Michael R. Cummings

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Principles and Issues

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To Lee Ann, my wife and partner, whose love and support have sustained me these many years.

About the Author

MICHAEL R. CUMMINGS received his Ph.D. in Biological Sciences from Northwestern University. His doctoral work, conducted in the laboratory of Dr. R. C. King, centered on ovarian development in *Drosophila melanogaster*. After a year on the faculty at Northwestern, he moved to the University of Illinois at Chicago, where for many years he held teaching and research positions. In 2003, he joined the faculty in the Department of Biological, Chemical, and Physical Sciences at Illinois Institute of Technology, where he is currently a Research Professor.

At the undergraduate level, he has focused on teaching genetics, human genetics for nonmajors, and general biology to majors and nonmajors. He has received awards given by the university faculty for outstanding teaching, has twice been voted by graduating seniors as the best teacher in their years on campus, and has received several teaching awards from student organizations.

His current research interests involve the organization of DNA sequences in the short-arm and centromere region of human chromosome 21. He is engaged in a collaborative effort to construct a physical map of this region of chromosome 21 for the purpose of exploring molecular mechanisms of chromosome interactions.

In addition to *Human Heredity*, Dr. Cummings is the author and coauthor of a number of other widely used college textbooks, including *Biology: Science and Life*; *Concepts of Genetics*; *Genetics: A Molecular Perspective*; *Essentials of Genetics*; and *Human Genetics and Society*. He has also written articles on aspects of genetics for the *McGraw-Hill Encyclopedia of Science and Technology* and has published a newsletter on advances in human genetics for instructors and students.

He and his wife, Lee Ann, are the parents of two adult children, Brendan and Kerry, and have two grandchildren, Colin and Maggie. He is an avid sailor, enjoys reading and collecting books (biography, history), appreciates music (baroque, opera, and urban electric blues), and is a long-suffering Cubs fan.

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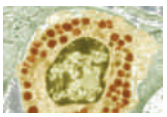

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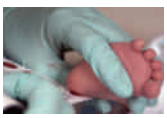

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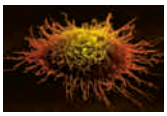

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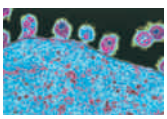

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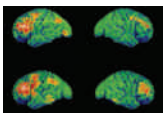

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Preface

THE PUBLICATION OF THE TENTH EDITION of a textbook offers an opportunity to look back at its beginnings. The first edition was published before the start of the Human Genome Project and the development of the myriad fields that end in "omics". Over ten editions, much of the book's contents have changed, but its continuing success rests on the fact that its rationale and aims have remained constant.

This book is written for a one-term human genetics course for students in the humanities, social sciences, business, engineering, and other fields. It assumes that the students who come to this course will have little or no background in biology, chemistry, or mathematics and will have personal, professional, or intellectual reasons for wanting to learn something about human genetics. The book is intended to serve those who will become *consumers* of genetic-based health care services and those who may become *providers* of health care services.

Because genetic knowledge and technology is rapidly being transferred to many areas of our society, it is imperative that the general public, elected officials, and policy makers outside the scientific community have a working knowledge of genetics to help shape how genetics and its associated technologies will be used in our society. To help communicate this knowledge, *Human Heredity* is written to transmit the principles of genetics in a straightforward and accessible way, without unnecessary jargon, detail, or the use of anecdotal stories in place of content. Some descriptive chemistry is used after an appropriate introduction and definition of terms. In the same vein, no advanced math skills are required to calculate elementary probabilities or to calculate genotype and allele frequencies.

Goals of the Text

From its beginnings, this book has held to a few simple goals for teaching students about human genetics. This tenth edition continues that tradition, with the following goals:

1. Present the concepts underlying human genetics in clear, concise, jargon-free language to give students a working knowledge of genetics. Each chapter presents a limited number of clearly stated concepts and examples to assist learning a complex topic.
2. Begin each chapter with a relevant example that nonmajors can understand and provide examples that students can apply to themselves, their families, and their work environments.
3. Examine the social, cultural, and ethical implications associated with the use of genetic technology.
4. Explain the origin, nature, and amount of genetic diversity present in the human population and how that diversity has been shaped by natural selection.

To achieve these goals, emphasis has been placed on clear writing and the use of accompanying photographs and artwork that teach rather than merely illustrate the ideas under discussion.

Organization

Although it is without formal divisions, the text is organized into four sections: Chapters 1 through 7 cover cell division, transmission of traits from generation to generation, and development. Chapters 8 through 12 emphasize molecular genetics, mutation, and cancer. Chapters 13 through 16 include recombinant DNA, genomics, and biotechnology. These chapters cover gene action, mutation, cloning, genomics, as well as genetic screening, genetic testing, and genetic counseling. Chapters 17 through 19 cover specialized topics: the immune system, the genetics of behavior, and population genetics and human evolution.

Instructors teaching genetics courses to nonmajors come from many different backgrounds and use a wide range of instructional formats, including active learning. To facilitate this array of approaches, the book is organized to allow both students and instructors to use the material no matter what order of topics is selected. After the first section, the chapters can be used in any order. Within each chapter, outlines and end-of-chapter activities let the instructor and students easily identify and explore central ideas.

What's New in the Tenth Edition

Each chapter has been updated to reflect the latest advances in genetics. Listed below are some of the most significant revisions in this edition.

Chapter 1: A Perspective on Human Genetics

- Revised and expanded.
- New case study added to Genetics in Practice.

Chapter 2: Cells and Cell Division

- Expanded coverage of genetic disorders associated with cellular structures.
- Updated section on role of cellular organelles in normal cell function.
- New case study added to Genetics in Practice.

Chapter 3: Transmission of Genes from Generation to Generation

- Section 3.1 revised and expanded, covering transmission of traits and genetic testing.
- New case study added to Genetics in Practice.

Chapter 4: Pedigree Analysis in Human Genetics

- New case study added to Genetics in Practice.

Chapter 5: The Inheritance of Complex Traits

- Expanded and updated coverage of multifactorial traits.
- New Figure 5.12b map of obesity in U.S.
- New Figure 5.14 Leptin cycle.

