

# Table of Contents



## 1

### The Molecular Basis of Heredity, Variation, and Evolution 1

#### 1.1 Modern Genetics Is in Its Second Century 2

The First Century of Modern Genetics 2

Genetics—Central to Modern Biology 4

#### 1.2 The Structure of DNA Suggests a Mechanism for Replication 6

The Discovery of DNA Structure 6

DNA Nucleotides 7

DNA Replication 8

#### 1.3 DNA Transcription and Messenger RNA Translation Express Genes 9

Genetic Analysis 1.1 10

Transcription 10

**Experimental Insight 1.1** 11

Translation 12

Genomes, Proteomes, and “-omic” Approaches 13

Genetic Analysis 1.2 14

#### 1.4 Evolution Has a Molecular Basis 15

Darwin's Theory of Evolution 16

Four Evolutionary Processes 17

Tracing Evolutionary Relationships 17

Genetic Analysis 1.3 20

*Case Study The Modern Human Family* 21

*Summary* 22 • *Keywords* 23 • *Problems* 24



## 2

### Transmission Genetics 26

#### 2.1 Gregor Mendel Discovered the Basic Principles of Genetic Transmission 27

Mendel's Modern Experimental Approach 28

Five Critical Experimental Innovations 29

#### 2.2 Monohybrid Crosses Reveal the Segregation of Alleles 31

Identifying Dominant and Recessive Traits 31

Evidence of Particulate Inheritance and Rejection of the Blending Theory 32

Segregation of Alleles 33

Hypothesis Testing by Test-Cross Analysis 34

Hypothesis Testing by  $F_2$  Self-Fertilization 35

#### 2.3 Dihybrid and Trihybrid Crosses Reveal the Independent Assortment of Alleles 36

Dihybrid-Cross Analysis of Two Genes 36

Genetic Analysis 2.1 37

Testing Independent Assortment by Test-Cross Analysis 39

Genetic Analysis 2.2 40

Testing Independent Assortment by Trihybrid-Cross Analysis 41

Probability Calculations in Genetics Problem Solving 42

The Rediscovery of Mendel's Work 42

Genetic Analysis 2.3 43

**Experimental Insight 2.1** 44

#### 2.4 Probability Theory Predicts Mendelian Ratios 44

The Product Rule 44

**Experimental Insight 2.2** 45

The Sum Rule 45

Conditional Probability 45

**Experimental Insight 2.3** 46

Binomial Probability 46

#### 2.5 Chi-Square Analysis Tests the Fit between Observed Values and Expected Outcomes 48

The Normal Distribution 48

Chi-Square Analysis 49

Chi-Square Analysis of Mendel's Data 50

#### 2.6 Autosomal Inheritance and Molecular Genetics Parallel the Predictions of Mendel's Hereditary Principles 51

Autosomal Dominant Inheritance 52

Autosomal Recessive Inheritance 53

Molecular Genetics of Mendel's Traits 54

**Case Study** *Inheritance of Sickle Cell Disease in Humans* 56

**Summary** 57 • **Keywords** 57 • **Problems** 58



## 3 Cell Division and Chromosome Heredity 64

### 3.1 Mitosis Divides Somatic Cells 65

Stages of the Cell Cycle 65

Substages of M Phase 66

Chromosome Distribution 67

Completion of Cell Division 68

Cell Cycle Checkpoints 69

Cell Cycle Mutations and Cancer 72

### 3.2 Meiosis Produces Gametes for Sexual Reproduction 72

Meiosis versus Mitosis 73

Meiosis I 75

Meiosis II 79

The Mechanistic Basis of Mendelian Ratios 79

Segregation in Single-Celled Diploids 81

### 3.3 The Chromosome Theory of Heredity Proposes That Genes Are Carried on Chromosomes 81

Genetic Analysis 3.1 83

X-Linked Inheritance 84

Testing the Chromosome Theory of Heredity 85

### 3.4 Sex Determination Is Chromosomal and Genetic 86

Sex Determination in *Drosophila* 86

Genetic Analysis 3.2 87

Mammalian Sex Determination 88

Diversity of Sex Determination 88

**Experimental Insight** 3.1 89

### 3.5 Human Sex-Linked Transmission Follows Distinct Patterns 90

Expression of X-Linked Recessive Traits 91

Genetic Analysis 3.3 93

X-Linked Dominant Trait Transmission 94

Y-Linked Inheritance 94

