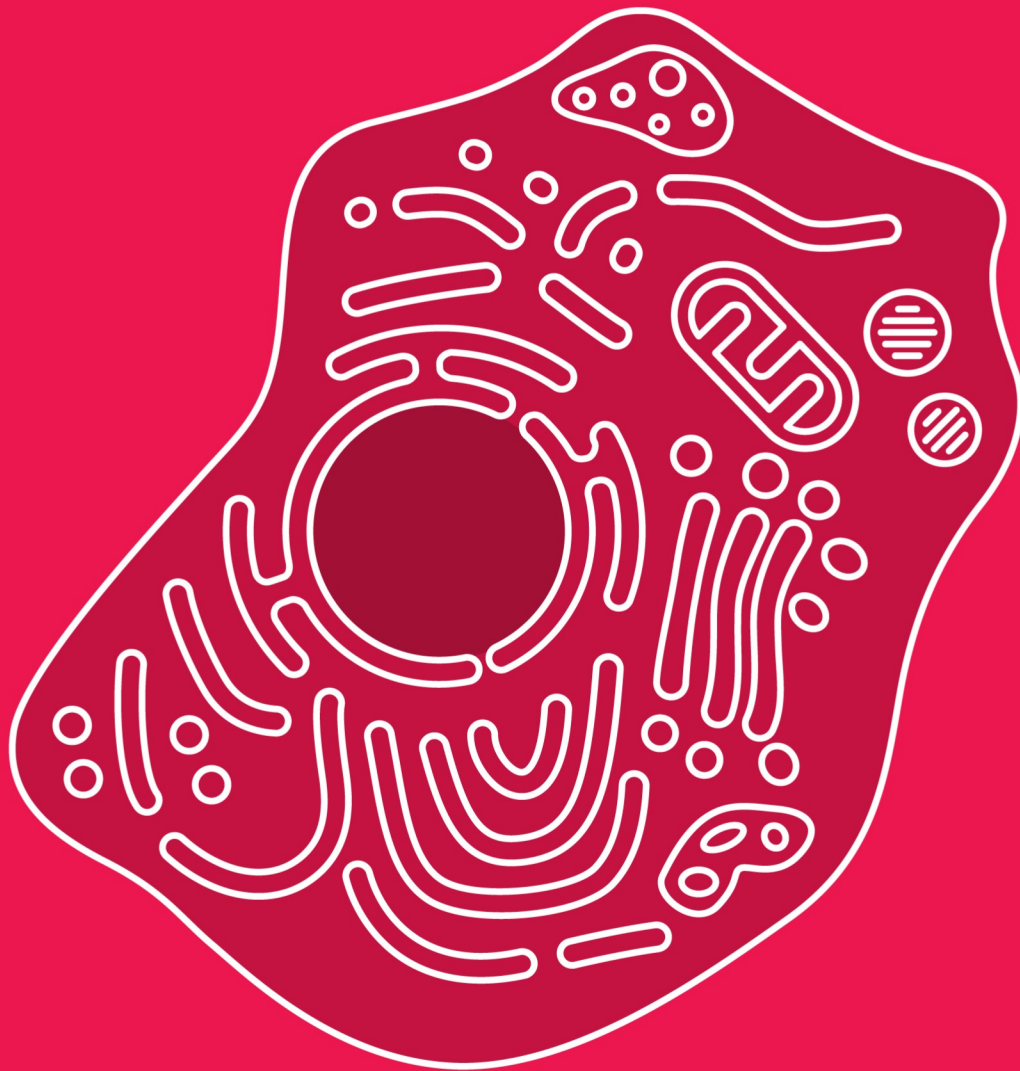


# Molecular Biology of **THE CELL**

Fifth Edition



ALBERTS   JOHNSON   LEWIS   RAFF   ROBERTS   WALTER

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# Preface

In many respects, we understand the structure of the universe better than the workings of living cells. Scientists can calculate the age of the Sun and predict when it will cease to shine, but we cannot explain how it is that a human being may live for eighty years but a mouse for only two. We know the complete genome sequences of these and many other species, but we still cannot predict how a cell will behave if we mutate a previously unstudied gene. Stars may be  $10^{43}$  times bigger, but cells are more complex, more intricately structured, and more astonishing products of the laws of physics and chemistry. Through heredity and natural selection, operating from the beginnings of life on Earth to the present day—that is, for about 20% of the age of the universe—living cells have been progressively refining and extending their molecular machinery, and recording the results of their experiments in the genetic instructions they pass on to their progeny.

With each edition of this book, we marvel at the new information that cell biologists have gathered in just a few years. But we are even more amazed and daunted at the sophistication of the mechanisms that we encounter. The deeper we probe into the cell, the more we realize how much remains to be understood. In the days of our innocence, working on the first edition, we hailed the identification of a single protein—a signal receptor, say—as a great step forward. Now we appreciate that each protein is generally part of a complex with many others, working together as a system, regulating one another's activities in subtle ways, and held in specific positions by binding to scaffold proteins that give the chemical factory a definite spatial structure. Genome sequencing has given us virtually complete molecular parts-lists for many different organisms; genetics and biochemistry have told us a great deal about what those parts are capable of individually and which ones interact with which others; but we have only the most primitive grasp of the dynamics of these biochemical systems, with all their interlocking control loops. Therefore, although there are great achievements to report, cell biologists face even greater challenges for the future.

In this edition, we have included new material on many topics, ranging from epigenetics, histone modifications, small RNAs, and comparative genomics, to genetic noise, cytoskeletal dynamics, cell-cycle control, apoptosis, stem cells, and novel cancer therapies. As in previous editions, we have tried above all to give readers a conceptual framework for the mass of information that we now have about cells. This means going beyond the recitation of facts. The goal is to learn how to put the facts to use—to reason, to predict, and to control the behavior of living systems.

To help readers on the way to an active understanding, we have for the first time incorporated end-of-chapter problems, written by John Wilson and Tim Hunt. These emphasize a quantitative approach and the art of reasoning from experiments. A companion volume, *Molecular Biology of the Cell, Fifth Edition: The Problems Book* (ISBN: 978-0-8153-4110-9), by the same authors, gives complete answers to these problems and also contains more than 1700 additional problems and solutions.

A further major adjunct to the main book is the attached Media DVD-ROM disc. This provides hundreds of movies and animations, including many that are new in this edition, showing cells and cellular processes in action and bringing the text to life; the disc now includes all the figures and tables from the main

book, pre-loaded into PowerPoint® presentations. Other ancillaries available for the book include a bank of test questions and lecture outlines, available to qualified instructors, and a set of 200 full-color overhead transparencies.

Different groups of readers will use different parts of the book. We anticipate that researchers, laboratories, and libraries will wish to have the full set of chapters in a single printed volume, as in the present Reference Edition. For those who prefer to have the core cell biology chapters in a somewhat more portable form, a Student Edition is also available, containing Chapters 1–20 as printed pages and Chapters 21–25 (on multicellular systems) in electronic (PDF) form on the accompanying disc.

Full details of the conventions adopted in the book are given in the Note to the Reader that follows this Preface. As explained there, we have taken a drastic approach in confronting the different rules for the writing of gene names in different species: throughout this book, we use the same style, regardless of species, and often in defiance of the usual species-specific conventions.

As always, we are indebted to many people. Full acknowledgments for scientific help are given separately, but we must here single out some exceptionally important contributions: Julie Theriot is almost entirely responsible for Chapters 16 (Cytoskeleton) and 24 (Pathogens, Infection, and Innate Immunity), and David Morgan likewise for Chapter 17 (Cell Cycle). Wallace Marshall and Laura Attardi provided substantial help with Chapters 8 and 20, respectively, as did Maynard Olson for the genomics section of Chapter 4, Xiaodong Wang for Chapter 18, and Nicholas Harberd for the plant section of Chapter 15.

We also owe a huge debt to the staff of Garland Publishing and others who helped convert writers' efforts into a polished final product. Denise Schanck directed the whole enterprise and shepherded the wayward authors along the road with wisdom, skill, and kindness. Nigel Orme put the artwork into its final form and supervised the visual aspects of the book, including the back cover, with his usual flair. Matthew Clements designed the book and its front cover. Emma Jeffcock laid out its pages with extraordinary speed and unflappable efficiency, dealing impeccably with innumerable corrections. Michael Morales managed the transformation of a mass of animations, video clips, and other materials into a user-friendly DVD-ROM. Eleanor Lawrence and Sherry Granum updated and enlarged the glossary. Jackie Harbor and Sigrid Masson kept us organized. Adam Sendroff kept us aware of our readers and their needs and reactions. Marjorie Anderson, Bruce Goatly, and Sherry Granum combed the text for obscurities, infelicities, and errors. We thank them all, not only for their professional skill and dedication and for efficiency far surpassing our own, but also for their unfailing helpfulness and friendship: they have made it a pleasure to work on the book.

Lastly, and with no less gratitude, we thank our spouses, families, friends and colleagues. Without their patient, enduring support, we could not have produced any of the editions of this book.



# Contents

<i>Special Features</i>	<i>viii</i>
<i>Detailed Contents</i>	<i>ix</i>
<i>Acknowledgments</i>	<i>xxvi</i>
<i>A Note to the Reader</i>	<i>xxxi</i>
<b>PART I</b>	<b>INTRODUCTION TO THE CELL</b>
1.	Cells and Genomes 1
2.	Cell Chemistry and Biosynthesis 45
3.	Proteins 125
<b>PART II</b>	<b>BASIC GENETIC MECHANISMS</b>
4.	DNA, Chromosomes, and Genomes 195
5.	DNA Replication, Repair, and Recombination 263
6.	How Cells Read the Genome: From DNA to Protein 329
7.	Control of Gene Expression 411
<b>PART III</b>	<b>METHODS</b>
8.	Manipulating Proteins, DNA, and RNA 501
9.	Visualizing Cells 579
<b>PART IV</b>	<b>INTERNAL ORGANIZATION OF THE CELL</b>
10.	Membrane Structure 617
11.	Membrane Transport of Small Molecules and the Electrical Properties of Membranes 651
12.	Intracellular Compartments and Protein Sorting 695
13.	Intracellular Vesicular Traffic 749
14.	Energy Conversion: Mitochondria and Chloroplasts 813
15.	Mechanisms of Cell Communication 879
16.	The Cytoskeleton 965
17.	The Cell Cycle 1053
18.	Apoptosis 1115
<b>PART V</b>	<b>CELLS IN THEIR SOCIAL CONTEXT</b>
19.	Cell Junctions, Cell Adhesion, and the Extracellular Matrix 1131
20.	Cancer 1205
21.	Sexual Reproduction: Meiosis, Germ Cells, and Fertilization 1269
22.	Development of Multicellular Organisms 1305
23.	Specialized Tissues, Stem Cells, and Tissue Renewal 1417
24.	Pathogens, Infection, and Innate Immunity 1485
25.	The Adaptive Immune System 1539
<i>Glossary</i>	<i>G–I</i>
<i>Index</i>	<i>I–I</i>
<i>Tables</i>	<i>The Genetic Code, Amino Acids T–I</i>

## Special Features

Table 1–1	Some Genomes That Have Been Completely Sequenced	p. 18
Table 1–2	The Numbers of Gene Families, Classified by Function, That Are Common to All Three Domains of the Living World	p. 24
Table 2–1	Covalent and Noncovalent Chemical Bonds	p. 53
Table 2–2	The Types of Molecules That Form a Bacterial Cell	p. 55
Table 2–3	Approximate Chemical Compositions of a Typical Bacterium and a Typical Mammalian Cell	p. 63
Table 2–4	Relationship Between the Standard Free-Energy Change, $\Delta G^\circ$ , and the Equilibrium Constant	p. 77
Panel 2–1	Chemical Bonds and Groups Commonly Encountered in Biological Molecules	pp. 106–107
Panel 2–2	Water and Its Influence on the Behavior of Biological Molecules	pp. 108–109
Panel 2–3	The Principal Types of Weak Noncovalent Bonds that Hold Macromolecules Together	pp. 110–111
Panel 2–4	An Outline of Some of the Types of Sugars Commonly Found in Cells	pp. 112–113
Panel 2–5	Fatty Acids and Other Lipids	pp. 114–115
Panel 2–6	A Survey of the Nucleotides	pp. 116–117
Panel 2–7	Free Energy and Biological Reactions	pp. 118–119
Panel 2–8	Details of the 10 Steps of Glycolysis	pp. 120–121
Panel 2–9	The Complete Citric Acid Cycle	pp. 122–123
Panel 3–1	The 20 Amino Acids Found in Proteins	pp. 128–129
Panel 3–2	Four Different Ways of Depicting a Small Protein, the SH2 Domain	pp. 132–133
Table 3–1	Some Common Types of Enzymes	p. 159
Panel 3–3	Some of the Methods Used to Study Enzymes	pp. 162–163
Table 4–1	Some Vital Statistics for the Human Genome	p. 206
Table 5–3	Three Major Classes of Transposable Elements	p. 318
Table 6–1	Principal Types of RNAs Produced in Cells	p. 336
Panel 8–1	Review of Classical Genetics	pp. 554–555
Table 10–1	Approximate Lipid Compositions of Different Cell Membranes	p. 624
Table 11–1	A Comparison of Ion Concentrations Inside and Outside a Typical Mammalian Cell	p. 652
Panel 11–2	The Derivation of the Nernst Equation	p. 670
Panel 11–3	Some Classical Experiments on the Squid Giant Axon	p. 679
Table 12–1	Relative Volumes Occupied by the Major Intracellular Compartments in a Liver Cell (Hepatocyte)	p. 697
Table 12–2	Relative Amounts of Membrane Types in Two Kinds of Eucaryotic Cells	p. 697
Table 14–1	Product Yields from the Oxidation of Sugars and Fats	p. 824
Panel 14–1	Redox Potentials	p. 830
Table 15–5	The Ras Superfamily of Monomeric GTPases	p. 926
Panel 16–2	The Polymerization of Actin and Tubulin	pp. 978–979
Panel 16–3	Accessory Proteins that Control the Assembly and Position of Cytoskeletal Filaments	pp. 994–995
Table 17–2	Summary of the Major Cell-Cycle Regulatory Proteins	p. 1066
Panel 17–1	The Principle Stages of M Phase (Mitosis and Cytokinesis) in an Animal Cell	pp. 1072–1073

# Detailed Contents

## Chapter 1 Cells and Genomes

### THE UNIVERSAL FEATURES OF CELLS ON EARTH

All Cells Store Their Hereditary Information in the Same Linear Chemical Code (DNA)	1
All Cells Replicate Their Hereditary Information by Templated Polymerization	2
All Cells Transcribe Portions of Their Hereditary Information into the Same Intermediary Form (RNA)	3
All Cells Use Proteins as Catalysts	4
All Cells Translate RNA into Protein in the Same Way	5
The Fragment of Genetic Information Corresponding to One Protein Is One Gene	6
Life Requires Free Energy	7
All Cells Function as Biochemical Factories Dealing with the Same Basic Molecular Building Blocks	8
All Cells Are Enclosed in a Plasma Membrane Across Which Nutrients and Waste Materials Must Pass	8
A Living Cell Can Exist with Fewer Than 500 Genes	9
Summary	10

### THE DIVERSITY OF GENOMES AND THE TREE OF LIFE

Cells Can Be Powered by a Variety of Free Energy Sources	11
Some Cells Fix Nitrogen and Carbon Dioxide for Others	12
The Greatest Biochemical Diversity Exists Among Prokaryotic Cells	13
The Tree of Life Has Three Primary Branches: Bacteria, Archaea, and Eucaryotes	14
Some Genes Evolve Rapidly; Others Are Highly Conserved	15
Most Bacteria and Archaea Have 1000–6000 Genes	16
New Genes Are Generated from Preexisting Genes	17
Gene Duplications Give Rise to Families of Related Genes Within a Single Cell	18
Genes Can Be Transferred Between Organisms, Both in the Laboratory and in Nature	19
Sex Results in Horizontal Exchanges of Genetic Information Within a Species	21
The Function of a Gene Can Often Be Deduced from Its Sequence	22
More Than 200 Gene Families Are Common to All Three Primary Branches of the Tree of Life	22
Mutations Reveal the Functions of Genes	23
Molecular Biologists Have Focused a Spotlight on <i>E. coli</i>	23
Summary	24

### GENETIC INFORMATION IN EUCARYOTES

Eucaryotic Cells May Have Originated as Predators	26
Modern Eucaryotic Cells Evolved from a Symbiosis	26
Eucaryotes Have Hybrid Genomes	27
Eucaryotic Genomes Are Big	30
Eucaryotic Genomes Are Rich in Regulatory DNA	30
The Genome Defines the Program of Multicellular Development	31
Many Eucaryotes Live as Solitary Cells: the Protists	31
A Yeast Serves as a Minimal Model Eucaryote	32
The Expression Levels of All The Genes of An Organism Can Be Monitored Simultaneously	33
To Make Sense of Cells, We Need Mathematics, Computers, and Quantitative Information	34
<i>Arabidopsis</i> Has Been Chosen Out of 300,000 Species As a Model Plant	35