Chapter 6: Cytogenetics: Karyotypes and Chromosome Aberrations

- Revised Section 6.1 Facing a Life-Changing Decision.
- Updated and expanded Exploring Genetics feature on non-invasive fetal testing.

Chapter 7: Development and Sex Determination

- Revised Section 7.1 Sex: Is It Nature or Nurture?
- New case study added to Genetics in Practice.

Chapter 8: The Structure, Replication, and Chromosomal Organization of DNA

- Revised Section 8.1 Are DNA Vaccines the Answer?
- Genetic Revolution feature updated and expanded.
- New case study added to Genetics in Practice.

Chapter 9: Gene Expression and Gene Regulation
- Revised Section 9.1 Cows as a Cause of Death.

Chapter 10: From Proteins to Phenotypes
- Revised Section 10.1 Protein Malfunctions Cause Genetic Disorders.
- New Figure 10.16 Global distribution of lactose intolerance.
- New Figure 10.18 Vegetables with taste differences.

Chapter 11: Genome Alterations: Mutation and Epigenetics (New Title)
- Revised Section 11.1 Are Some Flame Retardants Dangerous?
- New Exploring Genetics feature: Irradiated Food.
- New Section 11.9 Epigenetics Involves Reversible Alterations to the Genome.
- New Figure 11.18 Nucleosome structure.
- New Figure 11.19 Gene Silencing.
- New Figure 11.20 Methyl groups.
- New Figure 11.21 Beckwith-Weidemann syndrome.
- New case study added to Genetics in Practice.

Chapter 12: Genes and Cancer
- Revised Section 12.1 Decisions About Cancer Testing.
- Revised Section 12.8 Hybrid Genes and Cancer.
- Revised Section 12.9 Genomics, Epigenetics, and Cancer.

Chapter 13: An Introduction to Genetic Technology
- Revised Section 13.1 Making Choices About Biotechnology.
- New case study added to Genetics in Practice.

Chapter 14: Biotechnology and Society
- Revised Section 14.1 The Origin of DNA Profiles.
- Updated section on DNA Profiles are used in Forensics.
- Revised case study in Genetics in Practice.

Chapter 15: Genomes and Genomics
- Revised Section 15.1 Genomics and Personalized Medicine.
- Updated Table 15.4 Comparison of Selected Genomes.

Chapter 16: Reproductive Technology, Genetic Testing, and Gene Therapy
- Revised Section 16.1 Genetic Technology and Reproduction.
- New Figure 16.9 GIFT and ZIFT.
- New Figure 16.17 Target disorders for gene therapy.

Chapter 17: Genes and the Immune System
- Revised Section 17.1 Components of the Immune System are Genetically Controlled.
- Updated Exploring Genetics: Peanut Allergies are Increasing.
- Updated Table 17.4 Global HIV and AIDS Cases.

Chapter 18: Genetics of Behavior
- Revised Section 18.1 Human Behavior is a Complex Trait.

Chapter 19: Population Genetics and Human Evolution
- Revised Section 19.1 Natural Selection Drives Evolution.
- New Figure 19.12 Phylogenetic Tree of Human Species.
- Revised Section on Human and Chimpanzee Genomes.
- New section: Have We Identified all our Human Relatives?
- New Figure 19.16 Phylogeny of Human Species.

Features of the Book

Numbered Chapter Outlines

At the beginning of each chapter, an outline of the primary chapter headings provides an overview of the main concepts, secondary ideas, and examples. To help students grasp the central points, many of the headings are written as narratives or summaries of the ideas that follow. These outlines also serve as convenient starting points for students to review the material in each chapter. To make the outlines more useful, they have been numbered and used to organize the summary, the questions, and the problems at the end of each chapter. In this way, students can relate examples and questions to specific topics in the chapter more easily and clearly.

First Section Case Studies

The first section of each chapter contains a case study that is directly related to the main ideas of the chapter, often drawn from real life. Topics include the use of DNA fingerprinting in court cases, the cloning of milk cows, the use of exome sequencing to diagnose a genetic disorder, and the development of *in vitro* fertilization (IVF) and the birth of Louise Brown—the first IVF baby. These vignettes are designed to promote student interest in the topics covered in the chapter and to demonstrate that laboratory research often has a direct impact on everyday life. These case studies are linked to another case presented in the Genetics in Practice section at the end of the chapter, and to other cases available online.

The Genetic Revolution

The Genetic Revolution is a feature that emphasizes the past, present, and future impact of genetic technology on our daily lives, from genetic testing at birth to the future of cancer therapy.

Exploring Genetics

Exploring Genetics feature boxes present ideas and applications that are related to and extend the central concepts in a chapter. Some of these examine controversies that arise as genetic knowledge is transferred into technology and services.

Marginal Glossary

A glossary in the page margins gives students immediate access to definitions of terms as they are introduced in the text. This format also allows definitions to be identified when students are studying or preparing for examinations. The definitions have been gathered into an alphabetical glossary at the back of the book. Because an understanding of the concepts of genetics depends on understanding the relevant terms, more than 350 terms are included in the glossary. These glossary terms are also available on the website as flashcards.

End-of-Chapter Features

Genetics in Practice: Relevant Case Studies

A case study is included at the end of each chapter, illustrating the impact of genetics in our society. These contain scenarios and examples of genetic issues related to health, reproduction, personal decision making, public health, and ethics. Many of the case studies and the accompanying questions can be used for classroom discussions, student papers and presentations, and role playing. Other cases are located on the book's website along with links to resources for further research and exploration.

Summary

Each chapter ends with a summary that restates the major ideas covered in the chapter. The beginning outline and ending summary for each chapter use the same content and order to emphasize major concepts and their applications. Each point of the summary outline is followed by a brief restatement of the chapter material covered under the same heading. This helps students recall the concepts, topics, and examples presented in the chapter. It is hoped that this organization will minimize the chance that they will attempt to learn by rote memorization.

Questions and Problems

The summary's focus on the chapter's main points is continued in the ***Questions and Problems*** at the end of each chapter. The questions and problems are presented under the headings from the chapter outline. This allows students to relate the problems and questions to specific topics presented in the chapter, focus on concepts they find difficult, and work the problems that illustrate those topics. The questions and problems are designed to test students' knowledge of the facts and their ability to reason from the facts to conclusions. To this end, they use an objective question format and a problem-solving format. Because some quantitative skills are necessary in human genetics, almost all chapters include some problems that require students to organize the concepts in the chapter and use those concepts in reasoning to a conclusion. Answers to selected problems are provided in an appendix. Answers to all questions and problems are available in the Instructor's Manual and on the password-protected Biology CourseMate website.

