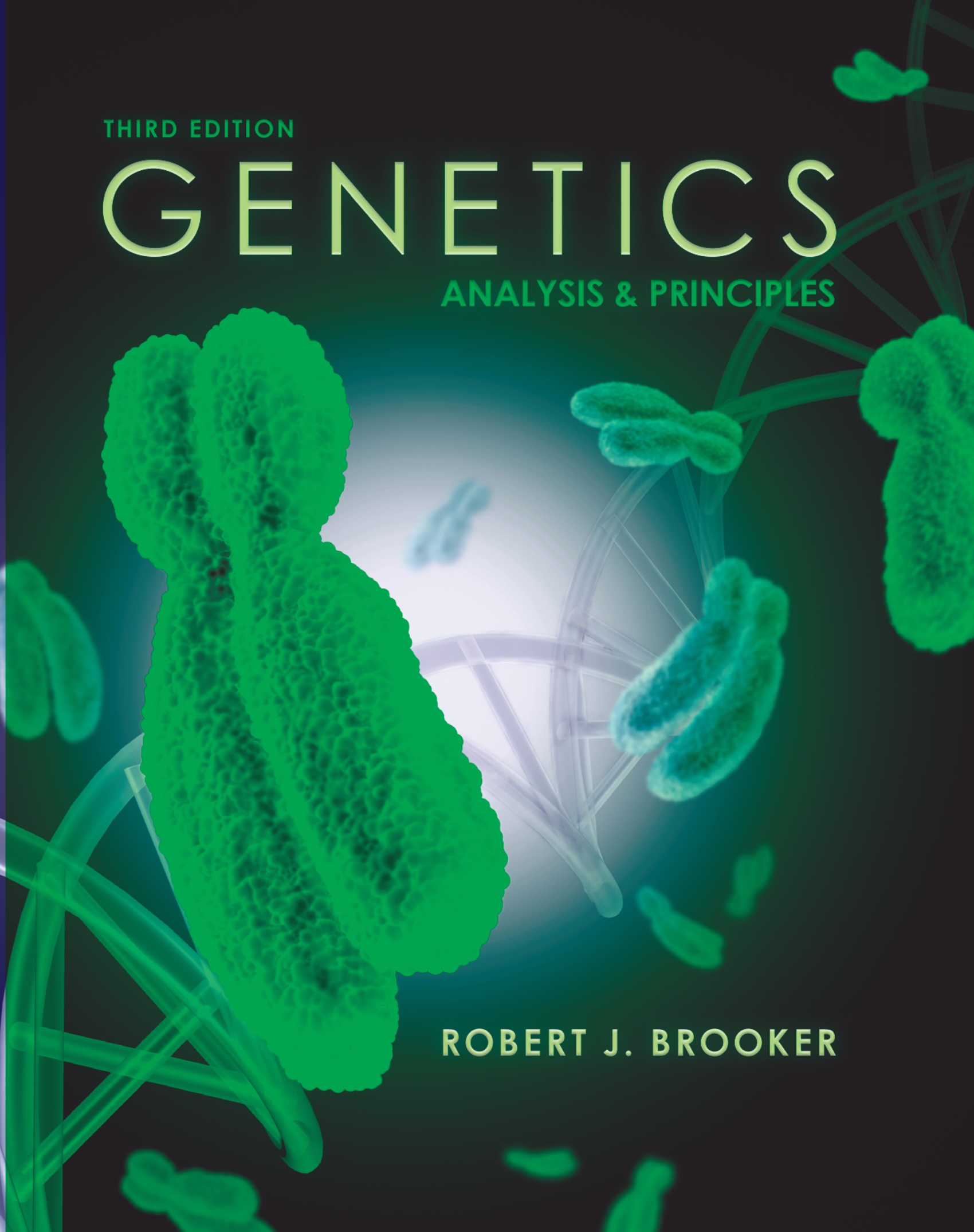
THIRD EDITION

GENETICS

ANALYSIS & PRINCIPLES



ROBERT J. BROOKER

:: ROBERT J. BROOKER

UNIVERSITY OF MINNESOTA–MINNEAPOLIS

third edition

GENETICS

ANALYSIS & PRINCIPLES

McGraw-Hill Higher Education

Boston Burr Ridge, IL Dubuque, IA New York San Francisco St. Louis
Bangkok Bogotá Caracas Kuala Lumpur Lisbon London Madrid Mexico City
Milan Montreal New Delhi Santiago Seoul Singapore Sydney Taipei Toronto

The McGraw-Hill Companies

McGraw-Hill Irwin

GENETICS: ANALYSIS & PRINCIPLES, THIRD EDITION

This book is printed on recycled, acid-free paper containing 10% postconsumer waste.

1 2 3 4 5 6 7 8 9 0 DOW/DOW 0 9 8

ISBN 978–0–07–299278–6
MHID 0–07–299278–6

Publisher: *Janice Roerig-Blong*
Executive Editor: *Patrick E. Reidy*
Senior Developmental Editor: *Lisa A. Bruflodt*
Marketing Manager: *Barbara Owca*
Senior Project Manager: *Jayne Klein*
Senior Production Supervisor: *Laura Fuller*
Senior Media Project Manager: *Jodi Banowetz*
Designer: *John Joran*
Interior Designer: *Rokusek Design, Inc.*
Cover Illustration: *Imagineering Media Services Inc.*
Senior Photo Research Coordinator: *John C. Leland*
Photo Research: *Pronk&Associates*
Supplement Producer: *Mary Jane Lampe*
Compositor: *Lachina Publishing Services*
Typeface: *10/12 Minion*
Printer: *R. R. Donnelley Williard, OH*

The credits section for this book begins on page 823 and is considered an extension of the copyright page.

Library of Congress Cataloging-in-Publication Data

Brooker, Robert J.
Genetics : analysis & principles / Robert J. Brooker. — 3rd ed.
p. cm.
Includes bibliographical references and index.
ISBN 978–0–07–299278–6 — ISBN 0–07–299278–6 (hard copy : alk. paper) 1. Genetics. I. Title.
QH430.B766 2009
576.5--dc22

2007038523

www.mhhe.com

ABOUT THE AUTHOR

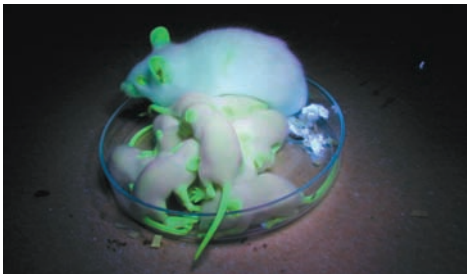
Robert J. Brooker is a Professor in the Department of Genetics, Cell Biology, and Development at the University of Minnesota–Minneapolis. He received his B.A. in Biology from Wittenberg University in 1978 and his Ph.D. in Genetics from Yale University in 1983. At Harvard, he conducted post-doctoral studies on the lactose permease, which is the product of the *lacY* gene of the *lac* operon. He continues his work on transporters at the University of Minnesota. Dr. Brooker's laboratory primarily investigates the structure, function, and regulation of iron transporters found in bacteria and *C. elegans*. At the University of Minnesota, he teaches undergraduate courses in biology, genetics, and cell biology.

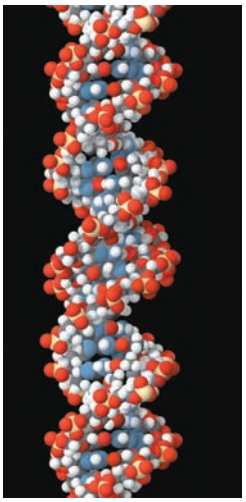
DEDICATION

To my wife, Deborah, and our children,
Daniel, Nathan, and Sarah

BRIEF CONTENTS

TABLE OF CONTENTS





PREFACE

In the third edition of *Genetics: Analysis & Principles,* the content has been updated to reflect current trends in the field. In addition, the presentation of the content has been improved in a way that fosters active learning. As an author, researcher, and teacher, I want a textbook that gets students actively involved in learning genetics. To achieve this goal, I have worked with a talented team of editors, illustrators, and media specialists who have helped me to make the third edition of *Genetics: Analysis & Principles* a fun learning tool. The features that we feel are most appealing to students, and which have been added to or improved upon in the third edition, are the following.

- **Interactive exercises** Education specialists have crafted interactive exercises in which the students can make their own choices in problem-solving activities, and predict what the outcomes will be. These exercises often focus on inheritance patterns and human genetic diseases. (For example, see Chapters 4 and 22.)
- **Animations** Our media specialists have created over 50 animations for a variety of genetic processes. These animations were made specifically for this textbook, and use the art from the textbook. The animations literally make many of the figures in the textbook "come to life."
- **Experiments** As in the previous editions, each chapter (beginning with Chapter 2) incorporates one or two experiments that are presented according to the scientific method. These experiments are not "boxed off" from the rest of the chapter. Rather, they are integrated within the chapters and flow with the rest of the text. As you are reading the experiments, you will simultaneously explore the scientific method and the genetic principles that have been discovered using this approach. For students, I hope this textbook will help you to see the fundamental connection between scientific analysis and principles. For both students and instructors, I expect that this strategy will make genetics much more fun to explore.
- **Art** The art has been further refined for clarity and completeness. This makes it easier and more fun for students to study the illustrations without having to go back and forth between the art and the text.
- **Engaging text** A strong effort has been made in the third edition to pepper the text with questions. Sometimes these are questions that scientists considered when they were conducting their research. Sometimes they are questions that the students might ask themselves when they are learning about genetics.

Overall, an effective textbook needs to accomplish three goals. First, it needs to provide comprehensive, accurate, and up-to-date content in its field. Second, it needs to provide students with an exposure to the techniques and skills that are needed for them to become successful in that field. And finally, it should inspire students so they want to pursue that field as a career. The hard work that has gone into the third edition of *Genetics: Analysis & Principles* has been aimed at achieving all three of these goals.

HOW WE EVALUATED YOUR NEEDS

ORGANIZATION

In surveying many genetics instructors, it became apparent that most people fall into two camps: **Mendel first** versus **Molecular first.** I have taught genetics both ways. As a teaching tool, this textbook has been written with these different teaching strategies in mind. The organization and content lend themselves to various teaching formats.

Chapters 2 through 8 are largely inheritance chapters, while Chapters 24 through 26 examine population and quantitative genetics. The bulk of the molecular genetics is found in Chapters 9 through 23, although I have tried to weave a fair amount of molecular genetics into Chapters 2 through 8 as well. The information in

Chapters 9 through 23 *does not assume* that a student has already covered Chapters 2 through 8. Actually, each chapter is written with the perspective that instructors may want to vary the order of their chapters to fit their students' needs.

For those who like to discuss inheritance patterns first, a common strategy would be to cover Chapters 1 through 8 first, and then possibly 24 through 26. (However, many instructors like to cover quantitative and population genetics at the end. Either way works fine.) The more molecular and technical aspects of genetics would then be covered in Chapters 9 through 23. Alternatively, if you like the "Molecular first" approach, you would probably cover Chapter 1, then skip to Chapters 9 through 23, then return to Chapters 2 through 8, and then cover Chapters 24 through 26 at the end of the course. This textbook was written in such a way that either strategy works just fine.

ACCURACY

Both the publisher and I acknowledge the fact that inaccuracies can be a source of frustration for both the instructor and students. Therefore, throughout the writing and production of this textbook we have worked very hard to catch and correct errors during each phase of development and production.

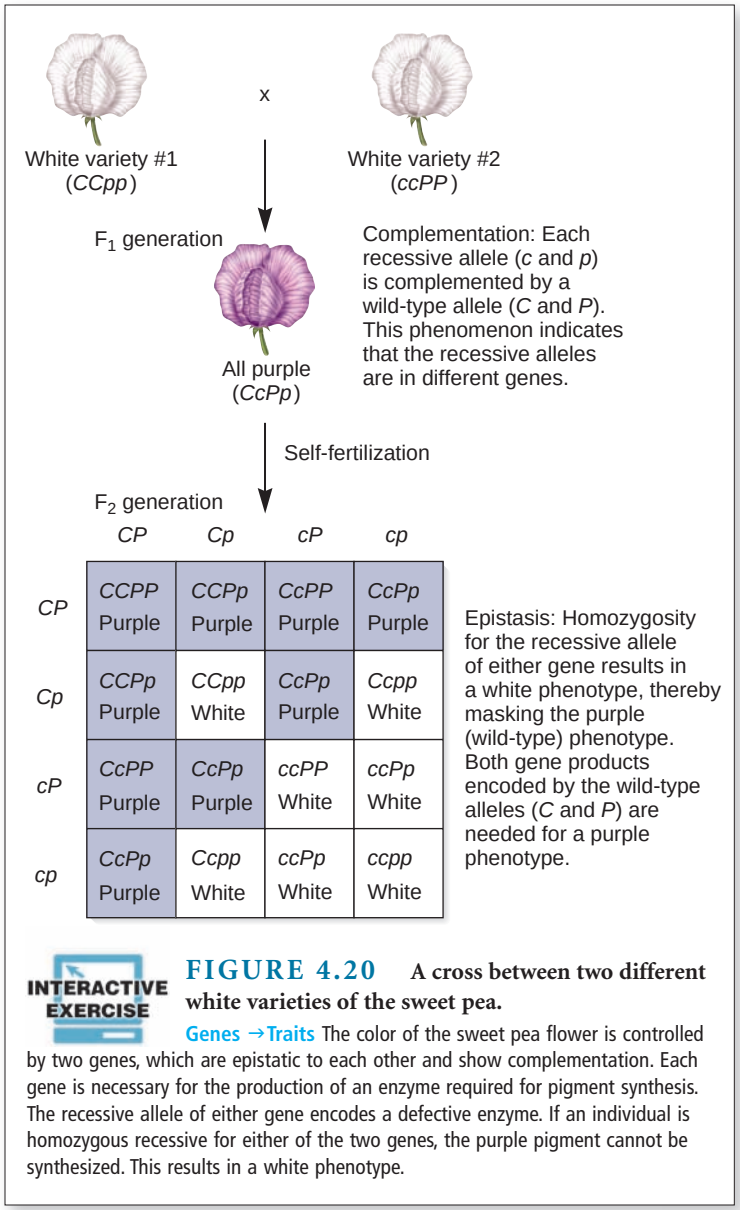
Each chapter has been reviewed by a minimum of ten people. At least eight of these people were faculty members who teach the course and/or conduct research in genetics. In addition, two development editors have gone through the material, at least twice, to check for accuracy in art, and consistency between the text and art. We also had a team of students work through all the problem sets and one development editor also checked them. The author personally checked every question and answer when the chapters were completed.

PEDAGOGY

Based on our discussions with instructors from many institutions, some common goals have emerged. Instructors want a broad textbook that clearly explains concepts in a way that is interesting, accurate, concise, and up-to-date. Likewise, most instructors want students to understand the experimentation that revealed these genetic concepts. In this textbook, concepts and experimentation are woven together to provide a story that enables students to learn the important genetic concepts that they will need in their future careers, and also to be able to explain the types of experiments that allowed researchers to derive such concepts. The end-of-chapter problem sets are categorized according to their main focus, either conceptual or experimental, although some problems contain a little of both. The problems are meant to strengthen students' abilities in a wide variety of ways.

- By bolstering their understanding of genetic principles.
- By enabling students to apply genetic concepts to new situations.
- By analyzing scientific data.
- By organizing their thoughts regarding a genetic topic.
- By improving their writing skills.

Finally, since genetics is such a broad discipline ranging from the molecular to the populational levels, many instructors have told us that it is a challenge for students to see both "the forest and the trees." It is commonly mentioned that students often have trouble connecting the concepts they have learned in molecular genetics with the traits that occur at the level of a whole organism (i.e., What does transcription have to do with blue eyes?). To try to make this connection more meaningful, certain figure legends in each chapter, designated **Genes→ Traits,** remind students that molecular and cellular phenomena ultimately lead to the traits that are observed in each species (for example, see Figure 4.20).



INTERACTIVE EXERCISE

FIGURE 4.20 A cross between two different white varieties of the sweet pea.

Genes →Traits The color of the sweet pea flower is controlled by two genes, which are epistatic to each other and show complementation. Each gene is necessary for the production of an enzyme required for pigment synthesis. The recessive allele of either gene encodes a defective enzyme. If an individual is homozygous recessive for either of the two genes, the purple pigment cannot be synthesized. This results in a white phenotype.

ILLUSTRATIONS

In surveying students whom I teach, I often hear it said that most of their learning comes from studying the figures. Likewise, instructors frequently use the illustrations from a textbook as a central teaching tool. For these reasons, the greatest amount of effort in improving the third edition has gone into the illustrations. The illustrations have been refined with four goals in mind:

1. **Completeness** For most figures, it should be possible to understand an experiment or genetic concept by looking at the illustration alone. Students have complained that it is difficult to understand the content of an illustration if they have to keep switching back and forth between the figure and text. In cases where an illustration shows the steps in a scientific process, the steps are described in brief statements that allow the students to understand the whole process (for example, see Figure 12.10). Likewise, such illustrations should make it easier for instructors to explain these processes in the classroom.
2. **Clarity** The figures have been extensively reviewed by students and instructors. This has helped us to avoid drawing things that may be confusing or unclear. I hope that no one looks at an element in any figure and wonders, "What is that thing?" Aside from being unmistakably drawn, all new elements within each figure are clearly labeled.
3. **Consistency** Before we began to draw the figures for the second edition, we generated a style sheet that contained recurring elements that are found in many places in the textbook. Examples include the DNA double helix, DNA polymerase, and fruit flies. We agreed upon the best way(s) to draw these elements and also what colors they should be. Therefore, as students and instructors progress through this textbook, they become accustomed to the way things should look.
4. **Realism** An important goal of this and previous editions is to make each figure as realistic as possible. When drawing macroscopic elements (for example, fruit flies, pea plants), the illustrations are based on real images, not on cartoonlike simplifications. Our most challenging goal, and one that we feel has been achieved most successfully, is the realism of our molecular drawings. Whenever possible, we have tried to depict molecular elements according to their actual structures, if such structures are known. For example, the ways we have drawn RNA polymerase, DNA polymerase, DNA helicase, and ribosomes are based on their crystal structures. When a student sees a figure in this textbook that illustrates an event in transcription, RNA polymerase is depicted in a way that is as realistic as possible (for example, see Figure 12.10).

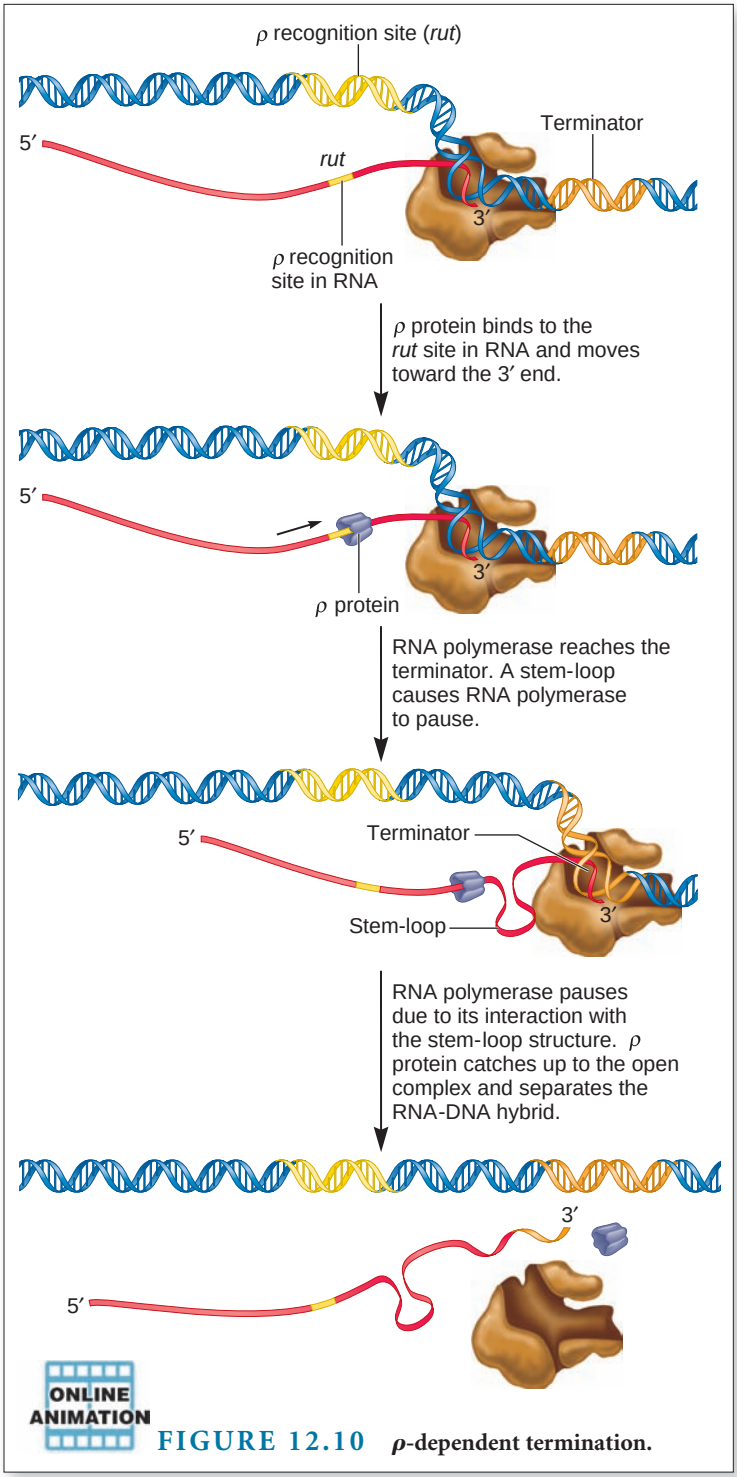


FIGURE 12.10 **ρ-dependent termination.**

WRITING STYLE

Motivation in learning often stems from enjoyment. If someone enjoys what they're reading, they are more likely to spend longer amounts of time with it and focus their attention more crisply. The writing style of this book is meant to be interesting, down to earth, and easy to follow. Each section of every chapter begins with an overview of the contents of that section, usually with a table or figure that summarizes the broad points. The section then examines how those broad points were discovered experimentally, as well as explaining many of the finer scientific details. Important terms are introduced in a boldface font. These terms are also found in the glossary.

There are various ways to make a genetics book interesting and inspiring. The subject matter itself is pretty amazing, so it's not difficult to build on that. In addition to describing the concepts and experiments in ways that motivate students, it is important to draw upon examples that bring the concepts to life. In a genetics book, many of these examples come from the medical realm. This textbook contains lots of examples of human diseases that exemplify some of the underlying principles of genetics. Students often say that they remember certain genetic concepts because they remember how defects in certain genes can cause disease. For example, defects in DNA repair genes cause a higher predisposition to develop cancer. In addition, I have tried to be evenhanded in providing examples from the microbial and plant world. Finally, students are often interested in applications of genetics that impact their everyday lives. Because we hear about genetics in the news on a daily basis, it's inspiring for students to learn the underlying basis for such technologies. Chapters 18 to 21 are devoted to genetic technologies, and applications of these and other technologies are found throughout this textbook. By the end of their genetics course, students should come away with a greater appreciation for the impact of genetics in their lives.

EXAMPLES OF SIGNIFICANT CONTENT CHANGES IN THE THIRD EDITION

- **Interactive Exercises** Many interactive exercises are available for students to understand inheritance patterns and human genetic diseases. These are indicated with an icon next to the relevant figures. They are largely found in Chapters 2, 4, 5, 7, and 22.
- **Animations** Nearly every chapter has one or more custom animations to help students understand genetic processes. These are also indicated by an icon next to the relevant figure.
- **Chapter 3 (Reproduction and Chromosome Transmission)** The illustrations and micrographs of mitosis and meiosis have been improved.
- **Chapter 4 (Extensions of Mendelian Inheritance)** The topic of suppressor mutations has been expanded.
- **Chapter 8 (Variation in Chromosome Structure and Number)** The technique of comparative genomic hybridization has been added, and included as a Feature Experiment.
- **Chapter 10 (Chromosome Organization and Molecular Structure)** An illustration and expanded discussion has been added for SMC proteins, which are involved with chromosome condensation and sister chromatid cohesion. Also, the histone code hypothesis is discussed and illustrated.
- **Chapter 11 (DNA Replication)** Illustrations in this chapter now depict the step-by-step formation of Okazaki fragments (for example, see Figure 11.10).
- **Chapter 13 (Translation of mRNA)** This chapter has undergone some reorganization to bring the basic concepts of translation to the first section.
- **Chapter 15 (Gene Regulation in Eukaryotes)** The topic of RNA interference has been expanded, including a Feature Experiment of the work of Fire and Mellow.
- **Chapter 16 (Gene Mutation and DNA Repair)** To complement some new material in Chapter 4, several examples of suppressor mutations are described. In addition, homologous recombination repair and nonhomologous end joining repair are illustrated and discussed within the context of repairing double-stranded DNA breaks.
- **Chapter 19 (Biotechnology)** Some new topics in biotechnology have been added including GloFish® and Bt corn.
- **Chapter 20 (Genomics I: Analysis of DNA)** The approach of shotgun DNA sequencing is greatly expanded along with complementary illustrations.
- **Chapter 21 (Genomics II: Functional Genomics, Proteomics, and Bioinformatics)** The method of chromatin immunoprecipitation (ChIP) has been added.
- **Chapter 22 (Medical Genetics and Cancer)** Several new topics have been added including the use of molecular markers in the mapping of human genetic diseases, and the molecular profiling of cancer cells using DNA microarrays.
- **Chapter 24 (Population Genetics)** This chapter contains an expanded discussion of natural selection with graphical representations of the various types. An entire new section on Sources of Genetic Variation has been added so students can appreciate how/why genetic variation is so prevalent.
- **Chapter 26 (Evolutionary Genetics)** The cladistic approach has been greatly expanded. In addition, an entire section on Evolutionary Developmental Biology (Evo-Devo) has been added.