1	The World of Animal Cells Is Represented By a Worm, a Fly, a Mouse, and a Human	36
1	Studies in <i>Drosophila</i> Provide a Key to Vertebrate Development	37
2	The Vertebrate Genome Is a Product of Repeated Duplication	38
2	Genetic Redundancy Is a Problem for Geneticists, But It Creates Opportunities for Evolving Organisms	39
3	The Mouse Serves as a Model for Mammals	39
3	Humans Report on Their Own Peculiarities	40
4	We Are All Different in Detail	41
5	Summary	42
6	Problems	42
7	References	44

## Chapter 2 Cell Chemistry and Biosynthesis

### THE CHEMICAL COMPONENTS OF A CELL

45	Cells Are Made From a Few Types of Atoms	45
46	The Outermost Electrons Determine How Atoms Interact	46
48	Covalent Bonds Form by the Sharing of Electrons	48
50	There Are Different Types of Covalent Bonds	50
51	An Atom Often Behaves as if It Has a Fixed Radius	51
51	Water Is the Most Abundant Substance in Cells	51
52	Some Polar Molecules Are Acids and Bases	52
53	Four Types of Noncovalent Attractions Help Bring Molecules Together in Cells	53
54	A Cell Is Formed from Carbon Compounds	54
55	Cells Contain Four Major Families of Small Organic Molecules	55
55	Sugars Provide an Energy Source for Cells and Are the Subunits of Polysaccharides	55
58	Fatty Acids Are Components of Cell Membranes, as Well as a Source of Energy	58
59	Amino Acids Are the Subunits of Proteins	59
61	Nucleotides Are the Subunits of DNA and RNA	61
62	The Chemistry of Cells Is Dominated by Macromolecules with Remarkable Properties	62
63	Noncovalent Bonds Specify Both the Precise Shape of a Macromolecule and its Binding to Other Molecules	63
65	Summary	65

### CATALYSIS AND THE USE OF ENERGY BY CELLS

66	Cell Metabolism Is Organized by Enzymes	66
66	Biological Order Is Made Possible by the Release of Heat Energy from Cells	66
68	Photosynthetic Organisms Use Sunlight to Synthesize Organic Molecules	68
70	Cells Obtain Energy by the Oxidation of Organic Molecules	70
71	Oxidation and Reduction Involve Electron Transfers	71
72	Enzymes Lower the Barriers That Block Chemical Reactions	72
74	How Enzymes Find Their Substrates: The Enormous Rapidity of Molecular Motions	74
75	The Free-Energy Change for a Reaction Determines Whether It Can Occur	75
76	The Concentration of Reactants Influences the Free-Energy Change and a Reaction's Direction	76
77	For Sequential Reactions, $\Delta G^\circ$ Values Are Additive	77
78	Activated Carrier Molecules Are Essential for Biosynthesis	78
79	The Formation of an Activated Carrier Is Coupled to an Energetically Favorable Reaction	79

ATP Is the Most Widely Used Activated Carrier Molecule	80	Molecular Tunnels Channel Substrates in Enzymes with Multiple Catalytic Sites	167
Energy Stored in ATP Is Often Harnessed to Join Two Molecules Together	81	Multienzyme Complexes Help to Increase the Rate of Cell Metabolism	168
NADH and NADPH Are Important Electron Carriers	82	The Cell Regulates the Catalytic Activities of its Enzymes	169
There Are Many Other Activated Carrier Molecules in Cells	83	Allosteric Enzymes Have Two or More Binding Sites That Interact	171
The Synthesis of Biological Polymers Is Driven by ATP Hydrolysis	84	Two Ligands Whose Binding Sites Are Coupled Must Reciprocally Affect Each Other's Binding	171
<i>Summary</i>	87	Symmetric Protein Assemblies Produce Cooperative Allosteric Transitions	172
<b>HOW CELLS OBTAIN ENERGY FROM FOOD</b>	<b>88</b>	The Allosteric Transition in Aspartate Transcarbamoylase Is Understood in Atomic Detail	173
Glycolysis Is a Central ATP-Producing Pathway	88	Many Changes in Proteins Are Driven by Protein Phosphorylation	175
Fermentations Produce ATP in the Absence of Oxygen	89	A Eucaryotic Cell Contains a Large Collection of Protein Kinases and Protein Phosphatases	176
Glycolysis Illustrates How Enzymes Couple Oxidation to Energy Storage	91	The Regulation of Cdk and Src Protein Kinases Shows How a Protein Can Function as a Microchip	177
Organisms Store Food Molecules in Special Reservoirs	91	Proteins That Bind and Hydrolyze GTP Are Ubiquitous Cellular Regulators	178
Most Animal Cells Derive Their Energy from Fatty Acids Between Meals	95	Regulatory Proteins Control the Activity of GTP-Binding Proteins by Determining Whether GTP or GDP Is Bound	179
Sugars and Fats Are Both Degraded to Acetyl CoA in Mitochondria	96	Large Protein Movements Can Be Generated From Small Ones	179
The Citric Acid Cycle Generates NADH by Oxidizing Acetyl Groups to CO <sub>2</sub>	97	Motor Proteins Produce Large Movements in Cells	181
Electron Transport Drives the Synthesis of the Majority of the ATP in Most Cells	100	Membrane-Bound Transporters Harness Energy to Pump Molecules Through Membranes	182
Amino Acids and Nucleotides Are Part of the Nitrogen Cycle	100	Proteins Often Form Large Complexes That Function as Protein Machines	184
Metabolism Is Organized and Regulated	101	Protein Machines with Interchangeable Parts Make Efficient Use of Genetic Information	184
<i>Summary</i>	103	The Activation of Protein Machines Often Involves Positioning Them at Specific Sites	185
<i>Problems</i>	103	Many Proteins Are Controlled by Multisite Covalent Modification	186
<i>References</i>	124	A Complex Network of Protein Interactions Underlies Cell Function	187
<b>Chapter 3 Proteins</b>	<b>125</b>	<i>Summary</i>	190
<b>THE SHAPE AND STRUCTURE OF PROTEINS</b>	<b>125</b>	<i>Problems</i>	191
The Shape of a Protein Is Specified by Its Amino Acid Sequence	125	<i>References</i>	193
Proteins Fold into a Conformation of Lowest Energy	130	<b>Chapter 4 DNA, Chromosomes, and Genomes</b>	<b>195</b>
The $\alpha$ Helix and the $\beta$ Sheet Are Common Folding Patterns	131	<b>THE STRUCTURE AND FUNCTION OF DNA</b>	<b>197</b>
Protein Domains Are Modular Units from which Larger Proteins Are Built	135	A DNA Molecule Consists of Two Complementary Chains of Nucleotides	197
Few of the Many Possible Polypeptide Chains Will Be Useful to Cells	136	The Structure of DNA Provides a Mechanism for Heredity	199
Proteins Can Be Classified into Many Families	137	In Eucaryotes, DNA Is Enclosed in a Cell Nucleus	200
Sequence Searches Can Identify Close Relatives	139	<i>Summary</i>	201
Some Protein Domains Form Parts of Many Different Proteins	140	<b>CHROMOSOMAL DNA AND ITS PACKAGING IN THE CHROMATIN FIBER</b>	<b>202</b>
Certain Pairs of Domains Are Found Together in Many Proteins	141	Eucaryotic DNA Is Packaged into a Set of Chromosomes	202
The Human Genome Encodes a Complex Set of Proteins, Revealing Much That Remains Unknown	142	Chromosomes Contain Long Strings of Genes	204
Larger Protein Molecules Often Contain More Than One Polypeptide Chain	142	The Nucleotide Sequence of the Human Genome Shows How Our Genes Are Arranged	205
Some Proteins Form Long Helical Filaments	143	Genome Comparisons Reveal Evolutionarily Conserved DNA Sequences	207
Many Protein Molecules Have Elongated, Fibrous Shapes	145	Chromosomes Exist in Different States Throughout the Life of a Cell	208
Many Proteins Contain a Surprisingly Large Amount of Unstructured Polypeptide Chain	146	Each DNA Molecule That Forms a Linear Chromosome Must Contain a Centromere, Two Telomeres, and Replication Origins	209
Covalent Cross-Linkages Often Stabilize Extracellular Proteins	147	DNA Molecules Are Highly Condensed in Chromosomes	210
Protein Molecules Often Serve as Subunits for the Assembly of Large Structures	148	Nucleosomes Are a Basic Unit of Eucaryotic Chromosome Structure	211
Many Structures in Cells Are Capable of Self-Assembly	149	The Structure of the Nucleosome Core Particle Reveals How DNA Is Packaged	212
Assembly Factors Often Aid the Formation of Complex Biological Structures	151	Nucleosomes Have a Dynamic Structure, and Are Frequently Subjected to Changes Catalyzed by ATP-Dependent Chromatin-Remodeling Complexes	215
<i>Summary</i>	152	Nucleosomes Are Usually Packed Together into a Compact Chromatin Fiber	216
<b>PROTEIN FUNCTION</b>	<b>152</b>	<i>Summary</i>	218
All Proteins Bind to Other Molecules	153	<b>THE REGULATION OF CHROMATIN STRUCTURE</b>	<b>219</b>
The Surface Conformation of a Protein Determines Its Chemistry	154	Some Early Mysteries Concerning Chromatin Structure	220
Sequence Comparisons Between Protein Family Members Highlight Crucial Ligand-Binding Sites	155		
Proteins Bind to Other Proteins Through Several Types of Interfaces	156		
Antibody Binding Sites Are Especially Versatile	156		
The Equilibrium Constant Measures Binding Strength	157		
Enzymes Are Powerful and Highly Specific Catalysts	158		
Substrate Binding Is the First Step in Enzyme Catalysis	159		
Enzymes Speed Reactions by Selectively Stabilizing Transition States	160		
Enzymes Can Use Simultaneous Acid and Base Catalysis	160		
Lysozyme Illustrates How an Enzyme Works	161		
Tightly Bound Small Molecules Add Extra Functions to Proteins	166		

Heterochromatin Is Highly Organized and Unusually Resistant to Gene Expression	220	DNA REPLICATION MECHANISMS	266
The Core Histones Are Covalently Modified at Many Different Sites	222	Base-Pairing Underlies DNA Replication and DNA Repair	266
Chromatin Acquires Additional Variety through the Site-Specific Insertion of a Small Set of Histone Variants	224	The DNA Replication Fork Is Asymmetrical	266
The Covalent Modifications and the Histone Variants Act in Concert to Produce a “Histone Code” That Helps to Determine Biological Function	224	The High Fidelity of DNA Replication Requires Several Proofreading Mechanisms	268
A Complex of Code-Reader and Code-Writer Proteins Can Spread Specific Chromatin Modifications for Long Distances Along a Chromosome	226	Only DNA Replication in the 5'-to-3' Direction Allows Efficient Error Correction	271
Barrier DNA Sequences Block the Spread of Reader–Writer Complexes and Thereby Separate Neighboring Chromatin Domains	227	A Special Nucleotide-Polymerizing Enzyme Synthesizes Short RNA Primer Molecules on the Lagging Strand	272
The Chromatin in Centromeres Reveals How Histone Variants Can Create Special Structures	228	Special Proteins Help to Open Up the DNA Double Helix in Front of the Replication Fork	273
Chromatin Structures Can Be Directly Inherited	230	A Sliding Ring Holds a Moving DNA Polymerase onto the DNA	273
Chromatin Structures Add Unique Features to Eucaryotic Chromosome Function	231	The Proteins at a Replication Fork Cooperate to Form a Replication Machine	275
Summary	233	A Strand-Directed Mismatch Repair System Removes Replication Errors That Escape from the Replication Machine	276
THE GLOBAL STRUCTURE OF CHROMOSOMES	233	DNA Topoisomerases Prevent DNA Tangling During Replication	278
Chromosomes Are Folded into Large Loops of Chromatin	234	DNA Replication Is Fundamentally Similar in Eucaryotes and Bacteria	280
Polytene Chromosomes Are Uniquely Useful for Visualizing Chromatin Structures	236	Summary	281
There Are Multiple Forms of Heterochromatin	238	THE INITIATION AND COMPLETION OF DNA REPLICATION IN CHROMOSOMES	281
Chromatin Loops Decondense When the Genes Within Them Are Expressed	239	DNA Synthesis Begins at Replication Origins	281
Chromatin Can Move to Specific Sites Within the Nucleus to Alter Their Gene Expression	239	Bacterial Chromosomes Typically Have a Single Origin of DNA Replication	282
Networks of Macromolecules Form a Set of Distinct Biochemical Environments inside the Nucleus	241	Eucaryotic Chromosomes Contain Multiple Origins of Replication	282
Mitotic Chromosomes Are Formed from Chromatin in Its Most Condensed State	243	In Eucaryotes DNA Replication Takes Place During Only One Part of the Cell Cycle	284
Summary	245	Different Regions on the Same Chromosome Replicate at Distinct Times in S Phase	285
HOW GENOMES EVOLVE	245	Highly Condensed Chromatin Replicates Late, While Genes in Less Condensed Chromatin Tend to Replicate Early	285
Genome Alterations Are Caused by Failures of the Normal Mechanisms for Copying and Maintaining DNA	246	Well-Defined DNA Sequences Serve as Replication Origins in a Simple Eucaryote, the Budding Yeast	286
The Genome Sequences of Two Species Differ in Proportion to the Length of Time That They Have Separately Evolved	247	A Large Multisubunit Complex Binds to Eucaryotic Origins of Replication	287
Phylogenetic Trees Constructed from a Comparison of DNA Sequences Trace the Relationships of All Organisms	248	The Mammalian DNA Sequences That Specify the Initiation of Replication Have Been Difficult to Identify	288
A Comparison of Human and Mouse Chromosomes Shows How the Structures of Genomes Diverge	249	New Nucleosomes Are Assembled Behind the Replication Fork	289
The Size of a Vertebrate Genome Reflects the Relative Rates of DNA Addition and DNA Loss in a Lineage	251	The Mechanisms of Eucaryotic Chromosome Duplication Ensure That Patterns of Histone Modification Can Be Inherited	290
We Can Reconstruct the Sequence of Some Ancient Genomes	251	Telomerase Replicates the Ends of Chromosomes	292
Multispecies Sequence Comparisons Identify Important DNA Sequences of Unknown Function	252	Telomere Length Is Regulated by Cells and Organisms	293
Accelerated Changes in Previously Conserved Sequences Can Help Decipher Critical Steps in Human Evolution	253	Summary	294
Gene Duplication Provides an Important Source of Genetic Novelty During Evolution	253	DNA REPAIR	295
Duplicated Genes Diverge	254	Without DNA Repair, Spontaneous DNA Damage Would Rapidly Change DNA Sequences	296
The Evolution of the Globin Gene Family Shows How DNA Duplications Contribute to the Evolution of Organisms	256	The DNA Double Helix Is Readily Repaired	296
Genes Encoding New Proteins Can Be Created by the Recombination of Exons	257	DNA Damage Can Be Removed by More Than One Pathway	297
Neutral Mutations Often Spread to Become Fixed in a Population, with a Probability that Depends on Population Size	257	Coupling DNA Repair to Transcription Ensures That the Cell's Most Important DNA Is Efficiently Repaired	299
A Great Deal Can Be Learned from Analyses of the Variation Among Humans	258	The Chemistry of the DNA Bases Facilitates Damage Detection	300
Summary	260	Special DNA Polymerases Are Used in Emergencies to Repair DNA	302
Problems	260	Double-Strand Breaks Are Efficiently Repaired	302
References	262	DNA Damage Delays Progression of the Cell Cycle	303
Chapter 5 DNA Replication, Repair, and Recombination	263	Summary	304
THE MAINTENANCE OF DNA SEQUENCES	263	HOMOLOGOUS RECOMBINATION	304
Mutation Rates Are Extremely Low	263	Homologous Recombination Has Many Uses in the Cell	304
Low Mutation Rates Are Necessary for Life as We Know It	265	Homologous Recombination Has Common Features in All Cells	305
Summary	265	DNA Base-Pairing Guides Homologous Recombination	305
		The RecA Protein and its Homologs Enable a DNA Single Strand to Pair with a Homologous Region of DNA Double Helix	307
		Branch Migration Can Either Enlarge Hetroduplex Regions or Release Newly Synthesized DNA as a Single Strand	308
		Homologous Recombination Can Flawlessly Repair Double-Stranded Breaks in DNA	308
		Cells Carefully Regulate the Use of Homologous Recombination in DNA Repair	310
		Holliday Junctions Are Often Formed During Homologous Recombination Events	311



Meiotic Recombination Begins with a Programmed Double-Strand Break	312
Homologous Recombination Often Results in Gene Conversion	314
Mismatch Proofreading Prevents Promiscuous Recombination Between Two Poorly Matched DNA Sequences	315
<i>Summary</i>	316

