GLOBAL EDITION

Essentials of Genetics

NINTH EDITION

William S. Klug • Michael R. Cummings
Charlotte A. Spencer • Michael A. Palladino

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Brief Contents

ESSENTIALS *of* GENETICS

Ninth Edition
Global Edition

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Preface

Essentials of Genetics is written for courses requiring a text that is briefer and less detailed than its more comprehensive companion, *Concepts of Genetics*. While coverage is thorough and modern, *Essentials* is written to be more accessible to biology majors, as well as to students majoring in a number of other disciplines, including agriculture, animal husbandry, chemistry, nursing, engineering, forestry, psychology, and wildlife management. Because *Essentials of Genetics* is shorter than many other texts, it is also more manageable in one-quarter and trimester courses.

Goals

In this edition of *Essentials of Genetics*, the two most important goals have been to introduce pedagogic innovations that enhance learning and to provide carefully updated, highly accessible coverage of genetic topics of both historical and modern significance. As new tools and findings of genetics research continue to emerge rapidly and grow in importance in the study of all subdisciplines of biology, instructors face tough choices about what content is truly essential as they introduce the discipline to novice students. We have thoughtfully revised each chapter in light of this challenge, by selectively scaling back the detail or scope of coverage in the more traditional chapters in order to provide expanded coverage and broader context for the more modern, cutting-edge topics. Our aim is to continue to provide efficient coverage of the fundamental concepts in transmission and molecular genetics that lay the groundwork for more in-depth coverage of emerging topics of growing importance—in particular, the many aspects of the genomic revolution that is already relevant to our day-to-day lives as well as the relatively new findings involving epigenetics and noncoding RNAs.

While we have adjusted this edition to keep pace with changing content and teaching practices, we remain dedicated to the core principles that underlie this book. Specifically, we seek to

- Emphasize concepts rather than excessive detail.
- Write clearly and directly to students in order to provide understandable explanations of complex analytical topics.
- Emphasize problem solving, thereby guiding students to think analytically and to apply and extend their knowledge of genetics.
- Provide the most modern and up-to-date coverage of this exciting field.
- Propagate the rich history of genetics that so beautifully elucidates how information is acquired as the discipline develops and grows.
- Create inviting, engaging, and pedagogically useful figures enhanced by meaningful photographs to support student understanding.
- Provide outstanding interactive media support to guide students in understanding important concepts through animations, tutorial exercises, and assessment tools.

The above goals serve as the cornerstone of *Essentials of Genetics*. This pedagogic foundation allows the book to accommodate courses with many different approaches and lecture formats. While the book presents a coherent table of contents that represents one approach to offering a course in genetics, chapters are nevertheless written to be independent of one another, allowing instructors to utilize them in various sequences.

New to This Edition

In addition to streamlining core chapters and updating information throughout the text, key improvements to this edition include three additional chapters in the Special Topics in Modern Genetics unit, end of chapter questions in Special Topics chapters, and a new feature exploring scientists' evolving understanding of the concept of the gene.

- **Special Topics in Modern Genetics** We have been pleased with the popular reception to the Special Topics in Modern Genetics chapters. Our goal has been to provide abbreviated, cohesive coverage of important topics in genetics that are not always easily located in textbooks. Professors have used these focused, flexible chapters in a multitude of ways: as the backbone of lectures, as inspiration for student assignments outside of class, and as the basis of group assignments and presentations.

  New to this edition are chapters on topics of great significance in genetics:

  - Emerging Roles of RNA
  - Genetically Modified Foods
  - Gene Therapy

  For all Special Topics chapters, we have added a series of questions that send the student back into the chapter to review key ideas or that provide the basis of personal contemplations and group discussions.
- **Evolving Concept of the Gene** Also new to this edition is a short feature, integrated in appropriate chapters, that highlights how scientists' understanding of a gene has changed over time. Since we cannot see genes, we must infer just what this unit of heredity is, based on experimental findings. By highlighting how scientists' conceptualization of the gene has advanced over time, we aim to help students appreciate the process of discovery

that has led to an ever more sophisticated understanding of hereditary information.

- **Concepts Question** A new feature, found as the second question in the Problems and Discussion Questions at the end of each chapter, asks the student to review and comment on common aspects of the Key Concepts, listed at the beginning of each chapter. This feature places added emphasis on our pedagogic approach of conceptual learning.
- **MasteringGenetics** This powerful online homework and assessment program guides students through complex topics in genetics, using in-depth tutorials that coach students to correct answers with hints and feedback specific to their misconceptions. New content for *Essentials of Genetics* includes a robust library of Practice Problems—found only in MasteringGenetics—that are like end of chapter questions in scope and difficulty. These questions include wrong answer feedback specific to a student's error, helping build students' problem-solving and critical thinking skills.

New and Updated Topics

While we have revised each chapter in the text to present the most current findings in genetics, below is a list of some of the most significant new and updated topics present in this edition.

Ch. 1: Introduction to Genetics • New chapter introduction vignette emphasizing translational medicine

Ch. 2: Mitosis and Meiosis • Updated coverage of kinetechore assembly and the concept of disjunction • Expanded coverage of checkpoints in cell cycle regulation

Ch. 4: Modification of Mendelian Ratios • New section on mitochondria, human health, and aging

Ch. 5: Sex Determination and Sex Chromosomes • Updated coverage on paternal age effects (PAEs) in humans • New content regarding the primary sex ratio in humans

Ch. 6: Chromosome Mutations • New information on Fragile X Syndrome and the *FMRI* gene • New information regarding gene families as linked to gene duplications

Ch. 7: Linkage and Chromosome Mapping in Eukaryotes • Introduction of "sequence maps" in humans based on the use of DNA markers

Ch. 10: DNA Replication and Recombination • Updated coverage of DNA Pol III holoenzyme • Revised figures involving DNA synthesis • New coverage of the initiation of bacterial DNA synthesis • New information on DNA recombination • New coverage of replication of telomeric DNA • Revision of the GTS essay: Telomeres: The Key to Immortality

Ch. 11: Chromosome Structure and DNA Sequence Organization • Updated coverage of chromatin remodeling • New information on H3 histone substitution in centromeric DNA • New coverage regarding the transcript of Alu sequences

Ch. 12: The Genetic Code and Transcription • Extended coverage of promoter elements in eukaryotes • Introduction of the process of RNA editing • Revision of figures involving ribosomes and transcription

Ch. 13: Translation and Proteins • Revision of all ribosome figures • New information on initiation, elongation during translation in eukaryotes

Ch. 14: Gene Mutation, DNA Repair, and Transposition • Reorganization and updates for mutation classification • Updated coverage of xeroderma pigmentosum and DNA repair mechanisms

Ch. 15: Regulation of Gene Expression • Updated coverage of gene regulation by riboswitches • Expanded coverage of chromatin modifications • Updated coverage of promoter and enhancer structures and functions • Updated coverage of the mechanisms of transcription activation and repression

Ch. 16: The Genetics of Cancer • New coverage of the progressive nature of colorectal cancers • Revised and updated coverage of driver and passenger mutations

Ch. 17: Recombinant DNA Technology • Streamlined content on recombinant DNA techniques to deemphasize older techniques and focus on more modern methods • New figure on FISH • Expanded coverage on next-generation and third-generation sequencing • New section on gene-targeting approaches includes content and figures on gene knockout animals and transgenic animals • Revised PDQ content

Ch. 18: Genomics, Bioinformatics, and Proteomics • Updated content on the Human Microbiome Project • New content introducing exome sequencing • Updated content on personal genome projects • Revised and expanded coverage of the Encyclopedia of DNA Elements (ENCODE) Project • New figure on genome sequencing technologies • New Case Study on the microbiome as a risk factor for disease

Ch. 19: Applications and Ethics of Genetic Engineering and Biotechnology • New section on synthetic biology for bioengineering applications • New material and figure on deducing fetal genome sequences from maternal blood • Revised and updated content on prenatal genetic testing • Moved content on GM crops to ST 5 • Moved content on gene therapy to ST 6 • Updated discussion on synthetic genomes • Revised and streamlined content on DNA microarrays given the changing role of microarrays in gene testing (relative to whole-genome, exome, and RNA sequencing) • New content on genetic analysis by sequencing individual

genomes for clinical purposes and single-cell sequencing • Revised ethics section to include additional discussion on the analysis of whole-genome sequences, preconception testing, DNA patents, and destiny predictions • Major revision of end of chapter questions • New GTS essay on the privacy and anonymity of genomic data • New Case Study on genetically modified bacteria for cancer treatment

