

# Contents

<b>PART I</b>	<b>INTRODUCTION TO THE CELL</b>	<b>1</b>
Chapter 1	Cells and Genomes	1
Chapter 2	Cell Chemistry and Bioenergetics	43
Chapter 3	Proteins	109
<b>PART II</b>	<b>BASIC GENETIC MECHANISMS</b>	<b>175</b>
Chapter 4	DNA, Chromosomes, and Genomes	175
Chapter 5	DNA Replication, Repair, and Recombination	237
Chapter 6	How Cells Read the Genome: From DNA to Protein	299
Chapter 7	Control of Gene Expression	369
<b>PART III</b>	<b>WAYS OF WORKING WITH CELLS</b>	<b>439</b>
Chapter 8	Analyzing Cells, Molecules, and Systems	439
Chapter 9	Visualizing Cells	529
<b>PART IV</b>	<b>INTERNAL ORGANIZATION OF THE CELL</b>	<b>565</b>
Chapter 10	Membrane Structure	565
Chapter 11	Membrane Transport of Small Molecules and the Electrical Properties of Membranes	597
Chapter 12	Intracellular Compartments and Protein Sorting	641
Chapter 13	Intracellular Membrane Traffic	695
Chapter 14	Energy Conversion: Mitochondria and Chloroplasts	753
Chapter 15	Cell Signaling	813
Chapter 16	The Cytoskeleton	889
Chapter 17	The Cell Cycle	963
Chapter 18	Cell Death	1021
Chapter 19	Cell Junctions and the Extracellular Matrix	1035
<b>PART V</b>	<b>CELLS IN THEIR SOCIAL CONTEXT</b>	<b>1035</b>
Chapter 20	Cancer	1091
Chapter 21	Development of Multicellular Organisms	1145
Chapter 22	Stem Cells and Tissue Renewal	1217
Chapter 23	Pathogens and Infection	1263
Chapter 24	The Innate and Adaptive Immune Systems	1297
Glossary		G: 1
Index		I: 1
Tables	The Genetic Code, Amino Acids	T: 1



# Special Features

TABLE 1-2	Some Model Organisms and Their Genomes	29
TABLE 2-1	Covalent and Noncovalent Chemical Bonds	45
TABLE 2-2	Relationship Between the Standard Free-Energy Change, $\Delta G^\circ$ , and the Equilibrium Constant	63
PANEL 2-1	Chemical Bonds and Groups Commonly Encountered in Biological Molecules	90
PANEL 2-2	Water and Its Influence on the Behavior of Biological Molecules	92
PANEL 2-3	The Principal Types of Weak Noncovalent Bonds that Hold Macromolecules Together	94
PANEL 2-4	An Outline of Some of the Types of Sugars Commonly Found in Cells	96
PANEL 2-5	Fatty Acids and Other Lipids	98
PANEL 2-6	A Survey of the Nucleotides	100
PANEL 2-7	Free Energy and Biological Reactions	102
PANEL 2-8	Details of the 10 Steps of Glycolysis	104
PANEL 2-9	The Complete Citric Acid Cycle	106
PANEL 3-1	The 20 Amino Acids Found in Proteins	112
TABLE 3-3	Some Molecules Covalently Attached to Proteins Regulate Protein Function	165
TABLE 4-1	Some Vital Statistics for the Human Genome	184
TABLE 5-4	Three Major Classes of Transposable Elements	288
TABLE 6-1	Principal Types of RNAs Produced in Cells	305
PANEL 7-1	Common Structural Motifs in Transcription Regulators	376
PANEL 8-1	DNA Sequencing Methods	478
PANEL 8-2	Review of Classical Genetics	486
TABLE 11-1	A Comparison of Inorganic Ion Concentrations Inside and Outside a Typical Mammalian Cell	598
PANEL 11-1	The Derivation of the Nernst Equation	616
TABLE 12-1	Relative Volumes Occupied by the Major Intracellular Compartments in a Liver Cell (Hepatocyte)	643
PANEL 14-1	Redox Potentials	765
TABLE 14-1	Product Yields from the Oxidation of Sugars and Fats	775
TABLE 15-3	Four Major Families of Trimeric G Proteins	846
TABLE 15-4	Some Signal Proteins That Act Via RTKs	850
TABLE 15-5	The Ras Superfamily of Monomeric GTPases	854
TABLE 15-6	Some Extracellular Signal Proteins That Act Through Cytokine Receptors and the JAK-STAT Signaling Pathway	864
PANEL 16-2	The Polymerization of Actin and Tubulin	902
TABLE 16-1	Chemical Inhibitors of Actin and Microtubules	904
PANEL 16-3	Actin Filaments	905
PANEL 16-4	Microtubules	933
TABLE 16-2	Major Types of Intermediate Filament Proteins in Vertebrate Cells	944
TABLE 17-1	The Major Cyclins and Cdks of Vertebrates and Budding Yeast	969
TABLE 17-2	Summary of the Major Cell Cycle Regulatory Proteins	973
PANEL 17-1	The Principal Stages of M Phase (Mitosis and Cytokinesis) in an Animal Cell	980
TABLE 19-1	Anchoring Junctions	1037
TABLE 19-2	Some Types of Collagen and Their Properties	1063
TABLE 19-3	Some Types of Integrins	1076
TABLE 22-1	Blood Cells	1241
TABLE 24-2	Properties of the Major Classes of Antibodies in Humans	1318
TABLE 24-3	Properties of Human Class I and Class II MHC Proteins	1330



# Detailed Contents

<b>Chapter 1 Cells and Genomes</b>	<b>1</b>	<b>The Frog and the Zebrafish Provide Accessible Models for Vertebrate Development</b>	<b>35</b>
<b>THE UNIVERSAL FEATURES OF CELLS ON EARTH</b>	<b>2</b>	<b>The Mouse Is the Predominant Mammalian Model Organism</b>	<b>35</b>
All Cells Store Their Hereditary Information in the Same Linear Chemical Code: DNA	2	Humans Report on Their Own Peculiarities	36
All Cells Replicate Their Hereditary Information by Templated Polymerization	3	We Are All Different in Detail	38
All Cells Transcribe Portions of Their Hereditary Information into the Same Intermediary Form: RNA	4	To Understand Cells and Organisms Will Require Mathematics, Computers, and Quantitative Information	38
All Cells Use Proteins as Catalysts	5	Summary	39
All Cells Translate RNA into Protein in the Same Way	6	Problems	39
Each Protein Is Encoded by a Specific Gene	7	References	41
Life Requires Free Energy	8	<b>Chapter 2 Cell Chemistry and Bioenergetics</b>	<b>43</b>
All Cells Function as Biochemical Factories Dealing with the Same Basic Molecular Building Blocks	8	<b>THE CHEMICAL COMPONENTS OF A CELL</b>	<b>43</b>
All Cells Are Enclosed in a Plasma Membrane Across Which Nutrients and Waste Materials Must Pass	8	Water Is Held Together by Hydrogen Bonds	44
A Living Cell Can Exist with Fewer Than 500 Genes	9	Four Types of Noncovalent Attractions Help Bring Molecules Together in Cells	44
Summary	10	Some Polar Molecules Form Acids and Bases in Water	45
<b>THE DIVERSITY OF GENOMES AND THE TREE OF LIFE</b>	<b>10</b>	A Cell Is Formed from Carbon Compounds	47
Cells Can Be Powered by a Variety of Free-Energy Sources	10	Cells Contain Four Major Families of Small Organic Molecules	47
Some Cells Fix Nitrogen and Carbon Dioxide for Others	12	The Chemistry of Cells Is Dominated by Macromolecules with Remarkable Properties	47
The Greatest Biochemical Diversity Exists Among Prokaryotic Cells	12	Noncovalent Bonds Specify Both the Precise Shape of a Macromolecule and Its Binding to Other Molecules	49
The Tree of Life Has Three Primary Branches: Bacteria, Archaea, and Eukaryotes	14	Summary	50
Some Genes Evolve Rapidly; Others Are Highly Conserved	15	<b>CATALYSIS AND THE USE OF ENERGY BY CELLS</b>	<b>51</b>
Most Bacteria and Archaea Have 1000–6000 Genes	16	Cell Metabolism Is Organized by Enzymes	51
New Genes Are Generated from Preexisting Genes	16	Biological Order Is Made Possible by the Release of Heat Energy from Cells	52
Gene Duplications Give Rise to Families of Related Genes Within a Single Cell	17	Cells Obtain Energy by the Oxidation of Organic Molecules	54
Genes Can Be Transferred Between Organisms, Both in the Laboratory and in Nature	18	Oxidation and Reduction Involve Electron Transfers	55
Sex Results in Horizontal Exchanges of Genetic Information Within a Species	19	Enzymes Lower the Activation-Energy Barriers That Block Chemical Reactions	57
The Function of a Gene Can Often Be Deduced from Its Sequence	20	Enzymes Can Drive Substrate Molecules Along Specific Reaction Pathways	58
More Than 200 Gene Families Are Common to All Three Primary Branches of the Tree of Life	20	How Enzymes Find Their Substrates: The Enormous Rapidity of Molecular Motions	59
Mutations Reveal the Functions of Genes	21	The Free-Energy Change for a Reaction, $\Delta G$ , Determines Whether It Can Occur Spontaneously	60
Molecular Biology Began with a Spotlight on <i>E. coli</i>	22	The Concentration of Reactants Influences the Free-Energy Change and a Reaction's Direction	61
Summary	22	The Standard Free-Energy Change, $\Delta G^\circ$ , Makes It Possible to Compare the Energetics of Different Reactions	61
<b>GENETIC INFORMATION IN EUKARYOTES</b>	<b>23</b>	The Equilibrium Constant and $\Delta G^\circ$ Are Readily Derived from Each Other	62
Eukaryotic Cells May Have Originated as Predators	24	The Free-Energy Changes of Coupled Reactions Are Additive	63
Modern Eukaryotic Cells Evolved from a Symbiosis	25	Activated Carrier Molecules Are Essential for Biosynthesis	63
Eukaryotes Have Hybrid Genomes	27	The Formation of an Activated Carrier Is Coupled to an Energetically Favorable Reaction	64
Eukaryotic Genomes Are Big	28	ATP Is the Most Widely Used Activated Carrier Molecule	65
Eukaryotic Genomes Are Rich in Regulatory DNA	29	Energy Stored in ATP Is Often Harnessed to Join Two Molecules Together	65
The Genome Defines the Program of Multicellular Development	29	NADH and NADPH Are Important Electron Carriers	67
Many Eukaryotes Live as Solitary Cells	30	There Are Many Other Activated Carrier Molecules in Cells	68
A Yeast Serves as a Minimal Model Eukaryote	30	The Synthesis of Biological Polymers Is Driven by ATP Hydrolysis	70
The Expression Levels of All the Genes of An Organism Can Be Monitored Simultaneously	32	Summary	73
Albino Drosophila Has Been Chosen Out of 300,000 Species as a Model Plant	32	<b>HOW CELLS OBTAIN ENERGY FROM FOOD</b>	<b>73</b>
The World of Animal Cells Is Represented By a Worm, a Fly, a Fish, a Mouse, and a Human	33	Glycolysis Is a Central ATP-Producing Pathway	74
Studies in <i>Drosophila</i> Provide a Key to Vertebrate Development	33	Fermentations Produce ATP in the Absence of Oxygen	75
The Vertebrate Genome Is a Product of Repeated Duplications	34		



