PART II THE RECOGNITION OF ANTIGEN

Chapter 4 Antigen Recognition by B-cell and T-cell Receptors

Chapter 5 The Generation of Lymphocyte Antigen Receptors

Chapter 6 Antigen Presentation to T Lymphocytes

## PART III THE DEVELOPMENT OF MATURE LYMPHOCYTE RECEPTOR REPERTOIRES

Chapter 7 Lymphocyte Receptor Signaling

Chapter 8 The Development of B and T Lymphocytes

## PART IV THE ADAPTIVE IMMUNE RESPONSE

Chapter 9 T Cell-Mediated Immunity

Chapter 10 The Humoral Immune Response

Chapter 11 Integrated Dynamics of Innate and Adaptive Immunity

Chapter 12 The Barrier Immune System

## PART V THE IMMUNE SYSTEM IN HEALTH AND DISEASE

Chapter 13 Failures of Host Defense Mechanisms

Chapter 14 Allergic Diseases and Hypersensitivity Reactions

Chapter 15 Autoimmunity and Transplantation

Chapter 16 Manipulation of the Immune Response

## APPENDICES

Note: Appendices II-IV are available on [digital.wwnorton.com/janeway10](http://digital.wwnorton.com/janeway10) and in the ebook.

Appendix I The Immunologist's Toolbox

eAppendix II CD Antigens

eAppendix III Cytokines and Their Receptors

eAppendix IV Chemokines and Their Receptors

Glossary

Credits

Index

iii	iv	vi	vii	ix
1	37	79	141	179
217	261	301	347	405
453	505	587	663	699
749	813	813	813	813
A-1	A-49	A-69	A-73	G-1
C-1	I-1			

# Detailed Contents

## Preface

- What's New in the Tenth Edition
- Resources for Instructors and Students
- Acknowledgments
- About the Authors

## PART I AN INTRODUCTION TO IMMUNO-BIOLOGY AND INNATE IMMUNITY

### Chapter 1 Basic Concepts in Immunology

The origins of vertebrate immune cells.

Principles of innate immunity.

- 1-1 Commensal organisms cause little host damage while pathogens damage host tissues by a variety of mechanisms.
- 1-2 Anatomic and chemical barriers are the first defense against pathogens.
- 1-3 The immune system is activated by inflammatory inducers that indicate the presence of pathogens or tissue damage.
- 1-4 The myeloid lineage comprises most of the cells of the innate immune system.
- 1-5 Sensor cells express pattern-recognition receptors that provide an initial discrimination between self and nonself.
- 1-6 Sensor cells induce an inflammatory response by producing mediators such as chemokines and cytokines.
- 1-7 Innate lymphoid cells and natural killer cells are effector cells that share similarities with lymphoid lineages of the adaptive immune system.

Summary.

Principles of adaptive immunity.

- 1-8 The interaction of antigens with antigen receptors induces lymphocytes to acquire effector and memory activity.
- 1-9 Antibodies and T-cell receptors are composed of constant and variable regions that provide distinct functions.
- 1-10 Antibodies and T-cell receptors recognize antigens by fundamentally different mechanisms.
- 1-11 Antigen-receptor genes are assembled by somatic gene rearrangements of incomplete receptor gene segments.
- 1-12 Lymphocytes activated by antigen give rise to clones of antigen-specific effector cells that mediate adaptive immunity.
- 1-13 Lymphocytes with self-reactive receptors are normally eliminated during development or are functionally inactivated.
- 1-14 Lymphocytes mature in the bone marrow or the thymus and then congregate in lymphoid tissues throughout the body.
- 1-15 Adaptive immune responses are initiated by antigen and antigen-presenting cells in peripheral lymphoid tissues.

iii	1-16	Lymphocytes encounter and respond to antigen in the peripheral lymphoid organs.	18
iv			
vi	1-17	Mucosal surfaces have specialized immune structures that orchestrate responses to environmental microbial encounters.	20
vii			
ix	1-18	Lymphocytes activated by antigen proliferate in the peripheral lymphoid organs, generating effector cells and immunological memory.	22
		Summary.	24
1		The effector mechanisms of immunity.	25
2	1-19	Innate immune responses can select from several effector modules to protect against different types of pathogens.	26
3			
	1-20	Antibodies protect against extracellular pathogens and their toxic products.	27
3			
	1-21	T cells orchestrate cell-mediated immunity and regulate B-cell responses to most antigens.	29
5			
	1-22	Inherited and acquired defects in the immune system result in increased susceptibility to infection.	31
6			
	1-23	Understanding adaptive immune responses is important for the control of allergies, autoimmune disease, and the rejection of transplanted organs.	32
7			
	1-24	Vaccination is the most effective means of controlling infectious diseases.	33
8			
	1-25	Emerging pathogens present new challenges for the immune system.	33
9		Summary.	34
		Summary to Chapter 1.	35
		References.	35
11			
11		<b>Chapter 2 Innate Immunity: The First Lines of Defense</b>	<b>37</b>
11		Anatomic barriers and initial chemical defenses.	38
	2-1	Infectious diseases are caused by diverse living agents that replicate in their hosts.	38
12			
	2-2	Epithelial surfaces of the body provide the first barrier against infection.	42
13			
	2-3	Infectious agents must overcome innate host defenses to establish a focus of infection.	44
13			
	2-4	Epithelial cells and phagocytes produce several kinds of antimicrobial molecules.	45
14		Summary.	49
		The complement system and innate immunity.	49
15			
	2-5	The complement system recognizes features of microbial surfaces and marks them for destruction by coating them with C3b.	51
16			
	2-6	The lectin pathway uses soluble receptors that recognize microbial surfaces to activate the complement cascade.	54
16			
	2-7	The classical pathway is initiated by activation of the C1 complex and is homologous to the lectin pathway.	57
16			
	2-8	Complement activation is largely confined to the surface on which it is initiated.	58
17			