## TRANSPOSITION AND CONSERVATIVE SITE-SPECIFIC RECOMBINATION 316

Through Transposition, Mobile Genetic Elements Can Insert Into Any DNA Sequence	317
DNA-Only Transposons Move by Both Cut-and-Paste and Replicative Mechanisms	317
Some Viruses Use a Transposition Mechanism to Move Themselves into Host Cell Chromosomes	319
Retroviral-like Retrotransposons Resemble Retroviruses, but Lack a Protein Coat	320
A Large Fraction of the Human Genome Is Composed of Nonretroviral Retrotransposons	321
Different Transposable Elements Predominate in Different Organisms	322
Genome Sequences Reveal the Approximate Times that Transposable Elements Have Moved	323
Conservative Site-Specific Recombination Can Reversibly Rearrange DNA	323
Conservative Site-Specific Recombination Was Discovered in Bacteriophage $\lambda$	324
Conservative Site-Specific Recombination Can Be Used to Turn Genes On or Off	324
<i>Summary</i>	326
<i>Problems</i>	327
<i>References</i>	328

## Chapter 6 How Cells Read the Genome: From DNA to Protein 329

### FROM DNA TO RNA 331

Portions of DNA Sequence Are Transcribed into RNA	332
Transcription Produces RNA Complementary to One Strand of DNA	333
Cells Produce Several Types of RNA	335
Signals Encoded in DNA Tell RNA Polymerase Where to Start and Stop	336
Transcription Start and Stop Signals Are Heterogeneous in Nucleotide Sequence	338
Transcription Initiation in Eucaryotes Requires Many Proteins	339
RNA Polymerase II Requires General Transcription Factors	340
Polymerase II Also Requires Activator, Mediator, and Chromatin-Modifying Proteins	342
Transcription Elongation Produces Superhelical Tension in DNA	343
Transcription Elongation in Eucaryotes Is Tightly Coupled to RNA Processing	345
RNA Capping Is the First Modification of Eucaryotic Pre-mRNAs	346
RNA Splicing Removes Intron Sequences from Newly Transcribed Pre-mRNAs	347
Nucleotide Sequences Signal Where Splicing Occurs	349
RNA Splicing Is Performed by the Spliceosome	349
The Spliceosome Uses ATP Hydrolysis to Produce a Complex Series of RNA–RNA Rearrangements	351
Other Properties of Pre-mRNA and Its Synthesis Help to Explain the Choice of Proper Splice Sites	352
A Second Set of snRNPs Splice a Small Fraction of Intron Sequences in Animals and Plants	353
RNA Splicing Shows Remarkable Plasticity	355
Spliceosome-Catalyzed RNA Splicing Probably Evolved from Self-Splicing Mechanisms	355
RNA-Processing Enzymes Generate the 3' End of Eucaryotic mRNAs	357
Mature Eucaryotic mRNAs Are Selectively Exported from the Nucleus	358
Many Noncoding RNAs Are Also Synthesized and Processed in the Nucleus	360
The Nucleolus Is a Ribosome-Producing Factory	362
The Nucleus Contains a Variety of Subnuclear Structures	363
<i>Summary</i>	366

## FROM RNA TO PROTEIN 366

An mRNA Sequence Is Decoded in Sets of Three Nucleotide	367
tRNA Molecules Match Amino Acids to Codons in mRNA	368
tRNAs Are Covalently Modified Before They Exit from the Nucleus	369
Specific Enzymes Couple Each Amino Acid to Its Appropriate tRNA Molecule	370
Editing by RNA Synthetases Ensures Accuracy	371
Amino Acids Are Added to the C-terminal End of a Growing Polypeptide Chain	373
The RNA Message Is Decoded in Ribosomes	373
Elongation Factors Drive Translation Forward and Improve Its Accuracy	377
The Ribosome Is a Ribozyme	378
Nucleotide Sequences in mRNA Signal Where to Start Protein Synthesis	379
Stop Codons Mark the End of Translation	381
Proteins Are Made on Polyribosomes	381
There Are Minor Variations in the Standard Genetic Code	382
Inhibitors of Prokaryotic Protein Synthesis Are Useful as Antibiotics	383
Accuracy in Translation Requires the Expenditure of Free Energy	385
Quality Control Mechanisms Act to Prevent Translation of Damaged mRNAs	385
Some Proteins Begin to Fold While Still Being Synthesized	387
Molecular Chaperones Help Guide the Folding of Most Proteins	388
Exposed Hydrophobic Regions Provide Critical Signals for Protein Quality Control	390
The Proteasome Is a Compartmentalized Protease with Sequestered Active Sites	391
An Elaborate Ubiquitin-Conjugating System Marks Proteins for Destruction	393
Many Proteins Are Controlled by Regulated Destruction	395
Abnormally Folded Proteins Can Aggregate to Cause Destructive Human Diseases	396
There Are Many Steps From DNA to Protein	399
<i>Summary</i>	399

## THE RNA WORLD AND THE ORIGINS OF LIFE 400

Life Requires Stored Information	401
Polynucleotides Can Both Store Information and Catalyze Chemical Reactions	401
A Pre-RNA World May Predate the RNA World	402
Single-Stranded RNA Molecules Can Fold into Highly Elaborate Structures	403
Self-Replicating Molecules Undergo Natural Selection	404
How Did Protein Synthesis Evolve?	407
All Present-Day Cells Use DNA as Their Hereditary Material	408
<i>Summary</i>	408
<i>Problems</i>	409
<i>References</i>	410

## Chapter 7 Control of Gene Expression 411

### AN OVERVIEW OF GENE CONTROL 411

The Different Cell Types of a Multicellular Organism Contain the Same DNA	411
Different Cell Types Synthesize Different Sets of Proteins	412
External Signals Can Cause a Cell to Change the Expression of Its Genes	413
Gene Expression Can Be Regulated at Many of the Steps in the Pathway from DNA to RNA to Protein	415
<i>Summary</i>	415

### DNA-BINDING MOTIFS IN GENE REGULATORY PROTEINS 416

Gene Regulatory Proteins Were Discovered Using Bacterial Genetics	416
The Outside of the DNA Helix Can Be Read by Proteins	416
Short DNA Sequences Are Fundamental Components of Genetic Switches	418
Gene Regulatory Proteins Contain Structural Motifs That Can Read DNA Sequences	418
The Helix–Turn–Helix Motif Is One of the Simplest and Most Common DNA-Binding Motifs	419

Homeodomain Proteins Constitute a Special Class of Helix–Turn–Helix Proteins	420	Expression of a Critical Gene Regulatory Protein Can Trigger the Expression of a Whole Battery of Downstream Genes	463
There Are Several Types of DNA-Binding Zinc Finger Motifs	421	Combinatorial Gene Control Creates Many Different Cell Types in Eucaryotes	464
$\beta$ sheets Can Also Recognize DNA	422	A Single Gene Regulatory Protein Can Trigger the Formation of an Entire Organ	465
Some Proteins Use Loops That Enter the Major and Minor Groove to Recognize DNA	423	The Pattern of DNA Methylation Can Be Inherited When Vertebrate Cells Divide	467
The Leucine Zipper Motif Mediates Both DNA Binding and Protein Dimerization	423	Genomic Imprinting Is Based on DNA Methylation	468
Heterodimerization Expands the Repertoire of DNA Sequences That Gene Regulatory Proteins Can Recognize	424	CG-Rich Islands Are Associated with Many Genes in Mammals	470
The Helix–Loop–Helix Motif Also Mediates Dimerization and DNA Binding	425	Epigenetic Mechanisms Ensure That Stable Patterns of Gene Expression Can Be Transmitted to Daughter Cells	471
It Is Not Yet Possible to Predict the DNA Sequences Recognized by All Gene Regulatory Proteins	426	Chromosome-Wide Alterations in Chromatin Structure Can Be Inherited	473
A Gel-Mobility Shift Assay Readily Detects Sequence-Specific DNA-Binding Proteins	427	The Control of Gene Expression Is Intrinsically Noisy	476
DNA Affinity Chromatography Facilitates the Purification of Sequence-Specific DNA-Binding Proteins	428	Summary	477
The DNA Sequence Recognized by a Gene Regulatory Protein Can Be Determined Experimentally	429	<b>POST-TRANSCRIPTIONAL CONTROLS</b>	477
Phylogenetic Footprinting Identifies DNA Regulatory Sequences Through Comparative Genomics	431	Transcription Attenuation Causes the Premature Termination of Some RNA Molecules	477
Chromatin Immunoprecipitation Identifies Many of the Sites That Gene Regulatory Proteins Occupy in Living Cells	431	Riboswitches Might Represent Ancient Forms of Gene Control	478
Summary	432	Alternative RNA Splicing Can Produce Different Forms of a Protein from the Same Gene	479
<b>HOW GENETIC SWITCHES WORK</b>	432	The Definition of a Gene Has Had to Be Modified Since the Discovery of Alternative RNA Splicing	480
The Tryptophan Repressor Is a Simple Switch That Turns Genes On and Off in Bacteria	433	Sex Determination in <i>Drosophila</i> Depends on a Regulated Series of RNA Splicing Events	481
Transcriptional Activators Turn Genes On	435	A Change in the Site of RNA Transcript Cleavage and Poly-A Addition Can Change the C-terminus of a Protein	482
A Transcriptional Activator and a Transcriptional Repressor Control the <i>Lac</i> Operon	435	RNA Editing Can Change the Meaning of the RNA Message	483
DNA Looping Occurs During Bacterial Gene Regulation	437	RNA Transport from the Nucleus Can Be Regulated	485
Bacteria Use Interchangeable RNA Polymerase Subunits to Help Regulate Gene Transcription	438	Some mRNAs Are Localized to Specific Regions of the Cytoplasm	486
Complex Switches Have Evolved to Control Gene Transcription in Eucaryotes	439	The 5' and 3' Untranslated Regions of mRNAs Control Their Translation	488
A Eucaryotic Gene Control Region Consists of a Promoter Plus Regulatory DNA Sequences	440	The Phosphorylation of an Initiation Factor Regulates Protein Synthesis Globally	488
Eucaryotic Gene Activator Proteins Promote the Assembly of RNA Polymerase and the General Transcription Factors at the Startpoint of Transcription	441	Initiation at AUG Codons Upstream of the Translation Start Can Regulate Eucaryotic Translation Initiation	489
Eucaryotic Gene Activator Proteins Also Modify Local Chromatin Structure	442	Internal Ribosome Entry Sites Provide Opportunities for Translation Control	491
Gene Activator Proteins Work Synergistically	444	Changes in mRNA Stability Can Regulate Gene Expression	492
Eucaryotic Gene Repressor Proteins Can Inhibit Transcription in Various Ways	445	Cytoplasmic Poly-A Addition Can Regulate Translation	493
Eucaryotic Gene Regulatory Proteins Often Bind DNA Cooperatively	445	Small Noncoding RNA Transcripts Regulate Many Animal and Plant Genes	493
Complex Genetic Switches That Regulate <i>Drosophila</i> Development Are Built Up from Smaller Modules	447	RNA Interference Is a Cell Defense Mechanism	495
The <i>Drosophila Eve</i> Gene Is Regulated by Combinatorial Controls	448	RNA Interference Can Direct Heterochromatin Formation	496
Complex Mammalian Gene Control Regions Are Also Constructed from Simple Regulatory Modules	450	RNA Interference Has Become a Powerful Experimental Tool	497
Insulators Are DNA Sequences That Prevent Eucaryotic Gene Regulatory Proteins from Influencing Distant Genes	452	Summary	497
Gene Switches Rapidly Evolve	453	Problems	497
Summary	453	References	499
<b>THE MOLECULAR GENETIC MECHANISMS THAT CREATE SPECIALIZED CELL TYPES</b>	454	<b>Chapter 8 Manipulating Proteins, DNA, and RNA</b>	501
DNA Rearrangements Mediate Phase Variation in Bacteria	454	<b>ISOLATING CELLS AND GROWING THEM IN CULTURE</b>	501
A Set of Gene Regulatory Proteins Determines Cell Type in a Budding Yeast	455	Cells Can Be Isolated from Intact Tissues	502
Two Proteins That Repress Each Other's Synthesis Determine the Heritable State of Bacteriophage Lambda	457	Cells Can Be Grown in Culture	502
Simple Gene Regulatory Circuits Can Be Used to Make Memory Devices	458	Eucaryotic Cell Lines Are a Widely Used Source of Homogeneous Cells	505
Transcriptional Circuits Allow the Cell to Carry Out Logic Operations	459	Embryonic Stem Cells Could Revolutionize Medicine	505
Synthetic Biology Creates New Devices from Existing Biological Parts	460	Somatic Cell Nuclear Transplantation May Provide a Way to Generate Personalized Stem Cells	507
Circadian Clocks Are Based on Feedback Loops in Gene Regulation	460	Hybridoma Cell Lines Are Factories That Produce Monoclonal Antibodies	508
A Single Gene Regulatory Protein Can Coordinate the Expression of a Set of Genes	462	Summary	510
		<b>PURIFYING PROTEINS</b>	510
		Cells Can Be Separated into Their Component Fractions	510
		Cell Extracts Provide Accessible Systems to Study Cell Functions	511
		Proteins Can Be Separated by Chromatography	512
		Affinity Chromatography Exploits Specific Binding Sites on Proteins	513
		Genetically-Engineered Tags Provide an Easy Way to Purify Proteins	514

Purified Cell-Free Systems Are Required for the Precise Dissection of Molecular Functions	516	Large Collections of Tagged Knockouts Provide a Tool for Examining the Function of Every Gene in an Organism	569
Summary	516	RNA Interference Is a Simple and Rapid Way to Test Gene Function	571
<b>ANALYZING PROTEINS</b>	<b>517</b>	Reporter Genes and <i>In Situ</i> Hybridization Reveal When and Where a Gene Is Expressed	572
Proteins Can Be Separated by SDS Polyacrylamide-Gel Electrophoresis	517	Expression of Individual Genes Can Be Measured Using Quantitative RT-PCR	573
Specific Proteins Can Be Detected by Blotting with Antibodies	518	Microarrays Monitor the Expression of Thousands of Genes at Once	574
Mass Spectrometry Provides a Highly Sensitive Method for Identifying Unknown Proteins	519	Single-Cell Gene Expression Analysis Reveals Biological "Noise"	575
Two-Dimensional Separation Methods are Especially Powerful	521	Summary	576
Hydrodynamic Measurements Reveal the Size and Shape of a Protein Complex	522	Problems	576
Sets of Interacting Proteins Can Be Identified by Biochemical Methods	523	References	578
Protein-Protein Interactions Can Also Be Identified by a Two-Hybrid Technique in Yeast	523	<b>Chapter 9 Visualizing Cells</b>	<b>579</b>
Combining Data Derived from Different Techniques Produces Reliable Protein-Interaction Maps	524	<b>LOOKING AT CELLS IN THE LIGHT MICROSCOPE</b>	<b>579</b>
Optical Methods Can Monitor Protein Interactions in Real Time	524	The Light Microscope Can Resolve Details 0.2 $\mu\text{m}$ Apart	580
Some Techniques Can Monitor Single Molecules	526	Living Cells Are Seen Clearly in a Phase-Contrast or a Differential-Interference-Contrast Microscope	583
Protein Function Can Be Selectively Disrupted with Small Molecules	527	Images Can Be Enhanced and Analyzed by Digital Techniques	583
Protein Structure Can Be Determined Using X-Ray Diffraction	527	Intact Tissues Are Usually Fixed and Sectioned before Microscopy	585
NMR Can Be Used to Determine Protein Structure in Solution	529	Specific Molecules Can Be Located in Cells by Fluorescence Microscopy	586
Protein Sequence and Structure Provide Clues About Protein Function	530	Antibodies Can Be Used to Detect Specific Molecules	588
Summary	531	Imaging of Complex Three-Dimensional Objects Is Possible with the Optical Microscope	589
<b>ANALYZING AND MANIPULATING DNA</b>	<b>532</b>	The Confocal Microscope Produces Optical Sections by Excluding Out-of-Focus Light	590
Restriction Nucleases Cut Large DNA Molecules into Fragments	532	Fluorescent Proteins Can Be Used to Tag Individual Proteins in Living Cells and Organisms	592
Gel Electrophoresis Separates DNA Molecules of Different Sizes	534	Protein Dynamics Can Be Followed in Living Cells	593
Purified DNA Molecules Can Be Specifically Labeled with Radioisotopes or Chemical Markers <i>in vitro</i>	535	Light-Emitting Indicators Can Measure Rapidly Changing Intracellular Ion Concentrations	596
Nucleic Acid Hybridization Reactions Provide a Sensitive Way of Detecting Specific Nucleotide Sequences	535	Several Strategies Are Available by Which Membrane-Impermeant Substances Can Be Introduced into Cells	597
Northern and Southern Blotting Facilitate Hybridization with Electrophoretically Separated Nucleic Acid Molecules	538	Light Can Be Used to Manipulate Microscopic Objects As Well As to Image Them	598
Genes Can Be Cloned Using DNA Libraries	540	Single Molecules Can Be Visualized by Using Total Internal Reflection Fluorescence Microscopy	599
Two Types of DNA Libraries Serve Different Purposes	541	Individual Molecules Can Be Touched and Moved Using Atomic Force Microscopy	600
cDNA Clones Contain Uninterrupted Coding Sequences	544	Molecules Can Be Labeled with Radioisotopes	600
Genes Can Be Selectively Amplified by PCR	544	Radioisotopes Are Used to Trace Molecules in Cells and Organisms	602
Cells Can Be Used As Factories to Produce Specific Proteins	546	Summary	603
Proteins and Nucleic Acids Can Be Synthesized Directly by Chemical Reactions	548	<b>LOOKING AT CELLS AND MOLECULES IN THE ELECTRON MICROSCOPE</b>	<b>604</b>
DNA Can Be Rapidly Sequenced	548	The Electron Microscope Resolves the Fine Structure of the Cell	604
Nucleotide Sequences Are Used to Predict the Amino Acid Sequences of Proteins	550	Biological Specimens Require Special Preparation for the Electron Microscope	605
The Genomes of Many Organisms Have Been Fully Sequenced	551	Specific Macromolecules Can Be Localized by Immunogold Electron Microscopy	606
Summary	552	Images of Surfaces Can Be Obtained by Scanning Electron Microscopy	607
<b>STUDYING GENE EXPRESSION AND FUNCTION</b>	<b>553</b>	Metal Shadowing Allows Surface Features to Be Examined at High Resolution by Transmission Electron Microscopy	608
Classical Genetics Begins by Disrupting a Cell Process by Random Mutagenesis	553	Negative Staining and Cryoelectron Microscopy Both Allow Macromolecules to Be Viewed at High Resolution	610
Genetic Screens Identify Mutants with Specific Abnormalities	556	Multiple Images Can Be Combined to Increase Resolution	610
Mutations Can Cause Loss or Gain of Protein Function	557	Different Views of a Single Object Can Be Combined to Give a Three-Dimensional Reconstruction	612
Complementation Tests Reveal Whether Two Mutations Are in the Same Gene or Different Genes	558	Summary	612
Genes Can Be Ordered in Pathways by Epistasis Analysis	558	Problems	614
Genes Identified by Mutations Can Be Cloned	559	References	615
Human Genetics Presents Special Problems and Special Opportunities	560	<b>Chapter 10 Membrane Structure</b>	<b>617</b>
Human Genes Are Inherited in Haplotype Blocks, Which Can Aid in the Search for Mutations That Cause Disease	561	<b>THE LIPID BILAYER</b>	<b>617</b>
Complex Traits Are Influenced by Multiple Genes	563	Phosphoglycerides, Sphingolipids, and Sterols Are the Major Lipids in Cell Membranes	618
Reverse Genetics Begins with a Known Gene and Determines Which Cell Processes Require Its Function	563	Phospholipids Spontaneously Form Bilayers	620
Genes Can Be Re-Engineered in Several Ways	564		
Engineered Genes Can Be Inserted into the Germ Line of Many Organisms	565		
Animals Can Be Genetically Altered	566		
Transgenic Plants Are Important for Both Cell Biology and Agriculture	568		