Ch. 20: Developmental Genetics • New introductory section on the key steps to the differentiated state • New section on the role of binary switch genes and regulatory programs in controlling organ formation, including new figures

Ch. 21: Quantitative Genetics and Multifactorial Traits • New section on limitations of heritability studies • Updated coverage of multifactorial genotypes and expanded coverage of the tomato genome and implications for future improvement in tomato strains • Revised coverage of eQTLS

Ch. 22: Population and Evolutionary Genetics • Revised and updated section on detecting genetic variation and the application of new technology to detect variation in DNA and in genomes • Extensively revised and updated section on the process of speciation • The section on use of phylogenetics to investigate evolutionary history has been improved and expanded with new examples • Information on human evolution has been completely revised and updated with new information about the genomics of extinct human species and their relationship to our species • Five new figures have been added throughout the chapter to accompany the added text

Special Topic 1: Epigenetics • Heavily revised section on imprinting • New ideas on the role of epigenetics in cancer accompany the coverage of the role of somatic mutation in cancer • New section on epigenetic modification of behavior in model organisms and humans

Special Topic 2: Emerging Roles of RNA • New chapter that focuses on the recently discovered functions of RNAs with an emphasis on noncoding RNAs • An introduction to CRISPR/Cas technology in gene editing • Explanation of mechanisms of microRNA and long noncoding RNA gene regulation • Discussion of extracellular RNAs in cell—cell communication and disease diagnosis • Coverage of RNA-induced transcriptional silencing

Special Topic 3: DNA Forensics • New coverage describing how DNA can be inadvertently transferred to a crime scene, leading to false arrests • New coverage of DNA phenotyping

Special Topic 4: Genomics and Personalized Medicine • New coverage on personal genomics and cancer, including a new story of one person's successful experience using "omics" profiling to select a personalized cancer treatment • Updated coverage of personalized medicine and disease diagnostics • Updated coverage of recent studies using "omics" profiles to predict and monitor disease states

Special Topic 5: Genetically Modified Foods • New chapter on genetically modified foods—the genetic technology behind them, the promises, debates, and controversies

Special Topic 6: Gene Therapy • New chapter on the modern aspects of gene therapy • Provides up-to-date applications of gene therapy in humans

Emphasis on Concepts

Essentials of Genetics focuses on conceptual issues in genetics and uses problem solving to develop a deep understanding of them. We consider a concept to be a cognitive unit of meaning that encompasses a related set of scientifically derived findings and ideas. As such, a concept provides broad mental imagery, which we believe is a very effective way to teach science, in this case, genetics. Details that might be memorized, but soon forgotten, are instead subsumed within a conceptual framework that is easily retained. Such a framework may be expanded in content as new information is acquired and may interface with other concepts, providing a useful mechanism to integrate and better understand related processes and ideas. An extensive set of concepts may be devised and conveyed to eventually encompass and represent an entire discipline—and this is our goal in this genetics textbook.

To aid students in identifying the conceptual aspects of a major topic, each chapter begins with a section called ***Chapter Concepts,*** which identifies the most important ideas about to be presented. Then, throughout each chapter, ***Essential Points*** are provided that establish the key issues that have been discussed. And in the ***How Do We Know?*** question that starts each chapter's problem set, students are asked to identify the experimental basis of important genetic findings presented in the chapter. As an extension of the learning approach in biology called "Science as a Way of Knowing," this feature enhances students' understanding of many key concepts covered in each chapter.

Collectively, these features help to ensure that students easily become aware of and understand the major conceptual issues as they confront the extensive vocabulary and the many important details of genetics. Carefully designed figures also support this approach throughout the book.

Emphasis on Problem Solving

Helping students develop effective problem-solving skills is one of the greatest challenges of a genetics course. The feature called ***Now Solve This,*** integrated throughout each chapter, asks students to link conceptual understanding in a more immediate way to problem solving. Each entry provides a problem for the student to solve that is closely related to the current text discussion. A pedagogic hint is

then provided to aid in arriving at the correct solution. All chapters conclude with ***Insights and Solutions,*** a popular and highly useful section that provides sample problems and solutions that demonstrate approaches useful in genetic analysis. These help students develop analytical thinking and experimental reasoning skills. Digesting the information in *Insights and Solutions* primes students as they move on to the lengthier ***Problems and Discussion Questions*** section that concludes each chapter. Here, we present questions that review topics in the chapter and problems that ask students to think in an analytical and applied way about genetic concepts. Problems are of graduated difficulty, with the most demanding near the end of each section. The addition of MasteringGenetics extends our focus on problem solving online, and it allows students to get help and guidance while practicing how to solve problems.

Continuing Features

The Ninth Edition has maintained a number of popular features that are pedagogically useful for students as they study genetics. Collectively, these create a platform that seeks to challenge students to think more deeply about, and thus understand more comprehensively, the information he or she has just finished studying.

- **Exploring Genomics** Appearing in numerous chapters, this feature illustrates the pervasiveness of genomics in the current study of genetics. Each entry asks students to access one or more genomics-related Web sites that collectively are among the best publicly available resources and databases. Students work through interactive exercises that ensure their familiarity with the type of genomic or proteomic information available. Exercises instruct students on how to explore specific topics and how to access significant data. Questions guide student exploration and challenge them to further explore the sites on their own. Importantly, *Exploring Genomics* integrates genomics information throughout the text, as this emerging field is linked to chapter content. This feature provides the basis for individual or group assignments in or out of the classroom.
- **Genetics, Technology, and Society Essays** Appearing in many chapters, this feature provides a synopsis of a topic related to a current finding in genetics that impacts directly on our current society. After each essay, a section entitled "Your Turn" appears in which questions are posed to students along with various resources to help answer them. This innovation provides yet another format to enhance classroom interactions.
- **Case Studies** This feature appears at the end of each chapter and provides the basis for enhanced classroom interactions. In each entry, a short scenario related to one of the chapter topics is presented, followed by several questions. These ask students to apply their newly acquired knowledge to real-life issues that may be explored in small-group discussions or serve as individual assignments.

For the Instructor

MasteringGenetics— http://www.masteringgenetics.com

MasteringGenetics engages and motivates students to learn and allows you to easily assign automatically graded activities. Tutorials provide students with personalized coaching and feedback. Using the gradebook, you can quickly monitor and display student results. MasteringGenetics easily captures data to demonstrate assessment outcomes. Resources include:

- In-depth tutorials that coach students with hints and feedback specific to their misconceptions.
- A new, robust library of **Practice Problems** offers more opportunities to assign challenging problems for student homework or practice. These questions include targeted wrong answer feedback to help students learn from their mistakes. They appear only in MasteringGenetics.
- An item library of assignable questions including end of chapter problems, test bank questions, and reading quizzes. You can use publisher-created prebuilt assignments to get started quickly. Each question can be easily edited to match the precise language you use.
- A gradebook that provides you with quick results and easy-to-interpret insights into student performance.

TestGen EQ Computerized Testing Software

Test questions are available as part of the TestGen EQ Testing Software, a text-specific testing program that is networkable for administering tests. It also allows instructors to view and edit questions, export the questions as tests, and print them out in a variety of formats.

For the Student

MasteringGenetics— http://www.masteringgenetics.com

Used by over a million science students, the Mastering platform is the most effective and widely used online tutorial, homework, and assessment system for the sciences. Perform better on exams with MasteringGenetics. As an instructor-assigned homework system, MasteringGenetics is designed to provide students with a variety of assessments to help them understand key topics and concepts and to build problem-solving skills. MasteringGenetics tutorials guide students through the toughest topics in genetics with self-paced tutorials that provide individualized coaching with hints and feedback specific to a student's individual misconceptions. Students can also explore MasteringGenetics' Study Area, which includes animations, the eText, *Exploring Genomics* exercises, and other study aids. The interactive eText allows students to access their text on mobile devices, highlight text, add study notes, review instructor's notes, and search throughout the text, 24/7.

