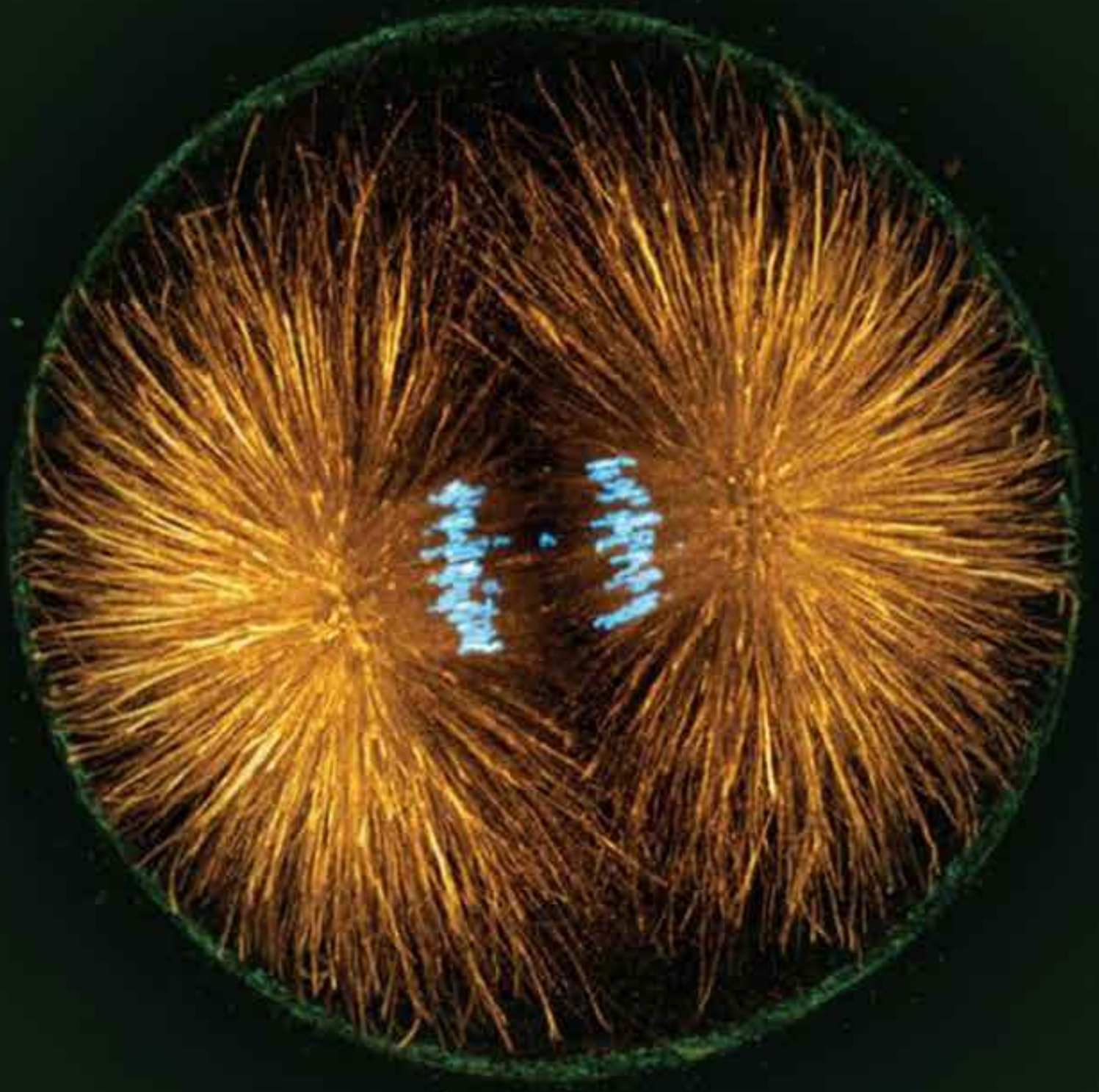
GENETICS 5E

ANALYSIS & PRINCIPLES



ROBERT J. BROOKER

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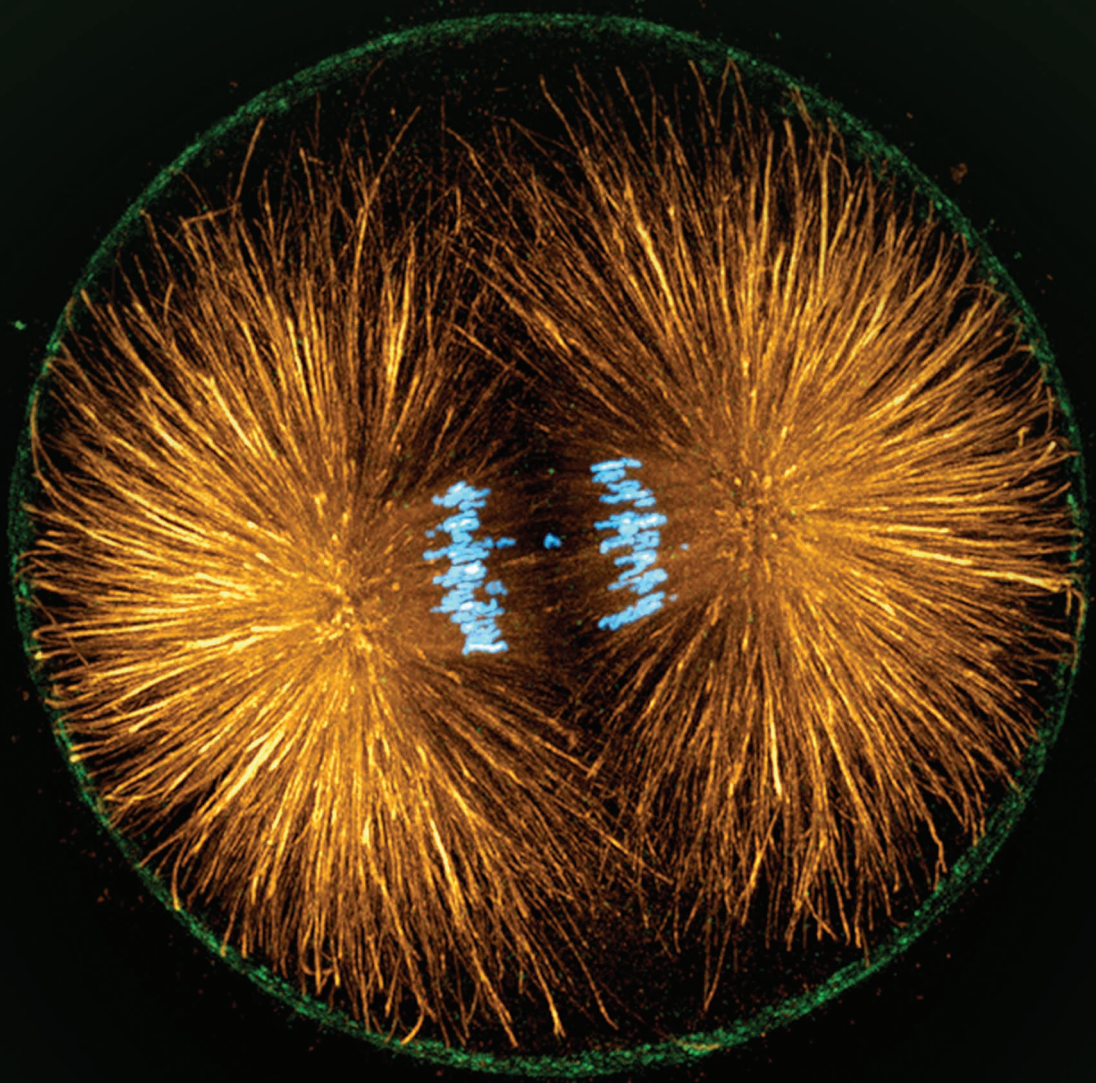

ROBERT J. BROOKER

University of Minnesota

Mc Graw Hill Education

GENETICS: ANALYSIS & PRINCIPLES, FIFTH EDITION

This book is printed on acid-free paper.

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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 postdoctoral 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

PREFACE

In the fifth 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 fifth edition of *Genetics: Analysis & Principles* a fun learning tool.

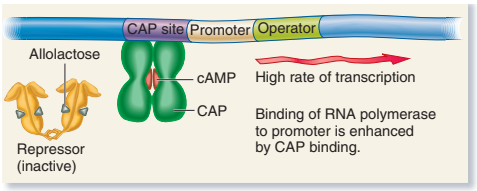
Overall, an effective textbook needs to accomplish four goals. First, it needs to provide comprehensive, accurate, and up-to-date content in its field. Second, it needs to expose students to the techniques and skills they will need to become successful in that field. Third, an effective textbook should have pedagogical features, such as formative assessment, that foster student learning. And finally, it should inspire students so they want to pursue that field as a career. The hard work that has gone into the fifth edition of *Genetics: Analysis & Principles* has been aimed at achieving all four of these goals!

FLIPPING THE CLASSROOM

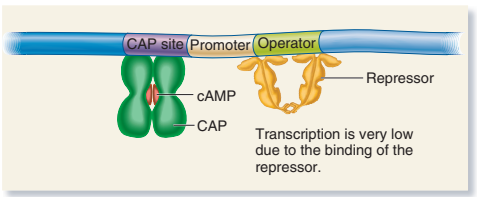
A recent trend in science education is the phenomenon that is sometimes called "flipping the classroom." This phrase refers to the idea that some of the activities that used to be done in class are now done outside of class, and vice versa. For example, instead of spending the entire class time lecturing over textbook and other materials, some of the class time is spent engaging students in various activities, such as problem solving, working through case studies, and designing experiments. This approach is called active learning. For many instructors, the classroom has become more learner centered rather teacher centered. A learner-centered classroom provides a rich environment in which students can interact with each other and with their instructors. Instructors and fellow students often provide formative assessment—immediate feedback that helps each student understand if his or her learning is on the right track.

What are some advantages of active learning? Educational studies reveal that active learning usually promotes greater learning gains. In addition, active learning often focuses on skill development rather than on the memorization of facts that are easily forgotten. Students become trained to "think like scientists" and to develop a skill set that enables them to apply scientific reasoning. A common concern among instructors who are beginning to try out active learning is that they think they will have less time to teach and therefore will cover less material. However, this may not be the case. Although students may be provided with online lectures, "flipping the classroom" typically gives students more responsibility for understanding the textbook material on their own. Along these lines, *Genetics: Analysis & Principles*, fifth edition, is intended to provide students with a resource that can be effectively used outside of the classroom. Here are several of the key pedagogical features:

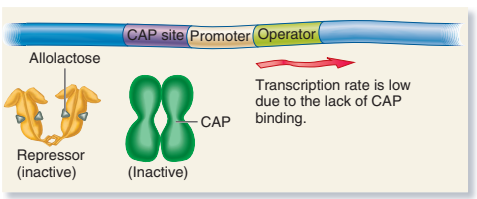
- Genes → Traits: Because genetics is such a broad discipline, ranging from the molecular level to populations, many



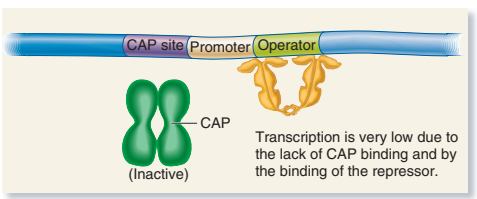
(a) Lactose, no glucose (high cAMP)



(b) No lactose or glucose (high cAMP)



(c) Lactose and glucose (low cAMP)



(d) Glucose, no lactose (low cAMP)

INTERACTIVE EXERCISE

FIGURE 14.8 The roles of the lac repressor and catabolite activator protein (CAP) in the regulation of the *lac* operon. This figure illustrates how the *lac* operon is regulated depending on its exposure to lactose or glucose.