SUGGESTIONS WELCOME!

It seems very appropriate to use the word evolution to describe the continued development of this textbook. I welcome any and all comments. The refinement of any science textbook requires input from instructors and their students. These include comments regarding writing, illustrations, supplements, factual content, and topics that may need greater or less emphasis. You are invited to contact me at:

Dr. Rob Brooker
Dept. of Genetics, Cell Biology, and Development
University of Minnesota
6-160 Jackson Hall
321 Church St.
Minneapolis, MN 55455
brook005@umn.edu

TEACHING AND LEARNING SUPPLEMENTS

McGraw-Hill offers various tools and technology products to support the third edition of *Genetics: Analysis & Principles.*

FOR THE INSTRUCTOR:

Online Learning Center (www.mhhe.com/brookergenetics3e)
The text specific website offers an extensive array of learning and teaching tools. In addition to student resources, the site also includes an instructor's manual, test bank, and lecture outlines.

Presentation Center
Complete set of electronic book images and assets for instructors
Build instructional materials wherever, whenever, and however you want! Accessed from your textbook's Online Learning Center, Presentation Center is an online digital library containing photos, artwork, animations, and other media types that can be used to create customized lectures, visually enhanced tests and quizzes, compelling course websites, or attractive printed support materials. All assets are copyrighted by McGraw-Hill Higher Education, but can be used by instructors for classroom purposes. The visual resources in this collection include:

- **Art** Full-color digital files of all illustrations in the book can be readily incorporated into lecture presentations, exams, or custom-made classroom materials. In addition, all files are pre-inserted into PowerPoint slides for ease of lecture preparation.
- **Photos** The photo collection contains digital files of photographs from the text, which can be reproduced for multiple classroom uses.
- **Tables** Every table that appears in the text has been saved in electronic form for use in classroom presentations and/or quizzes.
- **Animations** Numerous full-color animations illustrating important processes are also provided. Harness the visual impact of concepts in motion by importing these files into classroom presentations or online course materials.

Also residing on your textbook's Online Learning Center are:

- **PowerPoint Lecture Outlines** Ready-made presentations that combine art and lecture notes are provided for each chapter of the text.
- **PowerPoint Slides** For instructors who prefer to create their lectures from scratch, all illustrations, photos, and tables are pre-inserted by chapter into blank PowerPoint slides.

FOR THE STUDENT:

Student Study Guide/Solutions Manual
The solutions to the end-of-chapter problems and questions will aid the students in developing their problem-solving skills by providing the steps for each solution. The Study Guide follows the order of sections and subsections in the textbook and summarizes the main points in the text, figures, and tables. It also contains concept-building exercises, self-help quizzes, and practice exams.

Online Learning Center (www.mhhe.com/brookergenetics3e)
The text specific website offers an extensive array of learning tools, including a variety of quizzes for each chapter, interactive genetics problems, animations, and more.

ACKNOWLEDGMENTS

The production of a textbook is truly a collaborative effort, and I am greatly indebted to a variety of people. The first, second, and third editions went through multiple rounds of rigorous revisions that involved the input of faculty, students, editors, educational specialists, and media specialists. Their collective contributions are reflected in the final outcome.

Let me begin by acknowledging the many people at McGraw-Hill whose efforts are amazing. My highest praise goes to Lisa Bruflodt (Senior Developmental Editor), who managed and scheduled nearly every aspect of this project. I simply don't understand how one person can be so well organized and manage to stay calm at the same time. I also would like to thank Patrick Reidy (Executive Editor) for his patience in overseeing this project. He has the unenviable job of managing the budget for the book and that is not an easy task. I'm sure that he had some lively discussions with Janice Roerig-Blong (Publisher) during the course of this project. Other people at McGraw-Hill have played key roles in producing an actual book and the supplements that go along with it. In particular, Jayne Klein (Project Manager) has done a superb job of managing the components that need to be assembled to produce a book, along with Laura Fuller (Production Supervisor). I would also like to thank John Leland (Photo Research Coordinator), who acted as an interface between me and the photo company. In addition, my gratitude goes to John Joran (Designer), who provided much input into the internal design of the book as well as creating an awesome cover. Finally, I would like to thank Barb Owca (Marketing Manager), whose major efforts begin when the third edition comes out!

With regard to the content of the book, two editors worked closely with me in developing a book that is clear, consistent, and easy for students to follow. Deborah Brooker (Art/Text Coordinating Editor) analyzed all of the chapters in the textbook and made improvements with regard to art and text coordination. With great care, she examined the content in the text and determined if it matched what is found in the illustrations; she also checked every illustration for clarity and completeness. The high quality and pedagogy of the art are largely due to her efforts. She also scrutinized the text for clarity and logic. In addition, Joni Fraser (Freelance Development Editor) analyzed each chapter for its overall content and made many valuable suggestions for improvements. She did a great job of sharpening the writing. I am particularly grateful for her meticulous analysis of the problem sets. In her spare time, I think she may have worked all of

the problems. In addition to Deb and Joni, I would also like to thank Jane DeShaw (Freelance Copy Editor) for making grammatical improvements throughout the text and art.

I would also like to extend a special thanks to everyone at Imagineering, the art house that produced the illustrations in the second and third editions. Though we initially considered several art houses, when we saw how Imagineering could draw RNA polymerase, it was clear who the winner was. Their ability to draw three-dimensional molecular structures is outstanding. I am grateful to the many artists and contact people at Imagineering who have played important roles in developing the art for the second and third editions. Likewise, the people at Pronk & Associates have done a great job of locating many of the photographs that have been used in the third edition. Also, Lachina Publishing Services worked with great care in the paging of the book, making sure that the figures and relevant text are as close to each other as possible.

Finally, I want to thank the many scientists who reviewed the chapters of this textbook. Their broad insights and constructive suggestions were an important factor that shaped its final content and organization. I am truly grateful for their time and effort.

REVIEWERS

Shivanthi Anandan, *Drexel University*
Alan G. Atherly, *Iowa State University*
William Baird, *Clemson University*
Gail S. Begley, *Northeastern University*
Michael Benedik, *University of Houston*
Kelly Bidle, *Rider University*
Andrew J. Bohonak, *San Diego State University*
Mark A. Brick, *Colorado State University*
James J. Campanella, *Montclair State University*
Arden Campbell, *Iowa State University*
Gerard Campbell, *University of Pittsburgh*
Diane A. Caporale, *University of Wisconsin–Stevens Point*
J. Aaron Cassill, *University of Texas at San Antonio*
Richard W. Cheney, Jr., *Christopher Newport University*
Joseph P. Chinnici, *Virginia Commonwealth University*
Brian Condie, *University of Georgia*
Gregory Copenhaver, *University of North Carolina*
Stephen J. D'Surney, *University of Mississippi*
Sumana Datta, *Texas A&M University*
Jeff DeJong, *University of Texas at Dallas*
Robert S. Dotson, *Tulane University*
Johnny El-Rady, *University of South Florida*
Susan Elrod, *California Polytechnic State University*
Bert Ely, *University of South Carolina*
Les Erickson, *Salisbury University*
Michael L. Foster, *Eastern Kentucky University*
Robert G. Fowler, *San Jose State University*
Richard F. Gaber, *Northwestern University*
Sudhindra R. Gadagkar, *University of Dayton*
Matthew R. Gilg, *University of North Florida*
Jack R. Girton, *Iowa State University*
Michael A. Goldman, *San Francisco State University*
Elliott S. Goldstein, *Arizona State University*
Nels H. Granholm, *South Dakota State University*
Alison Hill, *Duke University*
Ralph Hillman, *Temple University*
David C. Hinkle, *University of Rochester*
J. Spencer Johnston, *Texas A&M University*
Gregg Jongeward, *University of the Pacific*
Christopher Kvaal, *St. Cloud State University*
Arlene T. Larson, *University of Colorado at Denver*
Elena Levine Keeling, *California Polytechnic State University*
Rebecca Lyczak, *Ursinus College*
Jocelyn Malamy, *University of Chicago*
Philip M. Mathis, *Middle Tennessee State University*
Terry R. McGuire, *Rutgers University*
Mark E. Meade, *Jacksonville State University*
Roderick M. Morgan, *Grand Valley State University*
Robert Moss, *Wofford College*
Jacqueline Peltier Horn, *Houston Baptist University*
David K. Peyton, *Morehead State University*
Chara J. Ragland, *Texas A&M University*
David H. Reed, *University of Mississippi*
Linda L. Restifo, *University of Arizona*
Inder Saxena, *University of Texas at Austin*
Deemah N. Schirf, *University of Texas at San Antonio*
Mark Schlueter, *Xavier University of Louisiana*
Ekaterina G. Sedia, *The Richard Stockton College of New Jersey*
Jeff Sekelsky, *University of North Carolina at Chapel Hill*
Richard N. Sherwin, *University of Pittsburgh*
Joan Smith Sonneborn, *University of Wyoming*
Adriana Stoica, *Georgetown University*
Martin Tracey, *Florida International University*
Carol Trent, *Western Washington University*
Sarah Ward, *Colorado State University*
Dan E. Wells, *University of Houston*
Douglas Wendell, *Oakland University*
Frederick Whipple, *California State University–Fullerton*
Mark Winey, *University of Colorado–Boulder*
David Wofford, *University of Florida*
Daniel Wang, *University of Miami*

ACCURACY CHECKERS

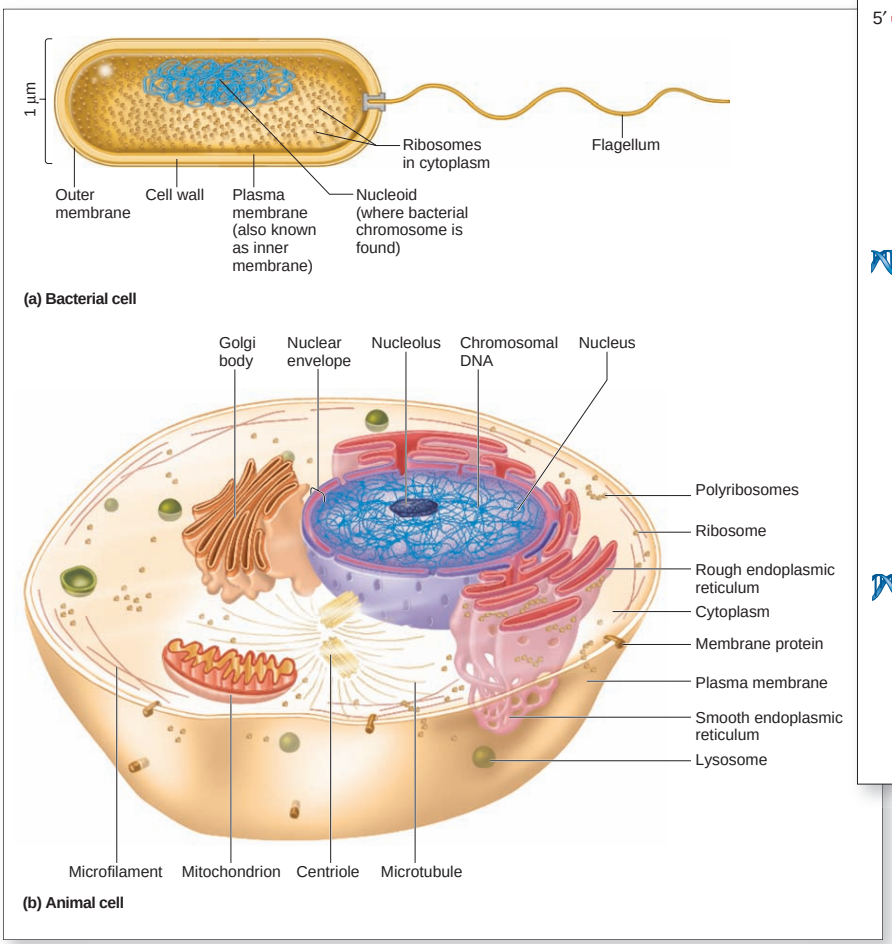
Ruth Ballard, *CSU–Sacramento*
Michel Baudry, *USC*
Michael Benedik, *University of Houston*
Carey Booth, *Portland State University*
Matt Bozovsky, *Loyola University*

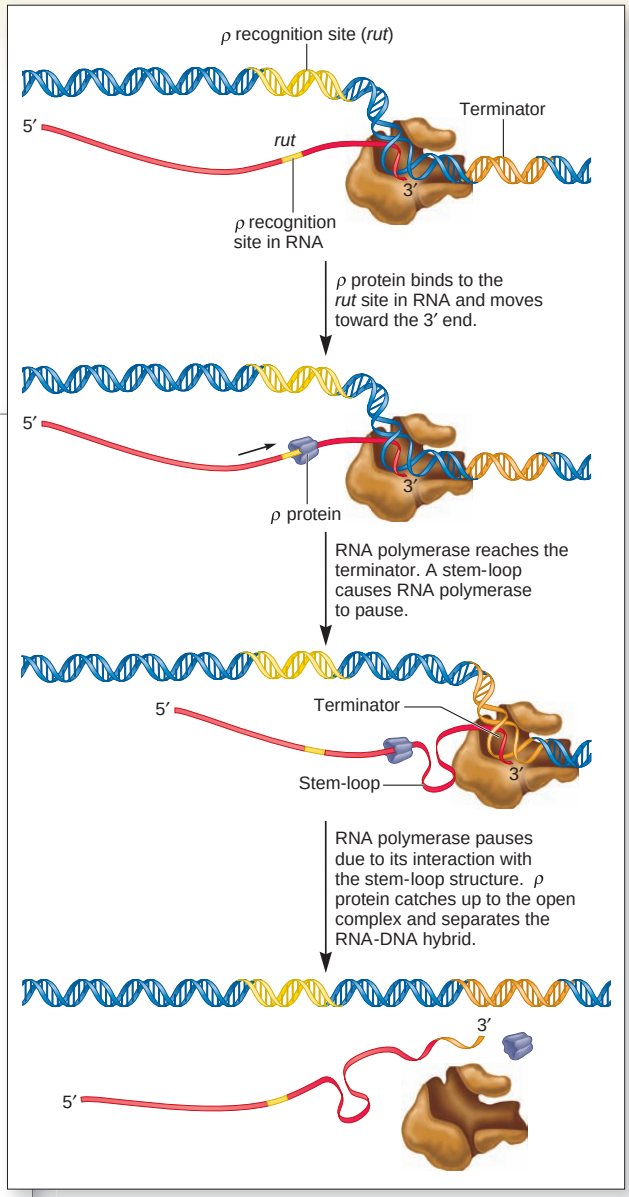
Joel Chandlee, *University of Rhode Island*
Henry Chang, *Purdue University*
Karen Cichy, *Michigan State University*
Brian Condie, *University of Georgia*
Erin Cram, *Northeastern University*
Jeff DeJong, *University of Texas at Dallas*
Rodney Dyer, *Virginia Commonwealth University*
Kevin Edwards, *Illinois State University*
Aboubaker Elkharroubi, *Johns Hopkins University*
Cedric Feschotte, *UT–Arlington*
David Foltz, *Louisiana State University*
Michael Foster, *Eastern Kentucky University*
Thomas Fowler, *Southern Illinois University*
Anne Galbraith, *UW–Lacrosse*
Jack Girton, *Iowa State University*
Elliott Goldstein, *ASU*
Christine Gray, *University of Puget Sound*
Tara Harmer Luke, *The Richard Stockton College of NJ*
Marilyn Hart, *Mankato State University*
Daryl Henderson, *Stony Brooker University*
Adam Hrincevich, *LSU*
Michael Ibba, *Ohio State University*
Margaret Jefferson, *CSU–LA*
David Kass, *Eastern Michigan University*
Cindy Malone, *CSU–Northridge*
John Mishler, *Delaware Valley College*
James Morris, *Clemson University*
Sang-Chul Nam, *Baylor University*
Daniel Odom, *California State University–Northridge*
Michael Polymenis, *Texas A&M University*
David Reed, *University of Mississippi*
Laurie Russell, *St. Louis University*
Mark Seeger, *Ohio State University*
Theresa Spradling, *University of Northern Iowa*
JD Swanson, *University of Central Arkansas*
James Thompson, *University of Oklahoma*
John Tomkiel, *U of NC–Greensboro*
Carol Trent, *Western Washington University*
Fyodor Urnov, *University of California–Berkeley*
Harald Vaessin, *Ohio State University*
Alan Waldman, *University of South Carolina*
Daniel Wang, *University of Miami*
Sarah Ward, *Colorado State University*
Matt White, *Ohio University*
Dwayne Wise, *Mississippi State University*
Yang Yen, *South Dakota State University*
Malcolm Zellars, *Georgia State University*
Jianzhi Zhang, *University of Michigan*

A Visual Guide to
GENETICS: ANALYSIS & PRINCIPLES

ROBERT J. BROOKER
UNIVERSITY OF MINNESOTA–MINNEAPOLIS

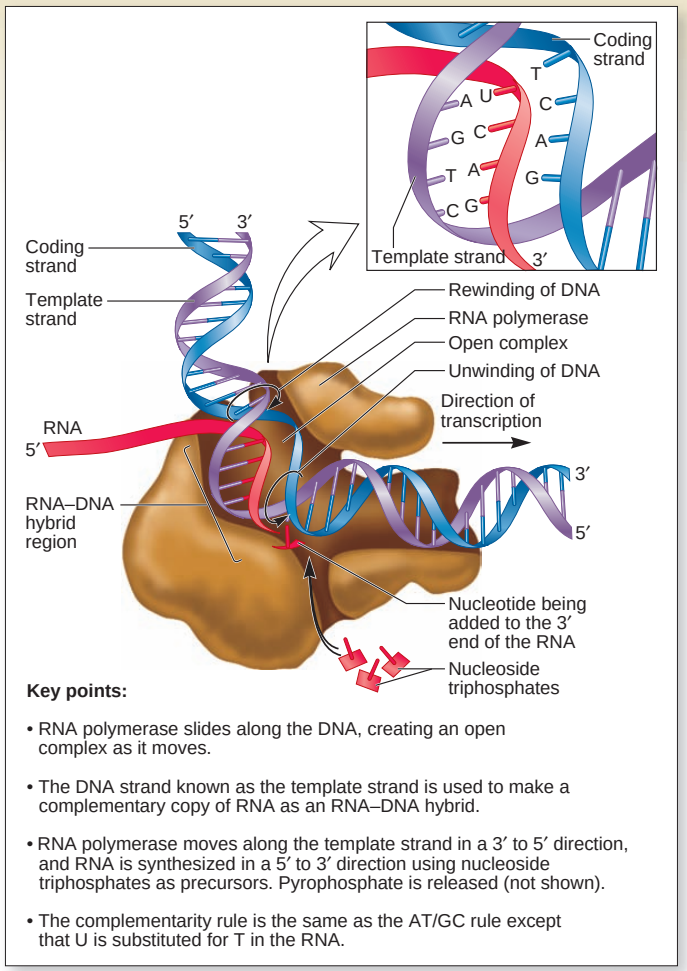
Brooker's Genetics *brings key concepts to life with its unique style of illustration.*





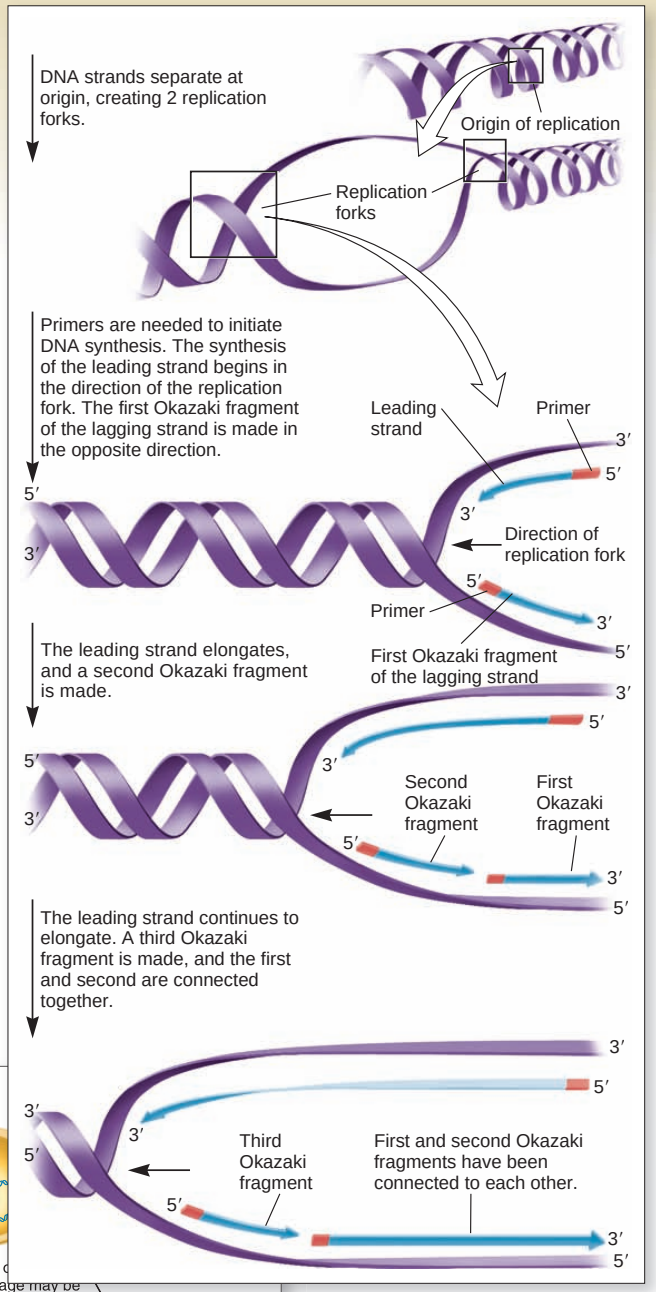
The digitally rendered images have a vivid three-dimensional look that will stimulate a student's interest and enthusiasm.

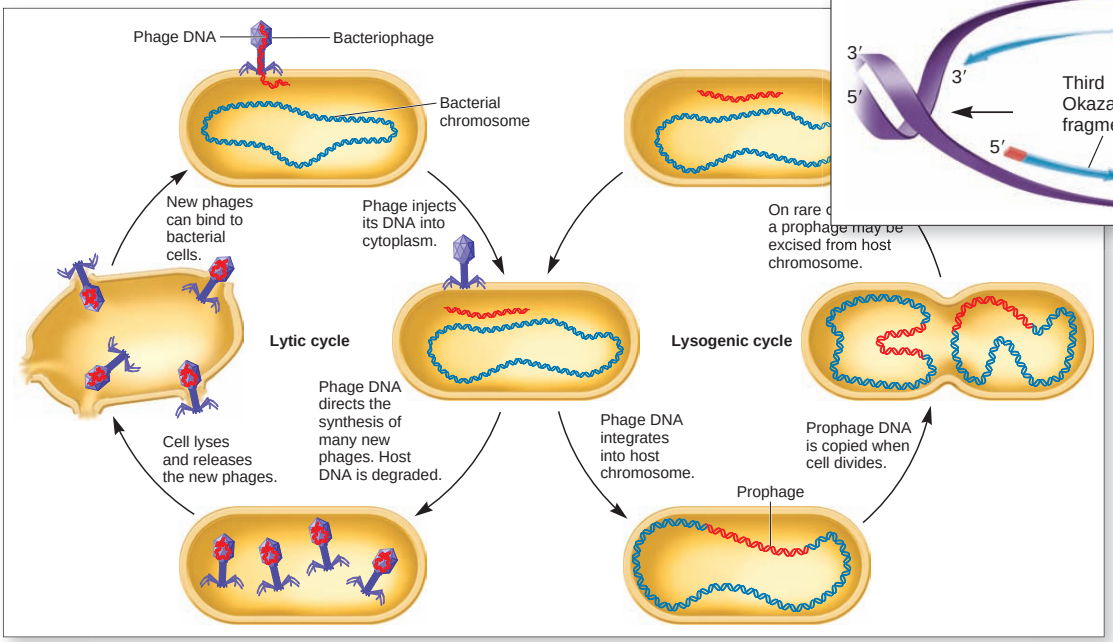
Each figure is carefully designed to follow closely with the text material.



Key points:

- RNA polymerase slides along the DNA, creating an open complex as it moves.
- The DNA strand known as the template strand is used to make a complementary copy of RNA as an RNA–DNA hybrid.
- RNA polymerase moves along the template strand in a 3′ to 5′ direction, and RNA is synthesized in a 5′ to 3′ direction using nucleoside triphosphates as precursors. Pyrophosphate is released (not shown).
- The complementarity rule is the same as the AT/GC rule except that U is substituted for T in the RNA.





Every illustration was drawn with four goals in mind: completeness, clarity, consistency, and realism.

Each chapter (beginning with Chapter 2) incorporates one or two experiments that are presented according to the scientific method. These experiments are integrated within the chapters and flow with the rest of the textbook. As you read the experiments, you will simultaneously explore the scientific method and the genetic principles learned from this approach.

STEP 1: BACKGROUND OBSERVATIONS

Each experiment begins with a description of the information that led researchers to study an experimental problem. Detailed information about the researchers and the experimental challenges they faced help students to understand actual research.