Pedagogical Features

Genomic Databases as Resources

To make students aware of the array of genomic resources available to them, genetic disorders mentioned in the book are referenced by their indexing numbers from the comprehensive catalog available online as *Online Mendelian Inheritance in Man* (*OMIM*). OMIM (updated daily) contains text, pictures, and videos, along with literature references. Through Entrez, OMIM is cross-linked to databases containing DNA sequences, protein sequences, chromosome maps, and other resources. Students and an informed public need to be aware of the existence and relevance of such databases, and to be up to date, textbooks must incorporate these resources.

Students can use OMIM to obtain detailed information about a genetic disorder, its mode of inheritance, its phenotype and clinical symptoms, mapping information, biochemical properties, the molecular nature of the disorder, and a bibliography of relevant papers. In the classroom, OMIM and its links are valuable resources for student projects and presentations.

Ancillary Materials

The ancillary materials that accompany this edition are designed to aid student learning as well as to assist the instructor in preparing lectures and examinations and in keeping abreast of the latest developments in the field. Instructor materials are available to qualified adopters. Please consult your local Cengage Learning sales representative for details. You may also visit the Brooks/Cole biology site at ***www.cengage.com/biology*** to see samples of these materials, request a desk copy, locate your sales representative, or purchase a copy online.

Electronic Test Bank

Over 1,100 test items consisting of multiple-choice, true/false, fill-in-the-blank, and short-answer questions. Included in Microsoft® Word format on the PowerLecture DVD.

Online Instructor's Manual

Includes chapter outlines, chapter summary, teaching/learning objectives, definitions of in-text terms, teaching hints, and answers to in-text questions. Included in Microsoft® Word format on the PowerLecture DVD.

Study Guide

Chapter summaries, learning objectives, and key terms, along with multiple-choice, fill-in-the-blank, true/false, discussion, and case-study questions to help students with retention and better test results.

PowerLecture

This convenient tool makes it easy for you to create customized lectures. Each chapter includes the following features, all organized by chapter: lecture slides, all chapter art and photos, animations, videos, Instructor's Manual, Test Bank, Examview® testing software, and JoinIn polling and quizzing slides. This single disc places all the media resources at your fingertips.

The Brooks/Cole Biology Video Library, featuring BBC Motion Gallery

Looking for an engaging way to launch your lectures? The Brooks/Cole series features short high-interest segments: Bone Marrow as a New Source for the Creation of Sperm, Repairing Damaged Hearts with Patients' Own Stem Cells, Genetically Modified Virus Used to Fight Cancer, and much more.

CengageNOW

Students: Save time, learn more, and succeed in the course with CengageNOW, an online set of resources (including Personalized Study Plans) that gives you the choices and tools you need to study smarter and get the grade. You will have access to hundreds of animations that clarify the illustrations in the text, videos, and quizzing to test your knowledge. You can also access live online tutoring from an experienced biology instructor. New to this edition are pop-up tutors that help clarify key topics by providing short video explanations. Get started today!

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Biology CourseMate

Cengage Learning's Biology CourseMate brings course concepts to life with interactive learning, study, and exam preparation tools that support the printed textbook or the included eBook. With CourseMate, professors can use the included Engagement Tracker to assess student preparation and engagement. Use the tracking tools to see progress for the class as a whole or for individual students.

Premium eBook

This complete online version of the text is integrated with multimedia resources and special study features, providing the motivation that so many students need for studying and the interactivity they need for learning. New to this edition are pop-up tutors that help clarify key topics by providing short video explanations.

A Problem-Based Guide to Basic Genetics

Provides students with a thorough and systematic approach to solving transmission genetics problems, along with numerous solved problems and practice problems. Written and illustrated by Donald Cronkite of Hope College.

Virtual Biology Laboratories: Genetics and Genetics 2 (Pedigree Analysis) Modules

These "virtual" online experiments expose students to the tools used in modern biology, support and illustrate lecture material, and allow students to "do" science by performing experiments, acquiring data, and using the data to explain biological phenomena.

Gene Discovery Lab

This is a CD-ROM lab manual that provides a virtual laboratory experience for the student in doing experiments in molecular biology. It includes experiments that use nine of the most common molecular techniques in biology, an overview of scientific method and experimental techniques, and Web links to provide access to data and other resources.

Acknowledgments

Over the course of ten editions, many reviewers, including those who helped with this edition have given their time to improve the pedagogy, presentation of concepts, and ways of inspiring students. From edition to edition, a number of reviewers went to extraordinary lengths to keep my ideas and writing on the straight and narrow path and to make suggestions that have greatly improved the book. George Hudock of Indiana University, H. Eldon Sutton of the University of Texas, and Werner Heim of Colorado College generously gave me access to their collective wisdom, and helped me learn and re-learn many of the nuances involved in writing about genetics. I am most grateful for their efforts.

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Jan Trybula, *State University of New York, Potsdam*
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Elizabeth T. Wood, *University of Arizona*
Denise Woodward, *Pennsylvania State University*

At Brooks/Cole, it was once again a pleasure to work with Peggy Williams, Senior Acquisitions Editor. Her vision about how to implement and increase the pedagogical value of texts has strengthened and enhanced the book. Tanya Nigh was the project manager who pulled together all the resources and people needed to put this edition together. The developmental editor, Liana Sarkisian, oversaw the preparation of this edition. Her attention to detail and gentle nudging kept the project on schedule.

Lauren Oliveira coordinated the Web-based features of the book. The layout was designed by RHDG, and the cover design was done by Jane Hambleton at Cuttriss & Hambleton. Photo research was handled by Scott Rosen of Bill Smith Group. His persistence in finding the right photo is evident throughout the text.

Christopher Black at Lachina Publishing Services eased the book through all the twists and turns along the way.

Contacting the Author

I welcome questions and comments from faculty and students about the book or about questions and issues related to human genetics. Please contact me at: cummings.chicago@gmail.com.

