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Human Genetics

Concepts and Applications

THIRTEENTH EDITION

Mc Graw Hill

Ricki Lewis

Thirteenth Edition

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Concepts and Applications

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HUMAN GENETICS

This book is printed on acid-free paper.

1 2 3 4 5 6 7 8 9 LWI 24 23 22 21 20

ISBN 978-1-260-57046-5
MHID 1-260-57046-0

Cover Image: *Portraits-Rawpixel.com/Shutterstock, Rawpixel Ltd/Getty Images, Kivilcim Pinar/iStock/Getty Images. World Map-vectorlight/Shutterstock. DNA-Olena_T/Getty Images.*

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About the Author

Courtesy of Larry Lewis

Ricki Lewis has built an eclectic career in communicating the excitement of genetics and genomics, combining skills as a geneticist and a journalist. She currently writes the popular weekly blog, DNA Science, at Public Library of Science and contributes frequent articles to Medscape Medical News and the Genetic Literacy Project. Dr. Lewis has authored or coauthored several university-level textbooks and is the author of the narrative nonfiction book, *The Forever Fix: Gene Therapy and the Boy Who Saved It*, as well as an essay collection, a novel, and a short "basics" book on human genetics. She teaches an online course on "Genethics" for the Alden March Bioethics Institute of Albany Medical College and is a genetic counselor for a private medical practice. Her passion is rare genetic diseases; she writes often about affected families who are pioneering DNA-based treatments.

Dedicated to the families who live with genetic diseases, the health care providers who help them, and the researchers who develop new tests and treatments.

Brief Contents

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Preface

The Evolution of *Human Genetics: Concepts and Applications*

This textbook began as a table of contents scribbled on a cocktail napkin at a publisher's meeting circa 1990, when genetics was on the precipice of becoming genomics. Since then, in addition to clearly explaining the basics of inheritance, the book has chronicled the beginnings of genome sequencing, the first clinical trials of gene therapy, the gradual expansion and explosion of genetic testing, and now the entrance of DNA information into our everyday lives.

In the middle editions, focus shifted to human genetics as the science of our diversity and introduced consumer DNA testing. That has now detonated as millions of people spit into tubes and swipe their cheeks to learn about their health, traits, families, and ancestry. At the same time, DNA evidence in forensic investigations has opened up new concerns about genetic privacy.

In 2019, the author learned, out-of-the-blue thanks to consumer DNA testing, of several half-siblings, and with further information, that she was donor-conceived. The impact was stunning, but ultimately positive. As a result, this edition of Human Genetics: Concepts and Applications *has been revised and updated with a new sensitivity to the power of genetic information, including a new chapter, "The Genetics of Identity." It covers genetic genealogy, privacy, and forensic DNA typing.*

What Sets This Book Apart

The vivid narrative writing style reflects Dr. Lewis's eclectic experience as a health and science writer, professor, speaker, and genetic counselor. Cases, historical asides, and descriptions of new technologies propel the clear explanations of concepts and mechanisms. In this new edition, a broader coverage of topics, yet with more practical information, prepares the reader to evaluate media reports, interpret genetic test results, and question their health care providers.

Updates to this edition include

- Using DNA to find the Golden State Killer
- The right *not* to know genetic information
- Percent of the genome that relatives share
- Genetics and transgender identity
- An astronaut's altered gene expression
- Tracking RNA to pinpoint time of death
- Inbreeding in Charles Darwin's family
- DNA typing reunites families
- Engineering a plant-based burger
- CRISPR, RNAi, antisense applications

Pie charts ease understanding of big data:

- Parts of a human genome (figure 11.14)
- Gene variant classification (figure 12B)
- Five sources of evolutionary change (figure 16.2)
- Ethnicity estimates (figure 18.12a)

A minor reorganization moves Genomes (in past editions under Technology, near the book's end) to follow Chromosomes (chapter 13), now that it is no longer futuristic. The new chapter 18, The Genetics of Identity, fits perfectly in the population genetics unit. Figures that did not add to content or concepts have been dropped, as have been Technology Timelines and some Glimpse of History boxes. These changes emphasize the Bioethics boxes, as the science of genetics becomes more a part of everyday life. Some boxes in past editions are now part of the text.

The Lewis Guided Learning System

Each chapter begins with two views of the content. *Learning Outcomes* embedded in the table of contents guide the student in setting goals and mastering material, while *The Big Picture* encapsulates the chapter's theme. The chapter opener essay and figure grab attention, pulling the reader into a true narrative.

Content flows logically through three to five major sections per chapter. Each section concludes with *Key Concepts Questions*. Answers to the questions marked with an asterisk are provided to the instructor in the Instructor Resources in Connect®. Instructors can choose to share these with the students.

Clinical Connections and *Bioethics* boxed readings pepper the chapters, each including challenging *Questions for Discussion*. *A Glimpse of History* boxes provide context and perspective.

Each chapter ends with a *Study Guide*. It includes a *Summary*, defined *Key Terms*, and straight recall *Review Questions*. Then follow *Applied Questions* that begin with one question that relates to the Chapter Opener, *Forensic Focus* questions, and *Case Studies and Research Results*. These types of inquiry challenge critical thinking and data evaluation skills.

Dynamic Art

Outstanding photographs and dimensional illustrations, vibrantly colored, are featured throughout *Human Genetics: Concepts and Applications*. Figure types include process figures with numbered steps, micro to macro representations, and the combination of art and photos to relate stylized drawings to real-life biological structures.

New to This Edition

The new edition embraces the broadening of human genetics from an academic and medical discipline to an informational science that can be highly personal, yet have societal impact. Changes to enhance learning include better contrast in figures, particularly for chromosomes; additional subheads; new figures, tables, and end-of-chapter questions; and key terms with definitions at the ends of chapters. Answers to even-numbered Key Concepts questions are available to instructors in the Instructor Resources in Connect®. Some *Glimpses of History* and all *Technology Timelines* have been cut.

Chapter 1 The Information in A Human Genome
- Types of discoveries from consumer DNA testing

Chapter 2 Cells
- Stem cell tourism

Chapter 4 Single-Gene Inheritance
- Monogenic versus complex traits
- The right *not* to know genetic information

Chapter 5 Beyond Mendel's Laws
- The complex inheritance of red hair

Chapter 6 Matters of Sex
- Transgender identity
- Brain cancer as a sex-influenced trait

Chapter 7 Complex Traits
- De-emphasis on European ancestry in examples
- Missing heritability indicating environmental component
- Polygenic risk scores

Chapter 9 DNA Structure and Replication
- Many small changes to improve clarity

Chapter 10 Gene Action: From DNA to Protein
- Altered gene expression in an astronaut
- A missing enzyme that knocks out nine others

Chapter 11 Gene Expression and Epigenetics
- Tracking RNA to pinpoint time of death
- Gene expression in the placenta

Chapter 13 Chromosomes
- Shifted focus to newer techniques

Chapter 14 Genomes (previously chapter 22)
- How a genomic view expands knowledge
- Sequencing the genomes of newborns

Chapter 15 Constant Allele Frequencies (formerly chapter 14)
- Tailoring genetic tests to population groups

Chapter 16 Changing Allele Frequencies (formerly chapter 15)
- Inbreeding in Charles Darwin's family
- One pie chart replaces several shape figures

Chapter 17 Human Ancestry and Evolution (formerly chapter 16)
- Interpreting Neanderthal DNA in consumer tests
- Migration through "vegetated corridors"

Chapter 18 Genetics of Identity
- New chapter, which blends tests and technologies used in ancestry and forensic testing
- DNA typing to reunite families
- Forensic DNA phenotyping to identify remains
- Limitations of forensic DNA evidence
- Capturing the Golden State Killer

Chapter 20 Cancer Genetics and Genomics (formerly chapter 18)
- Targeted treatments

Chapter 21 DNA Technologies (formerly chapter 19)
- Engineering a better veggie burger
- CRISPR patent battle
- Antisense and RNAi in agriculture and health care
- Editing the human germline

Chapter 22 Genetic Testing and Treatment (formerly chapter 20)
- Gene therapy vs. gene editing
- Pharmacogenetics and depression

Chapter 23 Reproductive Technologies (formerly chapter 21)
- Effect of pollution on female fertility
- Changes in sperm donation

New Figures

1.1 Consumer genetics
1.2 The cost of sequencing a human genome has plunged
1.7 A normal female karyotype
1.9 Percent of the genome shared with relatives
3.14 Oogenesis and spermatogenesis compared
3.24 The nuclear membrane of a dying cell in progeria
10A Multiple sulfatase deficiency
12.1 Somatic mutation puts patches on a golden retriever
12.10 A point mutation can alter a splice site
12.11 A pseudogene causes mutation
12B Gene variant classification
13A Trisomy vs. translocation in Down syndrome

15.1 Different populations have different frequencies of single-gene diseases
15.2 Microevolution and macroevolution in speech
15.7 Risk of inheriting CF
16.1 Inbreeding in the family of Charles Darwin
16.2 The five sources of evolutionary change at the population level
16.3 Types of genetic drift
16A Bili lights for Crigler-Najjar syndrome
16.4 A telltale mutation for PKU
17.17 Combinations of characteristics reflect ancestors from different populations
18.2-5 Applications of comparing 20 CODIS loci
18.8 Grandmothers of the Plaza de Mayo
18.9 Forensic DNA phenotyping
18.10 A maternal haplogroup
18.11 A paternal haplogroup
18.12 Ethnicity estimates
18.13 Centimorgans shared across chromosomal segments
18.14 Combining SNPs and STRs as a forensic tool
19.15 Herd immunity
20.17 PD-L1 immune checkpoint inhibitor
20.18 Chimeric antigen receptor T cell (CAR T) therapy
22.7 Comparison of gene therapy and gene editing

New Tables

5.2 Shared Centimorgans Indicate Relationships
18.2 A Maternal Lineage
18.3 Selected Y Haplogroups
18.4 Distribution of 3,000 SNP Profiles Across 26 Reference Populations
19A Human Organoids
20.2 Viruses That Can Cause Cancer
21.1 Key Biotechnology Inventions
21.3 Drugs Made in Transgenic Animals
21.4 Engineered Crops
22.5 Gene Therapies
23.1 Mutations That Interfere with Early Prenatal Development
23.2 Live Births Following IVF

New to Connect
Remote Proctoring & Browser-Locking Capabilities

New remote proctoring and browser-locking capabilities, hosted by Proctorio within Connect, provide control of the assessment environment by enabling security options and verifying the identity of the student.

Seamlessly integrated within Connect, these services allow instructors to control students' assessment experience by restricting browser activity, recording students' activity, and verifying students are doing their own work.

Instant and detailed reporting gives instructors an at-a-glance view of potential academic integrity concerns, thereby avoiding personal bias and supporting evidence-based claims.

Writing Assignment

Available within McGraw-Hill Connect® and McGraw-Hill Connect® Master, the Writing Assignment tool delivers a learning experience to help students improve their written communication skills and conceptual understanding. As an instructor you can assign, monitor, grade, and provide feedback on writing more efficiently and effectively.

ACKNOWLEDGMENTS

Human Genetics: Concepts and Applications, Thirteenth Edition, would not have been possible without the assistance of the editorial and production team: portfolio managers Ian Townsend and Andrew Urban, senior product developer Donna Nemmers, marketing manager Kelly Brown, project manager Kelly Hart, designer Beth Blech, content licensing specialist Beth Cray, and copyeditor Cheryl Ferguson. I am grateful to the reviewers of this textbook over the years, whose suggestions have contributed to its clarity and accuracy, and to readers of my weekly articles who have provided feedback on specific topics. As always, many thanks to my wonderful husband, Larry, for his support and encouragement.