### 3.6 Dosage Compensation Equalizes the Expression of Sex-Linked Genes 95

**Case Study** *The (Degenerative) Evolution of the  
Mammalian Y Chromosome* 96

**Summary** 98 • **Keywords** 99 • **Problems** 99



## 4 Inheritance Patterns of Single Genes and Gene Interaction 104

### 4.1 Interactions between Alleles Produce Dominance Relationships 105

The Molecular Basis of Dominance 105

Functional Effects of Mutation 106

Incomplete Dominance 108

Codominance 109

Dominance Relationships of ABO Alleles 109

Allelic Series 111

Genetic Analysis 4.1 112

Lethal Alleles 113

Sex-Limited Traits 117

Sex-Influenced Traits 117

Delayed Age of Onset 118

### 4.2 Some Genes Produce Variable Phenotypes 118

Incomplete Penetrance 118

Variable Expressivity 119

Gene–Environment Interactions 119

Pleiotropic Genes 121

### 4.3 Gene Interaction Modifies Mendelian Ratios 121

Gene Interaction in Pathways 121

The One Gene–One Enzyme Hypothesis 124

Genetic Dissection to Investigate Gene Action 125

**Experimental Insight** 4.1 125

Epistasis and Its Results 127

Genetic Analysis 4.2 128

### 4.4 Complementation Analysis Distinguishes Mutations in the Same Gene from Mutations in Different Genes 134

Genetic Analysis 4.3 135

**Case Study** Complementation Groups in a Human Cancer-Prone Disorder 137  
 Summary 137 • Keywords 138 • Problems 138



## 5 Genetic Linkage and Mapping in Eukaryotes 144

### 5.1 Linked Genes Do Not Assort Independently 145

Indications of Genetic Linkage 146  
 The Discovery of Genetic Linkage 148  
 Detecting Autosomal Genetic Linkage through Test-Cross Analysis 150  
 Genetic Analysis 5.1 152

### 5.2 Genetic Linkage Mapping Is Based on Recombination Frequency between Genes 153

The First Genetic Linkage Map 153  
 Map Units 154  
 Chi-Square Analysis of Genetic Linkage Data 154

### 5.3 Three-Point Test-Cross Analysis Maps Genes 154

Finding the Relative Order of Genes by Three-Point Mapping 154  
 Constructing a Three-Point Recombination Map 156  
 Determining Gamete Frequencies from Genetic Maps 159

### 5.4 Recombination Results from Crossing Over 160

Cytological Evidence of Recombination 160  
 Limits of Recombination along Chromosomes 160  
 Recombination within Genes 162  
 Genetic Analysis 5.2 163  
 Biological Factors Affecting Accuracy of Genetic Maps 164  
 Recombination Is Dominated by Hotspots 164  
 Correction of Genetic Map Distances 165

### 5.5 Linked Human Genes Are Mapped Using Lod Score Analysis 166

Allelic Phase 166  
 Lod Score Analysis 167  
**Experimental Insight 5.1** 169  
 Genetic Analysis 5.3 170

### 5.6 Recombination Affects Evolution and Genetic Diversity 170

### 5.7 Genetic Linkage in Haploid Eukaryotes Is Identified by Tetrad Analysis 171

Analysis of Unordered Tetrads 172  
 Ordered Ascus Analysis 173

### 5.8 Mitotic Crossover Produces Distinctive Phenotypes 175

**Case Study** Mapping the Gene for Cystic Fibrosis 177  
 Summary 178 • Keywords 179 • Problems 180



## 6 Genetic Analysis and Mapping in Bacteria and Bacteriophages 186

### 6.1 Bacteria Transfer Genes by Conjugation 187

Characteristics of Bacterial Genomes 188  
 Conjugation Identified 188  
 Research Technique 6.1 189  
 Transfer of the F Factor 192  
 Formation of an Hfr Chromosome 194  
 Hfr Gene Transfer 195

### 6.2 Interrupted Mating Analysis Produces Time-of-Entry Maps 197

Time-of-Entry Mapping Experiments 197  
 Consolidation of Hfr Maps 200  
 Genetic Analysis 6.1 202

### 6.3 Conjugation with F' Strains Produces Partial Diploids 203

Plasmids and Conjugation in Archaea 204

### 6.4 Bacterial Transformation Produces Genetic Recombination 204

Genetic Analysis 6.2 205  
 Steps in Transformation 206  
 Mapping by Transformation 206