The Lipid Bilayer Is a Two-Dimensional Fluid	621	Patch-Clamp Recording Indicates That Individual Gated Channels	680
The Fluidity of a Lipid Bilayer Depends on Its Composition	622	Open in an All-or-Nothing Fashion	
Despite Their Fluidity, Lipid Bilayers Can Form Domains of Different Compositions	624	Voltage-Gated Cation Channels Are Evolutionarily and Structurally Related	682
Lipid Droplets Are Surrounded by a Phospholipid Monolayer	625	Transmitter-Gated Ion Channels Convert Chemical Signals into Electrical Ones at Chemical Synapses	682
The Asymmetry of the Lipid Bilayer Is Functionally Important	626	Chemical Synapses Can Be Excitatory or Inhibitory	684
Glycolipids Are Found on the Surface of All Plasma Membranes	628	The Acetylcholine Receptors at the Neuromuscular Junction Are Transmitter-Gated Cation Channels	684
<i>Summary</i>	629	Transmitter-Gated Ion Channels Are Major Targets for Psychoactive Drugs	686
<b>MEMBRANE PROTEINS</b>	<b>629</b>	Neuromuscular Transmission Involves the Sequential Activation of Five Different Sets of Ion Channels	687
Membrane Proteins Can Be Associated with the Lipid Bilayer in Various Ways	629	Single Neurons Are Complex Computation Devices	688
Lipid Anchors Control the Membrane Localization of Some Signaling Proteins	630	Neuronal Computation Requires a Combination of at Least Three Kinds of K <sup>+</sup> Channels	689
In Most Transmembrane Proteins the Polypeptide Chain Crosses the Lipid Bilayer in an $\alpha$ -Helical Conformation	631	Long-Term Potentiation (LTP) in the Mammalian Hippocampus Depends on Ca <sup>2+</sup> Entry Through NMDA-Receptor Channels	691
Transmembrane $\alpha$ Helices Often Interact with One Another	632	<i>Summary</i>	692
Some $\beta$ Barrels Form Large Transmembrane Channels	634	<i>Problems</i>	693
Many Membrane Proteins Are Glycosylated	635	<i>References</i>	694
Membrane Proteins Can Be Solubilized and Purified in Detergents	636		
Bacteriorhodopsin Is a Light-Driven Proton Pump That Traverses the Lipid Bilayer as Seven $\alpha$ Helices	640		
Membrane Proteins Often Function as Large Complexes	642		
Many Membrane Proteins Diffuse in the Plane of the Membrane	642		
Cells Can Confine Proteins and Lipids to Specific Domains Within a Membrane	645		
The Cortical Cytoskeleton Gives Membranes Mechanical Strength and Restrict Membrane Protein Diffusion	646		
<i>Summary</i>	648		
<i>Problems</i>	648		
<i>References</i>	650		
<b>Chapter 11 Membrane Transport of Small Molecules and the Electrical Properties of Membranes</b>	<b>651</b>		
<b>PRINCIPLES OF MEMBRANE TRANSPORT</b>	<b>651</b>		
Protein-Free Lipid Bilayers Are Highly Impermeable to Ions	652		
There Are Two Main Classes of Membrane Transport Proteins: Transporters and Channels	652		
Active Transport Is Mediated by Transporters Coupled to an Energy Source	653		
<i>Summary</i>	654		
<b>TRANSPORTERS AND ACTIVE MEMBRANE TRANSPORT</b>	<b>654</b>		
Active Transport Can Be Driven by Ion Gradients	656		
Transporters in the Plasma Membrane Regulate Cytosolic pH	657		
An Asymmetric Distribution of Transporters in Epithelial Cells Underlies the Transcellular Transport of Solutes	658		
There Are Three Classes of ATP-Driven Pumps	659		
The Ca <sup>2+</sup> Pump Is the Best-Understood P-type ATPase	660		
The Plasma Membrane P-type Na <sup>+</sup> -K <sup>+</sup> Pump Establishes the Na <sup>+</sup> Gradient Across the Plasma Membrane	661		
ABC Transporters Constitute the Largest Family of Membrane Transport Proteins	663		
<i>Summary</i>	667		
<b>ION CHANNELS AND THE ELECTRICAL PROPERTIES OF MEMBRANES</b>	<b>667</b>		
Ion Channels Are Ion-Selective and Fluctuate Between Open and Closed States	667		
The Membrane Potential in Animal Cells Depends Mainly on K <sup>+</sup> Leak Channels and the K <sup>+</sup> Gradient Across the Plasma Membrane	669		
The Resting Potential Decays Only Slowly When the Na <sup>+</sup> -K <sup>+</sup> Pump Is Stopped	669		
The Three-Dimensional Structure of a Bacterial K <sup>+</sup> Channel Shows How an Ion Channel Can Work	671		
Aquaporins Are Permeable to Water But Impermeable to Ions	673		
The Function of a Neuron Depends on Its Elongated Structure	675		
Voltage-Gated Cation Channels Generate Action Potentials in Electrically Excitable Cells	676		
Myelination Increases the Speed and Efficiency of Action Potential Propagation in Nerve Cells	678		
		<b>Chapter 12 Intracellular Compartments and Protein Sorting</b>	<b>695</b>
		<b>THE COMPARTMENTALIZATION OF CELLS</b>	<b>695</b>
		All Eucaryotic Cells Have the Same Basic Set of Membrane-Enclosed Organelles	695
		Evolutionary Origins Explain the Topological Relationships of Organelles	697
		Proteins Can Move Between Compartments in Different Ways	699
		Signal Sequences Direct Proteins to the Correct Cell Address	701
		Most Organelles Cannot Be Constructed <i>De Novo</i> : They Require Information in the Organelle Itself	702
		<i>Summary</i>	704
		<b>THE TRANSPORT OF MOLECULES BETWEEN THE NUCLEUS AND THE CYTOSOL</b>	<b>704</b>
		Nuclear Pore Complexes Perforate the Nuclear Envelope	705
		Nuclear Localization Signals Direct Nuclear Proteins to the Nucleus	705
		Nuclear Import Receptors Bind to Both Nuclear Localization Signals and NPC proteins	707
		Nuclear Export Works Like Nuclear Import, But in Reverse	708
		The Ran GTPase Imposes Directionality on Transport Through NPCs	708
		Transport Through NPCs Can Be Regulated by Controlling Access to the Transport Machinery	709
		During Mitosis the Nuclear Envelope Disassembles	710
		<i>Summary</i>	712
		<b>THE TRANSPORT OF PROTEINS INTO MITOCHONDRIA AND CHLOROPLASTS</b>	<b>713</b>
		Translocation into Mitochondria Depends on Signal Sequences and Protein Translocators	713
		Mitochondrial Precursor Proteins Are Imported as Unfolded Polypeptide Chains	715
		ATP Hydrolysis and a Membrane Potential Drive Protein Import Into the Matrix Space	716
		Bacteria and Mitochondria Use Similar Mechanisms to Insert Porins into their Outer Membrane	717
		Transport Into the Inner Mitochondrial Membrane and Intermembrane Space Occurs Via Several Routes	717
		Two Signal Sequences Direct Proteins to the Thylakoid Membrane in Chloroplasts	719
		<i>Summary</i>	720
		<b>PEROXISOMES</b>	<b>721</b>
		Peroxisomes Use Molecular Oxygen and Hydrogen Peroxide to Perform Oxidative Reactions	721
		A Short Signal Sequence Directs the Import of Proteins into Peroxisomes	722
		<i>Summary</i>	723

<b>THE ENDOPLASMIC RETICULUM</b>	<b>723</b>	<b>TRANSPORT FROM THE TRANS GOLGI NETWORK TO LYOSOMES</b>	<b>779</b>
The ER Is Structurally and Functionally Diverse	724	Lysosomes Are the Principal Sites of Intracellular Digestion	779
Signal Sequences Were First Discovered in Proteins Imported into the Rough ER	726	Lysosomes Are Heterogeneous	780
A Signal-Recognition Particle (SRP) Directs ER Signal Sequences to a Specific Receptor in the Rough ER Membrane	727	Plant and Fungal Vacuoles Are Remarkably Versatile Lysosomes	781
The Polypeptide Chain Passes Through an Aqueous Pore in the Translocator	730	Multiple Pathways Deliver Materials to Lysosomes	782
Translocation Across the ER Membrane Does Not Always Require Ongoing Polypeptide Chain Elongation	731	A Mannose 6-Phosphate Receptor Recognizes Lysosomal Proteins in the <i>Trans</i> Golgi Network	783
In Single-Pass Transmembrane Proteins, a Single Internal ER Signal Sequence Remains in the Lipid Bilayer as a Membrane-Spanning $\alpha$ Helix	732	The M6P Receptor Shuttles Between Specific Membranes	784
Combinations of Start-Transfer and Stop-Transfer Signals Determine the Topology of Multipass Transmembrane Proteins	734	A Signal Patch in the Hydrolase Polypeptide Chain Provides the Cue for M6P Addition	785
Translocated Polypeptide Chains Fold and Assemble in the Lumen of the Rough ER	736	Defects in the GlcNAc Phosphotransferase Cause a Lysosomal Storage Disease in Humans	785
Most Proteins Synthesized in the Rough ER Are Glycosylated by the Addition of a Common <i>N</i> -Linked Oligosaccharide	736	Some Lysosomes Undergo Exocytosis	786
Oligosaccharides Are Used as Tags to Mark the State of Protein Folding	738	<i>Summary</i>	786
Improperly Folded Proteins Are Exported from the ER and Degraded in the Cytosol	739	<b>TRANSPORT INTO THE CELL FROM THE PLASMA MEMBRANE: ENDOCYTOSIS</b>	<b>787</b>
Misfolded Proteins in the ER Activate an Unfolded Protein Response	740	Specialized Phagocytic Cells Can Ingest Large Particles	787
Some Membrane Proteins Acquire a Covalently Attached Glycosylphosphatidylinositol (GPI) Anchor	742	Pinocytic Vesicles Form from Coated Pits in the Plasma Membrane	789
The ER Assembles Most Lipid Bilayers	743	Not All Pinocytic Vesicles Are Clathrin-Coated	790
<i>Summary</i>	745	Cells Use Receptor-Mediated Endocytosis to Import Selected Extracellular Macromolecules	791
<i>Problems</i>	746	Endocytosed Materials That Are Not Retrieved from Endosomes End Up in Lysosomes	792
<i>References</i>	748	Specific Proteins Are Retrieved from Early Endosomes and Returned to the Plasma Membrane	793
<b>Chapter 13 Intracellular Vesicular Traffic</b>	<b>749</b>	Multivesicular Bodies Form on the Pathway to Late Endosomes	795
<b>THE MOLECULAR MECHANISMS OF MEMBRANE TRANSPORT AND THE MAINTENANCE OF COMPARTMENTAL DIVERSITY</b>	<b>750</b>	Transcytosis Transfers Macromolecules Across Epithelial Cell Sheets	797
There Are Various Types of Coated Vesicles	751	Epithelial Cells Have Two Distinct Early Endosomal Compartments but a Common Late Endosomal Compartment	798
The Assembly of a Clathrin Coat Drives Vesicle Formation	754	<i>Summary</i>	799
Not All Coats Form Basket-like Structures	755	<b>TRANSPORT FROM THE TRANS GOLGI NETWORK TO THE CELL EXTERIOR: EXOCYTOSIS</b>	<b>799</b>
Phosphoinositides Mark Organelles and Membrane Domains	757	Many Proteins and Lipids Seem to Be Carried Automatically from the Golgi Apparatus to the Cell Surface	800
Cytoplasmic Proteins Regulate the Pinching-Off and Uncoating of Coated Vesicles	757	Secretory Vesicles Bud from the <i>Trans</i> Golgi Network	801
Monomeric GTPases Control Coat Assembly	758	Proteins Are Often Proteolytically Processed During the Formation of Secretory Vesicles	803
Not All Transport Vesicles Are Spherical	760	Secretory Vesicles Wait Near the Plasma Membrane Until Signaled to Release Their Contents	803
Rab Proteins Guide Vesicle Targeting	760	Regulated Exocytosis Can Be a Localized Response of the Plasma Membrane and Its Underlying Cytoplasm	804
SNAREs Mediate Membrane Fusion	762	Secretory Vesicle Membrane Components Are Quickly Removed from the Plasma Membrane	805
Interacting SNAREs Need to Be Pried Apart Before They Can Function Again	764	Some Regulated Exocytosis Events Serve to Enlarge the Plasma Membrane	805
Viral Fusion Proteins and SNAREs May Use Similar Fusion Mechanisms	764	Polarized Cells Direct Proteins from the <i>Trans</i> Golgi Network to the Appropriate Domain of the Plasma Membrane	805
<i>Summary</i>	766	Different Strategies Guide Membrane Proteins and Lipids Selectively to the Correct Plasma Membrane Domains	806
<b>TRANSPORT FROM THE ER THROUGH THE GOLGI APPARATUS</b>	<b>766</b>	Synaptic Vesicles Can Form Directly from Endocytic Vesicles	807
Proteins Leave the ER in COPII-Coated Transport Vesicles	767	<i>Summary</i>	809
Only Proteins That Are Properly Folded and Assembled Can Leave the ER	767	<i>Problems</i>	810
Vesicular Tubular Clusters Mediate Transport from the ER to the Golgi Apparatus	768	<i>References</i>	812
The Retrieval Pathway to the ER Uses Sorting Signals	769	<b>Chapter 14 Energy Conversion: Mitochondria and Chloroplasts</b>	<b>813</b>
Many Proteins Are Selectively Retained in the Compartments in Which They Function	771	<b>THE MITOCHONDRION</b>	<b>815</b>
The Golgi Apparatus Consists of an Ordered Series of Compartments	771	The Mitochondrion Contains an Outer Membrane, an Inner Membrane, and Two Internal Compartments	816
Oligosaccharide Chains Are Processed in the Golgi Apparatus	773	The Citric Acid Cycle Generates High-Energy Electrons	817
Proteoglycans Are Assembled in the Golgi Apparatus	775	A Chemiosmotic Process Converts Oxidation Energy into ATP	817
What Is the Purpose of Glycosylation?	776	NADH Transfers its Electrons to Oxygen Through Three Large Respiratory Enzyme Complexes	819
Transport Through the Golgi Apparatus May Occur by Vesicular Transport or Cisternal Maturation	777	As Electrons Move Along the Respiratory Chain, Energy Is Stored as an Electrochemical Proton Gradient Across the Inner Membrane	820
Golgi Matrix Proteins Help Organize the Stack	778	The Proton Gradient Drives ATP Synthesis	821
<i>Summary</i>	779		

