

Brief Contents

Unit I Defining and Working with GENES

- 1** Genes, Genomes, and Genetic Analysis
- 2** DNA Structure and Genetic Variation

Unit II Transmission Genetics

- 3** Mendelian Genetics: The Principles of Segregation and Assortment
- 4** The Chromosomal Basis of Inheritance
- 5** Genetic Linkage and Chromosome Mapping
- 6** Human Karyotypes and Chromosome Behavior
- 7** The Genetic Basis of Complex Traits
- 8** Genetics of Bacteria and Their Viruses

Unit III Organization and Replication of Chromosomes and DNA

- 9** Molecular Organization of Chromosomes and Genomes
- 10** DNA Replication and Sequencing
- 11** Mutation, Repair, and Recombination

Unit IV Gene Expression

- 12** Molecular Biology of Gene Expression
- 13** Molecular Mechanisms of Gene Regulation
- 14** Manipulating Genes and Genomes
- 15** Genetic Control of Development
- 16** Molecular Genetics of the Cell Cycle and Cancer

Unit V Variation

- 17** Mitochondrial DNA and Extranuclear Inheritance
- 18** Genes in Populations
- 19** Molecular and Human Evolutionary Genetics

1

2

40

81

82

120

159

200

245

279

319

320

353

382

423

424

466

519

568

609

649

650

677

717

Contents

Preface xv

The Student Experience xvi

What's New in the Ninth Edition xxii

Teaching Tools xxvi

Acknowledgments xxviii

About the Authors xxxi

Unit I Defining and Working with GENES

1

1 Genes, Genomes, and Genetic Analysis

2

*Learning Objectives & Science
Competencies* 3

1.1 DNA as the Genetic Material 4

Experimental Proof of the Genetic
Function of DNA 4

Genetic Role of DNA in Bacteriophages 6

1.2 DNA Structure and Replication 8

An Overview of DNA Replication 10

1.3 Genes and Proteins 11

Inborn Errors of Metabolism as
a Cause of Hereditary Disease 12

1.4 Genetic Analysis 15

Mutant Genes and Defective Proteins 16

Complementation Test for Mutations in the
Same Gene 19

Analysis of Complementation Data 20

Other Applications of Genetic Analysis 22

1.5 Gene Expression: The Central Dogma 23

Transcription 24

Translation 25

The Genetic Code 26

1.6 Mutation and Variation 28

Variation in Populations 29

1.7 Genes and Environment 30

1.8 The Molecular Unity of Life 31

Prokarya, Archaea, and Eukarya 32

Genomes and Proteomes 32

ROOTS OF DISCOVERY: The Black Urine Disease 14

ROOTS OF DISCOVERY: One Gene, One Enzyme 16

2 DNA Structure and Genetic Variation

40

*Learning Objectives & Science
Competencies* 41

2.1 Genetic Differences Among Individuals 41

DNA Markers as Landmarks
in Chromosomes 41

2.2 The Terminology of Genetic Analysis 43

2.3 The Molecular Structure of DNA 44

Polynucleotide Chains 44

The Double Helix 46

Base Pairing and Base Stacking 47

Antiparallel Strands 49

DNA Structure as Related to Function 50

2.4 The Separation and Identification of Genomic DNA Fragments 51

Restriction Enzymes and Site-Specific
DNA Cleavage 52

Gel Electrophoresis 54

Nucleic Acid Hybridization 56

2.5 Amplification of Specific DNA for Detection and Purification 58

Constraints on DNA Replication: Primers
and 5'-to-3' Strand Elongation 59

- The Polymerase Chain Reaction 60
- 2.6 Types of DNA Markers Present in Genomic DNA 64**
 - Restriction Fragment Length Polymorphisms 64
 - Single-Nucleotide Polymorphisms 64
 - Tandem Repeat Polymorphisms 67
 - Copy-Number Variation 70

2.7 Applications of DNA Markers 70

- Genetic Markers, Genetic Mapping, and "Disease Genes" 70
- Other Uses for DNA Markers 71

ROOTS OF DISCOVERY: The Double Helix 51

THE CUTTING EDGE: High-Throughput SNP Genotyping 68

Unit II Transmission Genetics

81

3 Mendelian Genetics: The Principles of Segregation and Assortment

82

Learning Objectives & Science Competencies 83

3.1 Morphological and Molecular Phenotypes 83

3.2 Segregation of a Single Gene 85

- Phenotypic Ratios in the F_2 Generation 87
- The Principle of Segregation 88
- Verification of Segregation 91
- The Testcross and the Backcross 92

