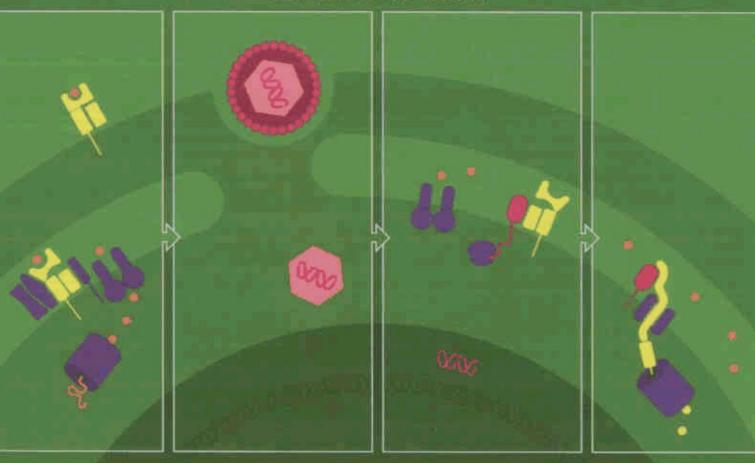
Immuno biology

SEVENTH EDITION



Kenneth Murphy - Paul Travers - Mark Walport

Contents

PARTI	AN INTRODUCTION TO IMMUNOBIOLOGY AND INNATE IMMU	NITY
Chapter 1	Basic Concepts in Immunology	1
Chapter 2	Innate Immunity	39
PART II	THE RECOGNITION OF ANTIGEN	
Chapter 3	Antigen Recognition by B-cell and T-cell Receptors	111
Chapter 4	The Generation of Lymphocyte Antigen Receptors	143
Chapter 5	Antigen Presentation to T Lymphocytes	181
PART III	THE DEVELOPMENT OF MATURE LYMPHOCYTE RECEPTOR REPERTOIRES	
Chapter 6	Signaling Through Immune System Receptors	219
Chapter 7	The Development and Survival of Lymphocytes	257
PART IV	THE ADAPTIVE IMMUNE RESPONSE	
Chapter 8	T Cell-Mediated Immunity	323
Chapter 9	The Humoral Immune Response	379
Chapter 10	Dynamics of Adaptive Immunity	421
Chapter 11	The Mucosal Immune System	459
PARTV	THE IMMUNE SYSTEM IN HEALTH AND DISEASE	
Chapter 12	Failures of Host Defense Mechanism	497
Chapter 13	Allergy and Hypersensitivity	555
Chapter 14	Autoimmunity and Transplantation	599
Chapter 15	Manipulation of the Immune Response	655
PART VI	THE ORIGINS OF IMMUNE RESPONSES	
Chapter 16	Evolution of the Immune System	711
Appendix I Ir	nmunologists' Toolbox	735
Appendix II (CD Antigens	783
Appendix III	Cytokines and their Receptors	799
Appendix IV	Chemokines and their Receptors	802
Appendix V	Immunological Constants	804
Biographies		805
Glossary		806
Index		835

Detailed Contents

AN INTRODUCTION TO IMMUNO-BIOLOGY AND INNATE IMMUNITY

Chapte	er 1 Basic Concepts in Immunology	1	1-23	for the control of allergies, autoimmune disease, and organ graft rejection. Vaccination is the most effective means of controlling	34
Princin	les of innate and adaptive immunity.	3	. 20	infectious diseases.	36
-	•		Summ	nary.	37
1-2	Functions of the immune response. The cells of the immune system derive from precursors in the bone marrow.	3 5	Summ	nary to Chapter 1.	37
	The myeloid lineage comprises most of the cells of the innate immune system.	5	Chap	oter 2 Innate Immunity	39
	The lymphoid lineage comprises the lymphocytes of		The fi	front line of host defense.	40
	the adaptive immune system and the natural killer cells of innate immunity.	8	2-1	Infectious diseases are caused by diverse living agents that replicate in their hosts.	41
	Lymphocytes mature in the bone marrow or the thymus and then congregate in lymphoid tissues throughout the body.	9	2-2	Infectious agents must overcome innate host defenses to establish a focus of infection.	44
	Most infectious agents activate the innate immune system and induce an inflammatory response.	10	2-3	The epithelial surfaces of the body make up the first lines of defense against infection.	46
	Activation of specialized antigen-presenting cells is a necessary first step for induction of adaptive immunity.	12	2-4	After entering tissues, many pathogens are recognized, ingested, and killed by phagocytes.	48
	The innate immune system provides an initial discrimination between self and nonself.	13	2-5	Pathogen recognition and tissue damage initiate an inflammatory response.	50
	Lymphocytes activated by antigen give rise to clones of antigen-specific effector cells that mediate	40	Summ	nary.	52
	adaptive immunity.	13	Patte	ern recognition in the innate immune system.	53
	Clonal selection of lymphocytes is the central principle of adaptive immunity.	14	2-6	Receptors with specificity for pathogen molecules recognize patterns of repeating structural motifs.	54
	The structure of the antibody molecule illustrates the central puzzle of adaptive immunity.	15	2-7	The Toll-like receptors are signaling receptors that distinguish different types of pathogen and help direct	•
1-12	Each developing lymphocyte generates a unique antigen receptor by rearranging its receptor gene segments.	16		an appropriate immune response.	56
1-13	Immunoglobulins bind a wide variety of chemical structures, whereas the T-cell receptor is specialized to recognize		2-8	The effects of bacterial lipopolysaccharide on macrophages are mediated by CD14 binding to TLR-4.	57
	toreign antigens as peptide fragments bound to proteins of the major histocompatibility complex.	17	2-9	The NOD proteins act as intracellular sensors of bacterial infection.	58
	The development and survival of lymphocytes is determined by signals received through their antigen receptors.	l 18	2-10	Activation of Toll-like receptors and NOD proteins triggers the production of pro-inflammatory cytokines and	
	Lymphocytes encounter and respond to antigen in the peripheral lymphoid organs.	18		chemokines, and the expression of co-stimulatory molecules.	58
	Interaction with other cells as well as with antigen is necessary for lymphocyte activation.	23	Summ	nary.	59
	Lymphocytes activated by antigen proliferate in the	23	The c	complement system and innate immunity.	61
	peripheral lymphoid organs, generating effector cells and immunological memory.	23	2-11	Complement is a system of plasma proteins that is activated by the presence of pathogens.	61
Summai	•	27	2-12	Complement interacts with pathogens to mark them for destruction by phagocytes.	62
	ector mechanisms of adaptive immunity.	27	2-13	The classical pathway is initiated by activation of the	
	Antibodies deal with extracellular forms of pathogens and their toxic products.	28	2-14	C1 complex. The lectin pathway is homologous to the classical pathway.	64 65
	T cells are needed to control intracellular pathogens and to activate B-cell responses to most antigens.	30	2-15	Complement activation is largely confined to the surface on which it is initiated.	67
	CD4 and CD8 T cells recognize peptides bound to two different classes of MHC molecules.	32	2-16	Hydrolysis of C3 causes initiation of the alternative pathway of complement.	69

1-22

Defects in the immune system result in increased susceptibility to infection.

