Table of Contents



The Molecular Basis of Heredity, Variation, and Evolution 33

1.1 Modern Genetics Is in Its Second Century 34

The First Century of Modern Genetics 34 Genetics—Central to Modern Biology 36

1.2 The Structure of DNA Suggests a Mechanism for Replication 38

The Discovery of DNA Structure 38 DNA Nucleotides 39 DNA Replication 40

1.3 DNA Transcription and Messenger RNA Translation Express Genes 41

Genetic Analysis 1.1 42
Transcription 42
Experimental Insight 1.1 43
Translation 44
Genomes, Proteomes, and "-omic" Approaches 45
Genetic Analysis 1.2 46

1.4 Evolution Has a Molecular Basis 47

Darwin's Theory of Evolution 48
Four Evolutionary Processes 49
Tracing Evolutionary Relationships 49
Genetic Analysis 1.3 52

Case Study The Modern Human Family 53
Summary 54 • Keywords 55 • Problems 56



Transmission Genetics 58

2.1 Gregor Mendel Discovered the Basic Principles of Genetic Transmission 59

Mendel's Modern Experimental
Approach 60

Five Critical Experimental Innovations 61

2.2 Monohybrid Crosses Reveal the Segregation of Alleles 63

Identifying Dominant and Recessive Traits 63

Evidence of Particulate Inheritance and Rejection of the Blending Theory 64

Segregation of Alleles 65

Hypothesis Testing by Test-Cross Analysis 66

Hypothesis Testing by F₂ Self-Fertilization 67

2.3 Dihybrid and Trihybrid Crosses Reveal the Independent Assortment of Alleles 68

Dihybrid-Cross Analysis of Two Genes 68

Genetic Analysis 2.1 69

Testing Independent Assortment by Test-Cross Analysis 71

Genetic Analysis 2.2 72

Testing Independent Assortment by Trihybrid-Cross Analysis 73

Probability Calculations in Genetics Problem Solving 74 The Rediscovery of Mendel's Work 74

Genetic Analysis 2.3 75

Experimental Insight 2.1 76 STEEDER

2.4 Probability Theory Predicts Mendelian Ratios 76

The Product Rule 76

Experimental Insight 2.2 77

The Sum Rule 77 Demonstrated xed Conditional Probability 77 ST 2020 Date 1

The second of th

Experimental Insight 2.3 78

Binomial Probability 78

2.5 Chi-Square Analysis Tests the Fit between Observed Values and Expected Outcomes 80

The Normal Distribution 80

Chi-Square Analysis 81

Chi-Square Analysis of Mendel's Data 82

2.6 Autosomal Inheritance and Molecular Genetics Parallel the Predictions of Mendel's Hereditary Principles 83

Autosomal Dominant Inheritance 84

Autosomal Recessive Inheritance 85

Molecular Genetics of Mendel's Traits 86

Case Study Inheritance of Sickle Cell Disease in Humans 88 Summary 89 · Keywords 89 · Problems 90



Cell Division and Chromosome Heredity 96

Mitosis Divides Somatic Cells 97

Stages of the Cell Cycle 97 Substages of M Phase 98 Chromosome Distribution 99 Completion of Cell Division 100 Cell Cycle Checkpoints 101 Cell Cycle Mutations and Cancer 104

3.2 Meiosis Produces Gametes for Sexual Reproduction 104

Meiosis versus Mitosis 105 Meiosis I 107 Meiosis II 111 The Mechanistic Basis of Mendelian Ratios 111 Segregation in Single-Celled Diploids 113

3.3 The Chromosome Theory of Heredity **Proposes That Genes Are Carried on** Chromosomes 113

Genetic Analysis 3.1 115 X-Linked Inheritance 116 Testing the Chromosome Theory of Heredity 117

3.4 Sex Determination Is Chromosomal and Genetic 118

Sex Determination in Drosophila 118 Genetic Analysis 3.2 119 Mammalian Sex Determination 120 Diversity of Sex Determination 120 Experimental Insight 3.1 121

3.5 Human Sex-Linked Transmission Follows Distinct Patterns 122

Expression of X-Linked Recessive Traits 123 Genetic Analysis 3.3 125 X-Linked Dominant Trait Transmission 126 Y-Linked Inheritance 126

