# 1  A Perspective on Human Genetics  

## 1.1 Genetics Is the Key to Biology  

## 1.2 What Are Genes and How Do They Work?  

Exploring Genetics: Genetic Disorders in Culture and Art  

## 1.3 How Are Genes Transmitted from Parents to Offspring?  

## 1.4 How Do Scientists Study Genes?  

Some basic methods in genetics  
Genetics is used in basic and applied research  

## 1.5 Has Genetics Affected Social Policy and Law?  

The misuse of genetics has affected social policy  
Eugenics was used to pass restrictive immigration laws in the United States  
Eugenics was used to restrict reproductive rights  

Exploring Genetics: Genetics, Eugenics, and Nazi Germany  
The decline of eugenics in the United States began with the rise of the Nazi movement  

Spotlight on . . . Eugenic Sterilization  

## 1.6 What Impact Is Genomics Having?  

Identifying and using genetic variation in genomics  
Health care uses genetic testing and genome scanning  
Stem-cell research offers hope for treating many diseases  
Biotechnology is impacting everyday life  

## 1.7 What Choices Do We Make in the Era of Genomics and Biotechnology?  

# 2  Cells and Cell Division  

## 2.1 The Chemistry of Cells  

Spotlight on . . . A Fatal Membrane Flaw  

## 2.2 Cell Structure Reflects Function  

There are two cellular domains: the plasma membrane and the cytoplasm  
Organelles are specialized structures in the cytoplasm  
The endoplasmic reticulum folds, sorts, and ships proteins  
Molecular sorting takes place in the Golgi complex  
Lysosomes are cytoplasmic disposal sites  
Mitochondria are sites of energy conversion  
The nucleus contains chromosomes  

## 2.3 The Cell Cycle Describes the Life History of a Cell  

Interphase has three stages  
Cell division by mitosis occurs in four stages
2.4 Mitosis Is Essential for Growth and Cell Replacement 32
2.5 Cell Division by Meiosis: The Basis of Sex 33
Meiosis I reduces the chromosome number 33
Meiosis II begins with haploid cells 33
Meiosis produces new combinations of genes in two ways 35
2.6 Formation of Gametes 38

3 Transmission of Genes from Generation to Generation 44
3.1 Heredity: How Are Traits Inherited? 45
Spotlight on ... Mendel and Test Anxiety 46
3.2 Mendel’s Experimental Design Resolved Many Unanswered Questions 46
3.3 Crossing Pea Plants: Mendel’s Study of Single Traits 47
What were the results and conclusions from Mendel’s first series of crosses? 48
The principle of segregation describes how a single trait is inherited 49
Exploring Genetics: Ockham’s Razor 50
3.4 More Crosses with Pea Plants: The Principle of Independent Assortment 51
Mendel performed crosses involving two traits 51
Analyzing the results and drawing conclusions 51
The principle of independent assortment explains the inheritance of two traits 52
3.5 Meiosis Explains Mendel’s Results: Genes Are on Chromosomes 55
Exploring Genetics: Evaluating Results: The Chi-Square Test 56
3.6 Mendelian Inheritance in Humans 57
Segregation and independent assortment occur with human traits 57
Pedigree construction is an important tool in human genetics 59
3.7 Variations on a Theme by Mendel 61
Incomplete dominance has a distinctive phenotype in heterozygotes 61
Codominant alleles are fully expressed in heterozygotes 62
Many genes have more than two alleles 63
Genes can interact to produce phenotypes 63

4 Pedigree Analysis in Human Genetics 70
4.1 Pedigree Analysis Is a Basic Method in Human Genetics 71
There are five basic patterns of Mendelian inheritance 72
Analyzing a pedigree 72
4.2 Autosomal Recessive Traits 73
Cystic fibrosis is an autosomal recessive trait 74
Exploring Genetics: Was Noah an Albino? 76
4.3 Autosomal Dominant Traits 77
Marfan syndrome is inherited as an autosomal dominant trait 77
4.4 Sex-Linked Inheritance Involves Genes on the X and Y Chromosomes 78
X-Linked dominant traits 79
X-Linked recessive traits 80
5 The Inheritance of Complex Traits 94

5.1 Some Traits Are Controlled by Two or More Genes 95
Phenotypes can be discontinuous or continuous 95
What are complex traits? 95

5.2 Polygenic Traits and Variation in Phenotype 97
Defining the genetics behind continuous phenotypic variation 97
How many genes control a polygenic trait? 98