2-9	The alternative pathway is an amplification loop for C3b formation that is accelerated by properdin in the presence of pathogens.	59	3-11	Certain NLR proteins react to infection or cellular damage by forming an inflammasome that induces cell death and secretion of inflammatory cytokines.	103
2-10	Membrane and plasma proteins that regulate the formation and stability of C3 convertases determine the extent of complement activation.	61	3-12	Activation of innate sensors in macrophages and dendritic cells triggers changes in gene expression that have far-reaching effects on the immune response.	106
2-11	Complement developed early in the evolution of multicellular organisms.	62	3-13	Toll signaling in <i>Drosophila</i> is downstream of a distinct set of pathogen-recognition molecules.	107
2-12	Surface-bound C3 convertase deposits large numbers of C3b fragments on pathogen surfaces and generates C5 convertase activity.	63	3-14	TLR and NOD genes have undergone extensive diversification in both invertebrates and some primitive chordates.	108
2-13	Ingestion of complement-tagged pathogens by phagocytes is mediated by receptors for the bound complement proteins.	64	Summary.	109	
2-14	The small fragments of some complement proteins initiate a local inflammatory response.	66	Consequences of innate immune activation.	109	
2-15	The terminal complement proteins polymerize to form pores in membranes that can kill certain pathogens.	66	3-15	Cytokines and their receptors fall into distinct families of structurally related proteins.	110
2-16	Complement-control proteins regulate all three pathways of complement activation and protect the host from their destructive effects.	68	3-16	Cytokine receptors of the hematopoietin superfamily are associated with the JAK family of tyrosine kinases, which activate STAT transcription factors.	112
2-17	Genetic and acquired disorders in complement regulation can produce various inflammatory conditions.	71	3-17	Chemokines released by macrophages and dendritic cells recruit effector cells to sites of infection.	114
2-18	Pathogens produce several types of proteins that can inhibit complement activation.	73	3-18	Cell-adhesion molecules control interactions between leukocytes and endothelial cells during an inflammatory response.	116
Summary.		74	3-19	Neutrophils make up the first wave of cells that cross the blood vessel wall to enter an inflamed tissue.	118
Summary to Chapter 2.		74	3-20	TNF- $\alpha$ is an important cytokine that triggers local containment of infection but induces shock when released systemically.	120
Discussion questions.		75	3-21	Cytokines made by macrophages and dendritic cells induce a systemic reaction known as the acute-phase response.	122
References.		75	3-22	Interferons induced by viral infection make several contributions to host defense.	124
<b>Chapter 3 Cellular Mechanisms of Innate Immunity</b>		<b>79</b>	3-23	Several types of innate lymphoid cells provide protection in early infection.	126
Pathogen recognition by cells of the innate immune system.		79	3-24	NK cells are activated by type I interferon and macrophage-derived cytokines.	128
3-1	After entering tissues, many microbes are recognized, ingested, and killed by phagocytes.	80	3-25	NK cells express activating and inhibitory receptors to distinguish between healthy and infected cells.	129
3-2	G protein-coupled receptors on phagocytes link microbe recognition with increased efficiency of intracellular killing.	83	3-26	NK-cell receptors belong to several structural families.	130
3-3	Microbial recognition and tissue damage initiate an inflammatory response.	87	3-27	NK cells express activating receptors that recognize ligands induced on infected cells or tumor cells.	133
3-4	Toll-like receptors represent an ancient pathogen-recognition system.	90	Summary.	134	
3-5	Mammalian Toll-like receptors are activated by many different pathogen-associated molecular patterns.	90	Summary to Chapter 3.	134	
3-6	TLR-4 recognizes bacterial lipopolysaccharide in association with the host accessory proteins MD-2 and CD14.	94	Discussion questions.	135	
3-7	TLRs activate NF $\kappa$ B, AP-1, and IRF transcription factors to induce the expression of inflammatory cytokines and type I interferons.	95	References.	136	
3-8	The RIG-I-like receptors detect cytoplasmic viral RNAs and activate MAVS to induce type I interferon production and pro-inflammatory cytokines.	96	<b>PART II THE RECOGNITION OF ANTIGEN</b>		
3-9	Cytosolic DNA activates the cGAS-STING pathway to induce production of type I interferons.	100	<b>Chapter 4 Antigen Recognition by B-cell and T-cell Receptors</b>	<b>141</b>	
3-10	NLRs comprise a large family of intracellular sensors with diverse functions.	102	The structure of a typical antibody molecule.	142	
			4-1	IgG antibodies consist of four polypeptide chains.	143
			4-2	Immunoglobulin heavy and light chains are composed of constant and variable regions.	144

4-3	The domains of an immunoglobulin molecule have similar structures.	144	Summary to Chapter 4.	174
4-4	The antibody molecule can readily be cleaved into functionally distinct fragments.	146	Discussion questions.	175
4-5	The hinge region of the immunoglobulin molecule allows flexibility in binding to multiple antigens.	147	References.	176
	Summary.	147		
	Structural variation in immunoglobulin constant regions.	148	<b>Chapter 5 The Generation of Lymphocyte Antigen Receptors</b>	<b>179</b>
4-6	Different classes of immunoglobulins are distinguished by the structure of their heavy-chain constant regions.	148	Primary immunoglobulin gene rearrangements and expression.	180
4-7	The constant region confers functional specialization on the antibody.	150	5-1 Complete immunoglobulin genes are generated by the somatic recombination of separate gene segments.	180
4-8	IgM and IgA can form polymers by interacting with the J chain.	151	5-2 Multiple contiguous V gene segments are present at each immunoglobulin locus.	182
	Summary.	152	5-3 Rearrangement of V, D, and J gene segments is guided by flanking DNA sequences.	184
	The interaction of the antibody molecule with specific antigen.	152	5-4 The reaction that recombines V, D, and J gene segments involves both lymphocyte-specific and ubiquitous DNA-modifying enzymes.	189
4-9	Localized regions of hypervariable sequence form the antigen-binding site.	152	5-5 The diversity of the immunoglobulin repertoire is generated by four main processes.	190
4-10	Antibodies bind antigens via contacts in CDRs that are complementary to the size and shape of the antigen.	153	5-6 The multiple inherited gene segments are used in different combinations.	191
4-11	Antibodies bind to conformational shapes on the surfaces of antigens using a variety of noncovalent forces.	155	5-7 Variable addition and subtraction of nucleotides at the junctions between gene segments contributes to the diversity of the third hypervariable region.	191
4-12	Antibody interaction with intact antigens is influenced by steric constraints.	156	5-8 IgM and IgD are derived from the same pre-mRNA transcript and are both expressed on the surface of mature B cells.	193
4-13	Some species generate antibodies with alternative structures.	157	5-9 Transmembrane and secreted forms of immunoglobulin are generated from different heavy-chain mRNA transcripts.	194
	Summary.	158	Summary.	196
	Antigen recognition by T cells.	159	T-cell receptor gene rearrangement.	196
4-14	The TCR $\alpha\beta$ heterodimer is very similar to a Fab fragment of immunoglobulin.	159	5-10 The T-cell receptor gene segments are arranged in a pattern similar to that of immunoglobulin gene segments and are rearranged by the same enzymes.	196
4-15	A T-cell receptor recognizes antigen in the form of a complex of a foreign peptide bound to an MHC molecule.	161	5-11 T-cell receptors concentrate diversity in the third hypervariable region.	199
4-16	There are two classes of MHC molecules with distinct subunit compositions but similar three-dimensional structures.	162	5-12 $\gamma\delta$ T-cell receptors are also generated by gene rearrangement.	200
4-17	Peptides are stably bound to MHC molecules and also serve to stabilize the MHC molecule on the cell surface.	164	Summary.	201
4-18	MHC class I molecules bind short peptides of 8–10 amino acids by both ends.	165	Evolution of the adaptive immune response.	201
4-19	The length of the peptides bound by MHC class II molecules is not constrained.	166	5-13 Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes.	202
4-20	The crystal structures of several peptide:MHC:T-cell receptor complexes show a similar orientation of the T-cell receptor over the peptide:MHC complex.	168	5-14 Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains.	203
4-21	The CD4 and CD8 cell-surface proteins of T cells directly contact MHC molecules and are required to make an effective response to antigen.	169	5-15 RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes.	205
4-22	The two classes of MHC molecules are expressed differentially on cells.	172	5-16 Different species generate immunoglobulin diversity in different ways.	207
4-23	A distinct subset of T cells bears an alternative receptor made up of $\gamma$ and $\delta$ chains.	173	5-17 Both $\alpha\beta$ and $\gamma\delta$ T-cell receptors are present in cartilaginous fishes.	210
	Summary.	174	5-18 MHC class I and class II molecules are also first found in the cartilaginous fishes.	210
			Summary.	211
			Summary to Chapter 5.	211