3.6 Dosage Compensation Equalizes the Expression of Sex-Linked Genes 127

Case Study The (Degenerative) Evolution of the Mammalian Y Chromosome 128 Summary 130 · Keywords 131 · Problems 131



Inheritance Patterns of Single Genes and Gene Interaction 136

4.1 Interactions between Alleles Produce **Dominance Relationships** 137

The Molecular Basis of Dominance 137 Functional Effects of Mutation 138 Incomplete Dominance 140 Codominance 141 Dominance Relationships of ABO Alleles 141 Allelic Series 143

Genetic Analysis 4.1 144 Lethal Alleles 145 Sex-Limited Traits 149 Sex-Influenced Traits 149 Delayed Age of Onset 150

4.2 Some Genes Produce Variable Phenotypes 150

Incomplete Penetrance 150 Variable Expressivity 151 Gene-Environment Interactions 151 Pleiotropic Genes 153

4.3 Gene Interaction Modifies Mendelian Ratios 153

Gene Interaction in Pathways 153 The One Gene-One Enzyme Hypothesis 156 Genetic Dissection to Investigate Gene Action 157 Experimental Insight 4.1 157 Epistasis and Its Results 159 Genetic Analysis 4.2 160

4.4 Complementation Analysis Distinguishes Mutations in the Same Gene from Mutations in Different Genes 166

Genetic Analysis 4.3 167

Case Study Complementation Groups in a Human Cancer-Prone Disorder 169 Summary 169 • Keywords 170 • Problems 170



Genetic Linkage and Mapping in Eukaryotes 176

5.1 Linked Genes Do Not Assort Independently 177

Genetic Analysis 5.1 184

Indications of Genetic Linkage 178
The Discovery of Genetic Linkage 180
Detecting Autosomal Genetic Linkage through
Test-Cross Analysis 182

5.2 Genetic Linkage Mapping Is Based on Recombination Frequency between Genes 185

The First Genetic Linkage Map 185

Map Units 186

Chi-Square Analysis of Genetic Linkage Data 186

5.3 Three-Point Test-Cross Analysis Maps Genes 186

Finding the Relative Order of Genes by Three-Point Mapping 186 Constructing a Three-Point Recombination Map 188 Determining Gamete Frequencies from Genetic Maps 191

5.4 Recombination Results from Crossing Over 192

Cytological Evidence of Recombination 192
Limits of Recombination along Chromosomes 192
Recombination within Genes 194
Genetic Analysis 5.2 195
Biological Factors Affecting Accuracy of Genetic

Maps 196
Recombination Is Dominated by Hotspots 196
Correction of Genetic Map Distances 197

5.5 Linked Human Genes Are Mapped Using Lod Score Analysis 198

Allelic Phase 198
Lod Score Analysis 199
Experimental Insight 5.1 201
Genetic Analysis 5.3 202

and Genetic Diversity 202 and I beside as

5.7 Genetic Linkage in Haploid Eukaryotes Is Identified by Tetrad Analysis 203

Analysis of Unordered Tetrads 204 Ordered Ascus Analysis 205

5.8 Mitotic Crossover Produces Distinctive Phenotypes 207

Case Study Mapping the Gene for Cystic Fibrosis 209 Summary 210 • Keywords 211 • Problems 212



Genetic Analysis and Mapping in Bacteria and Bacteriophages 218

6.1 Bacteria Transfer Genes by Conjugation 219

Conjugation Identified 220

Research Technique **6.1** 221

Transfer of the F Factor 224

Formation of an Hfr Chromosome 226

Hfr Gene Transfer 227

Characteristics of Bacterial Genomes 220

6.2 Interrupted Mating Analysis Produces Time-of-Entry Maps 229

Time-of-Entry Mapping Experiments 229
Consolidation of Hfr Maps 232
Genetic Analysis **6.1** 234

6.3 Conjugation with F' Strains Produces Partial Diploids 235

Plasmids and Conjugation in Archaea 236

6.4 Bacterial Transformation Produces Genetic Recombination 236

Genetic Analysis **6.2** 237
Steps in Transformation 238
Mapping by Transformation 238