5.3 The Additive Model for Polygenic Inheritance 99
Averaging out the phenotype is called regression to the mean 100

5.4 Multifactorial Traits: Polygenic Inheritance and Environmental Effects 100
The Genetic Revolution: Dissecting Genes and Environment in Spina Bifida 101
Several methods are used to study multifactorial traits 101

5.5 Heritability Measures the Genetic Contribution to Phenotypic Variation 103
Heritability estimates are based on known levels of genetic relatedness 103

5.6 Twin Studies and Multifactorial Traits 104
The biology of twins includes monozygotic and dizygotic twins 104
Concordance rates in twins 105
Exploring Genetics: Twins, Quintuplets, and Armadillos 106
We can study multifactorial traits such as obesity using twins and family studies 106
Spotlight on . . . Leptin and Female Athletes 108
What are some genetic clues to obesity? 108
Animal models of obesity 108
Scanning the genome for obesity-related genes 108

5.7 Genetics of Height: A Closer Look 109
Haplotypes and genome-wide association studies 110
Genes for human height: what have we learned so far? 110

5.8 Skin Color and IQ Are Complex Traits 111
Skin color is a multifactorial trait 111
Intelligence and intelligence quotient (IQ): are they related? 111
IQ values are heritable traits 112
What is the controversy about IQ and race? 112
Spotlight on . . . Building a Smarter Mouse 113
Scientists are searching for genes that control intelligence 114
Cytogenetics: Karyotypes and Chromosome Aberrations 120

6.1 The Human Chromosome Set 121

6.2 Making a Karyotype 124

6.3 Constructing and Analyzing Karyotypes 125
   What cells are obtained for chromosome studies? 126
   Amniocentesis collects cells from the fluid surrounding the fetus 127
   Chorionic villus sampling retrieves fetal tissue from the placenta 128

6.4 Variations in Chromosome Number 129
   Chromosome abnormalities in humans are common 130
   Polyploidy changes the number of chromosomal sets 130
   Triploidy 131
   Tetraploidy 131
   Aneuploidy changes the number of individual chromosomes 131
   Autosomal monosomy is a lethal condition 132
   Autosomal trisomy is relatively common 132
   Trisomy 13: Patau syndrome (47,+13) 132
   Trisomy 18: Edwards syndrome (47,+18) 133
   Trisomy 21: Down syndrome (47,+21) 134

6.5 What Are the Risks for Autosomal Trisomy? 134
   Maternal age is the leading risk factor for trisomy 135
   Why is maternal age a risk factor? 135

6.6 Aneuploidy of the Sex Chromosomes 136
   Turner syndrome (45,X) 136
   Klinefelter syndrome (47,XXY) 137
   XYY syndrome (47,XYY) 137
   What can we conclude about sex-chromosome aneuploidy? 138

6.7 Structural Changes Within Chromosomes 138
   Deletions involve loss of chromosomal material 139
   Translocations involve exchange of chromosomal parts 139

6.8 What Are Some Consequences of Aneuploidy? 140

6.9 Other Forms of Chromosome Changes 141
   Uniparental disomy 141
   Copy number variation 142
   Fragile sites appear as gaps or breaks in chromosomes 143

7 Development and Sex Determination 148

7.1 The Human Reproductive System 149
   The male reproductive system 149
   The female reproductive system 152
   Spotlight on . . . The Largest Cell 154
   Are there differences in the timing of meiosis and gamete formation in males and females? 154

7.2 A Survey of Human Development from Fertilization to Birth 155
   Development is divided into three trimesters 157
   Organ formation occurs in the first trimester 157
The second trimester is a period of organ maturation 157
Rapid growth takes place in the third trimester 158
Birth is hormonally induced 159

7.3 Teratogens Are a Risk to the Developing Fetus 160
Radiation, viruses, and chemicals can be teratogens 160
Fetal alcohol syndrome is a preventable tragedy 161

7.4 How Is Sex Determined? 161
Environmental interactions can help determine sex 162
Chromosomes can help determine sex 162
The human sex ratio changes with stages of life 162

7.5 Defining Sex in Stages: Chromosomes, Gonads, and Hormones 163
Exploring Genetics: Sex Testing in the Olympics—Biology and a Bad Idea 164
Sex differentiation begins in the embryo 165
Hormones help shape male and female phenotypes 165

7.6 Mutations Can Uncouple Chromosomal Sex from Phenotypic Sex 167
Androgen insensitivity can affect the sex phenotype 167
Exploring Genetics: Joan of Arc—Was It Really John of Arc? 168
Mutations can cause sex phenotypes to change at puberty 168