Genes → Traits The mechanism of catabolite repression provides the bacterium with the trait of being able to choose between two sugars. When exposed to both glucose and lactose, the bacterium chooses glucose first. After the glucose is used up, it then expresses the genes necessary for lactose metabolism. This trait allows the bacterium to more efficiently use sugars from its environment.

CONCEPT CHECK: Why is it beneficial for the bacterium to regulate the *lac* operon with both a repressor protein and an activator protein?

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 (see Figure 14.8).

- Learning Outcomes: Each section of every chapter begins with a set of learning outcomes. These outcomes help students understand what they should be able to do once they have mastered the material in that section.
- Formative Assessment: When students are expected to learn textbook material on their own, it is imperative that they are regularly given formative assessment so they can gauge whether they are mastering the material. Formative assessment is a major feature of this textbook and is bolstered by Connect—a state-of-the art digital assignment and assessment platform. In *Genetics: Analysis & Principles*, fifth edition, formative assessment is provided in multiple ways.

  1. Each section of every chapter ends with multiple-choice questions. Also, compared with the previous edition, many chapters in the fifth edition are divided into more sections that are shorter in length. Formative assessment at the end of each section allows students to evaluate their mastery of the material before moving on to the next section.
  2. Most figures have Concept Check questions so students can determine if they understand the key points in the figure.
  3. Extensive end-of chapter questions continue to provide students with feedback regarding their mastery of the material.
  4. Additional questions, including questions that pertain to every feature investigation, are found at the open-access companion website: www.mhhe.com/brookergenetics5e.
  5. The textbook material is supported by digital learning tools found in Connect. Questions and activities are assignable in Connect, but students also have access to our valuable adaptive study tool, LearnSmart, offered for the first time with the fifth edition of *Genetics: Analysis & Principles*.

Overall, the pedagogy of *Genetics: Analysis & Principles*, fifth edition, has been designed to foster student learning. Instead of being a collection of "facts and figures," *Genetics: Analysis and Principles*, fifth edition, by Robert Brooker, is intended to be an engaging and motivating textbook in which formative assessment allows students to move ahead and learn the material in a productive way. We welcome your feedback so we can make future editions even better!

HOW WE ARE MEETING YOUR NEEDS

Text 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, whereas Chapters 26 through 28 examine population and quantitative genetics. The bulk of the molecular genetics is found in Chapters 9 through 25, 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 25 does not assume that a student has already covered Chapters 2 through 8. In fact, 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 26 through 28. (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 25. Alternatively, if you like the "Molecular-first" approach, you would probably cover Chapter 1, then skip to Chapters 9 through 25, then return to Chapters 2 through 8, and then cover Chapters 26 through 28 at the end of the course. This textbook was written in such a way that either strategy works well.

Accuracy

Both the publisher and I acknowledge 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.

In addition to input from reviewers, a development editor has gone through the material to check for accuracy in art and consistency between the text and art. With regard to the problem sets, the author personally checked every question and answer when the chapters were completed.

Feature Experiments

As in 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 helps you to see the fundamental connection between scientific anal-

ysis and principles. For both students and instructors, I expect that this strategy makes genetics much more fun to explore.

Writing Style

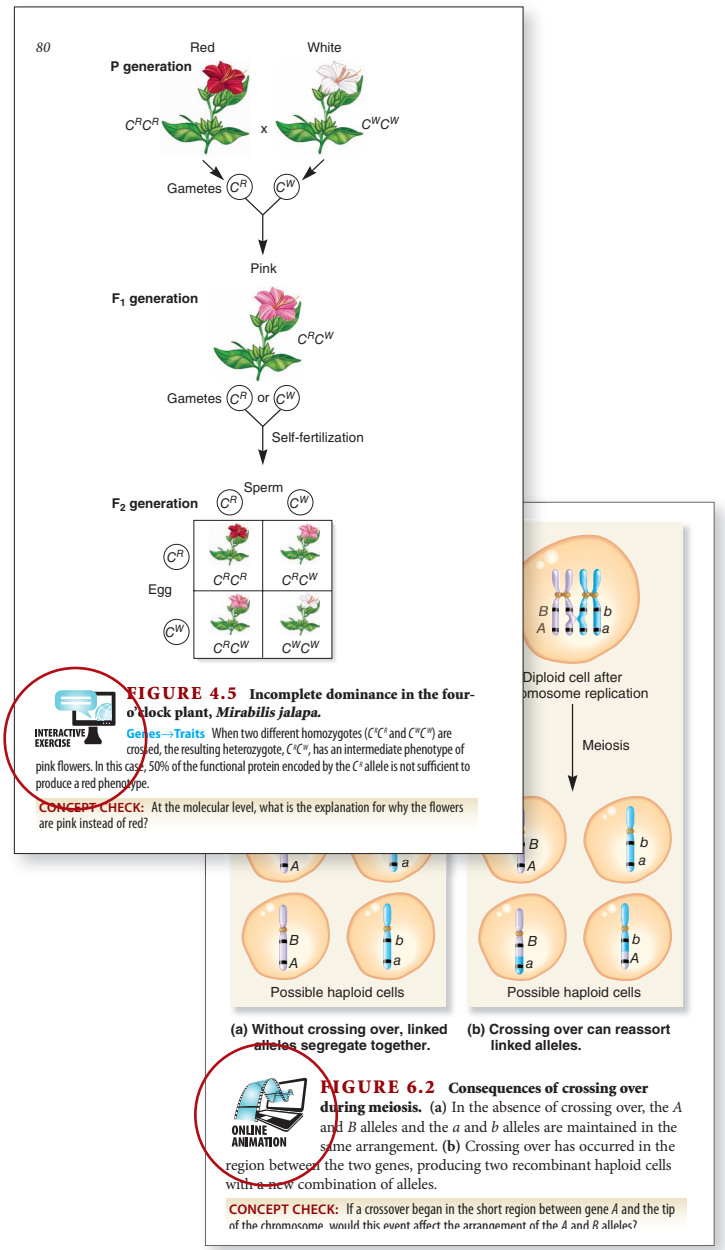
Motivation in learning often stems from enjoyment. If you enjoy what you're reading, you are more likely to spend more time with it and focus your attention more crisply. The writing style of this book is meant to be interesting, down to earth, and easy to follow. Each section of every chapter begins 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 at the end of the chapter and in the glossary.

A genetics book can be made interesting and inspiring in various ways. 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 on examples that bring the concepts to life. In a genetics book, many of these examples come from the realm of medicine and medical research. This textbook contains lots of examples of human diseases that exemplify some of the underlying principles of genetics. Students often say 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 for developing cancer. In addition, I have provided interesting examples from the microbial and plant world. Finally, students are often fascinated by applications of genetics that affect their everyday lives. Because we frequently hear about genetics in the news, it's inspiring for students to learn the underlying basis for such technologies. Chapters 20 to 23 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 influence of genetics in their lives.

Interactive Exercises and Animations

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 Interactive Exercises are an excellent tool for helping students test their understanding of inheritance patterns and human genetic diseases, but additional exercises also explore molecular concepts.

Our media specialists have also created over 55 animations for a variety of genetic processes. These animations were made specifically for this textbook and use the art from the textbook. The animations make many of the figures in the textbook "come to life." Icons are found in figure legends where the concept is supported by an Interactive Exercise or animation. The Interactive Exercises and animations are available through the Presentation Tools table in Connect, allowing professors to incorporate both into their classroom discussions. The Interactive Exercises are a great jumping off point for Active Learning discussions.



SIGNIFICANT CONTENT CHANGES IN THE FIFTH EDITION

- Each section of every chapter begins with Learning Outcomes and ends with multiple-choice questions. The answers to the multiple-choice questions are in the back of the book.
- Concept Check questions have been added to the figure legends of hundreds of figures, enabling students to determine if they understand key points in those figures. The answers to these questions are also in the back of the book.
- Many chapters have been divided into more sections that are shorter in length. This helps students to see the big

picture of each topic and provides an opportunity to include more formative assessment.
- Although the overall length of the fifth edition is not longer than the fourth edition, two new chapters have been added to this edition: Chapter 16. Eukaryotic Gene Regulation II: Epigenetics and Regulation at the RNA Level; and Chapter 17. Genetics of Viruses.

Examples of Specific Content Changes to Individual Chapters

- Chapter 2. Mendelian Inheritance: Divided into shorter sections that end in questions to help students gauge their understanding of Mendel's laws.
- Chapter 3. Chromosome Transmission During Cell Division and Sexual Reproduction: Improvement in the figures of mitosis and meiosis (see Figures 3.8 and 3.11).
- Chapter 4. Extensions of Mendelian Inheritance: This revised chapter begins with an overview that compares different inheritance patterns, and then the inheritance patterns are placed in their own sections that end with formative assessment questions. This approach should help students see the similarities and differences among the various patterns.
- Chapter 5. Non-Mendelian Inheritance: Epigenetic inheritance is now divided into two sections. One section is focused on dosage compensation and the other concerns genomic imprinting.
- Chapter 6. Genetic and Linkage Mapping in Eukaryotes: Contains a more streamlined presentation of mapping in haploid fungi.
- Chapter 7. Genetic Transfer and Mapping in Bacteria and Bacteriophages: Begins with an overview that compares different types of genetic transfer between bacteria, and then each form of transfer is highlighted within its own section. Mapping in bacteriophages has been separated into sections that focus on intergenic complementation and intragenic mapping.
- Chapter 8. Variation in Chromosome Structure and Number: The fifth edition contains a more streamlined presentation of natural and experimental mechanisms that produce variation in chromosome number.
- Chapter 9. Molecular Structure of DNA and RNA: The four levels of DNA structure are introduced in an overview section and then the different levels of DNA structure are presented in their own sections, followed by formative assessment questions.
- Chapter 10. Chromosome Organization and Molecular Structure: The information on viruses has been moved to Chapter 17, which is a new chapter in the fifth edition. Improvements have been made to several figures that depict chromatin structure (see Figures 10.11 and 10.18).
- Chapter 11. DNA Replication: The figure illustrating a three-dimensional view of DNA replication has been improved (see Figure 11.12).
- Chapter 12. Gene Transcription and RNA Modification: An improved figure has been added, which shows how sigma factor binds into the major groove (see Figure 12.6). A summary table has been added at the end of the chapter that compares transcription and RNA modification between bacteria and eukaryotes.
- Chapter 13. Translation of mRNA: The relationship between the genetic code to protein synthesis and the experimental determination of the genetic code have been placed into two separate sections. A new table has been added that describes how certain antibiotics inhibit translation (see Table 13.9).
- Chapter 14. Gene Regulation in Bacteria: The material on bacteriophage gene regulation has been moved to Chapter 17 (Genetics of Viruses). The *lac* operon and *trp* operon are now discussed in their own separate sections.
- Chapter 15. Gene Regulation in Eukaryotes I: Transcriptional Regulation: The material on eukaryotic gene regulation is now divided into two chapters. The first one focuses on transcriptional regulation. A new section has been added on the ENCODE Project.
- Chapter 16. Gene Regulation in Eukaryotes II: Epigenetics and Regulation at the RNA Level: This chapter has three new sections that focus on epigenetics during development and environmental factors that cause epigenetic changes. It includes seven new figures and three new tables.
- Chapter 17. Genetics of Viruses: This chapter incorporates some material from the fourth edition, such as bacteriophage gene regulation, but largely includes new material on viral reproductive cycles and gene regulation in HIV. It has eight new figures.
- Chapter 18. Gene Mutation and DNA Repair: The figure concerning trinucleotide repeat expansion has been revised (see Figure 18.12).
- Chapter 19. Recombination and Transposition at the Molecular Level: The figure concerning the function of transposase has been revised into a two-part figure that shows how transposase causes the transposon to loop out (see Figure 19.12).
- Chapter 20. DNA Technologies: Based on reviewer feedback, the order of topics in this chapter has been revised. DNA sequencing and site-directed mutagenesis come directly after cloning methods.
- Chapter 21. Biotechnology: Various topics, such as the use of transgenic crops, have been updated.
- Chapter 22. Genomics I: Analysis of DNA: A new section has been added on metagenomics.
- Chapter 23. Genomics II: Functional Genomics, Proteomics, and Bioinformatics: Includes updates to the topic of bioinformatics.
- Chapter 24. Medical Genetics and Cancer: This chapter ends with a new section on personalized medicine.
- Chapter 25. Developmental Genetics: Improvements in the color scheme of several figures will help students better understand certain key points of development.
- Chapter 26. Population Genetics: The chapter now contains an overview of microevolution, and then natural selection, genetic drift, migration, nonrandom mating, and sources of new genetic variation are covered in their own separate sections.