Understanding adaptive immune responses is important

34

2-17	Membrane and plasma proteins that regulate the formation and stability of C3 convertases determine the extent of complement activation under different circumstances.	69	3-5	The domains of an immunoglobulin molecule have similar structures.	116 118
2-18	Surface-bound C3 convertase deposits large numbers of		Summa	•	110
	C3b fragments on pathogen surfaces and generates C5 convertase activity.	73	The in antige	teraction of the antibody molecule with specific	118
2-19	Ingestion of complement-tagged pathogens by phagocytes is mediated by receptors for the bound complement proteins.	73	3-6	Localized regions of hypervariable sequence form the antigen-binding site.	118
2-20	Small fragments of some complement proteins can initiate a local inflammatory response.	75	3-7	Antibodies bind antigens via contacts with amino acids in CDRs, but the details of binding depend upon the size	
2-21	The terminal complement proteins polymerize to form pores in membranes that can kill certain pathogens.	75	3-8	and shape of the antigen. Antibodies bind to conformational shapes on the surfaces	119
2-22	Complement control proteins regulate all three pathways of complement activation and protect the host from its	70	3-9	of antigens. Antigen–antibody interactions involve a variety of forces.	120 121
Summa	destructive effects. ary.	78 81	Summa	-	122
Induce	ed innate responses to infection.	82	Antige	en recognition by T cells.	123
2-23	Activated macrophages secrete a range of cytokines that have a variety of local and distant effects.	83	3-10	The T-cell receptor is very similar to a Fab fragment of immunoglobulin.	123
2-24	Chemokines released by phagocytes and dendritic cells	83	3-11	A T-cell receptor recognizes antigen in the form of a complex of a foreign peptide bound to an MHC molecule.	125
2-25	recruit cells to sites of infection. Cell-adhesion molecules control interactions between leukocytes and endothelial cells during an inflammatory response.		3-12	There are two classes of MHC molecules with distinct subunit composition but similar three-dimensional structures.	126
2-26	Neutrophils make up the first wave of cells that cross the blood vessel wall to enter inflammatory sites.	88	3-13	Peptides are stably bound to MHC molecules, and also serve to stabilize the MHC molecule on the cell surface.	128
2-27	TNF- α is an important cytokine that triggers local containment of infection but induces shock when released systemically.	90	3-14	MHC class I molecules bind short peptides of 8–10 amino acids by both ends.	129
2-28	Cytokines released by phagocytes activate the acute-phase response.	92	3-15	The length of the peptides bound by MHC class II molecules is not constrained.	130
2-29	Interferons induced by viral infection make several contributions to host defense.	94	3-16	The crystal structures of several MHC:peptide:T-cell receptor complexes show a similar T-cell receptor	
2-30	NK cells are activated by interferons and	01	3-17	orientation over the MHC:peptide complex. The CD4 and CD8 cell-surface proteins of T cells are	132
0.04	macrophage-derived cytokines to serve as an early defense against certain intracellular infections.	95	3-18	required to make an effective response to antigen. The two classes of MHC molecules are expressed	133
2-31	NK cells possess receptors for self molecules that prevent their activation by uninfected cells.	96	3-19	differentially on cells. A distinct subset of T cells bears an alternative receptor	135
2-32	NK cells bear receptors that activate their killer function in response to ligands expressed on infected cells or tumor cells.	99		made up of γ and δ chains.	137 137
2-33	The NKG2D receptor activates a different signaling pathway from that of the other activating NK receptors.	100	Summ. Summ	ary. ary to Chapter 3.	138
2-34	Several lymphocyte subpopulations behave as innate-like	400			
Summa	lymphocytes.	100 102	Chap	ter 4 The Generation of Lymphocyte Antigen	ì
	ary to Chapter 2.	103		Receptors	143
			Prima	ry immunoglobulin gene rearrangement	144
n.	THE DECOCNITION OF ANTICE	= N I	4-1	Immunoglobulin genes are rearranged in antibody-producing cells.	144
Pa	THE RECOGNITION OF ANTIGI	ZIN	4-2	Complete genes that encode a variable region are generated by the somatic recombination of separate gene segments.	145
Chap	ter 3 Antigen Recognition by B-cell and T-cell Receptors	111	4-3	Multiple contiguous V gene segments are present at each immunoglobulin locus.	146
The s	tructure of a typical antibody molecule.	112	4-4	Rearrangement of V, D, and J gene segments is guided by flanking DNA sequences.	148
3-1	IgG antibodies consist of four polypeptide chains.	113	4-5	The reaction that recombines V, D, and J gene segments	
3-2	Immunoglobulin heavy and light chains are composed of constant and variable regions.	113		involves both lymphocyte-specific and ubiquitous DNA-modifying enzymes.	150
3-3	The antibody molecule can readily be cleaved into functionally distinct fragments.	114	4-6	The diversity of the immunoglobulin repertoire is generated by four main processes.	153
3-4	The immunoglobulin molecule is flexible, especially at the hinge region.	115	4-7	The multiple inherited gene segments are used in different combinations.	153

