# **Detailed Contents**

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

Chapte	er 1 Basic Concepts in Immunology	(1ini
The orig	gins of vertebrate immune cells.	2
Princip	les of innate immunity.	3
1-	Commensal organisms cause little host damage while pathogens damage host tissues by a variety of mechanisms.	3
1-2	Anatomic and chemical barriers are the first defense against pathogens.	5
1-3	The immune system is activated by inflammatory inducers that indicate the presence of pathogens or tissue damage.	6
1-4	The myeloid lineage comprises most of the cells of the innate immune system.	7
1-5	Sensor cells express pattern recognition receptors that provide an initial discrimination between self and nonself.	8
1-6	Sensor cells induce an inflammatory response by producing mediators such as chemokines and cytokines.	9
1-7	Innate lymphocytes and natural killer cells are effector cells that share similarities with lymphoid lineages of the adaptive immune system	11
Summa	y.	11
Princip	les of adaptive immunity.	11
1-8	The interaction of antigens with antigen receptors induces lymphocytes to acquire effector and memory activity.	12
1-9	Antibodies and T-cell receptors are composed of constant and variable regions that provide distinct functions.	13
1-10	Antibodies and T-cell receptors recognize antigens by fundamentally different mechanisms.	14
1-11	Antigen-receptor genes are assembled by somatic gene rearrangements of incomplete receptor gene segments.	15
1-12	Lymphocytes activated by antigen give rise to clones of antigen-specific effector cells that mediate adaptive immunity	15
1-13	Lymphocytes with self-reactive receptors are normally eliminated during development or are	10
1-14	Lymphocytes mature in the bone marrow or the thymus and then congregate in lymphoid tissues	10
1-15	throughout the body. Adaptive immune responses are initiated by antigen and antigen-presenting cells in	17
1-16	secondary lymphoid tissues.	18
	antigen in the peripheral lymphoid organs.	19
1-17	Mucosal surfaces have specialized immune	

structures that orchestrate responses to environmental microbial encounters.

22

1-18	Lymphocytes activated by antigen proliferate in	
	effector cells and immunological memory.	23
Summa	ary. In the encodes R beaubol and The Chelqu	24
The ef	fector mechanisms of immunity.	25
1-19	Innate immune responses can select from	
	different types of pathogens.	26
1-20	Antibodies protect against extracellular pathogens and their toxic products.	27
1-21	T cells orchestrate cell-mediated immunity and regulate B-cell responses to most antigens.	29
1-22	Inherited and acquired defects in the immune system result in increased susceptibility to infection.	31
1-23	Understanding adaptive immune responses is important for the control of allergies, autoimmune disease, and the rejection of transplanted organs.	32
1-24	Vaccination is the most effective means of controlling infectious diseases.	33
Summa	ary.	34
Summa	ary to Chapter 1.	34
Questio	ons. Consideration of the second of the second	35
Referen	nces.	36
Chapt	ter 2 Innate Immunity: The First Lines	
AND	of Defense	37
Anator	mic barriers and initial chemical defenses.	38
2-1	Infectious diseases are caused by diverse living agents that replicate in their hosts.	38
2-2	Epithelial surfaces of the body provide the first barrier against infection.	42
2-3	Infectious agents must overcome innate host defenses to establish a focus of infection.	44
2-4	Epithelial cells and phagocytes produce	45
Summa	ary.	48
The co	omplement system and innate immunity.	49
2-5	The complement system recognizes features of microbial surfaces and marks them for	
2-6	destruction by coating them with C3b. The lectin pathway uses soluble receptors that	50
	recognize microbial surfaces to activate the complement cascade.	53
2-7	The classical pathway is initiated by activation of the C1 complex and is homologous to the lectin pathway.	56
2-8	Complement activation is largely confined to the surface on which it is initiated.	57
2-9	The alternative pathway is an amplification loop for C3b formation that is accelerated by properdin in the presence of pathogens.	58
2-10	Membrane and plasma proteins that regulate the formation and stability of C3 convertases	
	determine the extent of complement activation.	60

2-11	Complement developed early in the evolution of multicellular organisms.	61
2-12	Surface-bound C3 convertase deposits large numbers of C3b fragments on pathogen surfaces	
2-13	Ingestion of complement-tagged pathogens by	62
	phagocytes is mediated by receptors for the bound complement proteins.	63
2-14	The small fragments of some complement proteins initiate a local inflammatory response.	65
2-15	The terminal complement proteins polymerize to form pores in membranes that can kill certain pathogens	66
2-16	Complement control proteins regulate all three pathways of complement activation and protect the host from their destructive effects.	67
2-17	Pathogens produce several types of proteins that can inhibit complement activation.	71
Summ	ary.	72
Summ	ary to Chapter 2.	73
Questi	ons.	74
Refere	nces.	75
Chap	ter 3 The Induced Responses of	
	Innate Immunity	77
Patter	n recognition by cells of the innate	77
3-1	After entering tissues, many microbes are	
	recognized, ingested, and killed by phagocytes.	78
3-2	G-protein-coupled receptors on phagocytes link	
	intracellular killing.	81
3-3	Microbial recognition and tissue damage initiate an	0.
2.4	inflammatory response.	85
3-4	recognition system.	87
3-5	Mammalian Toll-like receptors are activated by	
	many different pathogen-associated molecular patterns.	88
3-6	TLR-4 recognizes bacterial lipopolysaccharide in	
	association with the host accessory proteins MD-2 and CD14.	92
3-7	TLRs activate NF $\kappa$ B, AP-1, and IRF transcription	
	factors to induce the expression of inflammatory cytokines and type I interferons.	92
3-8	The NOD-like receptors are intracellular sensors of bacterial infection and cellular damage.	96
3-9	NLRP proteins react to infection or cellular damage through an inflammasome to induce	
	cell death and inflammation.	98
3-10	The RIG-I-like receptors detect cytoplasmic viral RNAs and activate MAVS to induce type I interferon	
	production and pro-inflammatory cytokines.	101
3-11	Cytosolic DNA sensors signal through STING to induce production of type I interferons.	103
3-12	Activation of innate sensors in macrophages and	qang
	dendritic cells triggers changes in gene expression	
	that have far-reaching effects on the	104
3-12	Toll signaling in Drasonhile is downstream of a	104
0-10	distinct set of pathogen-recognition molecules.	105

	diversification in both invertebrates and some	100
•	primitive chordates.	106
Summ	ary.	106
Induc	ed innate responses to infection.	107
3-15	Cytokines and their receptors fall into distinct families of structurally related proteins.	107
3-16	Cytokine receptors of the hematopoietin family are associated with the JAK family of tyrosine kinases, which activate STAT transcription factors.	109
3-17	Chemokines released by macrophages and dendritic cells recruit effector cells to sites of infection.	111
3-18	Cell-adhesion molecules control interactions between leukocytes and endothelial cells	110
0.10	during an inflammatory response.	113
3-19	cross the blood vessel wall to enter an inflamed	116
3-20	TNF- $\alpha$ is an important cytokine that triggers local containment of infection but induces	267
	shock when released systemically.	118
3-21	Cytokines made by macrophages and dendritic cells induce a systemic reaction known as the acute-phase response.	118
3-22	Interferons induced by viral infection make several contributions to host defense.	121
3-23	Several types of innate lymphoid cells provide protection in early infection.	124
3-24	NK cells are activated by type I interferon and macrophage-derived cytokines.	125
3-25	NK cells express activating and inhibitory receptors to distinguish between healthy and	4-17
	infected cells.	126
3-26	NK-cell receptors belong to several structural families, the KIRs, KLRs, and NCRs.	128
3-27	NK cells express activating receptors that recognize ligands induced on infected cells	
	or tumor cells.	130
Summ	ary.	131
Summ	ary to Chapter 3.	131
Questi	ons.	132
Refere	nces	133