3.3 Segregation of Two or More Genes 93

- The Principle of Independent Assortment 93
- The Testcross with Independently Assorting Genes 95
- Three or More Genes 95

3.4 Human Pedigree Analysis 97

- Characteristics of Dominant and Recessive Inheritance 97
- Most Human Genetic Variation Is Not "Bad" 99

Molecular Markers in Human Pedigrees 100

3.5 Incomplete Dominance and Epistasis 100

- Multiple Alleles 102
- Human ABO Blood Groups 103
- Epistasis 105

3.6 Probability in Genetic Analysis 107

- Elementary Outcomes and Events 108
- Probability of the Union of Events 109
- Probability of the Intersection of Events 109

3.7 Conditional Probability and Pedigrees 110

- Bayes' Theorem 111

ROOTS OF DISCOVERY: What Did Gregor Mendel Think He Discovered? 90

ROOTS OF DISCOVERY: This Land Is Your Land 101

4 The Chromosomal Basis of Inheritance

120

Learning Objectives & Science Competencies 121

4.1 The Stability of Chromosome Complements 121

4.2 Mitosis 123

- Prophase 124
- Metaphase 124
- Anaphase 126
- Telophase 126

4.3 Meiosis 126

- The First Meiotic Division: Reduction 129

The Second Meiotic Division: Equation 135

4.4 Sex-Chromosome Inheritance 136

- Chromosomal Determination of Sex 136
- X-Linked Inheritance 136
- Pedigree Characteristics of Human X-Linked Inheritance 140
- Heterogametic Females 141
- Nondisjunction as Proof of the Chromosome Theory of Heredity 141
- Sex Determination in *Drosophila* 142

- 4.5 Probability in the Prediction of Progeny Distributions 144**
 Using the Binomial Distribution in Genetics 145
 Meaning of the Binomial Coefficient 146
- 4.6 Testing Goodness of Fit to a Genetic Hypothesis 147**
 Random Variables and Distributions 147

The Chi-Square Method 148

Are Mendel's Data Too Good to Be True? 150

ROOTS OF DISCOVERY: Grasshopper, Grasshopper 134

ROOTS OF DISCOVERY: The White-Eyed Male 138

5 Genetic Linkage and Chromosome Mapping 159

Learning Objectives & Science Competencies 160

5.1 Linkage and Recombination of Genes in a Chromosome 161

- Coupling Versus Repulsion of Syntenic Alleles 162
 The Chi-Square Test for Linkage 163
 Each Pair of Linked Genes Has a Characteristic Frequency of Recombination 164
 Recombination in Females Versus Males 165

5.2 Genetic Mapping 165

- Map Distance and Frequency of Recombination 165
 Crossing Over 170
 Recombination Between Genes Results from a Physical Exchange Between Chromosomes 170
 Crossing Over Takes Place at the Four-Strand Stage of Meiosis 170

Multiple Crossovers 174

5.3 Genetic Mapping in a Three-Point Testcross 176

- Chromosome Interference in Double Crossovers 177
 Genetic Mapping Functions 178
 Genetic Map Distance and Physical Distance 179

5.4 Mapping by Tetrad Analysis 180

- Unordered Tetrads 180
 Ordered Tetrads 181

5.5 Genetic Mapping in Humans 184

- Inferring Linkage in Pedigrees 184
 Association Mapping 187

5.6 Special Features of Recombination 190

- Recombination Within Genes 190
 Mitotic Recombination 190

ROOTS OF DISCOVERY: Genes All in a Row 166

ROOTS OF DISCOVERY: Mapping Markers in the Human Genome 185

6 Human Karyotypes and Chromosome Behavior 200

Learning Objectives & Science Competencies 201

6.1 The Human Karyotype 201

- Standard Karyotypes 201
 The Centromere and Chromosome Stability 204
 Dosage Compensation of X-Linked Genes 205
 The Calico Cat 208
 Pseudoautosomal Inheritance 208
 Active Genes in the "Inactive" X Chromosome 209