### 6.5 Bacterial Transduction Is Mediated by Bacteriophages 206

Bacteriophage Life Cycles 207  
 Generalized Transduction 209  
 Cotransduction 209

Cotransduction Mapping 210

Specialized Transduction 212

## 6.6 Bacteriophage Chromosomes Are Mapped by Fine-Structure Analysis 213

Genetic Analysis 6.3 214

Genetic Complementation Analysis 215

Intragenic Recombination Analysis 216

Deletion-Mapping Analysis 216

## 6.7 Lateral Gene Transfer Alters Genomes 219

Lateral Gene Transfer and Genome Evolution 219

Identifying Lateral Gene Transfer in Genomes 220

*Case Study The Evolution of Antibiotic Resistance and Change in Medical Practice* 220

Summary 221 • Keywords 222 • Problems 222



# 7 DNA Structure and Replication 227

## 7.1 DNA Is the Hereditary Molecule of Life 228

Chromosomes Contain DNA 228

A Transformation Factor Responsible for Heredity 229

DNA Is the Transformation Factor 230

DNA Is the Hereditary Molecule 230

## 7.2 The DNA Double Helix Consists of Two Complementary and Antiparallel Strands 232

DNA Nucleotides 232

Genetic Analysis 7.1 234

Complementary DNA Nucleotide Pairing 234

The Twisting Double Helix 234

## 7.3 DNA Replication Is Semiconservative and Bidirectional 236

Three Competing Models of Replication 236

The Meselson-Stahl Experiment 236

Origin and Directionality of Replication in Bacterial DNA 237

Multiple Replication Origins in Eukaryotes 239

## 7.4 DNA Replication Precisely Duplicates the Genetic Material 241

DNA Sequences at Replication Origins 242

Replication Initiation 244

Continuous and Discontinuous Strand Replication 246

RNA Primer Removal and Okazaki Fragment Ligation 247

Simultaneous Synthesis of Leading and Lagging Strands 248

DNA Proofreading 249

Finishing Replication 251

Genetic Analysis 7.2 253

Telomeres, Aging, and Cancer 254

## 7.5 Molecular Genetic Analytical Methods Make Use of DNA Replication Processes 254

The Polymerase Chain Reaction 254

Separation of PCR Products 256

Dideoxynucleotide DNA Sequencing 256

New DNA-Sequencing Technologies: Next Generation and Third Generation 259

Genetic Analysis 7.3 260

*Case Study Use of PCR and DNA Sequencing to Analyze Huntington Disease Mutations* 261

Summary 263 • Keywords 264 • Problems 264



# 8 Molecular Biology of Transcription and RNA Processing 267

## 8.1 RNA Transcripts Carry the Messages of Genes 268

RNA Nucleotides and Structure 268

Identification of Messenger RNA 269

RNA Classification 270

## 8.2 Bacterial Transcription Is a Four-Stage Process 271

Bacterial RNA Polymerase 272

Bacterial Promoters 273

Transcription Initiation 273

Genetic Analysis 8.1 275

Transcription Elongation and Termination 276

Transcription Termination Mechanisms 276

## 8.3 Archaeal and Eukaryotic Transcription Displays Structural Homology and Common Ancestry 278

Eukaryotic and Archaeal RNA Polymerases 278

Consensus Sequences for Eukaryotic RNA Polymerase II Transcription 279

Research Technique 8.1 279

- Promoter Recognition 281
- Detecting Promoter Consensus Elements 282
- Enhancers and Silencers 282
- RNA Polymerase I Promoters 283
- RNA Polymerase III Promoters 284
- Termination in RNA Polymerase I or III 284
- Transcription 284
- Archaeal Transcription 285

## 8.4 Post-Transcriptional Processing Modifies RNA Molecules 285

- Capping 5' mRNA 285
- Polyadenylation of 3' Pre-mRNA 286
- The Torpedo Model of Transcription Termination 287
- Pre-mRNA Intron Splicing 287
- Splicing Signal Sequences 288
- Coupling of Pre-mRNA Processing Steps 289
- Alternative Transcripts of Single Genes 290
- Control of Alternative Splicing 294
- Intron Self-Splicing 294
- Genetic Analysis 8.2 295
- Ribosomal RNA Processing 296
- Transfer RNA Processing 297
- Post-Transcriptional RNA Editing 298
- Case Study* *Sexy Splicing: Alternative mRNA Splicing and Sex Determination in Drosophila* 299
- Summary* 300 • *Keywords* 301 • *Problems* 302