3-14 TLR and NOD genes have undergone extensive

### PART II THE RECOGNITION OF ANTIGEN

Chap	oter 4 Antigen Recognition by B-cell and T-cell Receptors	139
The s	tructure of a typical antibody molecule.	140
4-1	IgG antibodies consist of four polypeptide chains.	141
4-2	Immunoglobulin heavy and light chains are composed of constant and variable regions.	142
4-3	The domains of an immunoglobulin molecule have similar structures.	142
4-4	The antibody molecule can readily be cleaved into functionally distinct fragments.	144
4-5	The hinge region of the immunoglobulin molecule allows flexibility in binding to	
	multiple antigens.	145
Summ	nary.	145

The interaction of the antibody molecule with specific		146
4-6	Localized regions of hypervariable sequence	140
	form the antigen-binding site.	146
4-7	Antibodies bind antigens via contacts in CDRs that are complementary to the size and shape of the antigen.	147
4-8	Antibodies bind to conformational shapes on	
	the surfaces of antigens using a variety of noncovalent forces.	148
4-9	Antibody interaction with intact antigens is influenced by steric constraints.	150
4-10	Some species generate antibodies with alternative structures.	151
Summ	ary.	152
Antige	en recognition by T cells.	152
4-11	The TCR $\alpha$ : $\beta$ heterodimer is very similar to a Fab fragment of immunoglobulin.	153
4-12	A T-cell receptor recognizes antigen in the form of a complex of a foreign peptide bound to an MHC molecule.	155
4-13	There are two classes of MHC molecules with	
	distinct subunit compositions but similar three- dimensional structures.	155
4-14	Peptides are stably bound to MHC molecules, and	
	also serve to stabilize the MHC molecule on the cell surface.	158
4-15	MHC class I molecules bind short peptides of 8–10 amino acids by both ends.	158
4-16	The length of the peptides bound by MHC class II molecules is not constrained.	160
4-17	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.	161
4-18	The CD4 and CD8 cell-surface proteins of T cells directly contact MHC molecules and are required to make an effective response to antigen	162
4-19	The two classes of MHC molecules are expressed	105
4-20	A distinct subset of T cells bears an alternative	100
Summ	receptor made up of $\gamma$ and $\delta$ chains.	167
Summ	ary to Chapter 4	168
Questi	ons.	169
Refere	nces.	170
Chap	ter 5 The Generation of Lymphocyte	170
	Antigen Receptors	173
Prima	ry immunoglobulin gene rearrangement.	174
5-1	progenitors of antibody-producing cells.	174
5-2	Complete genes that encode a variable region are generated by the somatic recombination of separate gene segments.	175
5-3	Multiple contiguous V gene segments are present at each immunoglobulin locus.	176
5-4	Rearrangement of V, D, and J gene segments is guided by flanking DNA sequences.	178
5-5	The reaction that recombines V, D, and J gene	
	segments involves both lymphocyte-specific and ubiquitous DNA-modifying enzymes.	179

	The diversity of the immunoglobulin repertoire is generated by four main processes.	184
5-7	The multiple inherited gene segments are used in different combinations.	184
5-8	Variable addition and subtraction of nucleotides at the junctions between gene segments contributes to the diversity of the third hypervariable region.	185
Summa	ary.	186
T-cell I	receptor gene rearrangement.	187
5-9	The T-cell receptor gene segments are arranged in	
	a similar pattern to immunoglobulin gene segments and are rearranged by the same enzymes.	187
5-10	T-cell receptors concentrate diversity in the third hypervariable region.	189
5-11	$\gamma$ : $\delta$ T-cell receptors are also generated by gene rearrangement.	190
Summa	ary.	191
Struct	ural variation in immunoglobulin constant	
region	S.	191
5-12	Different classes of immunoglobulins are	
	distinguished by the structure of their heavy-	102
5 10	chain constant regions.	192
0-13	specialization on the antibody.	193
5-14	IgM and IgD are derived from the same pre-mRNA	
	transcript and are both expressed on the surface of	Patter
Super	mature B cells.	194
5-15	Transmembrane and secreted forms of immuno-	
	mRNA transcripts.	195
5-16	IgM and IgA can form polymers by interacting with	
	the J chain.	197
Summ	the J chain. ary.	197 198
Summ	the J chain. ary.	197 198 198
Summ Evolut 5-17	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity	197 198 198
Summ Evolut 5-17	the J chain. ary. tion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes.	197 198 <b>198</b> 198
Summ Evolut 5-17 5-18	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains.	197 198 <b>198</b> 198 200
Summ Evolut 5-17 5-18 5-19	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a	197 198 <b>198</b> 198 200
Summ. Evolut 5-17 5-18 5-19	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunoglobulin-like genes	197 198 198 198 200
Summ. Evolut 5-17 5-18 5-19	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes.	197 198 198 198 200 202
Summ. Evolut 5-17 5-18 5-19 5-20	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways.	197 198 198 198 200 202 202 203
Summ: Evolut 5-17 5-18 5-19 5-20 5-21	<ul> <li>the J chain.</li> <li>ary.</li> <li>ion of the adaptive immune response.</li> <li>Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes.</li> <li>Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains.</li> <li>RAG-dependent adaptive immunoglobulin-like genes appeared abruptly in the cartilaginous fishes.</li> <li>Different species generate immunoglobulin diversity in different ways.</li> <li>Both α:β and γ:δ T-cell receptors are present in</li> </ul>	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> </ol>
Summ. Evolut 5-17 5-18 5-19 5-20 5-21	the J chain. ary. <b>ion of the adaptive immune response.</b> Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha:\beta$ and $\gamma:\delta$ T-cell receptors are present in cartilaginous fishes.	197 198 198 200 202 203 206
Summ. Evolut 5-17 5-18 5-19 5-20 5-21 5-22	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha:\beta$ and $\gamma:\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes.	197 198 198 200 202 203 206 206
Summ. Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ	the J chain. ary. <b>ion of the adaptive immune response.</b> Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha$ : $\beta$ and $\gamma$ : $\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary.	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>206</li> <li>207</li> </ol>
Summ: Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ	the J chain. ary. <b>ion of the adaptive immune response.</b> Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha$ : $\beta$ and $\gamma$ : $\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5.	<ul> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>207</li> </ul>
Summ. Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha:\beta$ and $\gamma:\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons.	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>207</li> <li>208</li> </ol>
Summ. Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere	the J chain. ary. <b>ion of the adaptive immune response.</b> Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha$ : $\beta$ and $\gamma$ : $\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces.	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>208</li> <li>209</li> </ol>
Summ Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere Chap	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha:\beta$ and $\gamma:\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces. ter 6 Antigen Presentation to	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>208</li> <li>209</li> </ol>
Summ. Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere Chap	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both $\alpha:\beta$ and $\gamma:\delta$ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces. ter 6 Antigen Presentation to T Lymphocytes	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>208</li> <li>209</li> <li>213</li> </ol>
Summ Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere Chap	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both α:β and γ:δ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces. ter 6 Antigen Presentation to T Lymphocytes eneration of α:β T-cell receptor ligands.	197 198 198 200 202 203 206 206 207 207 208 209 213 214
Summ Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere Chap The g 6-1	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both α:β and γ:δ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces. ter 6 Antigen Presentation to T Lymphocytes eneration of α:β T-cell receptor ligands. Antigen presentation functions both in arming	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>208</li> <li>209</li> <li>213</li> <li>214</li> </ol>
Summ Evolut 5-17 5-18 5-19 5-20 5-21 5-22 Summ Summ Questi Refere Chap The g 6-1	the J chain. ary. ion of the adaptive immune response. Some invertebrates generate extensive diversity in a repertoire of immunoglobulin-like genes. Agnathans possess an adaptive immune system that uses somatic gene rearrangement to diversify receptors built from LRR domains. RAG-dependent adaptive immunity based on a diversified repertoire of immunoglobulin-like genes appeared abruptly in the cartilaginous fishes. Different species generate immunoglobulin diversity in different ways. Both α:β and γ:δ T-cell receptors are present in cartilaginous fishes. MHC class I and class II molecules are also first found in the cartilaginous fishes. ary. ary to Chapter 5. ons. nces. ter 6 Antigen Presentation to T Lymphocytes eneration of α:β T-cell receptor ligands. Antigen presentation functions both in arming effector T cells and in triggering their effector	<ol> <li>197</li> <li>198</li> <li>198</li> <li>200</li> <li>202</li> <li>203</li> <li>206</li> <li>207</li> <li>208</li> <li>209</li> <li>213</li> <li>214</li> </ol>

