

# Brief Contents

## Part One

### Introduction 1

- |   |                      |    |
|---|----------------------|----|
| 1 | Overview of Genetics | 1  |
| 2 | Cells                | 19 |
| 3 | Development          | 47 |

## Part Two

### Transmission Genetics 75

- |   |                                               |     |
|---|-----------------------------------------------|-----|
| 4 | Mendelian Inheritance                         | 75  |
| 5 | Extensions and Exceptions<br>to Mendel's Laws | 95  |
| 6 | Matters of Sex                                | 115 |
| 7 | Multifactorial Traits                         | 137 |
| 8 | The Genetics<br>of Behavior                   | 155 |

## Part Three

### DNA and Chromosomes 171

- |    |                                  |     |
|----|----------------------------------|-----|
| 9  | DNA Structure<br>and Replication | 171 |
| 10 | Gene Action<br>and Expression    | 189 |
| 11 | Gene Mutation                    | 211 |
| 12 | Chromosomes                      | 235 |

## Part Four

### Population Genetics 263

- |    |                                          |     |
|----|------------------------------------------|-----|
| 13 | When Allele Frequencies<br>Stay Constant | 263 |
| 14 | Changing Allele<br>Frequencies           | 277 |
| 15 | Human Origins<br>and Evolution           | 299 |

## Part Five

### Immunity and Cancer 323

- |    |                        |     |
|----|------------------------|-----|
| 16 | Genetics of Immunity   | 323 |
| 17 | The Genetics of Cancer | 351 |

## Part Six

### Genetic Technology 371

- |    |                                          |     |
|----|------------------------------------------|-----|
| 18 | Genetically Modified<br>Organisms        | 371 |
| 19 | Gene Therapy and<br>Genetic Counseling   | 389 |
| 20 | Agricultural<br>Biotechnology            | 407 |
| 21 | Reproductive<br>Technologies             | 425 |
| 22 | The Human Genome<br>Project and Genomics | 441 |

# List of Boxes

## Readings

|                                                                              |     |
|------------------------------------------------------------------------------|-----|
| 2.1 Inherited Illness at the Molecular Level                                 | 23  |
| 2.2 Inherited Diseases Caused by Faulty Ion Channels                         | 29  |
| 2.3 A Heart in the Wrong Place                                               | 30  |
| 3.1 The Strange Case of F.D.: A Human Partial Parthenogenote                 | 57  |
| 4.1 It's All in the Genes                                                    | 82  |
| 6.1 Of Preserved Eyeballs and Duplicated Genes—Color Blindness               | 122 |
| 7.1 Disentangling Genetic from Environmental Effects                         | 143 |
| 9.1 DNA Makes History                                                        | 181 |
| 11.1 Fragile X Syndrome—The First of the Triplet Repeat Disorders            | 224 |
| 12.1 HACs—Human Artificial Chromosomes                                       | 241 |
| 13.1 DNA Fingerprinting Relies on Molecular Genetics and Population Genetics | 270 |
| 14.1 Antibiotic Resistance—Stemming a Biological Arms Race                   | 286 |
| 14.2 Dogs and Cats: Products of Artificial Selection                         | 292 |
| 15.1 Tracing the Evolution of a Gene in Primates                             | 308 |
| 17.1 Retinoblastoma—The Two-Hit Hypothesis                                   | 359 |
| 17.2 Vegetables and Cancer Risk                                              | 366 |
| 22.1 The Search for the Huntington Disease Gene                              | 444 |

## In Their Own Words

|                                                                |     |
|----------------------------------------------------------------|-----|
| Living with Hemophilia                                         | 13  |
| Alkaptonuria                                                   | 101 |
| In Search of Heat-Loving Microorganisms                        | 185 |
| A Personal Look at Klinefelter Syndrome                        | 252 |
| Ashley's Message of Hope                                       | 253 |
| Innate Antibodies: An Ancient Protection Against Sperm or HIV? | 343 |
| Gene Therapy for Canavan Disease                               | 395 |

## Bioethics: Choices for the Future

|                                                                |     |
|----------------------------------------------------------------|-----|
| National Genetic Databases—Is GATTACA Coming?                  | 15  |
| Considering Cloning and Stem Cell Technology                   | 70  |
| Sex Reassignment: Making a Biological "He" into a Social "She" | 132 |
| Blaming Genes                                                  | 167 |
| Beryllium Screening                                            | 230 |
| Two Views of Neural Tube Defects                               | 318 |
| Pig Parts                                                      | 347 |
| The Ethics of Using a Recombinant Drug: EPO                    | 384 |
| Canavan Disease: Patients Versus Patents                       | 404 |
| The Butterfly That Roared                                      | 421 |
| Technology Too Soon? The Case of ICSI                          | 436 |