## 9 The Molecular Biology of Translation 305

### 9.1 Polypeptides Are Composed of Amino Acid Chains That Are Assembled at Ribosomes 306

- Amino Acid Structure 306
- Polypeptide and Transcript Structure 307
- Ribosome Structures 309
- Research Technique 9.1 310
- A Three-Dimensional View of the Ribosome 311

### 9.2 Translation Occurs in Three Phases 311

- Translation Initiation 311
- Polypeptide Elongation 315
- Genetic Analysis 9.1 317
- Translation Termination 318

### 9.3 Translation Is Fast and Efficient 319

- The Translational Complex 319
- Translation of Polycistronic mRNA 320

### 9.4 The Genetic Code Translates Messenger RNA into Polypeptide 320

- The Genetic Code Displays Third-Base Wobble 321
- Charging tRNA Molecules 322

### 9.5 Experiments Deciphered the Genetic Code 322

- No Overlap in the Genetic Code 323
- A Triplet Genetic Code 323
- No Gaps in the Genetic Code 324
- Genetic Analysis 9.2 325
- Deciphering the Genetic Code 326
- The (Almost) Universal Genetic Code 327
- Transfer RNAs and Genetic Code Specificity 328
- Genetic Analysis 9.3 329

### 9.6 Translation Is Followed by Polypeptide Folding, Processing, and Protein Sorting 330

- Posttranslational Polypeptide Processing 330
- The Signal Hypothesis 331
- Case Study* *Antibiotics and Translation Interference* 332
- Summary* 333 • *Keywords* 334 • *Problems* 334



## 10 The Integration of Genetic Approaches: Understanding Sickle Cell Disease 338

### 10.1 An Inherited Hemoglobin Variant Causes Sickle Cell Disease 339

- The First Patient with Sickle Cell Disease 339
- Hemoglobin Structure 340
- Globin Gene Mutations 340

### 10.2 Genetic Variation Can Be Detected by Examining DNA, RNA, and Proteins 341

- Gel Electrophoresis 342
- Hemoglobin Peptide Fingerprint Analysis 344
- Identification of DNA Sequence Variation 345
- Genetic Analysis 10.1 347
- Molecular Probes 348
- Electrophoretic Analysis of Sickle Cell Disease 349
- Research Technique 10.1 350

**10.3 Sickle Cell Disease Evolved by Natural Selection in Human Populations 353**

Research Technique 10.2 354

Genetic Analysis 10.2 356

Malaria Infection 357

Heterozygous Advantage 357

Evolution of  $\beta^C$  and  $\beta^E$  358*Case Study* Transmission and Molecular Genetic Analysis of *Thalassemia* 359