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As these acknowledgments make clear, a text such as this is a collective enterprise. All of the above individuals deserve to share in any success this text enjoys. We want them to know that our gratitude is equaled only by the extreme dedication evident in their efforts. Many, many thanks to them all.

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1 Introduction to Genetics

CHAPTER CONCEPTS

- Genetics in the twenty-first century is built on a rich tradition of discovery and experimentation stretching from the ancient world through the nineteenth century to the present day.
- Transmission genetics is the process by which traits controlled by genes are transmitted through gametes from generation to generation.
- Mutant strains can be used in genetic crosses to map the location and distance between genes on chromosomes.
- The Watson–Crick model of DNA structure explains how genetic information is stored and expressed. This discovery is the foundation of molecular genetics.
- Recombinant DNA technology revolutionized genetics, was the foundation for the Human Genome Project, and has generated new fields that combine genetics with information technology.
- Biotechnology provides genetically modified organisms and their products that are used across a wide range of fields including agriculture, medicine, and industry.
- Model organisms used in genetics research are now utilized in combination with recombinant DNA technology and genomics to study human diseases.
- Genetic technology is developing faster than the policies, laws, and conventions that govern its use.

Newer model organisms in genetics include the roundworm *Caenorhabditis elegans*, the zebrafish, *Danio rerio*, and the mustard plant *Arabidopsis thaliana*.

Information from the Human Genome Project and other areas of genetics is now having far-reaching effects on our daily lives. For example, researchers and clinicians are using genomic information to improve the quality of medical care via **translational medicine,** a process in which genetic findings are directly "translated" into new and improved methods of diagnosis and treatment. One important area of focus is cardiovascular disease, which is the leading cause of death worldwide. One of the key risk factors for development of this condition is the presence of elevated blood levels of "bad" cholesterol (low-density lipoprotein cholesterol, or LDL cholesterol). Although statin drugs are effective in lowering the blood levels of LDL cholesterol and reducing the risk of heart disease, up to 50 percent of treated individuals remain at risk, and serious side-effects prevent many others from using these drugs.

To gain a share of the estimated $25 billion market for treatment of elevated LDL levels, major pharmaceutical firms are developing a new generation of more effective cholesterol-lowering drugs. However, bringing a new drug to market is risky. Costs can run over $1 billion, and many drugs (up to 1 in 3) fail clinical trials and are withdrawn. In the search for a new strategy in drug development, human genetics is now playing an increasingly vital role. Blood levels of LDL in a population vary over a threefold range, and about 50 percent of this variation is genetic. Although many genes are involved, the role of one gene, *PCSK9,* in controlling LDL levels is an outstanding example of how a genetic approach has been successful in identifying drug targets and improving the chance that a new drug will be successful. The rapid transfer of basic

research on *PCSK9* to drug development and its use in treating patients is a pioneering example of translational medicine.

Soon after the *PCSK9* gene was identified, several mutant forms of this gene were found to be associated with extremely high levels of LDL cholesterol, resulting in a condition called familial hypercholesterolemia (FH). When this work came to the attention of researchers in Texas, they wondered whether other mutations in *PCSK9* might have the opposite effect and drastically lower LDL cholesterol levels. To test this idea, they turned to data from the Dallas Heart Study, which collected detailed clinical information, including LDL levels and DNA samples, from 3500 individuals. DNA sequencing of the *PSCK9* gene from participants with extremely low LDL levels identified two mutations that reduced blood levels of LDL by 40 percent. Other work showed that carriers of these mutations had an 88 percent lower risk of heart disease.

The PCSK9 protein binds to LDL receptors on liver cells, moving the receptors into the cell where they are broken down. However, if the PCSK9 protein does not bind to an LDL receptor, the receptor is returned to the cell surface where it can remove more LDL from the bloodstream. Carriers of either of the two mutations have much lower PCSK9 protein levels. As a result, liver cells in these individuals have many more LDL receptors, which, in turn, remove more LDL from the blood. Using this information, several pharmaceutical firms have developed antibody-based drugs that bind to the PCKS9 protein and prevent its interaction with LDL receptors, which, in turn, lowers LDL cholesterol levels. Successful clinical trials show that LDL blood levels can be reduced by up to 70 percent in the test population, and one of these drugs has been shown to reduce heart attacks and strokes by 50 percent. Ongoing clinical trials are drawing to a close, and it is expected that these drugs will soon be available to treat elevated cholesterol levels.

The example of the *PCSK9* gene clearly demonstrates that coupling genetic research with drug development will play a critical and exciting role in speeding the movement of research findings into medical practice.

This introductory chapter provides an overview of genetics and a survey of the high points in its history and gives a preliminary description of its central principles and emerging developments. All the topics discussed in this chapter will be explored in far greater detail elsewhere in the book. This text will enable you to achieve a thorough understanding of modern-day genetics and its underlying principles. Along the way, enjoy your studies, but take your responsibilities as a novice geneticist very seriously.

1.1 Genetics Has a Rich and Interesting History

We don't know when people first recognized the hereditary nature of certain traits, but archaeological evidence (e.g., pictorial representations, preserved bones and skulls, and dried seeds) documents the successful domestication of animals and the cultivation of plants thousands of years ago by the artificial selection of genetic variants from wild populations. Between 8000 and 1000 B.C., horses, camels, oxen, and wolves were domesticated, and selective breeding of these species soon followed. Cultivation of many plants, including maize, wheat, rice, and the date palm, began around 5000 B.C. Such evidence documents our ancestors' successful attempts to manipulate the genetic composition of species.

During the Golden Age of Greek culture, the writings of the Hippocratic School of Medicine (500–400 B.C.) and of the philosopher and naturalist Aristotle (384–322 B.C.) discussed heredity as it relates to humans. The Hippocratic treatise *On the Seed* argued that active "humors" in various parts of the body served as the bearers of hereditary traits. Drawn from various parts of the male body to the semen and passed on to offspring, these humors could be healthy or diseased, with the diseased humors accounting for the appearance of newborns with congenital disorders or deformities. It was also believed that these humors could be altered in individuals before they were passed on to offspring, explaining how newborns could "inherit" traits that their parents had "acquired" in response to their environment.

Aristotle extended Hippocrates' thinking and proposed that the male semen contained a "vital heat" with the capacity to produce offspring of the same "form" (i.e., basic structure and capacities) as the parent. Aristotle believed that this heat cooked and shaped the menstrual blood produced by the female, which was the "physical substance" that gave rise to an offspring. The embryo developed not because it already contained the parts of an adult in miniature form (as some Hippocratics had thought) but because of the shaping power of the vital heat. Although the ideas of Hippocrates and Aristotle sound primitive and naive today, we should recall that prior to the 1800s neither sperm nor eggs had been observed in mammals.

1600–1850: The Dawn of Modern Biology

Between about 300 B.C. and A.D. 1600, there were few significant new ideas about genetics. However, between 1600 and 1850, major strides provided insight into the biological basis of life. In the 1600s, William Harvey proposed the theory of **epigenesis,** which states that an organism develops from the fertilized embryo by a succession of developmental events that eventually transform the embryo into an adult. The theory of epigenesis directly conflicted with the theory of **preformation,** which stated that the sperm or the fertilized egg contains a complete miniature adult, called a **homunculus** (Figure 1–1). Around 1830, Matthias Schleiden and Theodor Schwann proposed the **cell theory,** stating that all organisms are composed of basic structural units called cells,

FIGURE 1–1 Depiction of the homunculus, a sperm containing a miniature adult, perfect in proportion and fully formed.
(Hartsoeker, N. Essay de dioptrique Paris, 1694, p. 246. National Library of Medicine)

which are derived from preexisting cells. The idea of **spontaneous generation,** the creation of living organisms from nonliving components, was disproved by Louis Pasteur later in the century, and living organisms were then considered to be derived from preexisting organisms and to consist of cells.

In the mid-1800s the revolutionary work of Charles Darwin and Gregor Mendel set the stage for the rapid development of genetics in the twentieth and twenty-first centuries.