- Chapter 27. Quantitative Genetics: This chapter in the fifth edition presents a more streamlined view of how quantitative loci are mapped. A section on the general features of heritability precedes a section on selective breeding.
- Chapter 28. Evolutionary Genetics: The cladistics method for constructing a phylogenetic tree is compared with the UPGMA method.

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:

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ONLINE TEACHING AND LEARNING RESOURCES

Help Your Students Prepare for Class

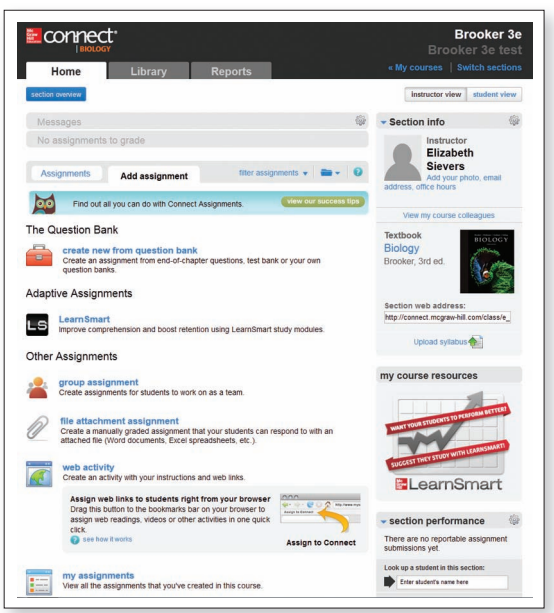
Digital resources can help you achieve your instructional goals—making your students more responsible for learning outside of class by meeting your students where they live: on the go and online. Use the text and digital tools to empower students to come to class more prepared and ready to engage!

McGraw-Hill Connect Genetics provides online presentation, assignment, and assessment solutions. It connects your students with the tools and resources they'll need to achieve success. With **Connect Genetics** you can deliver assignments, quizzes, and tests online. A robust set of questions and activities is presented in the Question Bank and a separate set of questions to use for exams is presented in the Test Bank. As an instructor, you can edit existing questions and author entirely new problems. Track individual student performance—by question, by assignment, or in relation to the class overall—with detailed grade reports. Integrate grade reports easily with Learning Management Systems such as Blackboard and Canvas—and much more. **ConnectPlus Genetics** provides students with all the advantages of Connect Biology plus 24/7 online access to an eBook. This media-rich version of the book is available through the McGraw-Hill ConnectPlus platform and allows seamless integration of text, media, and assessments.

To learn more, visit **www.mcgrawhillconnect.com**.

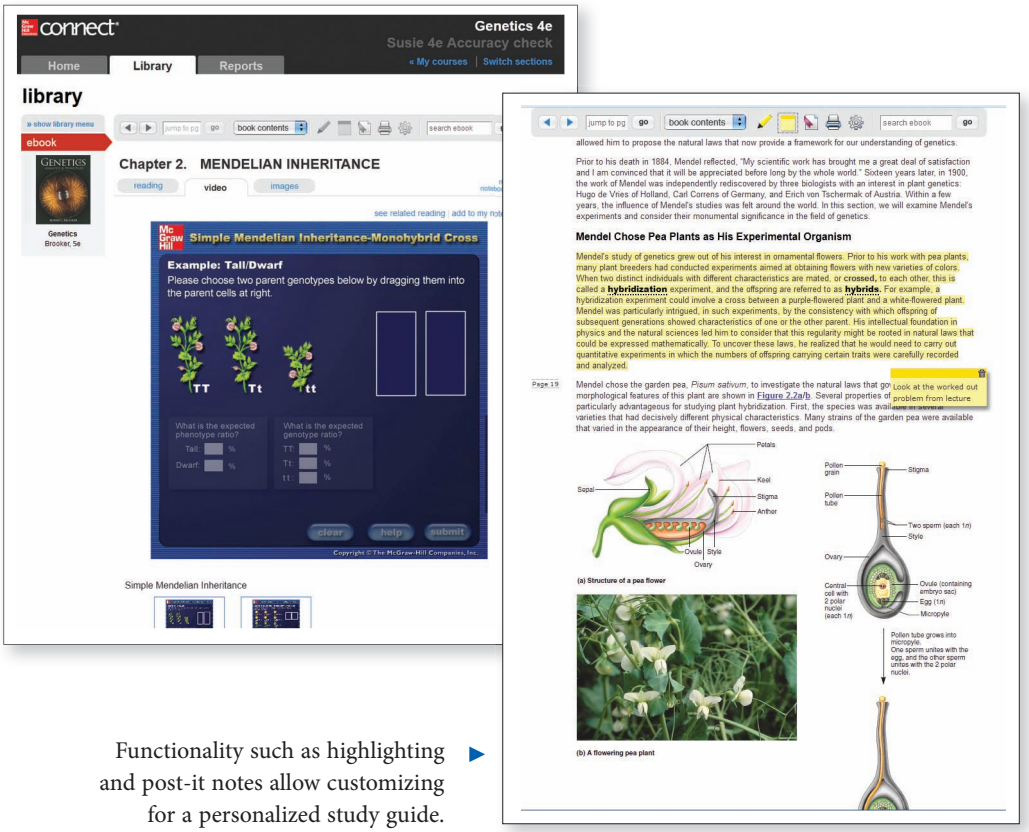
Help Your Students by Making Assignments—Reading, Homework, and LearnSmart

Connect content can be assigned as homework for before class to help students with basic concepts so they can better understand classroom presentations and projects. Quizzes taken after class can also evaluate their comprehension. These assignments support the rich assessment presented in the text so that student and professors can gauge the level of understanding of concepts and the mastery of skills.



Assignments can include reading assignments from the ConnectPlus eBook or SmartBook, homework or quizzes, LearnSmart, your own web or short answer activities, and more.

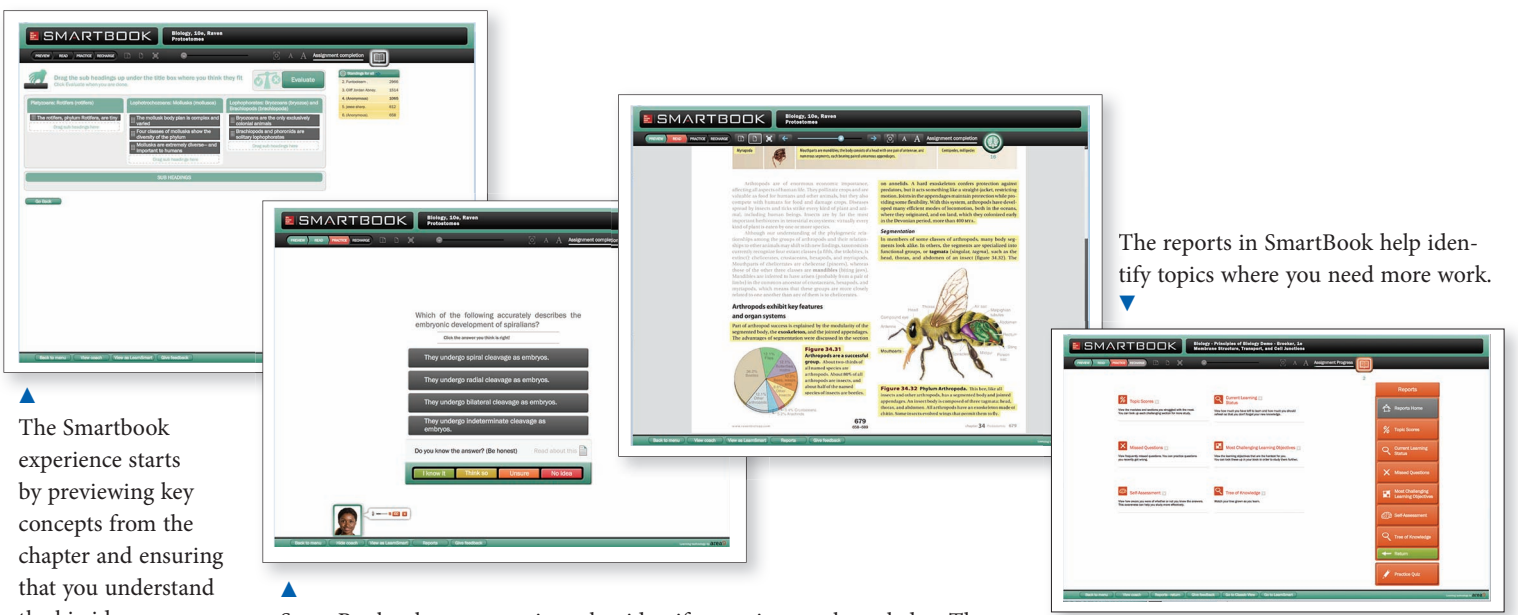
The interactive eBook takes the reading experience to a new level with links to animations and interactive exercises that supplement the text.



Functionality such as highlighting and post-it notes allow customizing for a personalized study guide.

SMARTBOOK™

Powered by an intelligent diagnostic and adaptive engine, **SmartBook** facilitates the reading process by identifying what content a student knows and doesn't know through adaptive assessments.

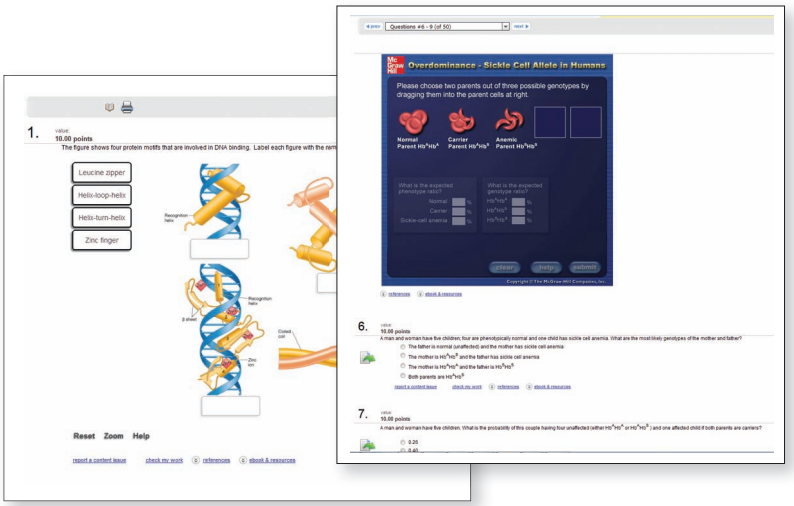


The Smartbook experience starts by previewing key concepts from the chapter and ensuring that you understand the big ideas.