EXPERIMENT 5A

Creighton and McClintock Showed That Crossing Over Produced New Combinations of Alleles and Resulted in the Exchange of Segments Between Homologous Chromosomes

As we have seen, Morgan's studies were consistent with the hypothesis that crossing over occurs between homologous chromosomes to produce new combinations of alleles. To obtain direct evidence that crossing over can result in genetic recombination, Harriet Creighton and Barbara McClintock used an interesting strategy involving parallel observations. In studies conducted in 1931, they first made crosses involving two linked genes to produce parental and recombinant offspring. Second, they used a microscope to view the structures of the chromosomes in the parents and in the offspring. Because the parental chromosomes had some unusual structural features, they could microscopically distinguish the two homologous chromosomes within a pair. As we will see, this enabled them to correlate the occurrence of recombinant offspring with microscopically observable exchanges in segments of homologous chromosomes.

Creighton and McClintock focused much of their attention on the pattern of inheritance of traits in corn. This species has 10 different chromosomes per set, which are named chromosome 1, chromosome 2, chromosome 3, and so on. In previous cytological examinations of corn chromosomes, some strains were found to have an unusual chromosome 9 with a darkly staining knob at one end. In addition, McClintock identified an abnormal version of chromosome 9 that also had an extra piece of chromosome 8 attached at the other end (**Figure 5.5a**). This chromosomal rearrangement is called a translocation.

Creighton and McClintock insightfully realized that this abnormal chromosome could be used to demonstrate that two homologous chromosomes physically exchange segments as a result of crossing over. They knew that a gene was located near the knobbed end of chromosome 9 that provided color to corn kernels. This gene existed in two alleles, the dominant allele *C* (colored) and the recessive allele *c* (colorless). A second gene, located near the translocated piece from chromosome 8, affected the texture of the kernel endosperm. The dominant allele *Wx* caused starchy endosperm, and the recessive *wx* allele caused waxy endosperm. Creighton and McClintock reasoned that a crossover involving a normal chromosome 9 and a knobbed/translocated chromosome 9 would produce a chromosome that had either a knob or a translocation, but not both. These two types of chromosomes would be distinctly different from either of the parental chromosomes (**Figure 5.5b**).

As shown in the experiment of **Figure 5.6**, Creighton and McClintock began with a corn strain that carried an abnormal chromosome that had a knob at one end and a translocation at the other. Genotypically, this chromosome was *C wx*. The cytologically normal chromosome in this strain was *c Wx*. This corn plant, termed parent A, had the genotype *Cc Wxwx*. It was crossed to a strain called parent B that carried two cytologically normal chromosomes and had the genotype *cc Wxwx*.

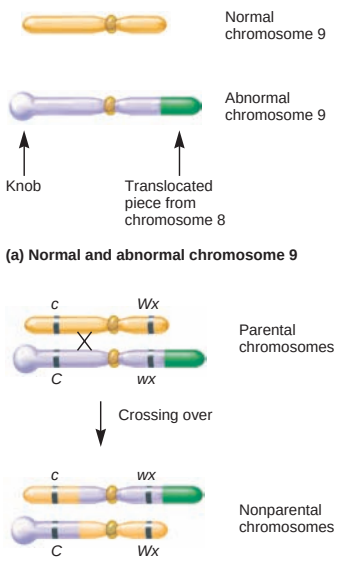


FIGURE 5.5 **Crossing over between a normal and abnormal chromosome 9 in corn.** (**a**) A normal chromosome 9 in corn is compared to an abnormal chromosome 9 that contains a knob at one end and a translocation at the opposite end. (**b**) A crossover produces a chromosome that contains only a knob at one end and another chromosome that contains only a translocation at the other end.

They then observed the kernels in two ways. First, they examined the phenotypes of the kernels to see if they were colored or colorless, and starchy or waxy. Second, the chromosomes in each kernel were examined under a microscope to determine their cytological appearance. Altogether, they observed a total of 25 kernels (see data of Figure 5.6).

THE HYPOTHESIS

Offspring with nonparental phenotypes are the product of a crossover. This crossover should create nonparental chromosomes via an exchange of chromosomal segments between homologous chromosomes.

STEP 2: HYPOTHESIS

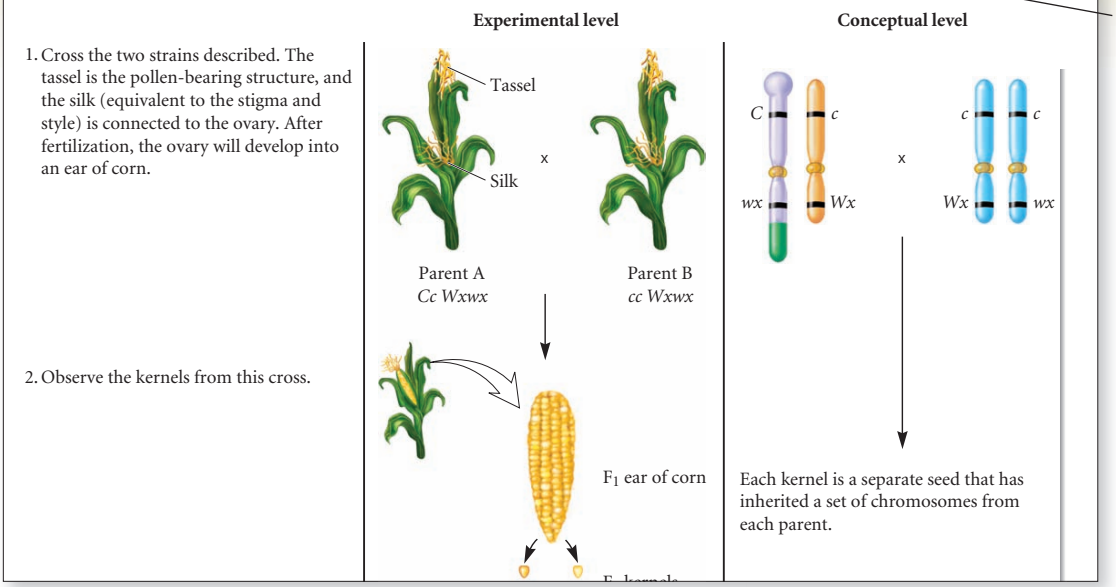
The student is given a statement describing the possible explanation for the observed phenomenon that will be tested. The hypothesis section reinforces the scientific method and allows students to experience the process for themselves.

STEP 3: TESTING THE HYPOTHESIS

This section illustrates the experimental process, including the actual steps followed by scientists to test their hypothesis. Science comes alive for students with this detailed look at experimentation.

TESTING THE HYPOTHESIS — FIGURE 5.6 Experimental correlation between genetic recombination and crossing over.

Starting materials: Two different strains of corn. One strain, referred to as parent A, had an abnormal chromosome 9 (knobbed/translocation) with a dominant *C* allele and a recessive *wx* allele. It also had a cytologically normal copy of chromosome 9 that carried the recessive *c* allele and the dominant *Wx* allele. Its genotype was *Cc Wxwx*. The other strain (referred to as parent B) had two normal versions of chromosome 9. The genotype of this strain was *cc Wxwx*.



STEP 4: THE DATA

Actual data from the original research paper help students understand how actual research results are reported. Each experiment's results are discussed in the context of the larger genetic principle to help students understand the implications and importance of the research.

THE DATA

Phenotype of F_1 *Kernel*	*Number of Kernels Analyzed*	*Cytological Appearance of a Chromosome in* F_1 *Offspring**		*Did a Crossover Occur During Gamete Formation in Parent A?*
Colored/waxy	3	Knobbed/translocation C wx	Normal w c x	o
Colorless/starchy	11	Knobless/normal c Wx	Normal W c x or c wx	No
Colorless/starchy	4	Knobless/translocation c wx	Normal c Wx	Yes
Colorless/waxy	2	Knobless/translocation c wx	Normal c wx	Yes
Colored/starchy	5	Knobbed/normal C Wx	Normal c Wx or c wx	Yes
Total	25			

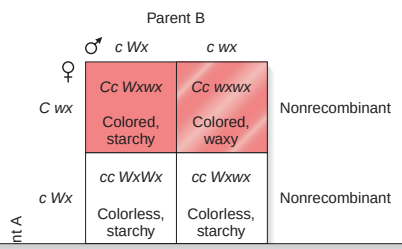
*In this table, the chromosome on the left was inherited from parent A, and the chromosome on the right was inherited from parent B.

STEP 5: INTERPRETING THE DATA

This discussion, which examines whether the experimental data supported or disproved the hypothesis, gives students an appreciation for scientific interpretation.

INTERPRETING THE DATA

By combining the gametes in a Punnett square, the following types of offspring can be produced:



Parent A	*Parent B*
C wx (nonrecombinant)	*c Wx*
c Wx (nonrecombinant)	*c wx*
C Wx (recombinant)	
c wx (recombinant)	

As seen in the Punnett square, two of the phenotypic categories, colored, starchy (*Cc Wxwx* or *Cc WxWx*) and colorless, starchy (*cc WxWx* or *cc Wxwx*), were ambiguous because they could arise from a nonrecombinant and from a recombinant gamete. In other words, these phenotypes could be produced whether or not recombination occurred in parent A. Therefore, let's focus on the two unambiguous phenotypic categories: colored, waxy (*Cc wxwx*) and colorless, waxy (*cc wxwx*). The colored, waxy phenotype could be

These problems are crafted to aid students in developing a wide range of skills. They also develop a student's cognitive, writing, analytical, computational, and collaborative abilities.

CONCEPTUAL QUESTIONS

Test the understanding of basic genetic principles. The student is given many questions with a wide range of difficulty. Some require critical thinking skills, and some require the student to write coherent essay questions.

Conceptual Questions

C1. What is the meaning of the term genetic material?

C2. After the DNA from type IIIS bacteria is exposed to type IIR bacteria, list all of the steps that you think must occur for the bacteria to start making a type IIIS capsule.

C3. Look up the meaning of the word transformation in a dictionary and explain whether it is an appropriate word to describe the transfer of genetic material from one organism to another.

C4. What are the building blocks of a nucleotide? With regard to the 5' and 3' positions on a sugar molecule, how are nucleotides linked together to form a strand of DNA?

C5. Draw the structure of guanine, guanosine, and deoxyguanosine triphosphate.

C6. Draw the structure of a phosphodiester linkage.

C7. Describe how bases interact with each other in the double helix. This discussion should address the issues of complementarity, hydrogen bonding, and base stacking.

C8. If one DNA strand is 5'–GGCATTACACTAGGCCT–3' what is the sequence of the complementary strand?

C9. What is meant by the term DNA sequence?

C10. Make a side-by-side drawing of two DNA helices, one with 10 base pairs (bp) per 360° turn and the other with 15 bp per 360° turn.

C11. Discuss the differences in the structural features of A DNA, B DNA, and Z DNA.

C12. What parts of a nucleotide (namely, phosphate, sugar, and/or bases) occupy the major and minor grooves of double-stranded DNA, and what parts are found in the DNA backbone? If a DNA-binding protein does not recognize a specific nucleotide sequence, do you expect that it recognizes the major groove, the minor groove, or the DNA backbone? Explain.

C16. Compare the structural features of a double-stranded RNA structure with those of a DNA double helix.

C17. Which of the following DNA double helices would be more difficult to separate into single-stranded molecules by treatment with heat, which breaks hydrogen bonds?

A. GGCGTACCAGCGCAT
CCGCATGGTCGCGTA

B. ATACGATTTACGAGA
TATGCTAAATGCTCT

Explain your choice.

C18. What structural feature allows DNA to store information?

C19. Discuss the structural significance of complementarity in DNA and in RNA.

C20. An organism has a G + C content of 64% in its DNA. What are the percentages of A, T, G, and C?

C21. Let's suppose you have recently identified an organism that was scraped from an asteroid that hit the earth. (Fortunately, no one was injured.) When you analyze this organism, you discover that its DNA is a triple helix, composed of six different nucleotides: A, T, G, C, X, and Y. You measure the chemical composition of the bases and find the following amounts of these six bases: A = 24%, T = 23%, G = 11%, C = 12%, X = 21%, Y = 9%. What rules would you propose govern triplex DNA formation in this organism? Note: There is more than one possibility.

C22. Upon further analysis of the DNA described in conceptual question C21, you discover that the triplex DNA in this alien organism is composed of a double helix, with the third helix wound within the major groove (just like the DNA in Figure 9.20). How would you propose that this DNA is able to replicate itself? In your answer, be specific about the base pairing rules within

EXPERIMENTAL QUESTIONS

Test the ability to analyze data, design experiments, or appreciate the relevance of experimental techniques.

Experimental Questions

E1. Genetic material acts as a blueprint for an organism's traits. Explain how the experiments of Griffith indicated that genetic material was being transferred to the type IIR bacteria.

E2. With regard to the experiment described in Figure 9.3, answer the following:

A. List several possible reasons why only a small percentage of the type IIR bacteria was converted to type IIIS.

B. Explain why an antibody must be used to remove the bacteria that are not transformed. What would the results look like, in all five cases, if the antibody/centrifugation step had not been included in the experimental procedure?

C. The DNA extract was treated with DNase, RNase, or protease. Why was this done? (In other words, what were the researchers trying to demonstrate?)

E3. An interesting trait that some bacteria exhibit is resistance to killing by antibiotics. For example, certain strains of bacteria are resistant to tetracycline, whereas other strains are sensitive to tetracycline. Describe an experiment you would carry out to demonstrate that tetracycline resistance is an inherited trait encoded by the DNA of the resistant strain.

E4. With regard to the experiment of Figure 9.6, answer the following:

A. Provide possible explanations why some of the DNA is in the supernatant.

B. Plot the results if the radioactivity in the pellet, rather than in the supernatant, had been measured.

C. Why were ^{32}P and ^{35}S chosen as radioisotopes to label the phages?

D. List possible reasons why less than 100% of the phage protein was removed from the bacterial cells during the shearing process.

E5. Does the experiment of Figure 9.6 rule out the possibility that RNA is the genetic material of T2 phage? Explain your answer. If it does not, could you modify the approach of Hershey and Chase to show that it is DNA and not RNA that is the genetic material of T2 bacteriophage? Note: It is possible to specifically label DNA or RNA by providing bacteria with radiolabeled thymine or uracil, respectively.

E6. In Chapter 9, we considered two experiments—one by Avery, MacLeod, and McCarty and the second by Hershey and Chase—that indicated DNA is the genetic material. Discuss the strengths

E7.

E8. answer the following:

A. What is the purpose of paper chromatography?

prior to its exposure to the plant tissue?

STUDENT DISCUSSION/ COLLARBORATION QUESTIONS

Encourage students to consider broad concepts and practical problems. Some questions require a substantial amount of computational activities, which can be worked on as a group.

Questions for Student Discussion/Collaboration

1. Try to propose structures for a genetic material that are substantially different from the double helix. Remember that the genetic material must have a way to store information and a way to be faithfully replicated.

2. How might you provide evidence that DNA is the genetic material in mice?

Note: All answers appear at the website for this textbook; the answers to even-numbered questions are in the back of the textbook.

www.mhhe.com/brookergenetics3e

Visit the Online Learning Center for practice tests, answer keys, and other learning aids for this chapter. Enhance your understanding of genetics with our interactive exercises, quizzes, animations, and much more.

1 OVERVIEW OF GENETICS

Hardly a week goes by without a major news story involving a genetic breakthrough. The increasing pace of genetic discoveries has become staggering. The Human Genome Project is a case in point. This project began in the United States in 1990, when the National Institutes of Health and the Department of Energy joined forces with international partners to decipher the massive amount of information contained in our **genome**—the DNA found within all of our chromosomes (**Figure 1.1**). Working collectively, a large group of scientists from around the world has produced a detailed series of maps that help geneticists navigate through human DNA. Remarkably, in only a decade, they determined the DNA sequence (read in the bases of A, T, G, and C) covering over 90% of the human genome. The first draft of this sequence, published in 2001, is nearly 3 billion nucleotide base pairs in length. The completed sequence, published in 2003, has an accuracy greater than 99.99%; fewer than one mistake was made in every 10,000 base pairs!

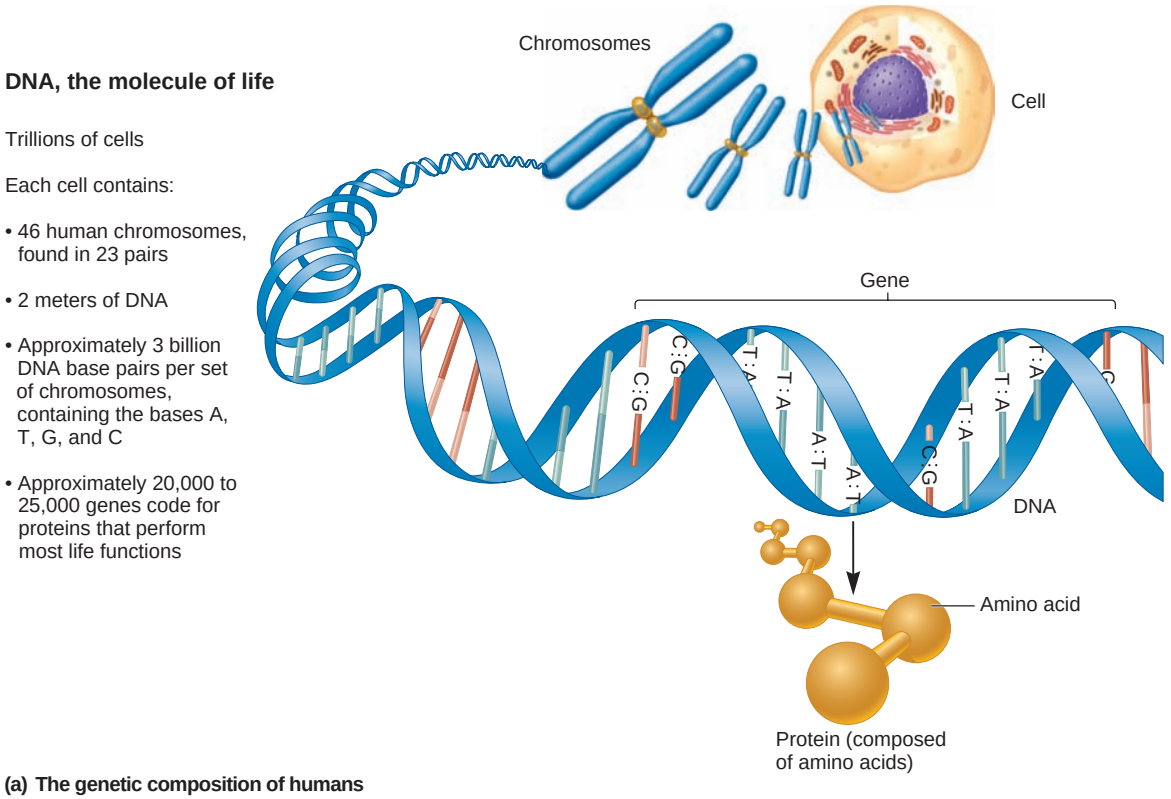
Studying the human genome allows us to explore fundamental details about ourselves at the molecular level. The results of the project are expected to shed considerable light on basic questions, like how many genes we have, how genes direct the activities of living cells, how species evolve, how single cells develop into complex tissues, and how defective genes cause disease. Furthermore, such understanding may lend itself to improvements in modern medicine by leading to better diagnoses of diseases and the development of new medicines to treat them.

As scientists have attempted to unravel the mysteries within our genes, this journey has involved the invention of many new technologies. This textbook emphasizes a large number of these modern approaches. Paradoxically, one could argue that these advancements may have a greater impact on our lives than the original discoveries upon which they were based. For example, the technology of gene cloning originally arose from discoveries concerning bacterial enzymes that "cut and paste" DNA fragments together. These scientific discoveries have made it possible to create medicines that would otherwise be difficult or impossible to make. An example is human recombinant insulin, termed *Humulin,* which is synthesized in a strain of *Escherichia coli* bacteria that has been genetically altered by the addition of the gene for human insulin. The bacteria are grown in a laboratory and make large amounts of human insulin. As discussed in Chapter 19, this insulin is purified and administered to many people with insulin-dependent diabetes.

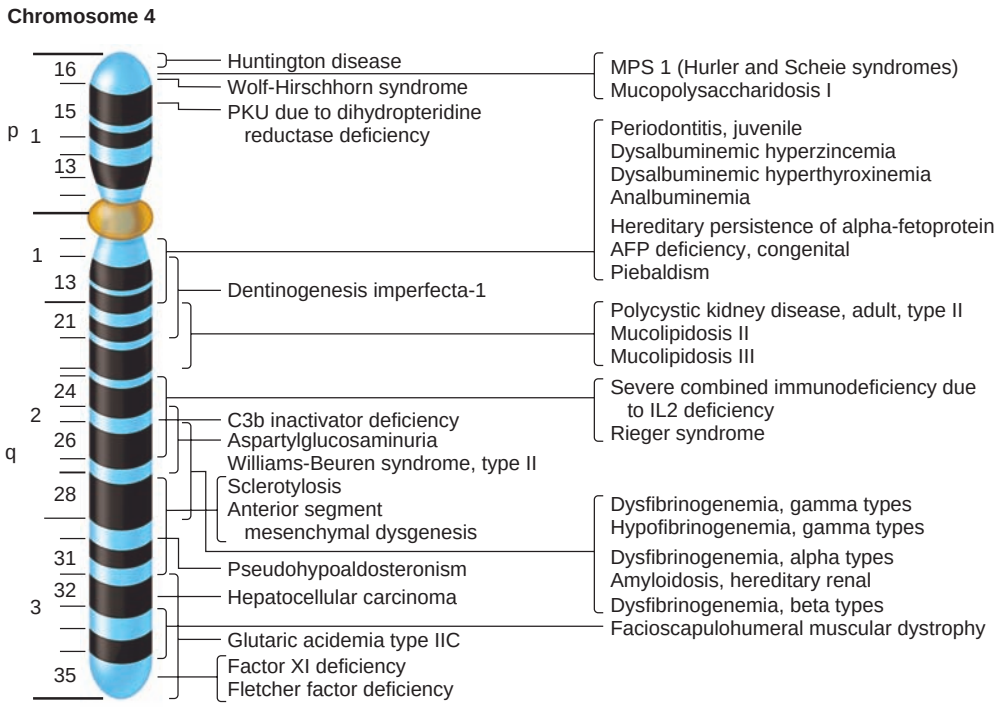
CHAPTER OUTLINE

Copycat, the first cloned pet. In 2002, the cat shown here, called Copycat, was produced by cloning, a procedure described in Chapter 19.

PART I
Introduction



(a) The genetic composition of humans



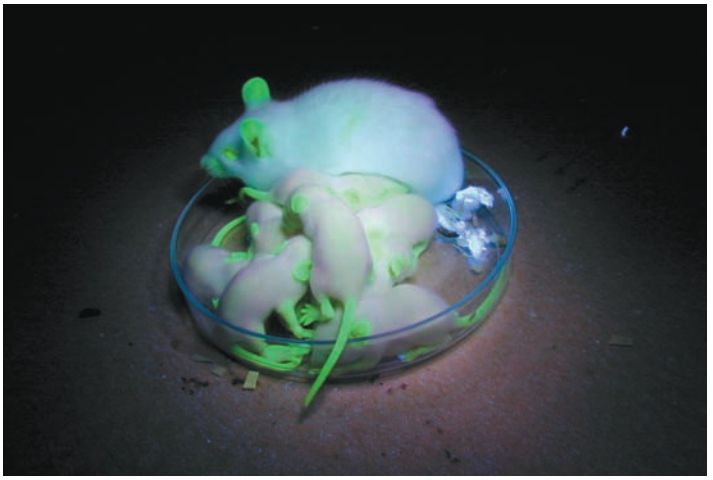
(b) Genes on one human chromosome that are associated with disease when mutant

FIGURE 1.1 **The Human Genome Project.** (**a**) The human genome is a complete set of human chromosomes. People have two sets of chromosomes, one from each parent. Collectively, each set of chromosomes is composed of a DNA sequence that is approximately 3 billion nucleotide base pairs long. Estimates suggest that each set contains about 20,000 to 25,000 different genes. This figure emphasizes the DNA found in the cell nucleus. Humans also have a small amount of DNA in their mitochondria, which has also been sequenced. (**b**) An important outcome of this work is the identification of genes that contribute to human diseases. This illustration depicts a map of a few genes that are located on human chromosome 4. When these genes carry certain rare mutations, they can cause the diseases designated in this figure.

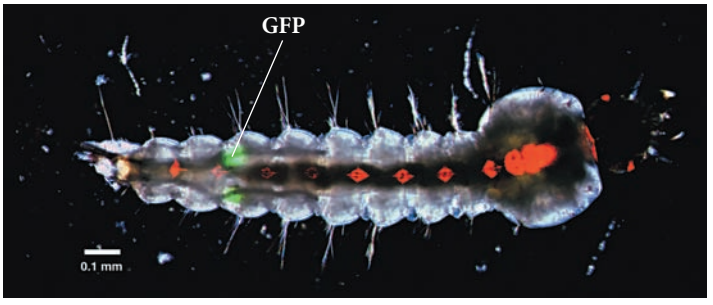
New genetic technologies are often met with skepticism and sometimes even with disdain. An example would be DNA fingerprinting, a molecular method to identify an individual based on a DNA sample (see Chapter 24). Though this technology is now relatively common in the area of forensic science, it was not always universally accepted. High-profile crime cases in the news cause us to realize that not everyone believes in DNA fingerprinting, in spite of its extraordinary ability to uniquely identify individuals. A second controversial example would be mammalian cloning. In 1997, Ian Wilmut and his colleagues created clones of sheep, using mammary cells from an adult animal (**Figure 1.2**). More recently, such cloning has been achieved in several mammalian species, including sheep, cows, mice, goats, pigs, and cats. In 2002, the first pet was cloned, a cat named Copycat (see photo at the beginning of the chapter). The cloning of mammals provides the potential for many practical applications. With regard to livestock, cloning would enable farmers to use cells from their best individuals to create genetically homogeneous herds. This could be advantageous in terms of agricultural yield, although such a genetically homogeneous herd may be more susceptible to certain diseases. However, people have become greatly concerned with the possibility of human cloning. This prospect has raised serious ethical questions. Within the past few years, legislative bills have been introduced that involve bans on human cloning.