Glycolysis Illustrates How Enzymes Couple Oxidation to Energy Storage	76	The Regulation of the Src Protein Kinase Reveals How a Protein Can Function as a Microprocessor	155
Organisms Store Food Molecules in Special Reservoirs	78	Proteins That Bind and Hydrolyze GTP Are Ubiquitous Cell Regulators	156
Most Animal Cells Derive Their Energy from Fatty Acids Between Meals	81	Regulatory Proteins GAP and GEF Control the Activity of GTP-Binding Proteins by Determining Whether GTP or GDP Is Bound	157
Sugars and Fats Are Both Degraded to Acetyl CoA in Mitochondria	81	Proteins Can Be Regulated by the Covalent Addition of Other Proteins	157
The Citric Acid Cycle Generates NADH by Oxidizing Acetyl Groups to CO <sub>2</sub>	82	An Elaborate Ubiquitin-Conjugating System Is Used to Mark Proteins	158
Electron Transport Drives the Synthesis of the Majority of the ATP in Most Cells	84	Protein Complexes with Interchangeable Parts Make Efficient Use of Genetic Information	159
Amino Acids and Nucleotides Are Part of the Nitrogen Cycle	85	A GTP-Binding Protein Shows How Large Protein Movements Can Be Generated	160
Metabolism Is Highly Organized and Regulated	87	Motor Proteins Produce Large Movements in Cells	161
Summary	88	Membrane-Bound Transporters Harness Energy to Pump Molecules Through Membranes	162
Problems	88	Proteins Often Form Large Complexes That Function as Protein Machines	164
References	108	Scaffolds Concentrate Sets of Interacting Proteins	164
		Many Proteins Are Controlled by Covalent Modifications That Direct Them to Specific Sites Inside the Cell	165
<b>Chapter 3 Proteins</b>	<b>109</b>	A Complex Network of Protein Interactions Underlies Cell Function	166
<b>THE SHAPE AND STRUCTURE OF PROTEINS</b>	<b>109</b>	Summary	166
The Shape of a Protein Is Specified by Its Amino Acid Sequence	109	Problems	170
Proteins Fold into a Conformation of Lowest Energy	114	References	172
The $\alpha$ Helix and the $\beta$ Sheet Are Common Folding Patterns	115		
Protein Domains Are Modular Units from Which Larger Proteins Are Built	117	<b>Chapter 4 DNA, Chromosomes, and Genomes</b>	<b>173</b>
Few of the Many Possible Polypeptide Chains Will Be Useful to Cells	118	<b>THE STRUCTURE AND FUNCTION OF DNA</b>	<b>175</b>
Proteins Can Be Classified into Many Families	119	A DNA Molecule Consists of Two Complementary Chains of Nucleotides	175
Some Protein Domains Are Found in Many Different Proteins	121	The Structure of DNA Provides a Mechanism for Heredity	177
Certain Pairs of Domains Are Found Together in Many Proteins	122	In Eukaryotes, DNA Is Enclosed in a Cell Nucleus	178
The Human Genome Encodes a Complex Set of Proteins, Revealing That Much Remains Unknown	122	Summary	179
Larger Protein Molecules Often Contain More Than One Polypeptide Chain	123	<b>CHROMOSOMAL DNA AND ITS PACKAGING IN THE CHROMATIN FIBER</b>	<b>179</b>
Some Globular Proteins Form Long Helical Filaments	123	Eukaryotic DNA Is Packaged into a Set of Chromosomes	180
Many Protein Molecules Have Elongated, Fibrous Shapes	124	Chromosomes Contain Long Strings of Genes	182
Proteins Contain a Surprisingly Large Amount of Intrinsically Disordered Polypeptide Chain	125	The Nucleotide Sequence of the Human Genome Shows How Our Genes Are Arranged	183
Covalent Cross-Linkages Stabilize Extracellular Proteins	127	Each DNA Molecule That Forms a Linear Chromosome Must Contain a Centromere, Two Telomeres, and Replication Origins	185
Protein Molecules Often Serve as Subunits for the Assembly of Large Structures	127	DNA Molecules Are Highly Condensed in Chromosomes	187
Many Structures in Cells Are Capable of Self-Assembly	128	Nucleosomes Are a Basic Unit of Eukaryotic Chromosome Structure	187
Assembly Factors Often Aid the Formation of Complex Biological Structures	130	The Structure of the Nucleosome Core Particle Reveals How DNA Is Packaged	188
Amyloid Fibrils Can Form from Many Proteins	130	Nucleosomes Have a Dynamic Structure, and Are Frequently Subjected to Changes Catalyzed by ATP-Dependent Chromatin Remodeling Complexes	190
Amyloid Structures Can Perform Useful Functions in Cells	132	Nucleosomes Are Usually Packed Together into a Compact Chromatin Fiber	191
Many Proteins Contain Low-complexity Domains that Can Form "Reversible Amyloids"	132	Summary	193
Summary	134	<b>CHROMATIN STRUCTURE AND FUNCTION</b>	<b>194</b>
<b>PROTEIN FUNCTION</b>	<b>134</b>	Heterochromatin Is Highly Organized and Restricts Gene Expression	194
All Proteins Bind to Other Molecules	134	The Heterochromatic State Is Self-Propagating	194
The Surface Conformation of a Protein Determines Its Chemistry	135	The Core Histones Are Covalently Modified at Many Different Sites	196
Sequence Comparisons Between Protein Family Members Highlight Crucial Ligand-Binding Sites	136	Chromatin Acquires Additional Variety Through the Site-Specific Insertion of a Small Set of Histone Variants	198
Proteins Bind to Other Proteins Through Several Types of Interfaces	137	Covalent Modifications and Histone Variants Act in Concert to Control Chromosome Functions	198
Antibody Binding Sites Are Especially Versatile	138	A Complex of Reader and Writer Proteins Can Spread Specific Chromatin Modifications Along a Chromosome	199
The Equilibrium Constant Measures Binding Strength	138	Barrier DNA Sequences Block the Spread of Reader-Writer Complexes and thereby Separate Neighboring Chromatin Domains	202
Enzymes Are Powerful and Highly Specific Catalysts	140	The Chromatin in Centromeres Reveals How Histone Variants Can Create Special Structures	203
Substrate Binding Is the First Step in Enzyme Catalysis	141	Some Chromatin Structures Can Be Directly Inherited	204
Enzymes Speed Reactions by Selectively Stabilizing Transition States	141		
Enzymes Can Use Simultaneous Acid and Base Catalysis	144		
Lysozyme Illustrates How an Enzyme Works	144		
Tightly Bound Small Molecules Add Extra Functions to Proteins	146		
Multienzyme Complexes Help to Increase the Rate of Cell Metabolism	148		
The Cell Regulates the Catalytic Activities of Its Enzymes	149		
Allosteric Enzymes Have Two or More Binding Sites That Interact	151		
Two Ligands Whose Binding Sites Are Coupled Must Reciprocally Affect Each Other's Binding	151		
Symmetric Protein Assemblies Produce Cooperative Allosteric Transitions	152		
Many Changes in Proteins Are Driven by Protein Phosphorylation	153		
A Eukaryotic Cell Contains a Large Collection of Protein Kinases and Protein Phosphatases	154		



Experiments with Frog Embryos Suggest that both Activating and Repressive Chromatin Structures Can Be Inherited Epigenetically	205	The Proteins at a Replication Fork Cooperate to Form a Replication Machine	249
Chromatin Structures Are Important for Eukaryotic Chromosome Function	206	A Strand-Directed Mismatch Repair System Removes Replication Errors That Escape from the Replication Machine	250
Summary	207	DNA Topoisomerases Prevent DNA Tangling During Replication	251
<b>THE GLOBAL STRUCTURE OF CHROMOSOMES</b>	<b>207</b>	DNA Replication Is Fundamentally Similar in Eukaryotes and Bacteria	253
Chromosomes Are Folded into Large Loops of Chromatin	207	Summary	254
Polytene Chromosomes Are Uniquely Useful for Visualizing Chromatin Structures	208	<b>THE INITIATION AND COMPLETION OF DNA REPLICATION IN CHROMOSOMES</b>	<b>254</b>
There Are Multiple Forms of Chromatin	210	DNA Synthesis Begins at Replication Origins	254
Chromatin Loops Decondense When the Genes Within Them Are Expressed	211	Bacterial Chromosomes Typically Have a Single Origin of DNA Replication	255
Chromatin Can Move to Specific Sites Within the Nucleus to Alter Gene Expression	212	Eukaryotic Chromosomes Contain Multiple Origins of Replication	256
Networks of Macromolecules Form a Set of Distinct Biochemical Environments inside the Nucleus	213	In Eukaryotes, DNA Replication Takes Place During Only One Part of the Cell Cycle	258
Mitotic Chromosomes Are Especially Highly Condensed	214	Different Regions on the Same Chromosome Replicate at Distinct Times in S Phase	258
Summary	216	A Large Multisubunit Complex Binds to Eukaryotic Origins of Replication	259
<b>HOW GENOMES EVOLVE</b>	<b>216</b>	Features of the Human Genome That Specify Origins of Replication Remain to Be Discovered	260
Genome Comparisons Reveal Functional DNA Sequences by their Conservation Throughout Evolution	217	New Nucleosomes Are Assembled Behind the Replication Fork	261
Genome Alterations Are Caused by Failures of the Normal Mechanisms for Copying and Maintaining DNA, as well as by Transposable DNA Elements	217	Telomerase Replicates the Ends of Chromosomes	262
The Genome Sequences of Two Species Differ in Proportion to the Length of Time Since They Have Separately Evolved	218	Telomeres Are Packaged Into Specialized Structures That Protect the Ends of Chromosomes	263
Phylogenetic Trees Constructed from a Comparison of DNA Sequences Trace the Relationships of All Organisms	219	Telomere Length Is Regulated by Cells and Organisms	264
A Comparison of Human and Mouse Chromosomes Shows How the Structures of Genomes Diverge	221	Summary	265
The Size of a Vertebrate Genome Reflects the Relative Rates of DNA Addition and DNA Loss in a Lineage	222	<b>DNA REPAIR</b>	<b>266</b>
We Can Infer the Sequence of Some Ancient Genomes	223	Without DNA Repair, Spontaneous DNA Damage Would Rapidly Change DNA Sequences	267
Multispecies Sequence Comparisons Identify Conserved DNA Sequences of Unknown Function	224	The DNA Double Helix Is Readily Repaired	268
Changes in Previously Conserved Sequences Can Help Decipher Critical Steps in Evolution	226	DNA Damage Can Be Removed by More Than One Pathway	269
Mutations in the DNA Sequences That Control Gene Expression Have Driven Many of the Evolutionary Changes in Vertebrates	227	Coupling Nucleotide Excision Repair to Transcription Ensures That the Cell's Most Important DNA Is Efficiently Repaired	271
Gene Duplication Also Provides an Important Source of Genetic Novelty During Evolution	227	The Chemistry of the DNA Bases Facilitates Damage Detection	271
Duplicated Genes Diverge	228	Special Translesion DNA Polymerases Are Used in Emergencies	273
The Evolution of the Globin Gene Family Shows How DNA Duplications Contribute to the Evolution of Organisms	229	Double-Strand Breaks Are Efficiently Repaired	273
Genes Encoding New Proteins Can Be Created by the Recombination of Exons	230	DNA Damage Delays Progression of the Cell Cycle	276
Neutral Mutations Often Spread to Become Fixed in a Population, with a Probability That Depends on Population Size	230	Summary	276
A Great Deal Can Be Learned from Analyses of the Variation Among Humans	232	<b>HOMOLOGOUS RECOMBINATION</b>	<b>276</b>
Summary	234	Homologous Recombination Has Common Features in All Cells	277
Problems	234	DNA Base-Pairing Guides Homologous Recombination	277
References	236	Homologous Recombination Can Flawlessly Repair Double-Strand Breaks in DNA	278
<b>Chapter 5 DNA Replication, Repair, and Recombination</b>	<b>237</b>	Strand Exchange Is Carried Out by the RecA/Rad51 Protein	279
<b>THE MAINTENANCE OF DNA SEQUENCES</b>	<b>237</b>	Homologous Recombination Can Rescue Broken DNA Replication Forks	280
Mutation Rates Are Extremely Low	237	Cells Carefully Regulate the Use of Homologous Recombination in DNA Repair	280
Low Mutation Rates Are Necessary for Life as We Know It	238	Homologous Recombination Is Crucial for Meiosis	282
Summary	239	Meiotic Recombination Begins with a Programmed Double-Strand Break	282
<b>DNA REPLICATION MECHANISMS</b>	<b>239</b>	Holliday Junctions Are Formed During Meiosis	284
Base-Pairing Underlies DNA Replication and DNA Repair	239	Homologous Recombination Produces Both Crossovers and Non-Crossovers During Meiosis	284
The DNA Replication Fork Is Asymmetrical	240	Homologous Recombination Often Results in Gene Conversion	286
The High Fidelity of DNA Replication Requires Several Proofreading Mechanisms	242	Summary	286
Only DNA Replication in the 5'-to-3' Direction Allows Efficient Error Correction	244	<b>TRANSPPOSITION AND CONSERVATIVE SITE-SPECIFIC RECOMBINATION</b>	<b>287</b>
A Special Nucleotide-Polymerizing Enzyme Synthesizes Short RNA Primer Molecules on the Lagging Strand	245	Through Transposition, Mobile Genetic Elements Can Insert Into Any DNA Sequence	288
Special Proteins Help to Open Up the DNA Double Helix in Front of the Replication Fork	246	DNA-Only Transposons Can Move by a Cut-and-Paste Mechanism	288
A Sliding Ring Holds a Moving DNA Polymerase Onto the DNA	246	Some Viruses Use a Transposition Mechanism to Move Themselves Into Host-Cell Chromosomes	290
		Retroviral-like Retrotransposons Resemble Retroviruses, but Lack a Protein Coat	291
		A Large Fraction of the Human Genome Is Composed of Nonretroviral Retrotransposons	291
		Different Transposable Elements Predominate in Different Organisms	292
		Genome Sequences Reveal the Approximate Times at Which Transposable Elements Have Moved	292