Discussion questions.	212	Summary.	255
References.	213	Summary to Chapter 6.	255
<b>Chapter 6 Antigen Presentation to T Lymphocytes</b>	<b>217</b>	Discussion questions.	256
The generation of $\alpha\beta$ T-cell receptor ligands.	218	References.	257
6-1 Antigen presentation functions both in arming effector T cells and in triggering their effector functions to attack pathogen-infected cells.	218	<b>PART III THE DEVELOPMENT OF MATURE LYMPHOCYTE RECEPTOR REPERTOIRES</b>	
6-2 Peptides are generated from ubiquitinated proteins in the cytosol by the proteasome.	220	<b>Chapter 7 Lymphocyte Receptor Signaling</b>	<b>261</b>
6-3 Peptides from the cytosol are transported by TAP into the endoplasmic reticulum and further processed before binding to MHC class I molecules.	222	General principles of signal transduction and propagation.	261
6-4 Newly synthesized MHC class I molecules are retained in the endoplasmic reticulum until they bind a peptide.	224	7-1 Transmembrane receptors convert extracellular signals into intracellular biochemical events.	262
6-5 Dendritic cells use cross-presentation to present exogenous proteins on MHC class I molecules so as to prime CD8 T cells.	226	7-2 Intracellular signal propagation is mediated by large multiprotein signaling complexes.	263
6-6 Peptide:MHC class II complexes are generated in acidified endocytic vesicles from proteins obtained through endocytosis, phagocytosis, and autophagy.	227	7-3 Small G proteins act as molecular switches in many different signaling pathways.	264
6-7 The invariant chain directs newly synthesized MHC class II molecules to acidified intracellular vesicles.	229	7-4 Signaling proteins are recruited to the membrane by a variety of mechanisms.	265
6-8 The MHC class II-like molecules HLA-DM and HLA-DO regulate exchange of CLIP for other peptides.	230	7-5 Post-translational modifications of proteins can both activate and inhibit signaling responses.	266
6-9 Cessation of MHC class II antigen processing occurs after dendritic-cell activation through reduced expression of the MARCH-1 E3 ligase.	233	7-6 The activation of many receptors generates small-molecule second messengers.	267
Summary.	234	Summary.	268
The major histocompatibility complex and its function.	235	Antigen receptor signaling and lymphocyte activation.	268
6-10 Many proteins involved in antigen processing and presentation are encoded by genes within the MHC.	235	7-7 Antigen receptors consist of variable antigen-binding chains associated with invariant chains that carry out the signaling function of the receptor.	268
6-11 The protein products of MHC class I and class II genes are highly polymorphic.	238	7-8 Antigen recognition by the T-cell receptor and its co-receptors transduces a signal across the plasma membrane to initiate signaling.	270
6-12 MHC polymorphism affects antigen recognition by T cells by influencing both peptide binding and the contacts between the T-cell receptor and MHC molecule.	240	7-9 Antigen recognition by the T-cell receptor and its co-receptors leads to phosphorylation of ITAMs by Src family kinases, generating the first intracellular signal in a signaling cascade.	272
6-13 Alloreactive T cells recognizing nonself MHC molecules are very abundant.	243	7-10 Phosphorylated ITAMs recruit and activate the tyrosine kinase ZAP-70.	273
6-14 Many T cells respond to superantigens.	245	7-11 ITAMs are also found in other receptors on leukocytes that signal for cell activation.	274
6-15 MHC polymorphism extends the range of antigens to which the immune system can respond.	246	7-12 Activated ZAP-70 phosphorylates adaptor proteins and promotes PI 3-kinase activation.	275
Summary.	246	7-13 Activated PLC- $\gamma$ generates the second messengers diacylglycerol and inositol trisphosphate that lead to transcription factor activation.	276
Recognition of nonpeptide ligands by unconventional T-cell subsets.	247	7-14 $\text{Ca}^{2+}$ entry activates the transcription factor NFAT.	277
6-16 A variety of genes with specialized functions in immunity are also encoded in the MHC.	247	7-15 Ras activation stimulates the mitogen-activated protein kinase (MAPK) relay and induces expression of the transcription factor AP-1.	278
6-17 Specialized MHC class I molecules act as ligands for the activation and inhibition of NK cells and unconventional T-cell subsets.	249	7-16 Protein kinase C activates the transcription factors $\text{NF}\kappa\text{B}$ and AP-1.	280
6-18 Members of the CD1 family of MHC class I-like molecules present lipid-based antigens to NKT cells.	251	7-17 PI 3-kinase activation up-regulates cellular metabolic pathways via the serine/threonine kinase Akt.	281
6-19 The nonclassical MHC class I molecule MR1 presents microbial riboflavin metabolites to MAIT cells.	253	7-18 T-cell receptor signaling leads to enhanced integrin-mediated cell adhesion.	283
6-20 $\gamma\delta$ T cells can recognize a variety of diverse ligands.	254	7-19 T-cell receptor signaling induces cytoskeletal reorganization by activating the small GTPase Cdc42.	283
		7-20 The logic of B-cell receptor signaling is similar to that of T-cell receptor signaling, but some of the signaling components are specific to B cells.	285