Finally, genetic technologies provide the means to modify the traits of animals and plants in ways that would have been unimaginable just a few decades ago. **Figure 1.3a** illustrates a bizarre example in which scientists introduced a gene from jellyfish into mice. As you may know, certain species of jellyfish emit a "green glow." These jellyfish have a gene that encodes a bioluminescent protein called green fluorescent protein (GFP). When exposed to blue or ultraviolet (UV) light, the protein emits a striking green-colored light. Scientists were able to clone the *GFP* gene from a sample of jellyfish cells and then introduce this gene into laboratory mice. The GFP protein is made throughout the cells of their bodies. As a result, their skin, eyes, and organs give off an eerie green glow when exposed to UV light. Only their fur does not glow.

FIGURE 1.2 **The cloning of a mammal.** The lamb on the left is Dolly, the first mammal to be cloned. She was cloned from the cells of a Finn Dorset (a white-faced sheep). The sheep on the right is Dolly's surrogate mother, a Blackface ewe. A description of how Dolly was created is presented in Chapter 19.



(a) GFP expressed in mice



(b) GFP expressed in the gonads of a male mosquito

FIGURE 1.3 **The introduction of a jellyfish gene into laboratory mice and mosquitoes.** **(a)** A gene that naturally occurs in the jellyfish encodes a protein called green fluorescent protein (GFP). The GFP gene was cloned and introduced into mice. When these mice are exposed to UV light, GFP emits a bright green color. These mice glow green, just like jellyfish! **(b)** GFP was introduced next to a gene sequence that causes the expression of GFP only in the gonads of male mosquitoes. This allows researchers to identify and sort males from females.

GFP allows researchers to identify particular proteins in cells or specific body parts. For example, Andrea Crisanti and colleagues have altered mosquitoes to express a green fluorescent protein only in the gonads of males (**Figure 1.3b**). This enables the researchers to identify and sort males and females. Why is this useful? The ability to rapidly sort mosquitoes makes it possible to produce populations of sterile males and then release the sterile males without the risk of releasing additional females. The release of sterile males may be effective at controlling mosquito populations because females only breed once before they die. Mating with a sterile male will prevent a female from producing offspring.

Overall, as we move forward in the twenty-first century, the excitement level in the field of genetics is high, perhaps higher than it has ever been. Nevertheless, the excitement generated by new genetic knowledge and technologies will also create many ethical and societal challenges. In this chapter, we will begin with an overview of genetics and then explore the various fields of genetics and their experimental approaches.

1.1 THE RELATIONSHIP BETWEEN GENES AND TRAITS

Genetics is the branch of biology that deals with heredity and variation. It stands as the unifying discipline in biology by allowing us to understand how life can exist at all levels of complexity, ranging from the molecular to the population level. Genetic variation is the root of the natural diversity that we observe among members of the same species as well as among different species.

Genetics is centered on the study of genes. A gene is classically defined as a unit of heredity, but such a vague definition does not do justice to the exciting characteristics of genes as intricate molecular units that manifest themselves as potent contributors to cell structure and function. At the molecular level, a **gene** is a segment of DNA that produces a functional product. The functional product of most genes is a polypeptide, which is a linear sequence of amino acids that folds into units that constitute proteins. In addition, genes are commonly described according to the way they affect **traits,** which are the characteristics of an organism. In humans, for example, we speak of traits such as eye color, hair texture, and height. The ongoing theme of this textbook is the relationship between genes and traits. As an organism grows and develops, its collection of genes provides a blueprint that determines its characteristics.

In this section of Chapter 1, we will examine the general features of life, beginning with the molecular level and ending with populations of organisms. As will become apparent, genetics is the common thread that explains the existence of life and its continuity from generation to generation. For most students, this chapter should serve as a cohesive review of topics they learned in other introductory courses such as General Biology. Even so, it is usually helpful to see the "big picture" of genetics before delving into the finer details that are covered in Chapters 2 through 26.

Living Cells Are Composed of Biochemicals

To fully understand the relationship between genes and traits, we need to begin with an examination of the composition of living organisms. Every cell is constructed from intricately organized chemical substances. Small organic molecules such as glucose and amino acids are produced from the linkage of atoms via chemical bonds. The chemical properties of organic molecules are essential for cell vitality in two key ways. First, the breakage of chemical bonds during the degradation of small molecules provides energy to drive cellular processes. A second important function of these small organic molecules is their role as the building blocks for the synthesis of larger molecules. Four important categories of larger cellular molecules are **nucleic acids** (i.e., DNA and RNA), **proteins, carbohydrates,** and **lipids.** Three of these—nucleic acids, proteins, and carbohydrates—form **macromolecules** that are composed of many repeating units of smaller building blocks. Proteins, RNA, and carbohydrates can be made from hundreds or even thousands of repeating building blocks. DNA is the largest macromolecule found in living cells. A single DNA molecule can be composed of a linear sequence of hundreds of millions of nucleotides!

The formation of cellular structures relies on the interactions of molecules and macromolecules. For example, nucleotides are the building blocks of DNA, which is a constituent of cellular chromosomes (**Figure 1.4**). In addition, the DNA is associated with a myriad of proteins that provide organization to the structure of chromosomes. Within a eukaryotic cell, the chromosomes are contained in a compartment called the cell nucleus. The nucleus is bounded by a membrane composed of lipids and proteins that shields the chromosomes from the rest of the cell. The organization of chromosomes within a cell nucleus protects the chromosomes from mechanical breakage and provides a single compartment for genetic activities such as gene transcription. As a general theme, the formation of large cellular structures arises from interactions among different molecules and macromolecules. These cellular structures, in turn, are organized to make a complete living cell.

Each Cell Contains Many Different Proteins That Determine Cellular Structure and Function

To a great extent, the characteristics of a cell depend on the types of proteins that it makes. As we will learn throughout this textbook, proteins are the "workhorses" of all living cells. The range of functions among different types of proteins is truly remarkable. Some proteins help determine the shape and structure of a given cell. For example, the protein known as tubulin can assemble into large structures known as microtubules, which provide the cell with internal structure and organization. Other proteins are inserted into cell membranes and aid in the transport of ions and small molecules across the membrane. Proteins may also function as biological motors. An interesting case is the protein known as myosin, which is involved in the contractile properties of muscle cells. Within multicellular organisms, certain proteins also function in cell-to-cell recognition and signaling. For example, hormones such as insulin are secreted by endocrine cells and

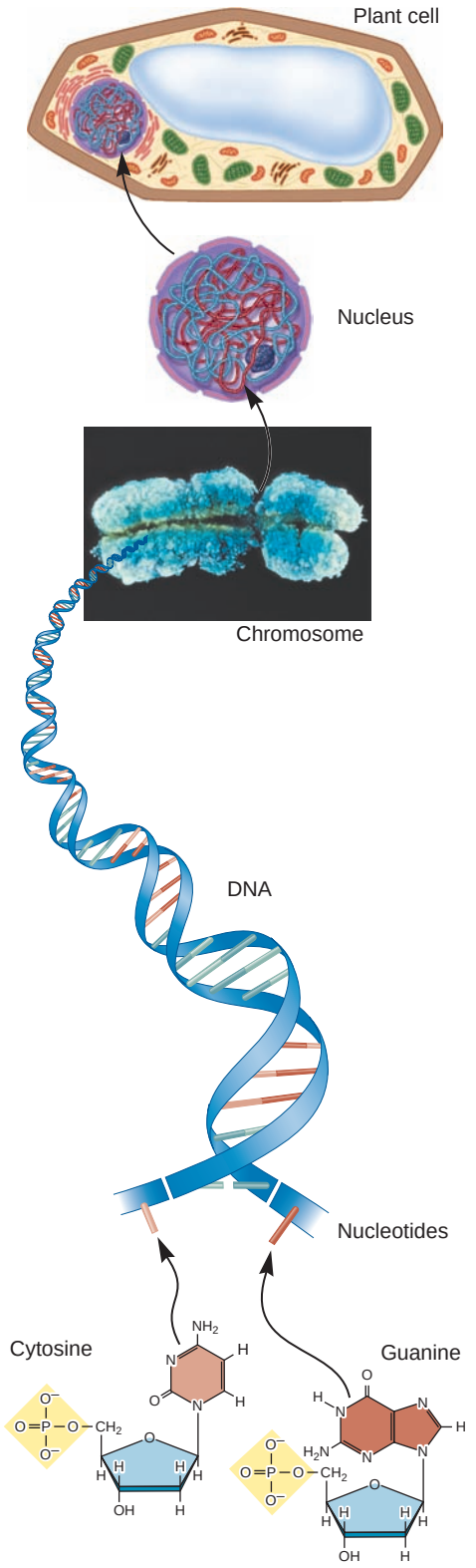


FIGURE 1.4 **Chemical composition of living cells.** Cellular structures are constructed from smaller building blocks. In this example, DNA is formed from the linkage of nucleotides to produce a very long macromolecule. The DNA associates with proteins to form a chromosome. The chromosomes are located within a membrane-bounded organelle called the nucleus, which, along with many different types of organelles, is found within a complete cell.

bind to the insulin receptor protein found within the plasma membrane of target cells.

Enzymes, which accelerate chemical reactions, are a particularly important category of proteins. Some enzymes play a role in the breakdown of molecules or macromolecules into smaller units. These are known as catabolic enzymes and are important in the utilization of energy. Alternatively, anabolic enzymes and accessory proteins function in the synthesis of molecules and macromolecules throughout the cell. The construction of a cell greatly depends on its proteins involved in anabolism because these are required to synthesize all cellular macromolecules.

Molecular biologists have come to realize that the functions of proteins underlie the cellular characteristics of every organism. At the molecular level, proteins can be viewed as the active participants in the enterprise of life.

DNA Stores the Information for Protein Synthesis

The genetic material is composed of a substance called **deoxyribonucleic acid,** abbreviated **DNA.** The DNA stores the information needed for the synthesis of all cellular proteins. In other words, the main function of the genetic blueprint is to code for the production of cellular proteins in the correct cell, at the proper time, and in suitable amounts. This is an extremely complicated task because living cells make thousands of different proteins. Genetic analyses have shown that a typical bacterium can make a few thousand different proteins, and estimates among higher eukaryotes range in the tens of thousands.

DNA's ability to store information is based on its molecular structure. DNA is composed of a linear sequence of **nucleotides.** Each nucleotide contains one nitrogen-containing base, either adenine (A), thymine (T), guanine (G), or cytosine (C). The linear order of these bases along a DNA molecule contains information similar to the way that groups of letters of the alphabet represent words. For example, the "meaning" of the sequence of bases ATGGGCCTTAGC differs from that of TTTAAGCTTGCC. DNA sequences within most genes contain the information to direct the order of amino acids within polypeptides according to the **genetic code.** In the code, a three-base sequence specifies one particular **amino acid** among the 20 possible choices. One or more polypeptides form a functional protein. In this way, the DNA can store the information to specify the proteins made by an organism.

DNA Sequence	Amino Acid Sequence
ATG GGC CTT AGC	METHIONINE GLYCINE LEUCINE SERINE
TTT AAG CTT GCC	PHENYLALANINE LYSINE LEUCINE ALANINE

In living cells, the DNA is found within large structures known as **chromosomes.** Figure 1.5 is a photograph of the 46 chromosomes contained in a cell from a human male. The DNA of an average human chromosome is an extraordinarily long, linear, double-stranded structure that contains well over a hundred

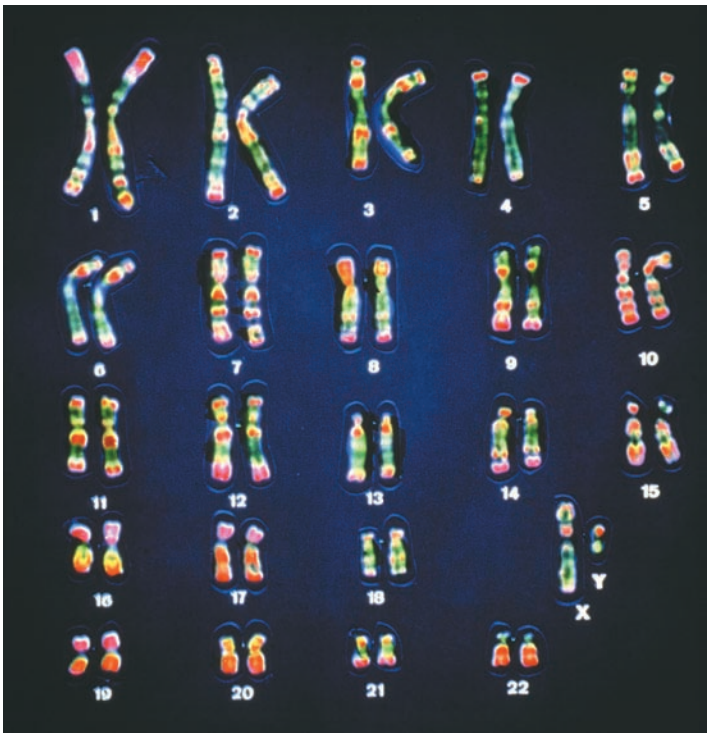
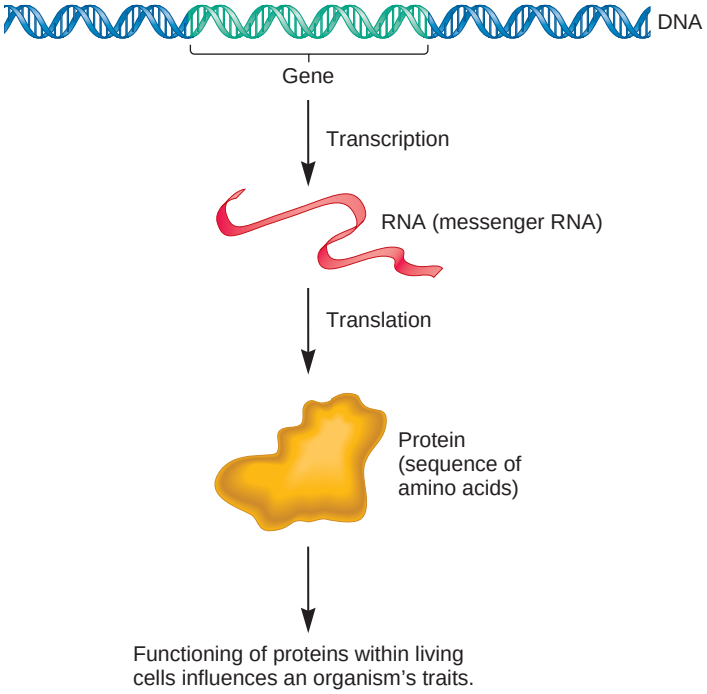


FIGURE 1.5 **A micrograph of the 46 chromosomes found in a cell from a human male.**



ONLINE ANIMATION

FIGURE 1.6 **Gene expression at the molecular level.** The expression of a gene is a multistep process. During transcription, one of the DNA strands is used as a template to make an RNA strand. During translation, the RNA strand is used to specify the sequence of amino acids within a polypeptide. One or more polypeptides produce a protein that functions within the cell, thereby influencing an organism's traits.

million nucleotides. Along the immense length of a chromosome, the genetic information is parceled into functional units known as genes. An average-sized human chromosome is expected to contain about 1,000 different genes.

The Information in DNA Is Accessed During the Process of Gene Expression

To synthesize its proteins, a cell must be able to access the information that is stored within its DNA. The process of using a gene sequence to affect the characteristics of cells and organisms is referred to as **gene expression.** At the molecular level, the information within genes is accessed in a stepwise process. In the first step, known as **transcription,** the DNA sequence within a gene is copied into a nucleotide sequence of **ribonucleic acid (RNA).** Most RNAs contain the information for the synthesis of a particular polypeptide. This type of RNA is called **messenger RNA (mRNA).** For polypeptide synthesis to occur, the sequence of nucleotides transcribed in an mRNA must be **translated** (using the genetic code) into the amino acid sequence of a polypeptide (Figure 1.6). After a polypeptide is made, it folds into a three-dimensional structure. As mentioned, a protein is a functional unit. Some proteins are composed of a single polypeptide, and other proteins consist of two or more polypeptides.

Gene expression results in the production of proteins with specific structures and functions. The unique relationship between gene sequences and protein structures is of paramount importance because the distinctive structure of each protein determines its function within a living cell or organism. Mediated by the process of gene expression, therefore, the sequence of nucleotides in DNA stores the information required for synthesizing proteins with specific structures and functions.

The Molecular Expression of Genes Within Cells Leads to an Organism's Traits

A trait is any characteristic that an organism displays. In genetics, we often focus our attention on **morphological traits** that affect the appearance of an organism. The color of a flower and the height of a pea plant are morphological traits. Geneticists frequently study these types of traits because they are easy to evaluate. For example, an experimenter can simply look at a plant and tell if it has red or white flowers. However, not all traits are morphological. **Physiological traits** affect the ability of an organism to function. For example, the rate at which a bacterium metabolizes a sugar such as lactose is a physiological trait. Like morphological traits, physiological traits are controlled, in part, by the expression of genes. **Behavioral traits** also affect the ways that an organism responds to its environment. An example would be the mating calls of bird species. In animals, the nervous system plays a key role in governing such traits.

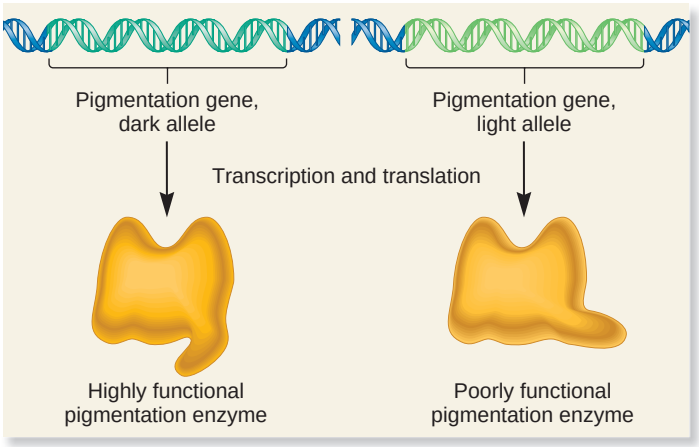
A difficult, yet very exciting, aspect of genetics is that our observations and theories span four levels of biological organization: molecules, cells, organisms, and populations. This can make it difficult to appreciate the relationship between genes and traits. To understand this connection, we need to relate the following phenomena:

1. Genes are expressed at the **molecular level.** In other words, gene transcription and translation lead to the production of a particular protein, which is a molecular process.
2. Proteins often function at the **cellular level.** The function of a protein within a cell will affect the structure and workings of that cell.
3. An organism's traits are determined by the characteristics of its cells. We do not have microscopic vision, yet when we view morphological traits, we are really observing the properties of an individual's cells. For example, a red flower has its color because the flower cells make a red pigment. The trait of red flower color is an observation at the **organism level.** Yet the trait is rooted in the molecular characteristics of the organism's cells.
4. A **species** is a group of organisms that maintains a distinctive set of attributes in nature. The occurrence of a trait within a species is an observation at the **population level.** Along with learning how a trait occurs, we also want to understand why a trait becomes prevalent in a particular species. In many cases, researchers discover that a trait predominates within a population because it promotes the reproductive success of the members of the population. This leads to the evolution of beneficial traits.

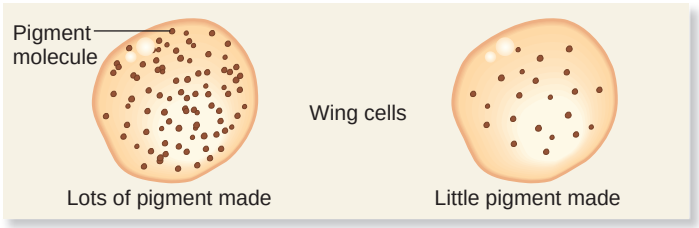
As a schematic example to illustrate the four levels of genetics, Figure 1.7 shows the trait of pigmentation in butterflies. One is light-colored and the other is very dark. Let's consider how we can explain this trait at the molecular, cellular, organism, and population levels.

At the molecular level, we need to understand the nature of the gene or genes that govern this trait. As shown in Figure 1.7a, a gene, which we will call the pigmentation gene, is responsible for the amount of pigment that is produced. The pigmentation gene can exist in two different forms called **alleles.** In this example, one allele confers a dark pigmentation and one causes a light pigmentation. Each of these alleles encodes a protein that functions as a pigment-synthesizing enzyme. However, the DNA sequences of the two alleles differ slightly from each other. This difference in the DNA sequence leads to a variation in the structure and function of the respective pigmentation enzymes.

At the cellular level (Figure 1.7b), the functional differences between the pigmentation enzymes affect the amount of pigment that is produced. The allele causing dark pigmentation, which is shown on the left, encodes a protein that functions very well. Therefore, when this gene is expressed in the cells of the wings, a large amount of pigment is made. By comparison, the allele causing light pigmentation encodes an enzyme that functions poorly. Therefore, when this allele is the only pigmentation gene that is expressed, little pigment is made.

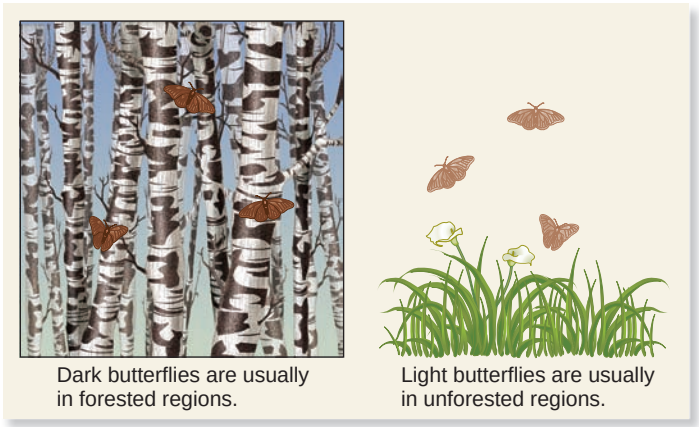


(a) Molecular level



(b) Cellular level

(c) Organism level



(d) Population level

FIGURE 1.7 **The relationship between genes and traits at the (a) molecular, (b) cellular, (c) organism, and (d) population levels.**

At the organism level (Figure 1.7c), the amount of pigment in the wing cells governs the color of the wings. If the pigment cells produce high amounts of pigment, the wings are dark-colored; if the pigment cells produce little pigment, the wings are light.

Finally, at the population level (Figure 1.7d), geneticists would like to know why a species of butterfly would contain some members with dark wings and other members with light wings. One possible explanation is differential predation. The butterflies with dark wings might avoid being eaten by birds if they happen to live within the dim light of a forest. The dark wings would help to camouflage the butterfly if it were perched on a dark surface such as a tree trunk. In contrast, the lightly colored wings would be an advantage if the butterfly inhabited a brightly lit meadow. Under these conditions, a bird may be less likely to notice a light-colored butterfly that is perched on a sunlit surface. A population geneticist might study this species of butterfly and find that the dark-colored members usually live in forested areas and the light-colored members reside in unforested regions.

Inherited Differences in Traits Are Due to Genetic Variation

In Figure 1.7, we considered how gene expression could lead to variation in a trait of an organism, such as dark- versus light-colored butterflies. Variation in traits among members of the same species is very common. For example, some people have brown hair, while others have blond hair; some petunias have white flowers, while others have purple flowers. These are examples of **genetic variation.** This term describes the differences in inherited traits among individuals within a population.

In large populations that occupy a wide geographic range, genetic variation can be quite striking. In fact, morphological differences have often led geneticists to misidentify two members of the same species as belonging to separate species. As an example, **Figure 1.8** compares four garter snakes that are members of the same species, *Thamnophis ordinoides.* They display dramatic differences in their markings. Such contrasting forms within a single species are termed **morphs.** You can easily imagine how someone might mistakenly conclude that these four snakes are not members of the same species.

Changes in the nucleotide sequence of DNA underlie the genetic variation that we see among individuals. Throughout this textbook, we will routinely examine how variation in the genetic material results in changes in the outcome of traits. At the molecular level, genetic variation can be attributed to different types of modifications.

1. Small or large differences can occur within gene sequences. These are called **gene mutations.** This type of variation, which produces two or more alleles of the same gene, was previously described in Figure 1.7. In many cases, gene mutations will alter the expression or function of the protein that the gene specifies.

FIGURE 1.8 **Four garter snakes showing different morphs within a single species.**

2. Major alterations can also occur in the structure of a chromosome. A large segment of a chromosome can be lost, rearranged, or reattached to another chromosome.
3. Variation may also occur in the total number of chromosomes. In some cases, an organism may inherit one too many or one too few chromosomes. In other cases, it may inherit an extra set of chromosomes.