7.7 Equalizing the Expression of X Chromosome Genes in Males and Females 169
Dosage compensation makes XX equal XY 169
Mice, Barr bodies, and X inactivation can help explain dosage compensation 169
Mammalian females can be mosaics for X chromosome gene expression 170
How and when are X chromosomes inactivated? 170

7.8 Sex-Related Phenotypic Effects 171
Sex-influenced traits 172
Sex-limited traits 172
Imprinted genes 172

8 The Structure, Replication, and Chromosomal Organization of DNA 176

8.1 DNA Is the Carrier of Genetic Information 177
DNA can transfer genetic traits between bacterial strains 178
DNA carries genetic information in viruses 179
Exploring Genetics: DNA for Sale 180

8.2 The Chemistry of DNA 181
Understanding the structure of DNA requires a review of some basic chemistry 181
Nucleotides are the building blocks of nucleic acids 181

8.3 The Watson-Crick Model of DNA Structure 183
The Genetic Revolution: What Happens When Your Genes Are Patented? 186

8.4 RNA Is a Single-Stranded Nucleic Acid 186

8.5 DNA Replication Depends on Complementary Base Pairing 187
Stages of DNA replication 188

8.6 The Organization of DNA in Chromosomes 189
Chromosomes have a complex structure 189
Centromeres and telomeres are specialized chromosomal regions 191
The nucleus has a highly organized architecture 191
9 Gene Expression and Gene Regulation 196

9.1 The Link Between Genes and Proteins 197
How are genes and enzymes related? 197
Genetic information is stored in DNA 197
The relationship between genes and proteins 198

9.2 The Genetic Code: The Key to Life 198

9.3 Tracing the Flow of Genetic Information from Nucleus to Cytoplasm 200
Spotlight on . . . Mutations in Splicing Sites and Genetic Disorders 201

9.4 Transcription Produces Genetic Messages 201
Messenger RNA is processed and spliced 202

9.5 Translation Requires the Interaction of Several Components 203
Amino acids are subunits of proteins 203
Messenger RNA, ribosomal RNA, and transfer RNA interact during translation 203
Translation produces polypeptides from information in mRNA 204
Exploring Genetics: Antibiotics and Protein Synthesis 205

9.6 Polypeptides Are Processed and Folded to Form Proteins 205
How many proteins can human cells make? 205
Proteins are sorted and distributed to their cellular locations 207

9.7 Protein Structure and Function Are Related 208
Improper protein folding can be a factor in disease 209

9.8 Several Mechanisms Regulate the Expression of Genes 210
Chromatin remodeling and access to promoters 210
DNA methylation can silence genes 211
RNA interference is one mechanism of post-transcriptional regulation 212
Translational and post-translational mechanisms regulate the production of proteins 213

10 From Proteins to Phenotypes 218

10.1 Proteins Are the Link Between Genes and the Phenotype 219

10.2 Enzymes and Metabolic Pathways 220

10.3 Phenylketonuria: A Mutation That Affects an Enzyme 221
How is the metabolism of phenylalanine related to PKU? 221
Spotlight on . . . Why Wrinkled Peas Are Wrinkled 222
How does the buildup of phenylalanine produce mental retardation? 222
How effective is testing for PKU in newborns? 223
PKU can be treated with a diet low in phenylalanine 223
How long must a PKU diet be maintained? 224
What happens when women with PKU have children? 224

10.4 Other Metabolic Disorders in the Phenylalanine Pathway 224
Exploring Genetics: Dietary Management and Metabolic Disorders 225

10.5 Genes and Enzymes of Carbohydrate Metabolism 225
Galactosemia is caused by an enzyme deficiency 226
Lactose intolerance is a genetic variation 227

10.6 Defects in Transport Proteins: Hemoglobin 228
Hemoglobin disorders 230
Spotlight on . . . Population Genetics of Sickle Cell Genes 230
Sickle cell anemia is an autosomal recessive disorder 230
Treatment for sickle cell anemia includes drugs for gene switching 230
12.6 Colon Cancer Is a Genetic Model for Cancer 277
FAP causes chromosome instability and colon cancer 278
HNPCC is caused by DNA repair defects 279

12.7 Hybrid Genes, Epigenetics, and Cancer 280
Some chromosome rearrangements cause leukemia 281

12.8 Genomics and Cancer 282
Sequencing cancer genomes identifies cancer-associated genes 282
Epigenetics and cancer 283
Targeted therapy offers a new approach to treating cancer 284
The Genetic Revolution: Cancer Stem Cells 285
Exploring Genetics: The Cancer Genome Atlas (TCGA) 286