Michael R. Cummings

Human Heredity

1 A Perspective on Human Genetics

CHAPTER OUTLINE

1.1 Mining Medical Records to Find Disease Genes

1.2 Genetics Is the Key to Biology

1.3 What Are Genes and How Do They Work?

Exploring Genetics Genetic Disorders in Culture and Art

1.4 How Are Genes Transmitted from Parents to Offspring?

1.5 How Do Scientists Study Genes?

1.6 Has Genetics Affected Social Policy and Law?

Exploring Genetics Genetics, Eugenics, and Nazi Germany

1.7 What Impact Is Genomics Having?

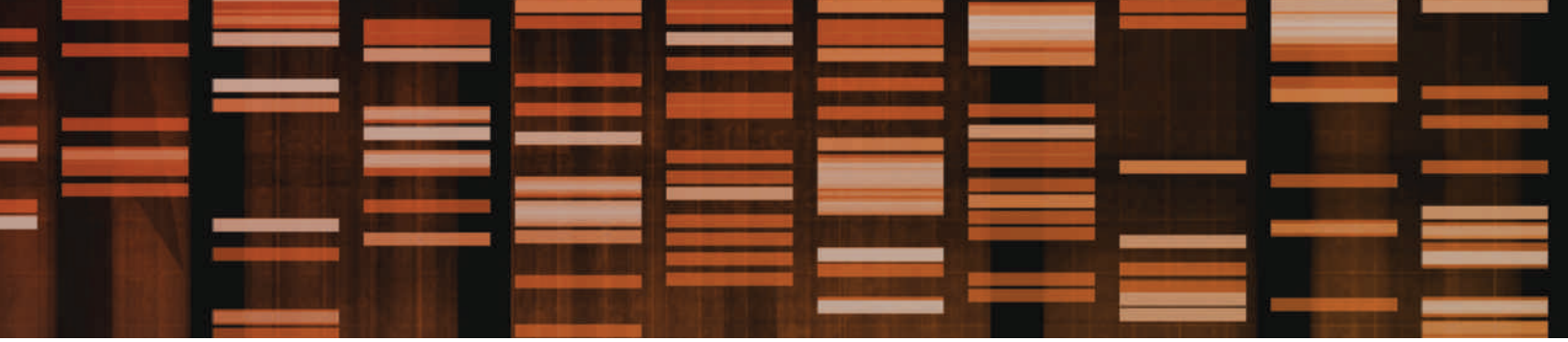
1.8 What Choices Do We Make in the Era of Genomics and Biotechnology?

1.1 Mining Medical Records to Find Disease Genes

About 15 years ago, Iceland passed a law allowing a biotech company, deCODE, to access and organize the medical records of all residents into a Health Sector database. The unusual step of allowing confidential medical records to be examined by a public corporation was part of a deCODE project to identify genes that predispose to complex disorders, such as diabetes and heart disease. deCODE compiled the genealogies of the approximately 800,000 Icelanders who have ever lived there since the colonization of the island in the ninth and tenth centuries and set up a bank of blood and tissue samples (for DNA extraction) provided by patients. These resources are powerful tools in the hunt for disease-causing genes. The law grants the company the right to sell this information (and the DNA samples) to third parties—including the research labs of pharmaceutical companies—with the hope that once disease genes are identified, diagnostic tests and therapies will follow quickly.

Why Iceland? Among the nations of the world, Iceland has one of the smallest and most genetically isolated populations, as well as very little genetic variation among members of the population. Small founding populations came to Iceland in the ninth and tenth centuries, and until about 50 years ago, Iceland was almost completely isolated from outside immigration. Plague (in the 1400s) and volcanoes (in the 1700s)

A crowd in Iceland reflects its narrow range of genetic diversity.



decimated the population, further reducing genetic variation. The present-day population of 290,000 inhabitants has a remarkably similar set of genes, making it easy for gene hunters to identify disease genes.

Why the controversy? Opponents point out that the privacy provisions of the law are inadequate and may violate the ethical principle that health records must be kept confidential. Abuses and misunderstandings may affect employment, insurance, and even marriage. In addition, critics question whether a single company should have exclusive rights to medical information and whether the Icelandic population will derive health benefits from this arrangement.

deCODE has now analyzed the medical records and DNA from over 100,000 individuals (more than half the country's adult population) and identified genetic risk factors for dozens of complex diseases, including cardiovascular disease, asthma, stroke, osteoporosis, and cancer. The company has developed and marketed DNA-based tests and genome scans for diseases including type II diabetes, cardiovascular disease, glaucoma, and several forms of cancer. In spite of their success in identifying mutations that cause complex diseases, deCode filed for bankruptcy in November 2009. The problem is that many of these diseases are too complex; each disease is caused by mutations in a large number of different genes, each of which has only a very small effect. Because each mutation is rare, there is little reason to develop diagnostic tests or drugs to treat such a small number of cases. In January 2010, deCode was sold to Saga Investments, which plans to redirect the company's research program and drop efforts to develop drugs based on its discoveries.

In spite of deCODE's problems, similar projects have sprung up in Great Britain, Estonia, Latvia, Singapore, and the Kingdom of Tonga. In the United States, programs using medical records and DNA samples from tens of thousands of individuals are under way at several research centers.

Underlying all these programs are serious bioethical issues centered on privacy, informed consent, commercialization, and corporate profit—profit derived from information gained through the medical records of and DNA from individuals. These important issues are at the heart of discussions and disagreements arising from the application of genetic technology. Scientists, physicians, politicians, and the public are debating the control and use of genetic information as well as the role of policy, law, and society in decisions about the use of genetic technology.

As research programs to identify genes associated with complex disorders proliferate, more and more people are being asked to participate in this work by donating a DNA sample and providing access to their medical records. If you were approached by a major medical center to be part of such a study, would you have privacy concerns about how your information would be used and who would have access to it? What do you know about U.S. laws designed to prevent genetic discrimination (GINA)? Do you think there is enough protection available to prevent your genetic information from being used to deny you employment or insurance? Would you agree to participate in such a research program?

In the Genetics in Practice section at the end of the chapter, you can read about a case that illustrates some of the unexpected and unintended consequences that can arise when disease genes are found.