6.5 Bacterial Transduction Is Mediated by Bacteriophages 238

Bacteriophage Life Cycles 239
Generalized Transduction 241
Cotransduction 241

Cotransduction Mapping	242
Specialized Transduction	244

6.6 Bacteriophage Chromosomes Are Mapped by Fine-Structure Analysis 245

Genetic Analysis 6.3 246
Genetic Complementation Analysis 247
Intragenic Recombination Analysis 248
Deletion-Mapping Analysis 248

6.7 Lateral Gene Transfer Alters Genomes 251

Lateral Gene Transfer and Genome Evolution 251 Identifying Lateral Gene Transfer in Genomes 252

Case Study The Evolution of Antibiotic Resistance and Change in Medical Practice 252 Summary 253 • Keywords 254 • Problems 254



DNA Structure and Replication 259

7.1 DNA Is the Hereditary Molecule of Life 260

Chromosomes Contain DNA 260
A Transformation Factor Responsible for Heredity 261
DNA Is the Transformation Factor 262
DNA Is the Hereditary Molecule 262

7.2 The DNA Double Helix Consists of Two Complementary and Antiparallel Strands 264

DNA Nucleotides 264

Genetic Analysis 7.1 266

Complementary DNA Nucleotide Pairing 266
The Twisting Double Helix 266

7.3 DNA Replication Is Semiconservative and Bidirectional 268

Three Competing Models of Replication 268

The Meselson-Stahl Experiment 268

Origin and Directionality of Replication in Bacterial DNA 269

Multiple Replication Origins in Eukaryotes 271

7.4 DNA Replication Precisely Duplicates the Genetic Material 273

DNA Sequences at Replication Origins 274

Replication Initiation 276

Continuous and Discontinuous Strand Replication 278

RNA Primer Removal and Okazaki Fragment Ligation 279 Simultaneous Synthesis of Leading and Lagging Strands 280

DNA Proofreading 281 Finishing Replication 283

Genetic Analysis 7.2 285

Telomeres, Aging, and Cancer 286

7.5 Molecular Genetic Analytical Methods Make Use of DNA Replication Processes 286

The Polymerase Chain Reaction 286

Separation of PCR Products 288

Dideoxynucleotide DNA Sequencing 288

New DNA-Sequencing Technologies: Next Generation and Third Generation 291

Genetic Analysis 7.3 292

Case Study Use of PCR and DNA Sequencing to Analyze Huntington Disease Mutations 293 Summary 295 • Keywords 296 • Problems 296



Molecular Biology of Transcription and RNA Processing 299

8.1 RNA Transcripts Carry the Messages of Genes 300

RNA Nucleotides and Structure 300
Identification of Messenger RNA 301
RNA Classification 302

8.2 Bacterial Transcription Is a Four-Stage Process 303

Bacterial RNA Polymerase 304
Bacterial Promoters 305
Transcription Initiation 305
Genetic Analysis 8.1 307
Transcription Elongation and Termination 308
Transcription Termination Mechanisms 308

8.3 Archaeal and Eukaryotic Transcription Displays Structural Homology and Common Ancestry 310

Eukaryotic and Archaeal RNA Polymerases 310 Consensus Sequences for Eukaryotic RNA Polymerase II Transcription 311

Research Technique 8.1 311

Promoter Recognition 313

Detecting Promoter Consensus Elements 314

Enhancers and Silencers 314

RNA Polymerase I Promoters 315

RNA Polymerase III Promoters 316

Termination in RNA Polymerase I or III

Transcription 316

Archaeal Transcription 317

8.4 Post-Transcriptional Processing Modifies RNA Molecules 317

Capping 5' mRNA 317

Polyadenylation of 3' Pre-mRNA 318

The Torpedo Model of Transcription
Termination 319

Pre-mRNA Intron Splicing 319

Splicing Signal Sequences 320

Coupling of Pre-mRNA Processing Steps 321

Alternative Transcripts of Single Genes 322

Control of Alternative Splicing 326

Intron Self-Splicing 326

Genetic Analysis **8.2** 327

Ribosomal RNA Processing 328

Transfer RNA Processing 329

Post-Transcriptional RNA Editing 330

Case Study Sexy Splicing: Alternative mRNA Splicing and Sex Determination in Drosophila 331
Summary 332 • Keywords 333 • Problems 334



