

# Contents

## 1 Introduction to Cell Biology 1

### 1.1 The Discovery of Cells 2

### 1.2 Basic Properties of Cells 3

- Cells Are Highly Complex and Organized 3
- Cells Possess a Generic Program and the Means to Use It 5
- Cells Are Capable of Producing More of Themselves 5
- Cells Acquire and Utilize Energy 5
- Cells Carry Out a Variety of Chemical Reactions 6
- Cells Engage in Mechanical Activities 6
- Cells Are Able to Respond to Stimuli 6
- Cells Are Capable of Self-Regulation 6
- Cells Evolve 7

### 1.3 Two Fundamentally Different Classes of Cells 7

- Characteristics That Distinguish Prokaryotic and Eukaryotic Cells 8
- Types of Prokaryotic Cells 14
- Types of Eukaryotic Cells: Cell Specialization 15
- The Sizes of Cells and Their Components 17
- Synthetic Biology 17
- **THE HUMAN PERSPECTIVE:** The Prospect of Cell Replacement Therapy 20

### 1.4 Viruses 23

- Viroids 26
- **EXPERIMENTAL PATHWAYS:** The Origin of Eukaryotic Cells 26

## 2 The Structure and Functions of Biological Molecules 32

### 2.1 Covalent Bonds 33

- Polar and Nonpolar Molecules 34
- Ionization 34

### 2.2 Noncovalent Bonds 34

- **THE HUMAN PERSPECTIVE:** Free Radicals as a Cause of Aging 35
- Ionic Bonds: Attractions between Charged Atoms 35
- Hydrogen Bonds 36
- Hydrophobic Interactions and van der Waals Forces 36
- The Life-Supporting Properties of Water 37

### 2.3 Acids, Bases, and Buffers 39

### 2.4 The Nature of Biological Molecules 40

- Functional Groups 41
- A Classification of Biological Molecules by Function 41

### 2.5 Four Types of Biological Molecules 42

- Carbohydrates 43

Lipids 47

Proteins 50

● **THE HUMAN PERSPECTIVE:** Protein Misfolding Can Have Deadly Consequences 66

Nucleic Acids 77

### 2.6 The Formation of Complex Macromolecular Structures 79

The Assembly of Tobacco Mosaic Virus Particles and Ribosomal Subunits 79

● **EXPERIMENTAL PATHWAYS:** Chaperones: Helping Proteins Reach Their Proper Folded State 80

