

Brief Contents

- 1** Genetics: The Study of Biological Information 1

PART I

Basic Principles: How Traits Are Transmitted 14

- 2** Mendel's Principles of Heredity 14
3 Extensions to Mendel's Laws 45
4 The Chromosome Theory of Inheritance 85
5 Linkage, Recombination, and the Mapping of Genes on Chromosomes 127

PART II

What Genes Are and What They Do 173

- 6** DNA Structure, Replication, and Recombination 173
7 Anatomy and Function of a Gene: Dissection Through Mutation 206
8 Gene Expression: The Flow of Information from DNA to RNA to Protein 254

PART III

Analysis of Genetic Information 298

- 9** Digital Analysis of Genomes 298
10 Analyzing Genomic Information 342

PART IV

How Genes Travel on Chromosomes 381

- 11** The Eukaryotic Chromosome 381
12 Chromosomal Rearrangements and Changes in Chromosome Number 409
13 Bacterial Genetics 459
14 Organellar Inheritance 491

PART V

How Genes Are Regulated 514

- 15** Gene Regulation in Prokaryotes 514
16 Gene Regulation in Eukaryotes 547

PART VI

Using Genetics 575

- 17** Manipulating the Genomes of Eukaryotes 575
18 The Genetic Analysis of Development 598
19 The Genetics of Cancer 631

PART VII

Beyond the Individual Gene and Genome 662

- 20** Variation and Selection in Populations 662
21 Genetics of Complex Traits 694

Contents

About The Authors iii
Preface x
Acknowledgements xxv

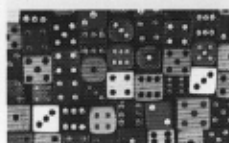
Introduction: Genetics in the Twenty-First Century 1

chapter 1

Genetics: The Study of Biological Information 1

- 1.1 DNA: The Fundamental Information
Molecule of Life 2
- 1.2 Proteins: The Functional Molecules
of Life Processes 3
- 1.3 Molecular Similarities of All
Life-Forms 4
- 1.4 The Modular Construction
of Genomes 6
- 1.5 Modern Genetic Techniques 8
- 1.6 Human Genetics and Society 10

PART I



Basic Principles: How Traits Are Transmitted 14

chapter 2

Mendel's Principles of Heredity 14

- 2.1 Background: The Historical Puzzle
of Inheritance 15
- 2.2 Genetic Analysis According to Mendel 20
- 2.3 Mendelian Inheritance in Humans 30

- *Genetics and Society: Developing Guidelines for
Genetic Screening* 34

chapter 3

Extensions to Mendel's Laws 45

- 3.1 Extensions to Mendel for Single-Gene
Inheritance 46

- 3.2 Extensions to Mendel for Multifactorial
Inheritance 55

- *Genetics and Society: Disease Prevention Versus
the Right to Privacy* 71

chapter 4

The Chromosome Theory of Inheritance 85

- 4.1 Chromosomes: The Carriers of Genes 86
- 4.2 Sex Chromosomes and Sex Determination 89
- 4.3 Mitosis: Cell Division That Preserves
Chromosome Number 92
- 4.4 Meiosis: Cell Divisions That Halve
Chromosome Number 98
- 4.5 Gametogenesis 106
- 4.6 Validation of the Chromosome
Theory 108
- 4.7 Sex-Linked and Sexually Dimorphic
Traits in Humans 114

- *Genetics and Society: Prenatal Genetic
Diagnosis* 89

- *Fast Forward: Transgenic Mice Prove That SRY
Is the Maleness Factor* 93

chapter 5

Linkage, Recombination, and the Mapping of Genes on Chromosomes 127

- 5.1 Gene Linkage and Recombination 128
- 5.2 Recombination: A Result of Crossing-Over
During Meiosis 132
- 5.3 Mapping: Locating Genes Along a
Chromosome 137
- 5.4 The Chi-Square Test and Linkage
Analysis 145
- 5.5 Tetrad Analysis in Fungi 149
- 5.6 Mitotic Recombination and Genetic Mosaics 157