4-8	Variable addition and subtraction of nucleotides at the			•	of MHC class II molecules with peptides.	193
	junctions between gene segments contributes to the diversity of the third hypervariable region.	154	5-10		oinding of peptides by MHC molecules provides e antigen presentation at the cell surface.	194
Summa	ary.	155	Summa	ary.		195
T-cell	receptor gene rearrangement.	155	The m	najor his	tocompatibility complex and its functions.	196
4-9	The T-cell receptor gene segments are arranged in a similar pattern to immunoglobulin gene segments and are rearranged by the same enzymes.	156	5-11	present	roteins involved in antigen processing and ation are encoded by genes within the major mpatibility complex.	197
4-10	T-cell receptors concentrate diversity in the third hypervariable region.	157	5-12	The pro	tein products of MHC class I and class II genes	199
4-11	$\gamma.\delta$ T-cell receptors are also generated by gene rearrangement.	158	5-13	MHC p	plymorphism affects antigen recognition by T cells by ing both peptide binding and the contacts between	/
Summa	ary.	159	C 44		eceptor and MHC molecule.	201
Struct	ural variation in immunoglobulin constant regions.	160	5-14		ctive T cells recognizing nonself MHC molecules y abundant.	204
4-12	Different classes of immunoglobulins are distinguished		5-15	•	cells respond to superantigens.	206
4-13	by the structure of their heavy-chain constant regions. The constant region confers functional specialization on	160	5-16	the imn	plymorphism extends the range of antigens to which nune system can respond.	207
4-14	the antibody. Mature naive B cells express both lgM and lgD at their	161	5-17		y of genes with specialized functions in immunity oncoded in the MHC.	208
4-15	surface. Transmembrane and secreted forms of immunoglobulin	163	5-18		ized MHC class I molecules act as ligands for the on and inhibition of NK cells.	209
7 10	are generated from alternative heavy-chain transcripts.	163	5-19	The CD	11 family of MHC class I-like molecules is encoded	
4-16	IgM and IgA can form polymers.	164			the MHC and presents microbial lipids to stricted T cells.	211
Summa	ary.	166	Summa		aniotod i dona.	212
Secon	dary diversification of the antibody repertoire.	167	Summa	ary to Ch	apter 5.	212
4-17	Activation-induced cytidine deaminase introduces mutations in genes transcribed in B cells.	168				
4-18	Rearranged V-region genes are further diversified by					
		169	Par	t III 📗	THE DEVELOPMENT OF MATU	RE
4-19	somatic hypermutation. In some species, most immunoglobulin gene		Par	t III	LYMPHOCYTE RECEPTOR	RE
	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to	169 171	Pai			IRE
4-19	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement.		Pai Chap		LYMPHOCYTE RECEPTOR	IRE
4-19 4-20 Summa	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response.	171 171 175			LYMPHOCYTE RECEPTOR REPERTOIRES	219
4-19 4-20 Summa	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response.	171 171	Chap	ter 6	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors	219
4-19 4-20 Summa Summa	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4.	171 171 175 175	Chap	ter 6 ral princ	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals	219 220
4-19 4-20 Summa Summa	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes	171 171 175 175	Chap	ter 6 ral princ Transminto intri	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large	219
4-19 4-20 Summa Summa Chapt The ge	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands.	171 171 175 175	Chap Gener 6-1 6-2	ter 6 ral princ Transminto intri Intracel multipro	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large otein signaling complexes.	219 220
4-19 4-20 Summa Summa Chapt The ga	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments.	171 171 175 175	Chap Gener 6-1 6-2 6-3	ter 6 ral princ Transminto intrinto intrintrinto intrintrintrintrintrintrintrintrintrintr	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals accellular biochemical events. lular signal transduction often takes place in large otein signaling complexes. ivation of some receptors generates small-molecule messengers.	219 220 220
4-19 4-20 Summa Summa Chapt The ge	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides	171 171 175 175 181 182	Chap Gener 6-1 6-2	ter 6 ral princ Transminto intrintracel multipre The acisecond Small C	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals accellular biochemical events. lular signal transduction often takes place in large otein signaling complexes. ivation of some receptors generates small-molecule	219 220 220 221
4-19 4-20 Summa Summa Chapt The ga	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively	171 171 175 175 175 181 182	Chap Gener 6-1 6-2 6-3	ter 6 ral prince Transminto intracel multipre The act second Small C differen Signalia	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large otein signaling complexes. ivation of some receptors generates small-molecule messengers. is proteins act as molecular switches in many	219 220 220 221 222
4-19 4-20 Summa Summa Chapt The ga 5-1 5-2	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively transported from the cytosol to the endoplasmic reticulum. Peptides for transport into the endoplasmic reticulum are generated in the cytosol. Retrograde transport from the endoplasmic reticulum to the cytosol enables exogenous proteins to be processed for cro	171 171 175 175 181 182 183 184 ss-	Chap Gener 6-1 6-2 6-3 6-4 6-5 6-6	ter 6 Transminto intrintracel multipro The aci second differen Signalir variety Signal membro	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large often signaling complexes. ivation of some receptors generates small-molecule messengers. a proteins act as molecular switches in many t signaling pathways. Ing proteins are recruited to the membrane by a of mechanisms. Iransduction proteins are organized in the plasma ane in structures called lipid rafts.	219 220 220 221 222 222
4-19 4-20 Summa Summa Chapt The ga 5-1 5-2 5-3	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively transported from the cytosol to the endoplasmic reticulum. Peptides for transport into the endoplasmic reticulum are generated in the cytosol. Retrograde transport from the endoplasmic reticulum to the cytosol enables exogenous proteins to be processed for cropresentation by MHC class I molecules. Newly synthesized MHC class I molecules are retained in	171 171 175 175 181 182 182 183 184 ss- 186	Chap Gener 6-1 6-2 6-3 6-4 6-5 6-6 6-7	ter 6 Transminto intrince multipre The act second Small Codifferent Signality variety Signal transminto intracel membra	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large of signaling complexes. ivation of some receptors generates small-molecule messengers. a proteins act as molecular switches in many t signaling pathways. and proteins are recruited to the membrane by a of mechanisms. ransduction proteins are organized in the piasma	219 220 220 221 222 224 224 225 226
4-19 4-20 Summa Summa The ge 5-1 5-2 5-3 5-4	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary, ary to Chapter 4. Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively transported from the cytosol to the endoplasmic reticulum. Peptides for transport into the endoplasmic reticulum are generated in the cytosol. Retrograde transport from the endoplasmic reticulum to the cytosol enables exogenous proteins to be processed for cropresentation by MHC class I molecules are retained in the endoplasmic reticulum until they bind a peptide. Many viruses produce immunoevasins that interfere with	171 171 175 175 181 182 182 183 184 ss- 186 187	Chap Gener 6-1 6-2 6-3 6-4 6-5 6-6 6-7 Summa	ter 6 Transminto intrinction intracel multipro The aci second Small Codifferen Signalir variety Signal membra. Protein signalir ary.	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. Itular signal transduction often takes place in large oftein signaling complexes. iivation of some receptors generates small-molecule messengers. A proteins act as molecular switches in many training pathways. In groteins are recruited to the membrane by a pof mechanisms. Iransduction proteins are organized in the plasma and in structures called lipid rafts. In degradation has an important role in terminating gresponses.	219 220 221 221 222 224 224 225 226 227
4-19 4-20 Summa Summa Chapt The ge 5-1 5-2 5-3 5-4 5-5	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. ter 5 Antigen Presentation to T Lymphocytes eneration of T-cell receptor ligands. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively transported from the cytosol to the endoplasmic reticulum. Peptides for transport into the endoplasmic reticulum are generated in the cytosol. Retrograde transport from the endoplasmic reticulum to the cytosol enables exogenous proteins to be processed for cropresentation by MHC class I molecules are retained in the endoplasmic reticulum until they bind a peptide. Many viruses produce immunoevasins that interfere with antigen presentation by MHC class I molecules. Peptides presented by MHC class II molecules are	171 171 175 175 181 182 182 183 184 ss- 186 187 189	Chap Gener 6-1 6-2 6-3 6-4 6-5 6-6 6-7 Summa	ter 6 Transminto intrinitracel multipro The aci second Small of different Signality variety Signal membra Protein signalirary.	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large oftein signaling complexes. ivation of some receptors generates small-molecule messengers. If proteins act as molecular switches in many transduction proteins are organized in the plasma and in structures called lipid rafts. Idegradation has an important role in terminating gresponses. Potor signaling and lymphocyte activation. Iniable chains of antigen receptors are associated with	219 220 221 222 224 224 225 226 227
4-19 4-20 Summa Summa Chapt The ge 5-1 5-2 5-3 5-4 5-5 5-6	somatic hypermutation. In some species, most immunoglobulin gene diversification occurs after gene rearrangement. Class switching enables the same assembled V _H exon to be associated with different C _H genes in the course of an immune response. ary. ary to Chapter 4. The MHC class I and class II molecules deliver peptides to the cell surface from two intracellular compartments. Peptides that bind to MHC class I molecules are actively transported from the cytosol to the endoplasmic reticulum. Peptides for transport into the endoplasmic reticulum are generated in the cytosol. Retrograde transport from the endoplasmic reticulum to the cytosol enables exogenous proteins to be processed for cropresentation by MHC class I molecules are retained in the endoplasmic reticulum until they bind a peptide. Many viruses produce immunoevasins that interfere with antigen presentation by MHC class I molecules.	171 171 175 175 181 182 182 183 184 ss- 186 187	Chap Gener 6-1 6-2 6-3 6-4 6-5 6-6 6-7 Summa	ter 6 Transminto intrinitracel multipro The aci second Small (different Signality variety) Signal membra Protein signalirary. en recep	LYMPHOCYTE RECEPTOR REPERTOIRES Signaling Through Immune System Receptors iples of signal transduction. embrane receptors convert extracellular signals acellular biochemical events. lular signal transduction often takes place in large otein signaling complexes. ivation of some receptors generates small-molecule messengers. a proteins act as molecular switches in many t signaling pathways. Ing proteins are recruited to the membrane by a of mechanisms. Iransduction proteins are organized in the plasma ane in structures called lipid rafts. Idegradation has an important role in terminating gresponses. Potor signaling and lymphocyte activation.	219 220 221 222 224 224 225 226 227