## 3 Bioenergetics, Enzymes, and Metabolism 86

### 3.1 Bioenergetics 87

The Laws of Thermodynamics and the Concept of Entropy 87

Free Energy 89

### 3.2 Enzymes as Biological Catalysts 94

The Properties of Enzymes 95

Overcoming the Activation Energy Barrier 96

The Active Site 97

Mechanisms of Enzyme Catalysis 99

Enzyme Kinetics 102

● **THE HUMAN PERSPECTIVE:** The Growing Problem of Antibiotic Resistance 106

### 3.3 Metabolism 108

An Overview of Metabolism 108

Oxidation and Reduction: A Matter of Electrons 109

The Capture and Utilization of Energy 110

Metabolic Regulation 115

## 4 Genes, Chromosomes, and Genomes 120

### 4.1 The Concept of a Gene as a Unit of Inheritance 121

### 4.2 Chromosomes: The Physical Carriers of the Genes 122

The Discovery of Chromosomes 122

Chromosomes as the Carriers of Genetic Information 123

Genetic Analysis in *Drosophila* 124

Crossing Over and Recombination 124

Mutagenesis and Giant Chromosomes 126

### 4.3 The Chemical Nature of the Gene 127

The Structure of DNA 127

The Watson-Crick Proposal 128

DNA Supercoiling 131

### 4.4 The Structure of the Genome 132

The Complexity of the Genome 133

- **THE HUMAN PERSPECTIVE:** Diseases that Result from Expansion of Trinucleotide Repeats 138
- 4.5 The Stability of the Genome 140**
  - Whole-Genome Duplication (Polyploidization) 140
  - Duplication and Modification of DNA Sequences 141
  - “Jumping Genes” and the Dynamic Nature of the Genome 142
- 4.6 Sequencing Genomes: The Footprints of Biological Evolution 145**
  - Comparative Genomics: “If It’s Conserved, It Must Be Important” 147
  - The Genetic Basis of “Being Human” 148
  - Genetic Variation Within the Human Species Population 150
  - **THE HUMAN PERSPECTIVE:** Application of Genomic Analyses to Medicine 151
  - **EXPERIMENTAL PATHWAYS:** The Chemical Nature of the Gene 154
- 5 The Path to Gene Expression 160**
  - 5.1 The Relationship between Genes, Proteins, and RNAs 161**
    - An Overview of the Flow of Information through the Cell 162
  - 5.2 An Overview of Transcription in Both Prokaryotic and Eukaryotic Cells 163**
    - Transcription in Bacteria 166
    - Transcription and RNA Processing in Eukaryotic Cells 167
  - 5.3 Synthesis and Processing of Eukaryotic Ribosomal and Transfer RNAs 169**
    - Synthesizing the rRNA Precursor 170
    - Processing the rRNA Precursor 171
    - Synthesis and Processing of the 5S rRNA 174
    - Transfer RNAs 174
  - 5.4 Synthesis and Processing of Eukaryotic Messenger RNAs 175**
    - The Machinery for mRNA Transcription 175
    - Split Genes: An Unexpected Finding 178
    - The Processing of Eukaryotic Messenger RNAs 182
    - Evolutionary Implications of Split Genes and RNA Splicing 188
    - Creating New Ribozymes in the Laboratory 188
  - 5.5 Small Regulatory RNAs and RNA Silencing Pathways 189**
    - **THE HUMAN PERSPECTIVE:** Clinical Applications of RNA Interference 192
    - MicroRNAs: Small RNAs that Regulate Gene Expression 193
    - piRNAs: A Class of Small RNAs that Function in Germ Cells 194
    - Other Noncoding RNAs 195
  - 5.6 Encoding Genetic Information 195**
    - The Properties of the Genetic Code 195
  - 5.7 Decoding the Codons: The Role of Transfer RNAs 198**
    - The Structure of tRNAs 199
  - 5.8 Translating Genetic Information 202**
    - Initiation 202
    - Elongation 205
    - Termination 208
    - mRNA Surveillance and Quality Control 208
    - Polyribosomes 209
    - **EXPERIMENTAL PATHWAYS:** The Role of RNA as a Catalyst 211
- 6 Controlling Gene Expression 217**
  - 6.1 Control of Gene Expression in Bacteria 218**
    - Organization of Bacterial Genomes 218
    - The Bacterial Operon 218
    - Riboswitches 221
  - 6.2 Control of Gene Expression in Eukaryotes: Structure and Function of the Cell Nucleus 222**
    - The Nuclear Envelope 222
    - Chromosomes and Chromatin 227
    - **THE HUMAN PERSPECTIVE:** Chromosomal Aberrations and Human Disorders 238
    - Epigenetics: There’s More to Inheritance than DNA 243
    - The Nucleus as an Organized Organelle 244
  - 6.3 An Overview of Gene Regulation in Eukaryotes 246**
  - 6.4 Transcriptional Control 248**
    - The Role of Transcription Factors in Regulating Gene Expression 251
    - The Structure of Transcription Factors 253
    - DNA Sites Involved in Regulating Transcription 256
    - Transcriptional Activation: The Role of Enhancers, Promoters, and Coactivators 259
    - Transcriptional Repression 264
  - 6.5 RNA Processing Control 267**
  - 6.6 Translational Control 270**
    - Initiation of Translation 270
    - Cytoplasmic Localization of mRNAs 271
    - The Control of mRNA Stability 272
    - The Role of MicroRNAs in Translational Control 273
  - 6.7 Posttranslational Control: Determining Protein Stability 275**
- 7 Replicating and Repairing DNA 279**
  - 7.1 DNA Replication 280**
    - Semiconservative Replication 280
    - Replication in Bacterial Cells 283

The Structure and Functions of DNA Polymerases 288  
 Replication in Eukaryotic Cells 292

## 7.2 DNA Repair 298

Nucleotide Excision Repair 299  
 Base Excision Repair 300  
 Mismatch Repair 301  
 Double-Strand Breakage Repair 301

## 7.3 Between Replication and Repair 302

● **THE HUMAN PERSPECTIVE:** The Consequences of DNA Repair Deficiencies 303

# 8 Cellular Membranes 306

## 8.1 An Overview of Membrane Functions 307

## 8.2 A Brief History of Studies on Plasma Membrane Structure 309

## 8.3 The Chemical Composition of Membranes 311

Membrane Lipids 311  
 The Asymmetry of Membrane Lipids 314  
 Membrane Carbohydrates 315

## 8.4 The Structure and Functions of Membrane Proteins 316

Integral Membrane Proteins 316  
 Studying the Structure and Properties of Integral Membrane Proteins 318  
 Peripheral Membrane Proteins 323  
 Lipid-Anchored Membrane Proteins 323