- *Fast Forward: Gene Mapping May Lead to a Cure for
Cystic Fibrosis* 143

- *Tools of Genetics: The Chi-Square Test for
Goodness of Fit* 147

- *Genetics and Society: Mitotic Recombination
and Cancer Formation* 159

PART II



What Genes Are and What They Do 173

chapter 6

DNA Structure, Replication, and Recombination 173

- 6.1 Experimental Evidence for DNA as the Genetic Material 174
- 6.2 The Watson and Crick Double Helix Model of DNA 179
- 6.3 Genetic Information in Nucleotide Sequence 185
- 6.4 DNA Replication 186
- 6.5 Recombination at the DNA Level 193

chapter 7

Anatomy and Function of a Gene: Dissection Through Mutation 206

- 7.1 Mutations: Primary Tools of Genetic Analysis 207
- 7.2 Molecular Mechanisms of Mutation 212
- 7.3 What Mutations Tell Us About Gene Structure 225
- 7.4 What Mutations Tell Us About Gene Function 233
- 7.5 A Comprehensive Example: Mutations That Affect Vision 241

- *Fast Forward: Trinucleotide Repeat Diseases: Huntington Disease and Fragile X Syndrome* 216

chapter 8

Gene Expression: The Flow of Information from DNA to RNA to Protein 254

- 8.1 The Genetic Code 255
- 8.2 Transcription: From DNA to RNA 264
- 8.3 Translation: From mRNA to Protein 273
- 8.4 Differences in Gene Expression Between Prokaryotes and Eukaryotes 281
- 8.5 The Effects of Mutations on Gene Expression and Function 283

- *Genetics and Society: HIV and Reverse Transcription* 268

PART III



Analysis of Genetic Information 298

chapter 9

Digital Analysis of Genomes 298

- 9.1 Fragmenting DNA 299
- 9.2 Cloning DNA Fragments 305
- 9.3 Sequencing DNA 309
- 9.4 Sequencing Genomes 313
- 9.5 Finding the Genes in Genomes 316
- 9.6 Genome Architecture and Evolution 321
- 9.7 Bioinformatics: Information Technology and Genomes 327
- 9.8 A Comprehensive Example: The Hemoglobin Genes 329

- *Tools of Genetics: Serendipity in Science: The Discovery of Restriction Enzymes* 301

chapter 10

Analyzing Genomic Information 342

- 10.1 Variation Among Genomes 343
- 10.2 Genotyping a Known Disease-Causing Mutation 347
- 10.3 Sampling DNA Variation in a Genome 353
- 10.4 Positional Cloning 357
- 10.5 The Era of Whole-Genome Sequencing 363

- *Tools of Genetics: The Lod Score Statistic* 361

PART IV



How Genes Travel on Chromosomes 381

chapter 11

The Eukaryotic Chromosome 381

- 11.1 Chromosomal DNA and Proteins 382
- 11.2 Chromosome Structure and Compaction 383

- 11.3 Chromosomal Packaging and Gene Expression 389
- 11.4 Replication of Eukaryotic Chromosomes 394
- 11.5 Chromosome Segregation 398
- 11.6 Artificial Chromosomes 401

chapter 12

Chromosomal Rearrangements and Changes in Chromosome Number 409

- 12.1 Rearrangements of Chromosomal DNA 410
- 12.2 The Effects of Rearrangements 416
- 12.3 Transposable Genetic Elements 426
- 12.4 Aberrations in Chromosome Number: Aneuploidy 433
- 12.5 Variation in Number of Chromosome Sets: Euploidy 438
- 12.6 Genome Restructuring and Evolution 443
- *Fast Forward: Programmed DNA Rearrangements and the Immune System* 412