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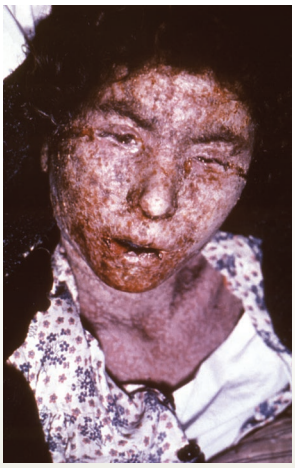
Applying Human Genetics

Chapter Openers

Matt Garcia



Source: CDC/Carl Flint; Armed Forces Institute of Pathology

A GLIMPSE OF HISTORY

The Human Touch

Clinical Connections

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Jane Ades/National Human Genome Research Institute

Bioethics

The Lewis Guided Learning System

In-Chapter Review Tools include summary tables and the end-of-chapter Study Guide, which has a summary of each section, Key Terms, and several sets of review questions, which are handy tools for reference and study. Boldfaced terms within the chapter and in the end-of-chapter Summary are defined in the Key Terms section of the Study Guide.

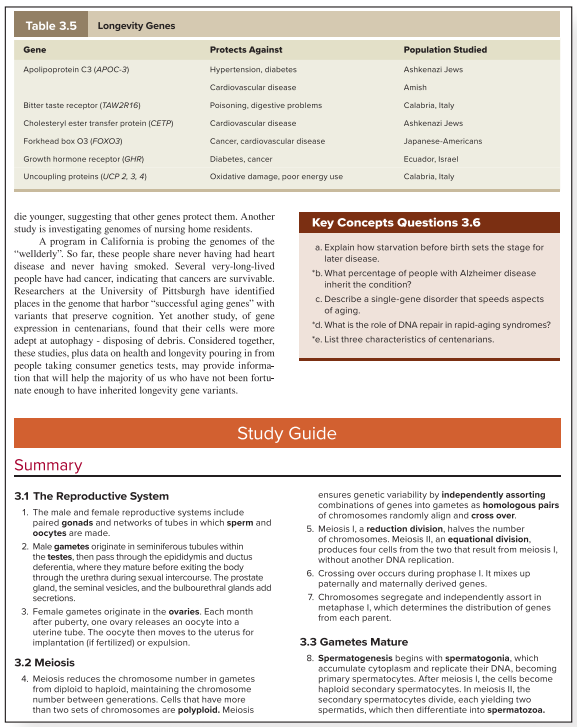


Table 3.5 Longevity Genes

Gene	Protects Against	Population Studied
Apolipoprotein C3 (*APOC-3*)	Hypertension, diabetes	Ashkenazi Jews
	Cardiovascular disease	Amish
Bitter taste receptor (*TAW2R16*)	Poisoning, digestive problems	Calabria, Italy
Cholesteryl ester transfer protein (*CETP*)	Cardiovascular disease	Ashkenazi Jews
Forkhead box O3 (*FOXO3*)	Cancer, cardiovascular disease	Japanese-Americans
Growth hormone receptor (*GHR*)	Diabetes, cancer	Ecuador, Israel
Uncoupling proteins (*UCP 2, 3, 4*)	Oxidative damage, poor energy use	Calabria, Italy

die younger, suggesting that other genes protect them. Another study is investigating genomes of nursing home residents.

A program in California is probing the genomes of the "wellderly". So far, these people share never having had heart disease and never having smoked. Several very-long-lived people have had cancer, indicating that cancers are survivable. Researchers at the University of Pittsburgh have identified places in the genome that harbor "successful aging genes" with variants that preserve cognition. Yet another study, of gene expression in centenarians, found that their cells were more adept at autophagy - disposing of debris. Considered together, these studies, plus data on health and longevity pouring in from people taking consumer genetics tests, may provide information that will help the majority of us who have not been fortunate enough to have inherited longevity gene variants.

Key Concepts Questions 3.6

a. Explain how starvation before birth sets the stage for later disease.
*b. What percentage of people with Alzheimer disease inherit the condition?
c. Describe a single-gene disorder that speeds aspects of aging.
*d. What is the role of DNA repair in rapid-aging syndromes?
*e. List three characteristics of centenarians.

Study Guide

Summary

3.1 The Reproductive System

1. The male and female reproductive systems include paired **gonads** and networks of tubes in which **sperm** and **oocytes** are made.
2. Male **gametes** originate in seminiferous tubules within the **testes**, then pass through the epididymis and ductus deferentia, where they mature before exiting the body through the urethra during sexual intercourse. The prostate gland, the seminal vesicles, and the bulbourethral glands add secretions.
3. Female gametes originate in the **ovaries**. Each month after puberty, one ovary releases an oocyte into a uterine tube. The oocyte then moves to the uterus for implantation (if fertilized) or expulsion.

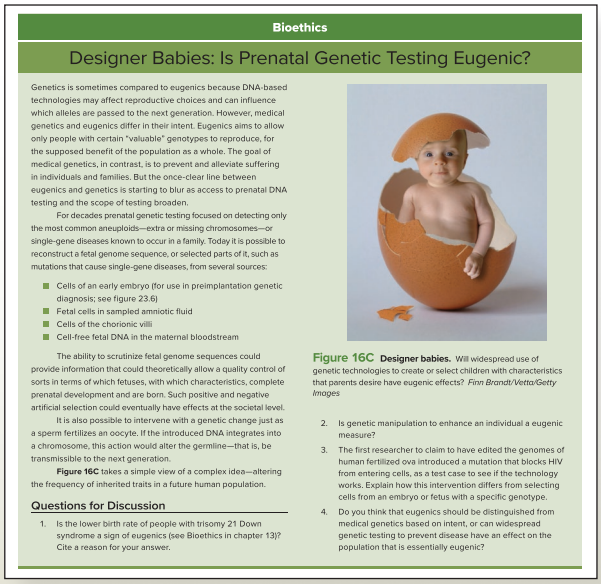
3.2 Meiosis

4. Meiosis reduces the chromosome number in gametes from diploid to haploid, maintaining the chromosome number between generations. Cells that have more than two sets of chromosomes are **polyploid.** Meiosis ensures genetic variability by **independently assorting** combinations of genes into gametes as **homologous pairs** of chromosomes randomly align and **cross over**.
5. Meiosis I, a **reduction division**, halves the number of chromosomes. Meiosis II, an **equational division**, produces four cells from the two that result from meiosis I, without another DNA replication.
6. Crossing over occurs during prophase I. It mixes up paternally and maternally derived genes.
7. Chromosomes segregate and independently assort in metaphase I, which determines the distribution of genes from each parent.

3.3 Gametes Mature

8. **Spermatogenesis** begins with **spermatogonia**, which accumulate cytoplasm and replicate their DNA, becoming primary spermatocytes. After meiosis I, the cells become haploid secondary spermatocytes. In meiosis II, the secondary spermatocytes divide, each yielding two spermatids, which then differentiate into **spermatozoa.**

Bioethics boxes include Questions for Discussion.



Bioethics

Designer Babies: Is Prenatal Genetic Testing Eugenic?

Genetics is sometimes compared to eugenics because DNA-based technologies may affect reproductive choices and can influence which alleles are passed to the next generation. However, medical genetics and eugenics differ in their intent. Eugenics aims to allow only people with certain "valuable" genotypes to reproduce, for the supposed benefit of the population as a whole. The goal of medical genetics, in contrast, is to prevent and alleviate suffering in individuals and families. But the once-clear line between eugenics and genetics is starting to blur as access to prenatal DNA testing and the scope of testing broaden.

For decades prenatal genetic testing focused on detecting only the most common aneuploids—extra or missing chromosomes—or single-gene diseases known to occur in a family. Today it is possible to reconstruct a fetal genome sequence, or selected parts of it, such as mutations that cause single-gene diseases, from several sources:

- Cells of an early embryo (for use in preimplantation genetic diagnosis; see figure 23.6)
- Fetal cells in sampled amniotic fluid
- Cells of the chorionic villi
- Cell-free fetal DNA in the maternal bloodstream

The ability to scrutinize fetal genome sequences could provide information that could theoretically allow a quality control of sorts in terms of which fetuses, with which characteristics, complete prenatal development and are born. Such positive and negative artificial selection could eventually have effects at the societal level.

It is also possible to intervene with a genetic change just as a sperm fertilizes an oocyte. If the introduced DNA integrates into a chromosome, this action would alter the germline—that is, be transmissible to the next generation.

Figure 16C takes a simple view of a complex idea—altering the frequency of inherited traits in a future human population.

Questions for Discussion

1. Is the lower birth rate of people with trisomy 21 Down syndrome a sign of eugenics (see Bioethics in chapter 13)? Cite a reason for your answer.

Figure 16C **Designer babies.** Will widespread use of genetic technologies to create or select children with characteristics that parents desire have eugenic effects? *Finn Brandt/Vetta/Getty Images*

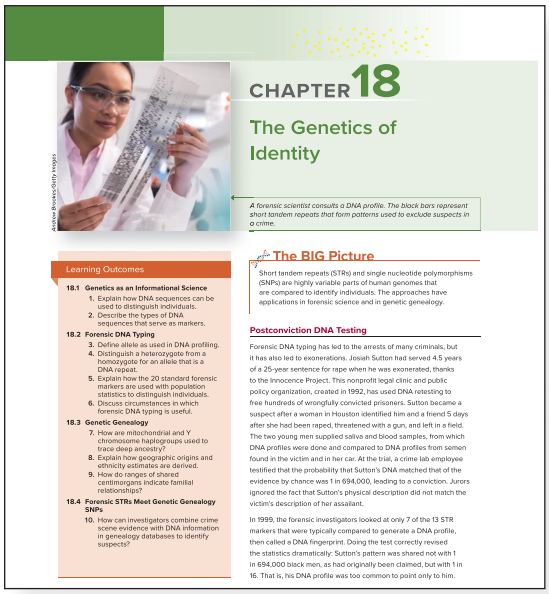
2. Is genetic manipulation to enhance an individual a eugenic measure?
3. The first researcher to claim to have edited the genomes of human fertilized ova introduced a mutation that blocks HIV from entering cells, as a test case to see if the technology works. Explain how this intervention differs from selecting cells from an embryo or fetus with a specific genotype.
4. Do you think that eugenics should be distinguished from medical genetics based on intent, or can widespread genetic testing to prevent disease have an effect on the population that is essentially eugenic?

Learning Outcomes preview major chapter topics in an inquiry-based format according to numbered sections.

The Big Picture encapsulates chapter content at the start.

Chapter Openers vividly relate content to real life.

Key Concepts Questions follow each numbered section.



CHAPTER 18

The Genetics of Identity

A forensic scientist consults a DNA profile. The black bars represent short tandem repeats that form patterns used to exclude suspects in a crime.

Learning Outcomes

18.1 Genetics as an Informational Science
1. Explain how DNA sequences can be used to distinguish individuals.
2. Describe the types of DNA sequences that serve as markers.

18.2 Forensic DNA Typing
3. Define allele as used in DNA profiling.
4. Distinguish a heterozygote from a homozygote for an allele that is a DNA repeat.
5. Explain how the 20 standard forensic markers are used with population statistics to distinguish individuals.
6. Discuss circumstances in which forensic DNA typing is useful.

18.3 Genetic Genealogy
7. How are mitochondrial and Y chromosome haplogroups used to trace deep ancestry?
8. Explain how geographic origins and ethnicity estimates are derived.
9. How do ranges of shared centimorgans indicate familial relationships?

18.4 Forensic STRs Meet Genetic Genealogy SNPs
10. How can investigators combine crime scene evidence with DNA information in genealogy databases to identify suspects?