- The Male 48
- The Female 48
- 3.2 Meiosis 49
- 3.3 Gamete Maturation 53
  - Sperm Development 53
  - Oocyte Development 55
- 3.4 Prenatal Development 56
  - Fertilization 56
  - Early Events—Cleavage and Implantation 57
  - The Embryo Forms 59
  - Supportive Structures 59
  - On the Matter of Multiples 59
  - The Embryo Develops 62
  - The Fetus 63
- 3.5 Birth Defects 64
  - The Critical Period 64
  - Teratogens 65
- 3.6 Maturation and Aging 67
  - Adult-Onset Inherited Disorders 67
  - Accelerated Aging Disorders 69
  - Is Longevity Inherited? 69

## Part Two

### Transmission Genetics 75

## Chapter 4

### Mendelian Inheritance 75

- 4.1 Following the Inheritance of One Gene—Segregation 75
  - Mendel the Man 76
  - Mendel's Experiments 76
  - Terms and Tools to Follow Segregating Genes 79

- 4.2 Single Gene Inheritance in Humans 80
  - Modes of Inheritance 80
  - On the Meaning of Dominance and Recessiveness 84
- 4.3 Following the Inheritance of Two Genes—Independent Assortment 85
- 4.4 Pedigree Analysis 87
  - Pedigrees Then and Now 87
  - Pedigrees Display Mendel's Laws 89

## Chapter 5

### Extensions and Exceptions to Mendel's Laws 95

- 5.1 When Gene Expression Appears to Alter Mendelian Ratios 96
  - Lethal Allele Combinations 96
  - Multiple Alleles 96
  - Different Dominance Relationships 97
  - Epistasis—When One Gene Affects Expression of Another 98
  - Penetrance and Expressivity 99
  - Pleiotropy—One Gene, Many Effects 100
  - Phenocopies—When It's Not in the Genes 102
  - Genetic Heterogeneity—More than One Way to Inherit a Trait 102
- 5.2 Maternal Inheritance and Mitochondrial Genes 103

- Mitochondrial Disorders 104
- Heteroplasmy Complicates Mitochondrial Inheritance 105
- Mitochondrial DNA Studies Clarify the Past 105

- 5.3 Linkage 106
  - Linkage Was Discovered in Pea Plants 106
  - Linkage Maps 107
  - Examples of Linked Genes in Humans 108
  - The Evolution of Gene Mapping 109

## Chapter 6

### Matters of Sex 115

- 6.1 Sexual Development 116
  - Sex Chromosomes 116
  - The Phenotype Forms 117
  - Gender Identity—Is Homosexuality Inherited? 119
- 6.2 Traits Inherited on Sex Chromosomes 120
  - X-Linked Recessive Inheritance 120
  - X-Linked Dominant Inheritance 125
- 6.3 X Inactivation Equalizes the Sexes 126
- 6.4 Gender Effects on Phenotype 128
  - Sex-limited Traits 129
  - Sex-influenced Traits 129
  - Genomic Imprinting 129

## Chapter 7

### Multifactorial Traits 137

- 7.1 Genes and the Environment  
Mold Most Traits 138  
Polygenic Traits Are  
Continuously  
Varying 139  
Fingerprint Patterns, Height,  
and Eye Color 139  
A Closer Look at Skin  
Color 140
- 7.2 Methods Used  
to Investigate Multifactorial  
Traits 142  
Empiric Risk 142  
Heritability—The Genetic  
Contribution to a  
Multifactorial Trait 144  
Adopted Individuals 145  
Twins 145  
Association Studies 147
- 7.3 Some Multifactorial  
Traits 149  
Heart Health 149  
Body Weight 151

## Chapter 8

### The Genetics of Behavior 155

- 8.1 Genes Contribute to Most  
Behavioral Traits 156
- 8.2 Eating Disorders 158
- 8.3 Sleep 159
- 8.4 Intelligence 160
- 8.5 Drug Addiction 161
- 8.6 Mood Disorders 163
- 8.7 Schizophrenia 164

## Part Three

### DNA and Chromosomes 171

## Chapter 9

### DNA Structure and Replication 171

- 9.1 Experiments Identify  
and Describe the  
Genetic Material 172  
DNA Is the Hereditary  
Molecule 172  
DNA Is the Hereditary  
Molecule—and Protein  
Is Not 172  
Deciphering the Structure  
of DNA 174
- 9.2 DNA Structure 176
- 9.3 DNA Replication—  
Maintaining Genetic  
Information 178  
Replication Is  
Semiconservative 178  
Steps and Participants  
in DNA Replication 180
- 9.4 PCR—Directing DNA  
Replication 183