Variations within the sequences of genes are a common source of genetic variation among members of the same species. In humans, familiar examples of variation involve genes for eye color, hair texture, and skin pigmentation. Chromosome variation—a change in chromosome structure and/or number—is also found, but this type of change is often detrimental. Many human genetic disorders are the result of chromosomal alterations. The most common example is Down syndrome, which is due to the presence of an extra chromosome (**Figure 1.9a**). By comparison, chromosome variation in plants is common and often can lead to strains of plants with superior characteristics, such as increased resistance to disease. Plant breeders have frequently exploited this observation. Cultivated varieties of wheat, for example, have many more chromosomes than the wild species (**Figure 1.9b**).

Traits Are Governed by Genes and by the Environment

In our discussion thus far, we have considered the role that genes play in the outcome of traits. Another critical factor is the **environment**—the surroundings in which an organism exists. A variety of factors in an organism's environment profoundly affect its morphological and physiological features. For example, a person's diet greatly influences many traits such as height, weight, and even intelligence. Likewise, the amount of sunlight a plant receives affects its growth rate and the color of its flowers. The

(a) (b)

FIGURE 1.9 **Examples of chromosome variation.** (**a**) A person with Down syndrome competing in the Special Olympics. This person has 47 chromosomes rather than the common number of 46, because she has an extra copy of chromosome 21. (**b**) A wheat plant. Bread wheat is derived from the contributions of three related species with two sets of chromosomes each, producing an organism with six sets of chromosomes.

term **norm of reaction** refers to the effects of environmental variation on an individual's traits.

External influences may dictate the way that genetic variation is manifested in an individual. An interesting example is the human genetic disease **phenylketonuria (PKU).** Humans possess a gene that encodes an enzyme known as phenylalanine hydroxylase. Most people have two functional copies of this gene. People with one or two functional copies of the gene can eat foods containing the amino acid phenylalanine and metabolize it properly.

A rare variation in the sequence of the phenylalanine hydroxylase gene results in a nonfunctional version of this protein. Individuals with two copies of this rare, inactive allele cannot metabolize phenylalanine. This occurs in about 1 in 8,000 births among Caucasians in the United States. When given a standard diet containing phenylalanine, individuals with this disorder are unable to break down this amino acid. Phenylalanine accumulates and is converted into phenylketones, which are detected in the urine. PKU individuals manifest a variety of detrimental traits, including mental retardation, underdeveloped

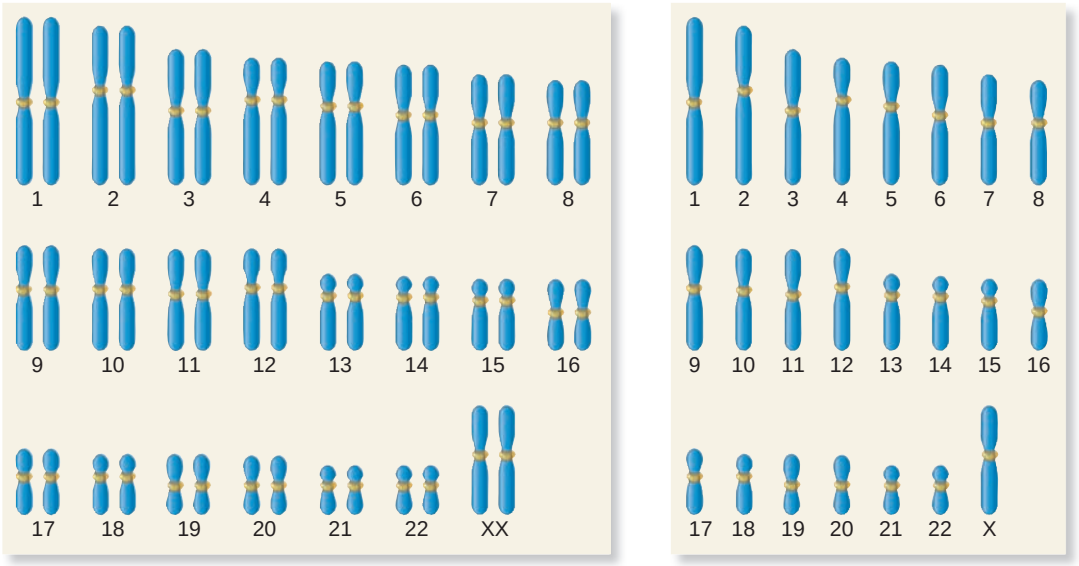
FIGURE 1.10 **Environmental influence on the outcome of PKU within a single family.** All three children pictured here have inherited the alleles that cause PKU. The child in the middle was raised on a phenylalanine-free diet and developed normally. The other two children were born before the benefits of a phenylalanine-free diet were known and were raised on diets that contained phenylalanine. Therefore, they manifest a variety of symptoms, including mental retardation. People born today with this disorder are usually diagnosed when infants. (*Photo from the March of Dimes Birth Defects Foundation.*)

teeth, and foul-smelling urine. In contrast, when PKU individuals are identified at birth and raised on a restricted diet that is low in phenylalanine, they develop normally (**Figure 1.10**). Fortunately, through routine newborn screening, most affected babies in the United States are now diagnosed and treated early. PKU provides a dramatic example of how the environment and an individual's genes can interact to influence the traits of the organism.

During Reproduction, Genes Are Passed from Parent to Offspring

Now that we have considered how genes and the environment govern the outcome of traits, we can turn to the issue of inheritance. A centrally important matter in genetics is the manner in which traits are passed from parents to offspring. The foundation for our understanding of inheritance came from the studies of Gregor Mendel in the nineteenth century. His work revealed that genetic determinants, which we now call genes, are passed from parent to offspring as discrete units. We can predict the outcome of genetic crosses based on Mendel's laws of inheritance.

The inheritance patterns identified by Mendel can be explained by the existence of chromosomes and their behavior during cell division. As in Mendel's pea plants, sexually reproducing species are commonly **diploid.** This means they contain two copies of each chromosome, one from each parent. The two



(a) Chromosomal composition found in most female human cells (46 chromosomes)

(b) Chromosomal composition found in a human gamete (23 chromosomes)

FIGURE 1.11 **The complement of human chromosomes in somatic cells and gametes.** **(a)** A schematic drawing of the 46 chromosomes of a human. With the exception of the sex chromosomes, these are always found in homologous pairs. **(b)** The chromosomal composition of a gamete, which contains only 23 chromosomes, one from each pair. This gamete contains an X chromosome. Half of the gametes from human males would contain a Y chromosome instead of the X chromosome.

copies are called **homologues** of each other. Because genes are located within chromosomes, diploid organisms have two copies of most genes. Humans, for example, have 46 chromosomes, which are found in homologous pairs (Figure 1.11a). With the exception of the sex chromosomes (namely, X and Y), each homologous pair contains the same kinds of genes. For example, both copies of human chromosome 12 carry the gene that encodes phenylalanine hydroxylase, which was discussed previously. Therefore, an individual has two copies of this gene. The two copies may or may not be identical alleles.

Most cells of the human body that are not directly involved in sexual reproduction contain 46 chromosomes. These cells are called **somatic cells.** In contrast, the **gametes**—sperm and egg cells—contain half that number and are termed **haploid** (Figure 1.11b). The union of gametes during fertilization restores the diploid number of chromosomes. The primary advantage of sexual reproduction is that it enhances genetic variation. For example, a tall person with blue eyes and a short person with brown eyes may have short offspring with blue eyes or tall offspring with brown eyes. Therefore, sexual reproduction can result in new combinations of two or more traits that differ from those of either parent.

The Genetic Composition of a Species Evolves over the Course of Many Generations

As we have just seen, sexual reproduction has the potential to enhance genetic variation. This can be an advantage for a population of individuals as they struggle to survive and compete within their natural environment. The term **biological evolution** refers to the phenomenon that the genetic makeup of a population can change over the course of many generations.

As suggested by Charles Darwin, the members of a species are in competition with each other for essential resources. Random genetic changes (i.e., mutations) occasionally occur within an individual's genes, and sometimes these changes lead to a modification of traits that promote reproductive success. For example, over the course of many generations, random gene mutations have lengthened the neck of the giraffe, enabling it to feed on leaves that are high in the trees. When a mutation creates a new allele that is beneficial, the allele may become prevalent in future generations because the individuals carrying the allele are more likely to reproduce and pass the beneficial allele to their offspring. This process is known as **natural selection.** In this way, a species becomes better adapted to its environment.

Over a long period of time, the accumulation of many genetic changes leads to rather striking modifications in a species' characteristics. As an example, Figure 1.12 depicts the evolution of the modern-day horse. A variety of morphological changes occurred, including an increase in size, fewer toes, and modified jaw structure.

1.2 FIELDS OF GENETICS

Genetics is a broad discipline encompassing molecular, cellular, organism, and population biology. Many scientists who are interested in genetics have been trained in supporting disciplines such as biochemistry, biophysics, cell biology, mathematics, microbi-

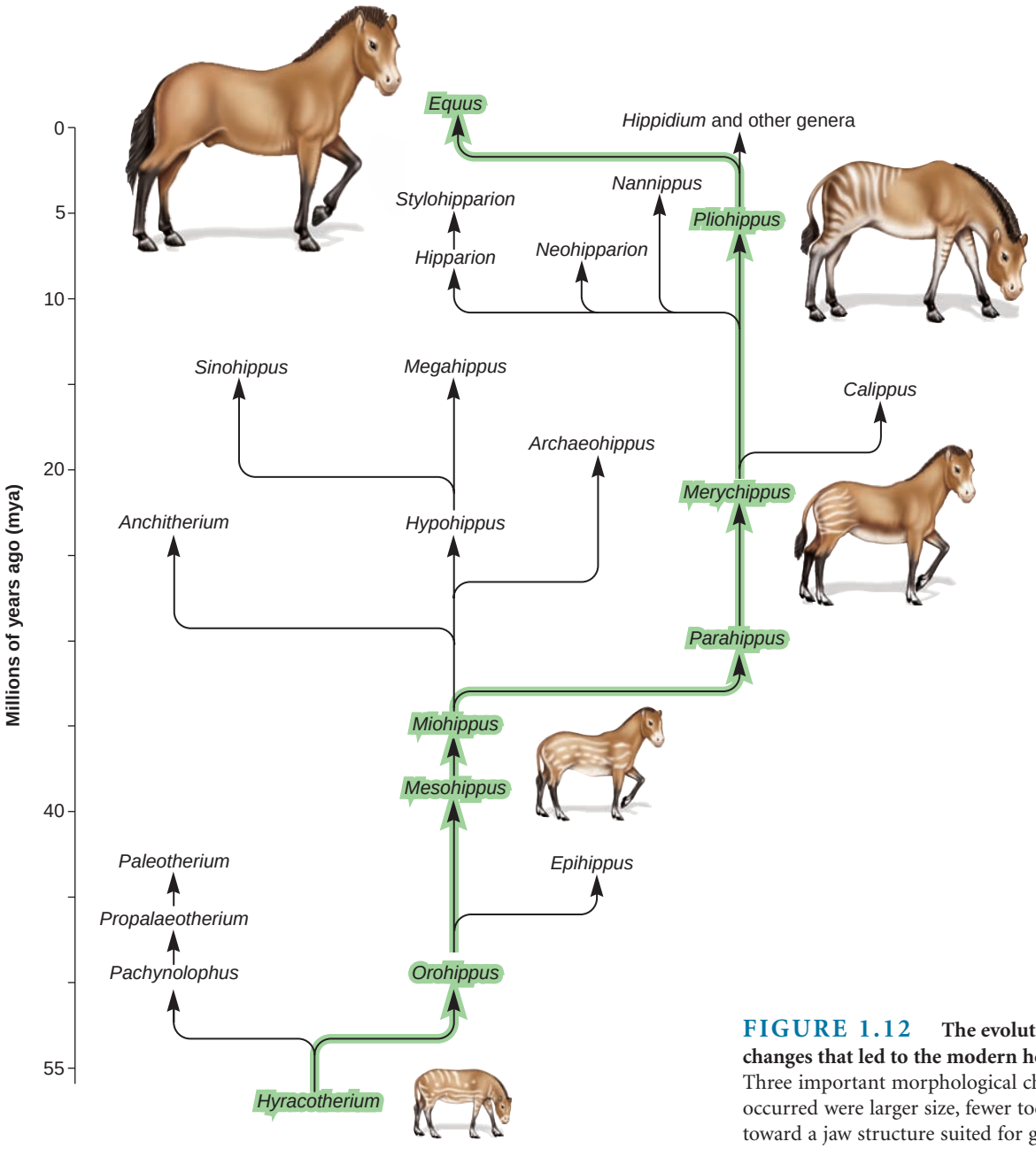


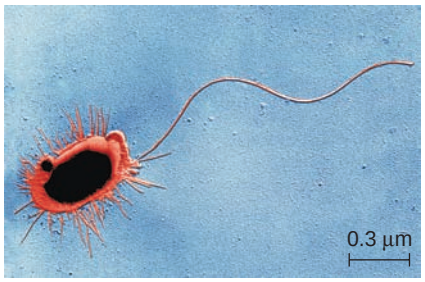
FIGURE 1.12 **The evolutionary changes that led to the modern horse, *Equus*.** Three important morphological changes that occurred were larger size, fewer toes, and a shift toward a jaw structure suited for grazing.

ology, population biology, ecology, agriculture, and medicine. Experimentally, geneticists often focus their efforts on **model organisms**—organisms studied by many different researchers so they can compare their results and determine scientific principles that apply more broadly to other species. **Figure 1.13** shows some common examples, including *Escherichia coli* (a bacterium), *Saccharomyces cerevisiae* (a yeast), *Drosophila melanogaster* (fruit fly), *Caenorhabditis elegans* (a nematode worm), *Danio rerio* (zebrafish), *Mus musculus* (mouse), and *Arabidopsis thaliana* (a flowering plant). By limiting their work to a few such model organisms, researchers can more easily unravel the genetic composition of a given species. Furthermore, the genes found in model organisms often function in a similar way to those found in humans.

The study of genetics has been traditionally divided into three areas: transmission, molecular, and population genetics, although overlap is found among these three fields. In this section, we will examine the general questions that scientists in these areas are attempting to answer.

Transmission Genetics Explores the Inheritance Patterns of Traits as They Are Passed from Parents to Offspring

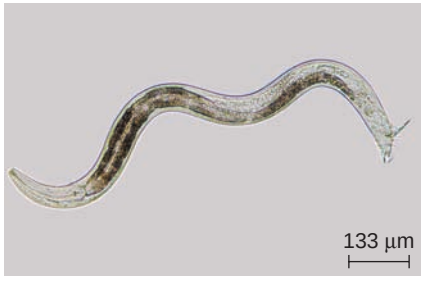
A scientist working in the field of transmission genetics examines the relationship between the transmission of genes from parent to offspring and the outcome of the offspring's traits. For example,



(a) *Escherichia coli*

(b) *Saccharomyces cerevisiae*

(c) *Drosophila melanogaster*



(d) *Caenorhabditis elegans*

(e) *Danio rerio*

(f) *Mus musculus*

(g) *Arabidopsis thaliana*

FIGURE 1.13 **Examples of model organisms studied by geneticists.** (**a**) *Escherichia coli* (a bacterium), (**b**) *Saccharomyces cerevisiae* (a yeast), (**c**) *Drosophila melanogaster* (fruit fly), (**d**) *Caenorhabditis elegans* (a nematode worm), (**e**) *Danio rerio* (zebrafish), (**f**) *Mus musculus* (mouse), and (**g**) *Arabidopsis thaliana* (a flowering plant).

how can two brown-eyed parents produce a blue-eyed child? Or why do tall parents tend to produce tall children, but not always? Our modern understanding of transmission genetics began with the studies of Gregor Mendel. His work provided the conceptual framework for transmission genetics. In particular, he originated the idea that genetic determinants, which we now call genes, are passed as discrete units from parents to offspring via sperm and egg cells. Since these pioneering studies of the 1860s, our knowledge of genetic transmission has greatly increased. Many patterns of genetic transmission are more complex than the simple Mendelian patterns that are described in Chapter 2. The additional complexities of transmission genetics are examined in Chapters 3 through 8.

Experimentally, the fundamental approach of a transmission geneticist is the **genetic cross.** A genetic cross involves breeding two selected individuals and the subsequent analysis of their offspring in an attempt to understand how traits are passed from parents to offspring. In the case of experimental organisms, the researcher chooses two parents with particular traits and then categorizes the offspring according to the traits they possess. In many cases, this analysis is quantitative in nature. For example, an experimenter may cross two tall pea plants and obtain 100 offspring that fall into two categories: 75 tall and 25 dwarf. As we will see in Chapter 2, the ratio of tall and dwarf offspring provides important information concerning the inheritance pattern of this trait.

Throughout Chapters 2 to 8, we will learn how researchers seek to answer many fundamental questions concerning the passage of traits from parents to offspring. Some of these questions are as follows:

What are the common patterns of inheritance for genes?
Chapters 2–4

When two or more genes are located on the same chromosome, how does this affect the pattern of inheritance? ***Chapters 5, 6***

Are there unusual patterns of inheritance that cannot be explained by the simple transmission of genes located on chromosomes in the cell nucleus? ***Chapter 7***

How do variations in chromosome structure or chromosome number occur, and how are they transmitted from parents to offspring? ***Chapter 8***

Molecular Genetics Is Focused on a Biochemical Understanding of the Hereditary Material

The goal of molecular genetics, as the name of the field implies, is to understand how the genetic material works at the molecular level. In other words, molecular geneticists want to understand the molecular features of DNA and how these features underlie the expression of genes. The experiments of molecular geneticists are usually conducted within the confines of a laboratory. Their efforts frequently progress to a detailed analysis of DNA, RNA, and/or protein, using a variety of techniques that are described throughout Parts III, IV, and V of this book.

Molecular geneticists often study mutant genes that have abnormal function. This is called a **genetic approach** to the study of a research question. In many cases, researchers analyze the effects of gene mutations that eliminate the function of a gene. This type of mutation is called a **loss-of-function mutation,** and the resulting gene is called a **loss-of-function allele.** By studying the effects of such mutations, the role of the functional, nonmutant gene is often revealed. For example, let's suppose that a particular plant species produces purple flowers. If a loss-of-function mutation within a given gene causes a plant to produce white flowers, one would suspect the role of the functional gene involves the production of purple pigmentation.

Studies within molecular genetics interface with other disciplines such as biochemistry, biophysics, and cell biology. In addition, advances within molecular genetics have shed considerable light on the areas of transmission and population genetics. Our quest to understand molecular genetics has spawned a variety of modern molecular technologies and computer-based approaches. Furthermore, discoveries within molecular genetics have had widespread applications in agriculture, medicine, and biotechnology.

Some general questions within the field of molecular genetics are the following:

What are the molecular structures of DNA and RNA? ***Chapters 9, 18***

What is the composition and conformation of chromosomes? ***Chapters 10, 20***

How is the genetic material copied? ***Chapter 11***

How are genes expressed at the molecular level? ***Chapters 12, 13, 18, 19, 21***

How is gene expression regulated so that it occurs under the appropriate conditions and in the appropriate cell type? ***Chapters 14, 15, 18, 23***

What is the molecular nature of mutations? How are mutations repaired? ***Chapter 16***

How does the genetic material become rearranged at the molecular level? ***Chapter 17***

What is the underlying relationship between genes and genetic diseases? ***Chapter 22***

How do genes govern the development of multicellular organisms? ***Chapter 23***

Population Genetics Is Concerned with Genetic Variation and Its Role in Evolution

The foundations of population genetics arose during the first few decades of the twentieth century. Although many scientists of this era did not accept the findings of Mendel and/or Darwin, the theories of population genetics provided a compelling way to connect the two viewpoints. Mendel's work and that of many succeeding geneticists gave insight into the nature of genes and how they are transmitted from parents to offspring. The work of Darwin provided a natural explanation for the various types of characteristics observed among the members of a species. To relate these two phenomena, population geneticists have developed mathematical theories to explain the prevalence of certain forms of genes within populations of individuals. The work of population geneticists helps us understand how the forces of nature have produced and favored the existence of individuals that carry particular genes.

Population geneticists are particularly interested in genetic variation and how that variation is related to an organism's environment. In this field, the prevalence of alleles within a population is of central importance. Some general questions in population genetics are the following:

Why are two or more different alleles of a gene maintained in a population? ***Chapter 24***

What factors alter the prevalence of alleles within a population? ***Chapter 24***

What are the contributions of genetics and environment in the outcome of a trait? ***Chapter 25***

How do genetics and the environment influence quantitative traits, such as size and weight? ***Chapter 25***

What factors have the most impact on the process of evolution? ***Chapter 26***

How does evolution occur at the molecular level? ***Chapter 26***

Genetics Is an Experimental Science

Science is a way of knowing about our natural world. The science of genetics allows us to understand how the expression of our genes produces the traits that we possess. Researchers typically follow two general types of scientific approaches—hypothesis testing and discovery-based science. In **hypothesis testing,** also called the **scientific method,** scientists follow a series of steps to reach verifiable conclusions about the world in which we live. Although scientists arrive at their theories in different ways, the scientific

method provides a way to validate (or invalidate) a particular hypothesis. Alternatively, research may also involve the collection of data without a preconceived hypothesis. For example, researchers might analyze the genes found in cancer cells to identify those genes that have become mutant. In this case, the scientists may not have a hypothesis about which particular genes may be involved. The collection and analysis of data without the need for a preconceived hypothesis is called **discovery-based science** or, simply, discovery science.

In traditional science textbooks, the emphasis often lies on the product of science. Namely, many textbooks are aimed primarily at teaching the student about the observations that scientists have made and the theories that they have proposed to explain these observations. Along the way, the student is provided with many bits and pieces of experimental techniques and data. Likewise, this textbook also provides you with many observations and theories. However, it attempts to go one step further. Each of the following chapters contains one or two experiments that have been "dissected" into five individual components to help you to understand the entire scientific process:

1. Background information is provided so that you may appreciate what previous observations were known prior to conducting the experiment.
2. Most experiments involve hypothesis testing. In those cases, the figure states the hypothesis that the scientists were trying to test. In other words, what scientific question was the researcher trying to answer?
3. Next, the figure follows the experimental steps the scientist took to test the hypothesis. The steps necessary to carry out the experiment are listed in the order they were conducted. The figure contains two parallel illustrations labeled Experimental Level and Conceptual Level. The illustration shown in the Experimental Level helps you to understand the techniques that were followed. The Conceptual Level helps you to understand what is actually happening at each step in the procedure.
4. The raw data for each experiment are then presented.
5. Last, an interpretation of the data is offered within the text.

The rationale behind this approach is that it enables you to see the experimental process from beginning to end. Hopefully, you will find this a more interesting and rewarding way to learn about genetics. As you read through the chapters, the experiments will help you to see the relationship between science and scientific theories.

As a student of genetics, you will be given the opportunity to involve your mind in the experimental process. As you are reading an experiment, you may find yourself thinking about different approaches and alternative hypotheses. Different people can view the same data and arrive at very different conclusions. As you progress through the experiments in this book, you will enjoy genetics far more if you try to develop your own skills at formulating hypotheses, designing experiments, and interpreting data. Also, some of the questions in the problem sets are aimed at refining these skills.

Finally, it is worthwhile to point out that science is a social discipline. As you develop your skills at scrutinizing experiments, it is fun to discuss your ideas with other people, including fellow students and faculty members. Keep in mind that you do not need to "know all the answers" before you enter into a scientific discussion. Instead, it is more rewarding to view science as an ongoing and never-ending dialogue.

PROBLEM SETS & INSIGHTS

Solved Problems

S1. A human gene called the *CF* gene (for cystic fibrosis) encodes a protein that functions in the transport of chloride ions across the cell membrane. Most people have two copies of a functional *CF* gene and do not have cystic fibrosis. However, a mutant version of the cystic fibrosis gene is found in some people. If a person has two mutant copies of the gene, he or she develops the disease known as cystic fibrosis. Are the following examples a description of genetics at the molecular, cellular, organism, or population level?

A. People with cystic fibrosis have lung problems due to a buildup of mucus in their lungs.

B. The mutant *CF* gene encodes a defective chloride transporter.

C. A defect in the chloride transporter causes a salt imbalance in lung cells.

D. Scientists have wondered why the mutant cystic fibrosis gene is relatively common. In fact, it is the most common mutant gene that causes a severe disease in Caucasians. Usually, mutant genes that cause severe diseases are relatively rare. One possible explanation why the *CF* gene is so common is that people who have one copy of the functional *CF* gene and one copy of the mutant gene may be more resistant to diarrheal diseases such as cholera. Therefore, even though individuals with two mutant copies are very sick, people with one mutant copy and one functional copy might have a survival advantage over people with two functional copies of the gene.

Answer:

A. Organism. This is a description of a trait at the level of an entire individual.

B. Molecular. This is a description of a gene and the protein it encodes.

C. Cellular. This is a description of how protein function affects the cell.

D. Population. This is a possible explanation why two versions of the gene occur within a population.

S2. Explain the relationship between the following pairs of terms:

A. RNA and DNA

B. RNA and transcription

C. Gene expression and trait

D. Mutation and allele

Answer:

A. DNA is the genetic material. DNA is used to make RNA. RNA is then used to specify a sequence of amino acids within a polypeptide.

B. Transcription is a process in which RNA is made using DNA as a template.

C. Genes are expressed at the molecular level to produce functional proteins. The functioning of proteins within living cells ultimately affects an organism's traits.