6-2	Peptides are generated from ubiquitinated proteins in the cytosol by the proteasome.	216
6-3	Peptides from the cytosol are transported by TAP into the endoplasmic reticulum and further processed before binding to MHC class I molecules	218
6-4	Newly synthesized MHC class I molecules are retained in the endoplasmic reticulum until they	210
	bind a peptide.	219
6-5	Dendritic cells use cross-presentation to present exogenous proteins on MHC class I molecules to prime CD8 T cells.	222
6-6	Peptide:MHC class II complexes are generated in acidified endocytic vesicles from proteins obtained through endocytosis, phagocytosis, and autophagy.	223
6-7	The invariant chain directs newly synthesized MHC class II molecules to acidified intracellular vesicles.	225
6-8	The MHC class II-like molecules HLA-DM and HLA-DO regulate exchange of CLIP for other	
	peptides.	226
6-9	Cessation of antigen processing occurs in dendritic cells after their activation through reduced	
0	expression of the MARCH-1 E3 ligase.	229
Summa	iry.	230
The m	ajor histocompatibility complex and its function.	231
6-10	Many proteins involved in antigen processing and presentation are encoded by genes within the MHC.	231
6-11	The protein products of MHC class I and class II genes are highly polymorphic.	234
6-12	MHC polymorphism affects antigen recognition by T cells by influencing both peptide binding and the contacts between T-cell receptor and MHC molecule.	235
6-13	Alloreactive T cells recognizing nonself MHC molecules are very abundant.	239
6-14	Many T cells respond to superantigens.	240
6-15	MHC polymorphism extends the range of antigens to which the immune system can respond.	241
Summa	ıry.	242
Gener	ation of ligands for unconventional	
T-cell s	ubsets.	242
6-16	A variety of genes with specialized functions in	18010
	immunity are also encoded in the MHC.	243
6-17	Specialized MHC class I molecules act as ligands for the activation and inhibition of NK cells and	0.45
6-18	Members of the CD1 family of MHC class I-like	245
	NKT cells.	246
6-19	The nonclassical MHC class I molecule MR1 presents microbial folate metabolites to MAIT cells.	248
6-20	$\gamma{:}\delta$ T cells can recognize a variety of diverse ligands.	249
Summa	ry.	250
Summa	ry to Chapter 6.	250
Questio	ns.	251
Referen	ces.	252
PART LYMF	III THE DEVELOPMENT OF MATURE HOCYTE RECEPTOR REPERTOIRES	

Chapter 7 Lymphocyte Receptor Signaling	257
General principles of signal transduction and	
propagation.	257

7-1	Transmembrane receptors convert extracellular signals into intracellular biochemical events.	258
7-2	Intracellular signal propagation is mediated by large multiprotein signaling complexes.	260
7-3	Small G proteins act as molecular switches in many different signaling pathways.	262
7-4	Signaling proteins are recruited to the membrane by a variety of mechanisms.	262
7-5	Post-translational modifications of proteins can both activate and inhibit signaling responses.	263
7-6	The activation of some receptors generates small- molecule second messengers.	264
Summa	ary.	265
Antige 7-7	n receptor signaling and lymphocyte activation. Antigen receptors consist of variable antigen-binding chains associated with invariant chains that carry out the signaling function of the receptor.	265 266
7-8	Antigen recognition by the T-cell receptor and its co-receptors transduces a signal across the plasma membrane to initiate signaling.	267
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.	268
7-10	Phosphorylated ITAMs recruit and activate the tyrosine kinase ZAP-70.	270
7-11	ITAMs are also found in other receptors on leukocytes that signal for cell activation.	270
7-12	Activated ZAP-70 phosphorylates scaffold proteins and promotes PI 3-kinase activation.	271
7-13	Activated PLC- $\gamma$ generates the second messengers diacylglycerol and inositol trisphosphate that lead to transcription factor activation.	272
7-14	Ca <sup>2+</sup> entry activates the transcription factor NFAT.	273
7-15	Ras activation stimulates the mitogen-activated protein kinase (MAPK) relay and induces expression	074
7-16	Protein kinase C activates the transcription factors	274
7-17	PI 3-kinase activation upregulates cellular metabolic pathways via the serine/threonine kinase Akt.	277
7-18	T-cell receptor signaling leads to enhanced integrin- mediated cell adhesion.	278
7-19	T-cell receptor signaling induces cytoskeletal reorganization by activating the small GTPase Cdc42.	279
7-20	The logic of B-cell receptor signaling is similar to that of T-cell receptor signaling, but some of the signaling	
Summa	components are specific to B cells. ary.	279 282
Co-sti	mulatory and inhibitory receptors modulate	
antiger	n receptor signaling in T and B lymphocytes.	282
19980	co-stimulatory signaling receptor for naive T-cell activation.	283
7-22	Maximal activation of PLC- $\gamma$ , which is important for transcription factor activation, requires a	001
7-00	TNE receptor superfamily members successful T	284
1-23	and B-cell activation.	284