Discussion questions.	212	Summary.	255
References.	213	Summary to Chapter 6.	255
<b>Chapter 6 Antigen Presentation to T Lymphocytes</b>	<b>217</b>	Discussion questions.	256
<b>The generation of <math>\alpha\beta</math> T-cell receptor ligands.</b>	<b>218</b>	References.	257
6-1 Antigen presentation functions both in arming effector T cells and in triggering their effector functions to attack pathogen-infected cells.	218	<b>PART III THE DEVELOPMENT OF MATURE LYMPHOCYTE RECEPTOR REPERTOIRES</b>	
6-2 Peptides are generated from ubiquitinated proteins in the cytosol by the proteasome.	220	<b>Chapter 7 Lymphocyte Receptor Signaling</b>	<b>261</b>
6-3 Peptides from the cytosol are transported by TAP into the endoplasmic reticulum and further processed before binding to MHC class I molecules.	222	General principles of signal transduction and propagation.	261
6-4 Newly synthesized MHC class I molecules are retained in the endoplasmic reticulum until they bind a peptide.	224	7-1 Transmembrane receptors convert extracellular signals into intracellular biochemical events.	262
6-5 Dendritic cells use cross-presentation to present exogenous proteins on MHC class I molecules so as to prime CD8 T cells.	226	7-2 Intracellular signal propagation is mediated by large multiprotein signaling complexes.	263
6-6 Peptide:MHC class II complexes are generated in acidified endocytic vesicles from proteins obtained through endocytosis, phagocytosis, and autophagy.	227	7-3 Small G proteins act as molecular switches in many different signaling pathways.	264
6-7 The invariant chain directs newly synthesized MHC class II molecules to acidified intracellular vesicles.	229	7-4 Signaling proteins are recruited to the membrane by a variety of mechanisms.	265
6-8 The MHC class II-like molecules HLA-DM and HLA-DO regulate exchange of CLIP for other peptides.	230	7-5 Post-translational modifications of proteins can both activate and inhibit signaling responses.	266
6-9 Cessation of MHC class II antigen processing occurs after dendritic-cell activation through reduced expression of the MARCH-1 E3 ligase.	233	7-6 The activation of many receptors generates small-molecule second messengers.	267
Summary.	234	Summary.	268
<b>The major histocompatibility complex and its function.</b>	<b>235</b>	Antigen receptor signaling and lymphocyte activation.	268
6-10 Many proteins involved in antigen processing and presentation are encoded by genes within the MHC.	235	7-7 Antigen receptors consist of variable antigen-binding chains associated with invariant chains that carry out the signaling function of the receptor.	268
6-11 The protein products of MHC class I and class II genes are highly polymorphic.	238	7-8 Antigen recognition by the T-cell receptor and its co-receptors transduces a signal across the plasma membrane to initiate signaling.	270
6-12 MHC polymorphism affects antigen recognition by T cells by influencing both peptide binding and the contacts between the T-cell receptor and MHC molecule.	240	7-9 Antigen recognition by the T-cell receptor and its co-receptors leads to phosphorylation of ITAMs by Src family kinases, generating the first intracellular signal in a signaling cascade.	272
6-13 Alloreactive T cells recognizing nonself MHC molecules are very abundant.	243	7-10 Phosphorylated ITAMs recruit and activate the tyrosine kinase ZAP-70.	273
6-14 Many T cells respond to superantigens.	245	7-11 ITAMs are also found in other receptors on leukocytes that signal for cell activation.	274
6-15 MHC polymorphism extends the range of antigens to which the immune system can respond.	246	7-12 Activated ZAP-70 phosphorylates adaptor proteins and promotes PI 3-kinase activation.	275
Summary.	246	7-13 Activated PLC- $\gamma$ generates the second messengers diacylglycerol and inositol trisphosphate that lead to transcription factor activation.	276
<b>Recognition of nonpeptide ligands by unconventional T-cell subsets.</b>	<b>247</b>	7-14 $\text{Ca}^{2+}$ entry activates the transcription factor NFAT.	277
6-16 A variety of genes with specialized functions in immunity are also encoded in the MHC.	247	7-15 Ras activation stimulates the mitogen-activated protein kinase (MAPK) relay and induces expression of the transcription factor AP-1.	278
6-17 Specialized MHC class I molecules act as ligands for the activation and inhibition of NK cells and unconventional T-cell subsets.	249	7-16 Protein kinase C activates the transcription factors NF $\kappa$ B and AP-1.	280
6-18 Members of the CD1 family of MHC class I-like molecules present lipid-based antigens to NKT cells.	251	7-17 PI 3-kinase activation up-regulates cellular metabolic pathways via the serine/threonine kinase Akt.	281
6-19 The nonclassical MHC class I molecule MR1 presents microbial riboflavin metabolites to MAIT cells.	253	7-18 T-cell receptor signaling leads to enhanced integrin-mediated cell adhesion.	283
6-20 $\gamma\delta$ T cells can recognize a variety of diverse ligands.	254	7-19 T-cell receptor signaling induces cytoskeletal reorganization by activating the small GTPase Cdc42.	283
		7-20 The logic of B-cell receptor signaling is similar to that of T-cell receptor signaling, but some of the signaling components are specific to B cells.	285