Charles Darwin and Evolution

With this background, we turn to a brief discussion of the work of Charles Darwin, who published *The Origin of Species* in 1859, describing his ideas about evolution. Darwin's geological, geographical, and biological observations convinced him that existing species arose by descent with modification from ancestral species. Greatly influenced by his voyage on the HMS *Beagle* (1831–1836), Darwin's thinking led him to formulate the theory of **natural selection,** which presented an explanation of the mechanism of evolutionary change. Formulated and proposed independently by Alfred Russel Wallace, natural selection is based on the observation that populations tend to contain more offspring than the environment can support, leading to a struggle for survival among individuals. Those individuals with heritable traits that allow them to adapt to their environment are better able to survive and reproduce than those with less adaptive traits. Over a long period of time, advantageous variations, even very slight ones, will accumulate. If a population carrying these inherited variations becomes reproductively isolated, a new species may result.

Darwin, however, lacked an understanding of the genetic basis of variation and inheritance, a gap that left his theory open to reasonable criticism well into the twentieth century. Shortly after Darwin published his book, Gregor Johann Mendel published a paper in 1866 showing how traits were passed from generation to generation in pea plants and offering a general model of how traits are inherited. His research was little known until it was partially duplicated and brought to light by Carl Correns, Hugo de Vries, and Erich Tschermak around 1900.

By the early part of the twentieth century, it became clear that heredity and development were dependent on genetic information residing in genes contained in chromosomes, which were then contributed to each individual by gametes—the so-called **chromosomal theory of inheritance.** The gap in Darwin's theory was closed, and Mendel's research has continued to serve as the foundation of genetics.

1.2 Genetics Progressed from Mendel to DNA in Less Than a Century

Because genetic processes are fundamental to life itself, the science of genetics unifies biology and serves as its core. The starting point for this branch of science was a monastery garden in central Europe in the late 1850s.

Mendel's Work on Transmission of Traits

Gregor Mendel, an Augustinian monk, conducted a decade-long series of experiments using pea plants. He applied quantitative data analysis to his results and showed that traits are passed from parents to offspring in predictable ways. He further concluded that each trait in the plant is controlled by a pair of factors (which we now call genes) and that during gamete formation (the formation of egg cells and sperm), members of a gene pair separate from each other. His work was published in 1866 but was largely unknown until it was cited in papers published by others around 1900. Once confirmed, Mendel's findings became recognized as explaining the transmission of traits in pea plants and all other higher organisms. His work forms the foundation for **genetics,** which is defined as the branch of biology concerned with the study of heredity and variation. Mendelian genetics will be discussed later in the text (see Chapters 3 and 4).

ESSENTIAL POINT

Mendel's work on pea plants established the principles of gene transmission from parent to offspring that serve as the foundation for the science of genetics. ■

The Chromosome Theory of Inheritance: Uniting Mendel and Meiosis

Mendel did his experiments before the structure and role of chromosomes were known. About 20 years after his work was published, advances in microscopy allowed researchers to identify chromosomes and establish that, in most eukaryotes, members of each species have a characteristic number of chromosomes called the **diploid number (2*n*)** in most of their cells. For example, humans have a diploid number of 46 (Figure 1–2). Chromosomes in diploid cells exist in pairs, called **homologous chromosomes.**

Researchers in the last decades of the nineteenth century also described chromosome behavior during two forms of cell division, **mitosis** and **meiosis.** In mitosis, chromosomes are copied and distributed so that each daughter cell receives a diploid set of chromosomes identical to those in the parental cell. Meiosis is associated with gamete formation. Cells produced by meiosis receive only one chromosome from each chromosome pair, and the resulting number of chromosomes is called the **haploid (*n*) number.** This reduction in chromosome number is essential if the offspring arising from the fusion of egg and sperm are to maintain the constant number of chromosomes characteristic of their parents and other members of their species.

Early in the twentieth century, Walter Sutton and Theodor Boveri independently noted that the behavior of chromosomes during meiosis is identical to the behavior of genes during gamete formation described by Mendel. For example, genes and chromosomes exist in pairs, and members of a gene pair and members of a chromosome pair separate from each other during gamete formation. Based on these parallels, Sutton and Boveri each proposed that genes are carried on chromosomes. They independently formulated the chromosome theory of inheritance, which states that inherited traits are controlled by genes residing on chromosomes faithfully transmitted through gametes, maintaining genetic continuity from generation to generation.

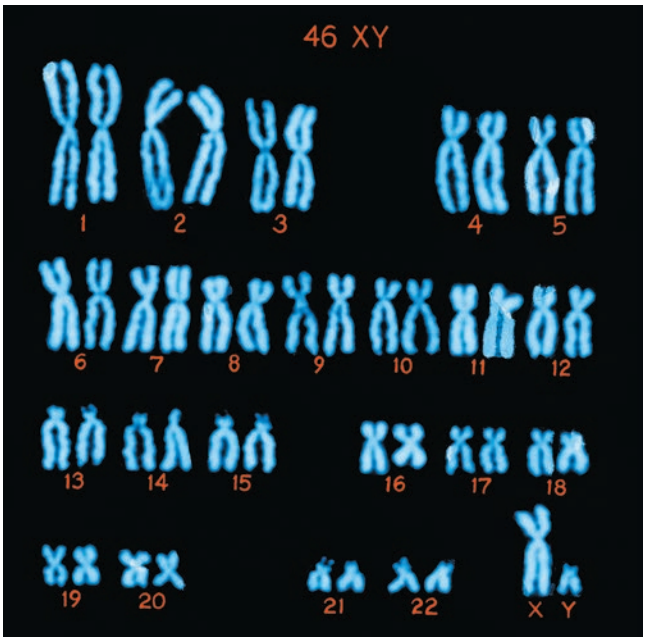


FIGURE 1–2 A colorized image of the human male chromosome set. Arranged in this way, the set is called a karyotype.

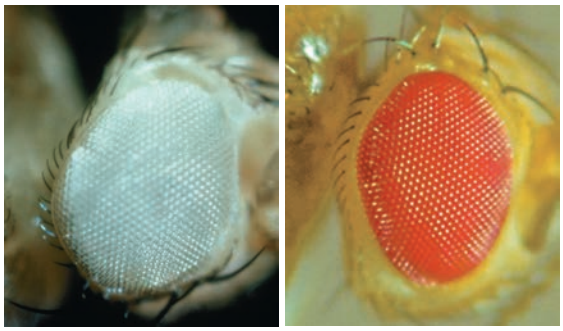


FIGURE 1–3 The white-eyed mutation in *D. melanogaster* (left) and the normal red eye color (right).

Genetic Variation

About the same time that the chromosome theory of inheritance was proposed, scientists began studying the inheritance of traits in the fruit fly, *Drosophila melanogaster*. Early in this work, a white-eyed fly (Figure 1–3) was discovered among normal (wild-type) red-eyed flies. This variant was produced by a **mutation** in one of the genes controlling eye color. Mutations are defined as any heritable change in the DNA sequence and are the source of all genetic variation.

ESSENTIAL POINT

The chromosome theory of inheritance explains how genetic information is transmitted from generation to generation. ■

The white-eye variant discovered in *Drosophila* is an **allele** of a gene controlling eye color. Alleles are defined as alternative forms of a gene. Different alleles may produce differences in the observable features, or **phenotype,** of an organism. The set of alleles for a given trait carried by an organism is called the **genotype.** Using mutant genes as markers, geneticists can map the location of genes on chromosomes.

The Search for the Chemical Nature of Genes: DNA or Protein?

Work on white-eyed *Drosophila* showed that the mutant trait could be traced to a single chromosome, confirming the idea that genes are carried on chromosomes. Once this relationship was established, investigators turned their attention to identifying which chemical component of chromosomes carries genetic information. By the 1920s, scientists knew that proteins and DNA were the major chemical

components of chromosomes. There are a large number of different proteins, and because of their universal distribution in the nucleus and cytoplasm, many researchers thought proteins were the carriers of genetic information.