6-10	Antigen binding leads to phosphorylation of the ITAM sequences associated with the antigen receptors.	231	Summa	ary.	272
6-11	In T cells, fully phosphorylated ITAMs bind the kinase		T-cell	development in the thymus.	273
6-12	ZAP-70 and enable it to be activated. Activated Syk and ZAP-70 phosphorylate scaffold proteins	233	7-7	T-cell progenitors originate in the bone marrow, but all the important events in their development occur in the thymus.	274
	that mediate many of the downstream effects of antigen receptor signaling.	233	7-8	T-cell precursors proliferate extensively in the thymus but most die there.	275
6-13	PLC- γ is activated by Tec tyrosine kinases.	234	7-9	Successive stages in the development of thymocytes are	_, ,
6-14	Activation of the small G protein Ras activates a MAP kinase cascade, resulting in the production of the transcription factor AP-1.	235	7-10	marked by changes in cell-surface molecules. Thymocytes at different developmental stages are found	277
6-15	The transcription factor NFAT is indirectly activated by Ca ²⁺ .	236	744	in distinct parts of the thymus.	279
6-16	The transcription factor NF κ B is activated by the actions of protein kinase C.		7-11	T cells with $\alpha:\beta$ or $\gamma:\delta$ receptors arise from a common progenitor.	280
6-17	The logic of B-cell receptor signaling is similar to that of T-cell receptor signaling but some of the signaling		7-12 7-13	T cells expressing particular γ - and δ -chain V regions arise in an ordered sequence early in life. Successful synthesis of a rearranged β chain allows the	282
6-18	components are specific to B cells. ITAMs are also found in other receptors on leukocytes that	239	7-10	production of a pre-T-cell receptor that triggers cell proliferation and blocks further β-chain gene	
	signal for cell activation.	240		rearrangement.	283
6-19	The cell-surface protein CD28 is a co-stimulatory receptor for naive T cells.	240	7-14	T-cell α -chain genes undergo successive rearrangements until positive selection or cell death intervenes.	286
6-20	Inhibitory receptors on lymphocytes help regulate immune responses.	242	Summa	ary.	288
Summa	ry.	244	Positi	ve and negative selection of T cells.	288
	receptors and signaling pathways.	244	7-15	The MHC type of the thymic stroma selects a repertoire of mature T cells that can recognize foreign antigens	000
6-21	Cytokines typically activate fast signaling pathways that end in the nucleus.	245	7-16	presented by the same MHC type. Only thymocytes whose receptors interact with	289
6-22	Cytokine receptors form dimers or trimers on ligand binding.	245		self-peptide:self-MHC complexes can survive and mature.	290
6-23	Cytokine receptors are associated with the JAK family of tyrosine kinases which activate STAT transcription factors.	245	7-17	Positive selection acts on a repertoire of T-cell receptors with inherent specificity for MHC molecules.	291
6-24 6-25	Cytokine signaling is terminated by a negative feedback mechanism. The receptors that induce apoptosis activate specialized	246	7-18	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.	292
6-26	intracellular proteases called caspases. The intrinsic pathway of apoptosis is mediated by release	247	7-19	Thymic cortical epithelial cells mediate positive selection of developing thymocytes.	293
6-27	of cytochrome <i>c</i> from mitochondria. Microbes and their products act via Toll-like receptors to	249	7-20	T cells that react strongly with ubiquitous self antigens are deleted in the thymus.	294
	activate NFκB.	249	7-21	Negative selection is driven most efficiently by bone	296
6-28	Bacterial peptides, mediators of inflammatory responses, and chemokines signal through members of the		7-22	marrow derived antigen-presenting cells. The specificity and/or the strength of signals for negative	
0	G-protein-coupled receptor family.	251	Comme	and positive selection must differ.	297
Summa	rry. rry to Chapter 6.	253 253	Summ	ary.	298
Camino	iy to onaptor of	200		val and maturation of lymphocytes in peripheral noid tissues.	299
Chap	ter 7 The Development and Survival of Lymphocytes	257	7-23	Different lymphocyte subsets are found in particular locations in peripheral lymphoid tissues.	299
Devel	opment of B lymphocytes	259	7-24	The development and organization of peripheral lymphoid	
7-1	Lymphocytes derive from hematopoietic stem cells in	209		tissues are controlled by proteins of the tumor necrosis factor family.	300
7-2	the bone marrow. B-cell development begins by rearrangement of the	259	7-25	The homing of lymphocytes to specific regions of peripheral lymphoid tissues is mediated by chemokines.	1 302
7-3	heavy-chain locus. The pre-B-cell receptor tests for successful production of	262	7-26	Lymphocytes that encounter sufficient quantities of self antigens for the first time in the periphery are eliminated or inactivated.	
	a complete heavy chain and signals for proliferation of pro-B cells.	264	7-27	Most immature B cells arriving in the spleen are short-lived and require cytokines and positive signals through the B-cell receptor for maturation and survival.	304
7-4	Pre-B-cell receptor signaling inhibits further heavy-chain locus rearrangement and enforces allelic exclusion.	266	7-28	B-1 cells and marginal zone B cells are distinct B-cell	
7 - 5	Pre-B cells rearrange the light-chain locus and express cell-surface immunoglobulin.	266	7-29	subtypes with unique antigen receptor specificity. T-cell homeostasis in the periphery is regulated by	306
7-6	Immature B cells are tested for autoreactivity before they leave the bone marrow.	268	Summ	cytokines and self-MHC interactions. ary.	307 307