chapter 13

Bacterial Genetics 459

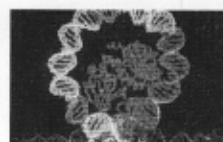
- 13.1 The Enormous Diversity of Bacteria 460
- 13.2 Bacterial Genomes 462
- 13.3 Bacteria as Experimental Organisms 466
- 13.4 Gene Transfer in Bacteria 468
- 13.5 Bacterial Genetic Analysis 479
- 13.6 A Comprehensive Example: How *N. gonorrhoeae* Became Resistant to Penicillin 481

chapter 14

Organellar Inheritance 491

- 14.1 Mitochondria and Their Genomes 492
- 14.2 Chloroplasts and Their Genomes 495
- 14.3 The Relationship Between Organellar and Nuclear Genomes 498
- 14.4 Non-Mendelian Inheritance of Mitochondria and Chloroplasts 500
- 14.5 Mutant Mitochondria and Human Disease 505
- *Genetics and Society: Mitochondrial DNA Tests as Evidence of Kinship in Argentine Courts* 502

PART V



How Genes Are Regulated 514

chapter 15

Gene Regulation in Prokaryotes 514

- 15.1 The Elements of Prokaryotic Gene Expression 515
- 15.2 Regulation of Transcription Initiation via DNA-Binding Proteins 516
- 15.3 RNA-Mediated Mechanisms of Gene Regulation 529
- 15.4 Discovering and Manipulating Bacterial Gene Regulatory Mechanisms 532
- 15.5 A Comprehensive Example: Control of Bioluminescence by Quorum Sensing 537

chapter 16

Gene Regulation in Eukaryotes 547

- 16.1 Overview of Eukaryotic Gene Regulation 548
- 16.2 Control of Transcription Initiation Through Enhancers 549
- 16.3 Epigenetics: Control of Transcription Initiation Through DNA Methylation 557
- 16.4 Regulation After Transcription 561
- 16.5 A Comprehensive Example: Sex Determination in *Drosophila* 564

PART VI



Using Genetics 575

chapter 17

Manipulating the Genomes of Eukaryotes 575

- 17.1 Creating Transgenic Organisms 576
- 17.2 Uses of Transgenic Organisms 579

17.3 Targeted Mutagenesis 584

17.4 Human Gene Therapy 590

■ *Tools of Genetics: Cloning by Somatic Cell Nuclear Transfer* 582

chapter 18

The Genetic Analysis of Development 598

- 18.1 Model Organisms: Prototypes for Developmental Genetics 599
- 18.2 Mutagenesis Screens 600
- 18.3 Determining Where and When Genes Act 606
- 18.4 Ordering Genes in a Pathway 609
- 18.5 A Comprehensive Example: Body Plan Development in *Drosophila* 610

chapter 19

The Genetics of Cancer 631

- 19.1 Characteristics of Cancer Cells 632
- 19.2 The Genetic Basis of Cancers 634
- 19.3 How Cell Division Is Normally Controlled 637
- 19.4 How Mutations Cause Cancer Phenotypes 644
- 19.5 Personalized Cancer Treatment 649

■ *Tools of Genetics: Analysis of Cell-Cycle Mutants in Yeast* 640

PART VII



Beyond the Individual Gene and Genome 662

chapter 20

Variation and Selection in Populations 662

- 20.1 The Hardy-Weinberg Law: Predicting Genetic Variation in "Ideal" Populations 663
- 20.2 What Causes Allele Frequencies to Change in Real Populations? 670
- 20.3 Ancestry and the Evolution of Modern Humans 680

chapter 21

Genetics of Complex Traits 694

- 21.1 Heritability: Genetic Versus Environmental Influences on Complex Traits 695
- 21.2 Mapping Quantitative Trait Loci (QTLs) 703

Guidelines for Gene Nomenclature A1

Brief Answer Section B1

Glossary G1

Credits C

Index I1