12.9 Cancer and the Environment 286
Some viral infections lead to cancer 287
What other environmental factors are related to cancer? 287

13 An Introduction to Genetic Technology 292

13.1 What Are Clones? 293
Animals can be cloned by several methods 293

13.2 Cloning Genes Is a Multistep Process 295
DNA can be cut at specific sites using restriction enzymes 296
Vectors serve as carriers of DNA to be cloned 297
Recombinant DNA molecules are inserted into host cells for cloning 297

13.3 Cloned Libraries 298

13.4 Finding a Specific Clone in a Library 298
Exploring Genetics: Asilomar: Scientists Get Involved 299
Spotlight on . . . Can We Clone Endangered Species? 300

13.5 A Revolution in Cloning: The Polymerase Chain Reaction 301

13.6 Analyzing Cloned Sequences 302
The Southern blot technique can be used to analyze cloned sequences 302
DNA sequencing is one form of genome analysis 303
Exploring Genetics: DNA Sequencing 306

13.7 DNA Microarrays Are Used to Analyze Gene Expression 306

14 Biotechnology and Society 312

14.1 Biopharming: Making Human Proteins in Animals 314
Human proteins can be made in animals 315
Transgenic plants may replace animal hosts for making human proteins 315

14.2 Using Stem Cells to Treat Disease 316
Stem cells provide insight into basic biological processes 317
Stem-cell-based therapies may treat many diseases 317

14.3 Genetically Modified Foods 318
Transgenic crop plants can be made resistant to herbicides and disease 318
Spotlight on . . . Bioremediation: Using Bugs to Clean Up Waste Sites 319
Enhancing the nutritional value of foods 320
Functional foods and health 321
What are some concerns about genetically modified organisms? 321
14.4 Transgenic Animals as Models of Human Diseases 322
Scientists use animal models to study human diseases 322

14.5 DNA Profiles as Tools for Identification 323
Making DNA profiles 323
DNA profiles are used in forensics 323
Exploring Genetics: Death of a Czar 325
DNA profiles have many other uses 326

14.6 Social and Ethical Questions About Biotechnology 326

15 Genomes and Genomics 332

15.1 Genome Sequencing Is an Extension of Genetic Mapping 333
Recombination frequencies are used to make genetic maps 334
Linkage and recombination can be measured by lod scores 335
Recombinant DNA technology radically changed gene-mapping efforts 336

15.2 Genome Projects Are an Outgrowth of Recombinant DNA Technology 337

15.3 Genome Projects Have Created New Scientific Fields 339

15.4 Genomics: Sequencing, Identifying, and Mapping Genes 340
Scientists can analyze genomic information with bioinformatics 341
Annotation is used to find where the genes are 341
Spotlight on . . . Our Genetic Relative 342
As genes are discovered, the function of their encoded proteins are studied 342

15.5 What Have We Learned So Far About the Human Genome? 342
New disease-related types of mutations have been discovered 343
Nucleotide variation in genomes is common 344

15.6 Using Genomics to Study a Human Genetic Disorder 345

15.7 Proteomics Is an Extension of Genomics 346

15.8 Ethical Concerns About Human Genomics 347
Exploring Genetics: Who Owns Your Genome? 348

16 Reproductive Technology, Genetic Testing, and Gene Therapy 354

16.1 Infertility Is a Common Problem 355
Infertility is a complex problem 355
Infertility in women has many causes 356
Infertility in men involves sperm defects 356
Spotlight on . . . Fatherless Mice 357
Other causes of infertility 357

16.2 Assisted Reproductive Technologies (ART) Expand Childbearing Options 357
Intrauterine insemination uses donor sperm 357
Egg retrieval or donation is an option 358
In vitro fertilization (IVF) is a widely used form of ART 359
GIFT and ZIFT are based on IVF 359
Surrogacy is a controversial form of ART 360
16.3 Ethical Issues in Reproductive Technology 361
Spotlight on . . . Reproductive Technologies from the Past 361
The use of ART carries risks to parents and children 361

16.4 Genetic Testing and Screening 362
Exploring Genetics: The Business of Making Babies 363
Newborn screening is universal in the United States 363
Both carrier and prenatal testing are done to screen for genetic disorders 363
The use of PGD raises ethical issues 364
Prenatal testing is associated with risks 366

16.5 Gene Therapy Promises to Correct Many Disorders 366
What are the strategies for gene transfer? 366
Gene therapy showed early promise 366
The Genetic Revolution: Should I Save Cord Blood? 367
There are ethical issues associated with gene therapy 368
Gene doping is a controversial form of gene therapy 369