Lymph	oid tun	nors.	308	8-17	T cells differentiate into several subsets of functionally	40
7-30	B-cell tu counter	mors often occupy the same site as their normal carts.	308	8-18	different effector cells. CD8 T cells can be activated in different ways to become	
7-31	T-cell de	mors correspond to a small number of stages of evelopment.	311	8-19	cytotoxic effector cells. Various forms of signal 3 induce the differentiation of naive CD4 T cells down distinct effector pathways. 35	
7-32	transloc	mphomas frequently carry chromosomal ations that join immunoglobulin loci to genes	312	8-20	Regulatory CD4 T cells are involved in controlling	
Summa	_	ulate cell growth.	312	Summa	•	
	ry to Cha	pter 7.	313		•	
				Gener cytok	al properties of effector T cells and their nes. 35	56
Par	t IV	THE ADAPTIVE IMMUNE		8-21	Effector T-cell interactions with target cells are initiated by antigen-nonspecific cell-adhesion molecules. 35	57
		RESPONSE		8-22	Binding of the T-cell receptor complex directs the release of effector molecules and focuses them on the target cell. 35	57
Chapt	er 8	T Cell-Mediated Immunity	323	8-23	The effector functions of T cells are determined by the array of effector molecules that they produce.	
Entry 6	of naive	T cells and antigen-presenting cells into		8-24	Cytokines can act locally or at a distance. 35	59
	eral lyn	phoid organs. cells migrate through peripheral lymphoid tissues,	325	8-25	Cytokines and their receptors fall into distinct families of structurally related proteins. 36	31
0-1		g the peptide:MHC complexes on dendritic	325	8-26	The TNF family of cytokines are trimeric proteins that are usually associated with the cell surface.	32
8-2		cyte entry into lymphoid tissues depends on		Summa	ary. 36	33
		ines and adhesion molecules.	326	T cell-	mediated cytotoxicity.	64
8-3	the entr	on of integrins by chemokines is responsible for y of naive T cells into lymph nodes.	327	8-27	Cytotoxic T cells can induce target cells to undergo programmed cell death. 36	
8-4	organs	sponses are initiated in peripheral lymphoid by activated dendritic cells.	331	8-28	Cytotoxic effector proteins that trigger apoptosis are contained in the granules of CD8 cytotoxic T cells.	
8-5	dendriti		332	8-29	Cytotoxic T cells are selective and serial killers of targets expressing a specific antigen.	
8-6	of patho	c cells process antigens from a wide array gens.	334	8-30	Cytotoxic T cells also act by releasing cytokines. 36	
8-7	Pathoge	en-induced TLR signaling in immature dendritic luces their migration to lymphoid organs and		Summ		
		es antigen processing.	336	Macro	phage activation by T _H 1 cells. 36	86
8-8		cytoid dendritic cells detect viral infections and e abundant type I interferons and pro-inflammatory		8-31	T _H 1 cells have a central role in macrophage activation. 36	39
8-9	cytokine		338	8-32	Activation of macrophages by T _H 1 cells promotes microbial killing and must be tightly regulated to avoid tissue damage. 37	70
•	induced naive T	by pathogens to present foreign antigens to	339	8-33	T _H 1 cells coordinate the host response to intracellular pathogens.	71
8-10		are highly efficient at presenting antigens that bind		Summa	ary. 37	72
C		surface immunoglobulin.	340	Summ	ary to Chapter 8. 37	72
Summa	•	ive T cells by pathogen-activated	342	Chap	ter 9 The Humoral Immune Response 37	70
	tic cells		343		·	
8-11		nesion molecules mediate the initial interaction			activation and antibody production. 38	31
8-12	Antigen	T cells with antigen-presenting cells. presenting cells deliver three kinds of signals	343	9-1	The humoral immune response is initiated when B cells that bind antigen are signaled by helper T cells or by certain microbial antigens alone.	Q 1
8-13		al expansion and differentiation of naive T cells. ependent co-stimulation of activated T cells	344	9-2	B-cell responses to antigen are enhanced by co-ligation	′'
0-10	induces	expression of the T-cell growth factor interleukin-2 high-affinity IL-2 receptor.	345	9-3	of the B-cell co-receptor. Helper T cells activate B cells that recognize the	32
8-14		can be modified by additional co-stimulatory	346	9-4	same antigen. Antigenic peptides bound to self-MHC class II molecules	33
8-15	Antigen eads to	recognition in the absence of co-stimulation functional inactivation or clonal deletion of			on B cells trigger helper T cells to make membrane-bound and secreted molecules that can activate a B cell.	34
8-16	periphe	al T cells. ating T cells differentiate into effector T cells that	347	9-5	B cells that have bound antigen via their B-cell receptor are trapped in the T-cell zones of secondary	
		equire co-stimulation to act.	349		lymphoid tissues. 38	36

9-6	Antibody-secreting plasma cells differentiate from activated B cells.	387	10-2	The nonspecific responses of innate immunity are necessary for an adaptive immune response to be	425
9-7	The second phase of a primary B-cell immune response occurs when activated B cells migrate to follicles and proliferate to form germinal centers.	388	10-3	initiated. Cytokines made in the earliest phase of an infection influence differentiation of CD4 T cells toward the	
9-8	Germinal center B cells undergo V-region somatic hypermutation, and cells with mutations that improve affinity for antigen are selected.	390	10-4	T _H 17 subset. Cytokines made in the later stages of an infection influence differentiation of CD4 T cells toward T _H 1	426
9-9	Class switching in thymus-dependent antibody responses requires expression of CD40 ligand by the helper T cell and is directed by cytokines.	392	10-5	or T_H2 cells. The distinct subsets of CD4 T cells can regulate each other's differentiation.	427 430
9-10	Ligation of the B-cell receptor and CD40, together with direct contact with T cells, are all required to sustain	002	10-6	Effector T cells are guided to sites of infection by chemokines and newly expressed adhesion molecules.	432
9-11	germinal center B cells. Surviving germinal center B cells differentiate into either	394	10-7	Differentiated effector T cells are not a static population but continue to respond to signals as they carry out their effector functions.	434
9-12	plasma cells or memory cells. B-cell responses to bacterial antigens with intrinsic	395	10-8	Primary CD8 T-cell responses to pathogens can occur in the absence of CD4 help.	435
9-13	ability to activate B cells do not require T-cell help. B-cell responses to bacterial polysaccharides do not require peptide-specific T-cell help.	396 397	10-9	Antibody responses develop in lymphoid tissues under the direction of CD4 helper T cells.	437
Summa		399	10-10	Antibody responses are sustained in medullary cords and bone marrow.	438
The di	stribution and functions of immunoglobulin es.	400	10-11	The effector mechanisms used to clear an infection depend on the infectious agent.	439
9-14	Antibodies of different isotypes operate in distinct places and have distinct effector functions.	400	10-12	Resolution of an infection is accompanied by the death of most of the effector cells and the generation of	444
9-15	Transport proteins that bind to the Fc regions of antibodies carry particular isotypes across epithelial barriers.	402	Summa	memory cells. ry.	441 441
9-16	High-affinity IgG and IgA antibodies can neutralize bacterial toxins.	404	lmmui	nological memory	442
9-17	High-affinity IgG and IgA antibodies can inhibit the infectivity of viruses.	405	10-13	Immunological memory is long-lived after infection or vaccination.	442
9-18 9-19	Antibodies can block the adherence of bacteria to host cells. Antibody:antigen complexes activate the classical pathway	406	10-14	Memory B-cell responses differ in several ways from those of naive B cells.	444
9-20	of complement by binding to C1q. Complement receptors are important in the removal of	406	10-15	Repeated immunization leads to increasing affinity of antibody due to somatic hypermutation and selection	
	immune complexes from the circulation.	408	10-16	by antigen in germinal centers. Memory T cells are increased in frequency compared	445
Summa The de	estruction of antibody-coated pathogens via	409		with naive T cells specific for the same antigen and have distinct activation requirements and cell-surface proteins that distinguish them from effector T cells.	446
	eptors. The Fc receptors of accessory cells are signaling receptors	409	10-17	Memory T cells are heterogeneous and include central memory and effector memory subsets.	449
9-22	specific for immunoglobulins of different classes. Fc receptors on phagocytes are activated by antibodies	410	10-18	CD4 T-cell help is required for CD8 T-cell memory and involves CD40 and IL-2 signaling.	450
9-22	bound to the surface of pathogens and enable the phagocytes to ingest and destroy pathogens.	411	10-19	In immune individuals, secondary and subsequent responses are mainly attributable to memory lymphocytes.	450
9-23	Fc receptors activate NK cells to destroy antibody-coated targets.	412	Summa	ary.	453
9-24	Mast cells, basophils, and activated eosinophils bind IgE antibody via the high-affinity Fcc receptor.	413	Summa	ary to Chapter 10.	454
9-25	IgE-mediated activation of accessory cells has an important role in resistance to parasite infection.	414	Chap	ter 11 The Mucosal Immune System	459
Summ	·	415	The o	rganization of the mucosal immune system.	459
	ary to Chapter 9.	416	11-1	The mucosal immune system protects the internal surfaces of the body.	4459
Chap	ter 10 Dynamics of Adaptive Immunity	421	11-2	The mucosal immune system may be the original vertebrate immune system.	461
The c	ourse of the immune response to infection.	422	11-3	Mucosa-associated lymphoid tissue is located in anatomically defined compartments in the gut.	462
10-1	The course of an infection can be divided into several distinct phases.	422	11-4	The intestine has distinctive routes and mechanisms of antigen uptake.	464