7-24	Inhibitory receptors on lymphocytes downregulate immune responses by interfering with co-stimulatory signaling pathways.	286
7-25	Inhibitory receptors on lymphocytes downregulate immune responses by recruiting protein or lipid	
	phosphatases.	287
Summa	ary.	288
Summa	ary to Chapter 7.	289
Questic	ons.	290
Referen	ices.	291
Chapt	ter 8 The Development of B and	295
Dovolo	amont of B lymphocytos	206
8-1	Lymphocytes derive from hematopoietic stem cells in the bone marrow.	297
8-2	B-cell development begins by rearrangement of the heavy-chain locus.	299
8-3	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	155
8-4	cell stage. Pre-B-cell receptor signaling inhibits further	302
	heavy-chain locus rearrangement and enforces allelic exclusion.	303
8-5	Pre-B cells rearrange the light-chain locus and express cell-surface immunoglobulin.	304
8-6	Immature B cells are tested for autoreactivity before they leave the bone marrow.	305
8-7	Lymphocytes that encounter sufficient quantities of self antigens for the first time in the periphery are eliminated or inactivated.	308
8-8	Immature 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.	309
8-9	B-1 B cells are an innate lymphocyte subset that arises early in development.	312
Summa	iry.	313
Develo	prent of T lymphocytes	315
8-10	T-cell progenitors originate in the bone marrow, but all the important events in their development	010
8-11	occur in the thymus. Commitment to the T-cell lineage occurs in the	315
8-12	thymus following Notch signaling. T-cell precursors proliferate extensively in the	317
8-13	thymus, but most die there. Successive stages in the development of	317
	thymocytes are marked by changes in cell-surface molecules.	319
8-14	Thymocytes at different developmental stages are found in distinct parts of the thymus.	321
8-15	T cells with $\alpha{:}\beta$ or $\gamma{:}\delta$ receptors arise from a common progenitor.	322
8-16	T cells expressing $\gamma$ : $\delta$ T-cell receptors arise in two distinct phases during development.	322
8-17	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.	324

8-18	T-cell $\alpha$ -chain genes undergo successive rearrangements until positive selection or cell death intervenes.	326
Summ	ary.	328
Positiv	ve and negative selection of T cells.	328
8-19	Only thymocytes whose receptors interact with self peptide:self MHC complexes can survive and mature.	328
8-20	Positive selection acts on a repertoire of T-cell receptors with inherent specificity for MHC molecules.	329
8-21	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.	330
8-22	Thymic cortical epithelial cells mediate positive selection of developing thymocytes.	331
8-23	T cells that react strongly with ubiquitous self antigens are deleted in the thymus.	332
8-24	Negative selection is driven most efficiently by bone marrow-derived antigen-presenting cells.	334
8-25	The specificity and/or the strength of signals for negative and positive selection must differ.	334
8-26	Self-recognizing regulatory T cells and innate T cells develop in the thymus.	335
8-27	The final stage of T-cell maturation occurs in the thymic medulla.	336
8-28	T cells that encounter sufficient quantities of self antigens for the first time in the periphery are	
	eliminated or inactivated.	336
Summa	ary.	337
Summa	ary to Chapter 8.	337
Questio	ons.	339
Referen	nces.	340

#### PART IV THE ADAPTIVE IMMUNE RESPONSE

Chapter 9 T-cell-Mediated Immunity

Develo organs	opment and function of secondary lymphoid s – sites for the initiation of adaptive immune	
respor	ISES.	347
9-1	T and B lymphocytes are found in distinct locations in secondary lymphoid tissues.	347
9-2	The development of secondary lymphoid tissues is controlled by lymphoid tissue inducer cells and proteins of the tumor necrosis factor family.	349
9-3	T and B cells are partitioned into distinct regions of secondary lymphoid tissues by the actions of chemokines.	350
9-4	Naive T cells migrate through secondary lymphoid tissues, sampling peptide:MHC complexes on dendritic cells.	35
9-5	Lymphocyte entry into lymphoid tissues depends on chemokines and adhesion molecules.	352
9-6	Activation of integrins by chemokines is responsible for the entry of naive T cells into lymph nodes.	353
9-7	The exit of T cells from lymph nodes is controlled by a chemotactic lipid.	355
9-8	T-cell responses are initiated in secondary lymphoid organs by activated dendritic cells.	356
9-9	Dendritic cells process antigens from a wide array	358

9-10	Microbe-induced TLR signaling in tissue-resident dendritic cells induces their migration to lymphoid organs and enhances antigen processing.	361
9-11	Plasmacytoid dendritic cells produce abundant type I interferons and may act as helper cells for antigen presentation by conventional dendritic cells.	363
9-12	Macrophages are scavenger cells that can be induced by pathogens to present foreign antigens to naive	
0.10	T cells.	363
9-13	that bind to their surface immunoglobulin.	364
Summa	ary.	500
Primin	g of naive I cells by pathogen-activated	366
9-14	Cell-adhesion molecules mediate the initial	
12743	interaction of naive T cells with antigen- presenting cells.	367
9-15	Antigen-presenting cells deliver multiple signals for	
	T cells.	368
9-16	CD28-dependent co-stimulation of activated T cells	
	induces expression of interleukin-2 and the	368
0.17	Additional co-stimulatory pathways are involved in	500
9-17	T-cell activation.	369
9-18	Proliferating T cells differentiate into effector T cells that do not require co-stimulation to act.	370
9-19	CD8 T cells can be activated in different ways to become cytotoxic effector cells.	372
9-20	CD4 T cells differentiate into several subsets of functionally different effector cells.	372
9-21	Cytokines induce the differentiation of naive CD4 T cells down distinct effector pathways.	375
9-22	CD4 T-cell subsets can cross-regulate each other's differentiation through the cytokines they produce.	377
9-23	Regulatory CD4 T cells are involved in controlling adaptive immune responses.	379
Summ	ary.	380
Gener their c	al properties of effector T cells and	380
9-24	Effector T-cell interactions with target cells are	
	initiated by antigen-nonspecific cell-adhesion	381
0-25	An immunological synapse forms between effector	001
5 25	T cells and their targets to regulate signaling and to direct the release of effector molecules.	381
9-26	The effector functions of T cells are determined by	9000
	the array of effector molecules that they produce.	383
9-27	Cytokines can act locally or at a distance.	383
9-28	T cells express several TNF-family cytokines as trimeric proteins that are usually associated with the cell surface	386
Summ	ary.	386
T-coll	-mediated cytotoxicity	387
9-29	Cytotoxic T cells induce target cells to undergo programmed cell death via extrinsic and intrinsic	207
9-30	The intrinsic pathway of apoptosis is mediated by	007
0.01	the release of cytochrome c from mitochondria.	389
9-31	contained in the granules of CD8 cytotoxic T cells.	390