The Proton Gradient Drives Coupled Transport Across the Inner Membrane	822	Mitochondria and Chloroplasts Have Diverse Genomes	859
Proton Gradients Produce Most of the Cell's ATP	822	Mitochondria and Chloroplasts Probably Both Evolved from Endosymbiotic Bacteria	859
Mitochondria Maintain a High ATP:ADP Ratio in Cells	823	Mitochondria Have a Relaxed Codon Usage and Can Have a Variant Genetic Code	861
A Large Negative Value of $\Delta G$ for ATP Hydrolysis Makes ATP Useful to the Cell	824	Animal Mitochondria Contain the Simplest Genetic Systems Known	862
ATP Synthase Can Function in Reverse to Hydrolyze ATP and Pump $H^+$	826	Some Organelle Genes Contain Introns	863
Summary	827	The Chloroplast Genome of Higher Plants Contains About 120 Genes	863
<b>ELECTRON-TRANSPORT CHAINS AND THEIR PROTON PUMPS</b>	<b>827</b>	Mitochondrial Genes Are Inherited by a Non-Mendelian Mechanism	864
Protons Are Unusually Easy to Move	827	Organelle Genes Are Maternally Inherited in Many Organisms	866
The Redox Potential Is a Measure of Electron Affinities	828	Petite Mutants in Yeasts Demonstrate the Overwhelming Importance of the Cell Nucleus for Mitochondrial Biogenesis	866
Electron Transfers Release Large Amounts of Energy	829	Mitochondria and Plastids Contain Tissue-Specific Proteins that Are Encoded in the Cell Nucleus	867
Spectroscopic Methods Identified Many Electron Carriers in the Respiratory Chain	829	Mitochondria Import Most of Their Lipids; Chloroplasts Make Most of Theirs	867
The Respiratory Chain Includes Three Large Enzyme Complexes Embedded in the Inner Membrane	831	Mitochondria May Contribute to the Aging of Cells and Organisms	868
An Iron–Copper Center in Cytochrome Oxidase Catalyzes Efficient $O_2$ Reduction	832	Why Do Mitochondria and Chloroplasts Have Their Own Genetic Systems?	868
Electron Transfers in the Inner Mitochondrial Membrane Are Mediated by Electron Tunneling during Random Collisions	834	Summary	870
A Large Drop in Redox Potential Across Each of the Three Respiratory Enzyme Complexes Provides the Energy for $H^+$ Pumping	835	<b>THE EVOLUTION OF ELECTRON-TRANSPORT CHAINS</b>	<b>870</b>
The $H^+$ Pumping Occurs by Distinct Mechanisms in the Three Major Enzyme Complexes	835	The Earliest Cells Probably Used Fermentation to Produce ATP	870
$H^+$ Ionophores Uncouple Electron Transport from ATP Synthesis	836	Electron-Transport Chains Enabled Anaerobic Bacteria to Use Nonfermentable Molecules as Their Major Source of Energy	871
Respiratory Control Normally Restrains Electron Flow Through the Chain	837	By Providing an Inexhaustible Source of Reducing Power, Photosynthetic Bacteria Overcame a Major Evolutionary Obstacle	872
Natural Uncouplers Convert the Mitochondria in Brown Fat into Heat-Generating Machines	838	The Photosynthetic Electron-Transport Chains of Cyanobacteria Produced Atmospheric Oxygen and Permitted New Life-Forms	873
The Mitochondrion Plays Many Critical Roles in Cell Metabolism	838	Summary	875
Bacteria Also Exploit Chemiosmotic Mechanisms to Harness Energy	839	Problems	877
Summary	840	References	878
<b>CHLOROPLASTS AND PHOTOSYNTHESIS</b>	<b>840</b>	<b>Chapter 15 Mechanisms of Cell Communication</b>	<b>879</b>
The Chloroplast Is One Member of the Plastid Family of Organelles	841	<b>GENERAL PRINCIPLES OF CELL COMMUNICATION</b>	<b>879</b>
Chloroplasts Resemble Mitochondria But Have an Extra Compartment	842	Extracellular Signal Molecules Bind to Specific Receptors	880
Chloroplasts Capture Energy from Sunlight and Use It to Fix Carbon	843	Extracellular Signal Molecules Can Act Over Either Short or Long Distances	881
Carbon Fixation Is Catalyzed by Ribulose Bisphosphate Carboxylase	844	Gap Junctions Allow Neighboring Cells to Share Signaling Information	884
Each $CO_2$ Molecule That Is Fixed Consumes Three Molecules of ATP and Two Molecules of NADPH	845	Each Cell Is Programmed to Respond to Specific Combinations of Extracellular Signal Molecules	884
Carbon Fixation in Some Plants Is Compartmentalized to Facilitate Growth at Low $CO_2$ Concentrations	846	Different Types of Cells Usually Respond Differently to the Same Extracellular Signal Molecule	885
Photosynthesis Depends on the Photochemistry of Chlorophyll Molecules	847	The Fate of Some Developing Cells Depends on Their Position in Morphogen Gradients	886
A Photochemical Reaction Center Plus an Antenna Complex Form a Photosystem	848	A Cell Can Alter the Concentration of an Intracellular Molecule Quickly Only If the Lifetime of the Molecule Is Short	886
In a Reaction Center, Light Energy Captured by Chlorophyll Creates a Strong Electron Donor from a Weak One	849	Nitric Oxide Gas Signals by Directly Regulating the Activity of Specific Proteins Inside the Target Cell	887
Noncyclic Photophosphorylation Produces Both NADPH and ATP	850	Nuclear Receptors Are Ligand-Modulated Gene Regulatory Proteins	889
Chloroplasts Can Make ATP by Cyclic Photophosphorylation Without Making NADPH	853	The Three Largest Classes of Cell-Surface Receptor Proteins Are Ion-Channel-Coupled, G-Protein-Coupled, and Enzyme-Coupled Receptors	891
Photosystems I and II Have Related Structures, and Also Resemble Bacterial Photosystems	853	Most Activated Cell-Surface Receptors Relay Signals Via Small Molecules and a Network of Intracellular Signaling Proteins	893
The Proton-Motive Force Is the Same in Mitochondria and Chloroplasts	853	Many Intracellular Signaling Proteins Function as Molecular Switches That Are Activated by Phosphorylation or GTP Binding	895
Carrier Proteins in the Chloroplast Inner Membrane Control Metabolite Exchange with the Cytosol	854	Intracellular Signaling Complexes Enhance the Speed, Efficiency, and Specificity of the Response	897
Chloroplasts Also Perform Other Crucial Biosyntheses	855	Modular Interaction Domains Mediate Interactions Between Intracellular Signaling Proteins	897
Summary	855	Cells Can Use Multiple Mechanisms to Respond Abruptly to a Gradually Increasing Concentration of an Extracellular Signal	899
<b>THE GENETIC SYSTEMS OF MITOCHONDRIA AND PLASTIDS</b>	<b>855</b>	Intracellular Signaling Networks Usually Make Use of Feedback Loops	901
Mitochondria and Chloroplasts Contain Complete Genetic Systems	856	Cells Can Adjust Their Sensitivity to a Signal	902
Organelle Growth and Division Determine the Number of Mitochondria and Plastids in a Cell	857	Summary	903

## SIGNALING THROUGH G-PROTEIN-COUPLED CELL-SURFACE RECEPTORS (GPCRS) AND SMALL INTRACELLULAR MEDIATORS 904

Trimeric G Proteins Relay Signals from GPCRs	905
Some G Proteins Regulate the Production of Cyclic AMP	905
Cyclic-AMP-Dependent Protein Kinase (PKA) Mediates Most of the Effects of Cyclic AMP	908
Some G Proteins Activate An Inositol Phospholipid Signaling Pathway by Activating Phospholipase C- $\beta$	909
Ca <sup>2+</sup> Functions as a Ubiquitous Intracellular Mediator	912
The Frequency of Ca <sup>2+</sup> Oscillations Influences a Cell's Response	912
Ca <sup>2+</sup> /Calmodulin-Dependent Protein Kinases (CaM-Kinases) Mediate Many of the Responses to Ca <sup>2+</sup> Signals in Animal Cells	914
Some G Proteins Directly Regulate Ion Channels	916
Smell and Vision Depend on GPCRs That Regulate Cyclic-Nucleotide-Gated Ion Channels	917
Intracellular Mediators and Enzymatic Cascades Amplify Extracellular Signals	919
GPCR Desensitization Depends on Receptor Phosphorylation	920
Summary	921

## SIGNALING THROUGH ENZYME-COUPLED CELL-SURFACE RECEPTORS 921

Activated Receptor Tyrosine Kinases (RTKs) Phosphorylate Themselves	922
Phosphorylated Tyrosines on RTKs Serve as Docking Sites for Intracellular Signaling Proteins	923
Proteins with SH2 Domains Bind to Phosphorylated Tyrosines	924
Ras Belongs to a Large Superfamily of Monomeric GTPases	926
RTKs Activate Ras Via Adaptors and GEFs: Evidence from the Developing <i>Drosophila</i> Eye	927
Ras Activates a MAP Kinase Signaling Module	928
Scaffold Proteins Help Prevent Cross-Talk Between Parallel MAP Kinase Modules	930
Rho Family GTPases Functionally Couple Cell-Surface Receptors to the Cytoskeleton	931
PI 3-Kinase Produces Lipid Docking Sites in the Plasma Membrane	932
The PI-3-Kinase-Akt Signaling Pathway Stimulates Animal Cells to Survive and Grow	934
The Downstream Signaling Pathways Activated By RTKs and GPCRs Overlap	935
Tyrosine-Kinase-Associated Receptors Depend on Cytoplasmic Tyrosine Kinases	935
Cytokine Receptors Activate the JAK-STAT Signaling Pathway, Providing a Fast Track to the Nucleus	937
Protein Tyrosine Phosphatases Reverse Tyrosine Phosphorylations	938
Signal Proteins of the TGF $\beta$ Superfamily Act Through Receptor Serine/Threonine Kinases and Smads	939
Serine/Threonine and Tyrosine Protein Kinases Are Structurally Related	941
Bacterial Chemotaxis Depends on a Two-Component Signaling Pathway Activated by Histidine-Kinase-Associated Receptors	941
Receptor Methylation Is Responsible for Adaptation in Bacterial Chemotaxis	943
Summary	944

## SIGNALING PATHWAYS DEPENDENT ON REGULATED PROTEOLYSIS OF LATENT GENE REGULATORY PROTEINS 946

The Receptor Protein Notch Is a Latent Gene Regulatory Protein	946
Wnt Proteins Bind to Frizzled Receptors and Inhibit the Degradation of $\beta$ -Catenin	948
Hedgehog Proteins Bind to Patched Relieving Its Inhibition of Smoothened	950
Many Stressful and Inflammatory Stimuli Act Through an NF $\kappa$ B-Dependent Signaling Pathway	952
Summary	954

## SIGNALING IN PLANTS 955

Multicellularity and Cell Communication Evolved Independently in Plants and Animals	955
Receptor Serine/Threonine Kinases Are the Largest Class of Cell-Surface Receptors in Plants	956

Ethylene Blocks the Degradation of Specific Gene Regulatory Proteins in the Nucleus	957
Regulated Positioning of Auxin Transporters Patterns Plant Growth	959
Phytochromes Detect Red Light, and Cryptochromes Detect Blue Light	960
Summary	961
Problems	962
References	964

## Chapter 16 The Cytoskeleton 965

### THE SELF-ASSEMBLY AND DYNAMIC STRUCTURE OF CYTOSKELETAL FILAMENTS 965

Cytoskeletal Filaments Are Dynamic and Adaptable	966
The Cytoskeleton Can Also Form Stable Structures	969
Each Type of Cytoskeletal Filament Is Constructed from Smaller Protein Subunits	970
Filaments Formed from Multiple Protofilaments Have Advantageous Properties	971
Nucleation Is the Rate-Limiting Step in the Formation of a Cytoskeletal Polymer	973
The Tubulin and Actin Subunits Assemble Head-to-Tail to Create Polar Filaments	973
Microtubules and Actin Filaments Have Two Distinct Ends That Grow at Different Rates	975
Filament Treadmilling and Dynamic Instability Are Consequences of Nucleotide Hydrolysis by Tubulin and Actin	976
Treadmilling and Dynamic Instability Aid Rapid Cytoskeletal Rearrangement	980
Tubulin and Actin Have Been Highly Conserved During Eucaryotic Evolution	982
Intermediate Filament Structure Depends on The Lateral Bundling and Twisting of Coiled Coils	983
Intermediate Filaments Impart Mechanical Stability to Animal Cells	985
Drugs Can Alter Filament Polymerization	987
Bacterial Cell Organization and Cell Division Depend on Homologs of the Eucaryotic Cytoskeleton	989
Summary	991

### HOW CELLS REGULATE THEIR CYTOSKELETAL FILAMENTS 992

A Protein Complex Containing $\gamma$ -Tubulin Nucleates Microtubules	992
Microtubules Emanate from the Centrosome in Animal Cells	992
Actin Filaments Are Often Nucleated at the Plasma Membrane	996
The Mechanism of Nucleation Influences Large-Scale Filament Organization	998
Proteins That Bind to the Free Subunits Modify Filament Elongation	999
Severing Proteins Regulate the Length and Kinetic Behavior of Actin Filaments and Microtubules	1000
Proteins That Bind Along the Sides of Filaments Can Either Stabilize or Destabilize Them	1001
Proteins That Interact with Filament Ends Can Dramatically Change Filament Dynamics	1002
Different Kinds of Proteins Alter the Properties of Rapidly Growing Microtubule Ends	1003
Filaments Are Organized into Higher-Order Structures in Cells	1005
Intermediate Filaments Are Cross-Linked and Bundled Into Strong Arrays	1005
Cross-Linking Proteins with Distinct Properties Organize Different Assemblies of Actin Filaments	1006
Filamin and Spectrin Form Actin Filament Webs	1008
Cytoskeletal Elements Make Many Attachments to Membrane	1009
Summary	1010

### MOLECULAR MOTORS 1010

Actin-Based Motor Proteins Are Members of the Myosin Superfamily	1011
There Are Two Types of Microtubule Motor Proteins: Kinesins and Dyneins	1014
The Structural Similarity of Myosin and Kinesin Indicates a Common Evolutionary Origin	1015
Motor Proteins Generate Force by Coupling ATP Hydrolysis to Conformational Changes	1016