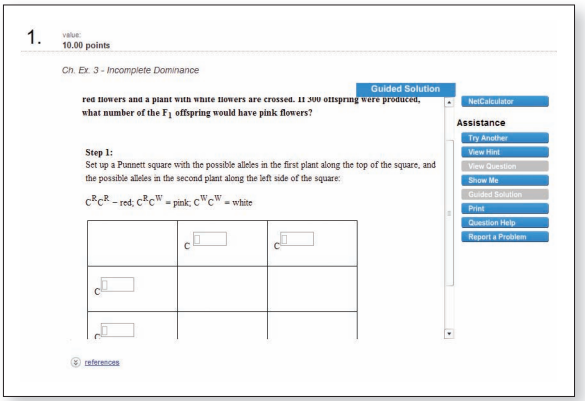
SmartBook asks you questions that identify gaps in your knowledge. The reading experience then continuously adapts in response to the assessments, highlighting the material you need to review based on what you don't know.

The reports in SmartBook help identify topics where you need more work.

Help your students prepare for class and revisit content by assigning homework in Connect and LearnSmart.

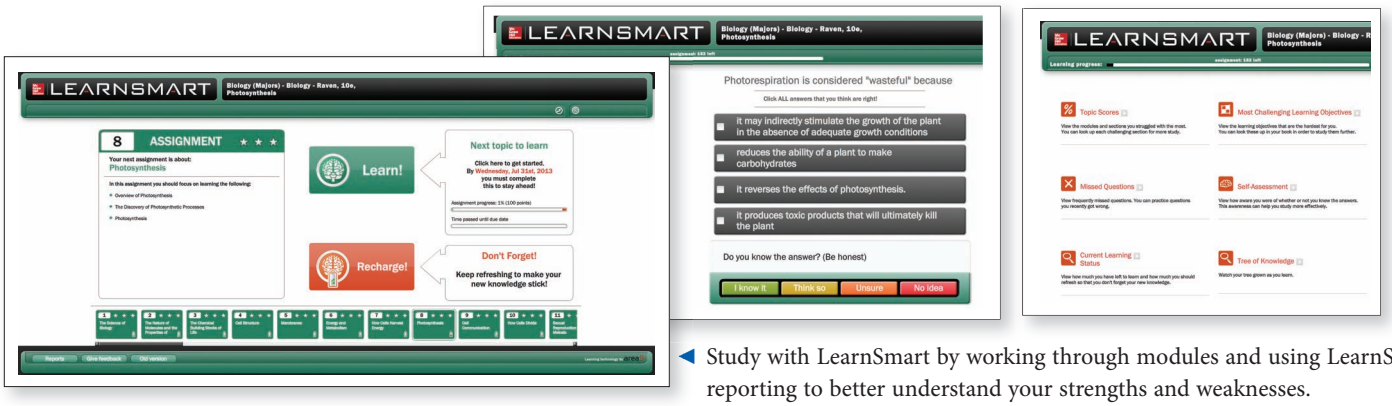


Interactive and traditional questions help assess your knowledge of the material. Having achieved a base level of knowledge, you will get more out of your time in class.



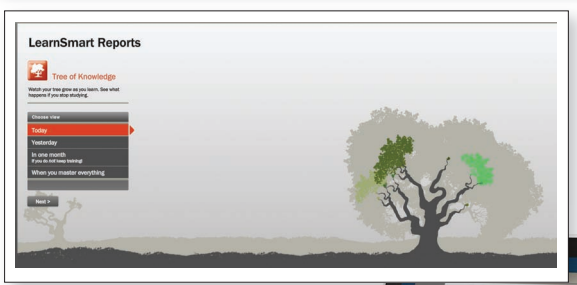
Quantitative questions help you challenge your students to apply material they learn in class and in the book.

LEARNSMART®



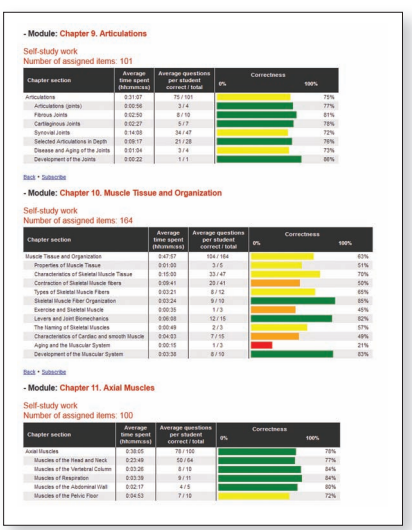
Study with LearnSmart by working through modules and using LearnSmart's reporting to better understand your strengths and weaknesses.

Gauge your students' progress using reports in LearnSmart and Connect. Students can run these same reports in LearnSmart to track their own progress.



The Tree of Knowledge tracks your progress, reporting on short-term successes and long-term retention.

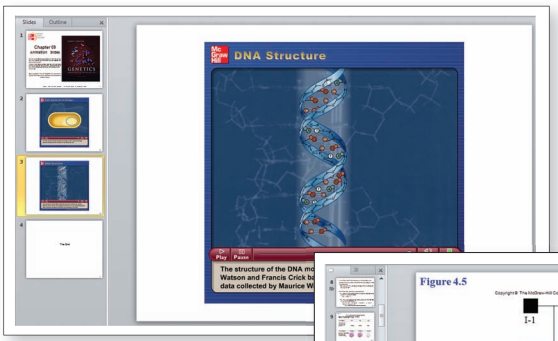
Download the LearnSmart app from iTunes or Google Play and work on LearnSmart from anywhere!



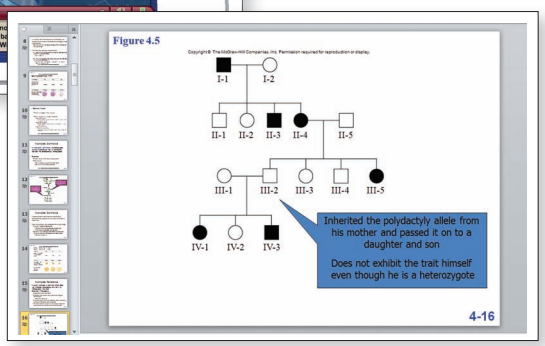
Reports in Connect and LearnSmart help you monitor student assignments and performance, allowing for "just-in-time" teaching to clarify concepts that are more difficult for your students to understand.

Presentation Tools

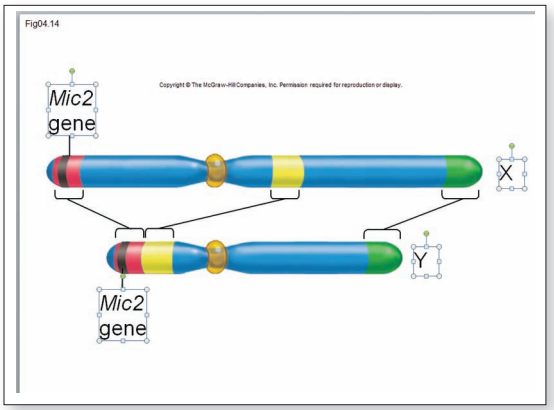
Within Connect, you will find presentation materials to enhance your class all in one place.



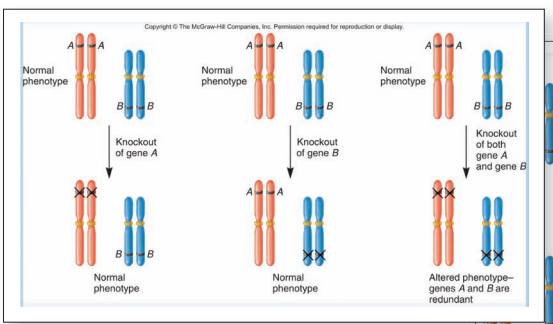
◀ Animation PowerPoints contain full-color animations illustrating important processes, which are fully embedded in PowerPoint slides for easy use in your presentations.

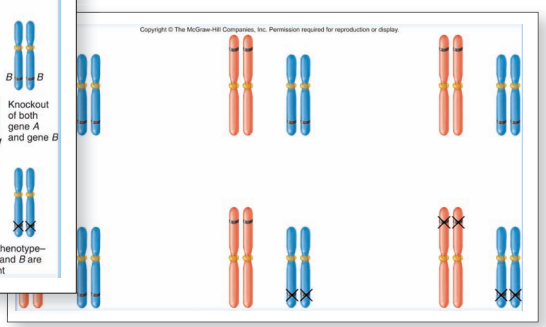


Lecture PowerPoints with animations fully embedded. ▶



▲ FlexArt PowerPoints contain editable art from the text. For all figures, labels and leader lines are editable and some figures also have editable or stepped out art allowing you to customize your PowerPoint presentations.





◀ Labeled and unlabeled JPEG files of all art and photos in the text to be readily incorporated into presentations, exams, or custom-made classroom materials.

Student Study Guide/Solutions Manual (ISBN: 0-07-767636-X)

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

ACKNOWLEDGMENTS

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

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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.

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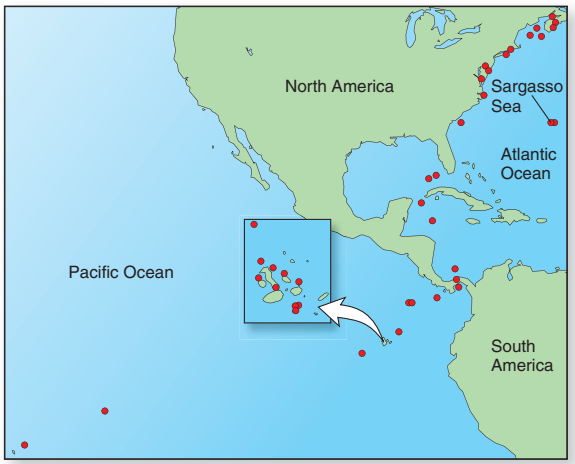
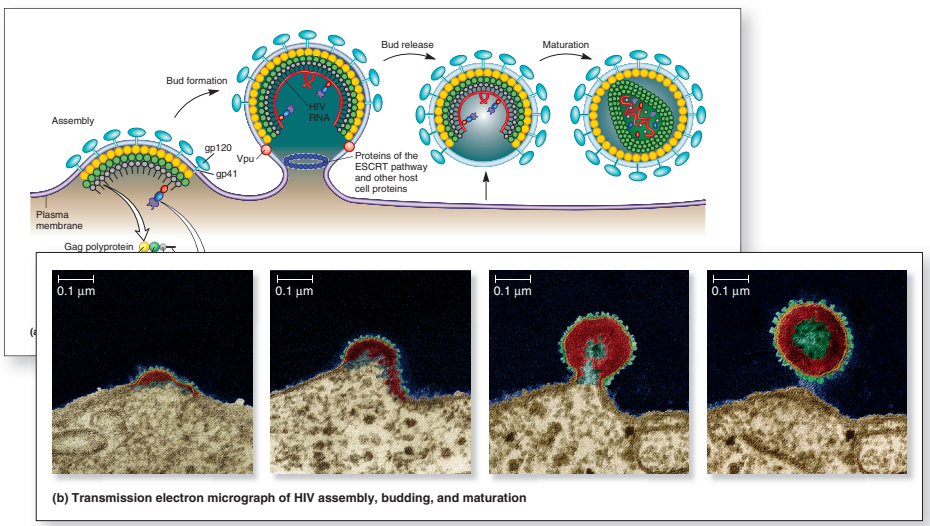
A Visual Guide to
GENETICS: ANALYSIS & PRINCIPLES

Instructional Art

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



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



(b) Transmission electron micrograph of HIV assembly, budding, and maturation

Many figures are supported with online Interactive Exercises and Online Animations that allow students an opportunity to delve into problem-solving activities through the Interactive Exercises and explore dynamic processes through the Online Animations. Icons indicate which figures are supported with these online features.