Conservative Site-Specific Recombination Can Reversibly Rearrange DNA	292	Proteins Are Made on Polyribosomes	349
Conservative Site-Specific Recombination Can Be Used to Turn Genes On or Off	294	There Are Minor Variations in the Standard Genetic Code	349
Bacterial Conservative Site-Specific Recombinases Have Become Powerful Tools for Cell and Developmental Biologists	294	Inhibitors of Prokaryotic Protein Synthesis Are Useful as Antibiotics	351
Summary	295	Quality Control Mechanisms Act to Prevent Translation of Damaged mRNAs	351
Problems	296	Some Proteins Begin to Fold While Still Being Synthesized	353
References	298	Molecular Chaperones Help Guide the Folding of Most Proteins	354
		Cells Utilize Several Types of Chaperones	355
		Exposed Hydrophobic Regions Provide Critical Signals for Protein Quality Control	357
<b>Chapter 6 How Cells Read the Genome: From DNA to Protein</b>	<b>299</b>	The Proteasome Is a Compartmentalized Protease with Sequestered Active Sites	357
<b>FROM DNA TO RNA</b>	<b>301</b>	Many Proteins Are Controlled by Regulated Destruction	359
RNA Molecules Are Single-Stranded	302	There Are Many Steps From DNA to Protein	361
Transcription Produces RNA Complementary to One Strand of DNA	302	Summary	362
RNA Polymerases Carry Out Transcription	303	<b>THE RNA WORLD AND THE ORIGINS OF LIFE</b>	<b>362</b>
Cells Produce Different Categories of RNA Molecules	305	Single-Stranded RNA Molecules Can Fold into Highly Elaborate Structures	363
Signals Encoded in DNA Tell RNA Polymerase Where to Start and Stop	306	RNA Can Both Store Information and Catalyze Chemical Reactions	364
Transcription Start and Stop Signals Are Heterogeneous in Nucleotide Sequence	307	How Did Protein Synthesis Evolve?	365
Transcription Initiation in Eukaryotes Requires Many Proteins	309	All Present-Day Cells Use DNA as Their Hereditary Material	365
RNA Polymerase II Requires a Set of General Transcription Factors	310	Summary	366
Polymerase II Also Requires Activator, Mediator, and Chromatin-Modifying Proteins	312	Problems	366
Transcription Elongation in Eukaryotes Requires Accessory Proteins	313	References	368
Transcription Creates Superhelical Tension	314		
Transcription Elongation in Eukaryotes Is Tightly Coupled to RNA Processing	315	<b>Chapter 7 Control of Gene Expression</b>	<b>369</b>
RNA Capping Is the First Modification of Eukaryotic Pre-mRNAs	316	<b>AN OVERVIEW OF GENE CONTROL</b>	<b>369</b>
RNA Splicing Removes Intron Sequences from Newly Transcribed Pre-mRNAs	317	The Different Cell Types of a Multicellular Organism Contain the Same DNA	369
Nucleotide Sequences Signal Where Splicing Occurs	319	Different Cell Types Synthesize Different Sets of RNAs and Proteins	370
RNA Splicing Is Performed by the Spliceosome	319	External Signals Can Cause a Cell to Change the Expression of Its Genes	372
The Spliceosome Uses ATP Hydrolysis to Produce a Complex Series of RNA–RNA Rearrangements	321	Gene Expression Can Be Regulated at Many of the Steps in the Pathway from DNA to RNA to Protein	372
Other Properties of Pre-mRNA and Its Synthesis Help to Explain the Choice of Proper Splice Sites	321	Summary	373
Chromatin Structure Affects RNA Splicing	323	<b>CONTROL OF TRANSCRIPTION BY SEQUENCE-SPECIFIC DNA-BINDING PROTEINS</b>	<b>373</b>
RNA Splicing Shows Remarkable Plasticity	323	The Sequence of Nucleotides in the DNA Double Helix Can Be Read by Proteins	373
Spliceosome-Catalyzed RNA Splicing Probably Evolved from Self-splicing Mechanisms	324	Transcription Regulators Contain Structural Motifs That Can Read DNA Sequences	374
RNA-Processing Enzymes Generate the 3' End of Eukaryotic mRNAs	324	Dimerization of Transcription Regulators Increases Their Affinity and Specificity for DNA	375
Mature Eukaryotic mRNAs Are Selectively Exported from the Nucleus	325	Transcription Regulators Bind Cooperatively to DNA	378
Noncoding RNAs Are Also Synthesized and Processed in the Nucleus	327	Nucleosome Structure Promotes Cooperative Binding of Transcription Regulators	379
The Nucleolus Is a Ribosome-Producing Factory	329	Summary	380
The Nucleus Contains a Variety of Subnuclear Aggregates	331	<b>TRANSCRIPTION REGULATORS SWITCH GENES ON AND OFF</b>	<b>380</b>
Summary	333	The Tryptophan Repressor Switches Genes Off	380
<b>FROM RNA TO PROTEIN</b>	<b>333</b>	Repressors Turn Genes Off and Activators Turn Them On	381
An mRNA Sequence Is Decoded in Sets of Three Nucleotides	334	An Activator and a Repressor Control the <i>Lac</i> Operon	382
tRNA Molecules Match Amino Acids to Codons in mRNA	334	DNA Looping Can Occur During Bacterial Gene Regulation	383
tRNAs Are Covalently Modified Before They Exit from the Nucleus	336	Complex Switches Control Gene Transcription in Eukaryotes	384
Specific Enzymes Couple Each Amino Acid to Its Appropriate tRNA Molecule	336	A Eukaryotic Gene Control Region Consists of a Promoter Plus Many <i>cis</i> -Regulatory Sequences	384
Editing by tRNA Synthetases Ensures Accuracy	338	Eukaryotic Transcription Regulators Work in Groups	385
Amino Acids Are Added to the C-terminal End of a Growing Polypeptide Chain	339	Activator Proteins Promote the Assembly of RNA Polymerase at the Start Point of Transcription	386
The RNA Message Is Decoded in Ribosomes	340	Eukaryotic Transcription Activators Direct the Modification of Local Chromatin Structure	386
Elongation Factors Drive Translation Forward and Improve Its Accuracy	343	Transcription Activators Can Promote Transcription by Releasing RNA Polymerase from Promoters	388
Many Biological Processes Overcome the Inherent Limitations of Complementary Base-Pairing	345	Transcription Activators Work Synergistically	388
Accuracy in Translation Requires an Expenditure of Free Energy	345	Eukaryotic Transcription Repressors Can Inhibit Transcription in Several Ways	389
The Ribosome Is a Ribozyme	346	Insulator DNA Sequences Prevent Eukaryotic Transcription	
Nucleotide Sequences in mRNA Signal Where to Start Protein Synthesis	347	Regulators from Influencing Distant Genes	391
Stop Codons Mark the End of Translation	348	Summary	392



**MOLECULAR GENETIC MECHANISMS THAT CREATE AND MAINTAIN SPECIALIZED CELL TYPES** 392

Complex Genetic Switches That Regulate *Drosophila* Development Are Built Up from Smaller Molecules 392

The *Drosophila Eve* Gene Is Regulated by Combinatorial Controls 394

Transcription Regulators Are Brought Into Play by Extracellular Signals 395

Combinatorial Gene Control Creates Many Different Cell Types 396

Specialized Cell Types Can Be Experimentally Reprogrammed to Become Pluripotent Stem Cells 398

Combinations of Master Transcription Regulators Specify Cell Types by Controlling the Expression of Many Genes 398

Specialized Cells Must Rapidly Turn Sets of Genes On and Off 399

Differentiated Cells Maintain Their Identity 400

Transcription Circuits Allow the Cell to Carry Out Logic Operations 402

Summary 404

**MEDIANISMS THAT REINFORCE CELL MEMORY IN PLANTS AND ANIMALS** 404

Patterns of DNA Methylation Can Be Inherited When Vertebrate Cells Divide 404

CG-Rich Islands Are Associated with Many Genes in Mammals 405

Genomic Imprinting Is Based on DNA Methylation 407

Chromosome-Wide Alterations in Chromatin Structure Can Be Inherited 409

Epigenetic Mechanisms Ensure That Stable Patterns of Gene Expression Can Be Transmitted to Daughter Cells 411

Summary 413

**POST-TRANSCRIPTIONAL CONTROLS** 413

Transcription Attenuation Causes the Premature Termination of Some RNA Molecules 414

Riboswitches Probably Represent Ancient Forms of Gene Control 414

Alternative RNA Splicing Can Produce Different Forms of a Protein from the Same Gene 415

The Definition of a Gene Has Been Modified Since the Discovery of Alternative RNA Splicing 416

A Change in the Site of RNA Transcript Cleavage and Poly-A Addition Can Change the C-terminus of a Protein 417

RNA Editing Can Change the Meaning of the RNA Message 418

RNA Transport from the Nucleus Can Be Regulated 419

Some mRNAs Are Localized to Specific Regions of the Cytosol 421

The 5' and 3' Untranslated Regions of mRNAs Control Their Translation 422

The Phosphorylation of an Initiation Factor Regulates Protein Synthesis Globally 423

Initiation at AUG Codons Upstream of the Translation Start Can Regulate Eukaryotic Translation Initiation 424

Internal Ribosome Entry Sites Provide Opportunities for Translational Control 425

Changes in mRNA Stability Can Regulate Gene Expression 426

Regulation of mRNA Stability Involves P-bodies and Stress Granules 427

Summary 428

**REGULATION OF GENE EXPRESSION BY NONCODING RNAs** 429

Small Noncoding RNA Transcripts Regulate Many Animal and Plant Genes Through RNA Interference 429

mRNAs Regulate mRNA Translation and Stability 429

RNA Interference Is Also Used as a Cell Defense Mechanism 431

RNA Interference Can Direct Heterochromatin Formation 432

siRNAs Protect the Germ Line from Transposable Elements 433

RNA Interference Has Become a Powerful Experimental Tool 433

Bacteria Use Small Noncoding RNAs to Protect Themselves from Viruses 433

Long Noncoding RNAs Have Diverse Functions in the Cell 435

Summary 436

Problems 436

References 438

**Chapter 8 Analyzing Cells, Molecules, and Systems** 439

**ISOLATING CELLS AND GROWING THEM IN CULTURE** 440

Cells Can Be Isolated from Tissues 440

Cells Can Be Grown in Culture 440

Eukaryotic Cell Lines Are a Widely Used Source of Homogeneous Cells 442

Hybridoma Cell Lines Are Factories That Produce Monoclonal Antibodies 444

Summary 445

**PURIFYING PROTEINS** 445

Cells Can Be Separated into Their Component Fractions 445

Cell Extracts Provide Accessible Systems to Study Cell Functions 447

Proteins Can Be Separated by Chromatography 448

Immunoprecipitation Is a Rapid Affinity Purification Method 449

Genetically Engineered Tags Provide an Easy Way to Purify Proteins 450

Purified Cell-free Systems Are Required for the Precise Dissection of Molecular Functions 451

Summary 451

**ANALYZING PROTEINS** 452

Proteins Can Be Separated by SDS Polyacrylamide-Gel Electrophoresis 452

Two-Dimensional Gel Electrophoresis Provides Greater Protein Separation 452

Specific Proteins Can Be Detected by Blotting with Antibodies 454

Hydrodynamic Measurements Reveal the Size and Shape of a Protein Complex 455

Mass Spectrometry Provides a Highly Sensitive Method for Identifying Unknown Proteins 455

Sets of Interacting Proteins Can Be Identified by Biochemical Methods 457

Optical Methods Can Monitor Protein Interactions 458

Protein Function Can Be Selectively Disrupted With Small Molecules 459

Protein Structure Can Be Determined Using X-Ray Diffraction 460

NMR Can Be Used to Determine Protein Structure in Solution 461

Protein Sequence and Structure Provide Clues About Protein Function 462

Summary 463

**ANALYZING AND MANIPULATING DNA** 463

Restriction Nucleases Cut Large DNA Molecules into Specific Fragments 464

Gel Electrophoresis Separates DNA Molecules of Different Sizes 465

Purified DNA Molecules Can Be Specifically Labeled with Radioisotopes or Chemical Markers *in vitro* 467

Genes Can Be Cloned Using Bacteria 467

An Entire Genome Can Be Represented in a DNA Library 469

Genomic and cDNA Libraries Have Different Advantages and Drawbacks 471

Hybridization Provides a Powerful, But Simple Way to Detect Specific Nucleotide Sequences 472

Genes Can Be Cloned *in vitro* Using PCR 473

PCR Is Also Used for Diagnostic and Forensic Applications 474

Both DNA and RNA Can Be Rapidly Sequenced 477

To Be Useful, Genome Sequences Must Be Annotated 477

DNA Cloning Allows Any Protein to be Produced in Large Amounts 483

Summary 484

**STUDYING GENE EXPRESSION AND FUNCTION** 485

Classical Genetics Begins by Disrupting a Cell Process by Random Mutagenesis 485

Genetic Screens Identify Mutants with Specific Abnormalities 488

Mutations Can Cause Loss or Gain of Protein Function 489

Complementation Tests Reveal Whether Two Mutations Are in the Same Gene or Different Genes 490

