

Contents

PREFACE xii

CHAPTER 1

Introduction to Genetics 1

- 1.1 Genetics Has a Rich and Interesting History 2
- 1.2 Genetics Progressed from Mendel to DNA in Less Than a Century 4
- 1.3 Discovery of the Double Helix Launched the Era of Molecular Genetics 6
- 1.4 Development of Recombinant DNA Technology Began the Era of DNA Cloning 8
- 1.5 The Impact of Biotechnology Is Continually Expanding 9
- 1.6 Genomics, Proteomics, and Bioinformatics Are New and Expanding Fields 12
- 1.7 Genetic Studies Rely on the Use of Model Organisms 12
- 1.8 We Live in the Age of Genetics 14

GENETICS, TECHNOLOGY, AND SOCIETY

Genetics and Society: The Application and Impact of Science and Technology 15

EXPLORING GENOMICS

Internet Resources for Learning about Genomics, Bioinformatics, and Proteomics 15

Case Study: Extending essential ideas of genetics beyond the classroom 16

Problems and Discussion Questions 16

CHAPTER 2

Mitosis and Meiosis 17

- 2.1 Cell Structure Is Closely Tied to Genetic Function 18
- 2.2 Chromosomes Exist in Homologous Pairs in Diploid Organisms 20
- 2.3 Mitosis Partitions Chromosomes into Dividing Cells 22
- 2.4 Meiosis Reduces the Chromosome Number from Diploid to Haploid in Germ Cells and Spores 26
- 2.5 The Development of Gametes Varies during Spermatogenesis and Oogenesis 30
- 2.6 Meiosis Is Critical to the Sexual Reproduction Cycle of All Diploid Organisms 32
- 2.7 Electron Microscopy Has Revealed the Cytological Nature of Mitotic and Meiotic Chromosomes 33

EXPLORING GENOMICS

PubMed: Exploring and Retrieving Biomedical Literature 34

Case Study: Timing is everything 35

Insights and Solutions 35

Problems and Discussion Questions 36

CHAPTER 3

Mendelian Genetics 37

- 3.1 Mendel Used a Model Experimental Approach to Study Patterns of Inheritance 38
- 3.2 The Monohybrid Cross Reveals How One Trait Is Transmitted from Generation to Generation 39
- 3.3 Mendel's Dihybrid Cross Generated a Unique F_2 Ratio 42
 - How Mendel's Peas Become Wrinkled: A Molecular Explanation 43
- 3.4 The Trihybrid Cross Demonstrates That Mendel's Principles Apply to Inheritance of Multiple Traits 44
- 3.5 Mendel's Work Was Rediscovered in the Early Twentieth Century 46
- 3.6 Independent Assortment Leads to Extensive Genetic Variation 48
 - Tay-Sachs Disease: The Molecular Basis of a Recessive Disorder in Humans 48
- 3.7 Laws of Probability Help to Explain Genetic Events 49
- 3.8 Chi-Square Analysis Evaluates the Influence of Chance on Genetic Data 49
- 3.9 Pedigrees Reveal Patterns of Inheritance of Human Traits 52

EXPLORING GENOMICS

Online Mendelian Inheritance in Man 54

Case Study: To test or not to test 55

Insights and Solutions 55

Problems and Discussion Questions 57

CHAPTER 4

Modification of Mendelian Ratios 60

- 4.1 Alleles Alter Phenotypes in Different Ways 61
- 4.2 Geneticists Use a Variety of Symbols for Alleles 62
- 4.3 Neither Allele Is Dominant in Incomplete, or Partial, Dominance 62
- 4.4 In Codominance, the Influence of Both Alleles in a Heterozygote Is Clearly Evident 63
- 4.5 Multiple Alleles of a Gene May Exist in a Population 64
- 4.6 Lethal Alleles Represent Essential Genes 65
 - The Molecular Basis of Dominance and Recessiveness: The Agouti Gene 66
- 4.7 Combinations of Two Gene Pairs with Two Modes of Inheritance Modify the 9:3:3:1 Ratio 66