9-32	Cytotoxic T cells are selective serial killers of targets expressing a specific antigen.	391	
9-33	Cytotoxic T cells also act by releasing cytokines.	392	
Summa	ry.	392	
Summary to Chapter 9.			
Questic	ns. mot sevelation sourced to levotter of aluditinos?	393	
Referen	Ces.	395	
Chapt	er 10 The Humoral Immune Response	399	
B-cell	activation by antigen and helper T cells.	400	
10-1	Activation of B cells by antigen involves signals from the B-cell receptor and either $T_{FH}$ cells or microbial antigens.	400	
10-2	Linked recognition of antigen by T cells and B cells promotes robust antibody responses.	402	
10-3	B cells that encounter their antigens migrate toward		
	the boundaries between B-cell and T-cell areas in	403	
10-4	T cells express surface molecules and cytokines that	100	
	development.	406	
10-5	Activated B cells differentiate into antibody-secreting plasmablasts and plasma cells.	406	
10-6	The second phase of a primary B-cell immune		
	response occurs when activated B cells migrate into follicles and proliferate to form germinal centers.	408	
10-7	Germinal center B cells undergo V-region somatic	n ein n	
10 1	hypermutation, and cells with mutations that improve affinity for antigen are selected.	410	
10-8	Positive selection of germinal center B cells involves contact with $\rm T_{FH}$ cells and CD40 signaling.	412	
10-9	Activation-induced cytidine deaminase (AID) introduces mutations into genes transcribed	10980	
	in B cells.	413	
10-10	Mismatch and base-excision repair pathways contribute to somatic hypermutation following initiation by AID	414	
10-11	AID initiates class switching to allow the same		
10 11	assembled $V_{H}$ exon to be associated with different		
	$C_H$ genes in the course of an immune response.	415	
10-12	Cytokines made by T <sub>FH</sub> cells direct the choice of isotype for class switching in T-dependent antibody	/19	
10.10	responses.	410	
10-13	eventually differentiate into either plasma cells or memory cells	419	
10-14	Some antigens do not require T-cell help to induce		
	B-cell responses.	419	
Summ	ary.	421	
The d	istributions and functions of immunoglobulin	422	
10-15	Antibodies of different classes operate in distinct places and have distinct effector functions.	423	
10-16	Polymeric immunoglobulin receptor binds to the Fc regions of IgA and IgM and transports them	577	
18340	across epithelial barriers.	425	
10-17	The neonatal Fc receptor carries IgG across the placenta and prevents IgG excretion from the body.	426	

10-18	High-affinity IgG and IgA antibodies can neutralize toxins and block the infectivity of viruses and bacteria.
10-19	Antibody:antigen complexes activate the classical pathway of complement by binding to C1g.
10-20	Complement receptors and Fc receptors both contribute to removal of immune complexes from the circulation.
Summ	ary.
The d	estruction of antibody-coated pathogens
via Fc	receptors.
10-21	The Fc receptors of accessory cells are signaling receptors specific for immunoglobulins of different classes.
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.
10-23	Fc receptors activate NK cells to destroy antibody-coated targets.
10-24	Mast cells and basophils bind IgE antibody via the high-affinity $Fc\epsilon$ receptor.
10-25	IgE-mediated activation of accessory cells has an important role in resistance to parasite infection.
Summ	ary.
Summ	ary to Chapter 10.
Questi	ons.
Refere	nces.
0	
Chap	ter II Integrated Dynamics of
STA	ation of inside and Adaptive initiality
respon	alion of innate and adaptive immunity in
11-1	The course of an infection can be divided into several distinct phases.
11-2	The effector mechanisms that are recruited to clear an infection depend on the infectious agent.
Summ	ary.
Effect	or T cells augment the effector functions of
innate	immune cells.
11-3	Effector T cells are guided to specific tissues and sites of infection by changes in their expression of
	adhesion molecules and chemokine receptors.

- anges in their expression of d chemokine receptors. 453 11-4 Pathogen-specific effector T cells are enriched at sites of infection as adaptive immunity progresses. 457 11-5 T<sub>H</sub>1 cells coordinate and amplify the host response to intracellular pathogens through classical activation of macrophages. 458 Activation of macrophages by T<sub>H</sub>1 cells must be 11-6 tightly regulated to avoid tissue damage. 460 11-7 Chronic activation of macrophages by T<sub>H</sub>1 cells mediates the formation of granulomas to contain intracellular pathogens that cannot be cleared. 461 11-8 Defects in type 1 immunity reveal its important role in the elimination of intracellular pathogens. 461 T<sub>H</sub>2 cells coordinate type 2 responses to expel 11-9 intestinal helminths and repair tissue injury. 462
- 11-10 T<sub>H</sub>17 cells coordinate type 3 responses to enhance the clearance of extracellular bacteria and fungi.

11-11	to signals as they carry out their effector functions.	46
11-12	Effector T cells can be activated to release	
Roeth	cytokines independently of antigen recognition.	46
11-13	Effector T cells demonstrate plasticity and cooperativity that enable adaptation during	
	anti-pathogen responses.	46
11-14	Integration of cell- and antibody-mediated	
	immunity is critical for protection against many	10
11-15	Primary CD8 T-cell responses to pathogens can	40
11 10	occur in the absence of CD4 T-cell help.	47
11-16	Resolution of an infection is accompanied by the	
	death of most of the effector cells and the generation of memory cells	4
Summa	arv.	4
Immu		1-
11-17	Immunological memory is long lived after infection	41
368	or vaccination.	4
11-18	Memory B-cell responses are more rapid and have	
	higher affinity for antigen compared with responses of naive B cells	4
11-19	Memory B cells can reenter germinal centers and	7
	undergo additional somatic hypermutation and	
	affinity maturation during secondary immune	1
11-20	MHC tetramers identify memory T cells that persist	-
-	at an increased frequency relative to their frequency	
Summ	as naive T cells.	4
11-21	Memory T cells arise from effector T cells that	4
11-22	Memory T cells are heterogeneous and include	-
	central memory, effector memory, and tissue-	
	resident subsets.	4
11-23	CD4 T-cell help is required for CD8 T-cell memory and involves CD40 and II -2 signaling	4
11-24	In immune individuals, secondary and subsequent	usinin
	responses are mainly attributable to memory	nera
	lymphocytes.	4
Summa	ary.	4
Summa	ary to Chapter 11.	4
Questio	ons.	4
Refere	nces.	4
Chap	ter 12 The Mucosal Immune System	49
The na	ature and structure of the mucosal	
immur	ne system. Honstalb of the discontration of the sension of	4
12-1	The mucosal immune system protects the internal surfaces of the body	1
12-2	Cells of the mucosal immune system are located	4
386	both in anatomically defined compartments and	
1	scattered throughout mucosal tissues.	4
12-3	The intestine has distinctive routes and mechanisms of antigen uptake	4
12-4	The mucosal immune system contains large	4
387	numbers of effector lymphocytes even in the	3
10.5	absence of disease.	5
12-5	The circulation of lymphocytes within the mucosal immune system is controlled by tissue-specific	
	adhesion molecules and chemokine receptors.	5