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

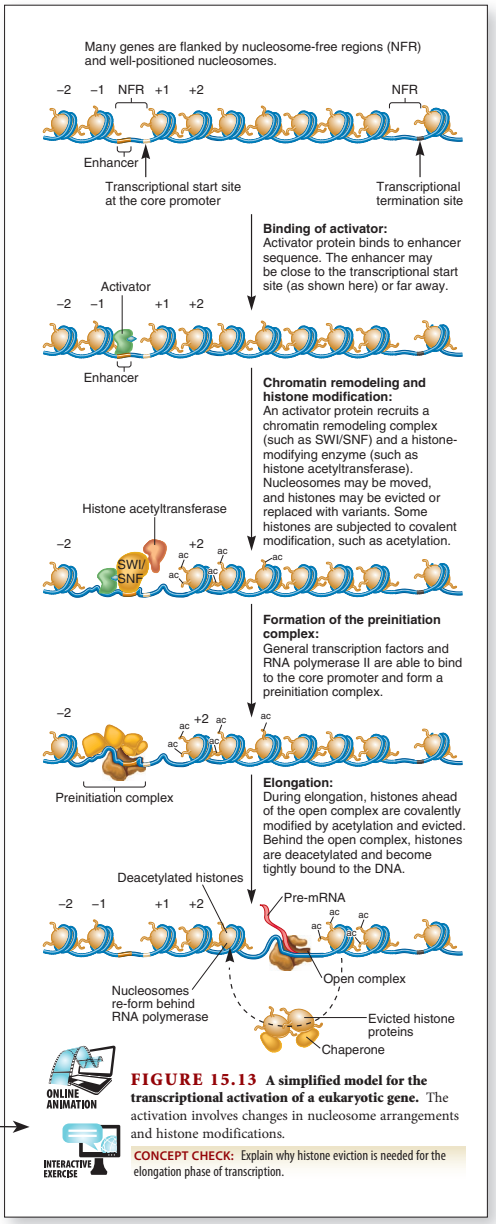


FIGURE 15.13 A simplified model for the transcriptional activation of a eukaryotic gene. The activation involves changes in nucleosome arrangements and histone modifications.

CONCEPT CHECK: Explain why histone eviction is needed for the elongation phase of transcription.

Learning Through Experimentation

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.

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

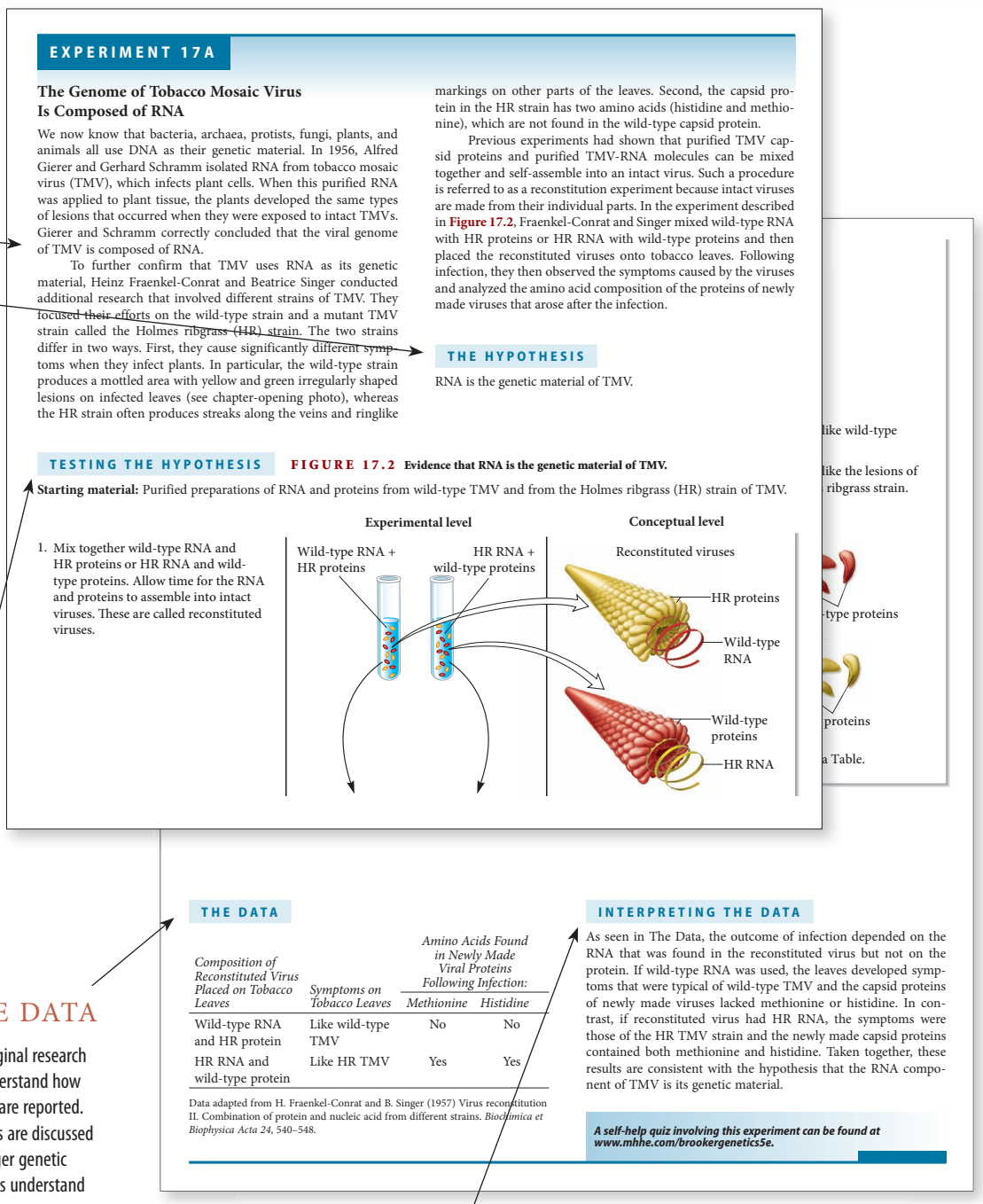
This section illustrates the experimental process, including the actual steps followed by scientists to test their hypothesis. Science comes alive for students with this detailed look at experimentation.

STEP 4: THE DATA

Actual data from the original research paper help students understand how real-life 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.

STEP 5: INTERPRETING THE DATA

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



EXPERIMENT 17A

The Genome of Tobacco Mosaic Virus Is Composed of RNA

We now know that bacteria, archaea, protists, fungi, plants, and animals all use DNA as their genetic material. In 1956, Alfred Gierer and Gerhard Schramm isolated RNA from tobacco mosaic virus (TMV), which infects plant cells. When this purified RNA was applied to plant tissue, the plants developed the same types of lesions that occurred when they were exposed to intact TMVs. Gierer and Schramm correctly concluded that the viral genome of TMV is composed of RNA.

To further confirm that TMV uses RNA as its genetic material, Heinz Fraenkel-Conrat and Beatrice Singer conducted additional research that involved different strains of TMV. They focused their efforts on the wild-type strain and a mutant TMV strain called the Holmes ribgrass (HR) strain. The two strains differ in two ways. First, they cause significantly different symptoms when they infect plants. In particular, the wild-type strain produces a mottled area with yellow and green irregularly shaped lesions on infected leaves (see chapter-opening photo), whereas the HR strain often produces streaks along the veins and ringlike markings on other parts of the leaves. Second, the capsid protein in the HR strain has two amino acids (histidine and methionine), which are not found in the wild-type capsid protein.

Previous experiments had shown that purified TMV capsid proteins and purified TMV-RNA molecules can be mixed together and self-assemble into an intact virus. Such a procedure is referred to as a reconstitution experiment because intact viruses are made from their individual parts. In the experiment described in **Figure 17.2**, Fraenkel-Conrat and Singer mixed wild-type RNA with HR proteins or HR RNA with wild-type proteins and then placed the reconstituted viruses onto tobacco leaves. Following infection, they then observed the symptoms caused by the viruses and analyzed the amino acid composition of the proteins of newly made viruses that arose after the infection.

THE HYPOTHESIS

RNA is the genetic material of TMV.

TESTING THE HYPOTHESIS **FIGURE 17.2** **Evidence that RNA is the genetic material of TMV.**

Starting material: Purified preparations of RNA and proteins from wild-type TMV and from the Holmes ribgrass (HR) strain of TMV.

1. Mix together wild-type RNA and HR proteins or HR RNA and wild-type proteins. Allow time for the RNA and proteins to assemble into intact viruses. These are called reconstituted viruses.

THE DATA

Composition of Reconstituted Virus Placed on Tobacco Leaves	*Symptoms on Tobacco Leaves*	*Amino Acids Found in Newly Made Viral Proteins Following Infection:*	
		Methionine	*Histidine*
Wild-type RNA and HR protein	Like wild-type TMV	No	No
HR RNA and wild-type protein	Like HR TMV	Yes	Yes

Data adapted from H. Fraenkel-Conrat and B. Singer (1957) Virus reconstitution II. Combination of protein and nucleic acid from different strains. *Biochimica et Biophysica Acta 24*, 540–548.

INTERPRETING THE DATA

As seen in The Data, the outcome of infection depended on the RNA that was found in the reconstituted virus but not on the protein. If wild-type RNA was used, the leaves developed symptoms that were typical of wild-type TMV and the capsid proteins of newly made viruses lacked methionine or histidine. In contrast, if reconstituted virus had HR RNA, the symptoms were those of the HR TMV strain and the newly made capsid proteins contained both methionine and histidine. Taken together, these results are consistent with the hypothesis that the RNA component of TMV is its genetic material.

A self-help quiz involving this experiment can be found at www.mhhe.com/brookergenetics5e.

Formative Assessment Throughout Each Chapter

Formative assessment provides a means for students to gauge their learning. Genetics: Analysis & Principles, *5e, has incorporated three new pedagogical features that should help students navigate this textbook.*

LEARNING OUTCOMES

Each section begins with one or more Learning Outcomes. These allow a student to appreciate the skills and knowledge they will gain if they master the material.

17.4 HIV REPRODUCTIVE CYCLE

Learning Outcomes:

1. Outline the organization of the HIV genome.
2. Explain how HIV is reverse transcribed and integrated into the DNA of its host cell.
3. Describe the steps that lead to the formation of new HIV particles.

In the previous section, we focused on the reproductive cycles of phage λ, which infects bacteria. In this section, we will focus on HIV, which infects helper T cells found in humans. T cells are a type of lymphocyte that play a key role in cell-mediated immunity. T cells are distinguished from other lymphocytes by the presence of T-cell receptors in their plasma membrane. T-cell receptors are responsible for recognizing antigens—molecules that elicit an immune response. The activation of T cells to fight

cellular digestion by nucleases. The p6 protein facilitates the incorporation of certain proteins, such as Vpr (described later), into HIV particles.

- ***pol:* Enzymes Needed for Viral Replication and Viral Assembly.** The *pol* gene encodes a polyprotein that is cleaved into three enzymes: HIV protease, reverse transcriptase, and integrase. The HIV protease processes proteins made from the HIV genome so they can assemble into mature HIV particles. Reverse transcriptase is required for the production of DNA from the RNA genome of HIV. A portion of reverse transcriptase called RNase H digests RNA during reverse transcription. Integrase is used to incorporate this DNA into the host genome.
- ***vif, vpu:* Proteins That Promote Infectivity and Budding.** The Vif protein is incorporated into mature HIV particles and promotes infectivity by interacting with host-cell proteins. The Vpu protein promotes budding.
- ***vpr, rev, tat, nef:* Proteins with Regulatory Functions.** The Vpr protein has several functions including the transport of the HIV genome into the cell nucleus. The

protein is able to form a capsid structure that encloses two molecules of HIV RNA along with several different proteins (see Figure 17.11b). The nucleocapsid and p6 proteins are found inside the capsid. They protect the HIV RNA from nuclease digestion and have binding sites that promote the incorporation of other proteins into the capsid. For example, p6 has binding sites for Vpr.