## Chapter 10

### Gene Action and Expression 189

- 10.1 Transcription—The Link  
Between Gene  
and Protein 190  
RNA Structure  
and Types 190  
Transcription Factors 192  
Steps of Transcription 193  
RNA Processing 194

### 10.2 Translating a Protein 196

- Deciphering the Genetic  
Code 196
- Building a Protein 199
- Protein Folding 201

### 10.3 The Human Genome Sequence Reveals Unexpected Complexity 203

- Genome Economy:  
Reconciling Gene  
and Protein  
Number 204
- What Does the Other 98.5  
Percent of the Human  
Genome Do? 206

## Chapter 11

### Gene Mutation 211

- 11.1 Mutations Can Alter  
Proteins—Three  
Examples 212  
The Beta Globin Gene 212  
Disorders of Orderly  
Collagen 214  
A Mutation That Causes  
Early-Onset Alzheimer  
Disease 215
- 11.2 Causes of Mutation 216  
Spontaneous  
Mutation 216  
Induced Mutations 218  
Natural Exposure  
to Mutagens 219
- 11.3 Types of Mutations 220  
Point Mutations 220  
Deletions and Insertions Can  
Cause Frameshifts 221  
Pseudogenes and  
Transposons Revisited 222

Expanding Repeats Lead to Protein Misfolding 222

11.4 The Importance of a Mutation's Position in the Gene 225

Globin Variants 225  
Inherited Susceptibility to Prion Disorders 226

11.5 Factors That Lessen the Effects of Mutation 227

11.6 DNA Repair 227

Types of DNA Repair 227  
DNA Repair Disorders 228

## Chapter 12

### Chromosomes 235

12.1 Portrait of a Chromosome 236

Telomeres and Centromeres Are Essential 237  
Karyotypes Are Chromosome Charts 238

12.2 Visualizing Chromosomes 240

Obtaining Cells for Chromosome Study 240  
Preparing Cells for Chromosome Observation 243

12.3 Abnormal Chromosome Number 246

Polyploidy 246  
Aneuploidy 246

12.4 Abnormal Chromosome Structure 252

Deletions and

Duplications 252

Translocations 253

Inversions 256

Isochromosomes and Ring Chromosomes 258

12.5 Uniparental Disomy—Two Genetic Contributions from One Parent 259

## Part Four

### Population Genetics 263

## Chapter 13

### When Allele Frequencies Stay Constant 263

13.1 The Importance of Knowing Allele Frequencies 264

13.2 When Allele Frequencies Stay Constant—Hardy-Weinberg Equilibrium 264

13.3 Practical Applications of Hardy-Weinberg Equilibrium 267

13.4 DNA Fingerprinting—A Practical Test of Hardy-Weinberg Assumptions 268  
DNA Patterns Distinguish Individuals 269  
Population Statistics Are Used to Interpret DNA Fingerprints 269  
DNA Fingerprinting to Identify World Trade Center Victims 272

## Chapter 14

### Changing Allele Frequencies 277

14.1 Nonrandom Mating 278

14.2 Migration 279

Historical Clues 279  
Geographical and Linguistic Clues 279

14.3 Genetic Drift 280

The Founder Effect 280  
Population Bottlenecks 282

14.4 Mutation 284

14.5 Natural Selection 284

Tuberculosis Ups and Downs—and Ups 284  
Evolving HIV 285  
Balanced Polymorphism 286

14.6 Gene Genealogy 292

PKU Revisited 292  
CF Revisited 293

## Chapter 15

### Human Origins and Evolution 299

15.1 Human Origins 300

The Australopithecines—And Others? 301  
*Homo* 303  
Modern Humans 304

15.2 Molecular Evolution 305

Comparing Genomes 305  
Comparing Chromosomes 306  
Comparing Protein Sequences 307  
Comparing DNA Sequences 310

- 15.3 Molecular Clocks 313
  - Neanderthals Revisited 313
  - Choosing Clues 313
- 15.4 Eugenics 316

## Part Five

### Immunity and Cancer 323

## Chapter 16

### Genetics of Immunity 323

- 16.1 The Importance of Cell Surfaces 324
  - Blood Groups 324
  - The Human Leukocyte Antigens 326
- 16.2 The Human Immune System 327
  - Physical Barriers and the Innate Immune Response 327
  - The Adaptive (Acquired) Immune Response 329
- 16.3 Abnormal Immunity 334
  - Inherited Immune Deficiencies 334
  - Acquired Immune Deficiency Syndrome 334
  - Autoimmunity 336
  - Allergies 338
- 16.4 Altering Immune Function 339
  - Vaccines 339
  - Immunotherapy 341
  - Transplantation 342
- 16.5 A Genomic View of Immunity—The Pathogen's Perspective 344
  - Crowd Diseases 345
  - Bioweapons 345