426

429

430 431

432

432

433

435

436

445

446

446

449 452

452

465

12-6	Priming of lymphocytes in one mucosal tissue may induce protective immunity at other mucosal surfaces.	502	
12-7	Distinct populations of dendritic cells control mucosal immune responses.	503	
12-8	Macrophages and dendritic cells have different roles in mucosal immune responses.	505	
12-9	Antigen-presenting cells in the intestinal mucosa acquire antigen by a variety of routes.	505	
12-10	Secretory IgA is the class of antibody associated with the mucosal immune system.	506	
12-11	T-independent processes can contribute to IgA production in some species.	509	
12-12	IgA deficiency is relatively common in humans but may be compensated for by secretory IgM.	509	
12-13	The intestinal lamina propria contains antigen- experienced T cells and populations of unusual innate lymphoid cells.	510	
12-14	The intestinal epithelium is a unique compartment		
	of the immune system.	511	
Summa	ary.	514	
The m	ucosal response to infection and regulation		
of muc	cosal immune responses.	514	
12-15	response and the development of protective immunity.	515	
12-16	Pathogens induce adaptive immune responses when innate defenses have been breached.	518	
12-17	Effector T-cell responses in the intestine protect the function of the epithelium.	518	
12-18	The mucosal immune system must maintain tolerance to harmless foreign antigens.	519	
12-19	The normal intestine contains large quantities of bacteria that are required for health.	520	
12-20	Innate and adaptive immune systems control microbiota while preventing inflammation without	501	
12-21	The intestinal microhiota plays a major role in	521	
12-21	shaping intestinal and systemic immune function.	522	
12-22	Full immune responses to commensal bacteria provoke intestinal disease.	524	
Summa	ary.	525	
Summa	ary to Chapter 12.	525	
Questio	ons.	526	
Referen	nces.	527	
PART V THE IMMUNE SYSTEM IN HEALTH AND DISEASE			

Chapt	ter 13	Failures of Host Defense	
		Mechanisms	533
Immur	nodeficie	ency diseases.	533
13-1	A histor	y of repeated infections suggests a	504
	diagnos	is of immunodeficiency.	534
13-2	Primary	immunodeficiency diseases are caused	
	by inher	ited gene defects.	534
13-3	Defects	in T-cell development can result in severe	505
	combine	eu immunodenciencies.	535

13-4	SCID can also be due to defects in the purine	500
10 5	salvage pathway.	538
13-5	can result in SCID.	538
13-6	Defects in signaling from T-cell antigen receptors can cause severe immunodeficiency.	539
13-7	Genetic defects in thymic function that block T-cell development result in severe immunodeficiencies.	539
13-8	Defects in B-cell development result in deficiencies in antibody production that cause an inability to clear extracellular bacteria and some viruses.	541
13-9	Immune deficiencies can be caused by defects in B-cell or T-cell activation and function that lead to abnormal antibody responses.	543
13-10	Normal pathways for host defense against different infectious agents are pinpointed by genetic deficiencies of cytokine pathways central to type $1/T_H 1$ and type $3/T_u 17$ responses.	546
13-11	Inherited defects in the cytolytic pathway of lymphocytes can cause uncontrolled lympho- proliferation and inflammatory responses to viral infections	548
13-12	X-linked lymphoproliferative syndrome is associated with fatal infection by Epstein–Barr virus and with the development of lymphomas	550
13-13	Immunodeficiency is caused by inherited defects	551
13-14	Defects in complement components and complement- regulatory proteins cause defective humoral immune	
13-15	Defects in phagocytic cells permit widespread	552
10.10	bacterial infections.	553
13-16	can cause uncontrolled inflammatory responses that result in 'autoinflammatory disease.'	556
13-17	Hematopoietic stem cell transplantation or gene therapy can be useful to correct genetic defects.	557
13-18	Noninherited, secondary immunodeficiencies are major predisposing causes of infection and death.	558
Summa	ıry.	559
Evasio	n and subversion of immune defenses.	560
13-19	different strategies to avoid detection by pattern recognition receptors and destruction by antibody,	500
13-20	Intracellular bacterial pathogens can evade the	500
13-21	immune system by seeking shelter within phagocytes.	563
10 21	parasites.	565
13-22	RNA viruses use different mechanisms of antigenic	
	variation to keep a step ahead of the adaptive immune system.	566
13-23	DNA viruses use multiple mechanisms to subvert NK-cell and CTL responses.	568
13-24	Some latent viruses persist <i>in vivo</i> by ceasing to replicate until immunity wanes.	571
Summa	ary.	573
Acquir	ed immune deficiency syndrome	573
13-25	HIV is a retrovirus that establishes a chronic	
	infection that slowly progresses to AIDS.	574