In 1944, Oswald Avery, Colin MacLeod, and Maclyn McCarty, researchers at the Rockefeller Institute in New York, published experiments showing that DNA was the carrier of genetic information in bacteria. This evidence, though clear-cut, failed to convince many influential scientists. Additional evidence for the role of DNA as a carrier of genetic information came from other researchers who worked with viruses. This evidence that DNA carries genetic information, along with other research over the next few years, provided solid proof that DNA, not protein, is the genetic material, setting the stage for work to establish the structure of DNA.

1.3 Discovery of the Double Helix Launched the Era of Molecular Genetics

Once it was accepted that DNA carries genetic information, efforts were focused on deciphering the structure of the DNA molecule and the mechanism by which information stored in it produces a phenotype.

The Structure of DNA and RNA

One of the great discoveries of the twentieth century was made in 1953 by James Watson and Francis Crick, who described the structure of DNA. DNA is a long, ladder-like macromolecule that twists to form a double helix (**Figure 1–4**). Each linear strand of the helix is made up of subunits called **nucleotides.** In DNA, there are four different nucleotides, each of which contains a nitrogenous base, abbreviated A (adenine), G (guanine), T (thymine), or C (cytosine). These four bases, in various sequence combinations, ultimately encode genetic information. The two strands of DNA are exact complements of one another, so that the rungs of the ladder in the double helix always consist of A═T and G═C base pairs. Along with Maurice Wilkins, Watson and Crick were awarded a Nobel Prize in 1962 for their work on the structure of DNA. We will discuss the structure of DNA later in the text (see Chapter 9).

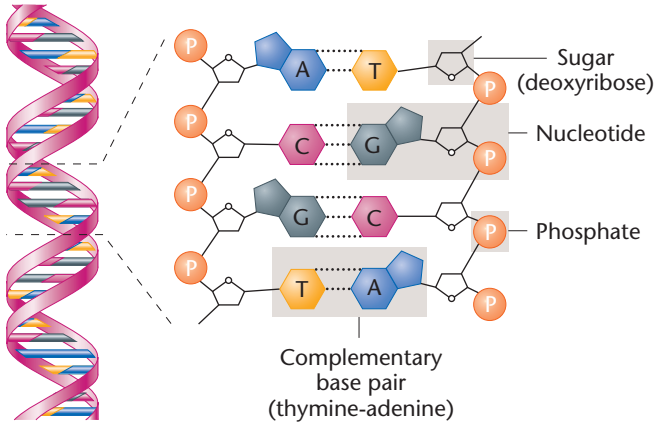


FIGURE 1–4 Summary of the structure of DNA, illustrating the arrangement of the double helix (on the left) and the chemical components making up each strand (on the right). The dotted lines on the right represent weak chemical bonds, called hydrogen bonds, which hold together the two strands of the DNA helix.

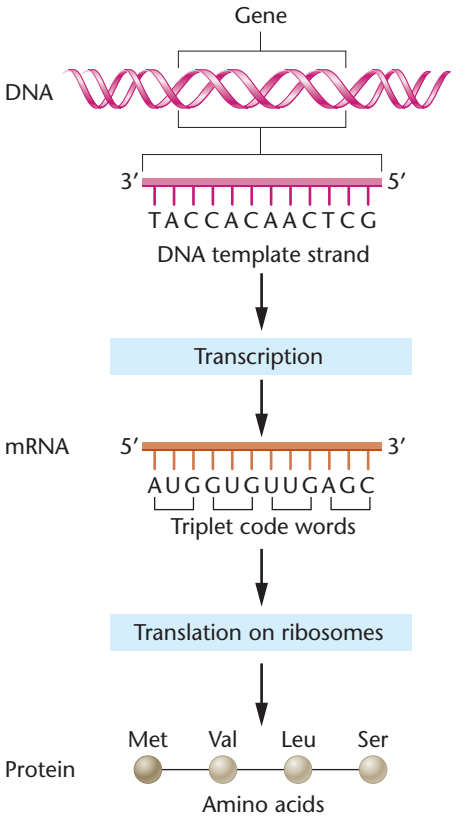


FIGURE 1–5 Gene expression consists of transcription of DNA into mRNA (top) and the translation (center) of mRNA (with the help of a ribosome) into a protein (bottom).

Another nucleic acid, RNA, is chemically similar to DNA but contains a different sugar (ribose rather than deoxyribose) in its nucleotides and contains the nitrogenous base uracil in place of thymine. RNA, however, is generally a single-stranded molecule.

Gene Expression: From DNA to Phenotype

The genetic information encoded in the order of nucleotides in DNA is expressed in a series of steps that results in the formation of a functional gene product. In the majority of cases, this product is a protein. In eukaryotic cells, the process leading to protein production begins in the nucleus with **transcription,** a process in which the nucleotide sequence in one strand of DNA is used to construct a complementary RNA sequence (top part of **Figure 1–5**). Once an RNA

molecule is produced, it moves to the cytoplasm, where the RNA—called **messenger RNA,** or **mRNA** for short—binds to **ribosomes.** The synthesis of proteins under the direction of mRNA is called **translation** (center part of Figure 1–5). The information encoded in mRNA (called the **genetic code**) consists of a linear series of nucleotide triplets. Each triplet, called a **codon,** is complementary to the information stored in DNA and specifies the insertion of a specific amino acid into a protein. Proteins (lower part of Figure 1–5) are polymers made up of amino acid monomers. There are 20 different amino acids commonly found in proteins.

Protein assembly is accomplished with the aid of adapter molecules called **transfer RNA (tRNA).** Within the ribosome, tRNAs recognize the information encoded in the mRNA codons and carry the proper amino acids for construction of the protein during translation.

We now know that gene expression can be more complex than outlined here. Some of these complexities will be discussed later in the text (see Chapters 13, 15, and Special Topic Chapter 1—Epigenetics).

Proteins and Biological Function

In most cases, proteins are the end products of gene expression. The diversity of proteins and the biological functions they perform—the diversity of life itself—arises from the fact that proteins are made from combinations of 20 different amino acids. Consider that a protein chain containing 100 amino acids can have at each position any one of 20 amino acids; the number of possible different 100 amino acid proteins, each with a unique sequence, is therefore equal to

$$20^{100}$$

Obviously, proteins are molecules with the potential for enormous structural diversity and serve as the mainstay of biological systems.

Enzymes form the largest category of proteins. These molecules serve as biological catalysts, lowering the energy of activation in reactions and allowing cellular metabolism to proceed at body temperature.

Proteins other than enzymes are critical components of cells and organisms. These include hemoglobin, the oxygen-binding molecule in red blood cells; insulin, a pancreatic hormone; collagen, a connective tissue molecule; and actin and myosin, the contractile muscle proteins. A protein's shape and chemical behavior are determined by its linear sequence of amino acids, which in turn are dictated by the stored information in the DNA of a gene that is transferred to RNA, which then directs the protein's synthesis.

Linking Genotype to Phenotype: Sickle-Cell Anemia

Once a protein is made, its biochemical or structural properties play a role in producing a phenotype. When mutation alters a gene, it may modify or even eliminate the encoded protein's usual function and cause an altered phenotype. To trace this chain of events, we will examine sickle-cell anemia, a human genetic disorder.

Sickle-cell anemia is caused by a mutant form of hemoglobin, the protein that transports oxygen from the lungs to cells in the body. Hemoglobin is a composite molecule made up of two different proteins, α-globin and β-globin, each encoded by a different gene. In sickle-cell anemia, a mutation in the gene encoding β-globin causes an amino acid substitution in 1 of the 146 amino acids in the protein. **Figure 1–6** shows the template DNA sequence, the corresponding mRNA codons, and the amino acids occupying positions 4–7 for the normal and mutant forms of β-globin. Notice that the mutation in sickle-cell anemia consists of a change in one DNA nucleotide, which leads to a change in codon 6 in mRNA from GAG to GUG, which in turn changes amino acid number 6 in β-globin from glutamic acid to valine. The other 145 amino acids in the protein are not changed by this mutation.