The BIG Picture

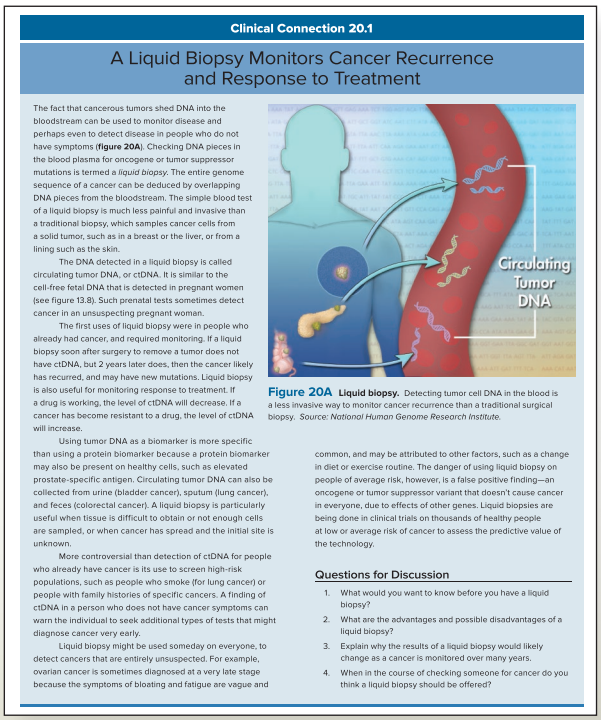
Short tandem repeats (STRs) and single nucleotide polymorphisms (SNPs) are highly variable parts of human genomes that are compared to identify individuals. The approaches have applications in forensic science and in genetic genealogy.

Postconviction DNA Testing

Forensic DNA typing has led to the arrests of many criminals, but it has also led to exonerations. Josiah Sutton had served 4.5 years of a 25-year sentence for rape when he was exonerated, thanks to the Innocence Project. This nonprofit legal clinic and public policy organization, created in 1992, has used DNA retesting to free hundreds of wrongfully convicted prisoners. Sutton became a suspect after a woman in Houston identified him and a friend 5 days after she had been raped, threatened with a gun, and left in a field. The two young men supplied saliva and blood samples, from which DNA profiles were done and compared to DNA profiles from semen found in the victim and in her car. At the trial, a crime lab employee testified that the probability that Sutton's DNA matched that of the evidence by chance was 1 in 694,000, leading to a conviction. Jurors ignored the fact that Sutton's physical description did not match the victim's description of her assailant.

In 1999, the forensic investigators looked at only 7 of the 13 STR markers that were typically compared to generate a DNA profile, then called a DNA fingerprint. Doing the test correctly revised the statistics dramatically: Sutton's pattern was shared not with 1 in 694,000 black men, as had originally been claimed, but with 1 in 16. That is, his DNA profile was too common to point only to him.

Clinical Connection boxes discuss how genetics and genomics impact health and health care and include questions for discussion.



Clinical Connection 20.1

A Liquid Biopsy Monitors Cancer Recurrence and Response to Treatment

The fact that cancerous tumors shed DNA into the bloodstream can be used to monitor disease and perhaps even to detect disease in people who do not have symptoms (**figure 20A**). Checking DNA pieces in the blood plasma for oncogene or tumor suppressor mutations is termed a *liquid biopsy*. The entire genome sequence of a cancer can be deduced by overlapping DNA pieces from the bloodstream. The simple blood test of a liquid biopsy is much less painful and invasive than a traditional biopsy, which samples cancer cells from a solid tumor, such as in a breast or the liver, or from a lining such as the skin.

The DNA detected in a liquid biopsy is called circulating tumor DNA, or ctDNA. It is similar to the cell-free fetal DNA that is detected in pregnant women (see figure 13.8). Such prenatal tests sometimes detect cancer in an unsuspecting pregnant woman.

The first uses of liquid biopsy were in people who already had cancer, and required monitoring. If a liquid biopsy soon after surgery to remove a tumor does not have ctDNA, but 2 years later does, then the cancer likely has recurred, and may have new mutations. Liquid biopsy is also useful for monitoring response to treatment. If a drug is working, the level of ctDNA will decrease. If a cancer has become resistant to a drug, the level of ctDNA will increase.

Using tumor DNA as a biomarker is more specific than using a protein biomarker because a protein biomarker may also be present on healthy cells, such as elevated prostate-specific antigen. Circulating tumor DNA can also be collected from urine (bladder cancer), sputum (lung cancer), and feces (colorectal cancer). A liquid biopsy is particularly useful when tissue is difficult to obtain or not enough cells are sampled, or when cancer has spread and the initial site is unknown.

More controversial than detection of ctDNA for people who already have cancer is its use to screen high-risk populations, such as people who smoke (for lung cancer) or people with family histories of specific cancers. A finding of ctDNA in a person who does not have cancer symptoms can warn the individual to seek additional types of tests that might diagnose cancer very early.

Liquid biopsy might be used someday on everyone, to detect cancers that are entirely unsuspected. For example, ovarian cancer is sometimes diagnosed at a very late stage because the symptoms of bloating and fatigue are vague and common, and may be attributed to other factors, such as a change in diet or exercise routine. The danger of using liquid biopsy on people of average risk, however, is a false positive finding—an oncogene or tumor suppressor variant that doesn't cause cancer in everyone, due to effects of other genes. Liquid biopsies are being done in clinical trials on thousands of healthy people at low or average risk of cancer to assess the predictive value of the technology.

Figure 20A **Liquid biopsy.** Detecting tumor cell DNA in the blood is a less invasive way to monitor cancer recurrence than a traditional surgical biopsy. *Source: National Human Genome Research Institute.*

Questions for Discussion

1. What would you want to know before you have a liquid biopsy?
2. What are the advantages and possible disadvantages of a liquid biopsy?
3. Explain why the results of a liquid biopsy would likely change as a cancer is monitored over many years.
4. When in the course of checking someone for cancer do you think a liquid biopsy should be offered?

Each chapter ends with a point-by-point **Summary**.

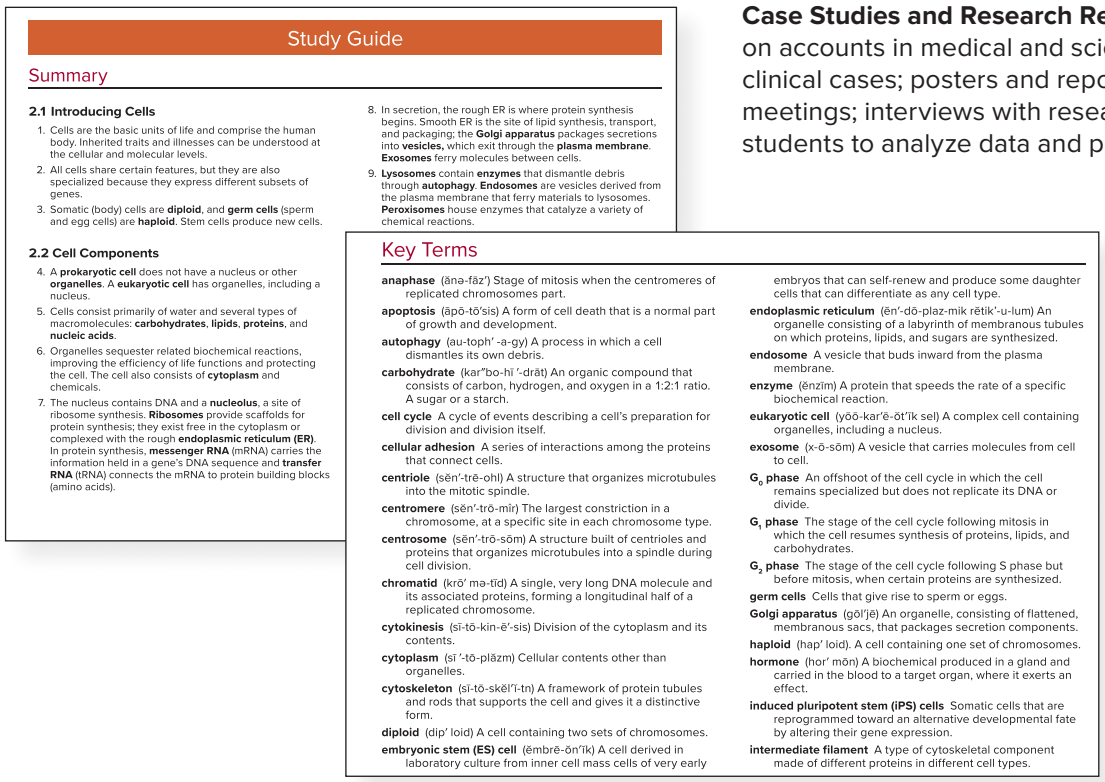
Key Terms that are boldfaced within the chapter are defined in the Key Terms section.

Review Questions assess content knowledge.

Applied Questions help students develop problem-solving skills. The first question in this section relates back to the chapter opener.

Forensics Focus questions probe the use of genetic information in criminal investigations.

Case Studies and Research Results use stories based on accounts in medical and scientific journals; real clinical cases; posters and reports from professional meetings; interviews with researchers; and fiction to ask students to analyze data and predict results.



Study Guide

Summary

2.1 Introducing Cells

1. Cells are the basic units of life and comprise the human body. Inherited traits and illnesses can be understood at the cellular and molecular levels.
2. All cells share certain features, but they are also specialized because they express different subsets of genes.
3. Somatic (body) cells are **diploid**, and **germ cells** (sperm and egg cells) are **haploid**. Stem cells produce new cells.

2.2 Cell Components

4. A **prokaryotic cell** does not have a nucleus or other **organelles**. A **eukaryotic cell** has organelles, including a nucleus.
5. Cells consist primarily of water and several types of macromolecules: **carbohydrates**, **lipids**, **proteins**, and **nucleic acids**.
6. Organelles sequester related biochemical reactions, improving the efficiency of life functions and protecting the cell. The cell also consists of **cytoplasm** and chemicals.
7. The nucleus contains DNA and a **nucleolus**, a site of ribosome synthesis. **Ribosomes** provide scaffolds for protein synthesis; they exist free in the cytoplasm or complexed with the rough **endoplasmic reticulum (ER)**. In protein synthesis, **messenger RNA** (mRNA) carries the information held in a gene's DNA sequence and **transfer RNA** (tRNA) connects the mRNA to protein building blocks (amino acids).
8. In secretion, the rough ER is where protein synthesis begins. Smooth ER is the site of lipid synthesis, transport, and packaging; the **Golgi apparatus** packages secretions into **vesicles,** which exit through the **plasma membrane**. **Exosomes** ferry molecules between cells.
9. **Lysosomes** contain **enzymes** that dismantle debris through **autophagy**. **Endosomes** are vesicles derived from the plasma membrane that ferry materials to lysosomes. **Peroxisomes** house enzymes that catalyze a variety of chemical reactions.