## 8.5 Membrane Lipids and Membrane Fluidity 324

The Importance of Membrane Fluidity 325  
 Maintaining Membrane Fluidity 325  
 Lipid Rafts 325

## 8.6 The Dynamic Nature of the Plasma Membrane 326

The Diffusion of Membrane Proteins after Cell Fusion 327  
 Restrictions on Protein and Lipid Mobility 328  
 The Red Blood Cell: An Example of Plasma Membrane Structure 331

## 8.7 The Movement of Substances Across Cell Membranes 333

The Energetics of Solute Movement 333  
 Diffusion of Substances through Membranes 335  
 Facilitated Diffusion 342  
 Active Transport 343  
 ● **THE HUMAN PERSPECTIVE:** Defects in Ion Channels and Transporters as a Cause of Inherited Disease 348

## 8.8 Membrane Potentials and Nerve Impulses 350

The Resting Potential 350  
 The Action Potential 351  
 Propagation of Action Potentials as an Impulse 353  
 Neurotransmission: Jumping the Synaptic Cleft 354

● **EXPERIMENTAL PATHWAYS:** The Acetylcholine Receptor 357

# 9 Mitochondrial Structure and Function 364

## 9.1 Mitochondrial Structure and Function 365

Mitochondrial Membranes 366  
 The Mitochondrial Matrix 368

## 9.2 Oxidative Metabolism in the Mitochondrion 369

The Tricarboxylic Acid (TCA) Cycle 371  
 The Importance of Reduced Coenzymes in the Formation of ATP 372

● **THE HUMAN PERSPECTIVE:** The Role of Anaerobic and Aerobic Metabolism in Exercise 374

## 9.3 The Role of Mitochondria in the Formation of ATP 375

Oxidation-Reduction Potentials 375  
 Electron Transport 376  
 Types of Electron Carriers 377

## 9.4 Translocation of Protons and the Establishment of a Proton-Motive Force 384

## 9.5 The Machinery for ATP Formation 385

The Structure of ATP Synthase 386  
 The Basis of ATP Formation According to the Binding Change Mechanism 387  
 Other Roles for the Proton-Motive Force in Addition to ATP Synthesis 391

## 9.6 Peroxisomes 392

● **THE HUMAN PERSPECTIVE:** Diseases that Result from Abnormal Mitochondrial or Peroxisomal Function 393

# 10 Chloroplast Structure and Function 397

## 10.1 Chloroplast Structure and Function 399

## 10.2 An Overview of Photosynthetic Metabolism 400

## 10.3 The Absorption of Light 402

Photosynthetic Pigments 402

## 10.4 Photosynthetic Units and Reaction Centers 404

Oxygen Formation: Coordinating the Action of Two Different Photosynthetic Systems 404  
 Killing Weeds by Inhibiting Electron Transport 411

## 10.5 Photophosphorylation 411

Noncyclic Versus Cyclic Photophosphorylation 412

## 10.6 Carbon Dioxide Fixation and the Synthesis of Carbohydrate 412

Carbohydrate Synthesis in C<sub>3</sub> Plants 412  
 Carbohydrate Synthesis in C<sub>4</sub> Plants 417  
 Carbohydrate Synthesis in CAM Plants 418

## 11 The Extracellular Matrix and Cell Interactions 421

### 11.1 The Extracellular Space 422

The Extracellular Matrix 422

### 11.2 Interactions of Cells with Extracellular Materials 430

Integrins 430

Focal Adhesions and Hemidesmosomes: Anchoring Cells to Their Substratum 433

### 11.3 Interactions of Cells with Other Cells 436

Selectins 437

The Immunoglobulin Superfamily 438

Cadherins 439

● **THE HUMAN PERSPECTIVE:** The Role of Cell Adhesion in Inflammation and Metastasis 441