Individuals with two mutant copies of the β-globin gene have sickle-cell anemia. Their mutant β-globin proteins cause hemoglobin molecules in red blood cells to polymerize when the blood's oxygen concentration is low, forming long chains of hemoglobin that distort the shape of red blood cells (**Figure 1–7**). The deformed cells are fragile and break easily, reducing the number of red blood cells in circulation (anemia is an insufficiency of red blood cells). Sickle-shaped blood cells block blood flow in capillaries and small blood vessels, causing severe pain and damage to the heart, brain, muscles, and kidneys. All the symptoms of this disorder are caused by a change in a single nucleotide in a gene that changes one amino acid out of 146 in the β-globin molecule, demonstrating the close relationship between genotype and phenotype.

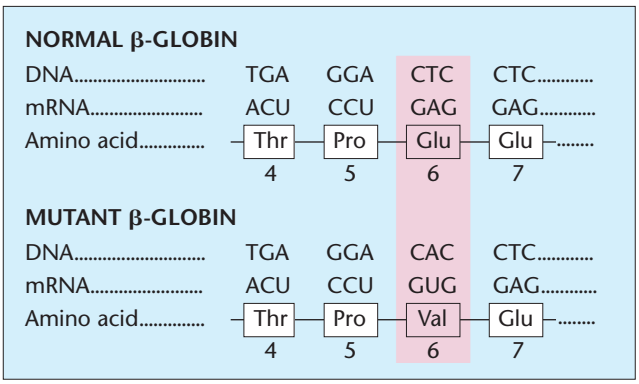


FIGURE 1–6 A single-nucleotide change in the DNA encoding β-globin (CTC→CAC) leads to an altered mRNA codon (GAG→GUG) and the insertion of a different amino acid (Glu→Val), producing the altered version of the β-globin protein that is responsible for sickle-cell anemia.

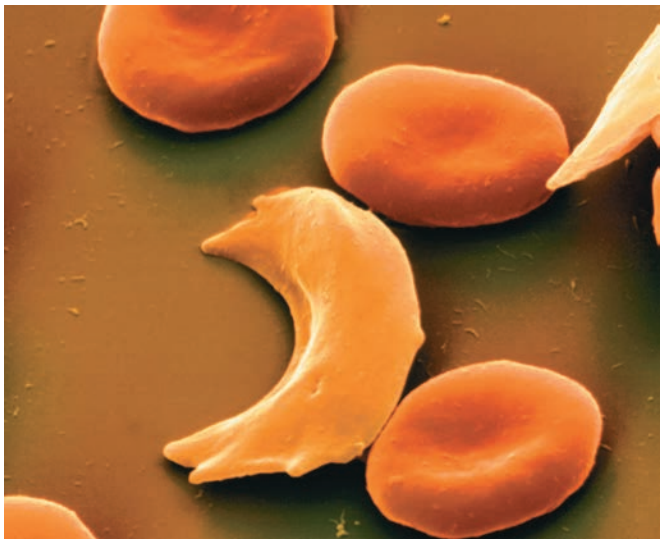


FIGURE 1–7 Normal red blood cells (round) and sickled red blood cells. The sickled cells block capillaries and small blood vessels.

ESSENTIAL POINT

The central dogma of molecular biology—that DNA is a template for making RNA, which in turn directs the synthesis of proteins—explains how genes control phenotypes. ■

1.4 Development of Recombinant DNA Technology Began the Era of DNA Cloning

The era of recombinant DNA began in the early 1970s, when researchers discovered that bacterial proteins called **restriction endonucleases,** which cut the DNA of invading viruses, could also be used to cut any organism's DNA at specific nucleotide sequences, producing a reproducible set of fragments.

Soon after, researchers discovered ways to insert the DNA fragments produced by the action of restriction enzymes into carrier DNA molecules called **vectors** to form **recombinant DNA** molecules. When transferred into bacterial cells, thousands of copies, or **clones,** of the combined vector and DNA fragments are produced during bacterial reproduction. Large amounts of cloned DNA fragments can be isolated from these bacterial host cells. These DNA fragments can be used to isolate genes, to study their organization and expression, and to study their nucleotide sequence and evolution.

Collections of clones that represent an organism's **genome,** defined as the complete haploid DNA content of a specific organism, are called genomic libraries. Genomic libraries are now available for hundreds of species.

Recombinant DNA technology has not only accelerated the pace of research but also given rise to the biotechnology industry, which has grown to become a major contributor to the U.S. economy.

1.5 The Impact of Biotechnology Is Continually Expanding

The use of recombinant DNA technology and other molecular techniques to make products is called **biotechnology.** In the United States, biotechnology has quietly revolutionized many aspects of everyday life; products made by biotechnology are now found in the supermarket, in health care, in agriculture, and in the court system. A later chapter (see Chapter 19) contains a detailed discussion of biotechnology, but for now, let's look at some everyday examples of biotechnology's impact.

Plants, Animals, and the Food Supply

The use of recombinant DNA technology to genetically modify crop plants has revolutionized agriculture. Genes for traits including resistance to herbicides, insects, and genes for nutritional enhancement have been introduced into crop plants. The transfer of heritable traits across species using recombinant DNA technology creates **transgenic organisms.** Herbicide-resistant corn and soybeans were first planted in the mid-1990s, and transgenic strains now represent about 88 percent of the U.S. corn crop and 93 percent of the U.S. soybean crop. It is estimated that more than 70 percent of the processed food in the United States contains ingredients from transgenic crops.

We will discuss the most recent findings involving genetically modified organisms later in the text (Special Topic Chapter 5—Genetically Modified Organisms).

New methods of cloning livestock such as sheep and cattle have also changed the way we use these animals. In 1996, Dolly the sheep (**Figure 1–8**) was cloned by nuclear transfer,

FIGURE 1–8 Dolly, a Finn Dorset sheep cloned from the genetic material of an adult mammary cell, shown next to her first-born lamb, Bonnie.

a method in which the nucleus of an adult cell is transferred into an egg that has had its nucleus removed. This method makes it possible to produce dozens or hundreds of genetically identical offspring with desirable traits and has many applications in agriculture, sports, and medicine.

Biotechnology has also changed the way human proteins for medical use are produced. Through use of gene transfer, transgenic animals now synthesize these therapeutic proteins. In 2009, an anticlotting protein derived from the milk of transgenic goats was approved by the U.S. Food and Drug Administration for use in the United States. Other human proteins from transgenic animals are now being used in clinical trials to treat several diseases. The biotechnology revolution will continue to expand as new methods are developed to make an increasing array of products.

Biotechnology in Genetics and Medicine

More than 10 million children or adults in the United States suffer from some form of genetic disorder, and every childbearing couple faces an approximately 3 percent risk of having a child with a genetic anomaly. The molecular basis for hundreds of genetic disorders is now known, and many of these genes have been mapped, isolated, and cloned. Biotechnology-derived whole-genome testing is now available to perform prenatal diagnosis of most if not all heritable disorders and to test parents for their status as "carriers" of inherited disorders. However, the use of genetic testing and related technologies raises ethical concerns that have yet to be fully resolved.

ESSENTIAL POINT

Biotechnology has revolutionized agriculture and the pharmaceutical industry, while genetic testing has had a profound impact on the diagnosis of genetic diseases. ■

1.6 Genomics, Proteomics, and Bioinformatics Are New and Expanding Fields

The use of recombinant DNA technology to create genomic libraries prompted scientists to consider sequencing all the clones in a library to derive the nucleotide sequence of an organism's genome. This sequence information would be used to identify each gene in the genome and establish its function.

One such project, the Human Genome Project, began in 1990 as an international effort to sequence the human genome. By 2003, the publicly funded Human Genome Project and a private, industry-funded genome project completed sequencing of the gene-containing portion of the genome.

As more genome sequences were acquired, several new biological disciplines arose. One, called **genomics** (the study of genomes), studies the structure, function, and evolution of genes and genomes. A second field, **proteomics,** identifies the set of proteins present in a cell under a given set of conditions, and studies their functions and interactions. To store, retrieve, and analyze the massive amount of data generated by genomics and proteomics, a specialized subfield of information technology called **bioinformatics** was created to develop hardware and software for processing and storing nucleotide and protein data.

Geneticists and other biologists now use information in databases containing nucleic acid sequences, protein sequences, and gene-interaction networks to answer experimental questions in a matter of minutes instead of months and years. A feature called "Exploring Genomics," located at the end of many of the chapters in this textbook, gives you the opportunity to explore these databases for yourself while completing an interactive genetics exercise.