Key Terms

anaphase (ănə-fāz') Stage of mitosis when the centromeres of replicated chromosomes part.

apoptosis (āpō-tō'sis) A form of cell death that is a normal part of growth and development.

autophagy (au-toph' -a-gy) A process in which a cell dismantles its own debris.

carbohydrate (kar"bo-hī '-drāt) An organic compound that consists of carbon, hydrogen, and oxygen in a 1:2:1 ratio. A sugar or a starch.

cell cycle A cycle of events describing a cell's preparation for division and division itself.

cellular adhesion A series of interactions among the proteins that connect cells.

centriole (sĕn'-trē-ōhl) A structure that organizes microtubules into the mitotic spindle.

centromere (sĕn'-trō-mĭr) The largest constriction in a chromosome, at a specific site in each chromosome type.

centrosome (sĕn'-trō-sōm) A structure built of centrioles and proteins that organizes microtubules into a spindle during cell division.

chromatid (krō' mə-tĭd) A single, very long DNA molecule and its associated proteins, forming a longitudinal half of a replicated chromosome.

cytokinesis (sī-tō-kin-ē'-sis) Division of the cytoplasm and its contents.

cytoplasm (sī '-tō-plăzm) Cellular contents other than organelles.

cytoskeleton (sī-tō-skĕl'ĭ-tn) A framework of protein tubules and rods that supports the cell and gives it a distinctive form.

diploid (dip' loid) A cell containing two sets of chromosomes.

embryonic stem (ES) cell (ĕmbrē-ŏn"ĭk) A cell derived in laboratory culture from inner cell mass cells of very early embryos that can self-renew and produce some daughter cells that can differentiate as any cell type.

endoplasmic reticulum (ĕn'-dō-plaz-mik rētik'-u-lum) An organelle consisting of a labyrinth of membranous tubules on which proteins, lipids, and sugars are synthesized.

endosome A vesicle that buds inward from the plasma membrane.

enzyme (ĕnzīm) A protein that speeds the rate of a specific biochemical reaction.

eukaryotic cell (yōō-kar'ē-ŏt'ĭk sel) A complex cell containing organelles, including a nucleus.

exosome (x-ō-sōm) A vesicle that carries molecules from cell to cell.

G_0 phase An offshoot of the cell cycle in which the cell remains specialized but does not replicate its DNA or divide.

G_1 phase The stage of the cell cycle following mitosis in which the cell resumes synthesis of proteins, lipids, and carbohydrates.

G_2 phase The stage of the cell cycle following S phase but before mitosis, when certain proteins are synthesized.

germ cells Cells that give rise to sperm or eggs.

Golgi apparatus (gōl'jē) An organelle, consisting of flattened, membranous sacs, that packages secretion components.

haploid (hap' loid). A cell containing one set of chromosomes.

hormone (hor' mōn) A biochemical produced in a gland and carried in the blood to a target organ, where it exerts an effect.

induced pluripotent stem (iPS) cells Somatic cells that are reprogrammed toward an alternative developmental fate by altering their gene expression.

intermediate filament A type of cytoskeletal component made of different proteins in different cell types.

Review Questions

1. Match each organelle to its function.

Organelle	Function
a. lysosome	1. lipid synthesis
b. rough ER	2. houses DNA
c. nucleus	3. energy extraction
d. smooth ER	4. dismantles debris
e. Golgi apparatus	5. detoxification
f. mitochondrion	6. protein synthesis
g. peroxisome	7. processes secretions

2. Describe a disease or symptoms that result when each of the following organelles or structures malfunctions.
   a. lysosome
   b. peroxisome
   c. mitochondrion
   d. cytoskeleton
   e. ion channel
3. What advantage does compartmentalization provide to a large and complex cell?
4. Distinguish between an exosome and an endosome.
5. Give two examples of how the plasma membrane functions as more than just a covering of the cell's insides.
6. List four types of controls on cell cycle rate.
7. How can all of a person's cells contain exactly the same genetic material, yet specialize as bone cells, nerve cells, muscle cells, and connective tissue cells?
8. Distinguish between
   a. a bacterial cell and a eukaryotic cell.

Applied Questions

1. The chapter opener describes diagnosing Rett syndrome, which affects neurons in the brain, from DNA extracted from a saved baby tooth. Explain why a mutation detected in one cell type can be used to help diagnose an inherited condition that affects a different cell type.
2. If you wanted to create a synthetic organelle to test new drugs for toxicity, which natural organelle's function would you try to replicate?
3. An inherited form of migraine is caused by a mutation in a gene *(SCN1A)* that encodes a sodium channel in neurons. What is a sodium channel, and in which cell structure is it located?
4. In a form of Parkinson disease, a protein called alpha synuclein accumulates because of impaired autophagy. Which organelle is implicated in this form of the disease?
5. Why wouldn't a cell in an embryo likely be in phase G_0?
6. Describe two ways to derive stem cells without using human embryos.
7. Two roommates regularly eat 100-calorie packages of cookies. After a semester of each roommate eating one package a night, and following similar diet and exercise plans otherwise, one roommate has gained 12 pounds, but the other's weight has stayed the same. If genetics does not account for the difference in weight gain, what other factor discussed in the chapter might?
8. A "telomere health DNA test" sold online promises to "track your cellular age based on your telomere length" so that you can "improve it." The company sells supplement packages to help in the quest for biological youth. What further information might be helpful in deciding whether to purchase this type of genetic test and the suggested supplements?

Forensics Focus

1. A man who owned a company that provides human tissues was sentenced to serve many years in prison for trafficking in body parts taken, without consent, from dismembered corpses from funeral homes. Thousands of parts from hundreds of bodies were used in surgical procedures, including hip replacements and dental implants. The most commonly used product was a bone paste. Many family members of the tissue sources testified at the trials. Explain why cells from bone tissue can be matched to blood or cheek lining cells from blood relatives.

Case Studies and Research Results

1. A boy with "congenital skin crease Kunze type" has rings of creases on his arms and legs, unusual facial features, intellectual disability, slow growth, and a cleft palate. He has a mutation in the gene *TUBB*, and his condition is termed a "tubulinopathy." What part of his cells is affected?
2. Members of a large, three-generation family in Italy do not notice burns, broken bones, or even red hot chili pepper powder injected under the skin. What might their abnormality be on a cellular level?
3. Researchers isolated stem cells from fat removed from people undergoing liposuction, a procedure to remove fat. The stem cells can give rise to muscle, fat, bone, and cartilage cells.
   a. Are the stem cells totipotent or pluripotent?
   b. Are these stem cells ES cells, iPS cells, or adult stem cells?

Dynamic Art Program

Multilevel Perspective

Illustrations depicting complex structures show microscopic and macroscopic views to help students see relationships among increasingly detailed drawings.

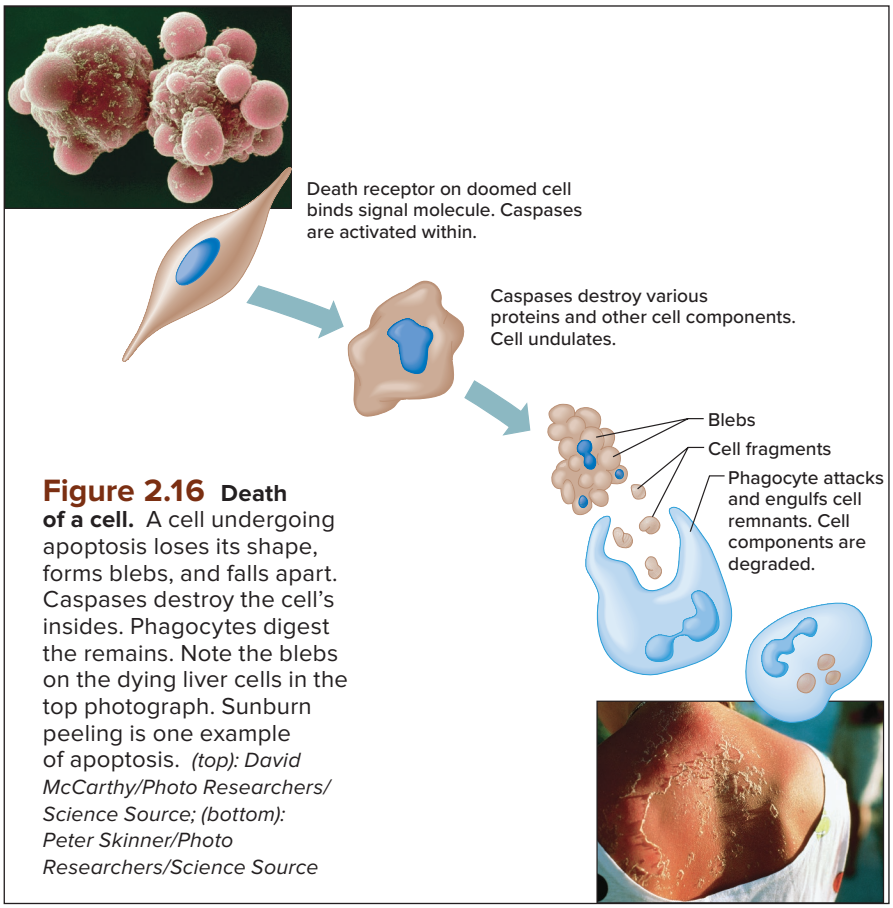


Figure 2.16 Death of a cell. A cell undergoing apoptosis loses its shape, forms blebs, and falls apart. Caspases destroy the cell's insides. Phagocytes digest the remains. Note the blebs on the dying liver cells in the top photograph. Sunburn peeling is one example of apoptosis. *(top): David McCarthy/Photo Researchers/ Science Source; (bottom): Peter Skinner/Photo Researchers/Science Source*

New Technologies

CAR T cell therapy harnesses a personalized immune response against cancer cells.

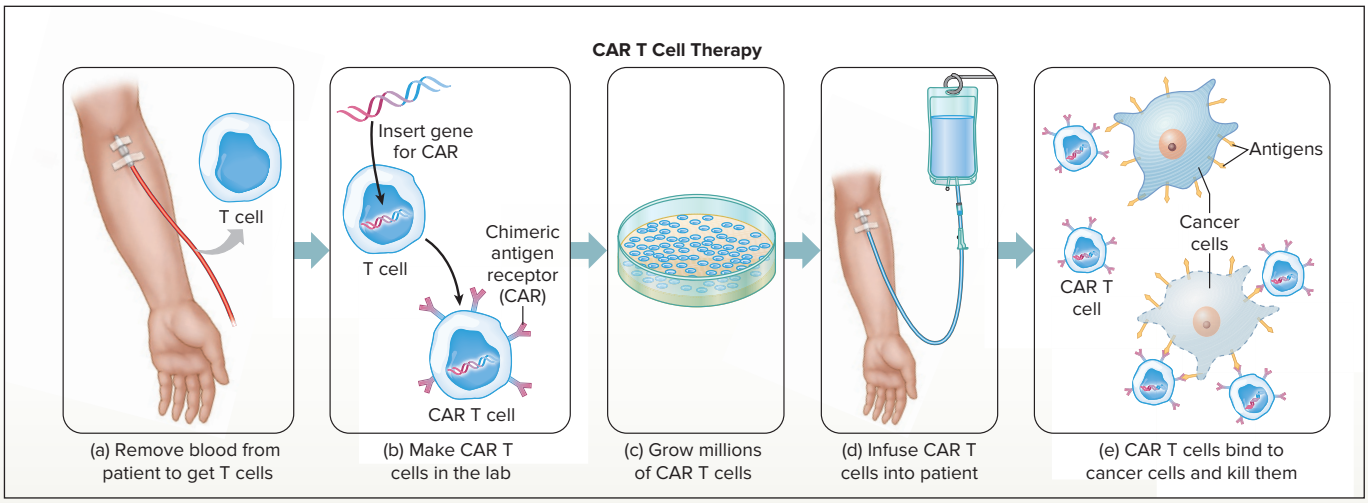


Figure 20.18 Chimeric antigen receptor therapy arms a patient's T cells to attack cancer cells. **(a)** A blood sample is taken from a patient and the T cells are separated. **(b)** In laboratory glassware, the patient's T cells are exposed to a gene modified to include the genetic instructions for both a T-cell receptor and an antibody. **(c)** Millions of copies of the modified T cells are cultured in the dish and then **(d)** transferred to the patient. The modified cells circulate and produce the hybrid protein that consists of both the T-cell receptor **(e)** and the antibody. The receptor guides the T cell to a cancer cell, where the antibody part binds, which alerts the immune system to send perforins that shatter the cancer cell and granulysins that dismantle the cancer cell from within. *(c): 2017 Terese Winslow LLC U.S. Govt. has certain rights*

Practical Information

Consumer genetics reveals information that may be pertinent to a person's health, traits, family, and ancestry.