11-5	The mucosal immune system contains large numbers of	400	lmmur	odeficiency diseases.	507
11.0	effector lymphocytes even in the absence of disease.	466	12-7	A history of repeated infections suggests a diagnosis of	
11-6	The circulation of lymphocytes within the mucosal immune system is controlled by tissue-specific adhesion molecules and chemokine receptors.	467	12-8	immunodeficiency. Inherited immunodeficiency diseases are caused by	507
11-7	Priming of lymphocytes in one mucosal tissue can induce		40.0	recessive gene defects.	508
11-8	protective immunity at other mucosal surfaces. Secretory IgA is the class of antibody associated with the	469	12-9	The main effect of low levels of antibody is an inability to clear extracellular bacteria.	509
11-9	mucosal immune system. IgA deficiency is common in humans but may be	469	12-10	Some antibody deficiencies can be due to defects in either B-cell or T-cell function.	512
11-10	overcome by secretory IgM. The mucosal immune system contains unusual	472	12-11	Defects in complement components cause defective humoral immune function.	514
11-10	T lymphocytes.	472	12-12	Defects in phagocytic cells permit widespread bacterial infections.	515
Summa	ry.	475	12-13	Defects in T-cell differentiation can result in severe	Ų i U
	ucosal response to infection and regulation of	476	12-14	combined immunodeficiencies. Defects in antigen receptor gene rearrangement result	517
	al immune responses.	4/0	12-14	in SCID.	519
11-11	Enteric pathogens cause a local inflammatory response and the development of protective immunity.	476	12-15	Defects in signaling from T-cell antigen receptors can cause severe immunodeficiency.	520
11-12	The outcome of infection by intestinal pathogens is determined by a complex interplay between the microorganism and the host immune response.	478	12-16	Genetic defects in thymic function that block T-cell development result in severe immunodeficiencies.	520
11-13	The mucosal immune system must maintain a balance between protective immunity and homeostasis to a large		12-17	The normal pathways for host defense against intracellular bacteria are pinpointed by genetic deficiencies of	E00
44 41	number of different foreign antigens.	480	12-18	IFN-γ and IL-12 and their receptors. X-linked lymphoproliferative syndrome is associated with	522
11-14	The healthy intestine contains large quantities of bacteria but does not generate productive immunity against them.	482	12-10	fatal infection by Epstein–Barr virus and with the development of lymphomas.	523
11-15	Full immune responses to commensal bacteria provoke	105	12-19	Genetic abnormalities in the secretory cytotoxic pathway	
11-16	intestinal disease. Intestinal helminths provoke strong T _H 2-mediated immune	485		of lymphocytes cause uncontrolled lymphoproliferation and inflammatory responses to viral infections.	523
11-17	responses. Other eukaryotic parasites provoke protective immunity	485	12-20	Bone marrow transplantation or gene therapy can be useful to correct genetic defects.	525
11-18	and pathology in the gut. Dendritic cells at mucosal surfaces favor the induction of	488	12-21	Secondary immunodeficiencies are major predisposing causes of infection and death.	526
	tolerance under physiological conditions and maintain the presence of physiological inflammation.	488	Summa		527
Summa		489	Acqui	red immune deficiency syndrome.	527
	ry to Chapter 11.	490	12-22	Most individuals infected with HIV progress over time to AIDS.	528
			12-23	HIV is a retrovirus that infects CD4 T cells, dendritic cells, and macrophages.	530
Pai	THE IMMUNE SYSTEM IN		12-24	Genetic variation in the host can alter the rate of progression of disease.	532
	HEALTH AND DISEASE		12-25	A genetic deficiency of the co-receptor CCR5 confers resistance to HIV infection <i>in vivo</i> .	532
Chapt	ter 12 Failures of Host Defense		12-26	HIV RNA is transcribed by viral reverse transcriptase into DNA that integrates into the host-cell genome.	534
	Mechanisms	497	12-27	Replication of HIV occurs only in activated T cells.	536
Evasio	on and subversion of immune defenses	498	12-28	Lymphoid tissue is the major reservoir of HIV infection.	537
12-1	Antigenic variation allows pathogens to escape from immunity.	498	12-29	An immune response controls but does not	
12-1	Some viruses persist <i>in vivo</i> by ceasing to replicate until	100	40.00	eliminate HIV.	538
12-3	immunity wanes. Some pathogens resist destruction by host defense	501	12-30	The destruction of immune function as a result of HIV infection leads to increased susceptibility to opportunistic infection and eventually to death.	540
12-4	mechanisms or exploit them for their own purposes. Immunosuppression or inappropriate immune responses	502	12-31	Drugs that block HIV replication lead to a rapid	0.10
	can contribute to persistent disease.	504		decrease in titer of infectious virus and an increase in CD4 T cells.	540
12-5	Immune responses can contribute directly to pathogenesis.	506	12-32	HIV accumulates many mutations in the course of infection, and drug treatment is soon followed by the outgrowth of	
12-6	Regulatory T cells can affect the outcome of infectious disease.	506	40.00	drug-resistant variants.	542
Summa		507	12-33	Vaccination against HIV is an attractive solution but poses many difficulties.	543