Modern Approaches to Understanding Gene Function

Historically, a method known as **classical** or **forward genetics** was used to study and understand gene function. In this approach geneticists relied on the use of naturally occurring mutations, or intentionally induced mutations (using chemicals, X-rays, or UV light as examples) to cause altered phenotypes in model organisms, and then worked through the lab-intensive and time-consuming process of identifying the genes that caused these new phenotypes. Such characterization often led to the identification of a gene or genes of interest, and once the technology advanced, the gene sequence could be determined.

Classical genetics approaches are still used, but as genome sequencing has become routine, molecular approaches to understanding gene function have changed considerably. These modern approaches are what we will highlight in this section.

For the past two decades or so, geneticists have relied on the use of molecular techniques in an approach referred to as **reverse genetics.** In reverse genetics, the DNA sequence for a particular gene of interest is known, but the role and function of the gene are typically not well understood. For example, molecular biology techniques such as **gene knockout** render targeted genes nonfunctional in model organisms or in cultured cells, allowing scientists to investigate the fundamental question of "what happens if this gene is disrupted?" After creating a knockout, scientists look for changes in phenotype, as well as alterations at the cellular and molecular level. The ultimate goal is to determine the function of the gene being studied.

ESSENTIAL POINT

Recombinant DNA technology gave rise to several new fields, including genomics, proteomics, and bioinformatics, which allow scientists to explore the structure and evolution of genomes and the proteins they encode. ■

1.7 Genetic Studies Rely on the Use of Model Organisms

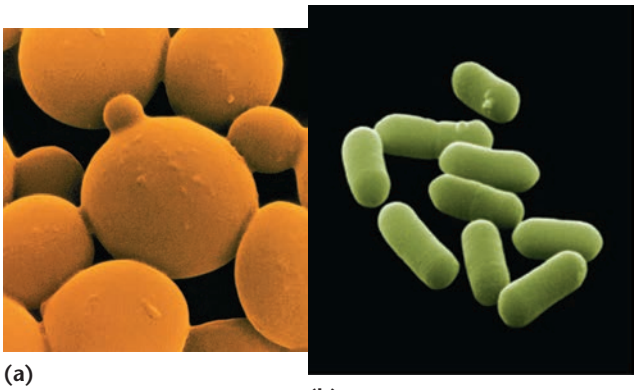
After the rediscovery of Mendel's work in 1900, research using a wide range of organisms confirmed that the principles of inheritance he described were of universal significance among plants and animals. Geneticists gradually came to focus attention on a small number of organisms, including the fruit fly (*Drosophila melanogaster*) and the mouse (*Mus musculus*) (**Figure 1–9**). This trend developed for two main reasons: first, it was clear that genetic mechanisms were the same in most organisms, and second, some organisms had characteristics that made them especially suitable for genetic research. They were easy to grow, had relatively short life cycles, produced many offspring, and their genetic analysis was fairly straightforward. Over time, researchers created a large catalog of mutant strains for these species, and the mutations were carefully studied, characterized, and mapped. Because of their well-characterized genetics, these species became **model genetic organisms,** defined as organisms used for the study of basic biological processes. In later chapters, we will see how discoveries in model organisms are shedding light on many aspects of biology, including aging, cancer, the immune system, and behavior.

The Modern Set of Genetic Model Organisms

Gradually, geneticists added other species to their collection of model organisms: viruses (such as the T phages and lambda phage) and microorganisms (the bacterium *Escherichia coli* and the yeast *Saccharomyces cerevisiae*) (**Figure 1–10**).

(a) (b)

FIGURE 1–9 The first generation of model organisms in genetic analysis included (a) the mouse, *Mus musculus,* and (b) the fruit fly, *Drosophila melanogaster*.



(a) (b)

FIGURE 1–10 Microbes that have become model organisms for genetic studies include (a) the yeast *Saccharomyces cerevisiae* and (b) the bacterium *Escherichia coli*.

More recently, additional species have been developed as model organisms, three of which are shown in the chapter opening photograph. Each species was chosen to allow study of some aspect of embryonic development. The nematode *Caenorhabditis elegans* was chosen as a model system to study the development and function of the nervous system because its nervous system contains only a few hundred cells and the developmental fate of these and all other cells in the body has been mapped out. *Arabidopsis thaliana,* a small plant with a short life cycle, has become a model organism for the study of many aspects of plant biology. The zebrafish, *Danio rerio,* is used to study vertebrate development: it is small, it reproduces rapidly, and its egg, embryo, and larvae are all transparent.

Model Organisms and Human Diseases

The development of recombinant DNA technology and the data from genome sequencing have confirmed that all life has a common origin. Because of this, genes with similar functions in different organisms tend to be similar or identical in structure and nucleotide sequence. Much of what scientists learn by studying the genetics of model organisms can therefore be applied to humans as a way of understanding and treating human diseases. In addition, the ability to create transgenic organisms by transferring genes between species has enabled scientists to develop models of human diseases in organisms ranging from bacteria to fungi, plants, and animals (**Table 1.1**).

The idea of studying a human disease such as colon cancer by using *E. coli* may strike you as strange, but the basic steps of DNA repair (a process that is defective in some forms of colon cancer) are the same in both organisms, and a gene involved (*mutL* in *E. coli* and *MLH1* in humans) is found in both organisms. More importantly, *E. coli* has the advantage of being easier to grow (the cells divide every 20 minutes), and researchers can easily create and study new mutations in the bacterial *mutL* gene in

TABLE 1.1 Model Organisms Used to Study Some Human Diseases

Organism	Human Diseases
E. coli	Colon cancer and other cancers
S. cerevisiae	Cancer, Werner syndrome
D. melanogaster	Disorders of the nervous system, cancer
C. elegans	Diabetes
D. rerio	Cardiovascular disease
M. musculus	Lesch–Nyhan disease, cystic fibrosis, fragile-X syndrome, and many other diseases

order to figure out how it works. This knowledge may eventually lead to the development of drugs and other therapies to treat colon cancer in humans.

The fruit fly, *Drosophila melanogaster,* is also being used to study a number of human diseases. Mutant genes have been identified in *D. melanogaster* that produce phenotypes with structural abnormalities of the nervous system and adult-onset degeneration of the nervous system. The information from genome-sequencing projects indicates that almost all these genes have human counterparts. For example, genes involved in a human disease of the retina called retinitis pigmentosa are identical to *Drosophila* genes involved in retinal degeneration. Study of these mutations in *Drosophila* is helping to dissect this disorder and to identify the function of the genes involved.

Another approach to studying diseases of the human nervous system is to transfer mutant human disease genes into *Drosophila* using recombinant DNA technology. The transgenic flies are then used for studying the mutant human genes themselves, other genes that affect the expression of the human disease genes, and the effects of therapeutic drugs on the action of those genes—all studies that are difficult or impossible to perform in humans. This gene transfer approach is being used to study almost a dozen human neurodegenerative disorders, including Huntington disease, Machado–Joseph disease, myotonic dystrophy, and Alzheimer disease.

Throughout the following chapters, you will encounter these model organisms again and again. Remember each time you meet them that they not only have a rich history in basic genetics research but are also at the forefront in the study of human genetic disorders and infectious diseases. As discussed in the next section, however, we have yet to reach a consensus on how and when some of this technology will be accepted as safe and ethically acceptable.

ESSENTIAL POINT

The study of model organisms for understanding human health and disease is one of many ways genetics and biotechnology are rapidly changing everyday life. ■

1.8 We Live in the Age of Genetics

Mendel described his decade-long project on inheritance in pea plants in an 1865 paper presented at a meeting of the Natural History Society of Brünn in Moravia. Less than 100 years later, the 1962 Nobel Prize was awarded to James Watson, Francis Crick, and Maurice Wilkins for their work on the structure of DNA. This time span encompassed the years leading up to the acceptance of Mendel's work, the discovery that genes are on chromosomes, the experiments that proved DNA encodes genetic information, and the elucidation of the molecular basis for DNA replication. The rapid development of genetics from Mendel's monastery garden to the Human Genome Project and beyond is summarized in a timeline in **Figure 1–11**.