	immune system.	576
13-27	Activated CD4 T cells are the major source of	
10.00	HIV replication.	578
13-28	transmitted and establishes infection.	579
13-29	HIV variants with tropism for different co-receptors play different roles in transmission and progression of disease.	580
13-30	A genetic deficiency of the co-receptor CCR5 confers resistance to HIV infection.	582
13-31	An immune response controls but does not eliminate HIV.	583
13-32	Lymphoid tissue is the major reservoir of HIV infection.	585
13-33	Genetic variation in the host can alter the rate of disease progression.	585
13-34	The destruction of immune function as a result of HIV infection leads to increased susceptibility to opportunistic infection and eventually to death.	587
13-35	Drugs that block HIV replication lead to a rapid decrease in titer of infectious virus and an increase in CD4 T cells.	588
13-36	In the course of infection HIV accumulates many mutations, which can result in the outgrowth of drug-resistant variants	590
13-37	Vaccination against HIV is an attractive solution	591
13-38	Prevention and education are important in controlling the spread of HIV and AIDS.	592
Summ	ary.	593
Summ	ary to Chapter 13.	594
Questi	ons.	50/
		594
Refere	nces.	595
Refere Chap	nces. ter 14 Allergy and Allergic Diseases	595 601
Refere Chap IgE ar 14-1	nces. ter 14 Allergy and Allergic Diseases id IgE-mediated allergic diseases. Sensitization involves class switching to IgE	595 601 602
Refere Chap IgE ar 14-1	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen.	595 601 602 603
Refere Chap IgE ar 14-1 14-2	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents.	595 595 601 602 603
Refere Chap IgE ar 14-1 14-2 14-3	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease.	595 595 601 602 603 605
Refere Chap IgE ar 14-1 14-2 14-3 14-4	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease.	595 595 601 602 603 605 607
Refere Chap IgE an 14-1 14-2 14-3 14-4 14-5	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses.	595 595 601 602 603 605 605 605 611
Refere Chap IgE ar 14-1 14-2 14-3 14-3 14-4 14-5 Summ	nces. ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses. ary.	595 595 601 602 603 605 607 605 611 612
Refere Chap IgE an 14-1 14-2 14-3 14-4 14-5 Summ Effect	nces. ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses. ary.	595 595 601 602 603 605 605 605 611 612
Refere Chap IgE ar 14-1 14-2 14-3 14-4 14-5 Summ Effect allergi 14-6	ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses. ary. or mechanisms in IgE-mediated c reactions.	595 595 601 602 603 605 607 609 611 612 612
Refere Chap IgE an 14-1 14-2 14-3 14-4 14-5 Summ Effect allergi 14-6	nces. ter 14 Allergy and Allergic Diseases d IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses. ary. or mechanisms in IgE-mediated c reactions. Most IgE is cell-bound and engages effector mechanisms of the immune system by pathways different from those of other antibody isotypes.	595 595 601 602 603 605 611 612 612 613
Refere Chap IgE an 14-1 14-2 14-3 14-4 14-5 Summ Effect allergi 14-6 14-7	nces. ter 14 Allergy and Allergic Diseases of IgE-mediated allergic diseases. Sensitization involves class switching to IgE production on first contact with an allergen. Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents. Genetic factors contribute to the development of IgE-mediated allergic disease. Environmental factors may interact with genetic susceptibility to cause allergic disease. Regulatory T cells can control allergic responses. ary. or mechanisms in IgE-mediated c reactions. Most IgE is cell-bound and engages effector mechanisms of the immune system by pathways different from those of other antibody isotypes. Mast cells reside in tissues and orchestrate allergic reactions.	595 595 601 602 603 605 605 611 612 612 613
Refere Chap IgE an 14-1 14-2 14-3 14-4 14-5 Summ Effect allergi 14-6 14-7 14-8	<ul> <li>Inces.</li> <li>Iter 14 Allergy and Allergic Diseases</li> <li>Id IgE-mediated allergic diseases.</li> <li>Sensitization involves class switching to IgE production on first contact with an allergen.</li> <li>Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents.</li> <li>Genetic factors contribute to the development of IgE-mediated allergic disease.</li> <li>Environmental factors may interact with genetic susceptibility to cause allergic disease.</li> <li>Regulatory T cells can control allergic responses.</li> <li>ary.</li> <li>Or mechanisms in IgE-mediated creactions.</li> <li>Most IgE is cell-bound and engages effector mechanisms of the immune system by pathways different from those of other antibody isotypes.</li> <li>Mast cells reside in tissues and orchestrate allergic reactions.</li> <li>Eosinophils and basophils cause inflammation and tissue damage in allergic reactions.</li> </ul>	595 595 601 602 603 605 607 605 611 612 613 613 614
Refere Chap IgE ar 14-1 14-2 14-3 14-4 14-5 Summ Effect allergi 14-6 14-7 14-8 14-9	<ul> <li>Allergy and Allergic Diseases</li> <li>Allergy and Allergic Diseases</li> <li>AlgE-mediated allergic diseases.</li> <li>Sensitization involves class switching to IgE production on first contact with an allergen.</li> <li>Although many types of antigens can cause allergic sensitization, proteases are common sensitizing agents.</li> <li>Genetic factors contribute to the development of IgE-mediated allergic disease.</li> <li>Environmental factors may interact with genetic susceptibility to cause allergic disease.</li> <li>Regulatory T cells can control allergic responses.</li> <li>ary.</li> <li>Or mechanisms in IgE-mediated creactions.</li> <li>Most IgE is cell-bound and engages effector mechanisms of the immune system by pathways different from those of other antibody isotypes.</li> <li>Mast cells reside in tissues and orchestrate allergic reactions.</li> <li>Eosinophils and basophils cause inflammation and tissue damage in allergic reactions.</li> </ul>	595 595 601 602 603 605 607 609 611 612 612 613 613 616

14-10	Allergen introduced into the bloodstream can cause	
	anaphylaxis.	619
14-11	Allergen inhalation is associated with the development of rhinitis and asthma.	621
14-12	Allergy to particular foods causes systemic reactions as well as symptoms limited to the gut.	624
14-13	IgE-mediated allergic disease can be treated by	
	symptoms or by desensitization techniques that aim at restoring biological tolerance to	
	the allergen.	625
Summ	ary.	627
Non-l	gE-mediated allergic diseases.	628
14-14	Non-IgE dependent drug-induced hypersensitivity reactions in susceptible individuals occur by binding	000
14-15	Systemic disease caused by immune-complex	020
571	quantities of poorly catabolized antigens.	628
14-16	Hypersensitivity reactions can be mediated by $T_H^1$ cells and CD8 cytotoxic T cells.	630
14-17	Celiac disease has features of both an allergic	634
Cumana		626
Summ	ary.	000
Summ	ary to Chapter 14.	030
Questi	ons.	637
Refere	nces.	638
Chap	ter 15 Autoimmunity and Transplantation	643
The m	aking and breaking of self-tolerance.	643
15-1	A critical function of the immune system is to discriminate self from nonself.	643
15-2	Multiple tolerance mechanisms normally prevent autoimmunity.	645
15-3	Central deletion or inactivation of newly formed lymphocytes is the first checkpoint of self-tolerance.	646
15-4	Lymphocytes that bind self antigens with relatively low affinity usually ignore them but in some	485
45.5	circumstances become activated.	647
15-5	induce immune attack but can serve as targets.	648
15-6	Autoreactive I cells that express particular cytokines may be nonpathogenic or may	640
15-7	Autoimmune responses can be controlled at	049
Summ	various stages by regulatory i cells. ary.	652
Autoir	nmune diseases and pathogenic mechanisms.	652
15-8	Specific adaptive immune responses to self	
533	antigens can cause autoimmune disease.	652
15-9	Autoimmunity can be classified into either organ- specific or systemic disease.	653
15-10	Multiple components of the immune system are typically recruited in autoimmune disease.	654
15-11	Chronic autoimmune disease develops through positive feedback from inflammation, inability to clear the self antigen, and a broadening of the	
	autoimmune response.	657

15-12	Both antibody and effector T cells can cause tissue damage in autoimmune disease.	659
15-13	Autoantibodies against blood cells promote their destruction.	661
15-14	The fixation of sublytic doses of complement to cells in tissues stimulates a powerful inflammatory response.	661
15-15	Autoantibodies against receptors cause disease by stimulating or blocking receptor function.	662
15-16	Autoantibodies against extracellular antigens cause inflammatory injury.	663
15-17	T cells specific for self antigens can cause direct tissue injury and sustain autoantibody responses.	665
Summa	ary.	668
The ge	enetic and environmental basis of autoimmunity.	669
15-18	Autoimmune diseases have a strong genetic component.	669
15-19	Genomics-based approaches are providing new insight into the immunogenetic basis of autoimmunity.	670
15-20	Many genes that predispose to autoimmunity fall into categories that affect one or more tolerance	074
15.01	Menagapia defecta of immune telerance	674
15-21	MHC gapes have an important role in controlling	074
10-22	susceptibility to autoimmune disease.	676
15-23	Genetic variants that impair innate immune	
	chronic inflammatory disease.	678
15-24	External events can initiate autoimmunity.	679
15-25	Infection can lead to autoimmune disease by providing an environment that promotes lymphocyte	000
15.00	activation.	680
15-20	pathogens and self molecules can lead to antiself responses and autoimmune disease.	680
15-27	Drugs and toxins can cause autoimmune syndromes.	682
15-28	Random events may be required for the initiation	000
~ ~ ~ ~	of autoimmunity.	682
Summ	ary.	082
Respo	onses to alloantigens and transplant rejection.	683
15-29	Graft rejection is an immunological response mediated primarily by T cells	683
15-30	Transplant rejection is caused primarily by the strong	1943
	immune response to nonself MHC molecules.	684
15-31	In MHC-identical grafts, rejection is caused by peptides from other alloantigens bound to graft	
	MHC molecules.	685
15-32	There are two ways of presenting alloantigens on the transplanted donor organ to the recipient's	696
15.33	Antibodies that react with endothelium cause	000
10-00	hyperacute graft rejection.	688
15-34	Late failure of transplanted organs is caused by chronic injury to the graft.	688
15-35	A variety of organs are transplanted routinely in clinical medicine.	689
15-36	The converse of graft rejection is graft-versus-	
	host disease.	691