As mentioned earlier, another polyprotein called the Gag-pol polyprotein plays a role in the maturation process, but is made in much lesser amounts than Gag polyprotein. As shown in Figure 17.15, a few copies of the Gag-pol polyprotein are incorporated into immature virus particles. When the Gag-pol polyprotein is cleaved by HIV protease, this releases more HIV protease, along with reverse transcriptase, and integrase. These proteins become captured within the capsid. As described in Figures 17.12 and 17.13, they are necessary for the reverse transcription and integration of the HIV genome in a newly infected host cell.

17.4 COMPREHENSION QUESTIONS

1. A viral protein that is needed to make HIV DNA is
   a. integrase. c. Vpr.
   b. reverse transcriptase. d. Gag polyprotein.
2. Which form of HIV RNA is packaged into HIV particles?
   a. Fully spliced c. Unspliced
   b. Incompletely spliced d. All of the above
3. After HIV components are made, what is the correct order of the stages that are needed to produce HIV particles?
   a. Maturation, budding, assembly
   b. Maturation, assembly, budding
   c. Assembly, budding, maturation
   d. Assembly, maturation, budding

COMPREHENSION QUESTIONS

Each section of every chapter ends with questions that help a student determine if they have learned the material and are ready to move on to the next section.

CONCEPT CHECK QUESTIONS

These are found within figure legends and help students determine their understanding of key points in the figure.

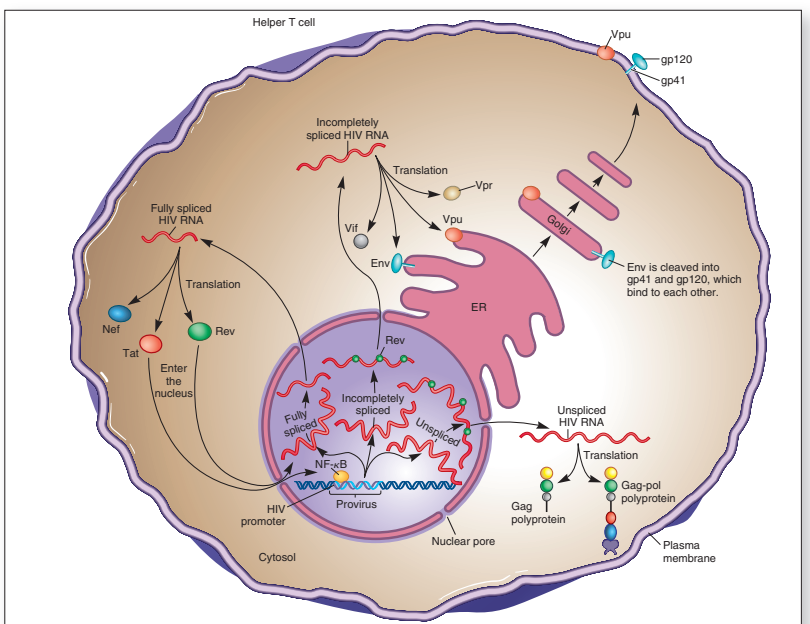


FIGURE 17.14 **Synthesis of new HIV components: HIV RNA and proteins.**

CONCEPT CHECK: Which form of HIV RNA, fully spliced, incompletely spiced, or unspliced, is needed during the early stage of synthesizing HIV components?

End-of-Chapter Support Materials

These study tools and problems are crafted to aid students in reviewing key information in the text and developing a wide range of problem-solving skills. They also develop a student's cognitive, writing, analytical, computational, and collaborative abilities.

KEY TERMS

Enhance student development of vital vocabulary necessary for the understanding and application of chapter content. Important terms are boldfaced throughout the chapter and page referenced at the end of each chapter for reflective study.

KEY TERMS

Page 393. epigenetics, epigenetic inheritance, transgenerational epigenetic inheritance, DNA methylation, chromatin remodeling, covalent histone modification, histone variants, feedback loops, noncoding RNAs
Page 394. *cis*-epigenetic mechanism, *trans*-epigenetic mechanism
Page 397. development, imprinting control region (ICR), differentially methylated region (DMR), de novo methylation
Page 398. maintenance methylation, X-chromosome inactivation (XCI), pluripotency factors, symmetry break
Page 400. trithorax group (TrxG), polycomb group (PcG), trimethylation, polycomb response element (PRE)
Page 404. oncogene
Page 405. alternative splicing
Page 406. constitutive exons, alternative exons, splicing factors, SR proteins, exon skipping
Page 407. polyA-binding protein, 3′-untranslated region (3′-UTR), AU-rich element (ARE)
Page 409. RNA interference (RNAi)
Page 410. microRNAs (miRNAs), short-interfering RNAs (siRNAs), RNA-induced silencing complex (RISC), processing body (P-body), iron regulatory protein (IRP), iron response element (IRE)

CHAPTER SUMMARY

Emphasizes the main concepts from each section of the chapter in a bulleted list form to provide students with a thorough review of the main topics covered.

CHAPTER SUMMARY

16.1 Overview of Epigenetics

- Epigenetics can be defined as the study of mechanisms that lead to changes in gene expression that are passed from cell to cell and are reversible but do not involve a change in the sequence of DNA. The transmission of epigenetic changes from one generation to the next is referred to as epigenetic inheritance.
- The most common types of molecular changes that underlie epigenetic control are DNA methylation, chromatin remodeling, covalent histone modification, the localization of histone variants, and feedback loops (see Table 16.1).
- Epigenetic changes can be established by transcription factors or noncoding RNAs (see Figure 16.1).
- Epigenetic changes may be maintained by *cis*- or *trans*-epigenetic mechanisms (see Figures 16.2, 16.3).
- Some epigenetic changes are programmed during development and others are caused by environmental agents (see Table 16.2).

PROBLEM SETS & INSIGHTS

Enhance student development

1. **Solved Problems:** Walk the student through the solutions of quantitative problems or provide explanations for the answers to more conceptual based questions.

PROBLEM SETS & INSIGHTS

Solved Problems

S1. Are the following examples best explained by genetic and/or epigenetic phenomena?

A. imprinting of the *Igf2* gene

B. variation in coat color in mice carrying the A^{vy} allele

C. formation of cancer cells

D. variation in flower color between different strains of pea plants, such as purple versus white

attached to DNA sites. After binding, the noncoding RNA can act as a bridge to attract other proteins to the site that cause epigenetic modifications, such as DNA methylation and covalent histone modifications.

S3. Prior to X-chromosome inactivation, what prevents the expression of the *Xist* gene?

Answer: Prior to X-chromosome inactivation, pluripotency factors promote the expression of the *Tsix* gene. The expression of the *Tsix* gene inhibits the expression of the *Xist* gene.

2. **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. Define epigenetics. Are all epigenetic changes passed from parent to offspring? Explain.

C2. List and briefly describe five types of molecular events that may underlie epigenetic gene regulation.

C3. Explain how epigenetic changes may be targeted to specific genes.

C4. What is the key difference between a *cis*- and *trans*-epigenetic mechanism that maintains an epigenetic modification? In Chapter 5, we considered genomic imprinting of the *Igf2* gene in which offspring express the copy of the gene they inherit from their father, but not the copy they inherit from their mother. Is this a *cis*- or *trans*-epigenetic mechanism?

C13. With regard to development, what would be the dire consequences if polycomb group complexes did not function properly?

C14. Using coat color in mice and the development of female honeybees as examples, how can dietary factors cause epigenetic modifications, leading to phenotypic effects?

C15. How can environmental agents that do not cause gene mutations contribute to cancer? Would these epigenetic changes be passed to offspring?

C16. Define alternative splicing. What are advantages and disadvantages of this process?

3. **Experimental Questions:** Test the ability to analyze data, design experiments, or appreciate the relevance of experimental techniques.

Experimental Questions

E1. A gene, which we will call gene *C*, can be epigenetically modified in such a way that its expression in some cells is permanently silenced. Describe how you could conduct cell fusion experiments to determine if a *cis*- or *trans*-epigenetic mechanism is responsible for maintaining the silencing of gene *C*.

E2. In the experiments described in Figure 16.7, explain the relationship between coat color and DNA methylation. How is coat color related to the diet of the mother?

E3. 5-Azocytidine is an inhibitor of DNA methyltransferase. If it were fed to female mice during pregnancy, explain how you think it would affect the coat color of offspring carrying the A^{vy} allele.

E4. A research study indicated that an agent in cigarette smoke caused the silencing of a tumor suppressor gene called *p53*. However, upon sequencing, no mutation was found in the DNA sequence for this gene. Give two possible explanations for these results.

E8. Chapter 20 describes a blotting method known as Northern blotting, in which a short segment of cloned DNA is used as a probe to detect RNA that is transcribed from a particular gene. The DNA probe, which is labeled, is complementary to the RNA that the researcher wishes to detect. After the probe DNA binds to the RNA within a blot of a gel, the RNA is visualized as a dark band. The method of Northern blotting can be used to determine the amount of a particular RNA transcribed in a given cell type. If one type of cell produces twice as much of a particular mRNA as another cell, the band appears twice as intense.

For this question, a researcher has a DNA probe complementary to the ferritin mRNA. This probe can be used to specifically detect the amount of ferritin mRNA on a gel. A researcher began with two flasks of human skin cells. One flask contained a very low concentration of iron, and the other flask had a high concentration of iron. The mRNA was isolated from these cells and then subjected

4. **Student Discussion/Collaboration 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. Go to the PubMed website and search words such as *epigenetic* and *cancer*. Scan through the journal articles you retrieve and make a list of environmental agents that may cause epigenetic changes that contribute to cancer.
2. Discuss the similarities and differences of phenotypic variation that are caused by epigenetic gene regulation versus variation in gene sequences (epigenetics versus genetics).
3. How are regulatory transcription factors (described in Chapter 15) and regulatory splicing factors (described in this chapter) similar in their mechanism of action? In your discussion, consider the domain structures of both types of proteins. How are they different?

Note: All answers appear at the website for this textbook; the answers to the even-numbered questions and all of the Concept Check and Comprehension Questions are in the back of the book.

CHAPTER OUTLINE

Carbon copy, the first cloned pet. *In 2002, the cat shown here, named Carbon copy (also called Copycat), was produced by cloning, a procedure described in Chapter 21.*

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, scientists from around the world 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) of over 90% of the human genome. The first draft of this sequence, published in 2001, showed that the human genome is approximately 3 billion nucleotide base pairs (bp) in length. The completed sequence, published in 2003, has an accuracy greater than 99.99%; less 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 Human Genome 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 treatments for them.

The journey to unravel the mysteries within our genes has involved the invention of many new technologies. For example, researchers have developed genetic techniques to produce medicines, such as human insulin, that would otherwise be difficult or impossible to make. Human insulin is synthesized in strains of *Escherichia coli* bacteria that have been genetically altered by the addition of genes that encode the polypeptides that form this hormone. The bacteria are grown in a laboratory and make large amounts of human insulin. As discussed in Chapter 19, the insulin is purified and administered to many people with insulin-dependent diabetes.

New genetic technologies are often met with skepticism and sometimes even with disdain. An example is DNA fingerprinting, a molecular method to identify an individual based on a DNA sample (see Chapter 26). 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.