Motor Protein Kinetics Are Adapted to Cell Functions	1020	Microtubule-Dependent Motor Proteins Govern Spindle Assembly and Function	1077
Motor Proteins Mediate the Intracellular Transport of Membrane-Enclosed Organelles	1021	Two Mechanisms Collaborate in the Assembly of a Bipolar Mitotic Spindle	1077
The Cytoskeleton Localizes Specific RNA Molecules	1022	Centrosome Duplication Occurs Early in the Cell Cycle	1078
Cells Regulate Motor Protein Function	1023	M-Cdk Initiates Spindle Assembly in Prophase	1078
<i>Summary</i>	1025	The Completion of Spindle Assembly in Animal Cells Requires Nuclear Envelope Breakdown	1079
<b>THE CYTOSKELETON AND CELL BEHAVIOR</b>	<b>1025</b>	Microtubule Instability Increases Greatly in Mitosis	1080
Sliding of Myosin II and Actin Filaments Causes Muscles to Contract	1026	Mitotic Chromosomes Promote Bipolar Spindle Assembly	1081
A Sudden Rise in Cytosolic $\text{Ca}^{2+}$ Concentration Initiates Muscle Contraction	1028	Kinetochores Attach Sister Chromatids to the Spindle	1082
Heart Muscle Is a Precisely Engineered Machine	1031	Bi-Orientation Is Achieved by Trial and Error	1083
Cilia and Flagella Are Motile Structures Built from Microtubules and Dyneins	1031	Multiple Forces Move Chromosomes on the Spindle	1085
Construction of the Mitotic Spindle Requires Microtubule Dynamics and the Interactions of Many Motor Proteins	1034	The APC/C Triggers Sister-Chromatid Separation and the Completion of Mitosis	1087
Many Cells Can Crawl Across A Solid Substratum	1036	Unattached Chromosomes Block Sister-Chromatid Separation: The Spindle Assembly Checkpoint	1088
Actin Polymerization Drives Plasma Membrane Protrusion	1037	Chromosomes Segregate in Anaphase A and B	1089
Cell Adhesion and Traction Allow Cells to Pull Themselves Forward	1040	Segregated Chromosomes Are Packaged in Daughter Nuclei at Telophase	1090
Members of the Rho Protein Family Cause Major Rearrangements of the Actin Cytoskeleton	1041	Meiosis Is a Special Form of Nuclear Division Involved in Sexual Reproduction	1090
Extracellular Signals Can Activate the Three Rho Protein Family Members	1043	<i>Summary</i>	1092
External Signals Can Dictate the Direction of Cell Migration	1045	<b>CYTOKINESIS</b>	<b>1092</b>
Communication Between the Microtubule and Actin Cytoskeletons Coordinates Whole-Cell Polarization and Locomotion	1046	Actin and Myosin II in the Contractile Ring Generate the Force for Cytokinesis	1093
The Complex Morphological Specialization of Neurons Depends on the Cytoskeleton	1047	Local Activation of RhoA Triggers Assembly and Contraction of the Contractile Ring	1094
<i>Summary</i>	1050	The Microtubules of the Mitotic Spindle Determine the Plane of Animal Cell Division	1095
<i>Problems</i>	1050	The Phragmoplast Guides Cytokinesis in Higher Plants	1097
<i>References</i>	1052	Membrane-Enclosed Organelles Must Be Distributed to Daughter Cells During Cytokinesis	1098
<b>Chapter 17 The Cell Cycle</b>	<b>1053</b>	Some Cells Reposition Their Spindle to Divide Asymmetrically	1099
<b>OVERVIEW OF THE CELL CYCLE</b>	<b>1054</b>	Mitosis Can Occur Without Cytokinesis	1099
The Eucaryotic Cell Cycle Is Divided into Four Phases	1054	The $G_1$ Phase Is a Stable State of Cdk Inactivity	1100
Cell-Cycle Control Is Similar in All Eucaryotes	1056	<i>Summary</i>	1101
Cell-Cycle Control Can Be Dissected Genetically by Analysis of Yeast Mutants	1056	<b>CONTROL OF CELL DIVISION AND CELL GROWTH</b>	<b>1101</b>
Cell-Cycle Control Can Be Analyzed Biochemically in Animal Embryos	1057	Mitogens Stimulate Cell Division	1102
Cell-Cycle Control Can Be Studied in Cultured Mammalian Cells	1059	Cells Can Delay Division by Entering a Specialized Nondividing State	1103
Cell-Cycle Progression Can Be Studied in Various Ways	1059	Mitogens Stimulate $G_1$ -Cdk and $G_1/S$ -Cdk Activities	1103
<i>Summary</i>	1060	DNA Damage Blocks Cell Division: The DNA Damage Response	1105
<b>THE CELL-CYCLE CONTROL SYSTEM</b>	<b>1060</b>	Many Human Cells Have a Built-In Limitation on the Number of Times They Can Divide	1007
The Cell-Cycle Control System Triggers the Major Events of the Cell Cycle	1060	Abnormal Proliferation Signals Cause Cell-Cycle Arrest or Apoptosis, Except in Cancer Cells	1107
The Cell-Cycle Control System Depends on Cyclically Activated Cyclin-Dependent Protein Kinases (Cdks)	1062	Organism and Organ Growth Depend on Cell Growth	1108
Inhibitory Phosphorylation and Cdk Inhibitory Proteins (CKIs) Can Suppress Cdk Activity	1063	Proliferating Cells Usually Coordinate Their Growth and Division	1108
The Cell-Cycle Control System Depends on Cyclical Proteolysis	1064	Neighboring Cells Compete for Extracellular Signal Proteins	1110
Cell-Cycle Control Also Depends on Transcriptional Regulation	1065	Animals Control Total Cell Mass by Unknown Mechanisms	1111
The Cell-Cycle Control System Functions as a Network of Biochemical Switches	1065	<i>Summary</i>	1112
<i>Summary</i>	1067	<i>Problems</i>	1112
<b>S PHASE</b>	<b>1067</b>	<i>References</i>	1113
S-Cdk Initiates DNA Replication Once Per Cycle	1067	<b>Chapter 18 Apoptosis</b>	<b>1115</b>
Chromosome Duplication Requires Duplication of Chromatin Structure	1069	Programmed Cell Death Eliminates Unwanted Cells	1115
Cohesins Help Hold Sister Chromatids Together	1070	Apoptotic Cells Are Biochemically Recognizable	1117
<i>Summary</i>	1071	Apoptosis Depends on an Intracellular Proteolytic Cascade That Is Mediated by Caspases	1118
<b>MITOSIS</b>	<b>1071</b>	Cell-Surface Death Receptors Activate the Extrinsic Pathway of Apoptosis	1120
M-Cdk Drives Entry Into Mitosis	1071	The Intrinsic Pathway of Apoptosis Depends on Mitochondria	1121
Dephosphorylation Activates M-Cdk at the Onset of Mitosis	1074	Bcl2 Proteins Regulate the Intrinsic Pathway of Apoptosis	1121
Condensin Helps Configure Duplicated Chromosomes for Separation	1075	IAPs Inhibit Caspases	1124
The Mitotic Spindle Is a Microtubule-Based Machine	1075	Extracellular Survival Factors Inhibit Apoptosis in Various Ways	1126
		Either Excessive or Insufficient Apoptosis Can Contribute to Disease	1127
		<i>Summary</i>	1128
		<i>Problems</i>	1128
		<i>References</i>	1129

## Chapter 19 Cell Junctions, Cell Adhesion, and the Extracellular Matrix

1131

### CADHERINS AND CELL–CELL ADHESION

1133

Cadherins Mediate $\text{Ca}^{2+}$ -Dependent Cell–Cell Adhesion in All Animals	1135
The Cadherin Superfamily in Vertebrates Includes Hundreds of Different Proteins, Including Many with Signaling Functions	1136
Cadherins Mediate Homophilic Adhesion	1137
Selective Cell–Cell Adhesion Enables Dissociated Vertebrate Cells to Reassemble into Organized Tissues	1139
Cadherins Control the Selective Assortment of Cells	1140
Twist Regulates Epithelial–Mesenchymal Transitions	1141
Catenins Link Classical Cadherins to the Actin Cytoskeleton	1142
Adherens Junctions Coordinate the Actin-Based Motility of Adjacent Cells	1142
Desmosome Junctions Give Epithelia Mechanical Strength	1143
Cell–Cell Junctions Send Signals into the Cell Interior	1145
Selectins Mediate Transient Cell–Cell Adhesions in the Bloodstream	1145
Members of the Immunoglobulin Superfamily of Proteins Mediate $\text{Ca}^{2+}$ -Independent Cell–Cell Adhesion	1146
Many Types of Cell Adhesion Molecules Act in Parallel to Create a Synapse	1147
Scaffold Proteins Organize Junctional Complexes	1148
Summary	1149

### TIGHT JUNCTIONS AND THE ORGANIZATION OF EPITHELIA

1150

Tight Junctions Form a Seal Between Cells and a Fence Between Membrane Domains	1150
Scaffold Proteins in Junctional Complexes Play a Key Part in the Control of Cell Proliferation	1153
Cell–Cell Junctions and the Basal Lamina Govern Apico–Basal Polarity in Epithelia	1155
A Separate Signaling System Controls Planar Cell Polarity	1157
Summary	1158

### PASSAGEWAYS FROM CELL TO CELL: GAP JUNCTIONS AND PLASMODESMATA

1158

Gap Junctions Couple Cells Both Electrically and Metabolically	1158
A Gap-Junction Connexon Is Made Up of Six Transmembrane Connexin Subunits	1159
Gap Junctions Have Diverse Functions	1161
Cells Can Regulate the Permeability of Their Gap Junctions	1161
In Plants, Plasmodesmata Perform Many of the Same Functions as Gap Junctions	1162
Summary	1163

### THE BASAL LAMINA

1164

Basal Laminae Underlie All Epithelia and Surround Some Nonepithelial Cell Types	1164
Laminin Is a Primary Component of the Basal Lamina	1165
Type IV Collagen Gives the Basal Lamina Tensile Strength	1166
Basal Laminae Have Diverse Functions	1167
Summary	1169

### INTEGRINS AND CELL–MATRIX ADHESION

1169

Integrins Are Transmembrane Heterodimers That Link to the Cytoskeleton	1170
Integrins Can Switch Between an Active and an Inactive Conformation	1170
Integrin Defects Are Responsible for Many Different Genetic Diseases	1172
Integrins Cluster to Form Strong Adhesions	1174
Extracellular Matrix Attachments Act Through Integrins to Control Cell Proliferation and Survival	1175
Integrins Recruit Intracellular Signaling Proteins at Sites of Cell–Substratum Adhesion	1176
Integrins Can Produce Localized Intracellular Effects	1177
Summary	1178

## THE EXTRACELLULAR MATRIX OF ANIMAL CONNECTIVE TISSUES

1178

The Extracellular Matrix Is Made and Oriented by the Cells Within It	1179
Glycosaminoglycan (GAG) Chains Occupy Large Amounts of Space and Form Hydrated Gels	1179
Hyaluronan Acts as a Space Filler and a Facilitator of Cell Migration During Tissue Morphogenesis and Repair	1180
Proteoglycans Are Composed of GAG Chains Covalently Linked to a Core Protein	1181
Proteoglycans Can Regulate the Activities of Secreted Proteins	1182
Cell-Surface Proteoglycans Act as Co-Receptors	1183
Collagens Are the Major Proteins of the Extracellular Matrix	1184
Collagen Chains Undergo a Series of Post-Translational Modifications	1186
Propeptides Are Clipped Off Procollagen After Its Secretion to Allow Assembly of Fibrils	1187
Secreted Fibril-Associated Collagens Help Organize the Fibrils	1187
Cells Help Organize the Collagen Fibrils They Secrete by Exerting Tension on the Matrix	1189
Elastin Gives Tissues Their Elasticity	1189
Fibronectin Is an Extracellular Protein That Helps Cells Attach to the Matrix	1191
Tension Exerted by Cells Regulates Assembly of Fibronectin Fibrils	1191
Fibronectin Binds to Integrins Through an RGD Motif	1193
Cells Have to Be Able to Degrade Matrix, as Well as Make it	1193
Matrix Degradation Is Localized to the Vicinity of Cells	1194
Summary	1195

### THE PLANT CELL WALL

1195

The Composition of the Cell Wall Depends on the Cell Type	1195
The Tensile Strength of the Cell Wall Allows Plant Cells to Develop Turgor Pressure	1197
The Primary Cell Wall Is Built from Cellulose Microfibrils Interwoven with a Network of Pectic Polysaccharides	1197
Oriented Cell-Wall Deposition Controls Plant Cell Growth	1199
Microtubules Orient Cell-Wall Deposition	1200
Summary	1202
Problems	1202
References	1204

## Chapter 20 Cancer

1205

### CANCER AS A MICROEVOLUTIONARY PROCESS

1205

Cancer Cells Reproduce Without Restraint and Colonize Other Tissues	1206
Most Cancers Derive from a Single Abnormal Cell	1207
Cancer Cells Contain Somatic Mutations	1208
A Single Mutation Is Not Enough to Cause Cancer	1209
Cancers Develop Gradually from Increasingly Aberrant Cells	1210
Cervical Cancers Are Prevented by Early Detection	1211
Tumor Progression Involves Successive Rounds of Random Inherited Change Followed by Natural Selection	1212
The Epigenetic Changes That Accumulate in Cancer Cells Involve Inherited Chromatin Structures and DNA Methylation	1213
Human Cancer Cells Are Genetically Unstable	1214
Cancerous Growth Often Depends on Defective Control of Cell Death, Cell Differentiation, or Both	1215
Cancer Cells Are Usually Altered in Their Responses to DNA Damage and Other Forms of Stress	1216
Human Cancer Cells Escape a Built-In Limit to Cell Proliferation	1217
A Small Population of Cancer Stem Cells Maintains Many Tumors	1217
How Do Cancer Stem Cells Arise?	1218
To Metastasize, Malignant Cancer Cells Must Survive and Proliferate in a Foreign Environment	1220
Tumors Induce Angiogenesis	1220
The Tumor Microenvironment Influences Cancer Development	1222
Many Properties Typically Contribute to Cancerous Growth	1223
Summary	1223

<b>THE PREVENTABLE CAUSES OF CANCER</b>	<b>1224</b>		
Many, But Not All, Cancer-Causing Agents Damage DNA	1225	There Is Still Much More to Do	1264
Tumor Initiators Damage DNA; Tumor Promoters Do Not	1226	<i>Summary</i>	1265
Viruses and Other Infections Contribute to a Significant Proportion of Human Cancers	1227	<i>Problems</i>	1265
Identification of Carcinogens Reveals Ways to Avoid Cancer	1229	<i>References</i>	1267
<i>Summary</i>	1230		
<b>FINDING THE CANCER-CRITICAL GENES</b>	<b>1230</b>	<b>Chapter 21 Sexual Reproduction: Meiosis, Germ Cells, and Fertilization</b>	<b>1269</b>
The Identification of Gain-of-Function and Loss-of-Function Mutations Requires Different Methods	1231	<b>OVERVIEW OF SEXUAL REPRODUCTION</b>	<b>1269</b>
Retroviruses Can Act as Vectors for Oncogenes That Alter Cell Behavior	1232	The Haploid Phase in Higher Eucaryotes Is Brief	1269
Different Searches for Oncogenes Have Converged on the Same Gene—Ras	1233	Meiosis Creates Genetic Diversity	1271
Studies of Rare Hereditary Cancer Syndromes First Identified Tumor Suppressor Genes	1234	Sexual Reproduction Gives Organisms a Competitive Advantage	1271
Tumor Suppressor Genes Can Also Be Identified from Studies of Tumors	1235	<i>Summary</i>	1272
Both Genetic and Epigenetic Mechanisms Can Inactivate Tumor Suppressor Genes	1235	<b>MEIOSIS</b>	<b>1272</b>
Genes Mutated in Cancer Can Be Made Overactive in Many Ways	1237	Gametes Are Produced by Two Meiotic Cell Divisions	1272
The Hunt for Cancer-Critical Genes Continues	1239	Duplicated Homologs (and Sex Chromosomes) Pair During Early Prophase I	1274
<i>Summary</i>	1240	Homolog Pairing Culminates in the Formation of a Synaptonemal Complex	1275
<b>THE MOLECULAR BASIS OF CANCER-CELL BEHAVIOR</b>	<b>1240</b>	Homolog Segregation Depends on Meiosis-Specific, Kinetochore-Associated Proteins	1276
Studies of Both Developing Embryos and Genetically Engineered Mice Have Helped to Uncover the Function of Cancer-Critical Genes	1241	Meiosis Frequently Goes Wrong	1278
Many Cancer-Critical Genes Regulate Cell Proliferation	1242	Crossing-Over Enhances Genetic Reassortment	1279
Distinct Pathways May Mediate the Disregulation of Cell-Cycle Progression and the Disregulation of Cell Growth in Cancer Cells	1244	Crossing-Over Is Highly Regulated	1280
Mutations in Genes That Regulate Apoptosis Allow Cancer Cells to Survive When They Should Not	1245	Meiosis Is Regulated Differently in Male and Female Mammals	1280
Mutations in the <i>p53</i> Gene Allow Many Cancer Cells to Survive and Proliferate Despite DNA Damage	1246	<i>Summary</i>	1281
DNA Tumor Viruses Block the Action of Key Tumor Suppressor Proteins	1247	<b>PRIMORDIAL GERM CELLS AND SEX DETERMINATION IN MAMMALS</b>	<b>1282</b>
The Changes in Tumor Cells That Lead to Metastasis Are Still Largely a Mystery	1249	Signals from Neighbors Specify PGCs in Mammalian Embryos	1282
Colorectal Cancers Evolve Slowly Via a Succession of Visible Changes	1250	PGCs Migrate into the Developing Gonads	1283
A Few Key Genetic Lesions Are Common to a Large Fraction of Colorectal Cancers	1251	The <i>Sry</i> Gene Directs the Developing Mammalian Gonad to Become a Testis	1283
Some Colorectal Cancers Have Defects in DNA Mismatch Repair	1254	Many Aspects of Sexual Reproduction Vary Greatly between Animal Species	1285
The Steps of Tumor Progression Can Often Be Correlated with Specific Mutations	1254	<i>Summary</i>	1286
Each Case of Cancer Is Characterized by Its Own Array of Genetic Lesions	1256	<b>EGGS</b>	<b>1287</b>
<i>Summary</i>	1256	An Egg Is Highly Specialized for Independent Development	1287
<b>CANCER TREATMENT: PRESENT AND FUTURE</b>	<b>1256</b>	Eggs Develop in Stages	1288
The Search for Cancer Cures Is Difficult but Not Hopeless	1257	Oocytes Use Special Mechanisms to Grow to Their Large Size	1290
Traditional Therapies Exploit the Genetic Instability and Loss of Cell-Cycle Checkpoint Responses in Cancer Cells	1257	Most Human Oocytes Die Without Maturing	1291
New Drugs Can Exploit the Specific Cause of a Tumor's Genetic Instability	1257	<i>Summary</i>	1292
Genetic Instability Helps Cancers Become Progressively More Resistant to Therapies	1259	<b>SPERM</b>	<b>1292</b>
New Therapies Are Emerging from Our Knowledge of Cancer Biology	1260	Sperm Are Highly Adapted for Delivering Their DNA to an Egg	1292
Small Molecules Can Be Designed to Inhibit Specific Oncogenic Proteins	1260	Sperm Are Produced Continuously in the Mammalian Testis	1293
Tumor Blood Vessels Are Logical Targets for Cancer Therapy	1262	Sperm Develop as a Syncytium	1294
Many Cancers May Be Treatable by Enhancing the Immune Response Against a Specific Tumor	1262	<i>Summary</i>	1296
Treating Patients with Several Drugs Simultaneously Has Potential Advantages for Cancer Therapy	1263	<b>FERTILIZATION</b>	<b>1297</b>
Gene Expression Profiling Can Help Classify Cancers into Clinically Meaningful Subgroups	1264	Ejaculated Sperm Become Capacitated in the Female Genital Tract	1297
		Capacitated Sperm Bind to the Zona Pellucida and Undergo an Acrosome Reaction	1298
		The Mechanism of Sperm–Egg Fusion Is Still Unknown	1298
		Sperm Fusion Activates the Egg by Increasing $\text{Ca}^{2+}$ in the Cytosol	1299
		The Cortical Reaction Helps Ensure That Only One Sperm Fertilizes the Egg	1300
		The Sperm Provides Centrioles as Well as Its Genome to the Zygote	1301
		IVF and ICSI Have Revolutionized the Treatment of Human Infertility	1301
		<i>Summary</i>	1303
		<i>References</i>	1304
		<b>Chapter 22 Development of Multicellular Organisms</b>	<b>1305</b>
		<b>UNIVERSAL MECHANISMS OF ANIMAL DEVELOPMENT</b>	<b>1305</b>
		Animals Share Some Basic Anatomical Features	1307