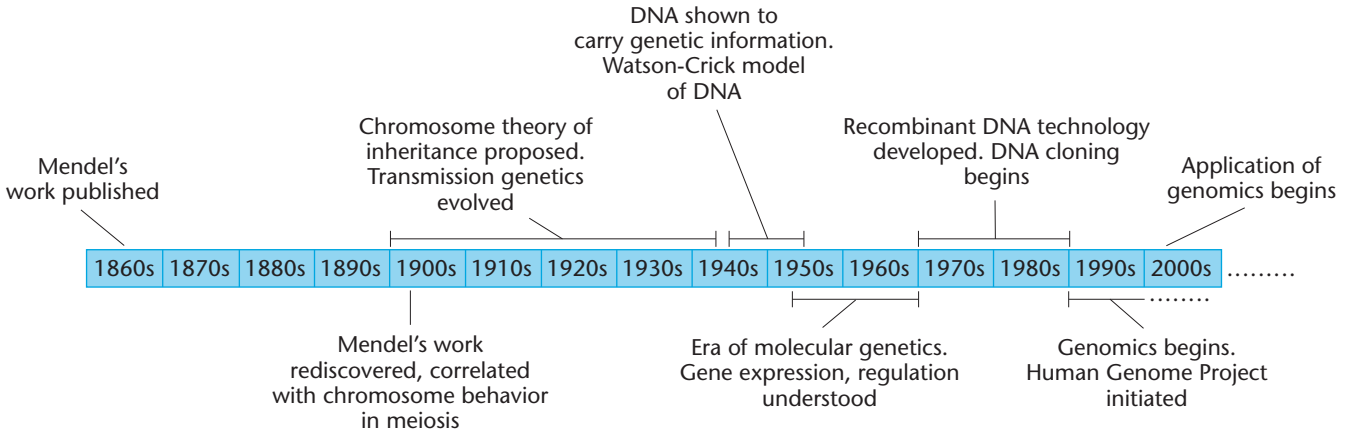


FIGURE 1–11 A timeline showing the development of genetics from Gregor Mendel's work on pea plants to the current era of genomics and its many applications in research, medicine, and society. Having a sense of the history of discovery in genetics should provide you with a useful framework as you proceed through this textbook.

The Nobel Prize and Genetics

No other scientific discipline has experienced the explosion of information and the level of excitement generated by the discoveries in genetics. This impact is especially apparent in the list of Nobel Prizes related to genetics, beginning with those awarded in the early and mid-twentieth century and continuing into the present (see inside front cover). Nobel Prizes in Medicine or Physiology and Chemistry have been consistently awarded for work in genetics and related fields. The first Nobel Prize awarded for such work was given to Thomas Morgan in 1933 for his research on the chromosome theory of inheritance. That award was followed by many others, including prizes for the discovery of genetic recombination, the relationship between genes and proteins, the structure of DNA, and the genetic code. In this century, geneticists continue to be recognized for their impact on biology in the current millennium, including Nobel Prizes awarded in 2002, 2006, 2007, and 2009. In 2010, the prize in Physiology or Medicine was given to Robert Edwards for the development of *in vitro* fertilization, and the 2012 prize was awarded to John Gurdon and Shinya Yamanaka for their work showing that adult cells can be reprogrammed to direct embryonic development and to form stem cells.

Genetics and Society

Just as there has never been a more exciting time to study genetics, the impact of this discipline on society has never been more profound. Genetics and its applications in biotechnology are developing much faster than the social conventions, public policies, and laws required to regulate their use. As a society, we are grappling with a host of sensitive genetics-related issues, including concerns about prenatal testing, genetic discrimination, ownership of genes, access to and safety of gene therapy, and genetic privacy. By the time you finish this course, you will have seen more than enough evidence to convince yourself that the present is the Age of Genetics, and you will understand the need to think about and become a participant in the dialogue concerning genetic science and its use.

ESSENTIAL POINT

Genetic technology is having a profound effect on society, but policies and legislation governing its use are lagging behind the resulting innovations. ■

Problems and Discussion Questions

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1. How does Mendel's work on the transmission of traits relate to our understanding of genetics today?

CONCEPT QUESTION

2. Review the Chapter Concepts list on p. 17. Most of these concepts are related to the discovery of DNA as the genetic material and the subsequent development of recombinant DNA technology. Write a brief essay that discusses the impact of recombinant DNA technology on genetics as we perceive the discipline today. ■
3. What is the chromosome theory of inheritance, and how is it related to Mendel's findings?
4. Define genotype and phenotype. Describe how they are related and how alleles fit into your definitions.
5. Given the state of knowledge at the time of the Avery, MacLeod, and McCarty experiment, why was it difficult for some scientists to accept that DNA is the carrier of genetic information?
6. What is a gene?
7. What is the structure of DNA? How does it differ from that of RNA?
8. Describe the central dogma of molecular genetics and how it serves as the basis of modern genetics.
9. Until the mid-1940s, many scientists considered proteins to be the likely candidates for the genetic material. Why?
10. Outline the roles played by restriction enzymes and vectors in cloning DNA.
11. Genetics is commonly seen as being grouped into several general areas: transmission, molecular, and population/evolution. Which biological processes are studied in transmission genetics?
12. Summarize the arguments for and against patenting genetically modified organisms.
13. We all carry about 20,000 genes in our genome. So far, patents have been issued for more than 6000 of these genes. Do you think that companies or individuals should be able to patent human genes? Why or why not?
14. Why do we use model organisms to study human genetic diseases?
15. If you knew that a devastating late-onset inherited disease runs in your family (in other words, a disease that does not appear until later in life) and you could be tested for it at the age of 20, would you want to know whether you are a carrier? Would your answer be likely to change when you reach age 40?
16. Why have the advances in bioinformatics kept pace with the advances in biotechnology, while the policies and legislation regarding the ethical issues involved have lagged behind?

2 Mitosis and Meiosis

CHAPTER CONCEPTS

- Genetic continuity between generations of cells and between generations of sexually reproducing organisms is maintained through the processes of mitosis and meiosis, respectively.
- Diploid eukaryotic cells contain their genetic information in pairs of homologous chromosomes, with one member of each pair being derived from the maternal parent and one from the paternal parent.
- Mitosis provides a mechanism by which chromosomes, having been duplicated, are distributed into progeny cells during cell reproduction.
- Mitosis converts a diploid cell into two diploid daughter cells.
- The process of meiosis distributes one member of each homologous pair of chromosomes into each gamete or spore, thus reducing the diploid chromosome number to the haploid chromosome number.
- Meiosis generates genetic variability by distributing various combinations of maternal and paternal members of each homologous pair of chromosomes into gametes or spores.
- During the stages of mitosis and meiosis, the genetic material is condensed into discrete structures called chromosomes.

Chromosomes in the prometaphase stage of mitosis, derived from a cell in the flower of *Haemanthus*.

Every living thing contains a substance described as the genetic material. Except in certain viruses, this material is composed of the nucleic acid DNA. DNA has an underlying linear structure possessing segments called genes, the products of which direct the metabolic activities of cells. An organism's DNA, with its arrays of genes, is organized into structures called **chromosomes,** which serve as vehicles for transmitting genetic information. The manner in which chromosomes are transmitted from one generation of cells to the next and from organisms to their descendants must be exceedingly precise. In this chapter we consider exactly how genetic continuity is maintained between cells and organisms.

Two major processes are involved in the genetic continuity of nucleated cells: **mitosis** and **meiosis.** Although the mechanisms of the two processes are similar in many ways, the outcomes are quite different. Mitosis leads to the production of two cells, each with the same number of chromosomes as the parent cell. In contrast, meiosis reduces the genetic content and the number of chromosomes by precisely half. This reduction is essential if sexual reproduction is to occur without doubling the amount of genetic material in each new generation. Strictly speaking, mitosis is that portion of the cell cycle during which the hereditary components are equally partitioned into daughter cells. Meiosis is part of a special type of cell division that leads to the production of sex cells: **gametes** or **spores.** This process is an essential step in the transmission of genetic information from an organism to its offspring.