Gene Products Can Be Ordered in Pathways by Epistasis Analysis 490

Mutations Responsible for a Phenotype Can Be Identified Through DNA Analysis 491

Rapid and Cheap DNA Sequencing Has Revolutionized Human Genetic Studies 491

Linked Blocks of Polymorphisms Have Been Passed Down from Our Ancestors 492

Polymorphisms Can Aid the Search for Mutations Associated with Disease 493

Genomics Is Accelerating the Discovery of Rare Mutations That Predispose Us to Serious Disease 493

Reverse Genetics Begins with a Known Gene and Determines Which Cell Processes Require Its Function 494

Animals and Plants Can Be Genetically Altered 495



The Bacterial CRISPR System Has Been Adapted to Edit Genomes in a Wide Variety of Species	497	Superresolution Fluorescence Techniques Can Overcome Diffraction-Limited Resolution	549
Large Collections of Engineered Mutations Provide a Tool for Examining the Function of Every Gene in an Organism	498	Superresolution Can Also be Achieved Using Single-Molecule Localization Methods	551
RNA Interference Is a Simple and Rapid Way to Test Gene Function	499	Summary	554
Reporter Genes Reveal When and Where a Gene Is Expressed	501	<b>LOOKING AT CELLS AND MOLECULES IN THE ELECTRON MICROSCOPE</b>	<b>554</b>
<i>In situ</i> Hybridization Can Reveal the Location of mRNAs and Noncoding RNAs	502	The Electron Microscope Resolves the Fine Structure of the Cell	554
Expression of Individual Genes Can Be Measured Using Quantitative RT-PCR	502	Biological Specimens Require Special Preparation for Electron Microscopy	555
Analysis of mRNAs by Microarray or RNA-seq Provides a Snapshot of Gene Expression	503	Specific Macromolecules Can Be Localized by Immunogold Electron Microscopy	556
Genome-wide Chromatin Immunoprecipitation Identifies Sites on the Genome Occupied by Transcription Regulators	505	Different Views of a Single Object Can Be Combined to Give a Three-Dimensional Reconstruction	557
Ribosome Profiling Reveals Which mRNAs Are Being Translated in the Cell	505	Images of Surfaces Can Be Obtained by Scanning Electron Microscopy	558
Recombinant DNA Methods Have Revolutionized Human Health	506	Negative Staining and Cryoelectron Microscopy Both Allow Macromolecules to Be Viewed at High Resolution	559
Transgenic Plants Are Important for Agriculture	507	Multiple Images Can Be Combined to Increase Resolution	561
Summary	508	Summary	562
<b>MATHEMATICAL ANALYSIS OF CELL FUNCTIONS</b>	<b>509</b>	Problems	563
Regulatory Networks Depend on Molecular Interactions	509	References	564
Differential Equations Help Us Predict Transient Behavior	512		
Both Promoter Activity and Protein Degradation Affect the Rate of Change of Protein Concentration	513	<b>Chapter 10 Membrane Structure</b>	<b>565</b>
The Time Required to Reach Steady State Depends on Protein Lifetime	514	<b>THE LIPID BILAYER</b>	<b>566</b>
Quantitative Methods Are Similar for Transcription Repressors and Activators	514	Phosphoglycerides, Sphingolipids, and Sterols Are the Major Lipids in Cell Membranes	566
Negative Feedback Is a Powerful Strategy in Cell Regulation	515	Phospholipids Spontaneously Form Bilayers	568
Delayed Negative Feedback Can Induce Oscillations	516	The Lipid Bilayer Is a Two-dimensional Fluid	569
DNA Binding By a Repressor or an Activator Can Be Cooperative	516	The Fluidity of a Lipid Bilayer Depends on Its Composition Despite Their Fluidity, Lipid Bilayers Can Form Domains of Different Compositions	572
Positive Feedback Is Important for Switchlike Responses and Bistability	518	Lipid Droplets Are Surrounded by a Phospholipid Monolayer	573
Robustness Is an Important Characteristic of Biological Networks	520	The Asymmetry of the Lipid Bilayer Is Functionally Important	573
Two Transcription Regulators That Bind to the Same Gene Promoter Can Exert Combinatorial Control	520	Glycolipids Are Found on the Surface of All Eukaryotic Plasma Membranes	575
An Incoherent Feed-forward Interaction Generates Pulses	522	Summary	576
A Coherent Feed-forward Interaction Detects Persistent Inputs	522	<b>MEMBRANE PROTEINS</b>	<b>576</b>
The Same Network Can Behave Differently in Different Cells Due to Stochastic Effects	523	Membrane Proteins Can Be Associated with the Lipid Bilayer in Various Ways	576
Several Computational Approaches Can Be Used to Model the Reactions in Cells	524	Lipid Anchors Control the Membrane Localization of Some Signaling Proteins	577
Statistical Methods Are Critical For the Analysis of Biological Data	524	In Most Transmembrane Proteins, the Polypeptide Chain Crosses the Lipid Bilayer in an $\alpha$ -Helical Conformation	579
Summary	525	Transmembrane $\alpha$ Helices Often Interact with One Another	580
Problems	525	Some $\beta$ Barrels Form Large Channels	580
References	528	Many Membrane Proteins Are Glycosylated	582
		Membrane Proteins Can Be Solubilized and Purified in Detergents	583
<b>Chapter 9 Visualizing Cells</b>	<b>529</b>	Bacteriorhodopsin Is a Light-driven Proton ( $H^+$ ) Pump That Traverses the Lipid Bilayer as Seven $\alpha$ Helices	586
<b>LOOKING AT CELLS IN THE LIGHT MICROSCOPE</b>	<b>529</b>	Membrane Proteins Often Function as Large Complexes	588
The Light Microscope Can Resolve Details 0.2 $\mu m$ Apart	530	Many Membrane Proteins Diffuse in the Plane of the Membrane	588
Photon Noise Creates Additional Limits to Resolution When Light Levels Are Low	532	Cells Can Confine Proteins and Lipids to Specific Domains Within a Membrane	590
Living Cells Are Seen Clearly in a Phase-Contrast or a Differential-Interference-Contrast Microscope	533	The Cortical Cytoskeleton Gives Membranes Mechanical Strength and Restricts Membrane Protein Diffusion	591
Images Can Be Enhanced and Analyzed by Digital Techniques	534	Membrane-bending Proteins Deform Bilayers	593
Intact Tissues Are Usually Fixed and Sectioned Before Microscopy	535	Summary	594
Specific Molecules Can Be Located in Cells by Fluorescence Microscopy	536	Problems	595
Antibodies Can Be Used to Detect Specific Molecules	539	References	596
Imaging of Complex Three-Dimensional Objects Is Possible with the Optical Microscope	540		
The Confocal Microscope Produces Optical Sections by Excluding Out-of-Focus Light	540	<b>Chapter 11 Membrane Transport of Small Molecules and the Electrical Properties of Membranes</b>	<b>597</b>
Individual Proteins Can Be Fluorescently Tagged in Living Cells and Organisms	542	<b>PRINCIPLES OF MEMBRANE TRANSPORT</b>	<b>597</b>
Protein Dynamics Can Be Followed in Living Cells	543	Protein-Free Lipid Bilayers Are Impermeable to Ions	598
Light-Emitting Indicators Can Measure Rapidly Changing Intracellular Ion Concentrations	546	There Are Two Main Classes of Membrane Transport Proteins: Transporters and Channels	598
Single Molecules Can Be Visualized by Total Internal Reflection Fluorescence Microscopy	547	Active Transport Is Mediated by Transporters Coupled to an Energy Source	599
Individual Molecules Can Be Touched, Imaged, and Moved Using Atomic Force Microscopy	548	Summary	600
		<b>TRANSPORTERS AND ACTIVE MEMBRANE TRANSPORT</b>	<b>600</b>
		Active Transport Can Be Driven by Ion-Concentration Gradients	601



Transporters in the Plasma Membrane Regulate Cytosolic pH	604	Nuclear Import Receptors Bind to Both Nuclear Localization Signals and NPC Proteins	652
An Asymmetric Distribution of Transporters in Epithelial Cells Underlies the Transcellular Transport of Solutes	605	Nuclear Export Works Like Nuclear Import, But in Reverse	652
There Are Three Classes of ATP-Driven Pumps	606	The Ran GTPase Imposes Directionality on Transport Through NPCs	653
ATP-type ATPase Pumps Ca <sup>2+</sup> into the Sarcoplasmic Reticulum in Muscle Cells	606	Transport Through NPCs Can Be Regulated by Controlling Access to the Transport Machinery	654
The Plasma Membrane Na <sup>+</sup> -K <sup>+</sup> Pump Establishes Na <sup>+</sup> and K <sup>+</sup> Gradients Across the Plasma Membrane	607	During Mitosis the Nuclear Envelope Disassembles	656
ABC Transporters Constitute the Largest Family of Membrane Transport Proteins	609	Summary	657
Summary	611	<b>THE TRANSPORT OF PROTEINS INTO MITOCHONDRIA AND CHLOROPLASTS</b>	658
<b>CHANNELS AND THE ELECTRICAL PROPERTIES OF MEMBRANES</b>	611	Translocation into Mitochondria Depends on Signal Sequences and Protein Translocators	659
Aquaporins Are Permeable to Water But Impermeable to Ions	612	Mitochondrial Precursor Proteins Are Imported as Unfolded Polypeptide Chains	660
Ion Channels Are Ion-Selective and Fluctuate Between Open and Closed States	613	ATP Hydrolysis and a Membrane Potential Drive Protein Import into the Matrix Space	661
The Membrane Potential in Animal Cells Depends Mainly on K <sup>+</sup> Leak Channels and the K <sup>+</sup> Gradient Across the Plasma Membrane	615	Bacteria and Mitochondria Use Similar Mechanisms to Insert Porins into their Outer Membrane	662
The Resting Potential Decays Only Slowly When the Na <sup>+</sup> -K <sup>+</sup> Pump Is Stopped	615	Transport into the Inner Mitochondrial Membrane and Intermembrane Space Occurs Via Several Routes	663
The Three-Dimensional Structure of a Bacterial K <sup>+</sup> Channel Shows How an Ion Channel Can Work	617	Two Signal Sequences Direct Proteins to the Thylakoid Membrane in Chloroplasts	664
Mechanosensitive Channels Protect Bacterial Cells Against Extreme Osmotic Pressures	619	Summary	666
The Function of a Neuron Depends on Its Elongated Structure	620	<b>PEROXISOMES</b>	666
Voltage-Gated Cation Channels Generate Action Potentials in Electrically Excitable Cells	621	Peroxisomes Use Molecular Oxygen and Hydrogen Peroxide to Perform Oxidation Reactions	666
The Use of Channelrhodopsins Has Revolutionized the Study of Neural Circuits	623	A Short Signal Sequence Directs the Import of Proteins into Peroxisomes	667
Myelination Increases the Speed and Efficiency of Action Potential Propagation in Nerve Cells	625	Summary	669
Patch-Clamp Recording Indicates That Individual Ion Channels Open in an All-or-Nothing Fashion	626	<b>THE ENDOPLASMIC RETICULUM</b>	669
Voltage-Gated Cation Channels Are Evolutionarily and Structurally Related	626	The ER Is Structurally and Functionally Diverse	670
Different Neuron Types Display Characteristic Stable Firing Properties	627	Signal Sequences Were First Discovered in Proteins Imported into the Rough ER	672
Transmitter-Gated Ion Channels Convert Chemical Signals into Electrical Ones at Chemical Synapses	627	A Signal-Recognition Particle (SRP) Directs the ER Signal Sequence to a Specific Receptor in the Rough ER Membrane	673
Chemical Synapses Can Be Excitatory or Inhibitory	629	The Polypeptide Chain Passes Through an Aqueous Channel in the Translocator	675
The Acetylcholine Receptors at the Neuromuscular Junction Are Excitatory Transmitter-Gated Cation Channels	630	Translocation Across the ER Membrane Does Not Always Require Ongoing Polypeptide Chain Elongation	677
Neurons Contain Many Types of Transmitter-Gated Channels	631	In Single-Pass Transmembrane Proteins, a Single Internal ER Signal Sequence Remains in the Lipid Bilayer as a Membrane-spanning $\alpha$ Helix	677
Many Psychoactive Drugs Act at Synapses	631	Combinations of Start-Transfer and Stop-Transfer Signals Determine the Topology of Multipass Transmembrane Proteins	679
Neuromuscular Transmission Involves the Sequential Activation of Five Different Sets of Ion Channels	632	ER Tail-anchored Proteins Are Integrated into the ER Membrane by a Special Mechanism	682
Single Neurons Are Complex Computation Devices	633	Translocated Polypeptide Chains Fold and Assemble in the Lumen of the Rough ER	682
Neuronal Computation Requires a Combination of at Least Three Kinds of K <sup>+</sup> Channels	634	Most Proteins Synthesized in the Rough ER Are Glycosylated by the Addition of a Common N-Linked Oligosaccharide	683
Long-Term Potentiation (LTP) in the Mammalian Hippocampus Depends on Ca <sup>2+</sup> Entry Through NMDA-Receptor Channels	636	Oligosaccharides Are Used as Tags to Mark the State of Protein Folding	685
Summary	637	Improperly Folded Proteins Are Exported from the ER and Degraded in the Cytosol	685
Problems	638	Misfolded Proteins in the ER Activate an Unfolded Protein Response	686
References	640	Some Membrane Proteins Acquire a Covalently Attached Glycosylphosphatidylinositol (GPI) Anchor	688
<b>Chapter 12 Intracellular Compartments and Protein Sorting</b>	641	The ER Assembles Most Lipid Bilayers	689
<b>THE COMPARTMENTALIZATION OF CELLS</b>	641	Summary	691
All Eukaryotic Cells Have the Same Basic Set of Membrane-enclosed Organelles	641	Problems	692
Evolutionary Origins May Help Explain the Topological Relationships of Organelles	643	References	694
Proteins Can Move Between Compartments in Different Ways	645	<b>Chapter 13 Intracellular Membrane Traffic</b>	695
Signal Sequences and Sorting Receptors Direct Proteins to the Correct Cell Address	647	<b>THE MOLECULAR MECHANISMS OF MEMBRANE TRANSPORT AND THE MAINTENANCE OF COMPARTMENTAL DIVERSITY</b>	697
Most Organelles Cannot Be Constructed De Novo: They Require Information in the Organelle Itself	648	There Are Various Types of Coated Vesicles	697
Summary	649	The Assembly of a Clathrin Coat Drives Vesicle Formation	697
<b>THE TRANSPORT OF MOLECULES BETWEEN THE NUCLEUS AND THE CYTOSOL</b>	649	Adaptor Proteins Select Cargo into Clathrin-Coated Vesicles	698
Nuclear Pore Complexes Perforate the Nuclear Envelope	649	Phosphoinositides Mark Organelles and Membrane Domains	700
Nuclear Localization Signals Direct Nuclear Proteins to the Nucleus	650		