Gene Content and Evolution of the Y Chromosome 209

6.2 Chromosome Abnormalities in Human Pregnancies 211

- Down Syndrome and Other Viable Trisomies 213
 Trisomic Segregation 214
 Sex-Chromosome Abnormalities 215
 Environmental Effects on Nondisjunction 216

6.3 Chromosomal Deletions and Duplications 217

- Deletions 217

- Deletion Mapping 218
- Duplications 219
- Unequal Crossing Over in Human Red-Green Color Blindness 220
- Copy-Number Variation with Reciprocal Risks of Autism and Schizophrenia 221
- Gene Duplication and the Evolution of New Proteins 224

6.4 Genetics of Chromosomal Inversions 225

- Paracentric Inversion (Not Including the Centromere) 226
- Pericentric Inversion (Including the Centromere) 227

6.5 Chromosomal Translocations 227

- Reciprocal Translocations 227

- Pseudolinkage in Heterozygotes 228

- Robertsonian Translocations and Trisomy 21 230

- Translocation Complexes in *Oenothera* 230

6.6 Genomic Position Effects on Gene Expression 232

6.7 Polyploidy in Plant Evolution 233

- Sexual Versus Asexual Polyploidization 235
- Autopolyploids and Allopolyploids 236
- Monoploid Organisms 238

ROOTS OF DISCOVERY: Lyonization of an X Chromosome 207

ROOTS OF DISCOVERY: The First Human Chromosomal Disorder Identified 212

7 The Genetic Basis of Complex Traits 245

Learning Objectives & Science Competencies 246

7.1 Complex Traits 246

- Continuous, Categorical, and Threshold Traits 247
- The Normal Distribution 247
- Reconciling Mendelian Inheritance with Continuous Traits 249

7.2 Causes of Variation 250

- Genotypic Variation 252
- Environmental Variation 253
- Genetics and Environment Combined 254
- Genotype-by-Environment Interaction and Association 255

7.3 Heritability 256

- The Number of Genes Affecting Complex Traits 257
- Broad-Sense Heritability 258
- Narrow-Sense Heritability 258
- Twin Studies 258

7.4 Correlation Between Relatives 259

- Covariance and Correlation 259
- The Graphical Meaning of a Correlation 260

7.5 Heritability and Selection 262

- Phenotypic Change with Individual Selection: A Prediction Equation 262
- Long-Term Artificial Selection 264
- Heritabilities of Threshold Traits 264

7.6 Misconceptions About Heritability 266

7.7 Identification of Genes Affecting Complex Traits 267

- Linkage Analysis in the Genetic Mapping of Quantitative-Trait Loci 267
- Genome-Wide Association Studies 268
- Candidate Genes for Complex Traits 269

ROOTS OF DISCOVERY: A Maize'n Grass 251

THE CUTTING EDGE: Crowd-Sourced Genomics 270

8 Genetics of Bacteria and Their Viruses 279

Learning Objectives & Science Competencies 280

8.1 Plasmids and Genetic Exchange 280

- The F Plasmid: A Conjugative Plasmid 281

8.2 Bacterial Genetics 282

- Mutant Phenotypes 282
- Isolating Auxotrophs 283
- Mechanisms of Genetic Exchange 284

8.3 DNA-Mediated Transformation 285

8.4 Genetic Exchange and Conjugation 286

Cointegrate Formation and Hfr Cells 287

Time-of-Entry Mapping 290

F' Plasmids 293

8.5 Transduction 294

The Phage Lytic Cycle 294

Generalized Transduction 294

8.6 Bacteriophage Genetics 297

Plaque Formation and Phage

Mutants 297

Genetic Recombination in the Lytic
Cycle 298Fine Structure of the *rII* Gene
in Bacteriophage T4 299**8.7 Lysogeny and Specialized
Transduction 303**Site-Specific Recombination
and Lysogeny 303

Specialized Transduction 309

**ROOTS OF DISCOVERY: The Sex Life
of Bacteria 293****ROOTS OF DISCOVERY: Artoo 304****THE CUTTING EDGE: Surviving in a Hostile
World 311****Unit III Organization and Replication of Chromosomes and DNA 319****9 Molecular Organization of Chromosomes and Genomes 320***Learning Objectives & Science
Competencies 321***9.1 Genome Size and Evolutionary
Complexity: The C-Value
Paradox 321****9.2 The Supercoiling of DNA 323**