- 4.8 Phenotypes Are Often Affected by More Than One Gene 67
- 4.9 Complementation Analysis Can Determine If Two Mutations Causing a Similar Phenotype Are Alleles of the Same Gene 72
- 4.10 Expression of a Single Gene May Have Multiple Effects 73
- 4.11 X-Linkage Describes Genes on the X Chromosome 73
- 4.12 In Sex-Limited and Sex-Influenced Inheritance, an Individual's Sex Influences the Phenotype 76
- 4.13 Genetic Background and the Environment Affect Phenotypic Expression 77
- 4.14 Extranuclear Inheritance Modifies Mendelian Patterns 80

GENETICS, TECHNOLOGY, AND SOCIETY

Improving the Genetic Fate of Purebred Dogs 84

- Case Study: A twin difference 85
- Insights and Solutions 85
- Problems and Discussion Questions 87

CHAPTER 5

Sex Determination and Sex Chromosomes 92

- 5.1 Life Cycles Depend on Sexual Differentiation 93
- 5.2 X and Y Chromosomes Were First Linked to Sex Determination Early in the Twentieth Century 96
- 5.3 The Y Chromosome Determines Maleness in Humans 97
- 5.4 The Ratio of Males to Females in Humans Is Not 1.0 101
- 5.5 Dosage Compensation Prevents Excessive Expression of X-Linked Genes in Humans and Other Mammals 102
- 5.6 The Ratio of X Chromosomes to Sets of Autosomes Determines Sex in *Drosophila* 104
- 5.7 Temperature Variation Controls Sex Determination in Reptiles 106

GENETICS, TECHNOLOGY, AND SOCIETY

A Question of Gender: Sex Selection in Humans 107

- Case Study: Doggone it! 108
- Insights and Solutions 108
- Problems and Discussion Questions 109

CHAPTER 6

Chromosome Mutations: Variation in Number and Arrangement 111

- 6.1 Variation in Chromosome Number: Terminology and Origin 112
- 6.2 Monosomy and Trisomy Result in a Variety of Phenotypic Effects 113
- 6.3 Polyploidy, in Which More Than Two Haploid Sets of Chromosomes Are Present, Is Prevalent in Plants 116

- 6.4 Variation Occurs in the Composition and Arrangement of Chromosomes 119
- 6.5 A Deletion Is a Missing Region of a Chromosome 119
- 6.6 A Duplication Is a Repeated Segment of a Chromosome 121
- 6.7 Inversions Rearrange the Linear Gene Sequence 123
 - Copy Number Variants (CNVs)—Duplications and Deletions at the Molecular Level 123
- 6.8 Translocations Alter the Location of Chromosomal Segments in the Genome 125
- 6.9 Fragile Sites in Human Chromosomes Are Susceptible to Breakage 127

GENETICS, TECHNOLOGY, AND SOCIETY

Down Syndrome, Prenatal Testing, and the New Eugenics 128

- Case Study: Fish tales 129
- Insights and Solutions 129
- Problems and Discussion Questions 130

CHAPTER 7

Linkage and Chromosome Mapping in Eukaryotes 132

- 7.1 Genes Linked on the Same Chromosome Segregate Together 133
- 7.2 Crossing Over Serves as the Basis of Determining the Distance between Genes during Mapping 136
- 7.3 Determining the Gene Sequence during Mapping Requires the Analysis of Multiple Crossovers 139
- 7.4 As the Distance between Two Genes Increases, Mapping Estimates Become More Inaccurate 145
- 7.5 Lod Score Analysis and Somatic Cell Hybridization Were Historically Important in Creating Human Chromosome Maps 147
- 7.6 Chromosome Mapping Is Now Possible Using DNA Markers and Annotated Computer Databases 148
- 7.7 Linkage and Mapping Studies Can Be Performed in Haploid Organisms 149
- 7.8 Other Aspects of Genetic Exchange 150
- 7.9 Did Mendel Encounter Linkage? 152
 - Why Didn't Gregor Mendel Find Linkage? 152

EXPLORING GENOMICS

Human Chromosome Maps on the Internet 153

- Case Study: Links to autism 153
- Insights and Solutions 154
- Problems and Discussion Questions 155