7-21	Antigen receptor signaling is a dynamic process that evolves over time.	287	8-12	T-cell precursors proliferate extensively in the thymus, but most die there.	321
	Summary.	288	8-13	Successive stages in the development of thymocytes are marked by changes in cell-surface molecules.	321
	Co-stimulatory and inhibitory receptors modulate antigen receptor signaling in T and B lymphocytes.	288	8-14	Commitment to the T-cell lineage occurs in the thymus after Notch signaling.	322
7-22	The cell-surface protein CD28 is a required co-stimulatory signaling receptor for naive T-cell activation.	289	8-15	After T-cell commitment, thymocyte development is regulated by T-cell receptor rearrangement, expression, and signaling.	325
7-23	Maximal activation of PLC- $\gamma$ , which is important for transcription factor activation, requires a co-stimulatory signal induced by CD28.	290	8-16	Thymocytes at different developmental stages are found in distinct parts of the thymus.	326
7-24	TNF receptor superfamily members augment T-cell and B-cell activation.	291	8-17	T cells with $\alpha\beta$ or $\gamma\delta$ receptors arise from a common progenitor.	326
7-25	Inhibitory receptors on lymphocytes down-regulate immune responses by interfering with co-stimulatory signaling pathways.	292	8-18	T cells expressing $\gamma\delta$ T-cell receptors arise in two distinct phases during development.	327
7-26	Inhibitory receptors on lymphocytes down-regulate immune responses by recruiting protein or lipid phosphatases.	293	8-19	Successful synthesis of a rearranged $\beta$ chain allows the production of a pre-T-cell receptor that triggers cell proliferation and blocks further $\beta$ -chain gene rearrangement.	329
7-27	Knowledge of lymphocyte receptor signaling pathways can be exploited to engineer chimeric antigen receptors.	295	8-20	T-cell $\alpha$ -chain genes undergo successive rearrangements until positive selection or cell death intervenes.	331
	Summary.	296		Summary.	332
	Summary to Chapter 7.	297		Positive and negative selection of T cells.	333
	Discussion questions.	297	8-21	Overview of positive and negative selection of $\alpha\beta$ lineage T cells.	333
	References.	298	8-22	Only thymocytes whose receptors interact with self peptide:self MHC complexes can survive and mature.	334
<b>Chapter 8</b>	<b>The Development of B and T Lymphocytes</b>	<b>301</b>	8-23	Positive selection coordinates the expression of CD4 or CD8 with the specificity of the T-cell receptor and the potential effector functions of the T cell.	335
	Development of B lymphocytes.	303	8-24	Thymic cortical epithelial cells mediate positive selection of developing thymocytes.	337
8-1	Lymphocytes derive from hematopoietic stem cells in the bone marrow.	303	8-25	T cells that react strongly with self antigens are deleted in the thymus.	338
8-2	Commitment to B cell, T cell, or innate lymphoid cell lineages is regulated by distinct networks of transcription factors.	305	8-26	The specificity and/or the strength of signals for negative and positive selection must differ.	339
8-3	B-cell development begins by rearrangement of the heavy-chain locus.	305	8-27	$\alpha\beta$ T cells diverge into multiple lineages at the CD4 <sup>+</sup> and CD8 <sup>+</sup> single-positive stage in the thymic medulla.	339
8-4	The pre-B-cell receptor tests for successful production of a complete heavy chain and signals for the transition from the pro-B cell to the pre-B cell stage.	308	8-28	Thymic emigration is controlled by signaling through a G protein-coupled receptor.	340
8-5	Pre-B-cell receptor signaling inhibits further heavy-chain locus rearrangement and enforces allelic exclusion.	310	8-29	T cells that encounter sufficient quantities of self antigens for the first time in the periphery are eliminated or inactivated.	341
8-6	Pre-B cells rearrange the light-chain locus and express cell-surface immunoglobulin.	310		Summary.	341
8-7	Immature B cells are tested for autoreactivity before they leave the bone marrow.	312		Summary to Chapter 8.	341
8-8	Lymphocytes that encounter sufficient quantities of self antigens in the periphery are eliminated.	313		Discussion questions.	342
8-9	Newly formed B cells arriving in the spleen turn over rapidly and require cytokines and positive signals through the B-cell receptor for maturation and long-term survival.	314		References.	343
8-10	B-1 B cells are an innate lymphocyte subset that arises early in development.	316	<b>PART IV THE ADAPTIVE IMMUNE RESPONSE</b>		
	Summary.	317	<b>Chapter 9</b>	<b>T Cell-Mediated Immunity</b>	<b>347</b>
	Development of T lymphocytes.	319		Development and function of secondary lymphoid organs—sites for the initiation of adaptive immune responses.	349
8-11	T-cell progenitors originate in the bone marrow, but all the important events in T-cell development occur in the thymus.	320	9-1	Secondary lymphoid structures are specialized to facilitate the interaction of circulating T and B lymphocytes with antigen.	349

10-19	Antigen:antibody complexes activate the classical pathway of complement by binding to C1q.	436	11-12	Effector T cells continue to respond to maturational and maintenance signals as they carry out their effector functions in target tissues.	476
10-20	Complement receptors and Fc receptors both contribute to removal of immune complexes from the circulation.	438	11-13	Effector T cells can be activated to release cytokines independently of antigen recognition.	478
Summary.		439	11-14	Effector CD4 T cells demonstrate plasticity and cooperativity that enable adaptation during antipathogen responses.	479
The destruction of antibody-coated pathogens via Fc receptors.		440	11-15	Integration of cell- and antibody-mediated immunity is critical for protection against many types of pathogens.	480
10-21	The Fc receptors of accessory cells are signaling receptors specific for immunoglobulins of different classes.	440	11-16	Resolution of an infection is accompanied by the death of most effector T cells and persistence of a small number of long-lived memory T cells.	482
10-22	Fc receptors on phagocytes are activated by antibodies bound to the surface of pathogens and enable the phagocytes to ingest and destroy pathogens.	441	Summary.		483
10-23	Fc receptors activate NK cells to destroy antibody-coated targets.	443	Immunological memory.		484
10-24	Mast cells and basophils bind IgE antibody via the high-affinity Fc $\epsilon$ receptor.	444	11-17	Immunological memory is long lived after infection or vaccination.	484
10-25	IgE-mediated activation of accessory cells has an important role in resistance to parasite infection.	445	11-18	MHC tetramers and adoptive transfers of clonal T-cell populations have enabled the study of T-cell memory.	485
Summary.		446	11-19	The developmental origins of memory T cells parallel those of effector T cells.	486
Summary to Chapter 10.		446	11-20	Memory T cells are heterogeneous and include central memory, effector memory, and tissue-resident subsets.	488
Discussion questions.		447	11-21	Circulating memory T cells acquire heightened sensitivity to IL-7 and/or IL-15 and undergo metabolic reprogramming to survive long-term.	491
References.		448	11-22	CD4 T-cell help is required for CD8 T-cell memory and involves CD40 and IL-2 signaling.	492
<b>Chapter 11 Integrated Dynamics of Innate and Adaptive Immunity</b>		<b>453</b>	11-23	Memory B-cell responses are more rapid and have higher affinity for antigen compared with responses of naive B cells.	494
Integration of innate and adaptive immunity in response to specific types of pathogens.		454	11-24	Memory B cells can reenter germinal centers and undergo additional somatic hypermutation and affinity maturation during secondary immune responses.	496
11-1	The course of an infection can be divided into several distinct phases.	454	11-25	In immune individuals, secondary and subsequent responses are mainly attributable to memory lymphocytes.	496
11-2	The effector mechanisms that are recruited to clear an infection can be organized into immune modules.	458	Summary.		498
11-3	Subsets of ILCs are early responders of the immune response.	460	Summary to Chapter 11.		498
Summary.		462	Discussion questions.		500
Effector CD4 T cells augment the effector functions of innate immune cells.		462	References.		500
11-4	Effector T cells are guided to specific tissues and sites of infection by changes in their expression of adhesion molecules and chemokine receptors.	463	<b>Chapter 12 The Barrier Immune System</b>		<b>505</b>
11-5	Pathogen-specific effector T cells are progressively enriched at sites of infection where they may undergo further maturation to acquire full effector function.	467	Organization of the mucosal immune system.		505
11-6	T <sub>H</sub> 1 cells coordinate and amplify the host response to intracellular pathogens through classical activation of macrophages.	467	12-1	The mucosal immune system protects the internal surfaces of the body.	506
11-7	Activation of macrophages by T <sub>H</sub> 1 cells must be tightly regulated to avoid tissue damage.	469	12-2	Immune cells of the mucosal immune system are located both within and outside of specialized lymphoid tissues in proximity to the epithelium.	510
11-8	Chronic activation of macrophages by T <sub>H</sub> 1 cells mediates the formation of granulomas to contain intracellular pathogens that cannot be cleared.	471	12-3	Maturation of the gut-associated lymphoid tissue is driven by acquisition of the commensal microbiota.	516
11-9	Defects in type 1 immunity reveal its important role in the elimination of intracellular pathogens.	471	Summary.		519
11-10	T <sub>H</sub> 2 cells coordinate type 2 responses to expel intestinal helminths and repair tissue injury.	472	Innate immune defenses of the intestinal immune system.		520
11-11	T <sub>H</sub> 17 cells coordinate type 3 responses to enhance the clearance of extracellular bacteria and fungi.	475	12-4	The intestines are lined by a diversity of epithelial cell types that develop from a common progenitor and play distinct roles in mucosal immunity.	520