Multicellular Animals Are Enriched in Proteins Mediating Cell Interactions and Gene Regulation	1308	Egg-Polarity, Gap, and Pair-Rule Genes Create a Transient Pattern That Is Remembered by Other Genes	1340
Regulatory DNA Defines the Program of Development	1309	Summary	1341
Manipulation of the Embryo Reveals the Interactions Between Its Cells	1310	<b>HOMEOTIC SELECTOR GENES AND THE PATTERNING OF THE ANTEROPOSTERIOR AXIS</b>	1341
Studies of Mutant Animals Identify the Genes That Control Developmental Processes	1311	The Hox Code Specifies Anterior-Posterior Differences	1342
A Cell Makes Developmental Decisions Long Before It Shows a Visible Change	1311	Homeotic Selector Genes Code for DNA-Binding Proteins That Interact with Other Gene Regulatory Proteins	1342
Cells Have Remembered Positional Values That Reflect Their Location in the Body	1312	The Homeotic Selector Genes Are Expressed Sequentially According to Their Order in the Hox Complex	1343
Inductive Signals Can Create Orderly Differences Between Initially Identical Cells	1313	The Hox Complex Carries a Permanent Record of Positional Information	1344
Sister Cells Can Be Born Different by an Asymmetric Cell Division	1313	The Anteroposterior Axis Is Controlled by <i>Hox</i> Selector Genes in Vertebrates Also	1344
Positive Feedback Can Create Asymmetry Where There Was None Before	1314	Summary	1347
Positive Feedback Generates Patterns, Creates All-or-None Outcomes, and Provides Memory	1315	<b>ORGANOGENESIS AND THE PATTERNING OF APPENDAGES</b>	1347
A Small Set of Signaling Pathways, Used Repeatedly, Controls Developmental Patterning	1316	Conditional and Induced Somatic Mutations Make it Possible to Analyze Gene Functions Late in Development	1348
Morphogens Are Long-Range Inducers That Exert Graded Effects	1316	Body Parts of the Adult Fly Develop From Imaginal Discs	1349
Extracellular Inhibitors of Signal Molecules Shape the Response to the Inducer	1317	Homeotic Selector Genes Are Essential for the Memory of Positional Information in Imaginal Disc Cells	1351
Developmental Signals Can Spread Through Tissue in Several Different Ways	1318	Specific Regulatory Genes Define the Cells That Will Form an Appendage	1351
Programs That Are Intrinsic to a Cell Often Define the Time-Course of Its Development	1319	The Insect Wing Disc Is Divided into Compartments	1352
Initial Patterns Are Established in Small Fields of Cells and Refined by Sequential Induction as the Embryo Grows	1319	Four Familiar Signaling Pathways Combine to Pattern the Wing Disc: Wingless, Hedgehog, Dpp, and Notch	1353
Summary	1320	The Size of Each Compartment Is Regulated by Interactions Among Its Cells	1353
<b>CAENORHABDITIS ELEGANS: DEVELOPMENT FROM THE PERSPECTIVE OF THE INDIVIDUAL CELL</b>	1321	Similar Mechanisms Pattern the Limbs of Vertebrates	1355
<i>Caenorhabditis elegans</i> Is Anatomically Simple	1321	Localized Expression of Specific Classes of Gene Regulatory Proteins Foreshadows Cell Differentiation	1356
Cell Fates in the Developing Nematode Are Almost Perfectly Predictable	1322	Lateral Inhibition Singles Out Sensory Mother Cells Within Proneural Clusters	1357
Products of Maternal-Effect Genes Organize the Asymmetric Division of the Egg	1323	Lateral Inhibition Drives the Progeny of the Sensory Mother Cell Toward Different Final Fates	1357
Progressively More Complex Patterns Are Created by Cell-Cell Interactions	1324	Planar Polarity of Asymmetric Divisions Is Controlled by Signaling via the Receptor Frizzled	1358
Microsurgery and Genetics Reveal the Logic of Developmental Control; Gene Cloning and Sequencing Reveal Its Molecular Mechanisms	1325	Asymmetric Stem-Cell Divisions Generate Additional Neurons in the Central Nervous System	1359
Cells Change Over Time in Their Responsiveness to Developmental Signals	1325	Asymmetric Neuroblast Divisions Segregate an Inhibitor of Cell Division into Just One of the Daughter Cells	1361
Heterochronic Genes Control the Timing of Development	1326	Notch Signaling Regulates the Fine-Grained Pattern of Differentiated Cell Types in Many Different Tissues	1362
Cells Do Not Count Cell Divisions in Timing Their Internal Programs	1327	Some Key Regulatory Genes Define a Cell Type; Others Can Activate the Program for Creation of an Entire Organ	1362
Selected Cells Die by Apoptosis as Part of the Program of Development	1327	Summary	1363
Summary	1328	<b>CELL MOVEMENTS AND THE SHAPING OF THE VERTEBRATE BODY</b>	1363
<b>DROSOPHILA AND THE MOLECULAR GENETICS OF PATTERN FORMATION: GENESIS OF THE BODY PLAN</b>	1328	The Polarity of the Amphibian Embryo Depends on the Polarity of the Egg	1364
The Insect Body Is Constructed as a Series of Segmental Units	1329	Cleavage Produces Many Cells from One	1365
<i>Drosophila</i> Begins Its Development as a Syncytium	1330	Gastrulation Transforms a Hollow Ball of Cells into a Three-Layered Structure with a Primitive Gut	1365
Genetic Screens Define Groups of Genes Required for Specific Aspects of Early Patterning	1332	The Movements of Gastrulation Are Precisely Predictable	1366
Interactions of the Oocyte With Its Surroundings Define the Axes of the Embryo: the Role of the Egg-Polarity Genes	1333	Chemical Signals Trigger the Mechanical Processes	1367
The Dorsoventral Signaling Genes Create a Gradient of a Nuclear Gene Regulatory Protein	1334	Active Changes of Cell Packing Provide a Driving Force for Gastrulation	1368
Dpp and Sog Set Up a Secondary Morphogen Gradient to Refine the Pattern of the Dorsal Part of the Embryo	1336	Changing Patterns of Cell Adhesion Molecules Force Cells Into New Arrangements	1369
The Insect Dorsoventral Axis Corresponds to the Vertebrate Ventrodorsal Axis	1336	The Notochord Elongates, While the Neural Plate Rolls Up to Form the Neural Tube	1370
Three Classes of Segmentation Genes Refine the Anterior-Posterior Maternal Pattern and Subdivide the Embryo	1336	A Gene-Expression Oscillator Controls Segmentation of the Mesoderm Into Somites	1371
The Localized Expression of Segmentation Genes Is Regulated by a Hierarchy of Positional Signals	1337	Delayed Negative Feedback May Generate the Oscillations of the Segmentation Clock	1373
The Modular Nature of Regulatory DNA Allows Genes to Have Multiple Independently Controlled Functions	1339	Embryonic Tissues Are Invaded in a Strictly Controlled Fashion by Migratory Cells	1373
		The Distribution of Migrant Cells Depends on Survival Factors as Well as Guidance Cues	1375



Left–Right Asymmetry of the Vertebrate Body Derives From Molecular Asymmetry in the Early Embryo	1376	The Basal Layer Contains Both Stem Cells and Transit Amplifying Cells	1422
<i>Summary</i>	1377	Transit amplifying Divisions Are Part of the Strategy of Growth Control	1423
<b>THE MOUSE</b>	<b>1378</b>	Stem Cells of Some Tissues Selectively Retain Original DNA Strands	1424
Mammalian Development Begins With a Specialized Preamble	1378	The Rate of Stem-Cell Division Can Increase Dramatically When New Cells Are Needed Urgently	1425
The Early Mammalian Embryo Is Highly Regulative	1380	Many Interacting Signals Govern Epidermal Renewal	1426
Totipotent Embryonic Stem Cells Can Be Obtained From a Mammalian Embryo	1380	The Mammary Gland Undergoes Cycles of Development and Regression	1426
Interactions Between Epithelium and Mesenchyme Generate Branching Tubular Structures	1381	<i>Summary</i>	1428
<i>Summary</i>	1382	<b>SENSORY EPITHELIA</b>	<b>1429</b>
<b>NEURAL DEVELOPMENT</b>	<b>1383</b>	Olfactory Sensory Neurons Are Continually Replaced	1429
Neurons Are Assigned Different Characters According to the Time and Place Where They Are Born	1383	Auditory Hair Cells Have to Last a Lifetime	1430
The Character Assigned to a Neuron at Its Birth Governs the Connections It Will Form	1385	Most Permanent Cells Renew Their Parts: the Photoreceptor Cells of the Retina	1432
Each Axon or Dendrite Extends by Means of a Growth Cone at Its Tip	1386	<i>Summary</i>	1433
The Growth Cone Pilots the Developing Neurite Along a Precisely Defined Path <i>In Vivo</i>	1387	<b>THE AIRWAYS AND THE GUT</b>	<b>1434</b>
Growth Cones Can Change Their Sensibilities as They Travel	1389	Adjacent Cell Types Collaborate in the Alveoli of the Lungs	1434
Target Tissues Release Neurotrophic Factors That Control Nerve Cell Growth and Survival	1389	Goblet Cells, Ciliated Cells, and Macrophages Collaborate to Keep the Airways Clean	1434
Neuronal Specificity Guides the Formation of Orderly Neural Maps	1391	The Lining of the Small Intestine Renews Itself Faster Than Any Other Tissue	1436
Axons From Different Regions of the Retina Respond Differently to a Gradient of Repulsive Molecules in the Tectum	1392	Wnt Signaling Maintains the Gut Stem-Cell Compartment	1438
Diffuse Patterns of Synaptic Connections Are Sharpened by Activity-Dependent Remodeling	1393	Notch Signaling Controls Gut Cell Diversification	1439
Experience Molds the Pattern of Synaptic Connections in the Brain	1395	Ephrin–Eph Signaling Controls the Migrations of Gut Epithelial Cells	1440
Adult Memory and Developmental Synapse Remodeling May Depend on Similar Mechanisms	1396	Wnt, Hedgehog, PDGF, and BMP Signaling Pathways Combine to Delimit the Stem-Cell Niche	1441
<i>Summary</i>	1397	The Liver Functions as an Interface Between the Digestive Tract and the Blood	1442
<b>PLANT DEVELOPMENT</b>	<b>1398</b>	Liver Cell Loss Stimulates Liver Cell Proliferation	1443
<i>Arabidopsis</i> Serves as a Model Organism for Plant Molecular Genetics	1398	Tissue Renewal Does Not Have to Depend on Stem Cells: Insulin-Secreting Cells in the Pancreas	1444
The <i>Arabidopsis</i> Genome Is Rich in Developmental Control Genes	1399	<i>Summary</i>	1445
Embryonic Development Starts by Establishing a Root–Shoot Axis and Then Halts Inside the Seed	1400	<b>BLOOD VESSELS, LYMPHATICS, AND ENDOTHELIAL CELLS</b>	<b>1445</b>
The Parts of a Plant Are Generated Sequentially by Meristems	1403	Endothelial Cells Line All Blood Vessels and Lymphatics	1445
Development of the Seedling Depends on Environmental Signals	1403	Endothelial Tip Cells Pioneer Angiogenesis	1446
Long-Range Hormonal Signals Coordinate Developmental Events in Separate Parts of the Plant	1403	Different Types of Endothelial Cells Form Different Types of Vessel	1447
The Shaping of Each New Structure Depends on Oriented Cell Division and Expansion	1406	Tissues Requiring a Blood Supply Release VEGF; Notch Signaling Between Endothelial Cells Regulates the Response	1448
Each Plant Module Grows From a Microscopic Set of Primordia in a Meristem	1407	Signals from Endothelial Cells Control Recruitment of Pericytes and Smooth Muscle Cells to Form the Vessel Wall	1450
Polarized Auxin Transport Controls the Pattern of Primordia in the Meristem	1408	<i>Summary</i>	1450
Cell Signaling Maintains the Meristem	1409	<b>RENEWAL BY MULTIPOTENT STEM CELLS: BLOOD CELL FORMATION</b>	<b>1450</b>
Regulatory Mutations Can Transform Plant Topology by Altering Cell Behavior in the Meristem	1410	The Three Main Categories of White Blood Cells Are Granulocytes, Monocytes, and Lymphocytes	1451
The Switch to Flowering Depends on Past and Present Environmental Cues	1412	The Production of Each Type of Blood Cell in the Bone Marrow Is Individually Controlled	1453
Homeotic Selector Genes Specify the Parts of a Flower	1413	Bone Marrow Contains Hemopoietic Stem Cells	1454
<i>Summary</i>	1415	A Multipotent Stem Cell Gives Rise to All Classes of Blood Cells	1456
<i>References</i>	1415	Commitment Is a Stepwise Process	1456
<b>Chapter 23 Specialized Tissues, Stem Cells, and Tissue Renewal</b>	<b>1417</b>	Divisions of Committed Progenitor Cells Amplify the Number of Specialized Blood Cells	1457
<b>EPIDERMIS AND ITS RENEWAL BY STEM CELLS</b>	<b>1417</b>	Stem Cells Depend on Contact Signals From Stromal Cells	1458
Epidermal Cells Form a Multilayered Waterproof Barrier	1419	Factors That Regulate Hemopoiesis Can Be Analyzed in Culture	1459
Differentiating Epidermal Cells Express a Sequence of Different Genes as They Mature	1420	Erythropoiesis Depends on the Hormone Erythropoietin	1459
Stem Cells in the Basal Layer Provide for Renewal of the Epidermis	1420	Multiple CSFs Influence Neutrophil and Macrophage Production	1460
The Two Daughters of a Stem Cell Do Not Always Have to Become Different	1421	The Behavior of a Hemopoietic Cell Depends Partly on Chance	1461
		Regulation of Cell Survival Is as Important as Regulation of Cell Proliferation	1462
		<i>Summary</i>	1462
		<b>GENESIS, MODULATION, AND REGENERATION OF SKELETAL MUSCLE</b>	<b>1463</b>
		Myoblasts Fuse to Form New Skeletal Muscle Fibers	1464

Muscle Cells Can Vary Their Properties by Changing the Protein Isoforms They Contain	1465
Skeletal Muscle Fibers Secrete Myostatin to Limit Their Own Growth	1465
Some Myoblasts Persist as Quiescent Stem Cells in the Adult	1466
<i>Summary</i>	1467

## FIBROBLASTS AND THEIR TRANSFORMATIONS: THE CONNECTIVE-TISSUE CELL FAMILY 1467

Fibroblasts Change Their Character in Response to Chemical Signals	1467
The Extracellular Matrix May Influence Connective-Tissue Cell Differentiation by Affecting Cell Shape and Attachment	1468
Osteoblasts Make Bone Matrix	1469
Most Bones Are Built Around Cartilage Models	1470
Bone Is Continually Remodeled by the Cells Within It	1472
Osteoclasts Are Controlled by Signals From Osteoblasts	1473
Fat Cells Can Develop From Fibroblasts	1474
Leptin Secreted by Fat Cells Provides Feedback to Regulate Eating	1475
<i>Summary</i>	1476

## STEM-CELL ENGINEERING 1476

Hemopoietic Stem Cells Can Be Used to Replace Diseased Blood Cells with Healthy Ones	1477
Epidermal Stem Cell Populations Can Be Expanded in Culture for Tissue Repair	1477
Neural Stem Cells Can Be Manipulated in Culture	1478
Neural Stem Cells Can Repopulate the Central Nervous System	1478
Stem Cells in the Adult Body Are Tissue-Specific	1479
ES Cells Can Make Any Part of the Body	1480
Patient-Specific ES Cells Could Solve the Problem of Immune Rejection	1481
ES Cells Are Useful for Drug Discovery and Analysis of Disease	1482
<i>Summary</i>	1482
<i>References</i>	1483