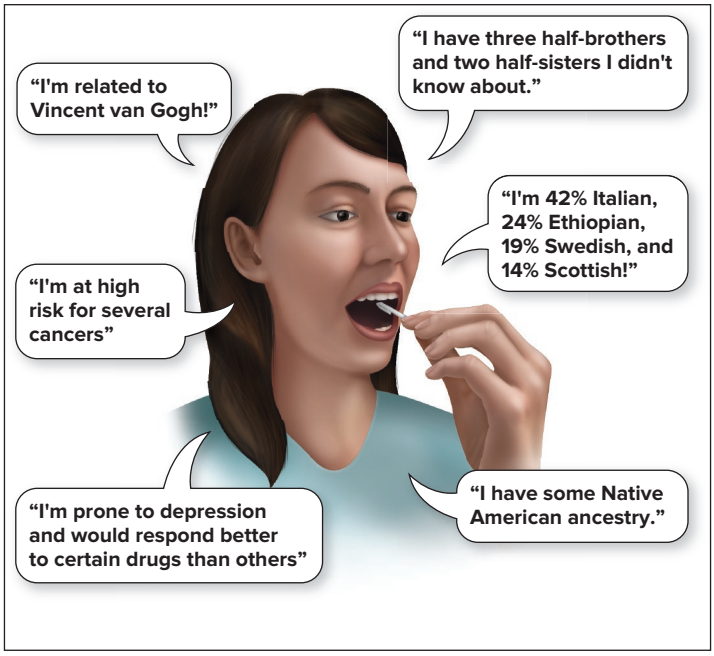


Figure 1.1 **Consumer genetics.** *DNA tests reveal several types of information and can bring surprises.*

Process Figures

Complex processes are broken down into a series of smaller steps that are easy to follow.

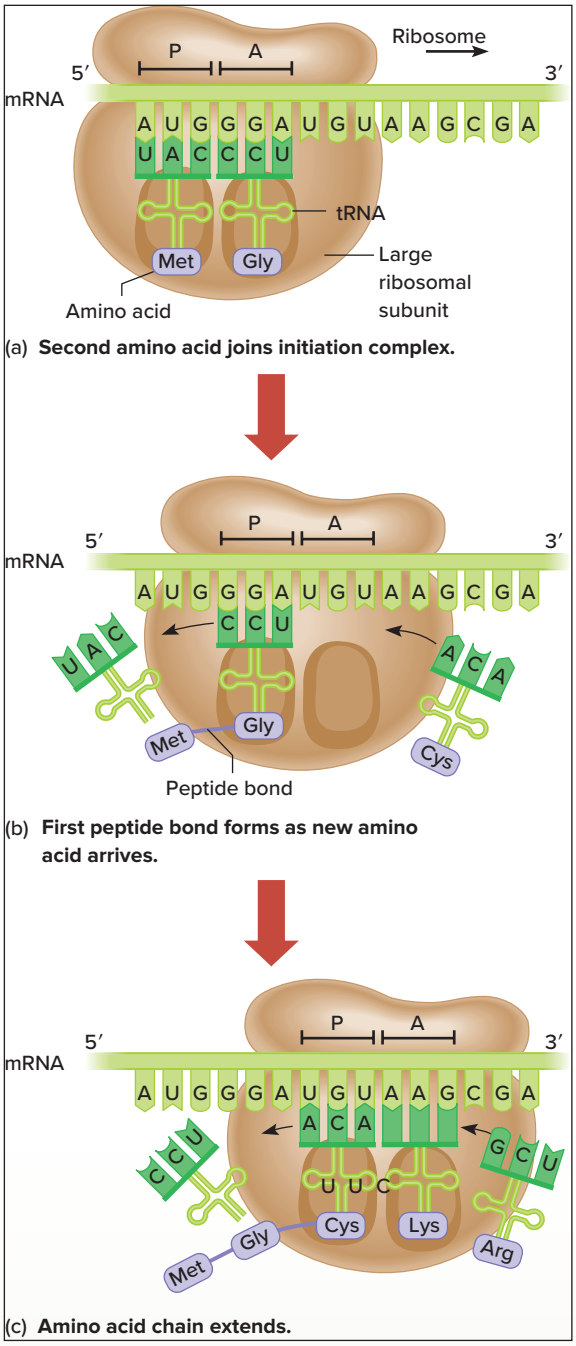


Figure 10.16 **Building a polypeptide.** **(a)** A large ribosomal subunit binds to the initiation complex, and a tRNA bearing a second amino acid (glycine, in this example) forms hydrogen bonds between its anticodon and the mRNA's second codon at the A site. The first amino acid, methionine, occupies the P site. **(b)** The methionine brought in by the first tRNA forms a peptide bond with the amino acid brought in by the second tRNA, and a third tRNA arrives, in this example carrying the amino acid cysteine, at the temporarily vacant A site. **(c)** A fourth and then fifth amino acid link to the growing polypeptide chain. The process continues until reaching a stop codon.

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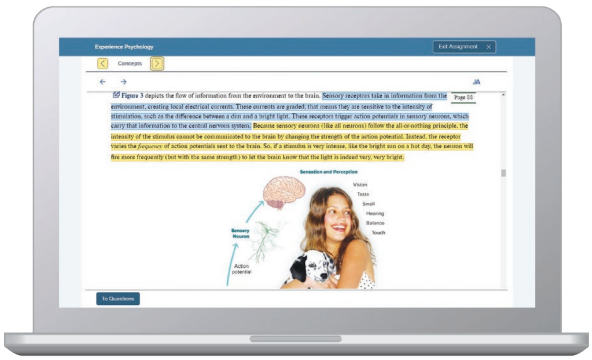

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CHAPTER 1

The Information in a Human Genome

A child's genome holds information on her health, where she came from, and what she might experience and achieve—but the environment is very important too in guiding who she is and will become.

Learning Outcomes

1.1 Introducing Genes and Genomes

1. Explain what genetics is and what it is not.
2. Distinguish among gene, exome, and genome.
3. Define *bioethics*.

1.2 Levels of Genetics and Genomics

4. List the levels of genetics.
5. Explain how DNA is maintained and how it provides the information to construct a protein.
6. Explain how a mutation can cause a disease.
7. State the basis of genetic diversity.
8. Explain the relationship between DNA and chromosomes.
9. Distinguish between Mendelian and complex traits.
10. Explain how genetics underlies evolution.

1.3 Applications of Genetics and Genomics

11. List some practical uses of DNA information.
12. Distinguish between traditional breeding and genetically modifying organisms.

1.4 A Global Perspective on Genomes

13. Explain how investigating genomes extends beyond interest in ourselves.

The BIG Picture

A human genome is a vast store of information encoded in the sequence of building blocks of the molecule deoxyribonucleic acid (DNA). Genetic information affects our health and traits, and holds clues to how we are biologically related to one another.

Eve's Genome

A baby is born. Drops of blood from her heel are placed into a small device that sends personal information into her electronic medical record. The device deciphers the entire sequence of DNA building blocks wound into the nucleus of a white blood cell. This is Eve's genome. Past, present, and future are encoded in nature's master informational molecule, deoxyribonucleic acid, or DNA—with room for environmental influences.

Eve's genome indicates overall good genetic health. She has a mild clotting disease that the nurse suspected when two gauze patches were needed to stop the bleeding from the heel stick. Two rare variants of the gene that causes cystic fibrosis (CF) mean that Eve is susceptible to certain respiratory infections and sensitive to irritants, but her parents knew that possibility from prenatal testing. Fortunately, the family lives in a rural area far from industrial pollution or wildfires, which will make it easier for Eve to avoid irritants such as smoke and dust.

The inherited traits that will emerge as Eve grows and develops range from interesting to important. Her hair will darken and curl, and variants of genes that contribute to bone development indicate that she'll have a small nose, broad forehead, and chiseled

cheekbones. If she follows a healthy diet, she'll be as tall as her parents. On the serious side, Eve has inherited a mutation in a gene that greatly raises her risk of developing certain types of cancers. Her genes predict a healthy heart, but she might develop diabetes unless she exercises regularly and limits carbohydrates in her diet.

Many traits are difficult to predict because of environmental influences, including experiences. What will Eve's personality be like? How intelligent will she be? How will she react to stress? What will be her passions?

Genome sequencing also reveals clues to Eve's past, which is of special interest to her father, who was adopted. She has gene variants common among the Eastern European population of her mother's origin, and others that match people from Morocco. Is that her father's heritage? Eve is the beautiful consequence of a mix of her parents' genomes, receiving half of her genetic material from each.

Do you want to know the information in your genome?

1.1 Introducing Genes and Genomes

Genetics is the study of inherited traits, rooted in DNA, and their variations and transmission. The field, a type of life science, began more than a century ago with plant breeding experiments. Genetics evolved during the last century from a minor medical discipline dealing with rare diseases to forming the underpinnings of the emerging field of precision medicine, discussed in section 1.3. Precision medicine attempts to prevent and treat disease based on individual differences in gene variants, environmental exposures, and lifestyle factors such as diet and exercise.

In this new century, genetics has exploded into a powerful source of information about our identities that can reveal or revise what we know about our pasts, reach diagnoses and target health treatments in the present, and predict our medical futures. Human genetics touches forensics, bioethics, psychology, and even history. Consumer genetics enables anyone to learn about their DNA by sending samples of saliva or cheek cells to companies (**figure 1.1**) that return and store DNA data.

Genetics is not the same as traditional genealogy, which considers relationships but not traits. The newer area of **genetic genealogy** considers how people are related and where their ancestors lived, using and comparing information from DNA sequences and evidence such as documents, old photographs, maps, and family stories and memories.

Figure 1.1 Consumer genetics. DNA tests reveal several types of information and can bring surprises.

Heredity is the transmission of traits and biological information between generations. Inherited traits range from obvious physical characteristics, such as freckles and red hair, to many aspects of health, including disease and risk of developing disease. Talents, quirks, personality traits, and other difficult-to-define characteristics might appear to be inherited if they affect several family members, but might also reflect shared genetic and environmental influences. Attributing some traits to genetics, such as sense of humor or whether or not one votes, are oversimplifications. These connections are associations, not causes.

Like all sciences, genetics has its own vocabulary. Some technical terms and expressions may be familiar, but actually have precise scientific definitions. Conversely, the language of genetics sometimes enters casual conversation. "*It's in her DNA*," for example, usually means an inborn trait, not a specific DNA sequence. The terms and concepts introduced in this chapter are explained and explored in detail in subsequent chapters. Boldfaced key terms are defined at the chapter's end.

Genes function as the units of heredity in that copies of genes are passed from one generation to the next. Genes are biochemical instructions that tell **cells**, the basic units of life, how to manufacture certain proteins. These proteins, in turn, impart or control the characteristics that create much of our individuality. A gene consists of the long molecule **deoxyribonucleic acid (DNA)**. The DNA transmits information in its sequence of four types of building blocks, which function like an alphabet. Most of a cell's DNA is in a structure called the **nucleus**.