Membrane-Bending Proteins Help Deform the Membrane During Vesicle Formation	701	Secretory Vesicle Membrane Components Are Quickly Removed from the Plasma Membrane	746
Cytoplasmic Proteins Regulate the Pinching-Off and Uncoating of Coated Vesicles	701	Some Regulated Exocytosis Events Serve to Enlarge the Plasma Membrane	748
Monomeric GTPases Control Coat Assembly	703	Polarized Cells Direct Proteins from the <i>Trans</i> Golgi Network to the Appropriate Domain of the Plasma Membrane	748
Not All Transport Vesicles Are Spherical	704	Summary	750
Rab Proteins Guide Transport Vesicles to Their Target Membrane	705	Problems	750
Rab Cascades Can Change the Identity of an Organelle	707	References	752
SNAREs Mediate Membrane Fusion	708		
Interacting SNAREs Need to Be Pried Apart Before They Can Function Again	709	<b>Chapter 14 Energy Conversion: Mitochondria and Chloroplasts</b>	<b>753</b>
Summary	710		
<b>TRANSPORT FROM THE ER THROUGH THE GOLGI APPARATUS</b>	<b>710</b>	<b>THE MITOCHONDRION</b>	<b>755</b>
Proteins Leave the ER in COPII-Coated Transport Vesicles	711	The Mitochondrion Has an Outer Membrane and an Inner Membrane	757
Only Proteins That Are Properly Folded and Assembled Can Leave the ER	712	The Inner Membrane Cristae Contain the Machinery for Electron Transport and ATP Synthesis	758
Vesicular Tubular Clusters Mediate Transport from the ER to the Golgi Apparatus	712	The Citric Acid Cycle in the Matrix Produces NADH	758
The Retrieval Pathway to the ER Uses Sorting Signals	713	Mitochondria Have Many Essential Roles in Cellular Metabolism	759
Many Proteins Are Selectively Retained in the Compartments in Which They Function	714	A Chemiosmotic Process Couples Oxidation Energy to ATP Production	761
The Golgi Apparatus Consists of an Ordered Series of Compartments	715	The Energy Derived from Oxidation Is Stored as an Electrochemical Gradient	762
Oligosaccharide Chains Are Processed in the Golgi Apparatus	716	Summary	763
Proteoglycans Are Assembled in the Golgi Apparatus	718	<b>THE PROTON PUMPS OF THE ELECTRON-TRANSPORT CHAIN</b>	<b>763</b>
What Is the Purpose of Glycosylation?	719	The Redox Potential Is a Measure of Electron Affinities	763
Transport Through the Golgi Apparatus May Occur by Cisternal Maturation	720	Electron Transfers Release Large Amounts of Energy	764
Golgi Matrix Proteins Help Organize the Stack	721	Transition Metal Ions and Quinones Accept and Release Electrons Readily	764
Summary	722	NADH Transfers Its Electrons to Oxygen Through Three Large Enzyme Complexes Embedded in the Inner Membrane	766
<b>TRANSPORT FROM THE <i>TRANS</i> GOLGI NETWORK TO LYSOSOMES</b>	<b>722</b>	The NADH Dehydrogenase Complex Contains Separate Modules for Electron Transport and Proton Pumping	768
Lysosomes Are the Principal Sites of Intracellular Digestion	722	Cytochrome <i>c</i> Reductase Takes Up and Releases Protons on the Opposite Side of the Crista Membrane, Thereby Pumping Protons	768
Lysosomes Are Heterogeneous	723	The Cytochrome <i>c</i> Oxidase Complex Pumps Protons and Reduces O <sub>2</sub> Using a Catalytic Iron-Copper Center	770
Plant and Fungal Vacuoles Are Remarkably Versatile Lysosomes	724	The Respiratory Chain Forms a Supercomplex in the Crista Membrane	772
Multiple Pathways Deliver Materials to Lysosomes	725	Protons Can Move Rapidly Through Proteins Along Predefined Pathways	773
Autophagy Degrades Unwanted Proteins and Organelles	726	Summary	774
A Mannose 6-Phosphate Receptor Sorts Lysosomal Hydrolases in the <i>Trans</i> Golgi Network	727	<b>ATP PRODUCTION IN MITOCHONDRIA</b>	<b>774</b>
Defects in the GlcNAc Phosphotransferase Cause a Lysosomal Storage Disease in Humans	728	The Large Negative Value of $\Delta G$ for ATP Hydrolysis Makes ATP Useful to the Cell	774
Some Lysosomes and Multivesicular Bodies Undergo Exocytosis	729	The ATP Synthase Is a Nanomachine that Produces ATP by Rotary Catalysis	776
Summary	729	Proton-driven Turbines Are of Ancient Origin	777
<b>TRANSPORT INTO THE CELL FROM THE PLASMA MEMBRANE: ENDOCYTOSIS</b>	<b>730</b>	Mitochondrial Cristae Help to Make ATP Synthesis Efficient	778
Pinocytic Vesicles Form from Coated Pits in the Plasma Membrane	731	Special Transport Proteins Exchange ATP and ADP Through the Inner Membrane	779
Not All Pinocytic Vesicles Are Clathrin-Coated	731	Chemiosmotic Mechanisms First Arose in Bacteria	780
Cells Use Receptor-Mediated Endocytosis to Import Selected Extracellular Macromolecules	732	Summary	782
Specific Proteins Are Retrieved from Early Endosomes and Returned to the Plasma Membrane	734	<b>CHLOROPLASTS AND PHOTOSYNTHESIS</b>	<b>782</b>
Plasma Membrane Signaling Receptors are Down-Regulated by Degradation in Lysosomes	735	Chloroplasts Resemble Mitochondria But Have a Separate Thylakoid Compartment	782
Early Endosomes Mature into Late Endosomes	735	Chloroplasts Capture Energy from Sunlight and Use It to Fix Carbon	783
<i>ESCRT</i> Protein Complexes Mediate the Formation of Intraluminal Vesicles in Multivesicular Bodies	736	Carbon Fixation Uses ATP and NADPH to Convert CO <sub>2</sub> into Sugars	784
Recycling Endosomes Regulate Plasma Membrane Composition	737	Sugars Generated by Carbon Fixation Can Be Stored as Starch or Consumed to Produce ATP	785
Specialized Phagocytic Cells Can Ingest Large Particles	738	The Thylakoid Membranes of Chloroplasts Contain the Protein Complexes Required for Photosynthesis and ATP Generation	786
Summary	740	Chlorophyll-Protein Complexes Can Transfer Either Excitation Energy or Electrons	787
<b>TRANSPORT FROM THE <i>TRANS</i> GOLGI NETWORK TO THE CELL EXTERIOR: EXOCYTOSIS</b>	<b>741</b>	A Photosystem Consists of an Antenna Complex and a Reaction Center	788
Many Proteins and Lipids Are Carried Automatically from the <i>Trans</i> Golgi Network (TGN) to the Cell Surface	741	The Thylakoid Membrane Contains Two Different Photosystems Working in Series	789
Secretory Vesicles Bud from the <i>Trans</i> Golgi Network	742		
Precursors of Secretory Proteins Are Proteolytically Processed During the Formation of Secretory Vesicles	743		
Secretory Vesicles Wait Near the Plasma Membrane Until Signaled to Release Their Contents	744		
For Rapid Exocytosis, Synaptic Vesicles Are Primed at the Presynaptic Plasma Membrane	744		
Synaptic Vesicles Can Form Directly from Endocytic Vesicles	746		