Topoisomerase Enzymes 324

**9.3 The Structure of Bacterial
Genomes 325**

Mobile DNA in Prokaryotes 325

Mobilization of Nonconjugative
Plasmids 326**9.4 The Structure of Eukaryotic
Genomes 328**The Nucleosome: The Structural Unit
of Chromatin 328

The Nucleosome Core Particle 328

Chromosome Territories in the
Nucleus 331

Chromosome Condensation 332

Polytene Chromosomes 333

**9.5 Analysis of Sequence Complexity in
Eukaryotic Genomes 334**

Kinetics of DNA Renaturation 334

Analysis of Genome Size and Repetitive
Sequences by Renaturation Kinetics 335**9.6 Unique and Repetitive Sequences in
Eukaryotic Genomes 336**

Unique Sequences 337

Highly Repetitive Sequences 337

Middle-Repetitive Sequences
and Transposable Elements 338Molecular Mechanisms of
Transposition 338Transposable Elements
in the Human Genome 340**9.7 Molecular Structure
of the Centromere 341****9.8 Molecular Structure of the Telomere 343**Telomere Length Limits the Number
of Cell Doublings 346**ROOTS OF DISCOVERY: Telomeres:
The Beginning of the End 346****10 DNA Replication and Sequencing 353***Learning Objectives & Science
Competencies 354***10.1 Problems of Initiation, Elongation, and
Incorporation Error 354****10.2 Semiconservative Replication of
Double-Stranded DNA 355**

The Meselson-Stahl Experiment 355

Theta Replication of Circular DNA
Molecules 357

Rolling-Circle Replication 360

10.3 Initiation of DNA Replication 361Unwinding, Stabilization, and Stress
Release 361Formation of the Primosome
Complex 362**10.4 The Elongation Process
and Proofreading 363**Discontinuous Replication of the
Lagging Strand 365

The Joining of Precursor Fragments 366

10.5 Terminating Replication 367**10.6 Replication in Eukaryotes 367**

Semiconservative Replication of DNA
in Chromosomes 368

Multiple Origins and Bidirectional
Replication in Eukaryotes 368

Initiation 370

Termination and the Problem
of Telomeres 372

10.7 Exploiting the System: DNA**Sequencing 372**

Sanger Sequencing 373

Next-Generation Sequencing 374

**ROOTS OF DISCOVERY: Replication
by Halves 358****11 Mutation, Repair, and Recombination****382**

Learning Objectives & Science

Competencies 383

11.1 Types of Mutations 383

Germ-Line and Somatic

Mutations 383

Conditional Mutations 383

Classification by Function 384

11.2 The Molecular Basis of Mutation 385

Nucleotide Substitutions 385

Missense Mutations: The Example
of Sickle-Cell Anemia 386

Insertions, Deletions, and Frameshift
Mutations 388

Dynamic Mutation of Trinucleotide
Repeats 389

Cytosine Methylation and Gene
Inactivation 391

**11.3 Transposable Elements as Agents of
Mutation 392****11.4 Spontaneous Mutation 393**

The Nonadaptive Nature
of Mutation 394

Estimation of Mutation Rates 395

Hotspots of Mutation 395

11.5 Mutagens 397

Depurination 397

Oxidation 398

Base-Analog Mutagens 399

Chemical Agents That Modify DNA 399

Ultraviolet Irradiation 400

Ionizing Radiation 401

Genetic Effects of the Chernobyl
Nuclear Accident 403

**11.6 Mechanisms of
DNA Repair 405**

Mismatch Repair 405

Base-Excision Repair 407

AP Repair 408

Nucleotide-Excision Repair 409

Photoreactivation 409

DNA Damage Bypass 409

Double-Strand Gap Repair 410

The SOS Repair System 411

**11.7 Reverse Mutations and Suppressor
Mutations 411**

Intragenic Suppression 412

Intergenic Suppression 412

The Ames Test for Mutagen/Carcinogen
Detection 413

**11.8 The Relationship Between Repair and
Recombination 414**

Double-Strand Break and Repair
Model 415

Hotspots of Recombination 416

ROOTS OF DISCOVERY: X-Ray Daze 404**Unit IV Gene Expression****423****12 Molecular Biology of Gene Expression****424**