The Molecular Biology of Translation 337

9.1 Polypeptides Are Composed of Amino Acid Chains That Are Assembled at Ribosomes 338

Amino Acid Structure 338

Polypeptide and Transcript Structure 339

Ribosome Structures 341

Research Technique 9.1 342

A Three-Dimensional View of the Ribosome 343

9.2 Translation Occurs in Three Phases 343

Translation Initiation 343
Polypeptide Elongation 347
Genetic Analysis **9.1** 349
Translation Termination 350

9.3 Translation Is Fast and Efficient 351 512 8.01

The Translational Complex 351

Translation of Polycistronic mRNA 352

9.4 The Genetic Code Translates Messenger RNA into Polypeptide 352

No Overlap in the Genetic Code 355

The Genetic Code Displays Third-Base Wobble 353 Charging tRNA Molecules 354

9.5 Experiments Deciphered the Genetic Code 354

A Triplet Genetic Code 355
No Gaps in the Genetic Code 356
Genetic Analysis 9.2 357
Deciphering the Genetic Code 358
The (Almost) Universal Genetic Code 359
Transfer RNAs and Genetic Code Specificity 360
Genetic Analysis 9.3 361

9.6 Translation Is Followed by Polypeptide Folding, Processing, and Protein Sorting 362

Posttranslational Polypeptide Processing 362
The Signal Hypothesis 363

Case Study Antibiotics and Translation
Interference 364
Summary 365 • Keywords 366 • Problems 366



The Integration of Genetic Approaches: Understanding Sickle Cell Disease 370

10.1 An Inherited Hemoglobin Variant Causes Sickle Cell Disease 371 000 grant Causes

The First Patient with Sickle Cell Disease 371
Hemoglobin Structure 372
Globin Gene Mutations 372