The complete set of genetic instructions characteristic of an organism, including protein-encoding genes and other DNA sequences, constitutes a **genome**. Nearly all

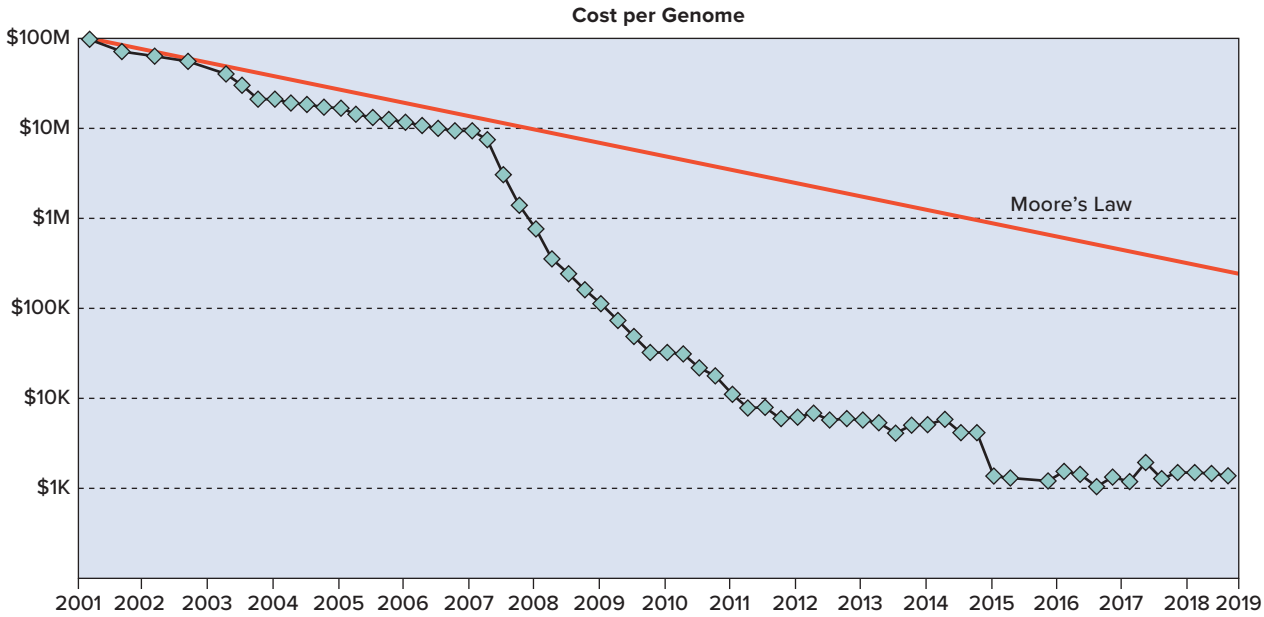


Figure 1.2 **The cost of sequencing a human genome has plunged.** Today people can be paid for use of their genetic information. *National Human Genome Research Institute*

of our cells contain two copies of the genome. Researchers published the deciphered sequences of the first human genomes in 2003, following a multi year, international effort. **Figure 1.2** shows how the cost of sequencing a human genome has plummeted since the first genomes were sequenced in the early 2000s. When the idea to sequence a human genome was proposed in 1990, the cost was estimated to be $1 billion. As technology steadily improved, the cost fell, drastically so in 2008, when a much more efficient method of sequencing genomes came into wide use. That is when the cost defied Moore's law, which is a term from business used to describe regular doubling of an event. Today, companies pay citizens for access to their genomes in doing research and developing products. Although millions of people have had their genomes sequenced, researchers are still analyzing what each of our genes does and how genes interact and respond to environmental stimuli.

Only about 1 percent of the 3.2 billion building blocks of our genomes specify proteins. This tiny slice of the genome, called the **exome**, is responsible for many aspects of health and our traits, including our differences.

The exome includes about 20,325 genes, accounting for about 85 percent of the genome known to contribute to genetic disease. Much of the rest of the genome controls how the body uses the genes of the exome. When genome sequencing was expensive, exome sequencing provided a shortcut to identify mutations that could explain a patient's mysterious symptoms and provide a diagnosis. Today sequencing genomes in search of a diagnosis is more economically feasible, as **Clinical Connection 1.1** discusses. Analyzing and comparing genomes constitutes the field of **genomics**.

Genetics directly affects our lives and those of our relatives, including our descendants. Principles of genetics also may be relevant in politics, economics, sociology, anthropology, art, the law, and athletics. Using genetic technologies forces us to wrestle with concepts of benefit and risk, even tapping our deepest feelings about right and wrong. The field of **bioethics** addresses concerns that arise from the use of new genetic technologies, including tests, treatments, privacy, and discrimination. Essays throughout this book address bioethical issues.

Key Concepts Questions 1.1

a. Distinguish between genetics and heredity.
*b. What is the type of chemical that makes up a gene?
c. Distinguish among a gene, an exome, and a genome.
*d. Define *bioethics*.

1.2 Levels of Genetics and Genomics

Genetics considers the transmission of information at several levels. It begins with the molecular level and broadens through cells, tissues and organs, individuals, families, and finally to populations and the evolution of species.

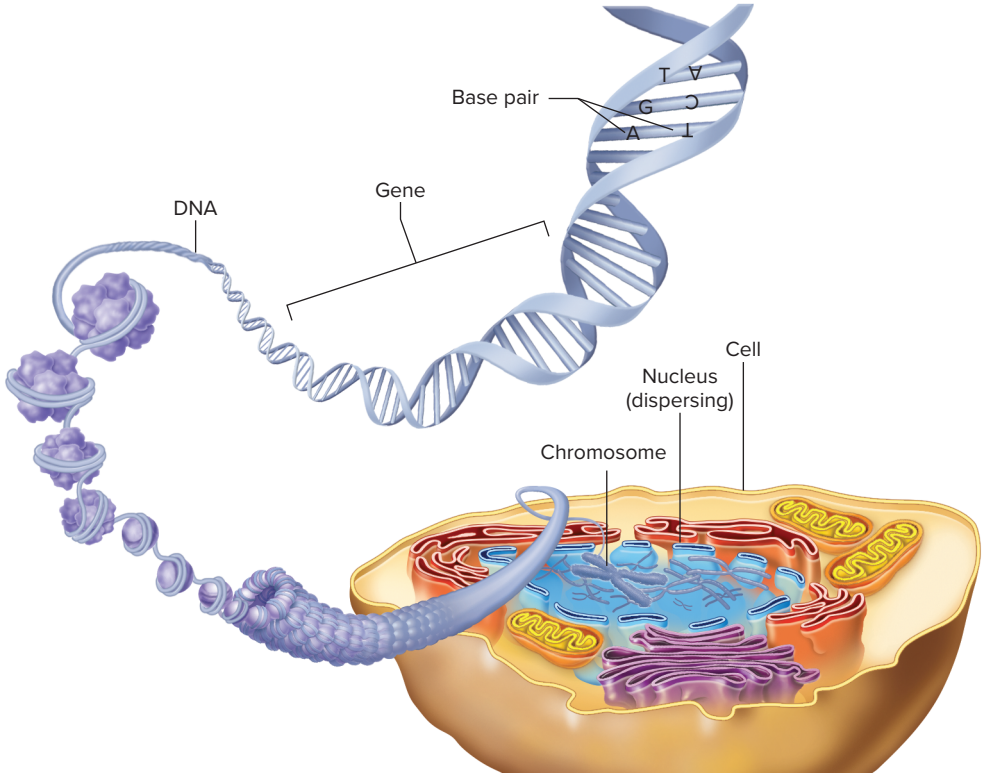


Figure 1.3 **Levels of genetics.** Genetics can be considered at several levels, from the sequences of DNA base pairs, to genes, to chromosomes, to genomes, to the more familiar individuals, families, and populations.

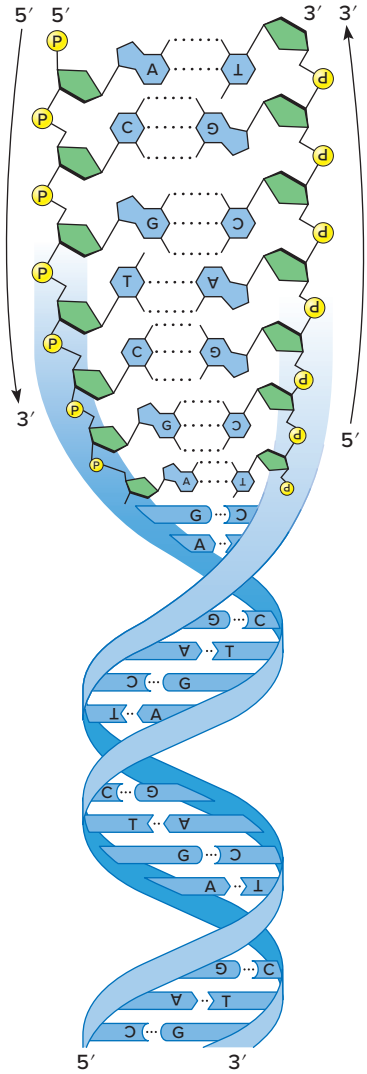


Figure 1.4 **The DNA double helix.** The 5′ and 3′ labels indicate the head-to-tail organization of the DNA double helix. A, C, T, and G are bases. S stands for sugar and P for phosphate. The green five-sided shapes represent the sugars. The dots that connect the bases into pairs represent hydrogen bonds.

Instructions and Information: DNA

A DNA molecule resembles a spiral staircase or double helix (**figure 1.3**). The "rails," or backbone, consist of alternating chemical groups (sugars and phosphates) and are the same in all DNA molecules. The two strands of the double helix are oriented in opposite directions, like two snakes biting each other's tails. The "steps" of the DNA double helix are pairs of the four types of building blocks, or **nitrogenous bases**: **adenine** (A) and **thymine** (T), which attract each other, and **cytosine** (C) and **guanine** (G), which attract each other (**figure 1.4**). The information that a DNA molecule imparts is in the sequences of A, T, C, and G.

The chemical structure of DNA gives the molecule two key abilities that are essential for being the basis of life: DNA can replicate itself when a cell divides and its information accessed to manufacture specific proteins.

In **DNA replication**, the chains of the double helix untwist and separate, and then each half builds a new partner chain from free DNA bases. In this way, the resulting "daughter" cells inherit identical copies of the genome during cell division. A and T recognize each other and attract, as do C and G. Chemical attractions called hydrogen bonds hold the bases of a pair together. Then **transcription** copies the sequence of part of one strand of a DNA molecule into a related type of molecule, messenger **ribonucleic acid (RNA)**. RNA molecules include a fifth type of base, **uracil** (U), in place of the T in DNA. Transcription is also called **gene expression**. In **translation**, each three RNA bases in a row attract another type of RNA that functions as a connector, bringing in a particular amino acid. The amino acids align and link like snap beads, forming a protein.

Proteins provide the traits associated with genes. The disease cystic fibrosis (CF) illustrates how a missing or abnormal protein causes the symptoms of an inherited disease (**figure 1.5**). In CF, the protein is the cystic fibrosis transmembrane conductance regulator (*CFTR*). The functioning protein works like a selective doorway in cells lining the airways and certain other body parts, thickening secretions when it doesn't work properly.