## Chapter 24 Pathogens, Infection, and Innate Immunity 1485

### INTRODUCTION TO PATHOGENS 1486

Pathogens Have Evolved Specific Mechanisms for Interacting with Their Hosts	1486
The Signs and Symptoms of Infection May Be Caused by the Pathogen or by the Host's Responses	1487
Pathogens Are Phylogenetically Diverse	1488
Bacterial Pathogens Carry Specialized Virulence Genes	1489
Fungal and Protozoan Parasites Have Complex Life Cycles with Multiple Forms	1494
All Aspects of Viral Propagation Depend on Host Cell Machinery	1496
Prions Are Infectious Proteins	1498
Infectious Disease Agents Are Linked To Cancer, Heart Disease, and Other Chronic Illnesses	1499
<i>Summary</i>	1501

### CELL BIOLOGY OF INFECTION 1501

Pathogens Cross Protective Barriers to Colonize the Host	1501
Pathogens That Colonize Epithelia Must Avoid Clearance by the Host	1502
Intracellular Pathogens Have Mechanisms for Both Entering and Leaving Host Cells	1504
Virus Particles Bind to Molecules Displayed on the Host Cell Surface	1505
Virions Enter Host Cells by Membrane Fusion, Pore Formation, or Membrane Disruption	1506
Bacteria Enter Host Cells by Phagocytosis	1507
Intracellular Eucaryotic Parasites Actively Invade Host Cells	1508
Many Pathogens Alter Membrane Traffic in the Host Cell	1511
Viruses and Bacteria Use the Host Cell Cytoskeleton for Intracellular Movement	1514
Viral Infections Take Over the Metabolism of the Host Cell	1517
Pathogens Can Alter the Behavior of the Host Organism to Facilitate the Spread of the Pathogen	1518

Pathogens Evolve Rapidly	1518
Antigenic Variation in Pathogens Occurs by Multiple Mechanisms	1519
Error-Prone Replication Dominates Viral Evolution	1520
Drug-Resistant Pathogens Are a Growing Problem	1521
<i>Summary</i>	1524

## BARRIERS TO INFECTION AND THE INNATE IMMUNE SYSTEM 1524

Epithelial Surfaces and Defensins Help Prevent Infection	1525
Human Cells Recognize Conserved Features of Pathogens	1526
Complement Activation Targets Pathogens for Phagocytosis or Lysis	1528
Toll-like Proteins and NOD Proteins Are an Ancient Family of Pattern Recognition Receptors	1530
Phagocytic Cells Seek, Engulf, and Destroy Pathogens	1531
Activated Macrophages Contribute to the Inflammatory Response at Sites of Infection	1533
Virus-Infected Cells Take Drastic Measures to Prevent Viral Replication	1534
Natural Killer Cells Induce Virus-Infected Cells to Kill Themselves	1535
Dendritic Cells Provide the Link Between the Innate and Adaptive Immune Systems	1536
<i>Summary</i>	1537
<i>References</i>	1537

## Chapter 25 The Adaptive Immune System 1539

### LYMPHOCYTES AND THE CELLULAR BASIS OF ADAPTIVE IMMUNITY 1540

Lymphocytes Are Required for Adaptive Immunity	1540
The Innate and Adaptive Immune Systems Work Together	1541
B Lymphocytes Develop in the Bone Marrow; T Lymphocytes Develop in the Thymus	1543
The Adaptive Immune System Works by Clonal Selection	1544
Most Antigens Activate Many Different Lymphocyte Clones	1545
Immunological Memory Involves Both Clonal Expansion and Lymphocyte Differentiation	1545
Immunological Tolerance Ensures That Self Antigens Are Not Normally Attacked	1547
Lymphocytes Continuously Circulate Through Peripheral Lymphoid Organs	1549
<i>Summary</i>	1551

### B CELLS AND ANTIBODIES 1551

B Cells Make Antibodies as Both Cell-Surface Antigen Receptors and Secreted Proteins	1552
A Typical Antibody Has Two Identical Antigen-Binding Sites	1552
An Antibody Molecule Is Composed of Heavy and Light Chains	1552
There Are Five Classes of Antibody Heavy Chains, Each with Different Biological Properties	1553
The Strength of an Antibody–Antigen Interaction Depends on Both the Number and the Affinity of the Antigen-Binding Sites	1557
Antibody Light and Heavy Chains Consist of Constant and Variable Regions	1558
The Light and Heavy Chains Are Composed of Repeating Ig Domains	1559
An Antigen-Binding Site Is Constructed from Hypervariable Loops	1560
<i>Summary</i>	1561

### THE GENERATION OF ANTIBODY DIVERSITY 1562

Antibody Genes Are Assembled From Separate Gene Segments During B Cell Development	1562
Imprecise Joining of Gene Segments Greatly Increases the Diversity of V Regions	1564
The Control of V(D)J Recombination Ensures That B Cells Are Monospecific	1565
Antigen-Driven Somatic Hypermutation Fine-Tunes Antibody Responses	1566
B Cells Can Switch the Class of Antibody They Make	1567
<i>Summary</i>	1568

<b>T CELLS AND MHC PROTEINS</b>	<b>1569</b>		
T Cell Receptors (TCRs) Are Antibodylike Heterodimers	1570	Most Developing Cytotoxic and Helper T Cells That Could Be Activated by Self-Peptide–MHC Complexes Are Eliminated in the Thymus	1586
Antigen Presentation by Dendritic Cells Can Either Activate or Tolerize T Cells	1571	Some Organ-Specific Proteins Are Ectopically Expressed in the Thymus Medulla	1587
Effector Cytotoxic T Cells Induce Infected Target Cells to Kill Themselves	1572	The Function of MHC Proteins Helps Explain Their Polymorphism	1588
Effector Helper T Cells Help Activate Other Cells of the Innate and Adaptive Immune Systems	1573	<i>Summary</i>	1588
Regulatory T Cells Suppress the Activity of Other T Cells	1574	<b>HELPER T CELLS AND LYMPHOCYTE ACTIVATION</b>	<b>1589</b>
T Cells Recognize Foreign Peptides Bound to MHC Proteins	1575	Activated Dendritic Cells Use Multiple Mechanisms to Activate T Cells	1590
MHC Proteins Were Identified in Transplantation Reactions Before Their Functions Were Known	1575	The Activation of T Cells Is Controlled by Negative Feedback	1591
Class I and Class II MHC Proteins Are Structurally Similar Heterodimers	1576	The Subclass of Effector Helper T Cell Determines the Nature of the Adaptive Immune Response	1592
An MHC Protein Binds a Peptide and Interacts with a T Cell Receptor	1577	T <sub>H</sub> 1 Cells Activate Infected Macrophages and Stimulate An Inflammatory Response	1594
MHC Proteins Help Direct T Cells to Their Appropriate Targets	1579	Antigen Binding to B Cell Receptors (BCRs) Is Only One Step in B Cell Activation	1595
CD4 and CD8 Co-Receptors Bind to Invariant Parts of MHC Proteins	1580	Antigen-Specific Helper T Cells Are Essential for Activating Most B Cells	1597
Cytotoxic T Cells Recognize Fragments of Foreign Cytosolic Proteins in Association with Class I MHC Proteins	1581	A Special Class of B Cells Recognize T-Cell-Independent Antigens	1598
Helper T Cells Respond to Fragments of Endocytosed Foreign Protein Associated with Class II MHC Proteins	1583	Immune Recognition Molecules Belong to the Ancient Ig Superfamily	1599
Potentially Useful T Cells Are Positively Selected in the Thymus	1585	<i>Summary</i>	1600
		<i>References</i>	1600

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# A Note to the Reader

## Structure of the Book

Although the chapters of this book can be read independently of one another, they are arranged in a logical sequence of five parts. The first three chapters of **Part I** cover elementary principles and basic biochemistry. They can serve either as an introduction for those who have not studied biochemistry or as a refresher course for those who have.

**Part II** deals with the storage, expression and transmission of genetic information.

**Part III** deals with the principles of the main experimental methods for investigating cells. It is not necessary to read these two chapters in order to understand the later chapters, but a reader will find it a useful reference.

**Part IV** discusses the internal organization of the cell.

**Part V** follows the behavior of cells in multicellular systems, starting with cell–cell junctions and extracellular matrix and concluding with two chapters on the immune system.

## End-of-Chapter Problems

A selection of problems, written by John Wilson and Tim Hunt, now appears in the text at the end of chapters 1–20. The complete solutions to these problems can be found in *Molecular Biology of the Cell, Fifth Edition: The Problems Book*.

## References

A concise list of selected references is included at the end of each chapter. These are arranged in alphabetical order under the main chapter section headings. These references frequently include the original papers in which important discoveries were first reported. Chapter 8 includes several tables giving the dates of crucial developments along with the names of the scientists involved. Elsewhere in the book the policy has been to avoid naming individual scientists.

## Media Codes

Media codes are integrated throughout the text to indicate when relevant videos and animations are available on the DVD-ROM. The four-letter codes are enclosed in brackets and highlighted in color, like this <ATCG>. The interface for the *Cell Biology Interactive* media player on the DVD-ROM contains a window where you enter the 4-letter code. When the code is typed into the interface, the corresponding media item will load into the media player.

## Glossary Terms

Throughout the book, **boldface type** has been used to highlight key terms at the point in a chapter where the main discussion of them occurs. *Italic* is used to set off important terms with a lesser degree of emphasis. At the end of the book is the expanded **glossary**, covering technical terms that are part of the common currency of cell biology; it is intended as a first resort for a reader who encounters an unfamiliar term used without explanation.

## Nomenclature for Genes and Proteins

Each species has its own conventions for naming genes; the only common feature is that they are always set in italics. In some species (such as humans), gene names are spelled out all in capital letters; in other species (such as zebrafish), all in lower case; in yet others (most mouse genes), with the first letter in upper case and rest in lower case; or (as in *Drosophila*) with different combinations of

upper and lower case, according to whether the first mutant allele to be discovered gave a dominant or recessive phenotype. Conventions for naming protein products are equally varied.

This typographical chaos drives everyone crazy. It is not just tiresome and absurd; it is also unsustainable. We cannot independently define a fresh convention for each of the next few million species whose genes we may wish to study. Moreover, there are many occasions, especially in a book such as this, where we need to refer to a gene generically, without specifying the mouse version, the human version, the chick version, or the hippopotamus version, because they are all equivalent for the purposes of the discussion. What convention then should we use?

We have decided in this book to cast aside the conventions for individual species and follow a uniform rule: we write all gene names, like the names of people and places, with the first letter in upper case and the rest in lower case, but all in italics, thus: *Apc*, *Bazooka*, *Cdc2*, *Dishevelled*, *Egl1*. The corresponding protein, where it is named after the gene, will be written in the same way, but in roman rather than italic letters: *Apc*, *Bazooka*, *Cdc2*, *Dishevelled*, *Egl1*. When it is necessary to specify the organism, this can be done with a prefix to the gene name.

For completeness, we list a few further details of naming rules that we shall follow. In some instances an added letter in the gene name is traditionally used to distinguish between genes that are related by function or evolution; for those genes we put that letter in upper case if it is usual to do so (*LacZ*, *RecA*, *HoxA4*). We use no hyphen to separate added letters or numbers from the rest of the name. Proteins are more of a problem. Many of them have names in their own right, assigned to them before the gene was named. Such protein names take many forms, although most of them traditionally begin with a lower-case letter (actin, hemoglobin, catalase), like the names of ordinary substances (cheese, nylon), unless they are acronyms (such as GFP, for Green Fluorescent Protein, or BMP4, for Bone Morphogenetic Protein #4). To force all such protein names into a uniform style would do too much violence to established usages, and we shall simply write them in the traditional way (actin, GFP, etc.). For the corresponding gene names in all these cases, we shall nevertheless follow our standard rule: *Actin*, *Hemoglobin*, *Catalase*, *Bmp4*, *Gfp*. Occasionally in our book we need to highlight a protein name by setting it in italics for emphasis; the intention will generally be clear from the context.

For those who wish to know them, the Table below shows some of the official conventions for individual species—conventions that we shall mostly violate in this book, in the manner shown.

ORGANISM	SPECIES-SPECIFIC CONVENTION		UNIFIED CONVENTION USED IN THIS BOOK	
	GENE	PROTEIN	GENE	PROTEIN
Mouse	<i>Hoxa4</i>	Hoxa4	<i>HoxA4</i>	HoxA4
	<i>Bmp4</i>	BMP4	<i>Bmp4</i>	BMP4
	<i>integrin <math>\alpha</math>-1, Itg<math>\alpha</math>1</i>	integrin $\alpha$ 1	<i>Integrin <math>\alpha</math>1, Itg<math>\alpha</math>1</i>	integrin $\alpha$ 1
Human	<i>HOXA4</i>	HOXA4	<i>HoxA4</i>	HoxA4
Zebrafish	<i>cyclops, cyc</i>	Cyclops, Cyc	<i>Cyclops, Cyc</i>	Cyclops, Cyc
<i>Caenorhabditis</i>	<i>unc-6</i>	UNC-6	<i>Unc6</i>	Unc6
<i>Drosophila</i>	<i>sevenless, sev</i> (named after recessive mutant phenotype)	Sevenless, SEV	<i>Sevenless, Sev</i>	Sevenless, Sev
	<i>Deformed, Dfd</i> (named after dominant mutant phenotype)	Deformed, DFD	<i>Deformed, Dfd</i>	Deformed, Dfd
Yeast				
<i>Saccharomyces cerevisiae</i> (budding yeast)	<i>CDC28</i>	Cdc28, Cdc28p	<i>Cdc28</i>	Cdc28
<i>Schizosaccharomyces pombe</i> (fission yeast)	<i>Cdc2</i>	Cdc2, Cdc2p	<i>Cdc2</i>	Cdc2
<i>Arabidopsis</i>	<i>GAI</i>	GAI	<i>Gai</i>	GAI
<i>E. coli</i>	<i>uvrA</i>	UvrA	<i>UvrA</i>	UvrA

## Ancillaries

### ***Molecular Biology of the Cell, Fifth Edition: The Problems Book*** **by John Wilson and Tim Hunt (ISBN: 978-0-8153-4110-9)**

*The Problems Book* is designed to help students appreciate the ways in which experiments and simple calculations can lead to an understanding of how cells work. It provides problems to accompany Chapters 1–20 of *Molecular Biology of the Cell*. Each chapter of problems is divided into sections that correspond to those of the main textbook and review key terms, test for understanding basic concepts, and pose research-based problems. *Molecular Biology of the Cell, Fifth Edition: The Problems Book* should be useful for homework assignments and as a basis for class discussion. It could even provide ideas for exam questions. Solutions for all of the problems are provided on the CD-ROM which accompanies the book. Solutions for the end-of-chapter problems in the main textbook are also found in *The Problems Book*.

### ***MBoC5 Media DVD-ROM***

The DVD included with every copy of the book contains the figures, tables, and micrographs from the book, pre-loaded into PowerPoint® presentations, one for each chapter. A separate folder contains individual versions of each figure, table, and micrograph in JPEG format. The panels are available in PDF format. There are also over 125 videos, animations, molecular structure tutorials, and high-resolution micrographs on the DVD. The authors have chosen to include material that not only reinforces basic concepts but also expands the content and scope of the book. The multimedia can be accessed either as individual files or through the *Cell Biology Interactive* media player. As discussed above, the media player has been programmed to work with the Media Codes integrated throughout the book. A complete table of contents and overview of all electronic resources is contained in the *MBoC5 Media Viewing Guide*, a PDF file located on the root level of the DVD-ROM and in the Appendix of the media player. The DVD-ROM also contains Chapters 21–25 which cover multicellular systems. The chapters are in PDF format and can be easily printed or searched using Adobe® Acrobat® Reader or other PDF software.

### **Teaching Supplements**

Upon request, teaching supplements for *Molecular Biology of the Cell* are available to qualified instructors.

### ***MBoC5 Transparency Set***

Provides 200 full-color overhead acetate transparencies of the most important figures from the book.

### ***MBoC5 Test Questions***

A selection of test questions will be available. Written by Kirsten Benjamin (Amyris Biotechnologies, Emeryville, California) and Linda Huang (University of Massachusetts, Boston), these thought questions will test students' understanding of the chapter material.

### ***MBoC5 Lecture Outlines***

Lecture outlines created from the concept heads for the text are provided.

### ***Garland Science Classwire™***

All of the teaching supplements on the DVD-ROM (these include figures in PowerPoint and JPEG format; Chapters 21–25 in PDF format; 125 videos, animations, and movies) and the test questions and lecture outlines are available to qualified instructors online at the Garland Science Classwire™ Web site. Garland Science Classwire™ offers access to other instructional resources from all of the Garland Science textbooks, and provides free online course management tools. For additional information, please visit <http://www.classwire.com/garlandscience> or e-mail [science@garland.com](mailto:science@garland.com). (*Classwire* is a trademark of Chalkfree, Inc.)

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# INTRODUCTION TO THE CELL

## Part I

### Chapters

- 1 Cells and Genomes
- 2 Cell Chemistry and Biosynthesis
- 3 Proteins