Learning Objectives & Science

Competencies 425

**12.1 Amino Acids, Polypeptides, and
Proteins 425****12.2 Colinearity Between Coding**

Sequences and Polypeptides 427

12.3 Overview of Transcription 428**12.4 Transcription in Prokaryotes 429**

Initiation 429

Genetic Evidence for Promoters 431

Elongation 431

Termination 432

12.5 Transcription in Eukaryotes 433

- RNA Polymerases 433
- Promoters and Promoter Recognition 434
- Initiation 435
- Elongation 435
- Termination 436

12.6 Messenger RNA and RNA**Processing 436**

- 5' Capping and 3' Polyadenylation 437
- Splicing of Intervening Sequences 437
- Characteristics of Human Transcripts 437
- Coupling of Transcription and RNA Processing 438
- Mechanism of RNA Splicing 439
- Effects of Intron Mutations 441
- Exon Shuffling in the Origin of New Genes 442

12.7 Protein Synthesis 443

- Initiation in Prokaryotes 443

- Initiation in Eukaryotes 445
- Elongation 445
- Release 447
- Translational Proofreading and Premature Termination 448
- Nonsense-Mediated Decay 449
- Polysomes 450

12.8 Protein Folding and Chaperones 451**12.9 The Standard Genetic Code 454**

- Genetic Evidence for a Triplet Code 454
- How the Code Was Cracked 456
- Features of the Standard Code 456
- Transfer RNA and Aminoacyl-tRNA Synthetase Enzymes 457
- Redundancy and Wobble 458
- Nonsense Suppression 458

ROOTS OF DISCOVERY: Messenger "Light" 432**ROOTS OF DISCOVERY: Poly-U 453****13 Molecular Mechanisms of Gene Regulation 466***Learning Objectives & Science Competencies 467***13.1 Transcriptional Regulation in Prokaryotes 467**

- Inducible and Repressible Systems of Negative Regulation 468
- Positive Regulation 469
- Stochastic Noise in Gene Expression 469

13.2 The Operon System of Gene Regulation 470

- Lac⁻ Mutants 470
- Inducible and Constitutive Synthesis and Repression 470
- Repressors, Operators, and Promoters 471
- The Operon System of Transcriptional Regulation 472
- Stochastic Noise in Lac Expression 473
- Positive Regulation of the Lactose Operon 473
- Regulation of the Tryptophan Operon 475

13.3 Regulation Through Transcription Termination 478

- Attenuation 478
- Riboswitches 481

13.4 Regulation in Bacteriophage Lambda 481**13.5 Transcriptional Regulation in Eukaryotes 484**

- Galactose Metabolism in Yeast 484
- Transcriptional Activator Proteins 486
- Transcriptional Enhancers and Transcriptional Silencers 488
- Deletion Scanning 488
- The Eukaryotic Transcription Complex 489
- Chromatin-Remodeling Complexes 491
- Alternative Promoters 493

13.6 Epigenetic Mechanisms of Transcriptional Regulation 497

- Cytosine Methylation 497
- Methylation and Transcriptional Inactivation 497
- Genomic Imprinting in the Female and Male Germ Lines 498