16.6 Genetic Counseling Assesses Reproductive Risks 369
Why do people seek genetic counseling? 370
How does genetic counseling work? 371

17 Genes and the Immune System 376

17.1 The Body Has Three Levels of Defense Against Infection 377
The skin is not part of the immune system but is a physical barrier 377
There are two parts to the immune system that protect against infection 377

17.2 The Inflammatory Response Is a General Reaction 378
Genetic disorders cause inflammatory diseases 378

17.3 The Complement System Kills Microorganisms 379

17.4 The Adaptive Immune Response Is a Specific Defense Against Infection 380
How does the immune response function? 381
The antibody-mediated immune response involves several stages 382
Antibodies are molecular weapons against antigens 384
T cells mediate the cellular immune response 385
The immune system has a memory function 386

17.5 Blood Types Are Determined by Cell-Surface Antigens 387
ABO blood typing allows for safe blood transfusions 387
Rh blood types can cause immune reactions between mother and fetus 388

17.6 Organ Transplants Must Be Immunologically Matched 388
Successful transplants depend on HLA matching 389
Copy number variation (CNV) and transplant success 390
Genetic engineering makes animal–human organ transplants possible 390

17.7 Disorders of the Immune System 391
Overreaction in the immune system causes allergies 391
Autoimmune reactions cause the immune system to attack the body 391
Exploring Genetics: Peanut Allergies Are Increasing 393
Genetic disorders can impair the immune system 393
HIV attacks the immune system 394
18 Genetics of Behavior 400

18.1 Models, Methods, and Phenotypes in Studying Behavior 401
There are several genetic models for inheritance and behavior 401
Methods of studying behavior genetics often involve twin studies 402
Phenotypes: how is behavior defined? 402
Exploring Genetics: Is Going to Medical School a Genetic Trait? 403
The nervous system is the focus of behavior genetics 403

18.2 Animal Models: The Search for Behavior Genes 404
Transgenic animals are used as models of human neurodegenerative disorders 404

18.3 Single Genes Affect the Nervous System and Behavior 405
Huntington disease is a model for neurodegenerative disorders 405
There is a genetic link between language and brain development 406

18.4 Single Genes Control Aggressive Behavior and Brain Metabolism 407
Geneticists have mapped a gene for aggression 408
There are problems with single-gene models for behavioral traits 409

18.5 The Genetics of Schizophrenia and Bipolar Disorder 409
Genetic models for schizophrenia and bipolar disorders 410
Genomic approaches to schizophrenia and bipolar disorder 411

18.6 Genetics and Social Behavior 411
Alzheimer disease is a complex disorder 411
Genomic approaches in AD 412
Alcoholism has several components 413

18.7 Summing Up: The Current Status of Human Behavior Genetics 414

19 Population Genetics and Human Evolution 418

19.1 How Can We Measure Allele Frequencies in Populations? 419
We can use the Hardy-Weinberg law to calculate allele and genotype frequencies 420
Spotlight on . . . Selective Breeding Gone Bad 420
Populations can be in genetic equilibrium 420

19.2 Using the Hardy-Weinberg Law in Human Genetics 420
The Hardy-Weinberg law can be used to calculate the frequency of alleles and genotypes 421
Heterozygotes for many genetic disorders are common in the population 421
Calculating the frequency of X-linked alleles 422

19.3 Measuring Genetic Diversity in Human Populations 423
Mutation generates new alleles but has little impact on allele frequency 423
Genetic drift can change allele frequencies 424
Natural selection acts on variation in populations 424

19.4 Natural Selection Affects the Frequency of Genetic Disorders 425
Exploring Genetics: Lactose Intolerance and Culture 426
Selection can rapidly change allele frequencies 426

19.5 Genetic Variation in Human Populations 427
Are there human races? 427
19.6 The Evolutionary History and Spread of Our Species (*Homo sapiens*) 430
Our evolutionary heritage begins with hominoids 430
Early humans emerged almost 5 million years ago 430
Our species, *Homo sapiens*, originated in Africa 431
Ancient migrations dispersed humans across the globe 431

19.7 Genomics and Human Evolution 432
The human and chimpanzee genomes are similar in many ways 432
The Genetic Revolution: Tracing Ancient Migrations 433
Neanderthals are not closely related to us 433
Chimpanzees, modern humans, and Neanderthals share a gene important in language development 434

Appendix: Answers to Selected Questions and Problems 441

Glossary 449

Index 457