D. Alleles are alternative forms of the same gene. For example, a particular human gene affects eye color. The gene can exist as a blue allele or a brown allele. The difference between these two alleles is caused by a mutation. Perhaps the brown allele was the first eye color allele in the human population. Within some ancestral person, however, a mutation may have occurred in the eye color gene that converted the brown allele to the blue allele. Now the human population has both the brown allele and the blue allele.

S3. How are genes passed from generation to generation?

Answer: When a diploid individual makes haploid cells for sexual reproduction, the cells contain half the number of chromosomes. When two haploid cells (e.g., sperm and egg) combine with each other, a zygote is formed that begins the life of a new individual. This zygote has inherited half of its chromosomes and, therefore, half of its genes from each parent. This is how genes are passed from parents to offspring.

Conceptual Questions

C1. Pick any example of a genetic technology and describe how it has directly impacted your life.

C2. At the molecular level, what is a gene? Where are genes located?

C3. Most genes encode proteins. Explain how the structure and function of proteins produce an organism's traits.

C4. Briefly explain how gene expression occurs at the molecular level.

C5. A human gene called the β-globin gene encodes a polypeptide that functions as a subunit of the protein known as hemoglobin. Hemoglobin is found within red blood cells; it carries oxygen. In human populations, the β-globin gene can be found as the common allele called the Hb^A allele, but it can also be found as the rare Hb^S allele. Individuals who have two copies of the Hb^S allele have the disease called sickle-cell disease. Are the following examples a description of genetics at the molecular, cellular, organism, or population level?

A. The Hb^S allele encodes a polypeptide that functions slightly differently from the polypeptide encoded by the Hb^A allele.

B. If an individual has two copies of the Hb^S allele, that person's red blood cells form a sickle shape.

C. Individuals who have two copies of the Hb^A allele do not have sickle-cell disease, but they are not resistant to malaria. People who have one Hb^A allele and one Hb^S allele do not have sickle-cell disease, and they are resistant to malaria. People who have two copies of the Hb^S allele have sickle-cell anemia, and this disease may significantly shorten their lives.

D. Individuals with sickle-cell disease have anemia because their red blood cells are easily destroyed by the body.

C6. What is meant by the term genetic variation? Give two examples of genetic variation not discussed in Chapter 1. What causes genetic variation at the molecular level?

C7. What is the cause of Down syndrome?

C8. Your textbook describes how the trait of phenylketonuria (PKU) is greatly influenced by the environment. Pick a trait in your favorite plant and explain how genetics and environment may play important roles.

C9. What is meant by the term diploid? Which cells of the human body are diploid, and which cells are not?

C10. What is a DNA sequence?

C11. What is the genetic code?

C12. Explain the relationships between the following pairs of genetic terms:

A. Gene and trait

B. Gene and chromosome

C. Allele and gene

D. DNA sequence and amino acid sequence

C13. With regard to biological evolution, which of the following statements is not correct? Explain why.

A. During its lifetime, an animal evolves to become better adapted to its environment.

B. The process of biological evolution has produced species that are better adapted to their environments.

C. When an animal is better adapted to its environment, the process of natural selection makes it more likely for that animal to reproduce.

C14. What are the primary interests of researchers working in the following fields of genetics?

A. Transmission genetics

B. Molecular genetics

C. Population genetics

Experimental Questions

E1. What is a genetic cross?

E2. The technique known as DNA sequencing (described in Chapter 18) enables researchers to determine the DNA sequence of genes. Would this technique be used primarily by transmission geneticists, molecular geneticists, or population geneticists?

E3. Figure 1.5 shows a micrograph of chromosomes from a normal human cell. If you performed this type of experiment using cells from a person with Down syndrome, what would you expect to see?

E4. Many organisms are studied by geneticists. Of the following species, do you think it would be more likely for them to be studied by a transmission geneticist, a molecular geneticist, or a population geneticist? Explain your answer. Note: More than one answer may be possible.

A. Dogs

B. *E. coli*

C. Fruit flies

D. Leopards

E. Corn

E5. Pick any trait you like in any species of wild plant or animal. The trait must somehow vary among different members of the species. For example, some butterflies have dark wings and others have light wings (see Figure 1.7).

A. Discuss all of the background information that you already have (from personal observations) regarding this trait.

B. Propose a hypothesis that would explain the genetic variation within the species. For example, in the case of the butterflies, your hypothesis might be that the dark butterflies survive better in dark forests, while the light butterflies survive better in lighter fields.

C. Describe the experimental steps you would follow to test your hypothesis.

D. Describe the possible data you might collect.

E. Interpret your data.

Note: When picking a trait to answer this question, do not pick the trait of wing color in butterflies.

Note: All answers appear at the website for this textbook; the answers to even-numbered questions are in the back of the textbook.

www.mhhe.com/brookergenetics3e

Visit the Online Learning Center for practice tests, answer keys, and other learning aids for this chapter. Enhance your understanding of genetics with our interactive exercises, quizzes, animations, and much more.

MENDELIAN INHERITANCE

2

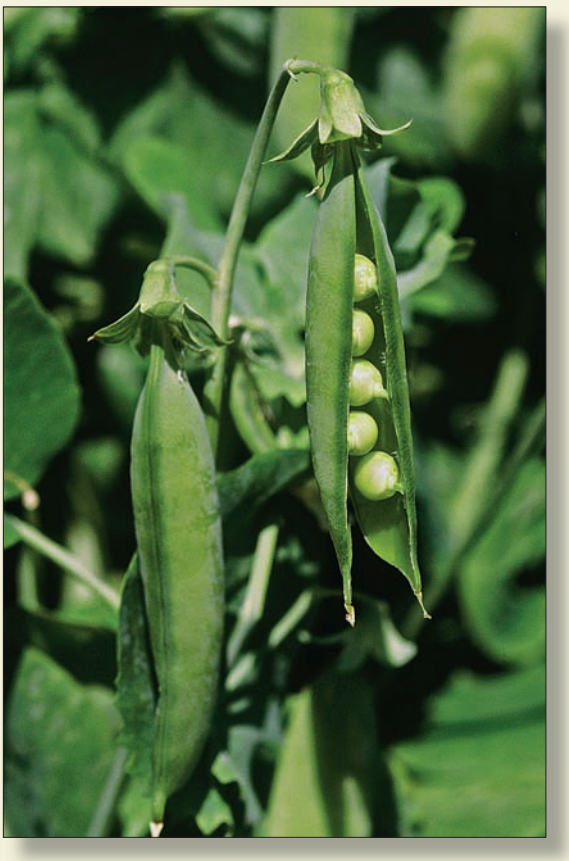
An appreciation for the concept of heredity can be traced far back in human history. Hippocrates, a famous Greek physician, was the first person to provide an explanation for hereditary traits (ca. 400 B.C.E.). He suggested that "seeds" are produced by all parts of the body, which are then collected and transmitted to the offspring at the time of conception. Furthermore, he hypothesized that these seeds cause certain traits of the offspring to resemble those of the parents. This idea, known as **pangenesis,** was the first attempt to explain the transmission of hereditary traits from generation to generation.

For the next 2,000 years, the ideas of Hippocrates were accepted by some and rejected by many. After the invention of the microscope in the late seventeenth century, some people observed sperm and thought they could see a tiny creature inside, which they termed a homunculus (little man). This homunculus was hypothesized to be a miniature human waiting to develop within the womb of its mother. Those who held that thought, known as spermists, suggested that only the father was responsible for creating future generations and that any resemblance between mother and offspring was due to influences "within the womb." During the same time, an opposite school of thought also developed. According to the ovists, the egg was solely responsible for human characteristics. The only role of the sperm was to stimulate the egg onto its path of development. Of course, neither of these ideas was correct.

The first systematic studies of genetic crosses were carried out by Joseph Kölreuter from 1761 to 1766. In crosses between different strains of tobacco plants, he found that the offspring were usually intermediate in appearance between the two parents. This led Kölreuter to conclude that both parents make equal genetic contributions to their offspring. Furthermore, his observations were consistent with **blending inheritance.** According to this view, the factors that dictate hereditary traits can blend together from generation to generation. The blended traits would then be passed to the next generation. The popular view before the 1860s, which combined the notions of pangenesis and blending inheritance, was that hereditary traits were rather malleable and could change and blend over the course of one or two generations. However, the pioneering work of Gregor Mendel would prove instrumental in refuting this viewpoint.

In Chapter 2, we will first examine the outcome of Mendel's crosses in pea plants. We begin our inquiry into genetics here because the inheritance patterns observed in peas are fundamentally related to inheritance patterns found in other eukaryotic species such as humans, mice, fruit flies, and corn. We will

CHAPTER OUTLINE



The garden pea, studied by Mendel.

PART II
Patterns of Inheritance

discover how Mendel's insights into the patterns of inheritance in pea plants revealed some simple rules that govern the process of inheritance. In Chapters 3 through 8, we will explore more complex patterns of inheritance and also consider the role that the chromosomes play as the carriers of the genetic material.

In the second part of this chapter, we will become familiar with general concepts in probability and statistics. How are statistical methods useful? First, probability calculations allow us to predict the outcomes of simple genetic crosses, as well as the outcomes of more complicated crosses described in later chapters. In addition, we will learn how to use statistics to test the validity of genetic hypotheses that attempt to explain the inheritance patterns of traits.

2.1 MENDEL'S LAWS OF INHERITANCE

Gregor Johann Mendel, born in 1822, is now remembered as the father of genetics (**Figure 2.1**). He grew up on a small farm in Hynčice (formerly Heinzendorf) in northern Moravia, which was then a part of Austria and is now a part of the Czech Republic. As a young boy, he worked with his father grafting trees to improve the family orchard. Undoubtedly, his success at grafting taught him that precision and attention to detail are important elements of success. These qualities would later be important in his experiments as an adult scientist. Instead of farming, however, Mendel was accepted into the Augustinian monastery of St. Thomas, completed his studies for the priesthood, and was ordained in 1847. Soon after becoming a priest, Mendel worked for a short time as a substitute teacher. To continue that role, he needed to obtain a teaching license from the government. Surprisingly, he failed the licensing exam due to poor answers in the areas of physics and natural history. Therefore, Mendel then enrolled at the University of Vienna to expand his knowledge in these two areas. Mendel's training in physics and mathematics taught him to perceive the world as an orderly place, governed by natural laws. In his studies, Mendel learned that these natural laws could be stated as simple mathematical relationships.

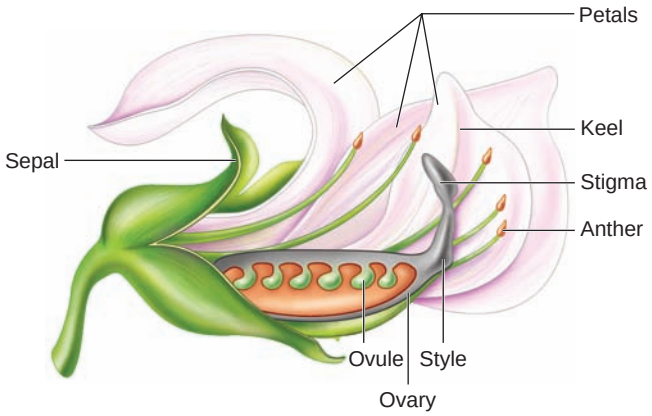
In 1856, Mendel began his historic studies on pea plants. For eight years, he grew and crossed thousands of pea plants on a small 115- by 23-foot plot. He kept meticulously accurate records that included quantitative data concerning the outcome of his crosses. He published his work, entitled "Experiments on Plant Hybrids," in 1866. This paper was largely ignored by scientists at that time, possibly because of its title or because it was published in a rather obscure journal (*The Proceedings of the Brünn Society of Natural History*). Another reason his work went unrecognized could be tied to a lack of understanding of chromosomes and their transmission, a topic we will discuss in Chapter 3. Nevertheless, Mendel's groundbreaking work allowed him to propose the natural laws that now provide a framework for our understanding of genetics.

Prior to his death in 1884, Mendel reflected, "My scientific work has brought me a great deal of satisfaction and I am convinced that it will be appreciated before long by the whole world." Sixteen years later, in 1900, the work of Mendel was independently rediscovered by three biologists with an interest in plant genetics: Hugo de Vries of Holland, Carl Correns of Germany, and Erich von Tschermak of Austria. Within a few years, the impact of Mendel's studies was felt around the world. In this section, we will examine Mendel's experiments and consider their monumental significance in the field of genetics.

FIGURE 2.1 **Gregor Johann Mendel, the father of genetics.**

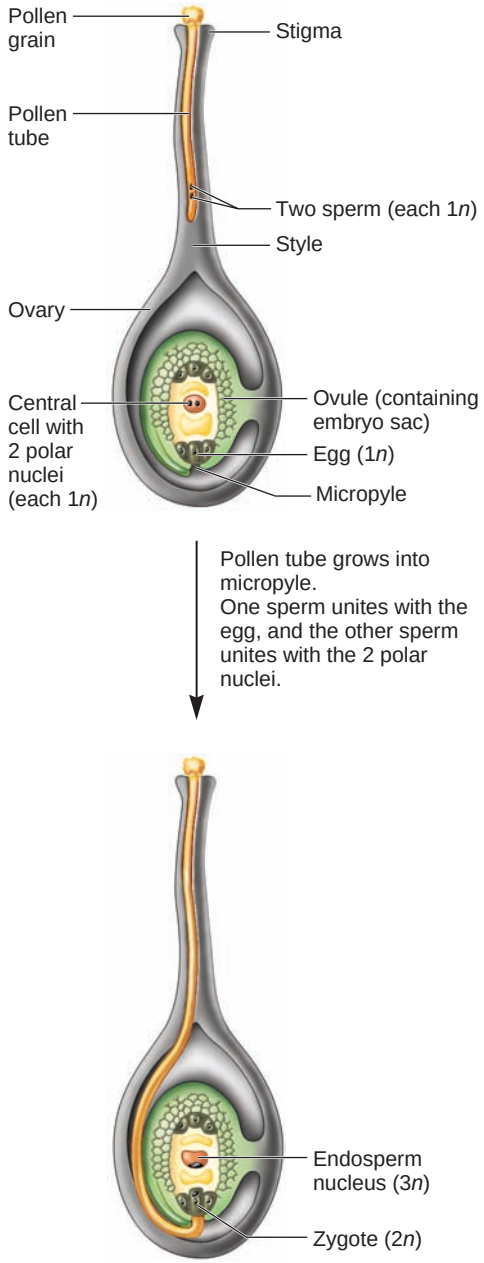
Mendel Chose Pea Plants as His Experimental Organism

Mendel's study of genetics grew out of his interest in ornamental flowers. Prior to his work with pea plants, many plant breeders had conducted experiments aimed at obtaining flowers with new varieties of colors. When two distinct individuals with different characteristics are mated or **crossed** to each other, this is called a **hybridization** experiment, and the offspring are referred to as **hybrids.** For example, a hybridization experiment could involve a cross between a purple-flowered plant and a white-flowered plant. Mendel was particularly intrigued, in such experiments, by the consistency with which offspring of subsequent generations showed characteristics of one or the other parent. His intellectual foundation in physics and the natural sciences led him



(a) Structure of a pea flower

(b) A flowering pea plant



(c) Pollination and fertilization in angiosperms

FIGURE 2.2 Flower structure and pollination in pea plants. (**a**) The pea flower can produce both pollen and egg cells. The pollen grains are produced within the anthers, and the egg cells are produced within the ovules that are contained within the ovary. A modified petal called a keel encloses the anthers and ovaries. (**b**) Photograph of a flowering pea plant. (**c**) A pollen grain must first land on the stigma. After this occurs, the pollen sends out a long tube through which two sperm cells travel toward an ovule to reach an egg cell. The fusion between a sperm and an egg cell results in fertilization and creates a zygote. A second sperm fuses with a central cell containing two polar nuclei to create the endosperm. The endosperm provides a nutritive material for the developing embryo.

to consider that this regularity might be rooted in natural laws that could be expressed mathematically. To uncover these laws, he realized that he would need to carry out quantitative experiments in which the numbers of offspring carrying certain traits were carefully recorded and analyzed.

Mendel chose the garden pea, *Pisum sativum*, to investigate the natural laws that govern plant hybrids. The morphological features of this plant are shown in **Figure 2.2a** and **b**. Several properties of this species were particularly advantageous for studying plant hybridization. First, the species was available in several varieties that had decisively different physical characteristics. Many strains of the garden pea were available that varied in the appearance of their height, flowers, seeds, and pods.

A second important issue is the ease of making crosses. In flowering plants, reproduction occurs by a pollination event (**Figure 2.2c**). Male gametes (**sperm**) are produced within **pollen grains** formed in the **anthers,** while the female gametes (**eggs**) are contained within **ovules** that form in the **ovaries.** For fertilization to occur, a pollen grain lands on the **stigma,** which

stimulates the growth of a pollen tube. This enables sperm cells to enter the stigma and migrate toward an ovule. Fertilization occurs when a sperm enters the micropyle, an opening in the ovule wall, and fuses with an egg cell. The term **gamete** is used to describe haploid reproductive cells that can unite to form a zygote. It should be emphasized, however, that the process that produces gametes in animals is quite different from the way that gametes are produced in plants and fungi. These processes are described in greater detail in Chapter 3.

In some experiments, Mendel wanted to carry out **self-fertilization,** which means that the pollen and egg are derived from the same plant. In peas, a modified petal known as the keel covers the reproductive structures of the plant. Because of this covering, pea plants naturally reproduce by self-fertilization. In fact, pollination occurs even before the flower opens. In other experiments, however, Mendel wanted to make crosses between different plants. How did he accomplish this goal? Fortunately, pea plants contain relatively large flowers that are easy to manipulate, making it possible to make crosses between two particular plants and study their outcomes. This process, known as **cross-fertilization,** requires that the pollen from one plant be placed on the stigma of another plant. This procedure is shown in **Figure 2.3.** Mendel was able to pry open immature flowers and remove the anthers before they produced pollen. Therefore, these flowers could not self-fertilize. He would then obtain pollen from another plant by gently touching its mature anthers with a paintbrush. Mendel applied this pollen to the stigma of the flower that already had its anthers removed. In this way, he was able to cross-fertilize his pea plants and thereby obtain any type of hybrid he wanted.

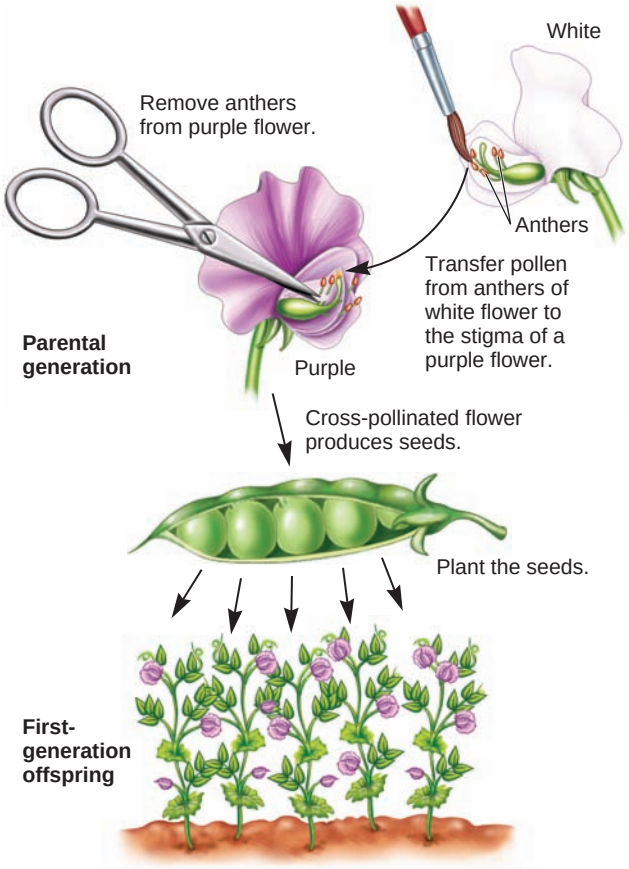


FIGURE 2.3 How Mendel cross-fertilized two different pea plants. This illustration depicts a cross between a plant with purple flowers and another plant with white flowers. The offspring from this cross are the result of pollination of the purple flower using pollen from a white flower.

Mendel Studied Seven Traits That Bred True

When he initiated his studies, Mendel obtained several varieties of peas that were considered to be distinct. These plants were different with regard to many morphological characteristics. Such characteristics of an organism are called characters, or **traits.** Over the course of two years, Mendel tested the strains to determine if their characteristics bred true. This means that a trait did not vary in appearance from generation to generation. For example, if the seeds from a pea plant were yellow, the next generation would also produce yellow seeds. Likewise, if these offspring were allowed to self-fertilize, all of their offspring would also produce yellow seeds, and so on. A variety that continues to produce the same characteristic after several generations of self-fertilization is called a **true-breeding line,** or **strain.**

Mendel next concentrated his efforts on the analysis of characteristics that were clearly distinguishable between different true-breeding lines. **Figure 2.4** illustrates the seven traits that Mendel eventually chose to follow in his breeding experiments. All seven were found in two variants. The term **variant** refers to a particular trait that may be found in two or more versions within a single species. For example, one trait he followed was height, which was found in two variants—tall and dwarf plants. Mendel studied this trait by crossing the variants to each other. A cross in which an experimenter is observing only one trait is called a **single-factor cross,** also called a **monohybrid cross.** When the two parents are different variants for a given trait, this type of cross produces single-trait hybrids, also known as **monohybrids.**

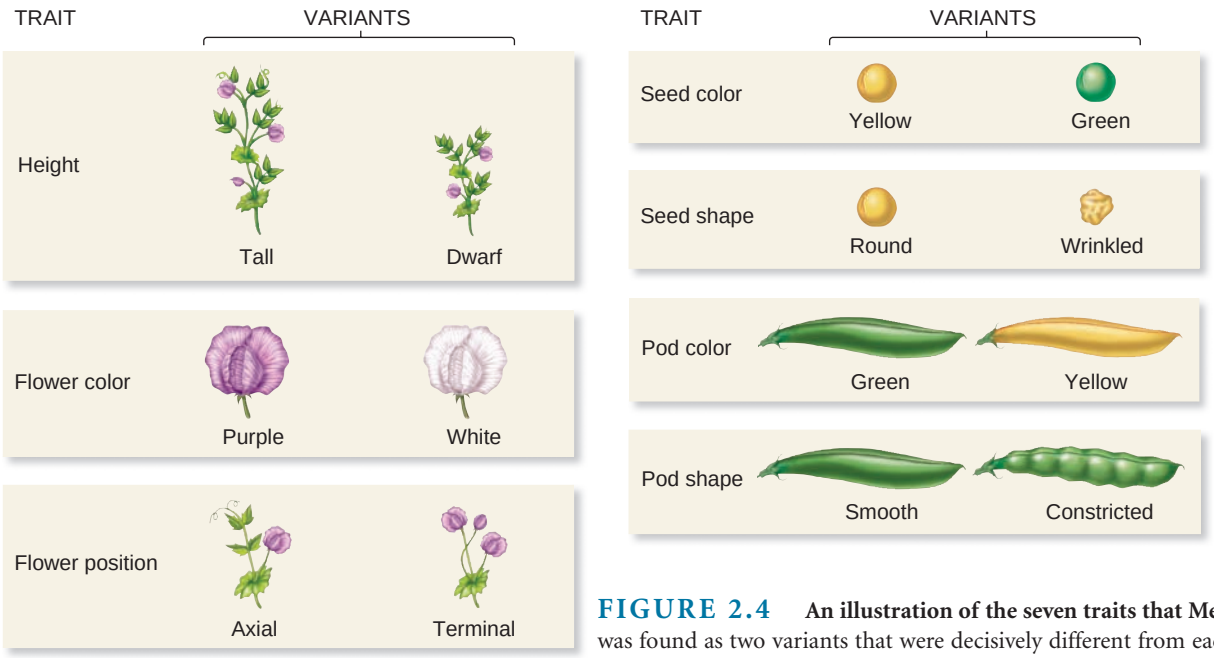


FIGURE 2.4 **An illustration of the seven traits that Mendel studied.** Each trait was found as two variants that were decisively different from each other.

EXPERIMENT 2A

Mendel Followed the Outcome of a Single Trait for Two Generations

Prior to conducting his studies, Mendel did not already have a hypothesis to explain the formation of hybrids. However, his educational background caused him to realize that a quantitative analysis of crosses may uncover mathematical relationships that would otherwise be mysterious. His experiments were designed to determine the relationships that govern hereditary traits. This rationale is called an **empirical approach.** Laws that are deduced from an empirical approach are known as empirical laws.

Mendel's experimental procedure is shown in **Figure 2.5**. He began with true-breeding plants that differed with regard to a single trait. These are termed the **parental generation,** or **P generation.** When the true-breeding parents were crossed to each other, this is called a P cross, and the offspring constitute the **F_1 generation,** for first filial generation. As seen in the data, all plants of the F_1 generation showed the phenotype of one parent but not the other. This prompted Mendel to follow the transmission of this trait for one additional generation. To do so, the plants of the F_1 generation were allowed to self-fertilize to produce a second generation called the **F_2 generation,** for second filial generation.