13.7 Regulation Through RNA Processing and Decay 499

- Alternative Splicing 499
- Messenger RNA Stability 499

13.8 Noncoding RNAs and Regulation 500

- Interfering RNAs 500
- Long Noncoding RNA 504

13.9 Translational Control 505

Regulatory RNAs Controlling
Translation 506

13.10 Programmed DNA

Rearrangements 507

Gene Amplification 507

Antibody and T-Cell Receptor
Variability 507

Mating-Type Interconversion 510

Transcriptional Control of Mating
Type 511

**ROOTS OF DISCOVERY: Operator?
Operator? 476**

ROOTS OF DISCOVERY: Double Trouble 502

14 Manipulating Genes and Genomes**519**

Learning Objectives & Science

Competencies 520

**14.1 Site-Specific DNA Cleavage and
Cloning Vectors 521**

Production of DNA Fragments
with Defined Ends 521

Recombinant DNA Molecules 522

Plasmid, Lambda, and Cosmid
Vectors 522

14.2 Cloning Strategies 524

Joining DNA Fragments 524

Insertion of a Particular DNA Molecule into
a Vector 526

The Use of Reverse Transcriptase: cDNA
and RT-PCR 526

**14.3 Detection of Recombinant
Molecules 528**

Gene Inactivation in the Vector
Molecule 528

Screening for Particular
Recombinants 530

14.4 Genomics 531

Genomic Sequencing 531

Sequencing the Human
Genome 532

Genome Annotation 533

Comparative Genomics 535

14.5 Functional Genomics 538

Chromatin Immunoprecipitation 543

Two-Hybrid Analysis of Protein-Protein
Interactions 544

14.6 Transgenic Organisms 547

Germ-Line Transformation in Animals 547

Genetic Engineering in Plants 551

Transformation Rescue 552

Site-Directed Mutagenesis
and Knockout Mutations 553

Gene Expression "Knockdown"
with RNAi 554

14.7 Gene Editing 555

CRISPR-Cas9 in Practice 555

**14.8 Some Applications of Genetic
Engineering 559**

Giant Salmon with Engineered

Growth Hormone 559

Nutritionally Engineered Rice 559

Production of Useful Proteins 560

Genetic Engineering with Animal
Viruses 560

ROOTS OF DISCOVERY: Hello, Dolly! 548

**THE CUTTING EDGE: Editing
the Muscular Dystrophy Gene 557**

15 Genetic Control of Development**568**

Learning Objectives & Science

Competencies 569

**15.1 Genetic Determinants of
Development 569****15.2 Early Embryonic Development in
Animals 570**

Autonomous Development
and Intercellular Signaling 570

Composition and Organization
of Oocytes 571

Early Development and Activation of the
Zygotic Genome 573

**15.3 Genetic Analysis of Development in the
Nematode 574**

Analysis of Cell Lineages 574

Mutations Affecting Cell Lineages 576

Programmed Cell Death 576

Loss-of-Function and Gain-of-Function
Alleles 576

Epistasis in the Analysis of Developmental Switches 579

15.4 Genetic Control of Development in *Drosophila* 582

Maternal-Effect Genes and Zygotic Genes 584

Genetic Basis of Pattern Formation in Early Development 585

Coordinate Genes 586

Gap Genes 589

Pair-Rule Genes 589

Segment-Polarity Genes 590

Interactions in the Regulatory Hierarchy 590

Metamorphosis of the Adult Fly 592

Homeotic Genes 592

Master Control Genes in Evolution 593

15.5 Regulatory RNAs in Development 595

Micro RNA-Based Regulation in *C. elegans* 595

miRNAs in *HOX* Gene Regulation 596

Long Intergenic Noncoding RNAs 597

15.6 Genetic Control of Development in Higher Plants 598

Flower Development in *Arabidopsis* 599

Combinatorial Determination of the Floral Organs 600

ROOTS OF DISCOVERY: Distinguished Lineages 575

ROOTS OF DISCOVERY: Embryogenesis 588

16 Molecular Genetics of the Cell Cycle and Cancer 609

Learning Objectives & Science Competencies 610

16.1 The Cell Cycle 610

Key Events in the Cell Cycle 610

Transcriptional Program of the Cell Cycle 612

16.2 Genetic Analysis of the Cell Cycle 613

Mutations Affecting Progression Through the Cell Cycle 613

16.3 Progression Through the Cell Cycle 615

Cyclins and Cyclin-Dependent Protein Kinases 615

Targets of the Cyclin-CDK Complexes 618

Triggers for the G₁/S and G₂/M Transitions 618

Protein Degradation Helps Regulate the Cell Cycle 620

16.4 Checkpoints in the Cell Cycle 621

The DNA Damage Checkpoint 622

The Centrosome Duplication Checkpoint 625

The Spindle Assembly Checkpoint 625

Consequences of Checkpoint Failure 625

16.5 Cancer Cells 626

Oncogenes and Proto-oncogenes 627

Tumor-Suppressor Genes 628

16.6 Hereditary Cancer Syndromes 631

Defects in DNA Repair 634

16.7 Genetics of the Acute Leukemias 636

16.8 The Genomics and Transcriptomics of Cancer 637

Pancreatic Cancer: The Mutational Landscape 638

Pancreatic Cancer: The Transcriptosomal Landscape 641

From Genes and Transcripts to Therapy? 641

ROOTS OF DISCOVERY: Cycle-Ops 617

ROOTS OF DISCOVERY: Two Hits, Two Errors 635

Unit V Variation 649

17 Mitochondrial DNA and Extranuclear Inheritance 650

Learning Objectives & Science Competencies 651

17.1 Origin and Molecular Genetics of Organelles 651

Organelle Genomes 652

RNA Editing 652

The Genetic Codes of Organelles 653

17.2 Patterns of Extranuclear Inheritance 655

Maternal Inheritance of Animal Mitochondria 655

Maternal Inheritance and Maternal Effects 656

Heteroplasmy 656

Mitochondrial Genetic Diseases 657
 Tracing Population History Through Mitochondrial DNA 658
 Cytoplasmic Male Sterility in Plants 659