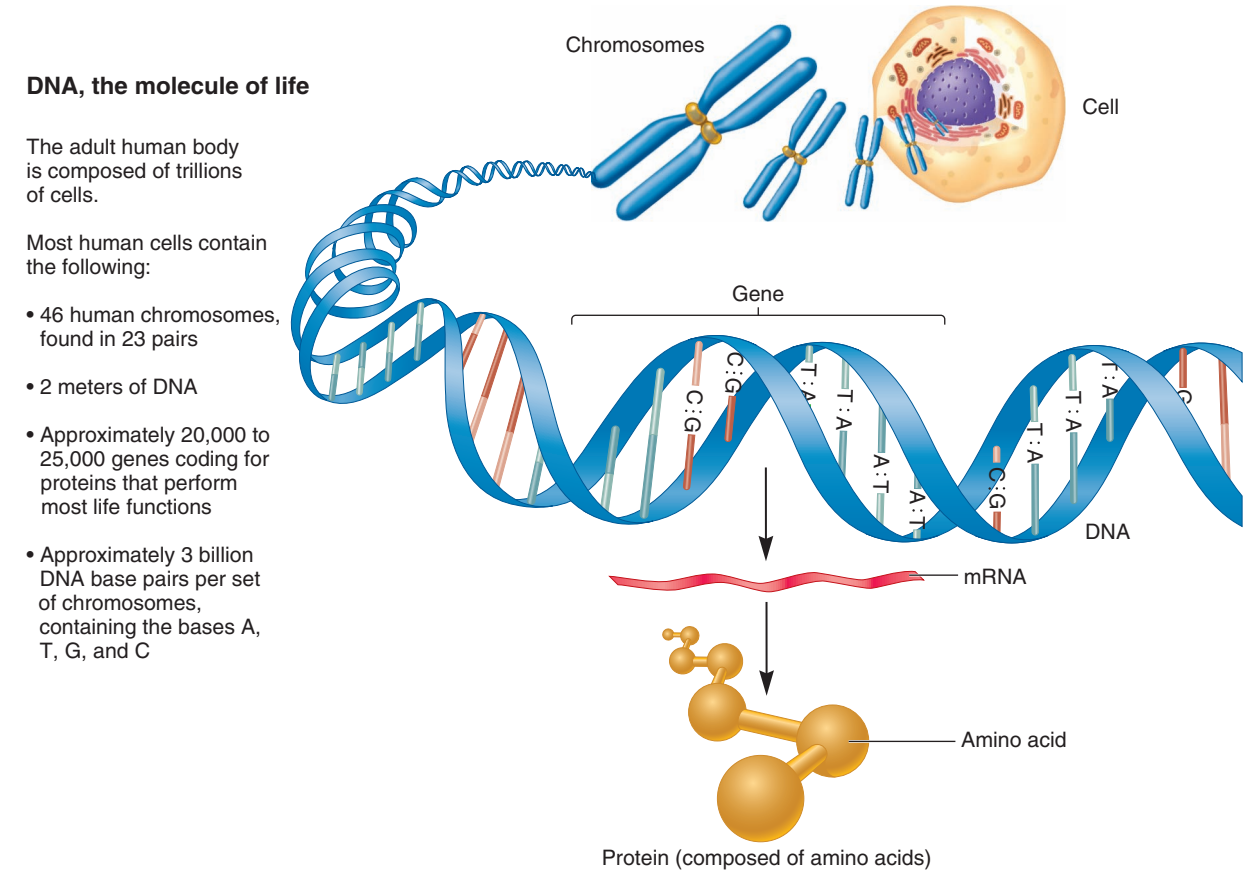


FIGURE 1.1 The human genome. The human genome is a complete set of human chromosomes. People have two sets of chromosomes—one from each parent—which are found in the cell nucleus. The Human Genome Project revealed that each set of chromosomes is composed of a DNA sequence that is approximately 3 billion nucleotide base pairs long. Estimates suggest that each set contains about 22,000 different genes. Most genes encode proteins. As discussed later, such genes are first transcribed into mRNA and then the mRNA is used to make proteins. 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.

CONCEPT CHECK: How might a better understanding of our genes be used in the field of medicine?

A second controversial example is 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 cows, mice, goats, pigs, and cats. In 2002, the first pet was cloned, a cat named Carbon copy, also known as 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, legislation has been introduced that involves 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 striking example in which scientists introduced a gene from jellyfish into mice. Certain species of jellyfish emit a "green glow" produced by 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 green fluorescent 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.

The expression of green fluorescent protein allows researchers to identify particular proteins in cells or specific body parts. For example, Andrea Crisanti and colleagues have altered mosquitoes to express GFP only in the gonads of males (**Figure 1.3b**). This

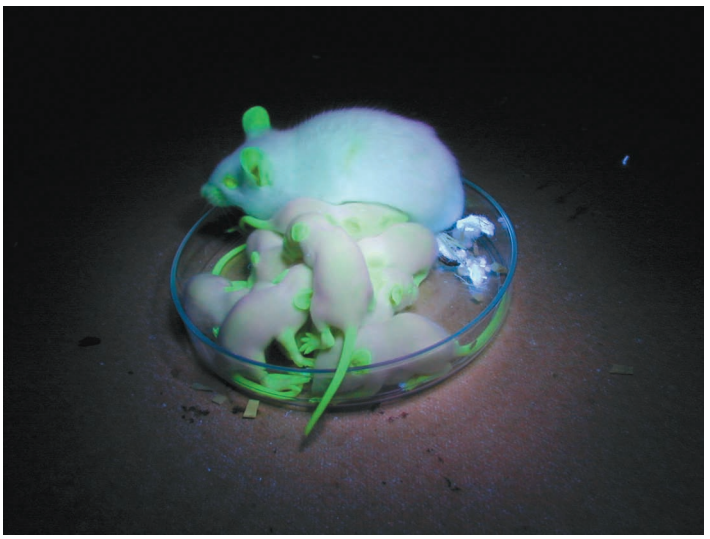
FIGURE 1.2 The cloning of a mammal. The lamb on the left is Dolly, the first mammal to be cloned. She was cloned from the cells of a Finn Dorset (a white-faced sheep). The sheep on the right is Dolly's surrogate mother, a Blackface ewe. A description of how Dolly was produced is presented in Chapter 21.

Photo courtesy of The Roslin Institute, The University of Edinburgh

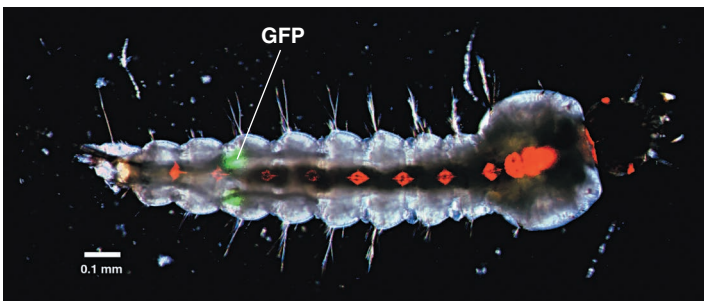
CONCEPT CHECK: What ethical issues may be associated with human cloning?

enables the researchers to identify and sort males from females. Why is this useful? Researchers can produce a population of mosquitoes and then sterilize the males. The ability to rapidly sort males and females makes it possible to release the sterile males without the risk of releasing additional females. The release of sterile males may be an effective means of controlling mosquito populations because females mate only once before they die. Mating with a sterile male prevents a female from producing offspring. In 2008, Osamu Shimomura, Martin Chalfie, and Roger Tsien received the Nobel Prize in chemistry for the discovery and the development of GFP, which has become a widely used tool in biology.

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 begin with an overview of genetics and then explore the various fields of genetics and their experimental approaches.



(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 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 the jellyfish! **(b)** The *GFP* gene 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.

CONCEPT CHECK: Why is it useful to sort male from female mosquitoes?

1.1 THE MOLECULAR EXPRESSION OF GENES

Learning Outcomes:

1. Describe the biochemical composition of cells.
2. Explain how proteins are largely responsible for cell structure and function.
3. Outline how DNA stores the information to make proteins.

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. 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 traits.

In this section of Chapter 1, we 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 an overview of topics they have 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 28.

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 breaking 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. RNA, proteins, 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 chromosomes (**Figure 1.4**). In addition, DNA is associated with many 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 double membrane composed of lipids and proteins that shields the chromosomes from the rest of the cell. The

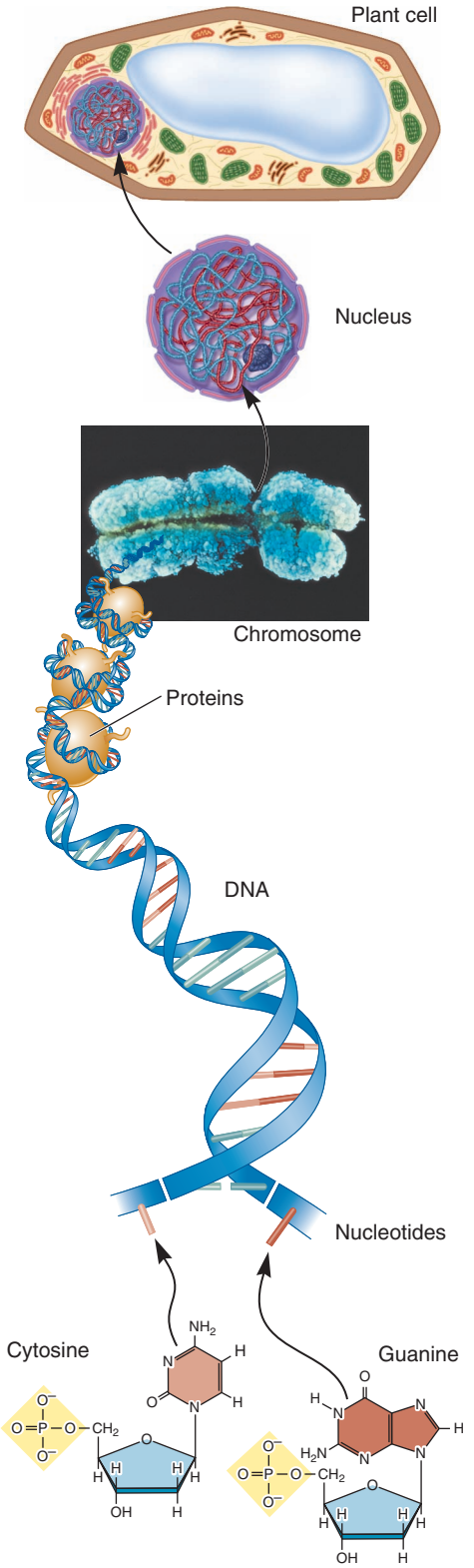


FIGURE 1.4 Molecular organization of a living cell. Cellular structures are constructed from smaller building blocks. In this example, DNA is formed from the linkage of nucleotides to produce a very long macromolecule. The DNA associates with proteins to form a chromosome. The chromosomes are located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

CONCEPT CHECK: Is DNA a small molecule, a macromolecule, or an organelle?

organization of chromosomes within a cell nucleus protects the chromosomes from mechanical damage 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 Cell Structure and Function

To a great extent, the characteristics of a cell depend on the types of proteins that it makes. All of the proteins that a cell makes at a given time is called its **proteome.** 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 assembles 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. **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 of living organisms 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 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 complex eukaryotic species range in the tens of thousands.