CHAPTER 8

Genetic Analysis and Mapping in Bacteria and Bacteriophages 159

- 8.1 Bacteria Mutate Spontaneously and Grow at an Exponential Rate 160

- 8.2 Conjugation Is One Means of Genetic Recombination in Bacteria 161
- 8.3 Rec Proteins Are Essential to Bacterial Recombination 168
- 8.4 The F Factor Is an Example of a Plasmid 168
- 8.5 Transformation Is Another Process Leading to Genetic Recombination in Bacteria 169
- 8.6 Bacteriophages Are Bacterial Viruses 170
- 8.7 Transduction Is Virus-Mediated Bacterial DNA Transfer 173
- 8.8 Bacteriophages Undergo Intergenic Recombination 175

GENETICS, TECHNOLOGY, AND SOCIETY

From Cholera Genes to Edible Vaccines 177

Case Study: To treat or not to treat 178

Insights and Solutions 178

Problems and Discussion Questions 179

CHAPTER 9

DNA Structure and Analysis 181

- 9.1 The Genetic Material Must Exhibit Four Characteristics 182
- 9.2 Until 1944, Observations Favored Protein as the Genetic Material 183
- 9.3 Evidence Favoring DNA as the Genetic Material Was First Obtained during the Study of Bacteria and Bacteriophages 183
- 9.4 Indirect and Direct Evidence Supports the Concept that DNA Is the Genetic Material in Eukaryotes 188
- 9.5 RNA Serves as the Genetic Material in Some Viruses 189
- 9.6 The Structure of DNA Holds the Key to Understanding Its Function 190
 - Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid 195
- 9.7 Alternative Forms of DNA Exist 196
- 9.8 The Structure of RNA Is Chemically Similar to DNA, but Single-Stranded 197
- 9.9 Many Analytical Techniques Have Been Useful during the Investigation of DNA and RNA 197

EXPLORING GENOMICS

Introduction to Bioinformatics: BLAST 200

Case Study: Zigs and zags of the smallpox virus 201

Insights and Solutions 201

Problems and Discussion Questions 201

CHAPTER 10

DNA Replication and Recombination 203

- 10.1 DNA Is Reproduced by Semiconservative Replication 204

- 10.2 DNA Synthesis in Bacteria Involves Five Polymerases, as Well as Other Enzymes 208
- 10.3 Many Complex Issues Must Be Resolved during DNA Replication 211
- 10.4 A Coherent Model Summarizes DNA Replication 214
- 10.5 Replication Is Controlled by a Variety of Genes 214
- 10.6 Eukaryotic DNA Replication Is Similar to Replication in Prokaryotes, but Is More Complex 215
- 10.7 The Ends of Linear Chromosomes Are Problematic during Replication 217
- 10.8 DNA Recombination, Like DNA Replication, Is Directed by Specific Enzymes 219

GENETICS, TECHNOLOGY, AND SOCIETY

Telomeres: The Key to Immortality? 221

Case Study: At loose ends 222

Insights and Solutions 222

Problems and Discussion Questions 222

CHAPTER 11

Chromosome Structure and DNA Sequence Organization 224

- 11.1 Viral and Bacterial Chromosomes Are Relatively Simple DNA Molecules 225
- 11.2 Mitochondria and Chloroplasts Contain DNA Similar to Bacteria and Viruses 226
- 11.3 Specialized Chromosomes Reveal Variations in the Organization of DNA 229
- 11.4 DNA Is Organized into Chromatin in Eukaryotes 231
- 11.5 Eukaryotic Genomes Demonstrate Complex Sequence Organization Characterized by Repetitive DNA 234
- 11.6 The Vast Majority of a Eukaryotic Genome Does Not Encode Functional Genes 236

EXPLORING GENOMICS

Database of Genomic Variants: Structural Variations in the Human Genome 237

Case Study: Art inspires learning 238

Insights and Solutions 238

Problems and Discussion Questions 238

CHAPTER 12

The Genetic Code and Transcription 240

- 12.1 The Genetic Code Exhibits a Number of Characteristics 241
- 12.2 Early Studies Established the Basic Operational Patterns of the Code 242

- 12.3 Studies by Nirenberg, Matthaei, and Others Deciphered the Code 242
- 12.4 The Coding Dictionary Reveals the Function of the 64 Triplets 246
- 12.5 The Genetic Code Has Been Confirmed in Studies of Bacteriophage MS2 248
- 12.6 The Genetic Code Is Nearly Universal 248
- 12.7 Different Initiation Points Create Overlapping Genes 249
- 12.8 Transcription Synthesizes RNA on a DNA Template 249
- 12.9 RNA Polymerase Directs RNA Synthesis 250
- 12.10 Transcription in Eukaryotes Differs from Prokaryotic Transcription in Several Ways 252
- 12.11 The Coding Regions of Eukaryotic Genes Are Interrupted by Intervening Sequences Called Introns 254
- 12.12 Transcription Has Been Visualized by Electron Microscopy 257