Photosystem II Uses a Manganese Cluster to Withdraw Electrons From Water	790	Some G Proteins Signal Via Phospholipids	836
The Cytochrome <i>b<sub>6</sub>-f</i> Complex Connects Photosystem II to Photosystem I	791	Ca <sup>2+</sup> Functions as a Ubiquitous Intracellular Mediator	838
Photosystem I Carries Out the Second Charge-Separation Step in the Z Scheme	792	Feedback Generates Ca <sup>2+</sup> Waves and Oscillations	838
The Chloroplast ATP Synthase Uses the Proton Gradient Generated by the Photosynthetic Light Reactions to Produce ATP	793	Ca <sup>2+</sup> /Calmodulin-Dependent Protein Kinases Mediate Many Responses to Ca <sup>2+</sup> Signals	840
All Photosynthetic Reaction Centers Have Evolved From a Common Ancestor	793	Some G Proteins Directly Regulate Ion Channels	843
The Proton-Motive Force for ATP Production in Mitochondria and Chloroplasts Is Essentially the Same	794	Smell and Vision Depend on GPCRs That Regulate Ion Channels	843
Osmotic Mechanisms Evolved in Stages	794	Nitric Oxide Is a Gaseous Signaling Mediator That Passes Between Cells	846
By Providing an Inexhaustible Source of Reducing Power, Photosynthetic Bacteria Overcame a Major Evolutionary Obstacle	796	Second Messengers and Enzymatic Cascades Amplify Signals	848
The Photosynthetic Electron-Transport Chains of Cyanobacteria Produced Atmospheric Oxygen and Permitted New Life-Forms	796	GPCR Desensitization Depends on Receptor Phosphorylation	848
Summary	798	Summary	849
<b>THE GENETIC SYSTEMS OF MITOCHONDRIA AND CHLOROPLASTS</b>	<b>800</b>	<b>SIGNALING THROUGH ENZYME-COUPLED RECEPTORS</b>	<b>850</b>
The Genetic Systems of Mitochondria and Chloroplasts Resemble Those of Prokaryotes	800	Activated Receptor Tyrosine Kinases (RTKs) Phosphorylate Themselves	850
Over Time, Mitochondria and Chloroplasts Have Exported Most of Their Genes to the Nucleus by Gene Transfer	801	Phosphorylated Tyrosines on RTKs Serve as Docking Sites for Intracellular Signaling Proteins	852
The Fission and Fusion of Mitochondria Are Topologically Complex Processes	802	Proteins with SH2 Domains Bind to Phosphorylated Tyrosines	852
Animal Mitochondria Contain the Simplest Genetic Systems Known	803	The GTPase Ras Mediates Signaling by Most RTKs	854
Mitochondria Have a Relaxed Codon Usage and Can Have a Variant Genetic Code	804	Ras Activates a MAP Kinase Signaling Module	855
Chloroplasts and Bacteria Share Many Striking Similarities	806	Scaffold Proteins Help Prevent Cross-talk Between Parallel MAP Kinase Modules	857
Organelle Genes Are Maternally Inherited in Animals and Plants	807	Rho Family GTPases Functionally Couple Cell-Surface Receptors to the Cytoskeleton	858
Mutations in Mitochondrial DNA Can Cause Severe Inherited Diseases	807	PI 3-Kinase Produces Lipid Docking Sites in the Plasma Membrane	859
The Accumulation of Mitochondrial DNA Mutations Is a Contributor to Aging	808	The PI-3-Kinase–Akt Signaling Pathway Stimulates Animal Cells to Survive and Grow	860
Why Do Mitochondria and Chloroplasts Maintain a Costly Separate System for DNA Transcription and Translation?	808	RTKs and GPCRs Activate Overlapping Signaling Pathways	861
Summary	809	Some Enzyme-Coupled Receptors Associate with Cytoplasmic Tyrosine Kinases	862
Problems	809	Cytokine Receptors Activate the JAK–STAT Signaling Pathway	863
References	811	Protein Tyrosine Phosphatases Reverse Tyrosine Phosphorylations	864
<b>Chapter 15 Cell Signaling</b>	<b>813</b>	Signal Proteins of the TGFβ Superfamily Act Through Receptor Serine/Threonine Kinases and Smads	865
<b>PRINCIPLES OF CELL SIGNALING</b>	<b>813</b>	Summary	866
Extracellular Signals Can Act Over Short or Long Distances	814	<b>ALTERNATIVE SIGNALING ROUTES IN GENE REGULATION</b>	<b>867</b>
Extracellular Signal Molecules Bind to Specific Receptors	815	The Receptor Notch Is a Latent Transcription Regulatory Protein	867
Each Cell Is Programmed to Respond to Specific Combinations of Extracellular Signals	816	Wnt Proteins Bind to Frizzled Receptors and Inhibit the Degradation of β-Catenin	868
There Are Three Major Classes of Cell-Surface Receptor Proteins	818	Hedgehog Proteins Bind to Patched, Relieving Its Inhibition of Smoothened	871
Cell-Surface Receptors Relay Signals Via Intracellular Signaling Molecules	819	Many Stressful and Inflammatory Stimuli Act Through an NFκB-Dependent Signaling Pathway	873
Intracellular Signals Must Be Specific and Precise in a Noisy Cytoplasm	820	Nuclear Receptors Are Ligand-Modulated Transcription Regulators	874
Intracellular Signaling Complexes Form at Activated Receptors	822	Circadian Clocks Contain Negative Feedback Loops That Control Gene Expression	876
Molecular Interaction Domains Mediate Interactions Between Intracellular Signaling Proteins	822	Three Proteins in a Test Tube Can Reconstitute a Cyanobacterial Circadian Clock	878
The Relationship Between Signal and Response Varies in Different Signaling Pathways	824	Summary	879
The Speed of a Response Depends on the Turnover of Signaling Molecules	825	<b>SIGNALING IN PLANTS</b>	<b>880</b>
Cells Can Respond Abruptly to a Gradually Increasing Signal	827	Multicellularity and Cell Communication Evolved Independently in Plants and Animals	880
Positive Feedback Can Generate an All-or-None Response	828	Receptor Serine/Threonine Kinases Are the Largest Class of Cell-Surface Receptors in Plants	881
Negative Feedback Is a Common Motif in Signaling Systems	829	Ethylene Blocks the Degradation of Specific Transcription Regulatory Proteins in the Nucleus	881
Cells Can Adjust Their Sensitivity to a Signal	830	Regulated Positioning of Auxin Transporters Patterns Plant Growth	882
Summary	831	Phytochromes Detect Red Light, and Cryptochromes Detect Blue Light	883
<b>SIGNALING THROUGH G-PROTEIN-COUPLED RECEPTORS</b>	<b>832</b>	Summary	885
Timing: G Proteins Relay Signals From GPCRs	832	Problems	886
Some G Proteins Regulate the Production of Cyclic AMP	833	References	887
Cyclic-AMP-Dependent Protein Kinase (PKA) Mediates Most of the Effects of Cyclic AMP	834	<b>Chapter 16 The Cytoskeleton</b>	<b>889</b>
		<b>FUNCTION AND ORIGIN OF THE CYTOSKELETON</b>	<b>889</b>
		Cytoskeletal Filaments Adapt to Form Dynamic or Stable Structures	890
		The Cytoskeleton Determines Cellular Organization and Polarity	892
		Filaments Assemble from Protein Subunits That Impart Specific Physical and Dynamic Properties	893



Accessory Proteins and Motors Regulate Cytoskeletal Filaments	894	Cell Polarization Is Controlled by Members of the Rho Protein Family	955
Bacterial Cell Organization and Division Depend on Homologs of Eukaryotic Cytoskeletal Proteins	896	Extracellular Signals Can Activate the Three Rho Protein Family Members	958
Summary	898	External Signals Can Dictate the Direction of Cell Migration	958
<b>ACTIN AND ACTIN-BINDING PROTEINS</b>	<b>898</b>	Communication Among Cytoskeletal Elements Coordinates Whole-Cell Polarization and Locomotion	959
Actin Subunits Assemble Head-to-Tail to Create Flexible, Polar Filaments	898	Summary	960
Nucleation Is the Rate-Limiting Step in the Formation of Actin Filaments	899	Problems	960
Actin Filaments Have Two Distinct Ends That Grow at Different Rates	900	References	962
ATP Hydrolysis Within Actin Filaments Leads to Treadmilling at Steady State	901	<b>Chapter 17 The Cell Cycle</b>	<b>963</b>
The Functions of Actin Filaments Are Inhibited by Both Polymer-stabilizing and Polymer-destabilizing Chemicals	904	<b>OVERVIEW OF THE CELL CYCLE</b>	<b>963</b>
Actin-Binding Proteins Influence Filament Dynamics and Organization	904	The Eukaryotic Cell Cycle Usually Consists of Four Phases	964
Monomer Availability Controls Actin Filament Assembly	906	Cell-Cycle Control Is Similar in All Eukaryotes	965
Actin-Nucleating Factors Accelerate Polymerization and Generate Branched or Straight Filaments	906	Cell-Cycle Progression Can Be Studied in Various Ways	966
Actin-Filament-Binding Proteins Alter Filament Dynamics	907	Summary	967
Severing Proteins Regulate Actin Filament Depolymerization	909	<b>THE CELL-CYCLE CONTROL SYSTEM</b>	<b>967</b>
Higher-Order Actin Filament Arrays Influence Cellular Mechanical Properties and Signaling	911	The Cell-Cycle Control System Triggers the Major Events of the Cell Cycle	967
Bacteria Can Hijack the Host Actin Cytoskeleton	913	The Cell-Cycle Control System Depends on Cyclically Activated Cyclin-Dependent Protein Kinases (Cdks)	968
Summary	914	Cdk Activity Can Be Suppressed By Inhibitory Phosphorylation and Cdk Inhibitor Proteins (CKIs)	970
<b>MYOSIN AND ACTIN</b>	<b>915</b>	Regulated Proteolysis Triggers the Metaphase-to-Anaphase Transition	970
Actin-Based Motor Proteins Are Members of the Myosin Superfamily	915	Cell-Cycle Control Also Depends on Transcriptional Regulation	971
Myosin Generates Force by Coupling ATP Hydrolysis to Conformational Changes	916	The Cell-Cycle Control System Functions as a Network of Biochemical Switches	972
Sliding of Myosin II Along Actin Filaments Causes Muscles to Contract	916	Summary	974
A Sudden Rise in Cytosolic Ca <sup>2+</sup> Concentration Initiates Muscle Contraction	920	<b>S PHASE</b>	<b>974</b>
Heart Muscle Is a Precisely Engineered Machine	923	S-Cdk Initiates DNA Replication Once Per Cycle	974
Actin and Myosin Perform a Variety of Functions in Non-Muscle Cells	923	Chromosome Duplication Requires Duplication of Chromatin Structure	975
Summary	925	Cohesins Hold Sister Chromatids Together	977
<b>MICROTUBULES</b>	<b>925</b>	Summary	977
Microtubules Are Hollow Tubes Made of Protofilaments	926	<b>MITOSIS</b>	<b>978</b>
Microtubules Undergo Dynamic Instability	927	M-Cdk Drives Entry Into Mitosis	978
Microtubule Functions Are Inhibited by Both Polymer-stabilizing and Polymer-destabilizing Drugs	929	Dephosphorylation Activates M-Cdk at the Onset of Mitosis	978
A Protein Complex Containing $\gamma$ -Tubulin Nucleates Microtubules	929	Condensin Helps Configure Duplicated Chromosomes for Separation	979
Microtubules Emanate from the Centrosome in Animal Cells	930	The Mitotic Spindle Is a Microtubule-Based Machine	982
Microtubule-Binding Proteins Modulate Filament Dynamics and Organization	932	Microtubule-Dependent Motor Proteins Govern Spindle Assembly and Function	983
Microtubule Plus-End-Binding Proteins Modulate Microtubule Dynamics and Attachments	932	Multiple Mechanisms Collaborate in the Assembly of a Bipolar Mitotic Spindle	984
Tubulin-Sequestering and Microtubule-Severing Proteins Destabilize Microtubules	935	Centrosome Duplication Occurs Early in the Cell Cycle	984
Two Types of Motor Proteins Move Along Microtubules	936	M-Cdk Initiates Spindle Assembly in Prophase	985
Microtubules and Motors Move Organelles and Vesicles	938	The Completion of Spindle Assembly in Animal Cells Requires Nuclear-Envelope Breakdown	985
Construction of Complex Microtubule Assemblies Requires Microtubule Dynamics and Motor Proteins	940	Microtubule Instability Increases Greatly in Mitosis	986
Motile Cilia and Flagella Are Built from Microtubules and Dyneins	941	Mitotic Chromosomes Promote Bipolar Spindle Assembly	986
Primary Cilia Play Important Signaling Functions in Animal Cells	942	Kinetochores Attach Sister Chromatids to the Spindle	987
Summary	943	Bi-orientation Is Achieved by Trial and Error	988
<b>INTERMEDIATE FILAMENTS AND SEPTINS</b>	<b>944</b>	Multiple Forces Act on Chromosomes in the Spindle	990
Intermediate Filament Structure Depends on the Lateral Bundling and Twisting of Coiled-Coils	945	The APC/C Triggers Sister-Chromatid Separation and the Completion of Mitosis	992
Intermediate Filaments Impart Mechanical Stability to Animal Cells	946	Unattached Chromosomes Block Sister-Chromatid Separation: The Spindle Assembly Checkpoint	993
Linker Proteins Connect Cytoskeletal Filaments and Bridge the Nuclear Envelope	948	Chromosomes Segregate in Anaphase A and B	994
Septins Form Filaments That Regulate Cell Polarity	949	Segregated Chromosomes Are Packaged in Daughter Nuclei at Telophase	995
Summary	950	Summary	995
<b>CELL POLARIZATION AND MIGRATION</b>	<b>951</b>	<b>CYTOKINESIS</b>	<b>996</b>
Many Cells Can Crawl Across a Solid Substratum	951	Actin and Myosin II in the Contractile Ring Generate the Force for Cytokinesis	996
Actin Polymerization Drives Plasma Membrane Protrusion	951	Local Activation of RhoA Triggers Assembly and Contraction of the Contractile Ring	997
Lamellipodia Contain All of the Machinery Required for Cell Motility	953	The Microtubules of the Mitotic Spindle Determine the Plane of Animal Cell Division	997
Myosin Contraction and Cell Adhesion Allow Cells to Pull Themselves Forward	954	The Phragmoplast Guides Cytokinesis in Higher Plants	1000
		Membrane-Enclosed Organelles Must Be Distributed to Daughter Cells During Cytokinesis	1001