10.2 Genetic Variation Can Be Detected by Examining DNA, RNA, and Proteins 373

Research Technique 10.1 382

Gel Electrophoresis 374

Hemoglobin Peptide Fingerprint Analysis 376

Identification of DNA Sequence Variation 377

Genetic Analysis 10.1 379

Molecular Probes 380

Electrophoretic Analysis of Sickle Cell Disease 383

10.3 Sickle Cell Disease Evolved by Natural Selection in Human Populations 385

Research Technique 10.2 386

Genetic Analysis 10.2 388

Malaria Infection 389

Heterozygous Advantage 389

Evolution of β^C and β^E 390

Case Study Transmission and Molecular Genetic Analysis of Thalassemia 391

Summary 392 · Keywords 392 · Problems 393



11 Chromosome Structure 397

11.1 Viruses Are Infectious Particles Containing Nucleic Acid Genomes 398

Viral Genomes 398

Viral Protein Packaging 398

11.2 Bacterial Chromosomes Are Organized by Proteins 400

Bacterial Genome Content 400
Bacterial Chromosome Compaction 400

11.3 Eukaryotic Chromosomes Are Organized into Chromatin 402

Chromatin Compaction 402

Histone Proteins and Nucleosomes 403

Higher Order Chromatin Organization and

Chromosome Structure 405

Nucleosome Distribution and Synthesis during Replication 406

Genetic Analysis 11.1 408

11.4 Chromatin Compaction Varies along the Chromosome 408

Chromosome Shape and Chromosome

Karyotypes 408

In Situ Hybridization 409

Imaging Chromosome Territory during

Interphase 411

Chromosome Banding 412

Heterochromatin and Euchromatin 413

Centromere Structure 413

Position Effect Variegation: Effect of Chromatin State on Transcription 414

Genetic Analysis 11.2 415

11.5 Chromatin Organizes Archaeal Chromosomes 416

Archaeal Chromosome and Genome

Characteristics 416

Archaeal Histones 417

Phylogenetic Origins of Histone Proteins 417

Case Study Fishing for Chromosome Abnormalities

in Cancer Cells 418

Summary 419 · Keywords 420 · Problems 420



Gene Mutation, DNA Repair, and Homologous Recombination 423

12.1 Mutations Are Rare and Occur at Random 424

Mutation Rates 424

Determination of Mutation Rate from Genome Sequence Analysis 425

12.2 Gene Mutations Modify DNA Sequence 425

Base-Pair Substitution Mutations 426

Experimental Insight 12.1 427

Frameshift Mutations 427

Regulatory Mutations 427

Forward Mutation and Reversion 429

12.3 Gene Mutations May Arise from Spontaneous Events 429

DNA Replication Errors 429

Genetic Analysis 12.1 432

Spontaneous Nucleotide Base Changes 432

DNA Nucleotide Lesions 434

12.4 Mutations May Be Induced by Chemicals or Ionizing Radiation 435

Chemical Mutagens 436

Radiation-Induced DNA Damage 438

The Ames Test 440

12.5 Repair Systems Correct Some DNA Damage 440

Direct Repair of DNA Damage 441

Genetic Analysis 12.2 442

DNA Damage Signaling Systems 445

DNA Damage Repair Disorders 446
Experimental Insight 12.2 447

12.6 Proteins Control Translesion DNA Synthesis and the Repair of Double-Strand Breaks 447

Translesion DNA Synthesis 447 Double-Strand Break Repair 448

12.7 DNA Double-Strand Breaks Initiate Homologous Recombination 449

The Holliday Model 450
The Bacterial RecBCD Pathway 450
The Double-Stranded Break Model of Meiotic Recombination 450
Holliday Junction Resolution 451

12.8 Gene Conversion Is Directed Mismatch Repair in Heteroduplex DNA 451

Case Study Li-Fraumeni Syndrome Is Caused by Inheritance of Mutations of p53 455 Summary 456 • Keywords 457 • Problems 457



Chromosome Aberrations and Transposition 462

13.1 Nondisjunction Leads to Changes in Chromosome Number 463

Euploidy and Aneuploidy 463

Chromosome Nondisjunction 463
Gene Dosage Alteration 464
Aneuploidy in Humans 465
Reduced Fertility in Aneuploidy 467
Mosaicism 467
Trisomy Rescue and Uniparental Disomy 468

13.2 Changes in Euploidy Result in Various Kinds of Polyploidy 469

Autopolyploidy and Allopolyploidy 469

Consequences of Polyploidy 470

Reduced Recessive Homozygosity 471

Polyploidy and Evolution 471

13.3 Chromosome Breakage Causes Mutation by Loss, Gain, and Rearrangement of Chromosomes 472

Partial Chromosome Deletion 472 Unequal Crossover 473

Detecting Duplication and Deletion 474

Deletion Mapping 474

Genetic Analysis 13.1 475

13.4 Chromosome Breakage Leads to Inversion and Translocation of Chromosomes 478

Chromosome Translocation 480

Genetic Analysis 13.2 477

13.5 Transposable Genetic Elements Move throughout the Genome 482

The Discovery of Transposition 483

Experimental Insight 13.1 484

The Characteristics and Classification of Transposable Elements 485

Experimental Insight 13.2 486

13.6 Transposition Modifies Bacterial Genomes 488

Insertion Sequences 488 Composite Transposons 489

13.7 Transposition Modifies Eukaryotic Genomes 489

Genetic Analysis 13.3 490

Drosophila P Elements 490

Retrotransposons 492

Case Study Human Chromosome Evolution 493 Summary 494 • Keywords 495 • Problems 495



14

Regulation of Gene Expression in Bacteria and Bacteriophage 500

14.1 Transcriptional Control of Gene Expression Requires DNA-Protein Interaction 501

Negative and Positive Control of Transcription 501 Regulatory DNA-Binding Proteins 502

14.2 The *lac* Operon Is an Inducible Operon System under Negative and Positive Control 504

Lactose Metabolism 504

lac Operon Structure 505

lac Operon Function 505

	Mutational	Analysis Deciphers	Genetic
	Regulation	of the lac Operon	508

Analysis of Structural Gene Mutations 508 lac Operon Regulatory Mutations 509

Molecular Analysis of the lac Operon 512

Genetic Analysis 14.1 513

Experimental Insight 14.1 514

14.4 Transcription from the Tryptophan Operon Is Repressible and Attenuated 515

Feedback Inhibition of Tryptophan Synthesis 516
Attenuation of the *trp* Operon 517
Attenuation Mutations 520
Attenuation in Other Amino Acid Operon Systems 520
Genetic Analysis 14.2 521