Adherens Junctions and Desmosomes: Anchoring Cells to Other Cells 443

The Role of Cell-Adhesion Receptors in Transmembrane Signaling 445

### 11.4 Tight Junctions: Sealing The Extracellular Space 446

### 11.5 Gap Junctions and Plasmodesmata: Mediating Intercellular Communication 448

Plasmodesmata 451

### 11.6 Cell Walls 452

## 12 Cellular Organelles and Membrane Trafficking 456

### 12.1 An Overview of the Endomembrane System 457

### 12.2 A Few Approaches to the Study of Endomembranes 459

Insights Gained from Autoradiography 459

Insights Gained from the Use of the Green Fluorescent Protein 459

Insights Gained from the Biochemical Analysis of Subcellular Fractions 461

Insights Gained from the Use of Cell-Free Systems 462

Insights Gained from the Study of Mutant Phenotypes 463

### 12.3 The Endoplasmic Reticulum 465

The Smooth Endoplasmic Reticulum 466

Functions of the Rough Endoplasmic Reticulum 466

From the ER to the Golgi Complex: The First Step in Vesicular Transport 475

### 12.4 The Golgi Complex 476

Glycosylation in the Golgi Complex 478

The Movement of Materials through the Golgi Complex 478

### 12.5 Types of Vesicle Transport and Their Functions 481

COPII-Coated Vesicles: Transporting Cargo from the ER to the Golgi Complex 482

COPI-Coated Vesicles: Transporting Escaped Proteins Back to the ER 484

Beyond the Golgi Complex: Sorting Proteins at the TGN 484

Targeting Vesicles to a Particular Compartment 486

### 12.6 Lysosomes 489

Autophagy 490

● **THE HUMAN PERSPECTIVE:** Disorders Resulting from Defects in Lysosomal Function 492

### 12.7 Plant Cell Vacuoles 493

### 12.8 The Endocytic Pathway: Moving Membrane and Materials into the Cell Interior 494

Endocytosis 494

Phagocytosis 501

### 12.9 Posttranslational Uptake of Proteins by Peroxisomes, Mitochondria, and Chloroplasts 502

Uptake of Proteins into Peroxisomes 502

Uptake of Proteins into Mitochondria 502

Uptake of Proteins into Chloroplasts 504

● **EXPERIMENTAL PATHWAYS:** Receptor-Mediated Endocytosis 505

## 13 The Cytoskeleton 510

### 13.1 Overview of the Major Functions of the Cytoskeleton 511

### 13.2 The Study of the Cytoskeleton 512

The Use of Live-Cell Fluorescence Imaging 512

The Use of In Vitro and In Vivo Single-Molecule Assays 513

The Use of Fluorescence Imaging Techniques to Monitor the Dynamics of the Cytoskeleton 515

### 13.3 Microtubules 516

Structure and Composition 516

Microtubule-Associated Proteins 517

Microtubules as Structural Supports and Organizers 518

Microtubules as Agents of Intracellular Motility 519

Motor Proteins that Traverse the Microtubular Cytoskeleton 520

Microtubule-Organizing Centers (MTOCs) 525

The Dynamic Properties of Microtubules 527

Cilia and Flagella: Structure and Function 531

● **THE HUMAN PERSPECTIVE:** The Role of Cilia in Development and Disease 535

### 13.4 Intermediate Filaments 540

Intermediate Filament Assembly and Disassembly 540

Types and Functions of Intermediate Filaments 542

### 13.5 Microfilaments 542

Microfilament Assembly and Disassembly 544

Myosin: The Molecular Motor of Actin Filaments 546

### 13.6 Muscle Contractility 550

The Sliding Filament Model of Muscle Contraction 552

### 13.7 Nonmuscle Motility 557

Actin-Binding Proteins 558

Examples of Nonmuscle Motility and Contractility 560

## 14 Cell Division 572

### 14.1 The Cell Cycle 573

Cell Cycles in Vivo 574

Control of the Cell Cycle 574

### 14.2 M Phase: Mitosis and Cytokinesis 581

Prophase 583

Prometaphase 588

Metaphase 590

Anaphase 592

Telophase 597

Motor Proteins Required for Mitotic Movements 597

Cytokinesis 597

### 14.3 Meiosis 602

The Stages of Meiosis 603

● **THE HUMAN PERSPECTIVE:** Meiotic Nondisjunction and Its Consequences 608

Genetic Recombination During Meiosis 610

● **EXPERIMENTAL PATHWAYS:** The Discovery and Characterization of MPF 611

## 15 Cell Signaling Pathways 617

### 15.1 The Basic Elements of Cell Signaling Systems 618

### 15.2 A Survey of Extracellular Messengers and Their Receptors 621

### 15.3 G Protein-Coupled Receptors and Their Second Messengers 621

Signal Transduction by G Protein-Coupled Receptors 622

● **THE HUMAN PERSPECTIVE:** Disorders Associated with G Protein-Coupled Receptors 625