Some Cells Reposition Their Spindle to Divide Asymmetrically	1001	Members of the Immunoglobulin Superfamily Mediate	
Meiosis Can Occur Without Cytokinesis	1002	Ca <sup>2+</sup> -Independent Cell–Cell Adhesion	1055
The G <sub>1</sub> Phase Is a Stable State of Cdk Inactivity	1002	Summary	1056
Summary	1004	<b>THE EXTRACELLULAR MATRIX OF ANIMALS</b>	<b>1057</b>
<b>MEIOSIS</b>	<b>1004</b>	The Extracellular Matrix Is Made and Oriented by the Cells	
Meiosis Includes Two Rounds of Chromosome Segregation	1004	Within It	1057
Duplicated Homologs Pair During Meiotic Prophase	1006	Glycosaminoglycan (GAG) Chains Occupy Large Amounts of	
Homolog Pairing Culminates in the Formation of a Synaptonemal		Space and Form Hydrated Gels	1058
Complex	1006	Hyaluronan Acts as a Space Filler During Tissue Morphogenesis	
Homolog Segregation Depends on Several Unique Features		and Repair	1059
of Meiosis I	1008	Proteoglycans Are Composed of GAG Chains Covalently	
Crossing-Over Is Highly Regulated	1009	Linked to a Core Protein	1059
Meiosis Frequently Goes Wrong	1010	Collagens Are the Major Proteins of the Extracellular Matrix	1061
Summary	1010	Secreted Fibril-Associated Collagens Help Organize the Fibrils	1063
<b>CONTROL OF CELL DIVISION AND CELL GROWTH</b>	<b>1010</b>	Cells Help Organize the Collagen Fibrils They Secrete by	
Mitogens Stimulate Cell Division	1011	Exerting Tension on the Matrix	1064
Cells Can Enter a Specialized Nondividing State	1012	Elastin Gives Tissues Their Elasticity	1065
Mitogens Stimulate G <sub>1</sub> -Cdk and G <sub>1</sub> /S-Cdk Activities	1012	Fibronectin and Other Multidomain Glycoproteins Help	
DNA Damage Blocks Cell Division: The DNA Damage Response	1014	Organize the Matrix	1066
Many Human Cells Have a Built-In Limitation on the Number		Fibronectin Binds to Integrins	1067
of Times They Can Divide	1016	Tension Exerted by Cells Regulates the Assembly of	
Abnormal Proliferation Signals Cause Cell-Cycle Arrest or		Fibronectin Fibrils	1068
Apoptosis, Except in Cancer Cells	1016	The Basal Lamina Is a Specialized Form of Extracellular Matrix	1068
Cell Proliferation Is Accompanied by Cell Growth	1016	Laminin and Type IV Collagen Are Major Components of the	
Proliferating Cells Usually Coordinate Their Growth and Division	1018	Basal Lamina	1069
Summary	1018	Basal Laminae Have Diverse Functions	1070
Problems	1019	Cells Have to Be Able to Degrade Matrix, as Well as Make It	1072
References	1020	Matrix Proteoglycans and Glycoproteins Regulate the	
<b>Chapter 18 Cell Death</b>	<b>1021</b>	Activities of Secreted Proteins	1073
Apoptosis Eliminates Unwanted Cells	1021	Summary	1074
Apoptosis Depends on an Intracellular Proteolytic Cascade		<b>CELL–MATRIX JUNCTIONS</b>	<b>1074</b>
That Is Mediated by Caspases	1022	Integrins Are Transmembrane Heterodimers That Link the	
Cell-Surface Death Receptors Activate the Extrinsic Pathway		Extracellular Matrix to the Cytoskeleton	1075
of Apoptosis	1024	Integrin Defects Are Responsible for Many Genetic Diseases	1076
The Intrinsic Pathway of Apoptosis Depends on Mitochondria	1025	Integrins Can Switch Between an Active and an Inactive	
Bcl-2 Proteins Regulate the Intrinsic Pathway of Apoptosis	1025	Conformation	1077
AP-1 Controls Caspases	1029	Integrins Cluster to Form Strong Adhesions	1079
Extracellular Survival Factors Inhibit Apoptosis in Various Ways	1029	Extracellular Matrix Attachments Act Through Integrins to	
Phagocytes Remove the Apoptotic Cell	1030	Control Cell Proliferation and Survival	1079
Either Excessive or Insufficient Apoptosis Can Contribute to		Integrins Recruit Intracellular Signaling Proteins at Sites of	
Disease	1031	Cell–Matrix Adhesion	1079
Summary	1032	Cell–Matrix Adhesions Respond to Mechanical Forces	1080
Problems	1033	Summary	1081
References	1034	<b>THE PLANT CELL WALL</b>	<b>1081</b>
<b>Chapter 19 Cell Junctions and the Extracellular</b>	<b>1035</b>	The Composition of the Cell Wall Depends on the Cell Type	1082
<b>Matrix</b>		The Tensile Strength of the Cell Wall Allows Plant Cells to	
<b>CELL–CELL JUNCTIONS</b>	<b>1038</b>	Develop Turgor Pressure	1083
Cadherins Form a Diverse Family of Adhesion Molecules	1038	The Primary Cell Wall Is Built from Cellulose Microfibrils	
Cadherins Mediate Homophilic Adhesion	1038	Interwoven with a Network of Pectic Polysaccharides	1083
Cadherin-Dependent Cell–Cell Adhesion Guides the		Oriented Cell Wall Deposition Controls Plant Cell Growth	1085
Organization of Developing Tissues	1040	Microtubules Orient Cell Wall Deposition	1086
Epithelial–Mesenchymal Transitions Depend on Control of		Summary	1087
Cadherins	1042	Problems	1087
Cadherins Link Classical Cadherins to the Actin Cytoskeleton	1042	References	1089
Adherens Junctions Respond to Forces Generated by the Actin		<b>Chapter 20 Cancer</b>	<b>1091</b>
Cytoskeleton	1042	<b>CANCER AS A MICROEVOLUTIONARY PROCESS</b>	<b>1091</b>
Tissue Remodeling Depends on the Coordination of Actin-		Cancer Cells Bypass Normal Proliferation Controls and	
Mediated Contraction With Cell–Cell Adhesion	1043	Colonize Other Tissues	1092
Diosmines Give Epithelia Mechanical Strength	1045	Most Cancers Derive from a Single Abnormal Cell	1093
Tight Junctions Form a Seal Between Cells and a Fence		Cancer Cells Contain Somatic Mutations	1094
Between Plasma Membrane Domains	1047	A Single Mutation Is Not Enough to Change a Normal Cell	
Tight Junctions Contain Strands of Transmembrane Adhesion		into a Cancer Cell	1094
Proteins	1047	Cancers Develop Gradually from Increasingly Aberrant Cells	1095
Snail-like Proteins Organize Junctional Protein Complexes	1049	Tumor Progression Involves Successive Rounds of Random	
Gap Junctions Couple Cells Both Electrically and Metabolically	1050	Inherited Change Followed by Natural Selection	1096
A Gap Junction Connexon Is Made of Six Transmembrane		Human Cancer Cells Are Genetically Unstable	1097
Connexin Subunits	1051	Cancer Cells Display an Altered Control of Growth	1098
In Plants, Plasmodesmata Perform Many of the Same Functions		Cancer Cells Have an Altered Sugar Metabolism	1098
as Gap Junctions	1053	Cancer Cells Have an Abnormal Ability to Survive Stress and	
Selectins Mediate Transient Cell–Cell Adhesions in the		DNA Damage	1099
Bloodstream	1054	Human Cancer Cells Escape a Built-in Limit to Cell Proliferation	1099
		The Tumor Microenvironment Influences Cancer Development	1100



Cancer Cells Must Survive and Proliferate in a Foreign Environment	1101	Many Cancers May Be Treatable by Enhancing the Immune Response Against the Specific Tumor	1137
Many Properties Typically Contribute to Cancerous Growth	1103	Cancers Evolve Resistance to Therapies	1139
Summary	1103	Combination Therapies May Succeed Where Treatments with One Drug at a Time Fail	1139
<b>CANCER-CRITICAL GENES: HOW THEY ARE FOUND AND WHAT THEY DO</b>	<b>1104</b>	We Now Have the Tools to Devise Combination Therapies Tailored to the Individual Patient	1140
The Identification of Gain-of-Function and Loss-of-Function Cancer Mutations Has Traditionally Required Different Methods	1104	Summary	1141
Retroviruses Can Act as Vectors for Oncogenes That Alter Cell Behavior	1105	Problems	1141
Different Searches for Oncogenes Converged on the Same Gene— <i>Ras</i>	1106	References	1143
Genes Mutated in Cancer Can Be Made Overactive in Many Ways	1106	<b>Chapter 21 Development of Multicellular Organisms</b>	<b>1145</b>
Studies of Rare Hereditary Cancer Syndromes First Identified Tumor Suppressor Genes	1107	<b>OVERVIEW OF DEVELOPMENT</b>	<b>1147</b>
Both Genetic and Epigenetic Mechanisms Can Inactivate Tumor Suppressor Genes	1108	Conserved Mechanisms Establish the Basic Animal Body Plan	1147
Systematic Sequencing of Cancer Cell Genomes Has Transformed Our Understanding of the Disease	1109	The Developmental Potential of Cells Becomes Progressively Restricted	1148
Many Cancers Have an Extraordinarily Disrupted Genome	1111	Cell Memory Underlies Cell Decision-Making	1148
Many Mutations in Tumor Cells are Merely Passengers	1111	Several Model Organisms Have Been Crucial for Understanding Development	1148
About One Percent of the Genes in the Human Genome Are Cancer-Critical	1112	Genes Involved in Cell–Cell Communication and Transcriptional Control Are Especially Important for Animal Development	1149
Disruptions in a Handful of Key Pathways Are Common to Many Cancers	1113	Regulatory DNA Seems Largely Responsible for the Differences Between Animal Species	1149
Mutations in the PI3K/Akt/mTOR Pathway Drive Cancer Cells to Grow	1114	Small Numbers of Conserved Cell–Cell Signaling Pathways Coordinate Spatial Patterning	1150
Mutations in the p53 Pathway Enable Cancer Cells to Survive and Proliferate Despite Stress and DNA Damage	1115	Through Combinatorial Control and Cell Memory, Simple Signals Can Generate Complex Patterns	1150
Genome Instability Takes Different Forms in Different Cancers	1116	Morphogens Are Long-Range Inductive Signals That Exert Graded Effects	1151
Cancers of Specialized Tissues Use Many Different Routes to Target the Common Core Pathways of Cancer	1117	Lateral Inhibition Can Generate Patterns of Different Cell Types	1151
Studies Using Mice Help to Define the Functions of Cancer-Critical Genes	1117	Short-Range Activation and Long-Range Inhibition Can Generate Complex Cellular Patterns	1152
Cancers Become More and More Heterogeneous as They Progress	1118	Asymmetric Cell Division Can Also Generate Diversity	1153
The Changes in Tumor Cells That Lead to Metastasis Are Still Largely a Mystery	1119	Initial Patterns Are Established in Small Fields of Cells and Refined by Sequential Induction as the Embryo Grows	1153
A Small Population of Cancer Stem Cells May Maintain Many Tumors	1120	Developmental Biology Provides Insights into Disease and Tissue Maintenance	1154
The Cancer Stem-Cell Phenomenon Adds to the Difficulty of Curing Cancer	1121	Summary	1154
Colorectal Cancers Evolve Slowly Via a Succession of Visible Changes	1122	<b>MECHANISMS OF PATTERN FORMATION</b>	<b>1155</b>
A Few Key Genetic Lesions Are Common to a Large Fraction of Colorectal Cancers	1123	Different Animals Use Different Mechanisms to Establish Their Primary Axes of Polarization	1155
Some Colorectal Cancers Have Defects in DNA Mismatch Repair	1124	Studies in <i>Drosophila</i> Have Revealed the Genetic Control Mechanisms Underlying Development	1157
The Steps of Tumor Progression Can Often Be Correlated with Specific Mutations	1125	Egg-Polarity Genes Encode Macromolecules Deposited in the Egg to Organize the Axes of the Early <i>Drosophila</i> Embryo	1157
Summary	1126	Three Groups of Genes Control <i>Drosophila</i> Segmentation Along the A-P Axis	1159
<b>CANCER PREVENTION AND TREATMENT: PRESENT AND FUTURE</b>	<b>1127</b>	A Hierarchy of Gene Regulatory Interactions Subdivides the <i>Drosophila</i> Embryo	1159
Epidemiology Reveals That Many Cases of Cancer Are Preventable	1127	Egg-Polarity, Gap, and Pair-Rule Genes Create a Transient Pattern That Is Remembered by Segment-Polarity and <i>Hox</i> Genes	1160
Sensitive Assays Can Detect Those Cancer-Causing Agents that Damage DNA	1127	<i>Hox</i> Genes Permanently Pattern the A-P Axis	1162
Fifty Percent of Cancers Could Be Prevented by Changes in Lifestyle	1128	<i>Hox</i> Proteins Give Each Segment Its Individuality	1163
Viruses and Other Infections Contribute to a Significant Proportion of Human Cancers	1129	<i>Hox</i> Genes Are Expressed According to Their Order in the <i>Hox</i> Complex	1163
Cancers of the Uterine Cervix Can Be Prevented by Vaccination Against Human Papillomavirus	1131	Trithorax and Polycomb Group Proteins Enable the <i>Hox</i> Complexes to Maintain a Permanent Record of Positional Information	1164
Infectious Agents Can Cause Cancer in a Variety of Ways	1132	The D-V Signaling Genes Create a Gradient of the Transcription Regulator Dorsal	1164
The Search for Cancer Cures Is Difficult but Not Hopeless	1132	A Hierarchy of Inductive Interactions Subdivides the Vertebrate Embryo	1166
Traditional Therapies Exploit the Genetic Instability and Loss of Cell-Cycle Checkpoint Responses in Cancer Cells	1132	A Competition Between Secreted Signaling Proteins Patterns the Vertebrate Embryo	1168
New Drugs Can Kill Cancer Cells Selectively by Targeting Specific Mutations	1133	The Insect Dorsoventral Axis Corresponds to the Vertebrate Ventral-Dorsal Axis	1169
PARP Inhibitors Kill Cancer Cells That Have Defects in <i>Brca1</i> or <i>Brca2</i> Genes	1133	<i>Hox</i> Genes Control the Vertebrate A-P Axis	1169
Small Molecules Can Be Designed to Inhibit Specific Oncogenic Proteins	1135	Some Transcription Regulators Can Activate a Program That Defines a Cell Type or Creates an Entire Organ	1170
		Notch-Mediated Lateral Inhibition Refines Cellular Spacing Patterns	1171