Summary 360 • Keywords 360 • Problems 361

 **11****Chromosome Structure 365****11.1 Viruses Are Infectious Particles Containing Nucleic Acid Genomes 366**

Viral Genomes 366

Viral Protein Packaging 366

**11.2 Bacterial Chromosomes Are Organized by Proteins 368**

Bacterial Genome Content 368

Bacterial Chromosome Compaction 368

**11.3 Eukaryotic Chromosomes Are Organized into Chromatin 370**

Chromatin Compaction 370

Histone Proteins and Nucleosomes 371

Higher Order Chromatin Organization and Chromosome Structure 373

Nucleosome Distribution and Synthesis during Replication 374

Genetic Analysis 11.1 376

**11.4 Chromatin Compaction Varies along the Chromosome 376**

Chromosome Shape and Chromosome Karyotypes 376

In Situ Hybridization 377

Imaging Chromosome Territory during Interphase 379

Chromosome Banding 380

Heterochromatin and Euchromatin 381

Centromere Structure 381

Position Effect Variegation: Effect of Chromatin State on Transcription 382

Genetic Analysis 11.2 383

**11.5 Chromatin Organizes Archaeal Chromosomes 384**

Archaeal Chromosome and Genome Characteristics 384

Archaeal Histones 385

Phylogenetic Origins of Histone Proteins 385

*Case Study* Fishing for Chromosome Abnormalities in Cancer Cells 386

Summary 387 • Keywords 388 • Problems 388

 **12****Gene Mutation, DNA Repair, and Homologous Recombination 391****12.1 Mutations Are Rare and Occur at Random 392**

Mutation Rates 392

Determination of Mutation Rate from Genome Sequence Analysis 393

**12.2 Gene Mutations Modify DNA Sequence 393**

Base-Pair Substitution Mutations 394

**Experimental Insight 12.1 395**

Frameshift Mutations 395

Regulatory Mutations 395

Forward Mutation and Reversion 397

**12.3 Gene Mutations May Arise from Spontaneous Events 397**

DNA Replication Errors 397

Genetic Analysis 12.1 400

Spontaneous Nucleotide Base Changes 400

DNA Nucleotide Lesions 402

**12.4 Mutations May Be Induced by Chemicals or Ionizing Radiation 403**

Chemical Mutagens 404

Radiation-Induced DNA Damage 406

The Ames Test 408

**12.5 Repair Systems Correct Some DNA Damage 408**

Direct Repair of DNA Damage 409

Genetic Analysis 12.2 410

DNA Damage Signaling Systems 413

DNA Damage Repair Disorders 414

Experimental Insight 12.2 415

## 12.6 Proteins Control Translesion DNA Synthesis and the Repair of Double-Strand Breaks 415

Translesion DNA Synthesis 415

Double-Strand Break Repair 416

## 12.7 DNA Double-Strand Breaks Initiate Homologous Recombination 417

The Holliday Model 418

The Bacterial RecBCD Pathway 418

The Double-Stranded Break Model of Meiotic Recombination 418

Holliday Junction Resolution 419

## 12.8 Gene Conversion Is Directed Mismatch Repair in Heteroduplex DNA 419

*Case Study* Li-Fraumeni Syndrome Is Caused by Inheritance of Mutations of p53 423