12-34	Prevention and education are one way in which the	545	Chapt	er 14	Autoimmunity and Transplantation	599
Summa	spread of HIV and AIDS can be controlled.	545	The ma	aking a	and breaking of self-tolerance	600
	ry to Chapter 12.	546	14-1		al function of the immune system is to inate self from nonself.	600
Chap	ter 13 Allergy and Hypersensitivity	555	14-2	Multiple autoim	e tolerance mechanisms normally prevent munity.	602
Sensit	ization and the production of IgE.	557	14-3		deletion or inactivation of newly formed cytes is the first checkpoint of self-tolerance.	603
13-1	Allergens are often delivered transmucosally at low dose, a route that favors IgE production.	557	14-4	affinity	pocytes that bind self antigens with relatively low usually ignore them but in some circumstances	603
13-2 13-3	Enzymes are frequent triggers of allergy. Class switching to IgE in B lymphocytes is favored by specific signals.	558 559	14-5	Antiger	ns in immunologically privileged sites do not induce	605
13-4	Both genetic and environmental factors contribute to the development of IgE-mediated allergy.	560	14-6	Autorea	active T cells that express particular cytokines may be	606
13-5	Regulatory T cells can control allergic responses.	565 565	14-7	Autoim	mune responses can be controlled at various by regulatory T cells.	607
Summa			Summa	-	• • •	609
	or mechanisms in allergic reactions.	566	Autoin	nmune	diseases and pathogenic mechanisms.	610
13-6	Most IgE is cell-bound and engages effector mechanisms of the immune system by different pathways from other antibody isotypes.	567	14-8	Specifi	c adaptive immune responses to self antigens use autoimmune disease.	610
13-7	Mast cells reside in tissues and orchestrate allergic reactions.	567	14-9		mune diseases can be classified into clusters e typically either organ-specific or systemic.	611
13-8	Eosinophils are normally under tight control to prevent inappropriate toxic responses.	569	14-10		e aspects of the immune system are typically and in autoimmune disease.	612
13-9	Eosinophils and basophils cause inflammation and tissue damage in allergic reactions.	571	14-11	feedba	c autoimmune disease develops through positive ck from inflammation, inability to clear the self	015
13-10	Allergic reactions can be divided into immediate and late-phase responses.	571	14-12	Both a	n, and a broadening of the autoimmune response. ntibody and effector T cells can cause tissue	615
13-11	The clinical effects of allergic reactions vary according to the site of mast-cell activation.	572	14-13	Autoar	e in autoimmune disease. Itibodies against blood cells promote their	617
13-12	Allergen inhalation is associated with the development of rhinitis and asthma.	574	14-14		ation of sublytic doses of complement to cells in	617
13-13 13-14	Skin allergy is manifested as urticaria or chronic eczema. Allergy to foods causes systemic reactions as well	576	14-15	Autoar	stimulates a powerful inflammatory response. Itibodies against receptors cause disease by	619
	as symptoms limited to the gut.	577	14-16		uting or blocking receptor function. Itibodies against extracellular antigens cause	620
13-15	Celiac disease is a model of antigen-specific immunopathology.	578	14 10	inflam	natory injury by mechanisms akin to type II and hypersensitivity reactions.	621
13-16	Allergy can be treated by inhibiting either IgE production or the effector pathways activated by the cross-linking of cell-surface IgE.	580	14-17		specific for self antigens can cause direct tissue and sustain autoantibody responses.	622
Summ	-	583	Summa	ary.		625
Hypei	sensitivity diseases.	583	The ge	enetic a	and environmental basis of autoimmunity.	626
13-17	Innocuous antigens can cause type II hypersensitivity reactions in susceptible individuals by binding to the		14-18 14-19		mune diseases have a strong genetic component. ct in a single gene can cause autoimmune	626
13-18	surfaces of circulating blood cells. Systemic disease caused by immune-complex formation	583	14-20	diseas	• -	627
10-10	can follow the administration of large quantities of poorly catabolized antigens.	583	14-20	geneti	basis of autoimmunity.	628
13-19	Delayed-type hypersensitivity reactions are mediated by T _H 1 cells and CD8 cytotoxic T cells.	585		that af	that predispose to autoimmunity fall into categories fect one or more of the mechanisms of tolerance.	631
13-20	Mutation in the molecular regulators of inflammation can cause hypersensitive inflammatory responses resulting	000	14-22	susce	genes have an important role in controlling of the state	631
	in 'autoinflammatory disease.'	588	14-23 14-24		al events can initiate autoimmunity. on can lead to autoimmune disease by providing	634
13-21	Crohn's disease is a relatively common inflammatory disease with a complex etiology.	590	14-25	an en	reactivity between foreign molecules on pathogens	634
Summ Summ	ary. ary to Chapter 13.	591 591	14-23	and se	elf molecules can lead to anti-self responses and immune disease.	635

14-26	Drugs and toxins can cause autoimmune syndromes.	636	Using	the immune response to attack tumors.	672
14-27	Random events may be required for the initiation of autoimmunity.	637	15-14	The development of transplantable tumors in mice led to the discovery of protective immune responses to	
Summa	ary.	637		tumors.	673
Poene	ances to allogations and transplant rejection	637	15-15	Tumors can escape rejection in many ways.	674
14-28	onses to alloantigens and transplant rejection. Graft rejection is an immunological response mediated primarily by T cells.	638	15-16	T lymphocytes can recognize specific antigens on human tumors, and adoptive T-cell transfer is being tested in cancer patients.	678
14-29	Matching donor and recipient at the MHC improves the outcome of transplantation.	639	15-17	Monocional antibodies against tumor antigens, alone or linked to toxins, can control tumor growth.	682
14-30	In MHC-identical grafts, rejection is caused by peptides from other alloantigens bound to graft MHC molecules.	640	15-18	Enhancing the immune response to tumors by vaccination holds promise for cancer prevention and therapy.	684
14-31	There are two ways of presenting alloantigens on the transplant to the recipient's T lymphocytes.	641	Summa	•	687
14-32	Antibodies reacting with endothelium cause hyperacute graft rejection.	642	-	oulating the immune response to fight infection.	687
14-33	Chronic organ rejection is caused by inflammatory	042	15-19	There are several requirements for an effective vaccine.	689
14-34	vascular injury to the graft. A variety of organs are transplanted routinely in	643	15-20	The history of vaccination against <i>Bordetella pertussis</i> illustrates the importance of developing an effective vaccina that is paragived to be seen	690
	clinical medicine.	644	15-21	vaccine that is perceived to be safe. Conjugate vaccines have been developed as a result of	090
14-35	The converse of graft rejection is graft-versus-host disease.	645	45.00	understanding how T and B cells collaborate in an immune response.	691
14-36	Regulatory T cells are involved in alloreactive immune responses.	646	15-22	The use of adjuvants is another important approach to enhancing the immunogenicity of vaccines.	693
14-37	The fetus is an allograft that is tolerated repeatedly.	647	15-23	Live-attenuated viral vaccines are usually more potent than 'killed' vaccines and can be made safer by the use of	
Summa	•	648		recombinant DNA technology.	695
Summe	ary to Chapter 14.	648	15-24	Live-attenuated bacterial vaccines can be developed by selecting nonpathogenic or disabled mutants.	696
Chap	ter 15 Manipulation of the Immune Response	655	15-25	Synthetic peptides of protective antigens can elicit protective immunity.	696
Extrin 15-1	sic regulation of unwanted immune responses. Corticosteroids are powerful anti-inflammatory drugs	655	15-26	The route of vaccination is an important determinant of success.	697
15-2	that alter the transcription of many genes. Cytotoxic drugs cause immunosuppression by killing	656	15-27	Protective immunity can be induced by injecting DNA encoding microbial antigens and human cytokines	
15-3	dividing cells and have serious side-effects.	657	15-28	into muscle. The effectiveness of a vaccine can be enhanced by	698
10-0	Cyclosporin A, tacrolimus (FK506), and rapamycin (sirolimus) are powerful immunosuppressive agents that interfere with T-cell signaling.	658	15-29	targeting it to sites of antigen presentation. An important question is whether vaccination can be used	699
15-4	immunosuppressive drugs are valuable probes of	030	10 20	therapeutically to control existing chronic infections.	700
15-5	intracellular signaling pathways in lymphocytes. Antibodies against cell-surface molecules have been	659	15-30	Modulation of the immune system might be used to inhibit immunopathological responses to infectious agents.	701
100	used to remove specific lymphocyte subsets or to inhibit		Summa		702
	cell function.	661	Summa	ary to Chapter 15.	703
15-6	Antibodies can be engineered to reduce their				
	immunogenicity in humans.	661			
15-7	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection.	661 662	Par	t VI THE ORIGINS OF IMMUNE	
15-7 15-8	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease.		Par	THE ORIGINS OF IMMUNE RESPONSES	
	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress	662		RESPONSES	711
15-8	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease. Depletion or inhibition of autoreactive lymphocytes can treat autoimmune disease. Interference with co-stimulatory pathways for the activation of lymphocytes could be a treatment for	662 664	Chap		711 712
15-8 15-9	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease. Depletion or inhibition of autoreactive lymphocytes can treat autoimmune disease. Interference with co-stimulatory pathways for the activation of lymphocytes could be a treatment for autoimmune disease. Induction of regulatory T cells by antibody therapy can	662 664	Chap	ter 16 Evolution of the Immune System tion of the innate immune system. The evolution of the immune system can be studied by	712
15-8 15-9 15-10 15-11	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease. Depletion or inhibition of autoreactive lymphocytes can treat autoimmune disease. Interference with co-stimulatory pathways for the activation of lymphocytes could be a treatment for autoimmune disease. Induction of regulatory T cells by antibody therapy can inhibit autoimmune disease.	662 664 666	Chap	ter 16 Evolution of the Immune System tion of the innate immune system. The evolution of the immune system can be studied by comparing the genes expressed by different species. Antimicrobial peptides are likely to be the most ancient	712 712
15-8 15-9 15-10 15-11 15-12	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease. Depletion or inhibition of autoreactive lymphocytes can treat autoimmune disease. Interference with co-stimulatory pathways for the activation of lymphocytes could be a treatment for autoimmune disease. Induction of regulatory T cells by antibody therapy can inhibit autoimmune disease. A number of commonly used drugs have immunomodulatory properties.	662 664 666 668	Chap Evolut	ter 16 Evolution of the Immune System tion of the innate immune system. The evolution of the immune system can be studied by comparing the genes expressed by different species. Antimicrobial peptides are likely to be the most ancient immune defenses. Toll-like receptors may represent the most ancient	712 712 713
15-8 15-9 15-10 15-11	immunogenicity in humans. Monoclonal antibodies can be used to prevent allograft rejection. Biological agents can be used to alleviate and suppress autoimmune disease. Depletion or inhibition of autoreactive lymphocytes can treat autoimmune disease. Interference with co-stimulatory pathways for the activation of lymphocytes could be a treatment for autoimmune disease. Induction of regulatory T cells by antibody therapy can inhibit autoimmune disease. A number of commonly used drugs have	662 664 666 668	Chap Evolu 16-1 16-2	ter 16 Evolution of the Immune System tion of the innate immune system. The evolution of the immune system can be studied by comparing the genes expressed by different species. Antimicrobial peptides are likely to be the most ancient immune defenses.	712 712