15-37	Regulatory T cells are involved in alloreactive	
	immune responses.	692
15-38	The fetus is an allograft that is tolerated repeatedly.	693
Summa	ıry.	694
Summa	iry to Chapter 15.	694
Questic	ons	695
Referen	ices.	696
Chapt	er 16 Manipulation of the	
	Immune Response	701
Treatm	ent of unwanted immune responses.	701
16-1	Corticosteroids are powerful anti-inflammatory drugs that alter the transcription of many genes.	702
16-2	Cytotoxic drugs cause immunosuppression by killing dividing cells and have serious side-effects.	703
16-3	Cyclosporin A, tacrolimus, rapamycin, and JAK inhibitors are effective immunosuppressive agents that interfere with various T-cell signaling pathways.	704
16-4	Antibodies against cell-surface molecules can be used to eliminate lymphocyte subsets or to inhibit lymphocyte function.	706
16-5	Antibodies can be engineered to reduce their immunogenicity in humans.	707
16-6	Monoclonal antibodies can be used to prevent allograft rejection.	708
16-7	Depletion of autoreactive lymphocytes can treat autoimmune disease.	710
16-8	Biologics that block TNF- $\alpha$ , IL-1, or IL-6 can alleviate autoimmune diseases.	711
16-9	Biologic agents can block cell migration to sites of inflammation and reduce immune responses.	712
16-10	Blockade of co-stimulatory pathways that activate lymphocytes can be used to treat autoimmune	710
16 11	disease.	/13
10-11	immunomodulatory properties.	713
16-12	Controlled administration of antigen can be used to manipulate the nature of an antigen-specific	714
Cumm	response.	714
Summa	ary.	714
Using 16-13	The development of transplantable tumors in mice	/16
16 14	responses to tumors.	716
10-14	evolve and can escape rejection in many ways.	717
16-15	T cells and form the basis of immunotherapies.	720
16-16	an effective treatment in some leukemias.	723
16-17	Monoclonal antibodies against tumor antigens, alone or linked to toxins, can control tumor growth.	724
16-18	Enhancing the immune response to tumors by vaccination holds promise for cancer prevention and therapy.	726
16-19	Checkpoint blockade can augment immune	
0	responses to existing tumors.	727
Summa	ary.	728

Fightin	g infectious diseases with vaccination.	729			
16-20	Vaccines can be based on attenuated pathogens or material from killed organisms.				
16-21	Most effective vaccines generate antibodies that prevent the damage caused by toxins or that neutralize the pathogen and stop infection.	731			
16-22	Effective vaccines must induce long-lasting protection while being safe and inexpensive.	732			
16-23	Live-attenuated viral vaccines are usually more potent than 'killed' vaccines and can be made safer by the use of recombinant DNA technology.	732			
16-24	Live-attenuated vaccines can be developed by selecting nonpathogenic or disabled bacteria or by creating genetically attenuated parasites (GAPs).	734			
16-25	The route of vaccination is an important determinant of success.	735			
16-26	Bordetella pertussis vaccination illustrates the importance of the perceived safety of a vaccine.	736			
16-27	Conjugate vaccines have been developed as a result of linked recognition between T and B cells.	737			
16-28	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.	738			
16-29	Adjuvants are important for enhancing the immunogenicity of vaccines, but few are approved for use in humans.	739			
16-30	Protective immunity can be induced by DNA-based vaccination.	740			
16-31	Vaccination and checkpoint blockade may be useful in controlling existing chronic infections.	741			
Summary.					
Summary to Chapter 16.					
Questions.					
References.					

## **APPENDICES**

Appe	endix I The Immunologist's Toolbox	749
A-1.	Immunization.	749
A-2	Antibody responses.	752
A-3	Affinity chromatography.	753
A-4	Radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA), and competitive	
	inhibition assay.	753
A-5	Hemagglutination and blood typing.	755
A-6	Coombs tests and the detection of rhesus	
	incompatibility.	756
A-7	Monoclonal antibodies.	757
A-8	Phage display libraries for antibody V-region production.	758
A-9	Generation of human monoclonal antibodies from	
	vaccinated individuals.	759
A-10	Microscopy and imaging using fluorescent dyes.	760
A-11	Immunoelectron microscopy.	761
A-12	Immunohistochemistry.	762
A-13	Immunoprecipitation and co-immunoprecipitation.	762

A-14	Immunob	olotting (Western blotting).	764	
A-15	5 Use of antibodies in the isolation and			
	character	rization of multiprotein complexes	704	
188	by mass	spectrometry.	764	
A-16	Isolation of peripheral blood lymphocytes by density gradient fractionation.			
A-17	Isolation blood.	of lymphocytes from tissues other than	766	
A-18	Flow cyto	ometry and FACS analysis.	767	
A-19	Lymphoo magnetic	yte isolation using antibody-coated beads.	770	
A-20	Isolation	of homogeneous T-cell lines.	770	
A-21	Limiting-	dilution culture.	771	
A-22	ELISPOT	assay.	773	
A-23	Identifica on cytoki	tion of functional subsets of T cells based ne production or transcription factor	773	
A 24	Identified	tion of T coll recentor oppositioity using ponti		
A-24	tetramers	a.	776	
A-25	Biosenso	or assays for measuring the rates of		
	for their I	igands.	777	
A-26	Assays o	f lymphocyte proliferation.	778	
A-27	Measure	ments of apoptosis.	779	
A-28	Assays fo	or cytotoxic T cells.	780	
A-29	Assays fo	or CD4 T cells.	782	
A-30	Transfer	of protective immunity.	782	
A-31	Adoptive	transfer of lymphocytes.	783	
A-32	Hematop	oietic stem-cell transfers.	784	
A-33	In vivo ad	ministration of antibodies.	785	
A-34	Transgen	ic mice.	786	
A-35	Gene kno	ockout by targeted disruption.	786	
A-36	Knockdo	wn of gene expression by		
	RNA inte	rference (RNAi).	790	
Appe	ndix II	CD antigens	791	
Appe	ndix III	Cytokines and their Receptors	811	
Appe	ndix IV	Chemokines and their Receptors	814	
Biogra	aphies		816	
Photograph Acknowledgments				
Gloss	ary		818	
Index			855	

clinit 15-36 The