*Summary* 424 • *Keywords* 425 • *Problems* 425



# 13

## Chromosome Aberrations and Transposition 430

## 13.1 Nondisjunction Leads to Changes in Chromosome Number 431

Euploidy and Aneuploidy 431

Chromosome Nondisjunction 431

Gene Dosage Alteration 432

Aneuploidy in Humans 433

Reduced Fertility in Aneuploidy 435

Mosaicism 435

Trisomy Rescue and Uniparental Disomy 436

## 13.2 Changes in Euploidy Result in Various Kinds of Polyploidy 437

Autopolyploidy and Allopolyploidy 437

Consequences of Polyploidy 438

Reduced Recessive Homozygosity 439

Polyploidy and Evolution 439

## 13.3 Chromosome Breakage Causes Mutation by Loss, Gain, and Rearrangement of Chromosomes 440

Partial Chromosome Deletion 440

Unequal Crossover 441

Detecting Duplication and Deletion 442

Deletion Mapping 442

Genetic Analysis 13.1 443

Genetic Analysis 13.2 445

## 13.4 Chromosome Breakage Leads to Inversion and Translocation of Chromosomes 446

Chromosome Inversion 446

Chromosome Translocation 448

## 13.5 Transposable Genetic Elements Move throughout the Genome 450

The Discovery of Transposition 451

Experimental Insight 13.1 452

The Characteristics and Classification of Transposable Elements 453

Experimental Insight 13.2 454

## 13.6 Transposition Modifies Bacterial Genomes 456

Insertion Sequences 456

Composite Transposons 457

## 13.7 Transposition Modifies Eukaryotic Genomes 457

Genetic Analysis 13.3 458

*Drosophila* P Elements 458

Retrotransposons 460

*Case Study* Human Chromosome Evolution 461

*Summary* 462 • *Keywords* 463 • *Problems* 463



# 14

## Regulation of Gene Expression in Bacteria and Bacteriophage 468

## 14.1 Transcriptional Control of Gene Expression Requires DNA-Protein Interaction 469

Negative and Positive Control of Transcription 469

Regulatory DNA-Binding Proteins 470

## 14.2 The *lac* Operon Is an Inducible Operon System under Negative and Positive Control 472

Lactose Metabolism 472

*lac* Operon Structure 473

*lac* Operon Function 473

- 14.3 Mutational Analysis Deciphers Genetic Regulation of the *lac* Operon** 476  
 Analysis of Structural Gene Mutations 476  
*lac* Operon Regulatory Mutations 477  
 Molecular Analysis of the *lac* Operon 480  
 Genetic Analysis 14.1 481  
 Experimental Insight 14.1 482
- 14.4 Transcription from the Tryptophan Operon Is Repressible and Attenuated** 483  
 Feedback Inhibition of Tryptophan Synthesis 484  
 Attenuation of the *trp* Operon 485  
 Attenuation Mutations 488  
 Attenuation in Other Amino Acid Operon Systems 488  
 Genetic Analysis 14.2 489
- 14.5 Bacteria Regulate the Transcription of Stress Response Genes and Translation and Archaea Regulate Transcription in a Bacteria-like Manner** 489  
 Alternative Sigma Factors and Stress Response 489  
 Translational Regulation in Bacteria 491  
 Transcriptional Regulation in Archaea 492
- 14.6 Antiterminators and Repressors Control Lambda Phage Infection of *E. coli*** 492  
 The Lambda Phage Genome 493  
 Early Gene Transcription 493  
 Cro Protein and the Lytic Cycle 496  
 The  $\lambda$  Repressor Protein and Lysogeny 496  
 Resumption of the Lytic Cycle Following Lysogeny Induction 497  
*Case Study* *Vibrio cholerae*—Stress Response Leads to Serious Infection 497  
*Summary* 498 • *Keywords* 499 • *Problems* 499



## 15

### Regulation of Gene Expression in Eukaryotes 504

- 15.1 Cis-Acting Regulatory Sequences Bind Trans-Acting Regulatory Proteins to Control Eukaryotic Transcription** 506  
 Transcriptional Regulatory Interactions 506  
 Integration and Modularity of Regulatory Sequences 507  
 Transcription Regulation by Enhancers and Silencers 508  
 Locus Control Regions 508  
 Mutations in Regulatory Sequences 509

- Enhancer-Sequence Conservation 510  
 Yeast Enhancer and Silencer Sequences 510  
 Insulator Sequences 511

### 15.2 Chromatin Remodeling and Modification Regulates Eukaryotic Transcription 512

- PEV Mutations 512  
 Overview of Chromatin Remodeling and Chromatin Modification 513  
 Open and Covered Promoters 514  
 Mechanisms of Chromatin Remodeling 514  
 Chemical Modifications of Chromatin 517  
 Genetic Analysis 15.1 518  
 An Example of Transcription Regulation in *S. cerevisiae* 520  
 Epigenetic Heritability 520  
 A Role for lncRNAs in Gene Regulation 521  
 Inactivation of Eutherian Mammalian Female X Chromosomes 521  
 Genomic Imprinting 522  
 Nucleotide Methylation 523

### 15.3 RNA-Mediated Mechanisms Control Gene Expression 524

- Gene Silencing by Double-Stranded RNA 524  
 Chromatin Modification by RNAi 526  
 The Evolution and Applications of RNAi 527  
*Case Study* *Environmental Epigenetics* 528  
*Summary* 529 • *Keywords* 529 • *Problems* 530



## 16

### Analysis of Gene Function by Forward Genetics and Reverse Genetics 533

- 16.1 Forward Genetic Screens Identify Genes by Their Mutant Phenotypes** 535  
 General Design of Forward Genetic Screens 535  
 Specific Strategies of Forward Genetic Screens 535  
 Analysis of Mutageneses 539  
 Genetic Analysis 16.1 540  
 Identifying Interacting and Redundant Genes Using Modifier Screens 540
- 16.2 Genes Identified by Mutant Phenotype Are Cloned Using Recombinant DNA Technology** 542  
 Cloning Genes by Complementation 542