1.2 Genetics Is the Key to Biology

With gene-hunting research programs like deCODE's becoming common, as we begin this book, we might pause and remember that genetics is more than a laboratory science; unlike some other areas of science, genetics and biotechnology have a direct impact on society.

Genetics The scientific study of heredity.

Trait Any observable property of an organism.

Perhaps as the first step in studying human genetics, we should ask, what *is* genetics? As a working definition, we can say that **genetics** is the scientific study of heredity. Like all definitions, this leaves a lot unsaid. To be more specific, what geneticists do is study how **traits** (such as eye color and hair color) and diseases (such as cystic fibrosis and sickle cell anemia) are passed from generation to generation. They also study the molecules that make up genes and gene products, as well as the way in which genes are turned on and off. Some geneticists study why variants of some genes occur more frequently in one population than in others. Other geneticists work in industry to develop products for agricultural and pharmaceutical firms. This work is part of the biotechnology industry, which is now a multi-billion-dollar component of the U.S. economy.

In a sense, genetics is the key to all of biology; genes control what cells look like and what they do, as well as how babies develop and how we reproduce. An understanding of what genes are, how they are passed from generation to generation, and how they work is essential to our understanding of all life on Earth, including our species, *Homo sapiens*.

In the chapters that follow, we will ask and answer many questions about genetics: How are genes passed from parents to their children? What are genes made of? Where are they located? How do they encode products called proteins, and how do proteins create the differences among individuals that we can see and study? Because this book is about human genetics, we will use human genetic disorders as examples of inherited traits (see Exploring Genetics: Genetic Disorders in Culture and Art). We will also examine how genetic knowledge and genetic technology interact with and shape many of our social, political, legal, and ethical institutions and policies.

Almost every day, the media carry a story about human genetics. These stories may report the discovery of a gene responsible for a genetic disorder, a controversy about genetic testing or a debate on the wisdom of genetically modifying our children. In many cases, as we will see, technology is far ahead of public policy and laws. To make informed decisions about genetics and biotechnology in your personal and professional life, you will need to have a foundation based on a knowledge of genetics. In the rest of this chapter, we will preview some of the concepts of human genetics that will be covered in more detail later in the book and introduce some of the social issues and controversies generated by genetic research. Many of these concepts and issues will be explored in more detail in the chapters that follow.

1.3 What Are Genes and How Do They Work?

Gene The fundamental unit of heredity and the basic structural and functional unit of genetics.

DNA A helical molecule consisting of two strands of nucleotides that is the primary carrier of genetic information.

Simply put, a **gene** is the basic structural and functional unit of genetics. In molecular terms, a gene is a string of chemical subunits (nucleotides) in a **DNA** molecule (Figure 1.1). (DNA is shorthand for deoxyribonucleic acid.) There are four different nucleotides in DNA, each composed of a sugar, a base, and a phosphate group. The nucleotides are abbreviated as single letters:

- A for adenine
- T for thymine
- G for guanine
- C for cytosine

Combinations of these four nucleotides in the form of genes store all the genetic information carried by an individual. The nucleotide sequence encoded in a gene defines the

Genetic Disorders in Culture and Art

It is difficult to pinpoint the time in history when the inheritance of specific traits in humans was first recognized. Descriptions of people with heritable disorders appear in myths and legends of many cultures. In some of these cultures, assigned social roles—from prophets and priests to kings and queens—were hereditary. The belief that certain traits were heritable helped shape the development of many social customs.

Steve Cole/Getty Images

In some societies, the birth of a deformed child was regarded as a sign of impending war or famine. Clay tablets excavated from Babylonian ruins record more than 60 types of birth defects, along with the dire consequences thought to accompany such births. Later societies, from Roman to those of eighteenth-century Europe, regarded malformed individuals (such as dwarfs) as curiosities rather than figures of impending doom; they were highly prized by royalty as courtiers and entertainers.

Over the millennia, artists have portrayed both famous and anonymous individuals with genetic disorders in paintings, sculptures, and other forms of the visual arts. These portrayals are detailed, highly accurate, and easily recognizable today. In fact, across time, culture, and artistic medium, affected individuals in these portraits often resemble each other more closely than they do their siblings, peers, or relatives. In some cases, the representations allow a disorder to be diagnosed at a distance of several thousand years.

Throughout the book, you will find fine-art representations of individuals with genetic disorders. These portraits represent a long-standing link between science and the arts in many cultures. They are not intended as a gallery of freaks or monsters but as a reminder that being human encompasses a wide range of conditions. A more thorough discussion of genetic disorders in art is in *Genetics and Malformations in Art* by J. Kunze and I. Nippert, published by Grosse Verläg, Berlin, 1986.