17.3 Vegetative Segregation 661

Leaf Variegation in Four-O'Clock Plants 661
 Respiration-Defective Mitochondrial Mutants in Yeast 663

17.4 Cytoplasmic Transmission of Symbionts 664

Bacterial Symbionts of Aphids 665
 Killer Strains of *Paramecium* 666
 Wolbachia in Arthropods 667

17.5 Maternal Effect in Snail Shell Coiling 670

ROOTS OF DISCOVERY: A Coming Together 654

ROOTS OF DISCOVERY: How the Aphids Got PVT 665

18 Genes in Populations 677

Learning Objectives & Science Competencies 678

18.1 Population Genetics 678

Allele Frequencies and Genotype Frequencies 678
 Random Mating and the Hardy-Weinberg Principle 680
 Implications of the Hardy-Weinberg Principle 681
 A Test for Random Mating 681
 Frequency of Heterozygous Genotypes 682
 Multiple Alleles 683
 DNA Typing 684
 X-Linked Genes 688
 Genetic Variation and Linkage 688

18.2 Inbreeding 691

The Inbreeding Coefficient 691
 Allelic Identity by Descent 692
 Calculation of the Inbreeding Coefficient from Pedigrees 693

Effects of Inbreeding 694

18.3 Genetics and Evolution 695

18.4 Mutation and Migration 696

Irreversible Mutation 696
 Reversible Mutation 697

18.5 Random Genetic Drift 698

Loss of Genetic Variation in Endangered Species 699

18.6 Natural Selection 701

Selection in a Laboratory Experiment 701
 Selection in Diploid Organisms 702
 Components of Fitness 703
 Selection-Mutation Balance 704
 Heterozygote Superiority 705
 Molecular Signals of Selection 706

ROOTS OF DISCOVERY: A Yule Message from Dr. Hardy 684

THE CUTTING EDGE: CRISPR-Cas9 for Disease Control? 708

19 Molecular and Human Evolutionary Genetics 717

Learning Objectives & Science Competencies 718

19.1 Molecular Evolutionary Analysis 718

Gene Trees 719
 Bootstrapping 721
 Gene Trees and Species Trees 721
 Molecular Clock of Evolutionary Change 722
 Rates of DNA Evolution 723
 Rates of Evolution in Protein-Coding Regions 724

Origins of New Genes: Orthologs and Paralogs 726

19.2 Ancient DNA 727

19.3 Where Humans Fit on the Tree of Life 729

Evidence That Humans Are Most Closely Related to Chimpanzees 729
 Similarities in Genomic DNA 729
 Analysis of Multiple Genetic Elements 729
 Differences Between Human and Chimpanzee Genomes 730

19.4 What Do the Genetic Differences Between Humans and Chimpanzees Mean? 732

Molecular Adaptations Unique to Humans 732

FOXP2: A Gene Related to Language 733

Gene-Expression Differences Between Humans and Chimpanzees 734

19.5 A Synopsis of Human Evolution 735

The Cast of Characters in Human Evolution 735

Models of Modern Human Origins 738

19.6 Genetic Evidence for Modern Human Origins 739

Tracing Human History Through Mitochondrial DNA 739

The Neandertal Genome 741

The Denisovan Genome 742

19.7 Measuring Human Diversity 743

Tracing Human History with Genetic Markers 743

The Apportionment of Within-Group and Between-Group Variation 746

Tracing Human History Through the Y Chromosome 746

19.8 Genetic Adaptations Unique to Humans 749

Amylase and Dietary Starch 749

Adaptation to Parasites and Disease 751

Evolutionary Adaptation Affecting Human Skin Color 752

THE CUTTING EDGE: The Peopling of Western Europe 747

ROOTS OF DISCOVERY: Starch Contrast 752

Appendix A: Answers to Even-Numbered Problems 759

Word Roots: Prefixes, Suffixes, and Combining Forms 778

Concise Dictionary of Genetics and Genomics 781

Index 808