Using Transposons to Clone Genes 543

Positional Cloning 544

Positional Cloning in Humans: The Huntington Disease Gene 548

Genome Sequencing to Determine Gene Identification 549

### 16.3 Reverse Genetics Investigates Gene Action by Progressing from Gene Identification to Phenotype 551

Use of Insertion Mutants in Reverse Genetics 552

RNA Interference in Gene Activity 552

Reverse Genetics by TILLING 554

### 16.4 Transgenes Provide a Means of Dissecting Gene Function 554

Genetic Analysis 16.2 556

Monitoring Gene Expression with Reporter Genes 556

Enhancer Trapping 559

Investigating Gene Function with Chimeric Genes 560

*Case Study Reverse Genetics and Genetic Redundancy in Flower Development* 561

Summary 563 • Keywords 564 • Problems 564



## 17

### Recombinant DNA Technology and Its Applications 567

#### 17.1 Specific DNA Sequences Are Identified and Manipulated Using Recombinant DNA Technology 568

Restriction Enzymes 568

**Experimental Insight 17.1** 569

Genetic Analysis 17.1 571

Molecular Cloning 572

DNA Libraries 577

Sequencing Long DNA Molecules 581

#### 17.2 Introducing Foreign Genes into Genomes Creates Transgenic Organisms 583

Expression of Heterologous Genes in Bacterial and Fungal Hosts 583

**Experimental Insight 17.2** 587

Transformation of Plant Genomes

by *Agrobacterium* 589

Transgenic Animals 594

Advances in Altering and Synthesizing DNA Molecules 598

Manipulation of DNA Sequences in Vivo 598

Genetic Analysis 17.2 600

#### 17.3 Gene Therapy Uses Recombinant DNA Technology 600

Two Forms of Gene Therapy 601

Gene Therapy in Humans 601

#### 17.4 Cloning of Plants and Animals Produces Genetically Identical Individuals 602

*Case Study Curing Sickle Cell Disease in Mice* 604

Summary 605 • Keywords 606 • Problems 606



## 18

### Genomics: Genetics from a Whole-Genome Perspective 611

#### 18.1 Structural Genomics Provides a Catalog of Genes in a Genome 612

The Clone-by-Clone Sequencing Approach 613

Whole-Genome Shotgun Sequencing 613

Metagenomics 616

#### 18.2 Annotation Ascribes Biological Function to DNA Sequences 617

**Experimental Insight 18.1** 618

Variation in Genome Organization among Species 620

Three Insights from Genome Sequences 621

#### 18.3 Evolutionary Genomics Traces the History of Genomes 622

**Research Technique 18.1** 623

The Tree of Life 624

Interspecific Genome Comparisons: Gene Content 624

**Research Technique 18.2** 626

Genetic Analysis 18.1 630

Interspecific Genome Comparisons: Genome Annotation 631

Interspecific Genome Comparisons: Gene Order 632

Intraspecific Genome Comparisons 634

Human Genetic Diversity 635

SNPs and Indels in Humans 635

Prenatal Genome Sequencing 636

## 18.4 Functional Genomics Aids in Elucidating Gene Function 636

Transcriptomics 636

Other "-omes" and "-omics" 638

Genomic Approaches to Reverse Genetics 641

Use of Yeast Mutants to Categorize Genes 641

Genetic Networks 642

**Case Study** *Genomic Analysis of Insect Guts May Fuel the World* 644

Summary 645 • Keywords 645 • Problems 646



# 19

## Organelle Inheritance and the Evolution of Organelle Genomes 649

### 19.1 Organelle Inheritance Transmits Genes Carried on Organelle Chromosomes 650

The Discovery of Organelle Inheritance 650

Homoplasmy and Heteroplasmy 651

Genome Replication in Organelles 652

Replicative Segregation of Organelle Genomes 653

### 19.2 Modes of Organelle Inheritance Depend on the Organism 654

Mitochondrial Inheritance in Mammals 654

Genetic Analysis 19.1 657

Mating Type and Chloroplast Segregation in *Chlamydomonas* 659

Genetic Analysis 19.2 660

Biparental Inheritance in *Saccharomyces cerevisiae* 661

Summary of Organelle Inheritance 662

### 19.3 Mitochondria Are the Energy Factories of Eukaryotic Cells 662

Mitochondrial Genome Structure and Gene Content 662

Mitochondrial Transcription and Translation 665

### 19.4 Chloroplasts Are the Sites of Photosynthesis 666

Chloroplast Genome Structure and Gene Content 667

Chloroplast Transcription and Translation 668

Editing of Chloroplast mRNA 668

## 19.5 The Endosymbiosis Theory Explains Mitochondrial and Chloroplast Evolution 668

**Experimental Insight 19.1** 669

Separate Evolution of Mitochondria and Chloroplasts 670

Continual DNA Transfer from Organelles 670

Encoding of Organellar Proteins 672

The Origin of the Eukaryotic Lineage 673

Secondary and Tertiary Endosymbioses 674