16-5	A second recognition system in <i>Drosophila</i> homologous to		Isolati	on of lymphocytes.	758
	the mammalian TNF receptor pathway provides protection from Gram-negative bacteria.	717	A-20	Isolation of peripheral blood lymphocytes by Ficoll-Hypaque™ gradient.	758
16-6	An ancestral complement system opsonizes pathogens for uptake by phagocytic cells.	717	A-21	Isolation of lymphocytes from tissues other than blood.	758
16-7	The lectin pathway of complement activation evolved in		A-22	Flow cytometry and FACS analysis.	759
	invertebrates.	719 720	A-23	Lymphocyte isolation using antibody-coated magnetic beads.	761
Summa		120	A-24	Isolation of homogeneous T-cell lines.	761
Evolu	tion of the adaptive immune response.	720	Chara	cterization of lymphocyte specificity, frequency,	
16-8	Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes.	721		inction.	762
16-9	Agnathans possess an adaptive immune system that uses		A-25	Limiting-dilution culture.	763
	somatic gene rearrangement to diversify receptors built from LRR domains.	722	A-26	ELISPOT assays.	763
16 10	Adaptive immunity based on a diversified repertoire of	122	A-27	Identification of functional subsets of T cells by staining for cytokines.	764
16-10	immunoglobulin-like genes appeared abruptly in the cartilaginous fish.	724	A-28	Identification of T-cell receptor specificity using MHC: peptide tetramers.	765
16-11	The target of the transposon is likely to have been a gene encoding a cell-surface receptor containing an		A-29	Assessing the diversity of the T-cell repertoire by 'spectratyping.'	766
16-12	immunoglobulin-like V domain. Different species generate immunoglobulin diversity in	725	A-30	Biosensor assays for measuring the rates of association and disassociation of antigen receptors for their ligands.	767
.0	different ways.	726	A-31	Stimulation of lymphocyte proliferation by treatment with	101
16-13	Both α:β and γ:δ T-cell receptors are present in	727		polyclonal mitogens or specific antigen.	769
10 14	cartilaginous fish. MHC class I and class II molecules are also first found	121	A-32	Measurements of apoptosis by the TUNEL assay.	770
16-14	in the cartilaginous fishes.	728	A-33	Assays for cytotoxic T cells.	770
Summ	_	729	A-34	Assays for CD4 T cells.	770
	ary to Chapter 16.	729	A-35	DNA microarrays.	772
			Detec	tion of immunity <i>in vivo</i> .	772
Appe	endix I Immunologists'Toolbox	735	A-36	Assessment of protective immunity.	772
• • •			A-37	Transfer of protective immunity.	773
	nization.	735	A-38	The tuberculin test.	774
A-1	Haptens.	736	A-39	Testing for allergic responses.	774
A-2	Routes of immunization.	738	A-40	Assessment of immune responses and immunological	
A-3	Effects of antigen dose.	738		competence in humans.	775
A-4	Adjuvants.	738	A-41	The Arthus reaction.	776
	etection, measurement, and characterization of	740	Manip	oulation of the immune system.	777
	odies and their use as research and diagnostic tools.		A-42	Adoptive transfer of lymphocytes.	777
A-5	Affinity chromatography.	741	A-43	Hematopoietic stem-cell transfers.	777
A-6	Radioimmunoassay (RIA), enzyme-linked immunosorbent	741	A-44	In vivo depletion of T cells.	777
۸ 7	assay (ELISA), and competitive inhibition assay.	743	A-45	In vivo depletion of B cells.	778
A-7 A-8	Hemagglutination and blood typing. Precipitin reaction.	743 744	A-46	Transgenic mice.	778
A-9	Equilibrium dialysis: measurement of antibody affinity and avidity.	745	A-47	Gene knockout by targeted disruption.	779
A-10	Anti-immunoglobulin antibodies.	746		All HOD Anthrone	700
A-11	Coombs tests and the detection of Rhesus incompatibility.	747	Appe	ndix II CD Antigens	783
A-12	Monoclonal antibodies.	749	Appe	ndix III Cytokines and their receptors	799
A-13	Phage display libraries for antibody V-region production.	750	Anne	ndix IV Chemokines and their receptors	802
A-14	Immunofluorescence microscopy.	751	• • •	·	
A-15	Immunoelectron microscopy.	753	Appe	ndix V Immunological constants	804
A-16 A-17	Immunohistochemistry. Immunoprecipitation and co-immunoprecipitation.	753 754	Biogr	aphies	805
A-18	Immunoprecipitation and communoprecipitation. Immunoblotting (Western blotting).	755	Gloss	eary	806
A-19	Use of antibodies in the isolation and identification of genes and their products.	756	Index	•	835
	genes and their products.	750	HIGGA		503