GENETICS, TECHNOLOGY, AND SOCIETY

Nucleic Acid-Based Gene Silencing: Attacking the Messenger 257

Case Study: A drug that sometimes works 258

Insights and Solutions 258

Problems and Discussion Questions 259

CHAPTER 13

Translation and Proteins 261

- 13.1 Translation of mRNA Depends on Ribosomes and Transfer RNAs 262
- 13.2 Translation of mRNA Can Be Divided into Three Steps 265
- 13.3 Crystallographic Analysis Has Revealed Many Details about the Functional Prokaryotic Ribosome 269
- 13.4 Translation Is More Complex in Eukaryotes 269
- 13.5 The Initial Insight that Proteins Are Important in Heredity Was Provided by the Study of Inborn Errors of Metabolism 270
- 13.6 Studies of *Neurospora* Led to the One-Gene:One-Enzyme Hypothesis 271
- 13.7 Studies of Human Hemoglobin Established that One Gene Encodes One Polypeptide 273
- 13.8 Variation in Protein Structure Is the Basis of Biological Diversity 276
- 13.9 Proteins Function in Many Diverse Roles 279

EXPLORING GENOMICS

Translation Tools and Swiss-Prot for Studying Protein Sequences 280

Case Study: Lost in translation 281

Insights and Solutions 281

Problems and Discussion Questions 282

CHAPTER 14

Gene Mutation, Transposition, and DNA Repair 284

- 14.1 Gene Mutations Are Classified in Various Ways 285
- 14.2 Spontaneous Mutations Arise from Replication Errors and Base Modifications 287
- 14.3 Induced Mutations Arise from DNA Damage Caused by Chemicals and Radiation 289
- 14.4 Organisms Use DNA Repair Systems to Counteract Mutations 292
- 14.5 The Ames Test Is Used to Assess the Mutagenicity of Compounds 296
- 14.6 DNA Sequencing Has Enhanced Our Understanding of Mutations in Humans 297
- 14.7 Geneticists Use Mutations to Identify Genes and Study Gene Function 298
- 14.8 Transposable Elements Move within the Genome and May Create Mutations 299

EXPLORING GENOMICS

Sequence Alignment to Identify a Mutation 303

Case Study: Genetic dwarfism 304

Insights and Solutions 305

Problems and Discussion Questions 305

CHAPTER 15

Regulation of Gene Expression 308

- 15.1 Prokaryotes Regulate Gene Expression in Response to Both External and Internal Conditions 309
- 15.2 Lactose Metabolism in *E. coli* Is Regulated by an Inducible System 309
- 15.3 The Catabolite-Activating Protein (CAP) Exerts Positive Control over the *lac* Operon 314
- 15.4 The Tryptophan (*trp*) Operon in *E. coli* Is a Repressible Gene System 315
- 15.5 Attenuation Is a Regulatory Mechanism in Some Prokaryotic Operons 317
- 15.6 Eukaryotic Gene Regulation Differs from That in Prokaryotes 317
- 15.7 Eukaryotic Gene Expression Is Influenced by Chromosome Organization and Chromatin Modifications 318
- 15.8 Eukaryotic Transcription Is Regulated at Specific *Cis*-Acting Sites 320
- 15.9 Eukaryotic Transcription Is Regulated by Transcription Factors that Bind to *Cis*-Acting Sites 323
- 15.10 Transcription Factors Bind to *Cis*-Acting sites and Interact with Basal Transcription Factors and Other Regulatory Proteins 324
- 15.11 Posttranscriptional Gene Regulation Occurs at All the Steps from RNA Processing to Protein Modification 325
- 15.12 RNA-induced Gene Silencing Controls Gene Expression in Several Ways 328