12-5	The intestinal epithelium contains conventional and unconventional T cells that are focused on barrier maintenance and defense.	528	Summary.	579
12-6	Innate lymphoid cells and unconventional lymphocytes are present in GALT and in the lamina propria and are rapid responders to microbes that breach the epithelium.	534	Summary to Chapter 12.	580
	Summary.	535	Discussion questions.	581
	The role of adaptive immunity in regulating the intestinal mucosal immune system at homeostasis.	536	References.	581
12-7	The mucosal immune system must establish and maintain tolerance to harmless foreign antigens.	536	<b>PART V THE IMMUNE SYSTEM IN HEALTH AND DISEASE</b>	
12-8	Macrophages and dendritic cells have complementary roles in the maintenance of immune tolerance in the intestines.	537	<b>Chapter 13 Failures of Host Defense Mechanisms</b>	<b>587</b>
12-9	The intestines have multiple routes for uptake and delivery of antigen to antigen-presenting cells.	540	Immunodeficiency diseases.	588
12-10	Intestinal dendritic cells favor the induction of antigen-specific T <sub>reg</sub> cells that are critical for the maintenance of mucosal immune homeostasis.	543	13-1 Primary immunodeficiency diseases are caused by inherited gene variants that typically cause recurrent infections early in life.	588
12-11	Lymphocytes primed within the mucosal immune system are directed to return to the mucosal tissue by tissue-specific adhesion molecules and chemokine receptors.	546	13-2 Defects in T-cell development can result in severe combined immune deficiencies.	589
12-12	Secretory IgA is the dominant class of antibody associated with the mucosal immune system at homeostasis.	547	13-3 SCID can also be due to defects in the purine salvage pathway.	592
12-13	T cell-independent processes can contribute to IgA production in some species.	550	13-4 Defects in antigen receptor gene rearrangement can result in SCID.	593
12-14	IgA deficiency is relatively common in humans but may be compensated for by secretory IgM.	551	13-5 Defects in signaling from T-cell antigen receptors can cause severe immunodeficiency.	594
12-15	Large numbers of antigen-experienced T cells are present in the intestinal lamina propria even in the absence of disease.	551	13-6 Genetic defects in thymic development or function that block T-cell development result in combined immunodeficiencies.	594
12-16	Priming of lymphocytes in one mucosal tissue may induce protective immunity at other mucosal surfaces.	552	13-7 Defects in B-cell development result in deficiencies in antibody production that cause an inability to clear extracellular bacteria.	596
	Summary.	553	13-8 Combined immunodeficiencies (CIDs) can be caused by defects in T-cell differentiation and function that impair activation of B cells, dendritic cells and macrophages, and innate effector cells.	598
	The intestinal immune response in host defense and immune-mediated disease.	553	13-9 B cell-specific activation defects cause hyper IgM syndromes that are limited to defects in the antibody response.	600
12-17	Enteric pathogens elicit 'danger signals' by activating pattern-recognition receptors that are sequestered in the intestinal epithelium.	554	13-10 Common variable immunodeficiency results from a variety of inherited defects that cause more limited defects in the antibody response.	600
12-18	Pathogens induce inflammatory adaptive immune responses when innate defenses have been breached.	556	13-11 Unidentified genetic defects cause isotype-specific antibody deficiencies.	601
12-19	Effector T-cell responses in the intestine protect the function of the epithelium.	557	13-12 Normal pathways for host defense against different infectious agents are pinpointed by genetic deficiencies of cytokine pathways central to type 1/T <sub>H</sub> 1 and type 3/T <sub>H</sub> 17 responses.	601
12-20	Noninvasive and invasive enteric bacterial pathogens use different strategies to colonize the intestines.	557	13-13 Inherited defects in the cytolytic pathway of lymphocytes can cause uncontrolled lymphoproliferation and inflammatory responses to viral infections.	603
12-21	Dysregulated immune responses to commensal bacteria provoke intestinal disease.	563	13-14 X-linked lymphoproliferative syndrome is associated with fatal infection by Epstein-Barr virus and the development of lymphomas.	605
	Summary.	564	13-15 Immunodeficiency is caused by inherited defects in the development of dendritic cells.	606
	Immunity at other barrier tissues.	564	13-16 Defects in complement components and complement-regulatory proteins cause defective humoral immune function and tissue damage.	607
12-22	Anatomy and mucosal immunity of the airways.	564	13-17 Defects in phagocytic cells result in widespread bacterial infections.	608
12-23	Respiratory immunity to inhaled pathogens; respiratory viruses.	567	13-18 Mutations in the molecular regulators of inflammation can cause uncontrolled inflammatory responses that result in 'autoinflammatory disease.'	612
12-24	Cutaneous immunity.	574		
12-25	The sensory nervous system communicates with the immune system to enhance defense against infections in the skin.	577		