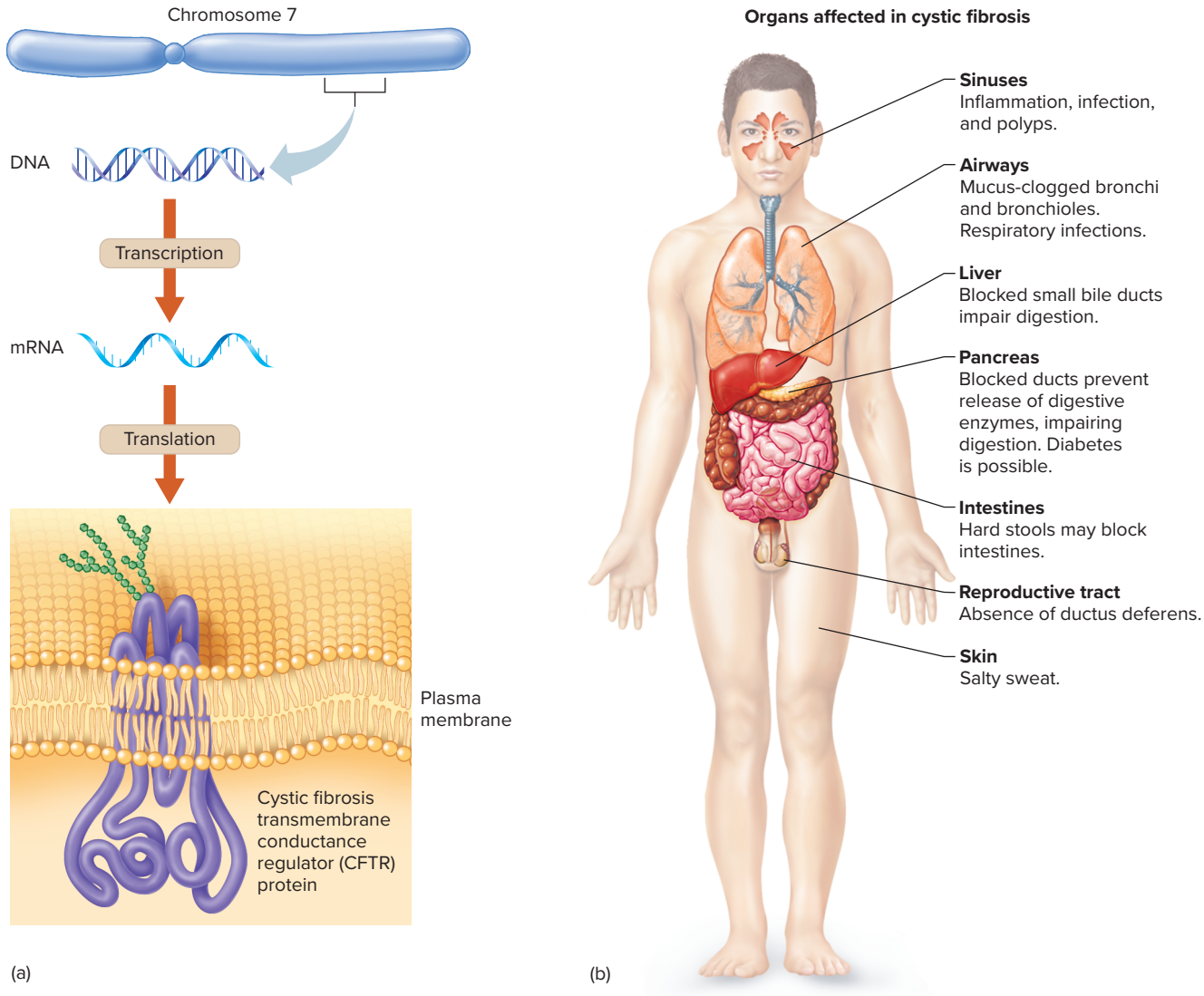


Figure 1.5 **From gene to protein to person. (a)** The gene encoding the CFTR protein, causing cystic fibrosis when in a variant form (a mutation), is part of the seventh largest chromosome. CFTR normally folds into a channel that regulates the flow of salt components (ions) into and out of cells lining the respiratory tract, pancreas, intestines, and elsewhere. **(b)** Cystic fibrosis causes several symptoms.

Source: Data from "Reverse genetics and cystic fibrosis" by M. C. Iannuzi and F. S. Collins. *American Journal of Respiratory Cellular and Molecular Biology* 2:309–316 [1990].

A change in a gene is a **mutation**, and it can have an effect at the whole-person level, such as causing a disease. **Figure 1.6** depicts the effect of a mutation in *CFTR*. A change of a "C" in the DNA sequence at a specific location in the gene to a "T" inserts the amino acid aspartic acid rather than the amino acid glycine as the protein forms. The resulting protein cannot open to the cell's surface, removing channels for certain salt components, causing the symptoms described in figure 1.5. Difficulty breathing, impaired digestion, and other symptoms result (see Clinical Connection 4.1).

The same protein-encoding gene may vary slightly in DNA base sequence from person to person. These gene variants are called **alleles**. The changes in DNA sequence that distinguish alleles arise by mutation. (The word *mutation* is also used as a noun to refer to the changed gene.) Once a gene mutates, the change is passed on when the cell that contains it replicates its DNA and divides. If the change is in a sperm or egg cell that becomes a fertilized egg, it is passed to the next generation.

Some mutations cause disease, and others provide variation such as freckled skin. Mutations can also help. One rare mutation makes a person's cells unable to manufacture a surface protein that binds HIV. These people are resistant to HIV infection. Mutations that have no detectable effect because they do not change the encoded protein in a way that affects its function are sometimes called gene variants. They are a little like a minor spelling error that does not obscure the meaning of a sentence.

The DNA sequences of the human genome are grouped among 23 structures called **chromosomes**. When a cell is not

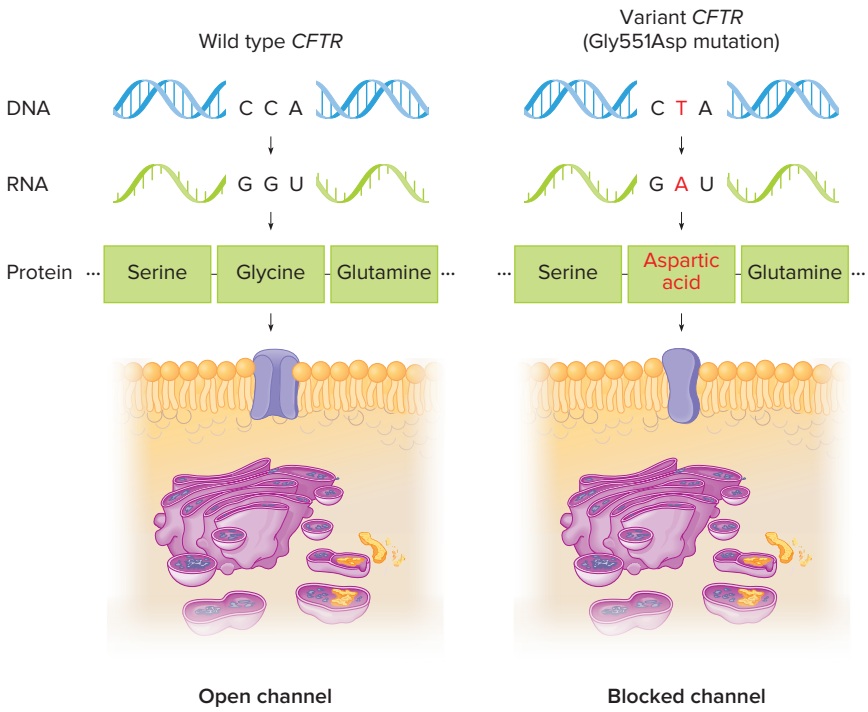


Figure 1.6 **A mutation can alter a protein, causing symptoms.** One type of mutation in the *CFTR* gene replaces one amino acid type (glycine) with another (aspartic acid) at a specific site, altering the encoded protein in a way that closes a type of ion channel that participates in secretion.

dividing, the chromosomes are in an unwound state within the nucleus. When a cell is dividing, the chromosomes wind up so tightly that they can be seen under a microscope when stained, appearing rod shaped. The DNA of a chromosome is continuous, but it includes hundreds of genes, plus other sequences.

A human **somatic cell** (non-sex cell) has 23 pairs of chromosomes, equaling two complete sets of genetic information (genomes). Twenty-two of these 23 pairs are **autosomes**, which do not differ between the sexes. The autosomes are numbered from 1 to 22, with 1 being the largest. The other two chromosomes, the X and the Y, are **sex chromosomes**.

In humans, a female has two X chromosomes and a male has one X and one Y chromosome. The Y chromosome bears genes that determine maleness. Charts called **karyotypes** display the chromosome pairs from largest to smallest (**figure 1.7**).

A trait caused predominantly by a single gene is termed Mendelian, named for Gregor Mendel, who discovered the patterns of trait transmission. Most characteristics are **complex traits**, which means that they are determined by one or more genes and environmental factors (**figure 1.8**). The more factors that contribute to a trait or illness—inherited or environmental—the more difficult it is to predict the risk of occurrence in a particular family member. The bone-thinning condition osteoporosis illustrates factors that can contribute to a disease. Mutations in several genes elevate osteoporosis risk by conferring susceptibility to fractures, but so do smoking, lack of weight-bearing exercise, and a calcium-poor diet.

The Body: Cells, Tissues, and Organs

A human body consists of approximately 30 trillion cells. All somatic cells except red blood cells contain two copies of the genome, but cells differ in appearance and activities because they use only some of their genes. Which genes a cell uses at any given time depends on environmental conditions inside and outside the body.

Like the internet, a genome contains a wealth of information, but only some of it is needed in a particular cell under particular circumstances. The use, or expression, of different subsets of genes to manufacture proteins drives the **differentiation**, or specialization, of distinctive cell types. An adipose cell is filled with fat, but not the contractile proteins of muscle cells. Both cell types, however, have two complete genomes. Groups of differentiated cells assemble and interact with each other and the nonliving materials that they secrete to form aggregates called **tissues**. Table 2.1 lists the four basic tissue types: connective tissues, epithelium (linings), muscle, and nervous. Altogether, they are composed of more than 290 types of cells.

Tissues intertwine and layer to form organs, which connect into organ systems. The stomach, for example, is a sac made of muscle that also has a lining of epithelial tissue, nervous tissue, and a supply of blood, which is a type of connective tissue. Many organs include rare, unspecialized **stem cells**.

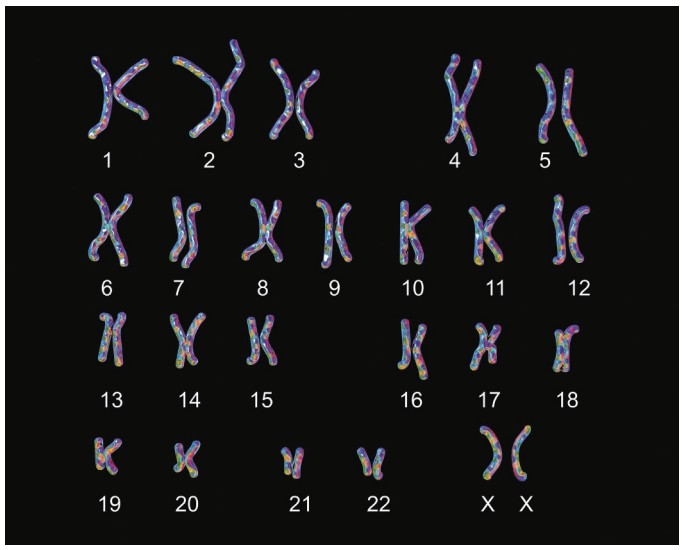
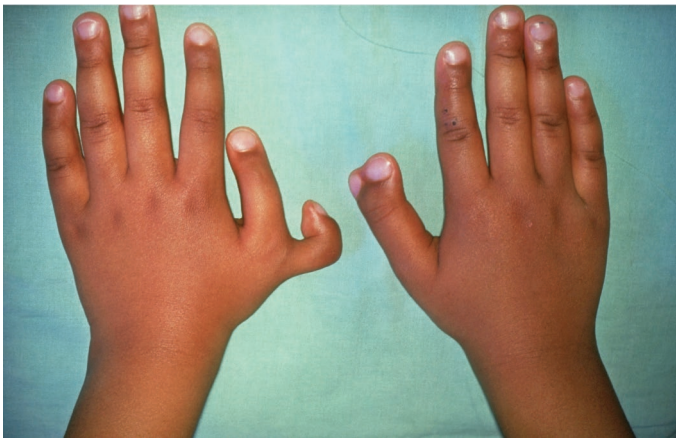


Figure 1.7 **A normal female karyotype.** *Kateryna Kon/Shutterstock*



(a)

(b)

Figure 1.8 **Mendelian versus complex traits.** **(a)** Polydactyly—extra fingers and/or toes—is a Mendelian trait (single gene). **(b)** Hair color is complex (also called multifactorial), controlled by at least three genes plus environmental influences, such as the bleaching effects of sun exposure. *(a): Lester V. Bergman/Getty Images; (b): Steve Mason/Getty Images*

A stem cell can divide to yield another stem cell and a cell that differentiates. Stem cells provide a reserve supply of cells that enable an organ to grow and repair damage.