EXPLORING GENOMICS**Tissue-Specific Gene Expression 330**

Case Study: A mysterious muscular dystrophy 330

Insights and Solutions 331

Problems and Discussion Questions 331

CHAPTER 16**Cancer and Regulation of the Cell Cycle 334**

16.1 Cancer Is a Genetic Disease at the Level of Somatic Cells 335

16.2 Cancer Cells Contain Genetic Defects Affecting Genomic Stability, DNA Repair, and Chromatin Modifications 337

16.3 Cancer Cells Contain Genetic Defects Affecting Cell-Cycle Regulation 338

16.4 Proto-oncogenes and Tumor-suppressor Genes Are Altered in Cancer Cells 340

16.5 Cancer Cells Metastasize, Invading Other Tissues 343

16.6 Predisposition to Some Cancers Can Be Inherited 344

16.7 Viruses Contribute to Cancer in Both Humans and Animals 345

16.8 Environmental Agents Contribute to Human Cancers 346

GENETICS, TECHNOLOGY, AND SOCIETY**Breast Cancer: The Double-Edged Sword of Genetic Testing 347**

Case Study: I thought it was safe 348

Insights and Solutions 348

Problems and Discussion Questions 349

CHAPTER 17**Recombinant DNA Technology and Gene Cloning 351**

17.1 An Overview of Recombinant DNA Technology 352

17.2 Constructing Recombinant DNA Molecules Requires Several Steps 352

17.3 Cloning DNA in Host Cells 356

17.4 The Polymerase Chain Reaction Makes DNA Copies without Host Cells 357

17.5 Recombinant Libraries Are Collections of Cloned Sequences 359

17.6 Specific Clones Can Be Recovered from a Library 361

17.7 Cloned Sequences Can Be Analyzed in Several Ways 362

17.8 DNA Sequencing Is the Ultimate Way to Characterize a Clone 366

EXPLORING GENOMICS**Manipulating Recombinant DNA: Restriction Mapping and Designing a Recombinant DNA Experiment 369**

Case Study: Should we worry about recombinant DNA technology? 370

Insights and Solutions 371

Problems and Discussion Questions 371

CHAPTER 18**Genomics, Bioinformatics, and Proteomics 375**

18.1 Whole-Genome Shotgun Sequencing Is a Widely Used Method for Sequencing and Assembling Entire Genomes 376

18.2 DNA Sequence Analysis Relies on Bioinformatics Applications and Genome Databases 380

18.3 Functional Genomics Attempts to Identify Potential Functions of Genes and Other Elements in a Genome 383

18.4 The Human Genome Project Reveals Many Important Aspects of Genome Organization in Humans 384

18.5 The "Omics" Revolution Has Created a New Era of Biological Research Methods 386

18.6 Prokaryotic and Eukaryotic Genomes Display Common Structural and Functional Features and Important Differences 387

18.7 Comparative Genomics Analyzes and Compares Genomes from Different Organisms 390

18.8 Metagenomics Applies Genomics Techniques to Environmental Samples 394

18.9 Transcriptome Analysis Reveals Profiles of Expressed Genes in Cells and Tissues 396

18.10 Proteomics Identifies and Analyzes the Protein Composition of Cells 398

EXPLORING GENOMICS**Contigs and Shotgun Sequencing 403**

Case Study: Bioprospecting in Darwin's wake 404

Insights and Solutions 404

Problems and Discussion Questions 405

CHAPTER 19**Applications and Ethics of Genetic Engineering and Biotechnology 407**

19.1 Genetically Engineered Organisms Synthesize a Wide Range of Biological and Pharmaceutical Products 408

19.2 Genetic Engineering of Plants Has Revolutionized Agriculture 411

19.3 Transgenic Animals with Genetically Enhanced Characteristics Have the Potential to Serve Important Roles in Agriculture and Biotechnology 414

- 19.4 Genetic Engineering and Genomics Are Transforming Medical Diagnosis 415
- 19.5 Genetic Engineering and Genomics Promise New, More Targeted Medical Therapies 421
- 19.6 DNA Profiles Identify Individuals 424
- 19.7 Genetic Engineering, Genomics, and Biotechnology Create Ethical, Social, and Legal Questions 427