Second Messengers 627

The Specificity of G Protein-Coupled Responses 630

Regulation of Blood Glucose Levels 631

The Role of GPCRs in Sensory Perception 634

### 15.4 Protein-Tyrosine Phosphorylation as a Mechanism for Signal Transduction 636

The Ras-MAP Kinase Pathway 640

Signaling by the Insulin Receptor 644

● **THE HUMAN PERSPECTIVE:** Signaling Pathways and Human Longevity 647

Signaling Pathways in Plants 648

### 15.5 The Role of Calcium as an Intracellular Messenger 648

Regulating Calcium Concentrations in Plant Cells 652

### 15.6 Convergence, Divergence, and Cross-Talk Among Different Signaling Pathways 653

Examples of Convergence, Divergence, and Cross-Talk Among Signaling Pathways 654

### 15.7 The Role of NO as an Intercellular Messenger 655

### 15.8 Apoptosis (Programmed Cell Death) 656

The Extrinsic Pathway of Apoptosis 658

The Intrinsic Pathway of Apoptosis 659

## 16 Cancer 664

### 16.1 Basic Properties of a Cancer Cell 665

### 16.2 The Causes of Cancer 667

### 16.3 The Genetics of Cancer 669

Tumor-Suppressor Genes and Oncogenes: Brakes and Accelerators 671

The Cancer Genome 683

Gene-Expression Analysis 685

### 16.4 New Strategies for Combating Cancer 687

Immunotherapy 688

Inhibiting the Activity of Cancer-Promoting Proteins 689

Inhibiting the Formation of New Blood

Vessels (Angiogenesis) 692

● **EXPERIMENTAL PATHWAYS:** The Discovery of Oncogenes 694

## 17 Immunity 699

### 17.1 An Overview of the Immune Response 700

Innate Immune Responses 700

Adaptive Immune Responses 703

### 17.2 The Clonal Selection Theory as It Applies to B Cells 704

Vaccination 706

### 17.3 T Lymphocytes: Activation and Mechanism of Action 707

### 17.4 Selected Topics on the Cellular and Molecular Basis of Immunity 710

The Modular Structure of Antibodies 710

DNA Rearrangements that Produce Genes Encoding B- and T-Cell Antigen Receptors 713

Membrane-Bound Antigen Receptor Complexes 716

The Major Histocompatibility Complex 716

Distinguishing Self from Nonself 721

Lymphocytes Are Activated by Cell-Surface Signals 722

Signal Transduction Pathways in Lymphocyte Activation 723

● **THE HUMAN PERSPECTIVE:** Autoimmune Diseases 724

● **EXPERIMENTAL PATHWAYS:** The Role of the Major Histocompatibility Complex in Antigen Presentation 727

## 18 Methods in Cell Biology 732

### 18.1 The Light Microscope 733

Resolution 733

Visibility 734

- Preparation of Specimens for Bright-Field Light Microscopy 735
  - Phase-Contrast Microscopy 735
  - Fluorescence Microscopy (and Related Fluorescence-Based Techniques) 736
  - Video Microscopy and Image Processing 738
  - Laser Scanning Confocal Microscopy 739
  - Super-Resolution Fluorescence Microscopy 740
  - 18.2 Transmission Electron Microscopy 740**
    - Specimen Preparation for Electron Microscopy 742
  - 18.3 Scanning Electron and Atomic Force Microscopy 746**
    - Atomic Force Microscopy 748
  - 18.4 The Use of Radioisotopes 748**
  - 18.5 Cell Culture 749**
  - 18.6 The Fractionation of a Cell's Contents by Differential Centrifugation 752**
  - 18.7 Isolation, Purification, and Fractionation of Proteins 752**
    - Selective Precipitation 752
    - Liquid Column Chromatography 753
    - Polyacrylamide Gel Electrophoresis 756
    - Protein Measurement and Analysis 757
  - 18.8 Determining the Structure of Proteins and Multisubunit Complexes 758**
  - 18.9 Fractionation of Nucleic Acids 760**
    - Separation of DNAs by Gel Electrophoresis 760
    - Separation of Nucleic Acids by Ultracentrifugation 760
  - 18.10 Nucleic Acid Hybridization 762**
  - 18.11 Chemical Synthesis of DNA 764**
  - 18.12 Recombinant DNA Technology 764**
    - Restriction Endonucleases 764
    - Formation of Recombinant DNAs 766
    - DNA Cloning 766
  - 18.13 Enzymatic Amplification of DNA by PCR 769**
    - Applications of PCR 770
  - 18.14 DNA Sequencing 771**
  - 18.15 DNA Libraries 773**
    - Genomic Libraries 773
    - cDNA Libraries 774
  - 18.16 DNA Transfer into Eukaryotic Cells and Mammalian Embryos 775**
  - 18.17 Determining Eukaryotic Gene Function by Gene Elimination or Silencing 778**
    - In Vitro Mutagenesis 778
    - Knockout Mice 778
    - RNA Interference 780
  - 18.18 The Use of Antibodies 780**
- Glossary G-1**
- Additional Readings A-1**
- Index I-1**