Relationships: From Individuals to Families

Two terms distinguish the alleles that are *present* in an individual from the alleles that are *expressed*. The **genotype** refers to the underlying DNA instructions (alleles present), whereas the **phenotype** is the visible trait, biochemical change, or effect on health (alleles expressed). Alleles are further distinguished by how many copies are necessary to affect the phenotype. A **dominant** allele has an effect when present in just one copy (on one chromosome), whereas a **recessive** allele must be present on both chromosomes of a pair to be expressed.

Individuals are genetically connected into families. A person has approximately half of his or her gene variants in common with each parent, sibling, and offspring, and one-quarter with each grandparent. First cousins share one-eighth of their gene variants. Charts called **pedigrees** depict the members of a family and indicate which individuals have particular inherited traits. **Figure 1.9** shows how the percent of the genome shared with a direct ancestor decreases as the generations go back and partners introduce new genomes. In this way, the proportion of the genome an individual shares with an ancestor halves at each generation.

The Bigger Picture: From Populations to Evolution

Above the family level of genetic organization is the population. In a strict biological sense, a population is a group of individuals that can have healthy offspring together. In a genetic sense, a population is a large collection of alleles, distinguished by their frequencies. People from a Swedish population, for example, would have a greater frequency of alleles that specify

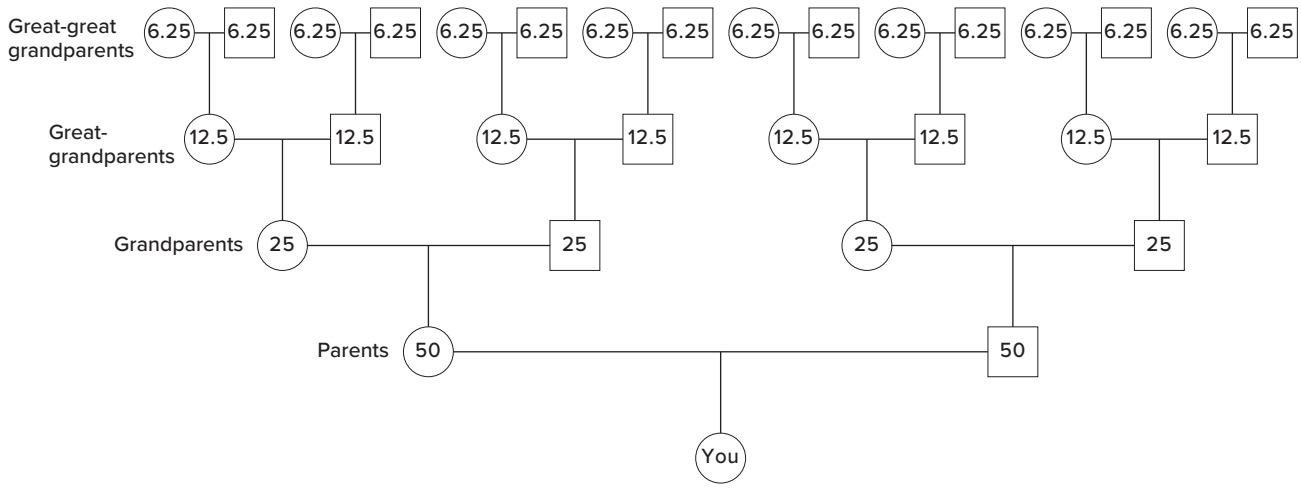


Figure 1.9 **Percent of the genome shared with relatives.** The percent of the DNA sequence that a person shares with ancestors halves at each generation.

light hair and skin than people from a population in Nigeria, who tend to have dark hair and skin. All the alleles in a population constitute the **gene pool**. (An individual does not have a gene pool.)

Population genetics is applied in health care, forensics, and other fields. It is also the basis of evolution, which is defined as changing allele frequencies in populations. Small-scale genetic changes in populations underlie the species distinctions we most often associate with evolution.

Comparing DNA sequences for individual genes, or the amino acid sequences of the proteins that the genes encode, can reveal how closely related different types of organisms are. The assumption is that the more similar the DNA sequences are, the more recently two species diverged from a shared ancestor, and the more closely related they are. This is a more plausible explanation than two species having evolved similar or identical gene sequences coincidentally. The same logic applies to family patterns of inherited traits. It is more likely that a brother and sister share approximately half of their gene variants because they have the same parents than that half of their genetic material is identical by chance.

More information is available in full genome sequences than in single genes. Humans, for example, share more than 98 percent of the DNA sequence with chimpanzees. Our genomes differ from theirs more in gene organization and in the number of copies of genes. Learning the functions of the human-specific genes may explain the differences between us and them—such as our sparse body hair and use of spoken language. Figure 17.16 highlights some of our distinctively human traits.

At the genome level, we are much more like each other genetically than are other mammals. Chimpanzees are more distinct from each other than we are! The most genetically diverse modern people are from Africa, where humanity arose. The gene variants among different modern ethnic groups include subsets of our ancestral African gene pool.

Key Concepts Questions 1.2

*a. List the levels of genetic information.

b. Explain how DNA carries and maintains information.

*c. List the nitrogenous bases that are part of DNA.

d. Explain how a mutation can cause a disease.

*e. Define *allele*.

*f. Name the two types of chromosomes.

g. Distinguish between Mendelian and complex traits.

*h. Define *gene expression*.

i. Distinguish between genotype and phenotype; dominant and recessive.

*j. Define *gene pool*.

k. Explain how comparing DNA sequences can clarify evolutionary relationships.

1.3 Applications of Genetics and Genomics

Genetics is impacting several areas of our lives, from health care choices, to what we eat, to unraveling our pasts and guiding our futures. "Citizen scientists" are discovering genetic information about themselves while helping researchers compile databases that will speed development of new diagnostic tests and treatments.

Thinking about genetics evokes fear, hope, anger, wonder, and despair, depending on context and circumstance. Following are a few uses of DNA information, then glimpses of applications of genetics and genomics that are explored more fully in subsequent chapters:

- Predicting shelf life of fruits and vegetables, detecting spoiled meat, identifying allergens, and indicating degree of fermentation in cheese
- Identifying victims of human trafficking at transportation centers by comparing the DNA of suspected victims to DNA from concerned relatives
- Detecting disease-causing mutations or abnormal chromosome numbers in a fetus from DNA in a pregnant woman's blood
- Identifying which of several pets produced feces, so a stool sample can be brought to a veterinarian to diagnose the sick animal
- Performing rapid diagnosis of an infectious disease on the battlefield
- Creating a tree of life depiction of how all species are related
- Selecting crops and show animals for breeding
- Choosing people to date
- Identifying criminals by comparing DNA from crime scenes, from a suspect, and to DNA from a suspect's relative who has uploaded information to a public genetic genealogy database
- Detecting tiny amounts of DNA in fur, feathers, or feces of rare or elusive species to sequence their genomes and learn more about them

Establishing Identity

Comparing DNA sequences among individuals can rule out identity, relationships, or ancestry, or indicate the probability that two individuals are related. The premise is that the more DNA sequences two individuals share, the more closely related they are.

DNA profiling refers to the techniques, statistical analyses, and machine learning approaches that are used to compare DNA sequences between and among individuals. It has varied applications. The term is most often used in the context of forensic science, which is the collecting of physical evidence of a crime. Comparing DNA collected at crime scenes to DNA in samples from suspects often leads to convictions, and also to reversing convictions erroneously made using other forms of evidence.

DNA profiling is also useful in identifying victims of natural disasters, such as violent storms and earthquakes. In happier circumstances, DNA profiles maintained in databases assist adopted individuals in locating blood relatives and children of sperm donors in finding their biological fathers and half-siblings. Chapter 18 explores the genetics of identity.

Another use of DNA profiling is to analyze food, because foods were once organisms, which have species-specific DNA sequences. Analyzing DNA sequences revealed horsemeat in meatballs sold at a restaurant chain, cheap fish sold as gourmet varieties, and worms in cans of sardines.

Illuminating History

DNA analysis is a time machine of sorts. It can connect past to present, from determining family relationships to establishing geographic origins of specific populations. DNA evidence sometimes confirms findings from anthropology and history and sometimes contradicts it.

DNA analysis confirmed that Thomas Jefferson had children with his slave Sally Hemings. The president was near Hemings 9 months before each of her seven children was born, and the children resembled him. Male descendants of Sally Hemings share an unusual Y chromosome sequence with the president's male relatives. His only son with his wife died in infancy, so researchers deduced the sequence of the president's Y chromosome from descendants of his uncle. Today the extended family holds reunions (**figure 1.10**).

DNA testing can provide views into past epidemics. For example, analysis of DNA in the mummy of the Egyptian king Tutankhamun, who died in 1323 B.C.E. at age 19, revealed DNA from the microorganism that causes malaria. The famous boy king likely died from complications of malaria following a leg fracture from weakened bones, rather than from intricate murder plots, a kick from a horse, or a fall from a chariot, as had been thought. His tomb included a cane and drugs, supporting the diagnosis based on DNA evidence.

Figure 1.10 DNA reveals and clarifies history. After DNA evidence showed that Thomas Jefferson likely fathered children with his slave Sally Hemings, confirming gossip of the time, descendants of both sides of the family met, and continue to do so. *Leslie Close/AP Photo*

Conservation Genetics

Combining analysis of genetic diversity with reproductive technologies creates a way to rebuild populations that are headed toward species extinction. This is the case for the northern white rhinoceros of Africa. The animals die after poachers remove their horns, which are displayed as decorations or ground up and used in medicines.

The last male northern white rhinoceros, named Sudan, died from an infection in 2018 at a nature conservancy in Kenya, leaving only Najin and her daughter Fatu, who are infertile. However, the genomes of cells from nine northern white rhinos stored at the San Diego Frozen Zoo reveal enough genetic diversity to suggest that researchers can bring back the species by borrowing from the genomes of the subspecies to the south. The southern rhino population is several thousand strong thanks to efforts to prevent poaching.

Researchers are working on three ways to bring back the animals:

- Treat defrosted northern white rhino cells with chemicals to make them differentiate as sperm and eggs, and then allow fertilization to occur in a lab dish. Transfer resulting embryos to the uteruses of surrogate southern rhinos.
- Transfer a nucleus from a frozen cell from a northern rhino to an egg from a southern rhino that has had its nucleus removed (this is cloning).
- Defrost northern rhino sperm and use them to fertilize southern white rhino eggs. Resulting offspring are then bred to reconstruct a northern white rhino population.

Precision Medicine

In several nations, people are volunteering to have their genomes sequenced so that researchers can learn more about health and disease. The DNA data are considered along with other types of information that can impact health, such as environmental exposures, exercise, diet, lifestyle factors, family histories, and the many microbes that live in and on the human body, collectively termed the **microbiome**. Evaluating genetic data is a large part of precision medicine, which is the tailoring of treatments to individuals.

On a smaller scale, a precision medicine approach consults DNA information to select drugs that are most likely to work and least likely to have side effects in a particular individual. This strategy, called **pharmacogenetics**, is already used to guide prescription of more than 150 drugs, according to the Food and Drug Administration. Some highly effective new drugs that collectively treat a variety of conditions, from cystic