GENETICS, TECHNOLOGY, AND SOCIETY

Personal Genome Projects and the Race for the \$1000 Genome 429

Case Study: A first for gene therapy 430

Insights and Solutions 430

Problems and Discussion Questions 431

CHAPTER 20

Developmental Genetics 433

- 20.1 Evolutionary Conservation of Developmental Mechanisms Can Be Studied Using Model Organisms 434
- 20.2 Genetic Analysis of Embryonic Development in *Drosophila* Reveals How the Body Axis of Animals Is Specified 434
- 20.3 Zygotic Genes Program Segment Formation in *Drosophila* 437
- 20.4 Homeotic Selector Genes Specify Parts of the Adult Body 439
- 20.5 Plants Have Evolved Developmental Systems That Parallel Those of Animals 442
- 20.6 Cell-Cell Interactions in Development Are Modeled in *C. elegans* 444
- 20.7 Transcriptional Networks Control Gene Expression in Development 446

GENETICS, TECHNOLOGY, AND SOCIETY

Stem Cell Wars 446

Case Study: One foot or another 447

Insights and Solutions 448

Problems and Discussion Questions 448

CHAPTER 21

Genetics and Behavior 450

- 21.1 Behavioral Differences between Genetic Strains Can Be Identified 451
- 21.2 The Behavior-First Approach Can Establish Genetic Strains with Behavioral Differences 453
- 21.3 The Gene-First Approach Uses Analysis of Mutant Alleles to Study Molecular Mechanisms That Underlie Behavior 455
- 21.4 Human Behavior Has Genetic Components 459

EXPLORING GENOMICS

HomoloGene: Searching for Behavioral Genes 462

Case Study: Primate models for human disorders 462

Insights and Solutions 463

Problems and Discussion Questions 463

CHAPTER 22

Quantitative Genetics and Multifactorial Traits 465

- 22.1 Not All Polygenic Traits Show Continuous Variation 466
- 22.2 Quantitative Traits Can Be Explained in Mendelian Terms 467
- 22.3 The Study of Polygenic Traits Relies on Statistical Analysis 469
- 22.4 Heritability Values Estimate the Genetic Contribution to Phenotypic Variability 471
- 22.5 Twin Studies Allow an Estimation of Heritability in Humans 475
- 22.6 Quantitative Trait Loci Can Be Mapped 476

GENETICS, TECHNOLOGY, AND SOCIETY

The Green Revolution Revisited: Genetic Research with Rice 477

Case Study: A flip of the genetic coin 478

Insights and Solutions 478

Problems and Discussion Questions 480

CHAPTER 23

Population and Evolutionary Genetics 483

- 23.1 Genetic Variation Is Present in Most Populations and Species 484
- 23.2 The Hardy-Weinberg Law Describes Allele Frequencies and Genotype Frequencies in Populations 486
- 23.3 The Hardy-Weinberg Law Can Be Applied to Human Populations 488
- 23.4 Natural Selection Is a Major Force Driving Allele Frequency Change 491
- 23.5 Mutation Creates New Alleles in a Gene Pool 493
- 23.6 Migration and Gene Flow Can Alter Allele Frequencies 494
- 23.7 Genetic Drift Causes Random Changes in Allele Frequency in Small Populations 494
- 23.8 Nonrandom Mating Changes Genotype Frequency but Not Allele Frequency 496
- 23.9 Reduced Gene Flow, Selection, and Genetic Drift Can Lead to Speciation 497
- 23.10 Genetic Differences Can Be Used to Reconstruct Evolutionary History 499

EXPLORING GENOMICS

The Y Chromosome Haplotype Reference Database (YHRD) 503

Case Study: An unexpected outcome 504

Insights and Solutions 504

Problems and Discussion Questions 504

CHAPTER 24

Conservation Genetics 507

24.1 Genetic Diversity Is the Goal of Conservation Genetics 509

24.2 Population Size Has a Major Impact on Species Survival 511

24.3 Genetic Effects Are More Pronounced in Small, Isolated Populations 512

24.4 Genetic Erosion Threatens Species' Survival 515

24.5 Conservation of Genetic Diversity Is Essential to Species Survival 516

GENETICS, TECHNOLOGY, AND SOCIETY

Gene Pools and Endangered Species: The Plight of the Florida Panther 519

Case Study: The flip side of the green revolution 520

Insights and Solutions 520

Problems and Discussion Questions 521

APPENDIX A ANSWERS TO SELECTED PROBLEMS A-1

APPENDIX B SELECTED READINGS B-1

GLOSSARY G-1

CREDITS C-1

INDEX I-1