14.5 Bacteria Regulate the Transcription of Stress Response Genes and Translation and Archaea Regulate Transcription in a Bacteria-like Manner 521

Alternative Sigma Factors and Stress Response 521 Translational Regulation in Bacteria 523 Transcriptional Regulation in Archaea 524

14.6 Antiterminators and Repressors Control Lambda Phage Infection of *E. coli* 524

The Lambda Phage Genome 525

Early Gene Transcription 525

Cro Protein and the Lytic Cycle 528

The λ Repressor Protein and Lysogeny 528

Resumption of the Lytic Cycle Following Lysogeny Induction 529

Case Study Vibrio cholerae—Stress Response Leads to Serious Infection 529 Summary 530 • Keywords 531 • Problems 531



Regulation of Gene Expression in Eukaryotes 536

15.1 Cis-Acting Regulatory Sequences Bind Trans-Acting Regulatory Proteins to Control Eukaryotic Transcription 538

Transcriptional Regulatory Interactions 538
Integration and Modularity of Regulatory Sequences 539
Transcription Regulation by Enhancers and Silencers 540
Locus Control Regions 540
Mutations in Regulatory Sequences 541

Enhancer-Sequence Conservation 542
Yeast Enhancer and Silencer Sequences 542
Insulator Sequences 543

15.2 Chromatin Remodeling and Modification Regulates Eukaryotic Transcription 544

PEV Mutations 544

Overview of Chromatin Remodeling and Chromatin Modification 545

Open and Covered Promoters 546

Mechanisms of Chromatin Remodeling 546

Chamical Modifications of Chromatin 540

Chemical Modifications of Chromatin 549

Genetic Analysis 15.1 550

An Example of Transcription Regulation in *S. cerevisiae* 552

Epigenetic Heritability 552

A Role for lncRNAs in Gene Regulation 553 Inactivation of Eutherian Mammalian Female X Chromosomes 553

Genomic Imprinting 554

Nucleotide Methylation 555

15.3 RNA-Mediated Mechanisms Control Gene Expression 556

Gene Silencing by Double-Stranded RNA 556
Chromatin Modification by RNAi 558
The Evolution and Applications of RNAi 559

Case Study Environmental Epigenetics 560
Summary 561 • Keywords 561 • Problems 562



16

Analysis of Gene Function by Forward Genetics and Reverse Genetics 565

16.1 Forward Genetic Screens Identify Genes by Their Mutant Phenotypes 567

General Design of Forward Genetic Screens 567 Specific Strategies of Forward Genetic Screens 567 Analysis of Mutageneses 571

Genetic Analysis 16.1 572

Identifying Interacting and Redundant Genes Using Modifier Screens 572

16.2 Genes Identified by Mutant Phenotype Are Cloned Using Recombinant DNA Technology 574

Cloning Genes by Complementation 574

Using Transposons to Clone Genes 575
Positional Cloning 576 576 September 2015
Positional Cloning in Humans: The Huntington Disease Gene 580
Genome Sequencing to Determine Gene Identification 581

16.3 Reverse Genetics Investigates Gene Action by Progressing from Gene Identification to Phenotype 583

Use of Insertion Mutants in Reverse Genetics 584 RNA Interference in Gene Activity 584 Reverse Genetics by TILLING 586

16.4 Transgenes Provide a Means of Dissecting Gene Function 586

Genetic Analysis 16.2 588

Monitoring Gene Expression with Reporter Genes 588 Enhancer Trapping 591 Investigating Gene Function with Chimeric Genes 592

Case Study Reverse Genetics and Genetic Redundancy in Flower Development 593 Summary 595 · Keywords 596 · Problems 596