**Case Study** *Ototoxic Deafness: A Mitochondrial Gene-Environment Interaction* 675

Summary 677 • Keywords 677 • Problems 678



# 20

## Developmental Genetics 681

### 20.1 Development Is the Building of a Multicellular Organism 682

Cell Differentiation 683

Pattern Formation 683

### 20.2 *Drosophila* Development Is a Paradigm for Animal Development 684

The Developmental Toolkit of *Drosophila* 686

Maternal Effects on Pattern Formation 687

Coordinate Gene Patterning of the Anterior-Posterior Axis 687

Domains of Gap Gene Expression 688

Regulation of Pair-Rule Genes 689

Specification of Parasegments by *Hox* Genes 691

Genetic Analysis 20.1 694

Downstream Targets of *Hox* Genes 695

*Hox* Genes in Metazoans 695

Stabilization of Cellular Memory by Chromatin Architecture 696

### 20.3 Cellular Interactions Specify Cell Fate 697

Inductive Signaling between Cells 697

Lateral Inhibition 700

Cell Death during Development 700

### 20.4 "Evolution Behaves Like a Tinkerer" 700

Evolution through Co-option 701

Constraints on Co-option 703

## 20.5 Plants Represent an Independent Experiment in Multicellular Evolution 703

Development at Meristems 703

Combinatorial Homeotic Activity in Floral-Organ Identity 704

Genetic Analysis 20.2 707

*Case Study* Cyclopia and Polydactyly—Different *Shh* Mutations with Distinctive Phenotypes 707

Summary 709 • Keywords 710 • Problems 710



## 21 Genetic Analysis of Quantitative Traits 713

### 21.1 Quantitative Traits Display Continuous Phenotypic Variation 714

Genetic Potential 714

Major Genes and Additive Gene Effects 715

Continuous Phenotypic Variation from Multiple Additive Genes 716

Allele Segregation in Quantitative Trait Production 716

Effects of Environmental Factors on Phenotypic Variation 719

Threshold Traits 719

### 21.2 Quantitative Trait Analysis Is Statistical 721

Statistical Description of Phenotypic Variation 721

Genetic Analysis 21.1 722

**Experimental Insight 21.1** 723

Partitioning Phenotypic Variance 725

Genetic Analysis 21.2 726

Partitioning Genetic Variance 726

### 21.3 Heritability Measures the Genetic Component of Phenotypic Variation 726

Broad Sense Heritability 727

Twin Studies 727

Narrow Sense Heritability and Artificial Selection 729

### 21.4 Quantitative Trait Loci Are the Genes That Contribute to Quantitative Traits 730

QTL Mapping Strategies 730

Identification of QTL Genes 732

Genome-Wide Association Studies 734

*Case Study* GWAS and Crohn's Disease 736

Summary 737 • Keywords 737 • Problems 738



## 22 Population Genetics and Evolution at the Population, Species, and Molecular Levels 742

### 22.1 The Hardy-Weinberg Equilibrium Describes the Relationship of Allele and Genotype Frequencies in Populations 743

Populations and Gene Pools 743

The Hardy-Weinberg Equilibrium 744

Determining Autosomal Allele Frequencies in Populations 746

The Hardy-Weinberg Equilibrium for More than Two Alleles 747

The Chi-Square Test of Hardy-Weinberg Predictions 748

### 22.2 Natural Selection Operates through Differential Reproductive Fitness within a Population 748

Differential Reproduction and Relative Fitness 748

Genetic Analysis 22.1 749

Directional Natural Selection 750

Natural Selection Favoring Heterozygotes 751

Convergent Evolution 752

### 22.3 Mutation Diversifies Gene Pools 753

Quantifying the Effects and Reverse Mutation Rates 753

Mutation-Selection Balance 753

Genetic Analysis 22.2 754

### 22.4 Migration Is Movement of Organisms and Genes between Populations 755

Effects of Gene Flow 755

Allele Frequency Equilibrium and Equalization 755

### 22.5 Genetic Drift Causes Allele Frequency Change by Sampling Error 756

The Founder Effect 756

Genetic Bottlenecks 757

### 22.6 Inbreeding Alters Genotype Frequencies 758

The Coefficient of Inbreeding 758

Inbreeding Depression 759

Genetic Analysis 22.3 760

## 22.7 Species and Higher Taxonomic Groups Evolve by the Interplay of Four Evolutionary Processes 760

- Processes of Speciation 761
- Reproductive Isolation and Speciation 761
- Contemporary Evolution in Darwin's Finches 764

## 22.8 Molecular Evolution Changes Genes and Genomes through Time 764

- Vertebrate Steroid Receptor Evolution 764
- Human Genetic Diversity and Evolution 766

**Case Study** CODIS—Using Population Genetics to Solve Crime and Identify Paternity 769  
**Summary** 771 • **Keywords** 772 • **Problems** 772

## References and Additional Reading R-1

## Appendix: Answers A-1

## Glossary G-1

## Credits C-1

## Index I-1