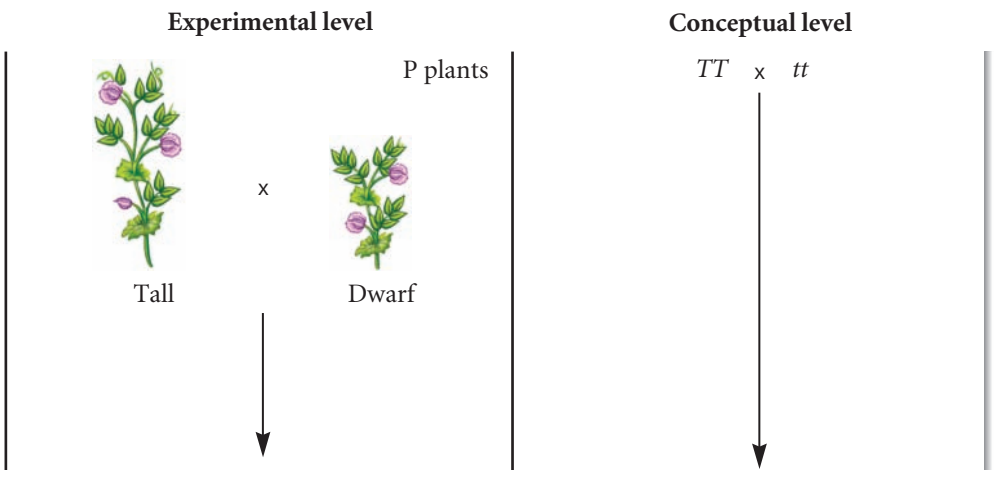
THE GOAL

Mendel speculated that the inheritance pattern for a single trait may follow quantitative natural laws. The goal of this experiment was to uncover such laws.

ACHIEVING THE GOAL — FIGURE 2.5 Mendel's analysis of single-factor crosses.

Starting material: Mendel began his experiments with true-breeding pea plants that varied with regard to only one of seven different traits (see Figure 2.4).

1. For each of seven traits, Mendel cross-fertilized two different true-breeding lines. Keep in mind that each cross involved two plants that differed in regard to only one of the seven traits studied. The illustration at the right shows one cross between a tall and dwarf plant. This is called a P (parental) cross.



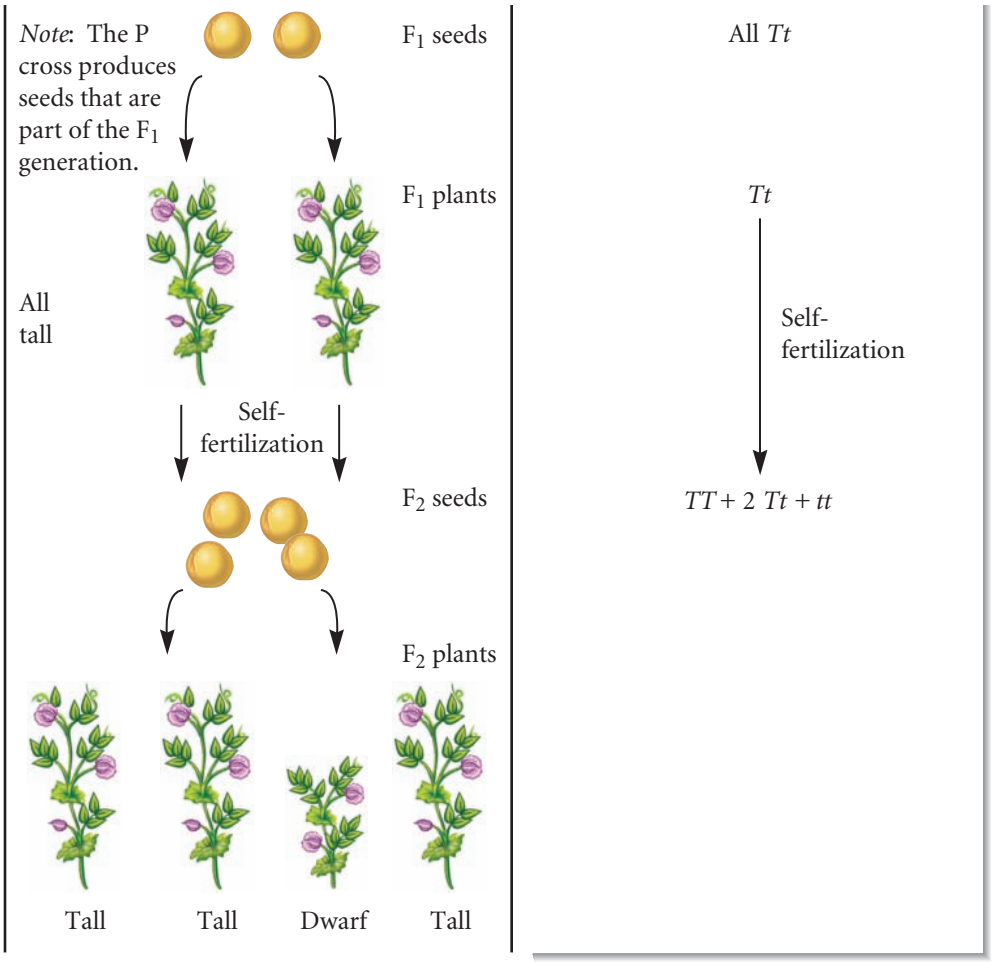
(continued)

2. Collect many seeds. The following spring, plant the seeds and allow the plants to grow. These are the plants of the F_1 generation.

3. Allow the F_1 generation plants to self-fertilize. This produces seeds that are part of the F_2 generation.

4. Collect the seeds and plant them the following spring to obtain the F_2 generation plants.

5. Analyze the characteristics found in each generation.



THE DATA

P Cross	*F_1 Generation*	*F_2 Generation*	*Ratio*
Tall × dwarf stem	All tall	787 tall, 277 dwarf	2.84:1
Purple × white flowers	All purple	705 purple, 224 white	3.15:1
Axial × terminal flowers	All axial	651 axial, 207 terminal	3.14:1
Yellow × green seeds	All yellow	6,022 yellow, 2,001 green	3.01:1
Round × wrinkled seeds	All round	5,474 round, 1,850 wrinkled	2.96:1
Green × yellow pods	All green	428 green, 152 yellow	2.82:1
Smooth × constricted pods	All smooth	882 smooth, 299 constricted	2.95:1
Total	All dominant	14,949 dominant, 5,010 recessive	2.98:1

INTERPRETING THE DATA

The data shown in Figure 2.5 are the results of producing an F_1 generation via cross-fertilization, and an F_2 generation via self-fertilization of the F_1 monohybrids. A quantitative analysis of these data allowed Mendel to propose three important ideas:

1. Mendel's data argued strongly against a blending mechanism of heredity. In all seven cases, the F_1 generation displayed characteristics that were distinctly like one of the two parents rather than traits intermediate in character. Using genetic terms that Mendel originated and are still used today, his first proposal was that the variant for one trait is **dominant** over another variant. For example, the variant of green pods is dominant to that of yellow pods. The term **recessive** is used to describe a variant that is masked by the presence of a dominant trait but reappears in subsequent generations. Yellow pods and dwarf stems are examples of recessive variants. They can also be referred to as recessive traits.
2. When a true-breeding plant with a dominant trait was crossed to a true-breeding plant with a recessive trait, the dominant trait was always observed in the F_1 generation. In the F_2 generation, some offspring displayed the dominant characteristic, while a smaller proportion showed the recessive trait. However, none of the offspring exhibited intermediate traits. How did Mendel explain this observation? Because the recessive trait appeared in the F_2 generation, he formed a second proposal—the genetic determinants of traits are passed along as "unit factors" from generation to generation. His data were consistent with a **particulate theory of inheritance,** in which the genes that govern traits are inherited as discrete units that remain

unchanged as they are passed from parent to offspring. Mendel called them unit factors, but we now call them genes.

3. A third important interpretation of Mendel's data is related to the proportions of offspring. When Mendel compared the numbers of dominant and recessive offspring in the F_2 generation, he noticed a recurring pattern. Within experimental variation, he always observed approximately a 3:1 ratio between the dominant trait and the recessive trait. Mendel was the first scientist to apply this type of quantitative analysis in a biological experiment. As described next, this quantitative approach allowed him to make a third proposal—genes **segregate** from each other during the process that gives rise to gametes.

A self-help quiz involving this experiment can be found at the Online Learning Center.

The 3:1 Phenotypic Ratio That Mendel Observed Is Consistent with the Segregation of Alleles, Now Known as Mendel's Law of Segregation

Mendel's research was aimed at understanding the laws that govern the inheritance of traits. At that time, scientists did not understand the molecular composition of the genetic material or its mode of transmission during gamete formation and fertilization. We now know that the genetic material is composed of deoxyribonucleic acid (DNA), a component of chromosomes. Each chromosome contains hundreds or thousands of shorter segments that function as genes—a term that was originally coined by the Danish botanist Wilhelm Johannsen in 1909. A **gene** is defined as a "unit of heredity" that may influence the outcome of an organism's traits. Each of the seven traits that Mendel studied is influenced by a different gene.

Most eukaryotic species, such as pea plants and humans, have their genetic material organized into pairs of chromosomes. For this reason, eukaryotes have two copies of most genes. These copies may be the same or they may differ. The term **allele** refers to different versions of the same gene. With this modern knowledge, the results shown in Figure 2.5 are consistent with the idea that each parent transmits only one copy of each gene (i.e., one allele) to each offspring. **Mendel's law of segregation** states that:

> *The two copies of a gene segregate (or separate) from each other during transmission from parent to offspring.*

Therefore, only one copy of each gene is found in a gamete. At fertilization, two gametes combine randomly, potentially producing different allelic combinations.

Let's use Mendel's cross of tall and dwarf pea plants to illustrate how alleles are passed from parents to offspring (**Figure 2.6**). The letters *T* and *t* are used to represent the alleles of the gene that determines plant height. By convention, the uppercase letter represents the dominant allele (*T* for tall height, in this case), and the recessive allele is represented by the same letter in lowercase (*t*, for dwarf height). For the P cross, both parents are true-breeding plants. Therefore, we know each has identical copies of the height gene. When an individual possesses two identical copies of a gene, the individual is said to be **homozygous** with respect to that gene. (The prefix *homo* means like, and the suffix *zygo* means pair.) In the P cross, the tall plant is homozygous for the tall allele *T*, while the dwarf plant is homozygous for the dwarf allele *t*. The term **genotype** refers to the genetic composition of an individual. *TT* and *tt* are the genotypes of the P generation in this experiment. The term **phenotype** refers to an observable characteristic of an organism. In the P generation, half of the plants are phenotypically tall and half are dwarf.

In contrast, the F_1 generation is **heterozygous,** with the genotype *Tt*, because every individual carries one copy of the tall allele and one copy of the dwarf allele. A heterozygous individual carries different alleles of a gene. (The prefix *hetero* means different.) Although these plants are heterozygous, their phenotypes are tall because they have a copy of the dominant tall allele.

The law of segregation predicts that the phenotypes of the F_2 generation will be tall and dwarf in a ratio of 3:1 (see Figure 2.6). Because the parents of the F_2 generation are heterozygous, each parent can transmit either a *T* allele or a *t* allele to a particular offspring, but not both, because each gamete carries only one of the two alleles. Therefore, *TT*, *Tt*, and *tt* are the possible genotypes of the F_2 generation (note that the genotype *Tt* is the same as *tT*). By randomly combining these alleles, the genotypes are produced in a 1:2:1 ratio. Because *TT* and *Tt* both produce tall phenotypes, a 3:1 phenotypic ratio is observed in the F_2 generation.

A Punnett Square Can Be Used to Predict the Outcome of Crosses

An easy way to predict the outcome of simple genetic crosses is to use a **Punnett square,** a method originally proposed by Reginald Punnett. To construct a Punnett square, you must know the genotypes of the parents. With this information, the Punnett square enables you to predict the types of offspring the parents are expected to produce and in what proportions. We will follow a step-by-step description of the Punnett square approach using a cross of heterozygous tall plants as an example.

Step 1. Write down the genotypes of both parents. In this example, a heterozygous tall plant is crossed to another heterozygous tall plant. The plant providing the pollen is considered the male parent and the plant providing the eggs, the female parent.

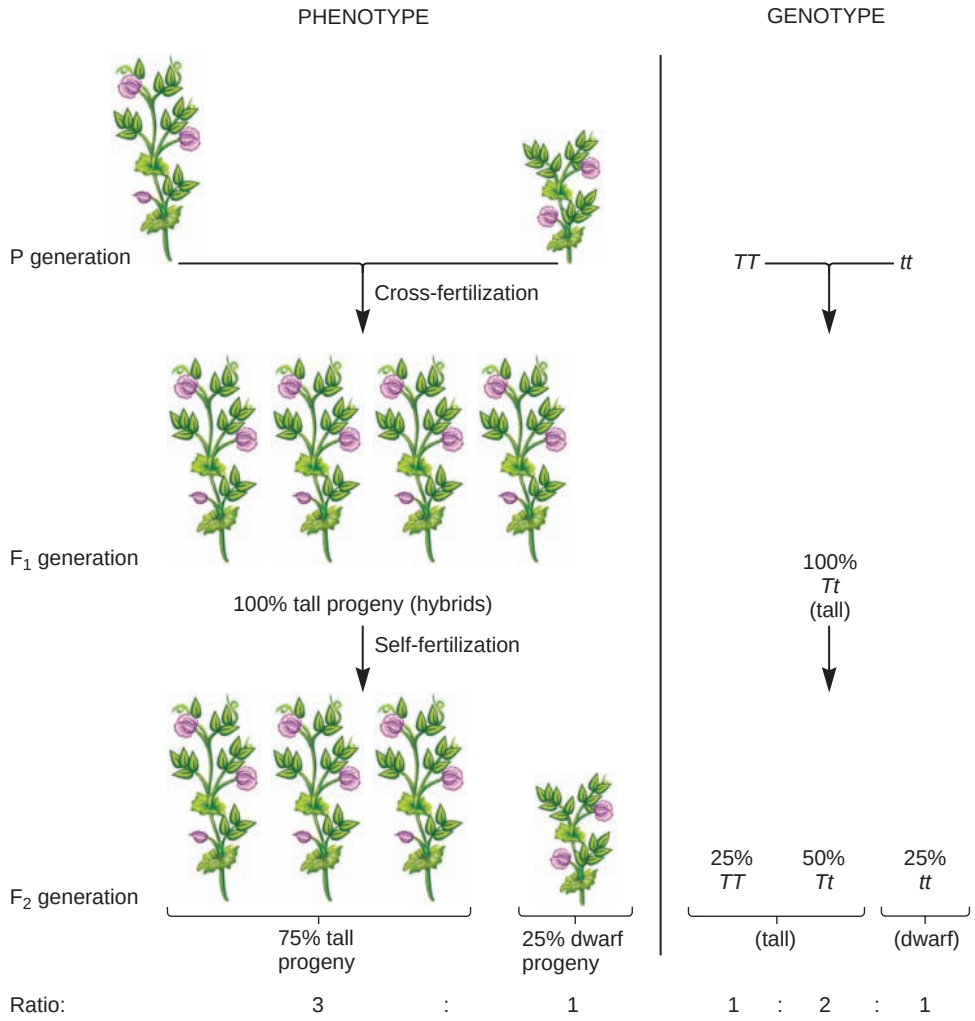
Male parent: *Tt*

Female parent: *Tt*

Step 2. *Write down the possible gametes that each parent can make.* Remember that the law of segregation tells us that a gamete can contain only one copy of each gene.

Male gametes: *T* or *t*

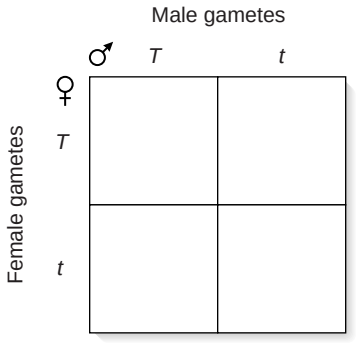
Female gametes: *T* or *t*



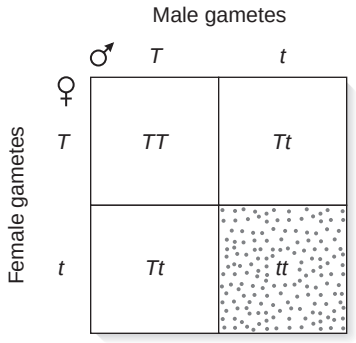
INTERACTIVE EXERCISE

FIGURE 2.6 **Mendel's law of segregation.** This illustration shows a cross between a true-breeding tall plant and a true-breeding dwarf plant and the subsequent segregation of the tall (*T*) and dwarf (*t*) alleles in the F_1 and F_2 generations.

Step 3. *Create an empty Punnett square.* In the examples shown in this textbook, the number of columns equals the number of male gametes, and the number of rows equals the number of female gametes. Our example has two rows and two columns. Place the male gametes across the top of the Punnett square and the female gametes along the side.



Step 4. *Fill in the possible genotypes of the offspring by combining the alleles of the gametes in the empty boxes.*



Step 5. *Determine the relative proportions of genotypes and phenotypes of the offspring.* The genotypes are obtained directly from the Punnett square. They are contained

within the boxes that have been filled in. In this example, the genotypes are *TT*, *Tt*, and *tt* in a 1:2:1 ratio. To determine the phenotypes, you must know the dominant/recessive relationship between the alleles. For plant height, we know that *T* (tall) is dominant to *t* (dwarf). The genotypes *TT* and *Tt* are tall, whereas the genotype *tt* is dwarf. Therefore, our Punnett square shows us that the ratio of phenotypes is 3:1, or 3 tall plants : 1 dwarf plant. Additional problems of this type are provided in the Solved Problems at the end of this chapter.

EXPERIMENT 2B

Mendel Also Analyzed Crosses Involving Two Different Traits

Though his experiments described in Figure 2.5 revealed important ideas regarding hereditary laws, Mendel realized that additional insights might be uncovered if he conducted more complicated experiments. In particular, he conducted crosses in which he simultaneously investigated the pattern of inheritance for two different traits. In other words, he carried out **two-factor crosses,** also called **dihybrid crosses,** in which he followed the inheritance of two different traits within the same groups of individuals. For example, let's consider an experiment in which one of the traits was seed shape, found in round or wrinkled variants; the second trait was seed color, which existed as yellow and green variants. In this dihybrid cross, Mendel followed the inheritance pattern for both traits simultaneously.

What results are possible from a dihybrid cross? One possibility is that the genetic determinants for two different traits are always linked to each other and inherited as a single unit (**Figure 2.7a**). If this were the case, the F_1 offspring could produce only two types of gametes, *RY* and *ry*. A second possibility is that they are not linked and can assort themselves independently into haploid gametes (**Figure 2.7b**). According to independent assortment, an F_1 offspring could produce four types of gametes, *RY*, *Ry*, *rY*, and *ry*. Keep in mind that the results of Figure 2.5 have already shown us that a gamete carries only one allele for each gene.

The experimental protocol of one of Mendel's two-factor crosses is shown in **Figure 2.8**. He began with two different strains of true-breeding pea plants that were different with regard to two traits. In this example, one plant was produced from seeds that were round and yellow; the other plant from seeds that were wrinkled and green. When these plants were crossed, the seeds, which contain the plant embryo, are considered part of the F_1 generation. As expected, the data revealed that the F_1 seeds displayed a phenotype of round and yellow. This was observed because round and yellow are dominant traits. It is the F_2 generation that supports the independent assortment model and refutes the linkage model.

THE HYPOTHESES

The inheritance pattern for two different traits follows one or more quantitative natural laws. Two possible hypotheses are described in Figure 2.7.

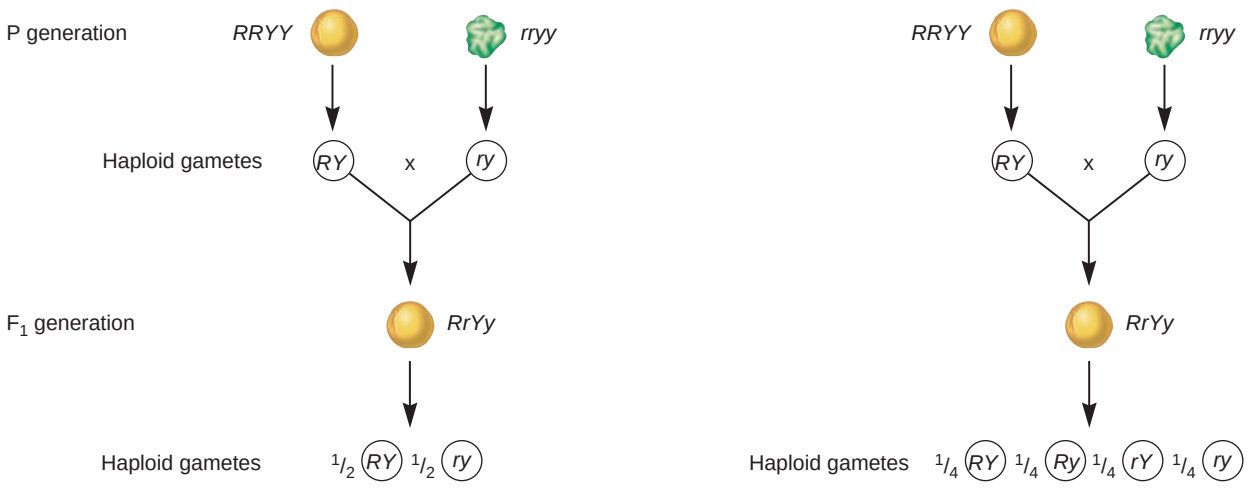
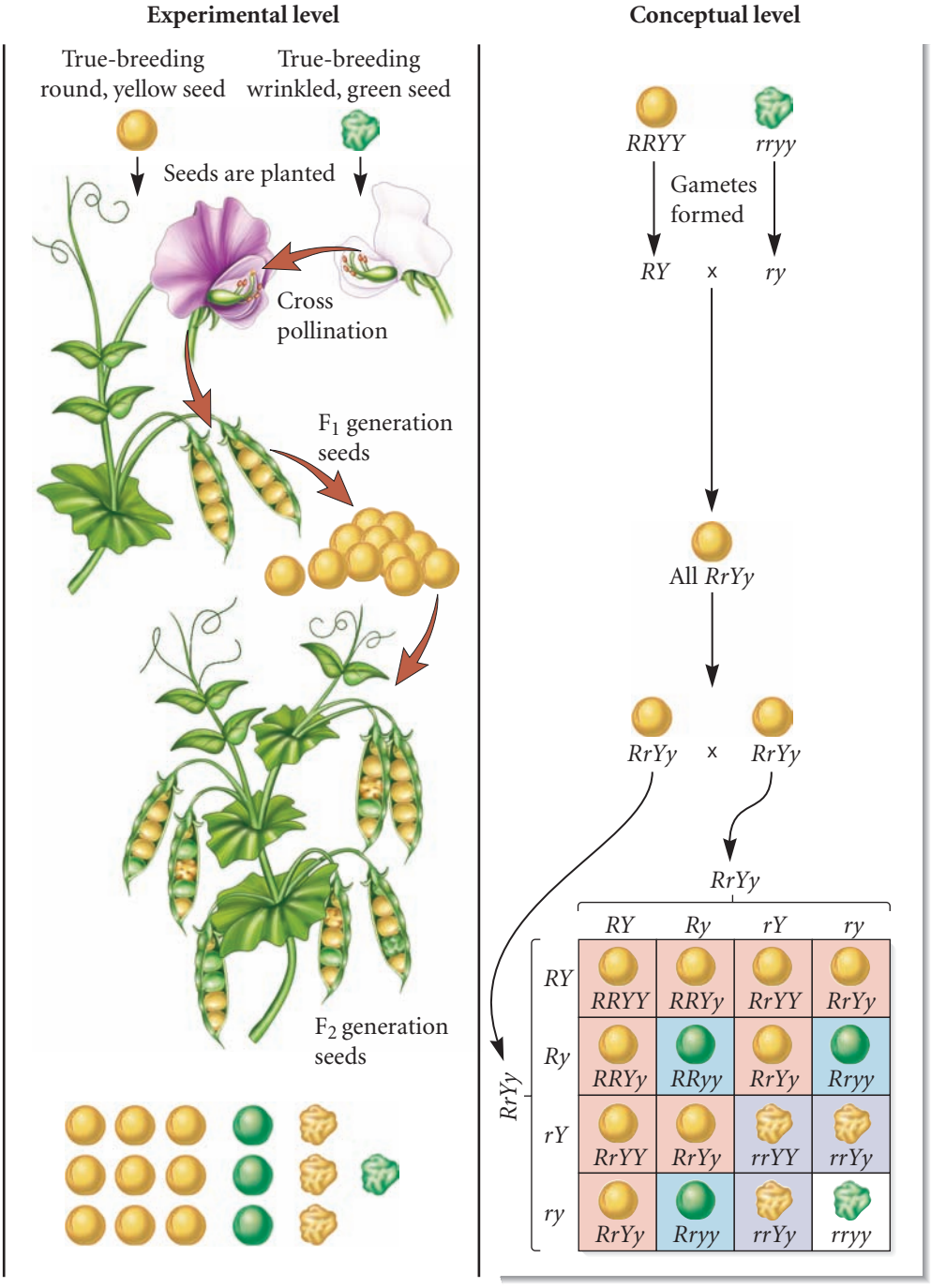


FIGURE 2.7 **Two hypotheses to explain how two different genes assort during gamete formation.** (**a**) According to the linked hypothesis, the two genes always stay associated with each other. (**b**) In contrast, the independent assortment hypothesis proposes that the two different genes randomly segregate into haploid cells.

TESTING THE HYPOTHESES — FIGURE 2.8 Mendel's analysis of two-factor crosses.

Starting material: In this experiment, Mendel began with two types of true-breeding pea plants that were different with regard to two traits. One plant had round, yellow seeds (*RRYY*); the other plant had wrinkled, green seeds (*rryy*).