## Chapter 17

### The Genetics of Cancer 351

- 17.1 Cancer as a Genetic Disorder 352
  - Cancer in Families 352
  - Loss of Cell Cycle Control 353
  - Inherited Versus Sporadic Cancer 354
- 17.2 Characteristics of Cancer Cells 354
- 17.3 Genes That Cause Cancer 356
  - Oncogenes 356
  - Tumor Suppressors 358
- 17.4 A Series of Genetic Changes Causes Some Cancers 363
  - A Rapidly Growing Brain Tumor 363
  - Colon Cancer 363
- 17.5 Cancer Prevention, Diagnosis, and Treatment 364
  - Diet-Cancer Associations 364
  - Diagnosing and Treating Cancer 365

## Part Six

### Genetic Technology 371

## Chapter 18

### Genetically Modified Organisms 371

- 18.1 Of Pigs and Patents 372
- 18.2 Recombinant DNA Technology 373

- Constructing Recombinant DNA Molecules 374
- Selecting Recombinant DNA Molecules 376
- Isolating the Gene of Interest 376
- Applications of Recombinant DNA Technology 377

- 18.3 Transgenic Organisms 378
  - Delivering DNA 378
  - Transgenic Pharming from Milk and Semen 379
- 18.4 Gene Targeting 382
  - Gene-Targeted Mice as Models 383
  - When Knockouts Are Normal 385

## Chapter 19

### Gene Therapy and Genetic Counseling 389

- 19.1 Gene Therapy Successes and Setbacks 390
  - Adenosine Deaminase Deficiency—Early Success 390
  - Ornithine Transcarbamylase Deficiency—A Setback 392
  - A Success in the Making—Canavan Disease 393
- 19.2 The Mechanics of Gene Therapy 394
  - Treating the Phenotype 394
  - Germline Versus Somatic Gene Therapy 395
  - Sites of Somatic Gene Therapy 395
  - Gene Delivery 398

- 19.3 A Closer Look: Treating Sickle Cell Disease 399
- 19.4 Genetic Screening and Genetic Counseling 401
- Genetic Counselors Provide Diverse Services 401
- Scene from a Sickle Cell Disease Clinic 403
- Genetic Counseling Quandaries and Challenges 403
- Perspective: A Slow Start, But Great Promise 403

## Chapter 20

### Agricultural Biotechnology 407

- 20.1 Traditional Breeding Compared to Biotechnology 409
- Similar Steps, Different Degree of Precision 409
- Government Regulation of Crops 411
- Biotechnology Provides Different Routes to Solving a Problem 411
- 20.2 Types of Plant Manipulations 412
- Altering Plants at the Gene Level 412
- Altering Plants at the Cellular Level 415
- 20.3 Release of Genetically Modified Organisms into the Environment 417

- Microcosm Experiments 417
- Field Tests 417
- Bioremediation 418

- 20.4 Economic, Ecological, and Evolutionary Concerns 418

- 20.5 The Impact of Genomics 420

## Chapter 21

### Reproductive Technologies 425

- 21.1 New Ways to Make Babies 426
- Grandmother and Mother at the Same Time 426
- Midlife Motherhood 426
- A Five-Year Wait 426
- 21.2 Infertility and Subfertility 427
- Male Infertility 427
- Female Infertility 428
- Infertility Tests 430
- 21.3 Assisted Reproductive Technologies 430
- Donated Sperm—Artificial Insemination 430
- A Donated Uterus—Surrogate Motherhood 431
- In Vitro* Fertilization 432
- Gamete Intrafallopian Transfer 432
- Oocyte Banking and Donation 433
- Preimplantation Genetic Screening and Diagnosis 433

- 21.4 On the Subject of "Spares" 435

## Chapter 22

### The Human Genome Project and Genomics 441

- 22.1 Genome Sequencing: A Continuation of Genetics 442
- 22.2 The Origin of the Idea 446
- The Sanger Method of DNA Sequencing 446
- The Project Starts 448
- 22.3 Technology Drives the Sequencing Effort 448
- 22.4 Genome Information Answers and Raises Questions 450
- The Definition of a Gene 450
- Nonhuman Genome Projects 450
- Epilogue: Genome Information Will Affect You 452

- Answers to End-of-Chapter Questions A-1
- Glossary G-1
- Credits C-1
- Index I-1