13-19	Factor-replacement therapies, hematopoietic stem-cell transplantation, and gene therapy can be used successfully to correct genetic defects.	613	Summary.	655
13-20	Noninherited, secondary immunodeficiencies are major predisposing causes of infection and death.	615	Summary to Chapter 13.	656
	Summary.	616	Discussion questions.	656
	Evasion and subversion of immune defenses.	616	References.	657
13-21	Extracellular bacterial pathogens have evolved different strategies to avoid detection by pattern-recognition receptors and destruction by antibody, complement, and antimicrobial peptides.	617	<b>Chapter 14 Allergic Diseases and Hypersensitivity Reactions</b>	<b>663</b>
13-22	Intracellular bacterial pathogens can evade the immune system by seeking shelter within phagocytes.	622	IgE and IgE-mediated allergic diseases.	664
13-23	Immune evasion is also practiced by protozoan parasites.	623	14-1 Sensitization involves class switching to IgE production on first contact with an allergen.	665
13-24	Many viruses target type I and type III interferon pathways to impair host antiviral defense.	625	14-2 Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents.	666
13-25	RNA viruses use different mechanisms of antigenic variation to keep a step ahead of the adaptive immune system.	625	14-3 Genetic factors contribute to the development of IgE-mediated allergic disease.	667
13-26	DNA viruses use multiple mechanisms to subvert CTL and NK-cell responses.	628	14-4 Environmental factors may interact with genetic susceptibility to cause allergic disease.	669
13-27	Viruses that establish latency persist <i>in vivo</i> by ceasing to replicate until immunity wanes.	631	Summary.	671
13-28	DNA and RNA viruses can induce exhaustion of CTL and NK cell responses, thereby impairing the antiviral response.	633	Effector mechanisms in IgE-mediated allergic reactions.	671
	Summary.	633	14-5 Most IgE is cell-bound and engages effector mechanisms of the immune system by pathways different from those of other antibody isotypes.	671
	Acquired immune deficiency syndrome.	634	14-6 Mast cells reside in tissues and orchestrate allergic reactions.	673
13-29	HIV is a retrovirus that establishes a chronic infection that slowly progresses to AIDS.	636	14-7 Eosinophils and basophils cause inflammation and tissue damage in allergic reactions.	675
13-30	HIV infects and replicates within cells of the immune system.	636	14-8 IgE-mediated allergic reactions have a rapid onset but can also lead to chronic responses.	677
13-31	Activated CD4 T cells are the major source of HIV replication.	638	14-9 Allergen introduced into the bloodstream can cause anaphylaxis and urticaria.	679
13-32	There are several routes by which HIV is transmitted and establishes infection.	641	14-10 Allergen inhalation is associated with the development of rhinitis and asthma.	681
13-33	HIV variants with tropism for different co-receptors play different roles in transmission and progression of disease.	641	14-11 Allergy to particular foods causes systemic reactions as well as symptoms limited to the gut.	682
13-34	A genetic deficiency of the co-receptor CCR5 confers resistance to HIV infection.	644	14-12 IgE-mediated allergic disease can be treated by inhibiting effector pathways or by desensitization to restore biological tolerance.	684
13-35	An immune response controls but does not eliminate HIV.	644	Summary.	686
13-36	Lymphoid tissue is the major reservoir of HIV infection.	646	Non-IgE-mediated allergic diseases.	686
13-37	Genetic variation in the host can alter the rate of HIV disease progression.	647	14-13 Non-IgE-dependent drug-induced hypersensitivity reactions in susceptible individuals occur by binding of the drug to the surface of circulating blood cells.	687
13-38	The destruction of immune function as a result of HIV infection leads to increased susceptibility to opportunistic infection and eventually to death.	649	14-14 Systemic disease caused by immune-complex formation can follow the administration of large quantities of poorly catabolized antigens.	687
13-39	Drugs that block HIV replication lead to a rapid decrease in titer of infectious virus and an increase in CD4 T cells.	649	14-15 Hypersensitivity reactions can be mediated by TH1 cells and cytotoxic CD8 T cells.	689
13-40	In the course of infection, HIV accumulates many mutations, which can result in the outgrowth of drug-resistant variants.	652	14-16 Celiac disease has features of both an allergic response and autoimmunity.	692
13-41	HIV treatment and prophylaxis are leading to a decline in the spread of HIV and AIDS.	652	Summary.	694
13-42	Vaccination against HIV remains an attractive solution but poses many difficulties.	653	Summary to Chapter 14.	694
			Discussion questions.	695
			References.	695
			<b>Chapter 15 Autoimmunity and Transplantation</b>	<b>699</b>
			The making and breaking of self-tolerance.	699
			15-1 Multiple mechanisms normally contribute to prevent autoimmunity.	699

15-2	Lymphocytes that bind self antigens with relatively low affinity usually ignore them but in some circumstances become activated.	702	15-26	The fetus is an allograft that is tolerated repeatedly.	741
15-3	Antigens in immunologically privileged sites do not induce immune attack but can serve as targets.	703	Summary.		742
15-4	Autoimmune responses can be controlled at various stages by regulatory T cells.	704	Summary to Chapter 15.		743
Summary.		705	Discussion questions.		744
Autoimmune diseases and pathogenic mechanisms.		706	References.		744
15-5	Autoimmunity can be classified into either organ-specific or systemic disease.	706	<b>Chapter 16 Manipulation of the Immune Response</b>		<b>749</b>
15-6	Multiple components of the immune system are typically recruited in autoimmune disease.	707	Fighting infectious diseases with vaccination.		749
15-7	Chronic autoimmune disease develops through positive feedback from inflammation, inability to clear the self antigen, and a broadening of the autoimmune response.	709	16-1	Vaccines can be based on attenuated pathogens or material from killed organisms.	750
15-8	Both antibody and effector T cells can cause tissue damage in autoimmune disease.	711	16-2	Most effective vaccines generate antibodies that prevent damage caused by toxins or that neutralize pathogens and stop infection.	752
15-9	Autoantibodies against blood cells promote their destruction.	713	16-3	Effective vaccines must induce long-lasting protection while being safe and inexpensive.	753
15-10	The fixation of sublytic doses of complement to cells in tissues stimulates a powerful inflammatory response.	713	16-4	Live-attenuated viral vaccines are usually more potent than 'killed' vaccines.	753
15-11	Autoantibodies against receptors cause disease by stimulating or blocking receptor function.	714	16-5	Live-attenuated viral vaccines can be made safer by the use of recombinant DNA technology.	754
15-12	Autoantibodies against extracellular antigens cause inflammatory injury.	715	16-6	Vaccines against bacteria or parasites can be developed using nonpathogenic or disabled bacteria or genetically attenuated parasites (GAPs).	755
15-13	T cells specific for self antigens can cause direct tissue injury and sustain autoantibody responses.	717	16-7	Conjugate vaccines rely on linked recognition between T and B cells.	756
Summary.		721	16-8	Adjuvants enhance the immunogenicity of vaccines, but few are approved for use in humans.	758
The genetic and environmental basis of autoimmunity.		721	16-9	Protective immunity can be induced by RNA- and DNA-based vaccination.	759
15-14	Autoimmune diseases have a strong genetic component.	722	16-10	The route of vaccination is an important determinant of success.	760
15-15	Monogenic defects of immune tolerance.	722	16-11	<i>Bordetella pertussis</i> vaccination illustrates the importance of the perceived safety of a vaccine.	761
15-16	MHC genes have an important role in controlling susceptibility to autoimmune disease.	727	16-12	Peptide-based vaccines can elicit protective immunity, but they require adjuvants and must be targeted to the appropriate cells and cell compartment to be effective.	762
15-17	Genetic variants that impair innate immune responses can predispose to T cell-mediated chronic inflammatory disease.	727	16-13	Vaccination and checkpoint blockade may be useful in controlling existing chronic infections.	763
15-18	Cross-reactivity between foreign molecules on pathogens and self molecules can promote autoimmune disease.	730	Summary.		763
Summary.		731	Using the immune response to attack tumors.		764
Responses to alloantigens and transplant rejection.		732	16-14	The development of transplantable tumors in mice led to the discovery of protective immune responses to tumors.	764
15-19	Transplant rejection is mediated primarily by T-cell responses to MHC molecules.	732	16-15	Tumors are 'edited' by the immune system as they evolve and can escape rejection in many ways.	765
15-20	Rejection of MHC-identical grafts is caused by peptides from other alloantigens bound to graft MHC molecules.	734	16-16	Tumor-rejection antigens can be recognized by T cells and form the basis of immunotherapies.	769
15-21	Alloreactive T cells reject transplanted organs by direct and indirect allorecognition.	735	16-17	Checkpoint blockade can augment immune responses to existing tumors.	771
15-22	Antibodies that react with endothelium cause hyperacute graft rejection.	737	16-18	T cells expressing chimeric antigen receptors are an effective treatment in some leukemias.	773
15-23	Late failure of transplanted organs is caused by chronic injury to the graft.	737	16-19	Monoclonal antibodies against tumor antigens, alone or linked to toxins, can control tumor growth.	774
15-24	A variety of organs are transplanted routinely in clinical medicine.	738	16-20	Enhancing the immune response to tumors by vaccination holds promise for cancer prevention and therapy.	776
15-25	The converse of graft rejection is graft-versus-host disease.	740	Summary.		777