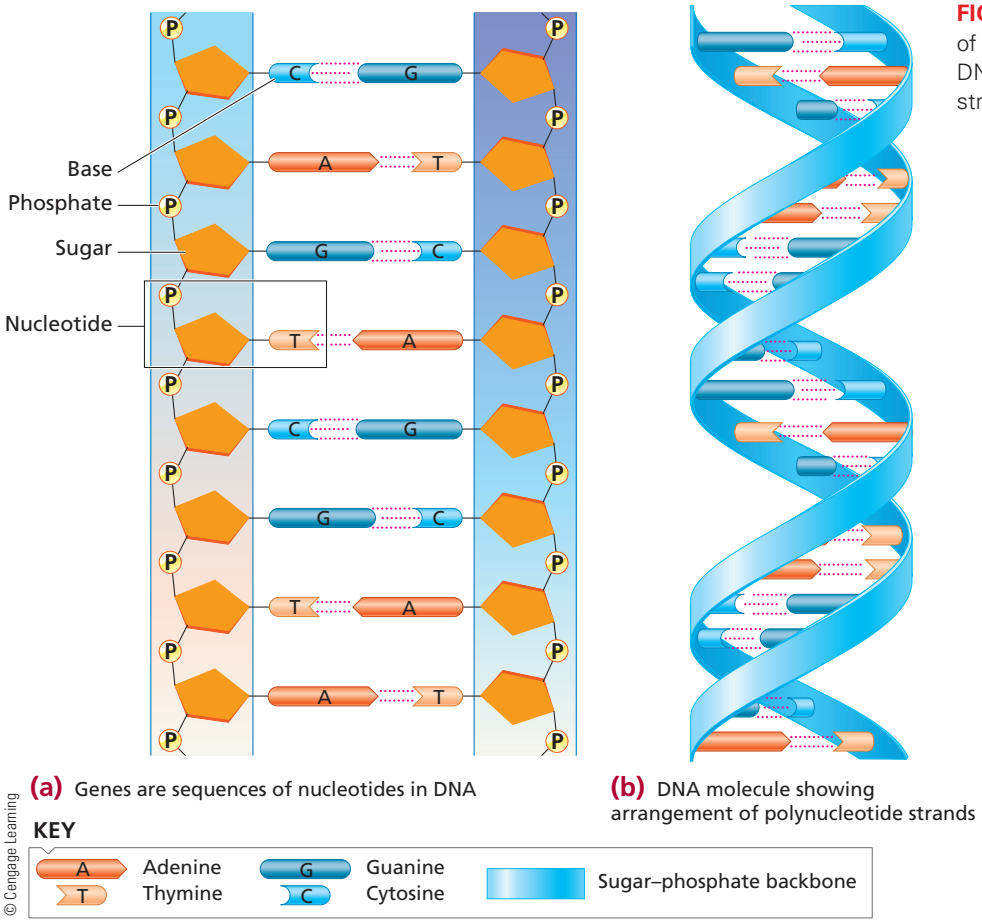
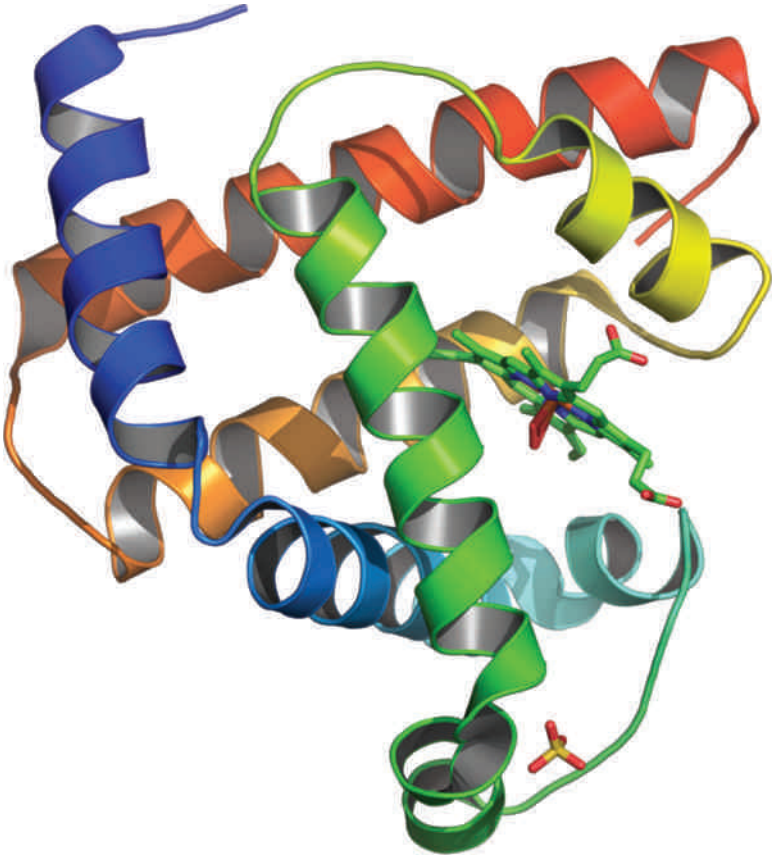


FIGURE 1.1 (a) Genes are composed of a sequence of nucleotides in a DNA molecule. (b) The double helix structure of DNA.



Carl Fürstenberg

FIGURE 1.2 The three-dimensional structure of a protein.

chemical subunits (amino acids) that make up gene products (proteins). When a gene is activated, its stored information is decoded and used to make a polypeptide, which folds into a three-dimensional shape and becomes a functional protein (Figure 1.2). The action of proteins produces characteristics we can see (such as eye color or hair color) or measure (blood proteins or height). Understanding how different proteins are produced and how they work in the cell are important parts of genetics. We will cover these topics in Chapters 9 and 10.

We can also define genes by their properties. Genes are copied (replicated), they undergo change (mutate), they are expressed (they can be switched on or off), and they can move from one chromosome to another (recombine). In later chapters, we will explore these properties and see how they are involved in genetic diseases.

National Library of Medicine

FIGURE 1.3 Gregor Mendel, the Augustinian monk whose work on pea plants provided the foundation for genetics as a scientific discipline.

1.4 How Are Genes Transmitted from Parents to Offspring?

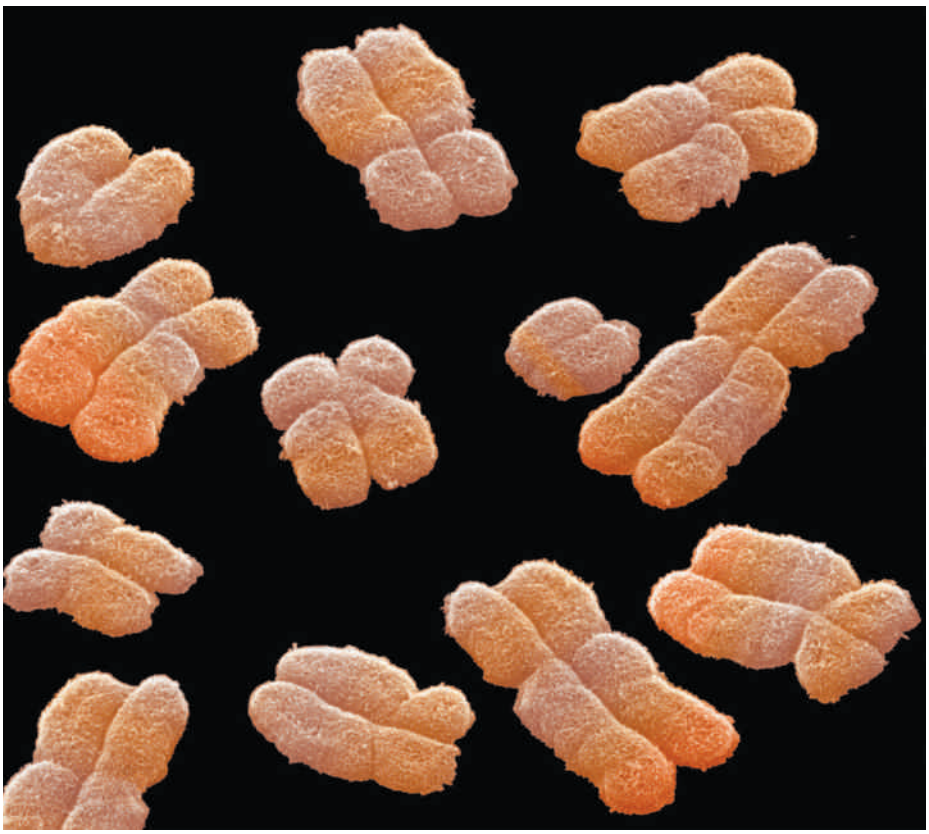
Thanks to the work of Gregor Mendel (Figure 1.3), a European monk who lived in the nineteenth century, we know how genes are passed from parents to offspring in plants and animals, including humans. When Mendel began his experiments, many people thought that traits carried by parents were blended together in their offspring. According to this idea, crossing a plant with red flowers and one with white flowers should produce plants with pink flowers (the pink color is a blend of red and white). Mendel's experiments on pea plants showed that genes are passed intact from generation to generation and that traits are not blended. As we will see, however, things are not always simple. There are cases in which crossing plants with red flowers and plants with white flowers *does* produce plants with pink flowers. We will discuss these cases