Recombinant DNA Technology and Its Applications 599

17.1 Specific DNA Sequences Are Identified and Manipulated Using Recombinant DNA

Restriction Enzymes 600

Experimental Insight 17.1 601

Genetic Analysis 17.1 603

Molecular Cloning 604

DNA Libraries 609

Sequencing Long DNA Molecules 613

17.2 Introducing Foreign Genes into Genomes **Creates Transgenic Organisms** 615

Expression of Heterologous Genes in Bacterial and Fungal Hosts 615

Experimental Insight 17.2 619

Transformation of Plant Genomes by Agrobacterium 621

Transgenic Animals 626 go of moral animals

Advances in Altering and Synthesizing DNA Molecules 630

Manipulation of DNA Sequences in Vivo 630 Genetic Analysis 17.2 632

17.3 Gene Therapy Uses Recombinant DNA Technology 632

Two Forms of Gene Therapy 633 Gene Therapy in Humans 633

17.4 Cloning of Plants and Animals Produces Genetically Identical Individuals 634

Case Study Curing Sickle Cell Disease in Mice 636 Summary 637 • Keywords 638 • Problems 638



Genomics: Genetics from a Whole-Genome Perspective 643

18.1 Structural Genomics Provides a Catalog of Genes in a Genome 644

The Clone-by-Clone Sequencing Approach 645 Whole-Genome Shotgun Sequencing 645 Metagenomics 648

18.2 Annotation Ascribes Biological Function to DNA Sequences 649

Experimental Insight 18.1 650

Variation in Genome Organization among Species 652 Three Insights from Genome Sequences 653

18.3 Evolutionary Genomics Traces the History of Genomes 654

Research Technique 18.1 655

The Tree of Life 656

Interspecific Genome Comparisons: Gene Content 656 manual smons lambdor

Research Technique 18.2 658

Genetic Analysis 18.1 662

Interspecific Genome Comparisons: Genome Annotation 663

Interspecific Genome Comparisons: Gene Order 664

Intraspecific Genome Comparisons 666

Human Genetic Diversity 667

SNPs and Indels in Humans 667

Prenatal Genome Sequencing 668

18.4	Functional Genomics Aids in Elucidating
	Gene Function 668

Transcriptomics 668

Other "-omes" and "-omics" 670

Genomic Approaches to Reverse Genetics 673

Use of Yeast Mutants to Categorize Genes 673

Genetic Networks 674

Case Study Genomic Analysis of Insect Guts May Fuel the World 676

Summary 677 • Keywords 677 • Problems 678



19

Organelle Inheritance and the Evolution of Organelle Genomes 681

19.1 Organelle Inheritance Transmits Genes Carried on Organelle Chromosomes 682

The Discovery of Organelle Inheritance 682
Homoplasmy and Heteroplasmy 683
Genome Replication in Organelles 684
Replicative Segregation of Organelle Genomes 685

19.2 Modes of Organelle Inheritance Depend on the Organism 686

Mitochondrial Inheritance in Mammals 686

Genetic Analysis 19.1 689

Mating Type and Chloroplast Segregation in *Chlamydomonas* 691

Genetic Analysis 19.2 692

Biparental Inheritance in *Saccharomyces* cerevisiae 693

Summary of Organelle Inheritance 694

19.3 Mitochondria Are the Energy Factories of Eukaryotic Cells 694

Mitochondrial Genome Structure and Gene
Content 694
Mitochondrial Transcription and Translation 697

19.4 Chloroplasts Are the Sites of Photosynthesis 698

Chloroplast Genome Structure and Gene Content 699 Chloroplast Transcription and Translation 700 Editing of Chloroplast mRNA 700

19.5 The Endosymbiosis Theory Explains Mitochondrial and Chloroplast Evolution 700

Experimental Insight 19.1 701

Separate Evolution of Mitochondria and Chloroplasts 702 Continual DNA Transfer from Organelles 702 Encoding of Organellar Proteins 704

The Origin of the Eukaryotic Lineage 705 Secondary and Tertiary Endosymbioses 706

Case Study Ototoxic Deafness: A Mitochondrial Gene–Environment Interaction 707 Summary 709 • Keywords 709 • Problems 710