Treatment of unwanted immune responses.	778	A-10	Generation of human monoclonal antibodies from vaccinated individuals.	A-13
16-21 Corticosteroids are powerful anti-inflammatory drugs that alter the transcription of many genes.	779	A-11	Microscopy and imaging using fluorescent dyes.	A-13
16-22 Cytotoxic drugs cause immunosuppression by killing dividing cells and have serious side effects.	780	A-12	Immunoelectron microscopy.	A-15
16-23 Cyclosporin A, tacrolimus, and rapamycin are effective immunosuppressive agents that interfere with various T-cell signaling pathways.	781	A-13	Immunohistochemistry.	A-15
16-24 JAK inhibitors can be used to treat autoimmune and inflammatory diseases.	783	A-14	Immunoprecipitation and co-immunoprecipitation.	A-16
16-25 Antibodies against cell-surface molecules can be used to eliminate lymphocyte subsets or to inhibit lymphocyte function.	783	A-15	Immunoblotting (western blotting).	A-17
16-26 Antibodies can be engineered to reduce their immunogenicity in humans.	784	A-16	Use of antibodies in the isolation and characterization of multiprotein complexes by mass spectrometry.	A-18
16-27 Monoclonal antibodies can be used to prevent allograft rejection.	785	A-17	Isolation of peripheral blood lymphocytes by density-gradient fractionation.	A-20
16-28 Depletion of autoreactive lymphocytes can treat autoimmune disease.	787	A-18	Isolation of lymphocytes from tissues other than blood.	A-20
16-29 Biologics that block TNF- $\alpha$ , IL-1, or IL-6 can alleviate autoimmune diseases.	788	A-19	Flow cytometry and FACS analysis.	A-21
16-30 Biologics can block cell migration to sites of inflammation and reduce immune responses.	789	A-20	Lymphocyte isolation using antibody-coated magnetic beads.	A-23
16-31 Blockade of co-stimulatory pathways that activate lymphocytes can be used to treat autoimmune disease.	790	A-21	Isolation of homogeneous T-cell lines.	A-24
16-32 Some commonly used drugs have immunomodulatory properties.	791	A-22	ELISPOT assay.	A-24
16-33 Controlled administration of antigen can be used to manipulate the nature of an antigen-specific response.	791	A-23	Identification of functional subsets of T cells based on cytokine production or transcription factor expression.	A-25
Summary.	792	A-24	Identification of T or B lymphocytes on the basis of antigen receptor specificity.	A-28
Summary to Chapter 16.	792	A-25	Biosensor assays for measuring the rates of association and dissociation of antigen receptors for their ligands.	A-28
Discussion questions.	794	A-26	Assays of lymphocyte proliferation.	A-30
References.	794	A-27	Measurements of apoptosis.	A-32
		A-28	Assays for cytotoxic T cells.	A-33
		A-29	Assays for CD4 T cells.	A-34
		A-30	Transfer of protective immunity.	A-35
		A-31	Adoptive transfer of lymphocytes.	A-36
		A-32	Assessment of lymphocyte tissue residency by parabiosis.	A-37
		A-33	Hematopoietic stem-cell transfers.	A-38
		A-34	<i>In vivo</i> administration of antibodies.	A-38
		A-35	Transgenic mice.	A-39
		A-36	Gene knockout by targeted disruption.	A-40
		A-37	Knockdown of gene expression by RNA interference (RNAi).	A-43
		A-38	Cell-lineage tracing techniques.	A-44
		A-39	Single-cell analysis	A-45
			<b>eAppendix II CD Antigens</b>	<b>A-49</b>
			<b>eAppendix III Cytokines and Their Receptors</b>	<b>A-69</b>
			<b>eAppendix IV Chemokines and Their Receptors</b>	<b>A-73</b>
			Glossary	G-1
			Credits	C-1
			Index	I-1
<b>Appendix I The Immunologist's Toolbox</b>	<b>A-1</b>			
A-1 Immunization.	A-1			
A-2 Antibody responses.	A-4			
A-3 Affinity chromatography.	A-5			
A-4 Radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), and competitive inhibition assay.	A-5			
A-5 Multiplex bead assay for detection of cytokines, antibody responses, or antigens.	A-7			
A-6 Hemagglutination and blood typing.	A-8			
A-7 Coombs tests and the detection of rhesus incompatibility.	A-9			
A-8 Monoclonal antibodies.	A-11			
A-9 Phage display libraries for antibody V-region production.	A-12			