in Chapter 3 and show that crosses between plants with red flowers and plants with white flowers that produce plants with pink flowers do not contradict the principles of inheritance discovered by Mendel.

Working at a monastery in what is now the Czech Republic, Mendel conducted research on the inheritance of traits in pea plants for more than a decade. He chose parental plants that each had a different distinguishing characteristic, called a trait. For example, Mendel bred tall pea plants with short pea plants. Plant height is the trait in this case and has two variations: tall and short. He also bred plants carrying green seeds with plants having yellow seeds. In this work, seed color is the trait; green and yellow are the variations of the trait he studied. In these breeding experiments, he wanted to see how seed color was passed from generation to generation.

Mendel kept careful records of the number and type of traits present in each generation. He also recorded the number of individual plants that carried each trait. He discovered patterns in the way traits were passed from parent to offspring through several generations. On the basis of those patterns, Mendel developed clear ideas about how traits are inherited. He concluded that traits such as plant height and flower color are passed from generation to generation by "factors" that are passed from parent to offspring. What he called "factors" we now call genes. Mendel reasoned that each parent carries two genes (a gene pair) for a specific trait (flower color, plant height, etc.) but that each parent contributes only one of those genes to its offspring; otherwise, the number of genes for a trait would double in each generation and soon reach astronomical numbers.

Mendel proposed that the two copies of a gene separate from each other during the formation of egg and sperm. As a result, only one copy of each gene is present in a sperm or egg. When an egg and sperm fuse at fertilization, the genes from the mother and father become members of a new gene pair in the offspring. In the mid-twentieth century, researchers discovered that genes are made of DNA and that this molecule is part of cellular structures known as chromosomes. Chromosomes (Figure 1.4) are found in the nucleus of human cells and other higher organisms. As we will see in Chapter 2, the separation of genes during the formation of the sperm and egg and the reunion



Andrew Syred/Photo Researchers, Inc.

FIGURE 1.4 Replicated human chromosomes as seen by scanning electron microscopy.

Transmission genetics The branch of genetics concerned with the mechanisms by which genes are transferred from parent to offspring.

Pedigree analysis The construction of family trees and their use to follow the transmission of genetic traits in families. It is the basic method of studying the inheritance of traits in humans.

Cytogenetics The branch of genetics that studies the organization and arrangement of genes and chromosomes by using the techniques of microscopy.

Karyotype A complete set of chromosomes from a cell that has been photographed during cell division and arranged in a standard sequence.

Molecular genetics The study of genetic events at the biochemical level.

Recombinant DNA technology A series of techniques in which DNA fragments from an organism are linked to self-replicating vectors to create recombinant DNA molecules, which are replicated or cloned in a host cell.

Clones Genetically identical molecules, cells, or organisms, all derived from a single ancestor.

Gene therapy Procedure in which normal genes are transplanted into humans carrying defective copies, as a means of treating genetic diseases.

of genes at fertilization is explained by the behavior of chromosomes in a form of cell division called meiosis.

When Mendel published his work on the inheritance of traits in pea plants (discussed in Chapter 3), there was no well-accepted idea of how traits were transmitted from parents to offspring; his evidence changed that situation. To many, Mendel was the first geneticist and the founder of genetics, a field that has expanded in numerous directions in the last 125 years. If you want to read more about the beginnings of genetics, the story of Mendel's work is told in an engaging book entitled *The Monk in the Garden: The Lost and Found Genius of Gregor Mendel, the Father of Genetics* by Robin M. Henig.

1.5 How Do Scientists Study Genes?

Ideas that form the foundation of genetics were discovered by studying many different organisms, including bacteria, yeast, insects, and plants, as well as humans. Because genetic mechanisms (and often genes) are the same across species, discoveries made in one organism (such as yeast) can be applied to other species, including humans. This close genetic relationship allows researchers to study human genetic disorders using experimental organisms, including insects, yeast, and mice. Although geneticists study many different species, they use a relatively small set of investigative methods, some of which are outlined in the following section.

Some basic methods in genetics.

The most basic approach studies the pattern of inheritance as traits are passed from generation to generation; this is called **transmission genetics** (Chapters 3 and 4). Using experimental organisms, geneticists study how traits such as height, eye color, flower color, and so on, are passed from parents to offspring. These experimental results are analyzed to establish how a trait is inherited. As we discussed in an earlier section, Gregor Mendel did the first significant work in transmission genetics, using pea plants as his experimental organism. His methods form the foundation of transmission genetics—methods that are still used today.

To study the inheritance of traits in humans, a more indirect method called **pedigree analysis** is used. Pedigree analysis begins by reconstructing the pattern of inheritance generated by a trait as it passes through several generations. These results are used to determine how a trait is inherited and to establish the risk of having affected children (Figure 1.5). Pedigrees are constructed from information obtained from interviews, medical files, letters, diaries, photographs, and family records.