1. Cross the two true-breeding plants to each other. This produces F_1 generation seeds.
2. Collect many seeds and record their phenotype.
3. F_1 seeds are planted and grown, and the F_1 plants are allowed to self-fertilize. This produces seeds that are part of the F_2 generation.
4. Analyze the characteristics found in the F_2 generation seeds.



THE DATA

P cross	*F_1 generation*	*F_2 generation*
Round, yellow × wrinkled, green seeds	All round, yellow	315 round, yellow seeds 108 round, green seeds 101 wrinkled, yellow seeds 32 wrinkled, green seeds

INTERPRETING THE DATA

The F_2 generation had seeds that were round and green and seeds that were wrinkled and yellow. These two categories of F_2 seeds are called **nonparentals** because these combinations of traits were not found in the true-breeding plants of the parental generation. The occurrence of nonparental variants contradicts the linkage model. According to the linkage model, the *R* and *Y* variants should be linked together and so should the *r* and *y* variants.

If this were the case, the F_1 plants could produce gametes that are only *RY* or *ry*. These would combine to produce *RRYY* (round, yellow), *RrYy* (round, yellow), or *rryy* (wrinkled, green) in a 1:2:1 ratio. Nonparental seeds could not be produced. However, Mendel did not obtain this result. Instead, he observed a phenotypic ratio of 9:3:3:1 in the F_2 generation.

Mendel's results from many dihybrid experiments rejected the hypothesis of linked assortment and, instead, supported the hypothesis that different traits assort themselves independently during reproduction. Using the modern notion of genes, **Mendel's law of independent assortment** states:

> *Two different genes will randomly assort their alleles during the formation of haploid cells.*

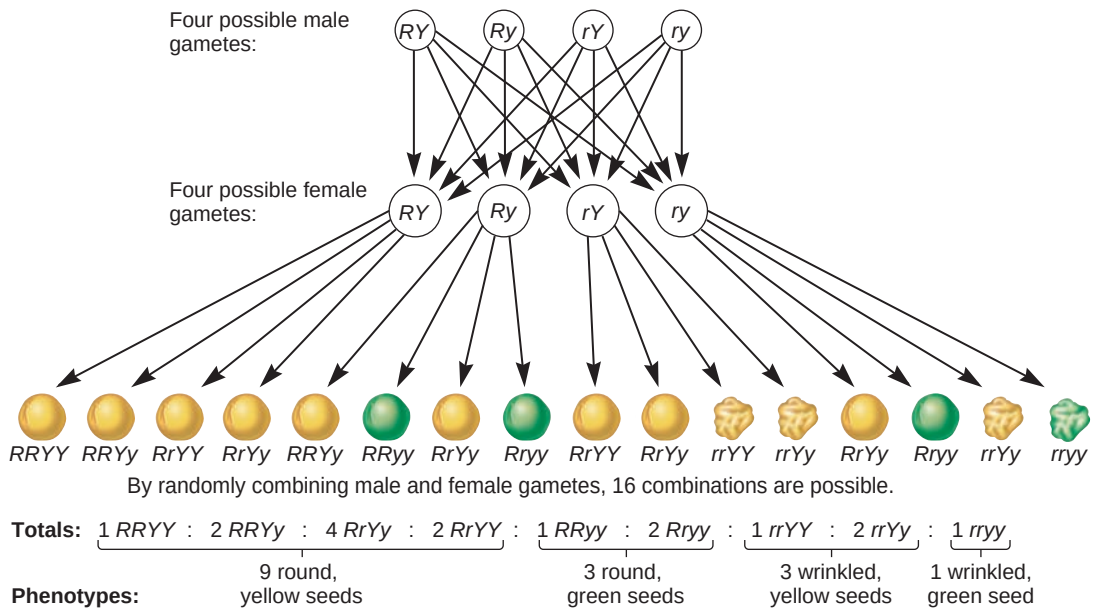
In other words, the allele for one gene will be found within a resulting gamete independently of whether the allele for a different gene is found in the same gamete. Using the example given in Figure 2.8, the round and wrinkled alleles will be assorted into haploid gametes independently of the yellow and green alleles. Therefore, a heterozygous *RrYy* parent can produce four different gametes—*RY*, *Ry*, *rY*, and *ry*—in equal proportions.

In an F_1 self-fertilization experiment, any two gametes can combine randomly during fertilization. This allows for 4^2, or 16, possible offspring, although some offspring will be genetically identical to each other. As shown in **Figure 2.9**, these 16 possible combinations result in seeds with the following phenotypes: 9 round, yellow; 3 round, green; 3 wrinkled, yellow; and 1 wrinkled, green. This 9:3:3:1 ratio is the expected outcome when a dihybrid is allowed to self-fertilize. Mendel was clever enough to realize that the data for his dihybrid experiments were close to a 9:3:3:1 ratio. In Figure 2.8, for example, his F_1 generation produced F_2 seeds with the following characteristics: 315 round, yellow seeds; 108 round, green seeds; 101 wrinkled, yellow seeds; and 32 wrinkled, green seeds. If we divide each of these numbers by 32 (the number of plants with wrinkled, green seeds), the phenotypic ratio of the F_2 generation is 9.8:3.2:3.4:1.0. Within experimental error, Mendel's data approximated the predicted 9:3:3:1 ratio for the F_2 generation.

The law of independent assortment held true for all seven traits that Mendel studied in pea plants. However, in other cases, the inheritance pattern of two different genes is consistent with the linkage model described earlier in Figure 2.7a. In Chapter 5, we will examine the inheritance of genes that are linked to each other because they are physically within the same chromosome. As we will see, linked genes do not assort independently.

An important consequence of the law of independent assortment is that a single individual can produce a vast array of genetically different gametes. As mentioned in Chapter 1, diploid species have pairs of homologous chromosomes, which may differ with respect to the alleles they carry. When an offspring receives a combination of alleles that differs from those in the parental generation, this phenomenon is termed **genetic recombination.** One mechanism that accounts for genetic recombination is independent assortment. A second mechanism, discussed in Chapter 5, is crossing over, which can reassort alleles that happen to be linked along the same chromosome.

The phenomenon of independent assortment is rooted in the random pattern by which the homologues assort themselves



INTERACTIVE EXERCISE

FIGURE 2.9 Mendel's law of independent assortment.

Genes→Traits The cross is between two parents that are heterozygous for seed shape and seed color (*RrYy* × *RrYy*). Four types of male gametes are possible: *RY, Ry, rY,* and *ry*. Likewise, four types of female gametes are possible: *RY, Ry, rY,* and *ry*. These four types of gametes are the result of the independent assortment of the seed shape and seed color alleles relative to each other. During fertilization, any one of the four types of male gametes can combine with any one of the four types of female gametes. This results in 16 types of offspring, each one containing two copies of the seed shape gene and two copies of the seed color gene.

during the process of meiosis, a topic addressed in Chapter 3. If a species contains a large number of homologous chromosomes, this creates the potential for an enormous amount of genetic diversity. For example, human cells contain 23 pairs of homologous chromosomes. These pairs can randomly assort into gametes during meiosis. The number of different gametes an individual can make equals 2^n, where n is the number of pairs of chromosomes. Therefore, humans can make 2^{23}, or over 8 million, possible gametes, due to independent assortment. The capacity to make so many genetically different gametes enables a species to produce individuals with many different combinations of traits. This allows environmental forces to select for those combinations of traits that favor reproductive success.

A self-help quiz involving this experiment can be found at the Online Learning Center.

A Punnett Square Can Also Be Used to Solve Independent Assortment Problems

As already depicted in Figure 2.8, we can use a Punnett square to predict the outcome of crosses involving two or more genes that assort independently. Let's see how such a Punnett square is made by considering a cross between two plants that are heterozygous for height and seed color (**Figure 2.10**). This cross is *TtYy* × *TtYy*. When we construct a Punnett square for this cross, we must keep in mind that each gamete has a single allele for each of two genes. In this example, the four possible gametes from each parent are

TY, *Ty*, *tY*, and *ty*

In this dihybrid experiment, we need to make a Punnett square containing 16 boxes. The phenotypes of the resulting offspring are predicted to occur in a ratio of 9:3:3:1.

In crosses involving three or more genes, the construction of a single large Punnett square to predict the outcome of crosses becomes very unwieldy. For example, in a trihybrid cross between two pea plants that are *Tt Rr Yy*, each parent can make 2^3, or 8, possible gametes. Therefore, the Punnett square must contain $8 \times 8 = 64$ boxes. As a more reasonable alternative, we can consider each gene separately and then algebraically combine them by multiplying together the expected outcomes for each gene. Two such methods, termed the **multiplication method** and the **forked-line method,** are shown in solved problem S3 at the end of this chapter.

Independent assortment is also revealed by a **dihybrid testcross.** In this type of experiment, dihybrid individuals are mated to individuals that are doubly homozygous recessive for the two traits. For example, individuals with a *TtYy* genotype could be crossed to *ttyy* plants. As shown here, independent assortment would predict a 1:1:1:1 ratio among the resulting offspring.

	TY	*Ty*	*tY*	*ty*
ty	*TtYy* Tall, yellow	*Ttyy* Tall, green	*ttYy* Dwarf, yellow	*ttyy* Dwarf, green

Cross: *TtYy* x *TtYy*

♂ / ♀	*TY*	*Ty*	*tY*	*ty*
TY	*TTYY* Tall, yellow	*TTYy* Tall, yellow	*TtYY* Tall, yellow	*TtYy* Tall, yellow
Ty	*TTYy* Tall, yellow	*TTyy* Tall, green	*TtYy* Tall, yellow	*Ttyy* Tall, green
tY	*TtYY* Tall, yellow	*TtYy* Tall, yellow	*ttYY* Dwarf, yellow	*ttYy* Dwarf, yellow
ty	*TtYy* Tall, yellow	*Ttyy* Tall, green	*ttYy* Dwarf, yellow	*ttyy* Dwarf, green

Genotypes: 1 *TTYY* : 2 *TTYy* : 4 *TtYy* : 2 *TtYY* : 1 *TTyy* : 2 *Ttyy* : 1 *ttYY* : 2 *ttYy* : 1 *ttyy*

Phenotypes: 9 tall plants with yellow seeds : 3 tall plants with green seeds : 3 dwarf plants with yellow seeds : 1 dwarf plant with green seeds

FIGURE 2.10 **A Punnett square for a dihybrid cross.** The Punnett square shown here involves a cross between two pea plants that are heterozygous for height and seed color. The cross is *TtYy* × *TtYy*.

Modern Geneticists Are Often Interested in the Relationship Between the Molecular Expression of Genes and the Outcome of Traits

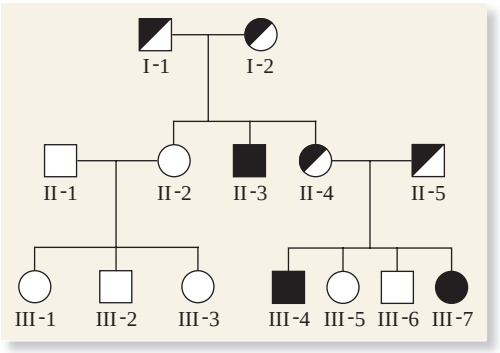
Mendel's work with pea plants was critically important because his laws of inheritance pertain to all eukaryotic organisms, such as fruit flies, corn, roundworms, mice, and humans, that transmit their genes through sexual reproduction. During the past several decades, many researchers have focused their attention on the relationship between the phenotypic appearance of traits and the molecular expression of genes. This theme will recur throughout the textbook (and we will draw attention to it by designating certain figure legends with a "Genes → Traits" label). As mentioned in Chapter 1, most genes encode proteins that function within living cells. The specific function of individual proteins affects the outcome of an individual's traits. A genetic approach can help us understand the relationship between a protein's function and its effect on phenotype. Most commonly, a geneticist will try to identify an individual that has a defective copy of a gene to see how that will affect the phenotype of the organism. These defective genes are called **loss-of-function alleles,** and they provide geneticists with a great amount of information. Unknowingly, Gregor Mendel had studied seven loss-of-function alleles among his strains of plants. The recessive characteristics in his pea plants were due to genes that had been rendered defective by a mutation. Such alleles are often inherited in a recessive manner, though this is not always the case.

How are loss-of-function alleles informative? In many cases, such alleles provide critical clues concerning the purpose of the protein's function within the organism. For example, we expect the gene affecting flower color (purple versus white) to encode a protein that is necessary for pigment production. This protein may function as an enzyme that is necessary for the synthesis of purple pigment. Furthermore, a reasonable guess is that the white allele is a loss-of-function allele that is unable to express this protein and therefore cannot make the purple pigment. To confirm this idea, a biochemist could analyze the petals from purple and white flowers and try to identify the protein that is defective or missing in the white petals but functionally active in the purple ones. The identification and characterization of this protein would provide a molecular explanation for this phenotypic characteristic.

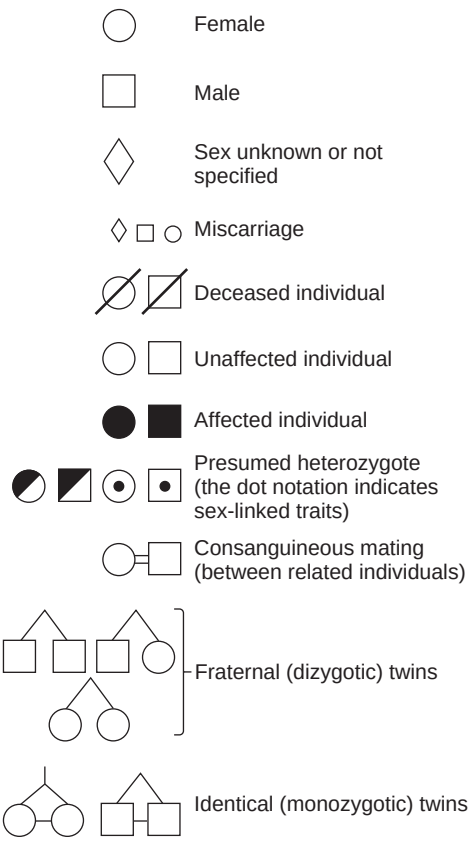
Pedigree Analysis Can Be Used to Follow the Mendelian Inheritance of Traits in Humans

Before we end our discussion of simple Mendelian traits, let's address the question of how we can analyze inheritance patterns among humans. In his experiments, Mendel selectively made crosses and then analyzed a large number of offspring. When studying human traits, however, researchers cannot control parental crosses. Instead, they must rely on the information that is contained within family trees. This type of approach, known as a **pedigree analysis,** is aimed at determining the type of inheritance pattern that a gene will follow. Although this method may be less definitive than the results described in Mendel's experiments, a pedigree analysis can often provide important clues concerning the pattern of inheritance of traits within human families. An expanded discussion of human pedigrees is provided in Chapter 22, which concerns the inheritance patterns of many different human diseases.

In order to discuss the applications of pedigree analyses, we need to understand the organization and symbols of a pedigree (**Figure 2.11**). The oldest generation is at the top of the pedigree, and the most recent generation is at the bottom. Vertical



(a) Human pedigree showing cystic fibrosis



(b) Symbols used in a human pedigree

FIGURE 2.11 **Pedigree analysis. (a)** A family pedigree in which some of the members are affected with cystic fibrosis. Individuals I-1, I-2, II-4, and II-5 are depicted as presumed heterozygotes because they produce affected offspring. **(b)** The symbols used in a pedigree analysis. Note: In pedigrees shown in this textbook, such as those found in the problem sets, the heterozygotes are not shown as half-filled symbols. Most pedigrees throughout the book show individuals' phenotypes—open symbols are unaffected individuals and filled (closed) symbols are affected individuals.

lines connect each succeeding generation. A man (square) and woman (circle) who produce one or more offspring are directly connected by a horizontal line. A vertical line connects parents with their offspring. If parents produce two or more offspring, the group of siblings (brothers and sisters) is denoted by two or more individuals projecting from the same horizontal line.

When a pedigree involves the transmission of a human trait or disease, affected individuals are depicted by filled symbols (in this case, black) that distinguish them from unaffected individuals. Each generation is given a roman numeral designation, and individuals within the same generation are numbered from left to right. A few examples of the genetic relationships in Figure 2.11a are described here:

Individuals I-1 and I-2 are the grandparents of III-1, III-2, III-3, III-4, III-5, III-6, and III-7

Individuals III-1, III-2, and III-3 are brother and sisters

Individual III-4 is affected by a genetic disease

The symbols shown in Figure 2.11 depict certain individuals, such as I-1, I-2, II-4, and II-5, as presumed heterozygotes because they are unaffected with a disease but produce homozygous offspring that are affected with a recessive genetic disease. However, in many pedigrees, such as those found in the problem sets at the end of the chapter, the inheritance pattern may not be known, so the symbols reflect only phenotypes. In most pedigrees, affected individuals are shown with closed symbols, and unaffected individuals, including those that might be heterozygous for a recessive disease, are depicted with open symbols.

Pedigree analysis is commonly used to determine the inheritance pattern of human genetic diseases. Human geneticists are routinely interested in knowing whether a genetic disease is inherited as a recessive or dominant trait. One way to discern the dominant/recessive relationship between two alleles is by a pedigree analysis. Genes that play a role in disease may exist as a normal allele or a mutant allele that causes disease symptoms. If the disease follows a simple Mendelian pattern of inheritance and is caused by a recessive allele, an individual must inherit two copies of the mutant allele to exhibit the disease. Therefore, a recessive pattern of inheritance makes two important predictions. First, two heterozygous normal individuals will, on average, have 1/4 of their offspring affected. Second, all offspring of two affected individuals will be affected. Alternatively, a dominant trait predicts that affected individuals will have inherited the gene from at least one affected parent (unless a new mutation has occurred during gamete formation).

The pedigree in Figure 2.11a concerns a human genetic disease known as cystic fibrosis (CF). Among Caucasians, approximately 3% of the population are heterozygous carriers of this recessive allele. In homozygotes, the disease symptoms include abnormalities of the pancreas, intestine, sweat glands, and lungs. These abnormalities are caused by an imbalance of ions across the plasma membrane. In the lungs, this leads to a buildup of thick, sticky mucus. Respiratory problems may lead to early death, although modern treatments have greatly increased the life span of CF patients. In the late 1980s, the gene for CF was identified. The CF gene encodes a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). This protein regulates the ion balance across the cell membrane in tissues of the pancreas, intestine, sweat glands, and lungs. The mutant allele causing CF alters the encoded CFTR protein. The altered CFTR protein is not correctly inserted into the plasma membrane, resulting in a decreased function that causes the ionic imbalance. As seen in the pedigree, the pattern of affected and unaffected individuals is consistent with a recessive mode of inheritance. Two unaffected individuals can produce an affected offspring. Although not shown in this pedigree, a recessive mode of inheritance is also characterized by the observation that two affected individuals will produce 100% affected offspring. However, for human genetic diseases that limit survival and/or fertility, there may never be cases where two affected individuals produce offspring.

2.2 PROBABILITY AND STATISTICS

A powerful application of Mendel's work is that the laws of inheritance can be used to predict the outcome of genetic crosses. In agriculture, for example, plant and animal breeders are concerned with the types of offspring their crosses will produce. This information is used to produce commercially important crops and livestock. In addition, people are often interested in predicting the characteristics of the children they may have. This may be particularly important to individuals who carry alleles that cause inherited diseases. Of course, we cannot see into the future and definitively predict what will happen. Nevertheless, genetic counselors can help couples to predict the likelihood of having an affected child. This probability is one factor that may influence a couple's decision whether to have children.

In this section, we will see how probability calculations are used in genetic problems to predict the outcome of crosses. To compute probability, we will use three mathematical operations known as the sum rule, the product rule, and the binomial expansion equation. These methods allow us to determine the probability that a cross between two individuals will produce a particular outcome. To apply these operations, we must have some knowledge regarding the genotypes of the parents and the pattern of inheritance of a given trait.

Probability calculations can also be used in hypothesis testing. In many situations, a researcher would like to discern the genotypes and patterns of inheritance for traits that are not yet understood. A traditional approach to this problem is to conduct crosses and then analyze their outcomes. The proportions of offspring may provide important clues that allow the experimenter to propose a hypothesis, based on the quantitative laws of inheritance, that explains the transmission of the trait from parent to offspring. Statistical methods, such as the chi square test, can then be used to evaluate how well the observed data from crosses fit the expected data. We will end this chapter with an example that applies the chi square test to a genetic cross.

Probability Is the Likelihood That an Event Will Occur

The chance that an event will occur in the future is called the event's **probability.** For example, if you flip a coin, the probability

is 0.50, or 50%, that the head side will be showing when the coin lands. Probability depends on the number of possible outcomes. In this case, two possible outcomes (heads or tails) are equally likely. This allows us to predict a 50% chance that a coin flip will produce heads. The general formula for probability (P) is

$$\text{Probability} = \frac{\text{Number of times an event occurs}}{\text{Total number of events}}$$

$$P_{\text{heads}} = 1 \text{ heads} / (1 \text{ heads} + 1 \text{ tails}) = 1/2 = 50\%$$

In genetic problems, we are often interested in the probability that a particular type of offspring will be produced. Recall that when two heterozygous tall pea plants (*Tt*) are crossed, the phenotypic ratio of the offspring is 3 tall:1 dwarf. This information can be used to calculate the probability for either type of offspring.

$$\text{Probability} = \frac{\text{Number of individuals with a given phenotype}}{\text{Total number of individuals}}$$

$$P_{\text{tall}} = 3 \text{ tall} / (3 \text{ tall} + 1 \text{ dwarf}) = 3/4 = 75\%$$

$$P_{\text{dwarf}} = 1 \text{ dwarf} / (3 \text{ tall} + 1 \text{ dwarf}) = 1/4 = 25\%$$

The probability is 75% of obtaining a tall plant and 25% of obtaining a dwarf plant. When we add together the probabilities of all the possible outcomes (tall and dwarf), we should get a sum of 100% (here, 75% + 25% = 100%).

A probability calculation allows us to predict the likelihood that an event will occur in the future. The accuracy of this prediction, however, depends to a great extent on the size of the sample. For example, if we toss a coin six times, our probability prediction would suggest that 50% of the time we should get heads (i.e., three heads and three tails). In this small sample size, however, we would not be too surprised if we came up with four heads and two tails. Each time we toss a coin, there is a random chance that it will be heads or tails. The deviation between the observed and expected outcomes is called the **random sampling error.** In a small sample, the error between the predicted percentage of heads and the actual percentage observed may be quite large. By comparison, if we flipped a coin 1,000 times, the percentage of heads would be fairly close to the predicted 50% value. In a larger sample, we expect the random sampling error to be a much smaller percentage.

The Sum Rule Can Be Used to Predict the Occurrence of Mutually Exclusive Events

Now that we have an understanding of probability, we can see how mathematical operations using probability values allow us to predict the outcome of genetic crosses. Our first genetic problem involves the use of the **sum rule,** which states that *the probability that one of two or more mutually exclusive events will occur is equal to the sum of the individual probabilities of the events.* As an example, let's consider a cross between two mice that are both heterozygous for genes affecting the ears and tail. One gene can be found as an allele designated *de*, which is a recessive allele that causes droopy ears; the normal allele is *De.* An allele of a second gene causes a crinkly tail. This crinkly tail allele (*ct*) is recessive to the normal allele (*Ct*). If a cross is made between two heterozygous mice (*Dede Ctct*), the predicted ratio of offspring is 9 with normal ears and normal tails, 3 with normal ears and crinkly tails, 3 with droopy ears and normal tails, and 1 with droopy ears and a crinkly tail. These four phenotypes are mutually exclusive. For example, a mouse with droopy ears and a normal tail cannot have normal ears and a crinkly tail.

The sum rule allows us to determine the probability that we will obtain any one of two or more different types of offspring. For example, in a cross between two heterozygotes (*Dede Ctct* × *Dede Ctct*), we can ask the following question: What is the probability that an offspring will have normal ears and a normal tail or have droopy ears and a crinkly tail? In other words, if we closed our eyes and picked an offspring out of a litter from this cross, what are the chances that we would be holding a mouse that has normal ears and a normal tail or a mouse with droopy ears and a crinkly tail? In this case, the investigator wants to predict whether one of two mutually exclusive events will occur. A strategy for solving such genetic problems using the sum rule is described here.

The Cross: *Dede Ctct* × *Dede Ctct*

The Question: What is the probability that an offspring will have normal ears and a normal tail or have droopy ears and a crinkly tail?

Step 1. *Calculate the individual probabilities of each phenotype.* This can be accomplished using a Punnett square.

The probability of normal ears and a normal tail is $9/(9 + 3 + 3 + 1) = 9/16$

The probability of droopy ears and a crinkly tail is $1/(9 + 3 + 3 + 1) = 1/16$

Step 2. *Add together the individual probabilities.*

$$9/16 + 1/16 = 10/16$$

This means that 10/16 is the probability that an offspring will have either normal ears and a normal tail or droopy ears and a crinkly tail. We can convert 10/16 to 0.625, which means that 62.5% of the offspring are predicted to have normal ears and a normal tail or droopy ears and a crinkly tail.

The Product Rule Can Be Used to Predict the Probability of Independent Events

We can use probability to make predictions regarding the likelihood of two or more independent outcomes from a genetic cross. When we say that events are independent, we mean that the occurrence of one event does not affect the probability of another event. As an example, let's consider a rare, recessive human trait known as congenital analgesia. Persons with this trait can distinguish between sharp and dull, and hot and cold, but do not perceive extremes of sensation as being painful. The first case of congenital analgesia, described in 1932, was a man who made his living entertaining the public as a "human pincushion."