DNA's ability to store information is based on its structure. DNA is composed of a linear sequence of **nucleotides.** Each nucleotide contains one of four nitrogen-containing bases: 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 micrograph of the 46 chromosomes contained in a cell from a human male, otherwise known as a karyotype. The DNA of an average human

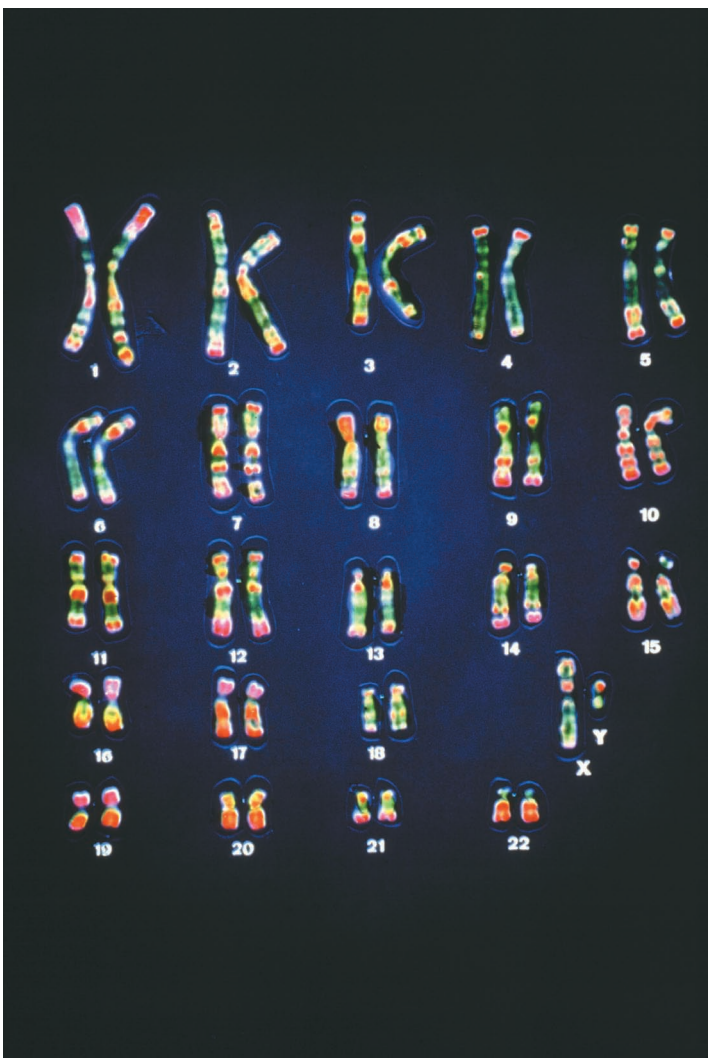


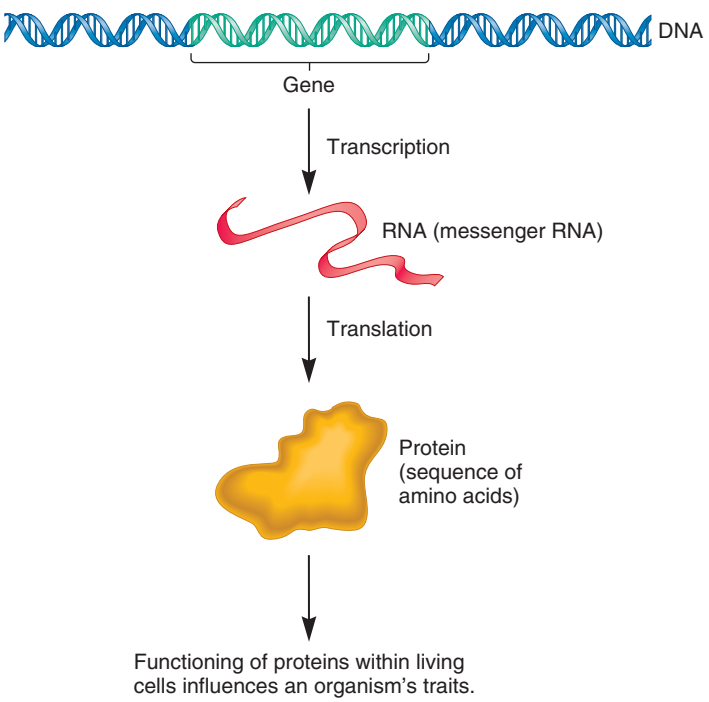
FIGURE 1.5 **A micrograph of the 46 chromosomes found in a cell from a human male.**

CONCEPT CHECK: Which types of macromolecules are found in chromosomes?

chromosome is an extraordinarily long, linear, double-stranded structure that contains well over a hundred 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 1000 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 (**Figure 1.6**). In the first step, known as **transcription,** the DNA sequence within a gene is copied into a nucleotide sequence of **ribonucleic acid (RNA). Protein-encoding genes** (also called **structural genes**) carry the information for the amino acid sequence of a polypeptide. When a protein-encoding gene is transcribed, the first product is an RNA molecule known as **messenger RNA (mRNA).** During polypeptide synthesis—a process called **translation**—the sequence of nucleotides within the mRNA determines the sequence of amino acids in a polypeptide. One or more polypeptides then fold and assemble into a functional protein. The synthesis of functional proteins ultimately determines an organism's traits. As discussed further in Chapter 12 (look ahead to Figure 12.1), the pathway of gene expression from DNA to RNA to protein is called the **central dogma of genetics** (also called the central dogma of molecular biology). It forms a cornerstone of our understanding of genetics at the molecular level.



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.

CONCEPT CHECK: Where is the information to make a polypeptide stored?

1.1 COMPREHENSION QUESTIONS

1. Which of the following is not a constituent of a cell's proteome?
   a. An enzyme
   b. A cytoskeletal protein
   c. A transport protein in the plasma membrane
   d. An mRNA
2. A gene is a segment of DNA that has the information to produce a functional product. The functional product of most genes is
   a. DNA. c. a polypeptide.
   b. mRNA. d. all of the above.
3. The function of the genetic code is to
   a. promote transcription.
   b. specify the amino acids within a polypeptide.
   c. alter the sequence of DNA.
   d. none of the above.
4. The process of transcription directly results in the synthesis of
   a. DNA. c. a polypeptide.
   b. RNA. d. all of the above.

1.2 THE RELATIONSHIP BETWEEN GENES AND TRAITS

Learning Outcomes:

1. Explain how the expression of genes leads to an organism's traits.
2. Define genetic variation.
3. Discuss the relationship between genes and traits.
4. Describe how genes are transmitted in sexually reproducing species.
5. Outline the process of evolution.

A trait is any characteristic that an organism displays. In genetics, we often focus our attention on **morphological traits** that affect the appearance, form, and structure 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 an organism responds to its environment. An example is the mating calls of bird species. In animals, the nervous system plays a key role in governing such traits. In this section, we will examine the relationship between the expression of genes and an organism's traits.

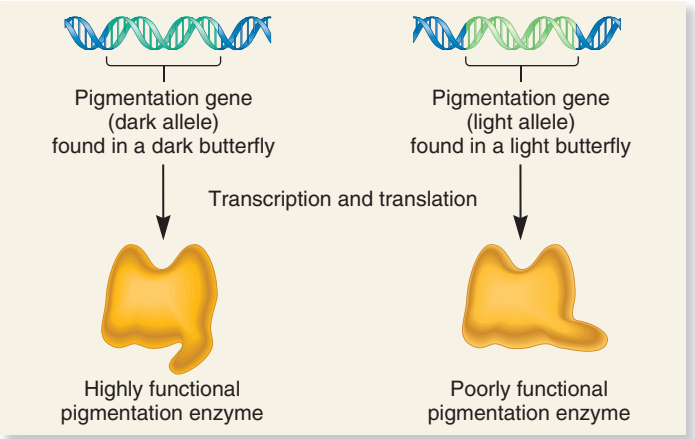
The Molecular Expression of Genes Leads to an Organism's Traits

A complicated, 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:

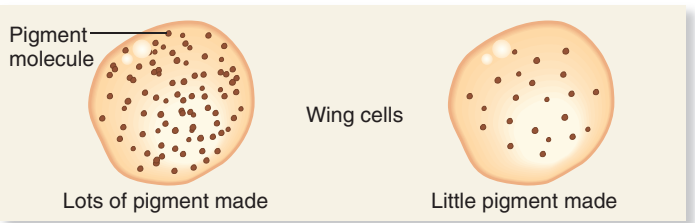
1. Genes are expressed at the **molecular level.** In other words, gene transcription and translation lead to the production of a particular protein, which is a molecular process.
2. Proteins often function at the **cellular level.** The function of a protein within a cell affects the structure and workings 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 dark-colored and the other is very light. 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 produced. The pigmentation gene exists in two different versions. Alternative versions of a specific gene are called **alleles.** In this example, one allele confers a dark pigmentation and the other causes a light pigmentation. Each of these alleles encodes a protein that functions as a pigment-synthesizing enzyme. However, the DNA sequences of

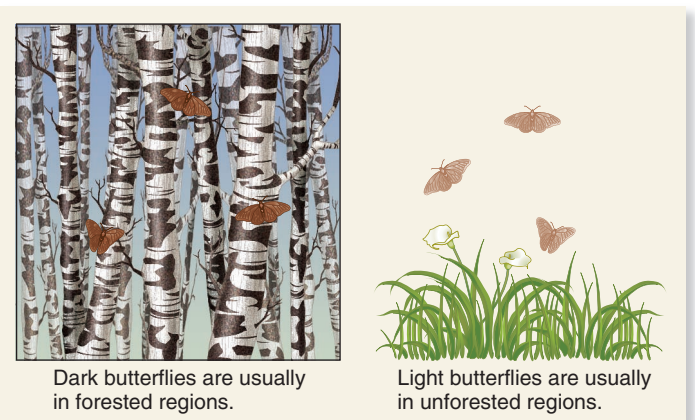


(a) Molecular level



(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.**

CONCEPT CHECK: Which butterfly has a more active pigment-producing enzyme, the dark- or light-colored one?

FIGURE 1.8 **Two dyeing poison frogs (*Dendrobates tinctorius*) showing different morphs within a single species.**

CONCEPT CHECK: Why do these two frogs look so different?

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 two pigmentation enzymes affect the amount of pigment 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 expressed, little pigment is made.

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 leads to variation in a trait of organisms, 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, and others have blond hair; some petunias have white flowers and some 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** shows two dyeing poison frogs that are members of the same species, *Dendrobates tinctorius.* 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 frogs 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 an organism's 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. When such changes initially occur, they are called **gene mutations.** Mutations result in genetic variation in which a gene is found in two or more alleles, as previously described in Figure 1.7. In many cases, gene mutations alter the expression or function of the protein that the gene encodes.
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 of sequences within 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 or number (or both)—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 leads to 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 determining an organism's 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

(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. Cultivated wheat is derived from the contributions of three wild species with two sets of chromosomes each, producing an organism with six sets of chromosomes.

CONCEPT CHECK: Do these examples constitute variation in chromosome structure or variation in chromosome number?

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.

An interesting example of the interplay between genes and the environment involves the human genetic disease **phenylketonuria (PKU).** Humans have 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 gene that encodes phenylalanine hydroxylase results in a nonfunctional version of this enzyme. Individuals with two copies of this rare, inactive allele cannot metabolize phenylalanine properly. 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. Individuals with PKU can manifest a variety of detrimental traits, including mental impairment, underdeveloped teeth, and foul-smelling urine. Fortunately, through routine newborn screening in the United States, PKU is now diagnosed early. Part of the treatment is a diet that restricts phenylalanine, which is present in high-protein foods such as eggs, meat, and dairy products. Restricting phenylalanine allows the affected child to develop normally. 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. How are traits passed from parents to offspring? The foundation for our understanding of inheritance came from Gregor Mendel's study of pea plants in the nineteenth century. His work revealed that the genetic determinants that govern traits, which we now call genes, are passed from parent to offspring as discrete units. We can predict the outcome of many 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 copies are called **homologs** 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 1.10a**). With the exception of the sex chromosomes (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, which 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 (23) and are termed **haploid** (**Figure 1.10b**). 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,** or simply, **evolution,** refers to the phenomenon that the genetic makeup of a population changes from one generation to the next.

As suggested by Charles Darwin, the members of a species are in competition with one another 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,