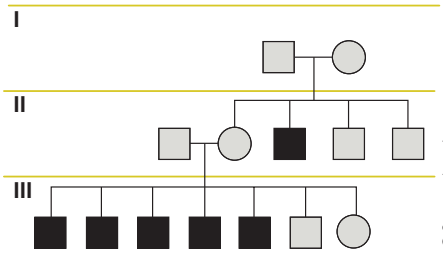


FIGURE 1.5 A pedigree represents the inheritance of a trait through several generations of a family. In this pedigree, males are symbolized by squares, females by circles. Darker symbols indicate those expressing the trait being studied; lighter symbols indicate unaffected individuals.

Cytogenetics is a branch of genetics that studies chromosome number and structure (discussed in Chapter 6). At the beginning of the twentieth century, observations on chromosome behavior were used to propose (correctly) that genes are located on chromosomes. Cytogenetics is one of the most important investigative approaches in human genetics and is used, among other things, to map genes and study chromosome structure and abnormalities. In clinical settings, cytogeneticists prepare **karyotypes** (Figure 1.6), standardized arrangements of chromosomes that are used to diagnose or rule out certain genetic disorders. In a karyotype, chromosomes are arranged by size, shape, and other characteristics that we will describe in Chapter 6.

A third approach, **molecular genetics**, has had the greatest impact on human genetics over the last several decades. Molecular genetics uses **recombinant DNA technology** to identify, isolate, produce **clones** (multiple copies), and analyze genes. These methods have greatly advanced our knowledge of how genes are organized and how they work at the molecular level. This technology is used for prenatal diagnosis of genetic disorders and in **gene therapy** to transfer human genes as a

treatment for genetic disorders. Cloned genes also can be transferred between individuals and between species to produce transgenic organisms. Transgenic organisms (also called genetically modified organisms—GMOs) are used in laboratory research, agriculture, and the pharmaceutical industry.

Recombinant DNA technology was used in the Human Genome Project to sequence the human **genome**, the complete set of genetic information we all carry, and has generated a new field of genetics called **genomics**. Scientists working in genomics use information from genome projects to study the origin, function, and evolution of genes and their interactions. New genomics technology is now being used to identify the genetic components of complex diseases such as diabetes, obesity, cardiovascular disease, and neurological disorders (including Alzheimer and Parkinson's) and is revolutionizing the study of human genetics.

The development and use of recombinant DNA technology has generated debate about the social, legal, and ethical aspects of genetics, including the genetic modification of plants and animals, the use of genetic testing for employment and insurance, and the modification of humans by gene therapy.

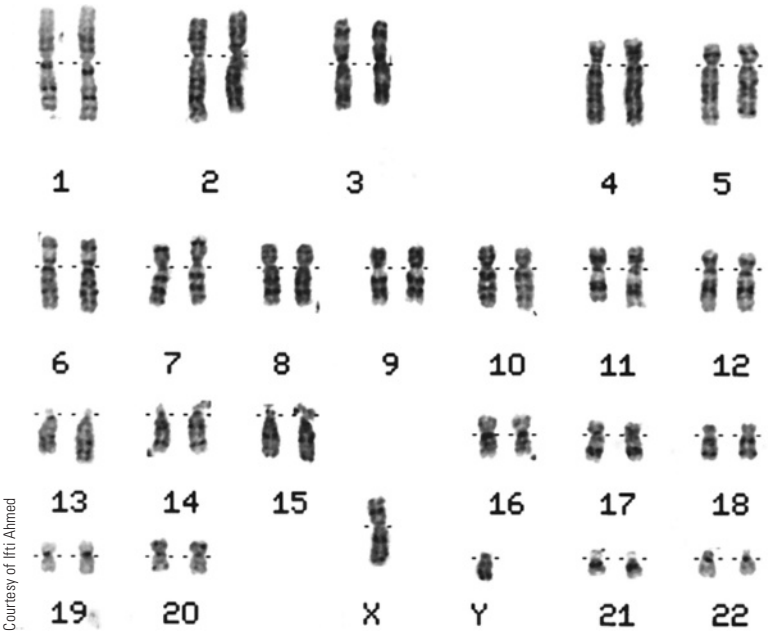


FIGURE 1.6 A karyotype arranges the chromosomes in a standard format so that they can be analyzed for abnormalities. This karyotype is that of a normal male.

A fourth approach studies the distribution of genes in populations. Population geneticists are interested in the forces that change the frequency of genes in a population over many generations and the way those changes are involved in evolution. **Population genetics** defines how much genetic variation exists in populations and how forces such as migration, population size, and natural selection change this variation. The coupling of population genetics with genomic technology has helped us understand the evolutionary history of our species and the migrations that distributed humans across Earth. This technology has been used to develop methods of DNA fingerprinting and DNA identification, techniques widely used in paternity testing and forensics.

Genome The set of DNA sequences carried by an individual.

Genomics The study of the organization, function, and evolution of genomes.

Population genetics The branch of genetics that studies inherited variation in populations of individuals and the forces that alter gene frequency.

Genetics is used in basic and applied research.

Genetics is a discipline that crosses and recrosses the line between basic research and applied research, often blurring distinctions between the two. In general, scientists do basic research in laboratory and field settings to understand how something works or why it works the way it does. In basic research, there is no immediate goal of solving a practical problem or making a commercial product; knowledge itself is the goal. In turn, the results of basic research generate new ideas and more basic research. In this way, we gain detailed information about how things work inside cells, why animals behave in certain ways, and how plants turn carbon dioxide into sugar. Among other things, basic research in genetics has provided us with details about genes, how they work, and, more importantly, what happens when they don't work properly.

Applied research is usually done to solve a practical problem or turn a discovery into a commercial service or product. Applied research uses basic methods such as transmission genetics to study the way in which a trait is inherited, but it also uses biotechnology to make products such as transgenic organisms, medicines, and nutritionally enhanced foods. In agriculture, applied genetic research has increased crop yields, lowered the fat content of pork, and created new forms of corn and soybeans that are disease resistant. In medicine, new diagnostic tests, the synthesis of customized proteins for treating disease, and the production of vaccines are just a few examples of applied genetic research.