Asymmetric Cell Divisions Make Sister Cells Different	1173	Ephrin–Eph Signaling Drives Segregation of the Different Gut Cell Types	1224
Differences in Regulatory DNA Explain Morphological Differences	1174	Notch Signaling Controls Gut Cell Diversification and Helps Maintain the Stem-Cell State	1224
Summary	1175	The Epidermal Stem-Cell System Maintains a Self-Renewing Waterproof Barrier	1225
<b>DEVELOPMENTAL TIMING</b>	<b>1176</b>	Tissue Renewal That Does Not Depend on Stem Cells: Insulin-Secreting Cells in the Pancreas and Hepatocytes in the Liver	1226
Molecular Lifetimes Play a Critical Part in Developmental Timing	1176	Some Tissues Lack Stem Cells and Are Not Renewable	1227
A Gene-Expression Oscillator Acts as a Clock to Control Vertebrate Segmentation	1177	Summary	1227
Intracellular Developmental Programs Can Help Determine the Time-Course of a Cell's Development	1179	<b>FIBROBLASTS AND THEIR TRANSFORMATIONS: THE CONNECTIVE-TISSUE CELL FAMILY</b>	<b>1228</b>
Cells Rarely Count Cell Divisions to Time Their Development	1180	Fibroblasts Change Their Character in Response to Chemical and Physical Signals	1228
MicroRNAs Often Regulate Developmental Transitions	1180	Osteoblasts Make Bone Matrix	1229
Hormonal Signals Coordinate the Timing of Developmental Transitions	1182	Bone Is Continually Remodeled by the Cells Within It	1230
Environmental Cues Determine the Time of Flowering	1182	Osteoclasts Are Controlled by Signals From Osteoblasts	1232
Summary	1184	Summary	1232
<b>MORPHOGENESIS</b>	<b>1184</b>	<b>GENESIS AND REGENERATION OF SKELETAL MUSCLE</b>	<b>1232</b>
Cell Migration Is Guided by Cues in the Cell's Environment	1185	Myoblasts Fuse to Form New Skeletal Muscle Fibers	1233
The Distribution of Migrant Cells Depends on Survival Factors	1186	Some Myoblasts Persist as Quiescent Stem Cells in the Adult	1234
Changing Patterns of Cell Adhesion Molecules Force Cells into New Arrangements	1187	Summary	1235
Repulsive Interactions Help Maintain Tissue Boundaries	1188	<b>BLOOD VESSELS, LYMPHATICS, AND ENDOTHELIAL CELLS</b>	<b>1235</b>
Groups of Similar Cells Can Perform Dramatic Collective Rearrangements	1188	Endothelial Cells Line All Blood Vessels and Lymphatics	1235
Planar Cell Polarity Helps Orient Cell Structure and Movement in Developing Epithelia	1189	Endothelial Tip Cells Pioneer Angiogenesis	1236
Interactions Between an Epithelium and Mesenchyme Generate Branching Tubular Structures	1190	Tissues Requiring a Blood Supply Release VEGF	1237
An Epithelium Can Bend During Development to Form a Tube or Inside	1192	Signals from Endothelial Cells Control Recruitment of Pericytes and Smooth Muscle Cells to Form the Vessel Wall	1238
Summary	1193	Summary	1238
<b>GROWTH</b>	<b>1193</b>	<b>A HIERARCHICAL STEM-CELL SYSTEM: BLOOD CELL FORMATION</b>	<b>1239</b>
The Proliferation, Death, and Size of Cells Determine Organism Size	1194	Red Blood Cells Are All Alike; White Blood Cells Can Be Grouped in Three Main Classes	1239
Animals and Organs Can Assess and Regulate Total Cell Mass	1194	The Production of Each Type of Blood Cell in the Bone Marrow Is Individually Controlled	1240
Intercellular Signals Stimulate or Inhibit Growth	1196	Bone Marrow Contains Multipotent Hematopoietic Stem Cells, Able to Give Rise to All Classes of Blood Cells	1242
Summary	1197	Commitment Is a Stepwise Process	1243
<b>NEURAL DEVELOPMENT</b>	<b>1198</b>	Divisions of Committed Progenitor Cells Amplify the Number of Specialized Blood Cells	1243
Neurons Are Assigned Different Characters According to the Time and Place of Their Birth	1199	Stem Cells Depend on Contact Signals From Stromal Cells	1244
The Growth Cone Pilots Axons Along Specific Routes Toward Their Targets	1201	Factors That Regulate Hematopoiesis Can Be Analyzed in Culture	1244
A Variety of Extracellular Cues Guide Axons to their Targets	1202	Erythropoiesis Depends on the Hormone Erythropoietin	1244
The Formation of Orderly Neural Maps Depends on Neuronal Specificity	1204	Multiple CSFs Influence Neutrophil and Macrophage Production	1245
Both Dendrites and Axonal Branches From the Same Neuron Avoid One Another	1206	The Behavior of a Hematopoietic Cell Depends Partly on Chance	1245
Target Tissues Release Neurotrophic Factors That Control Nerve Cell Growth and Survival	1208	Regulation of Cell Survival Is as Important as Regulation of Cell Proliferation	1246
Formation of Synapses Depends on Two-Way Communication Between Neurons and Their Target Cells	1209	Summary	1247
Synaptic Pruning Depends on Electrical Activity and Synaptic Signaling	1211	<b>REGENERATION AND REPAIR</b>	<b>1247</b>
Neurons That Fire Together Wire Together	1211	Planarian Worms Contain Stem Cells That Can Regenerate a Whole New Body	1247
Summary	1213	Some Vertebrates Can Regenerate Entire Organs	1248
Problems	1213	Stem Cells Can Be Used Artificially to Replace Cells That Are Diseased or Lost: Therapy for Blood and Epidermis	1249
References	1215	Neural Stem Cells Can Be Manipulated in Culture and Used to Repopulate the Central Nervous System	1250
<b>Chapter 22 Stem Cells and Tissue Renewal</b>	<b>1217</b>	Summary	1251
<b>STEM CELLS AND RENEWAL IN EPITHELIAL TISSUES</b>	<b>1217</b>	<b>CELL REPROGRAMMING AND PLURIPOTENT STEM CELLS</b>	<b>1251</b>
The Lining of the Small Intestine Is Continually Renewed Through Cell Proliferation in the Crypts	1218	Nuclei Can Be Reprogrammed by Transplantation into Foreign Cytoplasm	1252
Stem Cells of the Small Intestine Lie at or Near the Base of Each Crypt	1219	Reprogramming of a Transplanted Nucleus Involves Drastic Epigenetic Changes	1252
The Two Daughters of a Stem Cell Face a Choice	1219	Embryonic Stem (ES) Cells Can Generate Any Part of the Body	1253
Notch Signaling Maintains the Gut Stem-Cell Compartment	1220	A Core Set of Transcription Regulators Defines and Maintains the ES Cell State	1254
Stem Cells at the Crypt Base Are Multipotent, Giving Rise to the Full Range of Differentiated Intestinal Cell Types	1220	Fibroblasts Can Be Reprogrammed to Create Induced Pluripotent Stem Cells (iPS Cells)	1254
The Two Daughters of a Stem Cell Do Not Always Have to Become Different	1222	Reprogramming Involves a Massive Upheaval of the Gene Control System	1255
Prothymic Cells Create the Stem-Cell Niche	1222	An Experimental Manipulation of Factors that Modify Chromatin Can Increase Reprogramming Efficiencies	1256
A Single Lgr5-expressing Cell in Culture Can Generate an Entire Organized Crypt-Villus System	1223	ES and iPS Cells Can Be Guided to Generate Specific Adult Cell Types and Even Whole Organs	1256



Cells of One Specialized Type Can Be Forced to Transdifferentiate Directly Into Another	1258
ES and iPS Cells Are Useful for Drug Discovery and Analysis of Disease	1258
Summary	1260
Problems	1260
References	1262

## Chapter 23 Pathogens and Infection 1263

<b>INTRODUCTION TO PATHOGENS AND THE HUMAN MICROBIOTA</b>	<b>1263</b>
The Human Microbiota Is a Complex Ecological System That Is Important for Our Development and Health	1264
Pathogens Interact with Their Hosts in Different Ways	1264
Pathogens Can Contribute to Cancer, Cardiovascular Disease, and Other Chronic Illnesses	1265
Pathogens Can Be Viruses, Bacteria, or Eukaryotes	1266
Bacteria Are Diverse and Occupy a Remarkable Variety of Ecological Niches	1267
Bacterial Pathogens Carry Specialized Virulence Genes	1268
Bacterial Virulence Genes Encode Effector Proteins and Secretion Systems to Deliver Effector Proteins to Host Cells	1269
Fungal and Protozoan Parasites Have Complex Life Cycles Involving Multiple Forms	1271
All Aspects of Viral Propagation Depend on Host Cell Machinery	1273
Summary	1275
<b>CELL BIOLOGY OF INFECTION</b>	<b>1276</b>
Pathogens Overcome Epithelial Barriers to Infect the Host	1276
Pathogens That Colonize an Epithelium Must Overcome Its Protective Mechanisms	1276
Extracellular Pathogens Disturb Host Cells Without Entering Them	1277
Intracellular Pathogens Have Mechanisms for Both Entering and Leaving Host Cells	1278
Viruses Bind to Virus Receptors at the Host Cell Surface	1279
Viruses Enter Host Cells by Membrane Fusion, Pore Formation, or Membrane Disruption	1280
Bacteria Enter Host Cells by Phagocytosis	1281
Intracellular Eukaryotic Parasites Actively Invade Host Cells	1282
Some Intracellular Pathogens Escape from the Phagosome into the Cytosol	1284
Many Pathogens Alter Membrane Traffic in the Host Cell to Survive and Replicate	1284
Viruses and Bacteria Use the Host-Cell Cytoskeleton for Intracellular Movement	1286
Viruses Can Take Over the Metabolism of the Host Cell	1288
Pathogens Can Evolve Rapidly by Antigenic Variation	1289
Error-Prone Replication Dominates Viral Evolution	1291
Drug-Resistant Pathogens Are a Growing Problem	1291
Summary	1294
Problems	1294
References	1296

## Chapter 24 The Innate and Adaptive Immune Systems 1297

<b>THE INNATE IMMUNE SYSTEM</b>	<b>1298</b>
Epithelial Surfaces Serve as Barriers to Infection	1298
Pattern Recognition Receptors (PRRs) Recognize Conserved Features of Pathogens	1298
There Are Multiple Classes of PRRs	1299
Activated PRRs Trigger an Inflammatory Response at Sites of Infection	1300
Phagocytic Cells Seek, Engulf, and Destroy Pathogens	1301
Complement Activation Targets Pathogens for Phagocytosis or Lysis	1302
Virus-Infected Cells Take Drastic Measures to Prevent Viral Replication	1303
Natural Killer Cells Induce Virus-Infected Cells to Kill Themselves	1304
Dendritic Cells Provide the Link Between the Innate and Adaptive Immune Systems	1305
Summary	1305

<b>OVERVIEW OF THE ADAPTIVE IMMUNE SYSTEM</b>	<b>1307</b>
B Cells Develop in the Bone Marrow, T Cells in the Thymus	1308
Immunological Memory Depends On Both Clonal Expansion and Lymphocyte Differentiation	1309
Lymphocytes Continuously Recirculate Through Peripheral Lymphoid Organs	1311
Immunological Self-Tolerance Ensures That B and T Cells Do Not Attack Normal Host Cells and Molecules	1313
Summary	1315
<b>B CELLS AND IMMUNOGLOBULINS</b>	<b>1315</b>
B Cells Make Immunoglobulins (Igs) as Both Cell-Surface Antigen Receptors and Secreted Antibodies	1315
Mammals Make Five Classes of Igs	1316
Ig Light and Heavy Chains Consist of Constant and Variable Regions	1318
Ig Genes Are Assembled From Separate Gene Segments During B Cell Development	1319
Antigen-Driven Somatic Hypermutation Fine-Tunes Antibody Responses	1321
B Cells Can Switch the Class of Ig They Make	1322
Summary	1323
<b>T CELLS AND MHC PROTEINS</b>	<b>1324</b>
T Cell Receptors (TCRs) Are Ig-like Heterodimers	1325
Activated Dendritic Cells Activate Naïve T Cells	1326
T Cells Recognize Foreign Peptides Bound to MHC Proteins	1326
MHC Proteins Are the Most Polymorphic Human Proteins Known	1330
CD4 and CD8 Co-receptors on T Cells Bind to Invariant Parts of MHC Proteins	1331
Developing Thymocytes Undergo Negative and Positive Selection	1332
Cytotoxic T Cells Induce Infected Target Cells to Kill Themselves	1333
Effector Helper T Cells Help Activate Other Cells of the Innate and Adaptive Immune Systems	1335
Naïve Helper T Cells Can Differentiate Into Different Types of Effector T Cells	1335
Both T and B Cells Require Multiple Extracellular Signals For Activation	1336
Many Cell-Surface Proteins Belong to the Ig Superfamily	1338
Summary	1339
Problems	1340
References	1342

Glossary G:1

Index I:1

Tables T:1