20

Developmental Genetics 713

20.1 Development Is the Building of a Multicellular Organism 714

Cell Differentiation 715
Pattern Formation 715

20.2 Drosophila Development Is a Paradigm for Animal Development 716

The Developmental Toolkit of *Drosophila* 718

Maternal Effects on Pattern Formation 719

Coordinate Gene Patterning of the Anterior—Posterior Axis 719

Domains of Gap Gene Expression 720

Regulation of Pair-Rule Genes 721

Specification of Parasegments by *Hox*Genes 723

Genetic Analysis 20.1 726

Downstream Targets of *Hox* Genes 727 *Hox* Genes in Metazoans 727

Stabilization of Cellular Memory by Chromatin Architecture 728

20.3 Cellular Interactions Specify Cell Fate 729

Inductive Signaling between Cells 729

Lateral Inhibition 732

Cell Death during Development 732

20.4 "Evolution Behaves Like a Tinkerer" 732

Evolution through Co-option 733 Constraints on Co-option 735

20.5 Plants Represent an Independent Experiment in Multicellular Evolution 735

Development at Meristems 735 Combinatorial Homeotic Activity in Floral-Organ Identity 736

Genetic Analysis 20.2 739

Case Study Cyclopia and Polydactyly—Different Shh Mutations with Distinctive Phenotypes 739 Summary 741 • Keywords 742 • Problems 742



21Genetic Analysis of Quantitative Traits 745

21.1 Quantitative Traits Display Continuous Phenotype Variation 746

Genetic Potential 746

Major Genes and Additive Gene Effects 747

Continuous Phenotypic Variation from Multiple Additive Genes 748

Allele Segregation in Quantitative Trait Production 748

Effects of Environmental Factors on Phenotypic Variation 751

Threshold Traits 751

21.2 Quantitative Trait Analysis Is Statistical 753

Statistical Description of Phenotypic Variation 753

Genetic Analysis 21.1 754

Experimental Insight 21.1 755

Partitioning Phenotypic Variance 757

Genetic Analysis 21.2 758

Partitioning Genetic Variance 758

21.3 Heritability Measures the Genetic Component of Phenotypic Variation 758

Broad Sense Heritability 759
Twin Studies 759
Narrow Sense Heritability and Artificial Selection 761

21.4 Quantitative Trait Loci Are the Genes That Contribute to Quantitative Traits 762

QTL Mapping Strategies 762
Identification of QTL Genes 764
Genome-Wide Association Studies 766

Case Study GWAS and Crohn's Disease 768
Summary 769 • Keywords 769 • Problems 770



Population Genetics and Evolution at the Population, Species, and Molecular Levels 774

22.1 The Hardy-Weinberg Equilibrium Describes the Relationship of Allele and Genotype Frequencies in Populations 775

Populations and Gene Pools 775

The Hardy-Weinberg Equilibrium 776

Determining Autosomal Allele Frequencies in Populations 778

The Hardy-Weinberg Equilibrium for More than Two Alleles 779

The Chi-Square Test of Hardy-Weinberg Predictions 780

22.2 Natural Selection Operates through Differential Reproductive Fitness within a Population 780

Differential Reproduction and Relative Fitness 780

Genetic Analysis 22.1 781

Directional Natural Selection 782

Natural Selection Favoring Heterozygotes 783

Convergent Evolution 784

22.3 Mutation Diversifies Gene Pools 785

Quantifying the Effects and Reverse Mutation Rates 785 Mutation–Selection Balance 785 Genetic Analysis 22.2 786

22.4 Migration Is Movement of Organisms and Genes between Populations 787

Effects of Gene Flow 787 Allele Frequency Equilibrium and Equalization 787

22.5 Genetic Drift Causes Allele Frequency Change by Sampling Error 788

The Founder Effect 788

Genetic Bottlenecks 789

22.6 Inbreeding Alters Genotype Frequencies 790

The Coefficient of Inbreeding 790
Inbreeding Depression 791
Genetic Analysis 22.3 792

22.7 Species and Higher Taxonomic Groups Evolve by the Interplay of Four Evolutionary Processes 792

Processes of Speciation 793
Reproductive Isolation and Speciation 793
Contemporary Evolution in Darwin's Finches 796

22.8 Molecular Evolution Changes Genes and Genomes through Time 796

Vertebrate Steroid Receptor Evolution 796

Human Genetic Diversity and Evolution 798

Case Study CODIS—Using Population Genetics to Solve Crime and Identify Paternity 801
Summary 803 • Keywords 804 • Problems 804

References and Additional Reading 809

Appendix: Answers 817

Glossary 837

Credits 859

Index 863