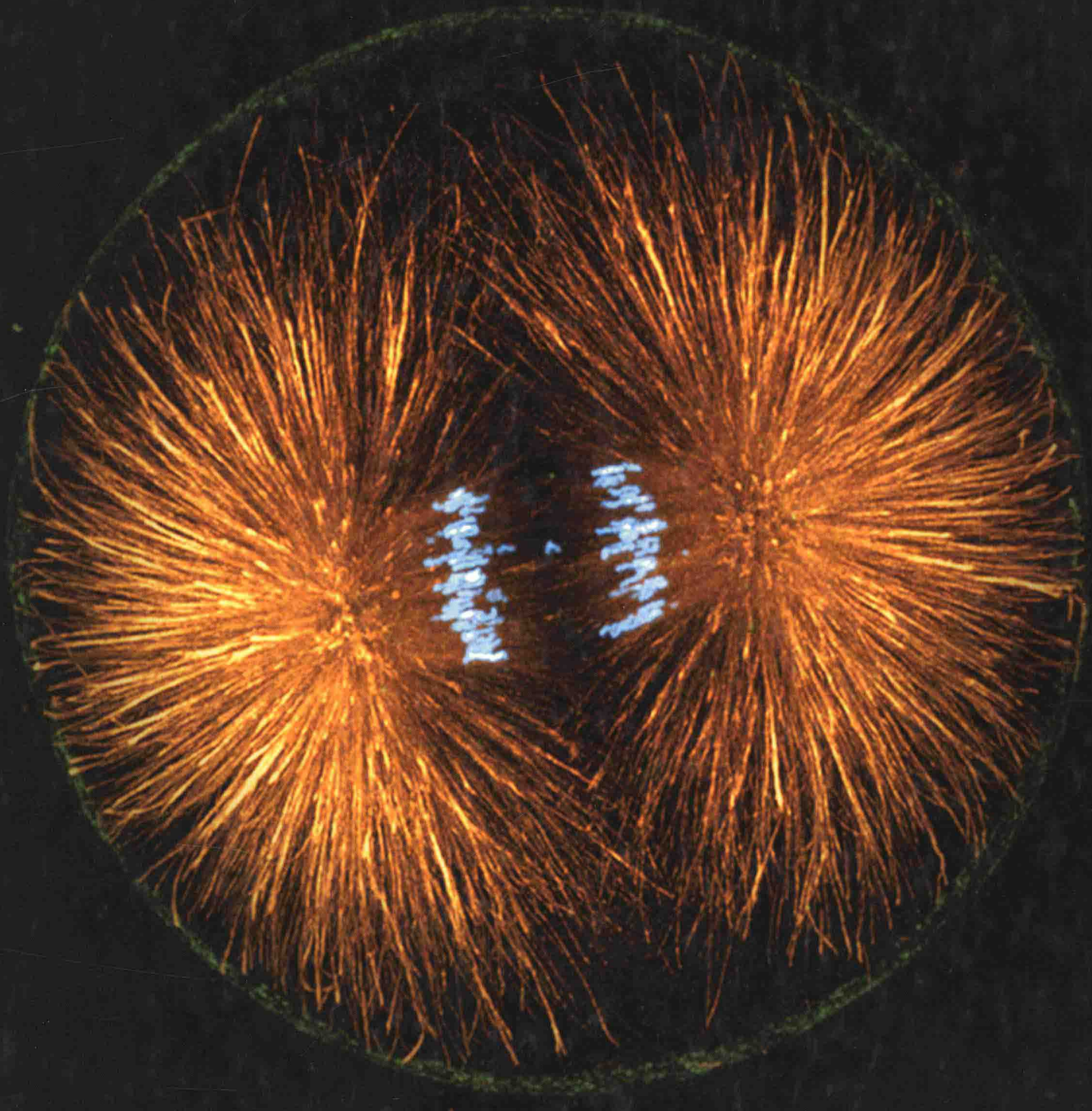
GENETICS 5E

ANALYSIS & PRINCIPLES



ROBERT J. BROOKER

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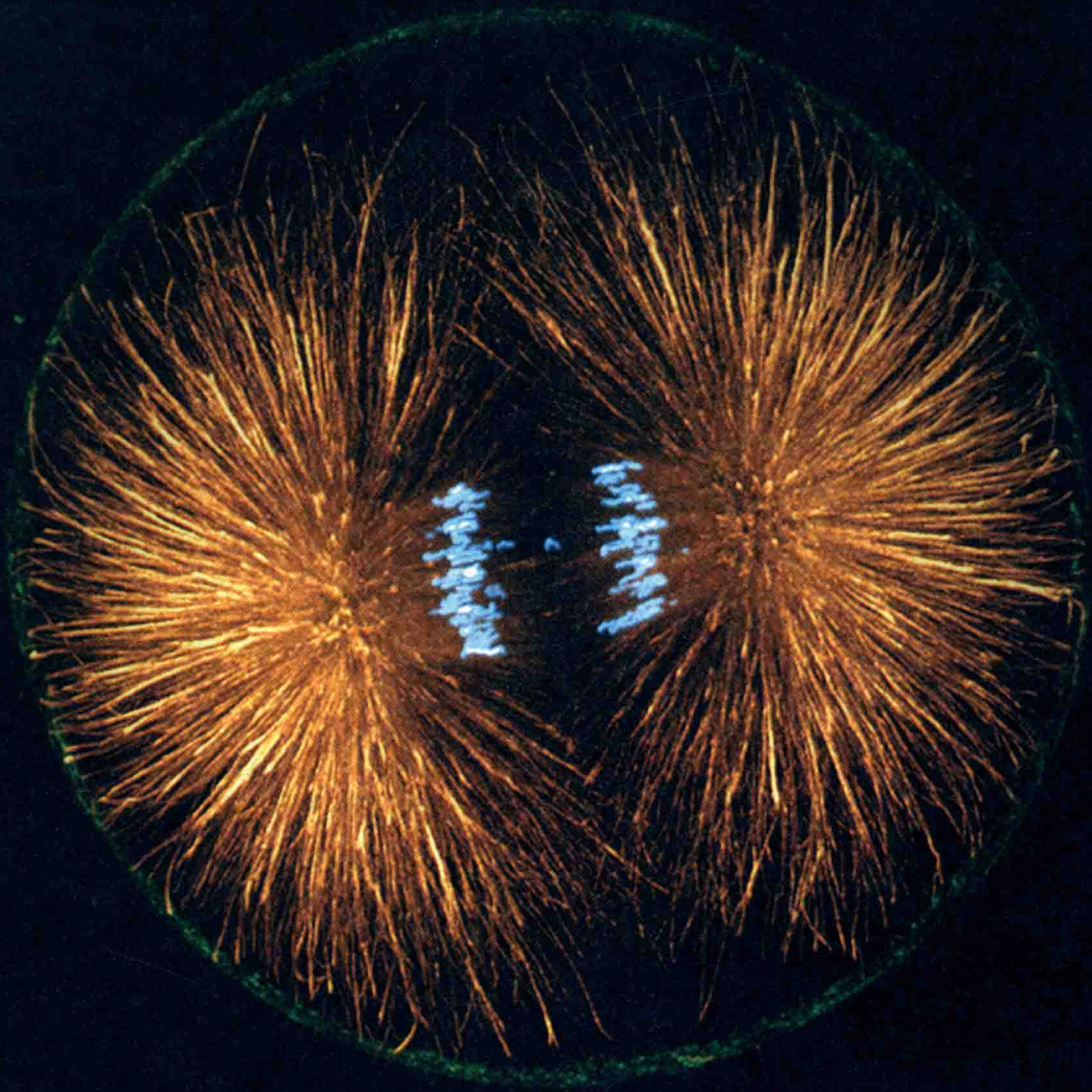

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Mc Graw Hill Education

GENETICS: ANALYSIS & PRINCIPLES, FIFTH EDITION

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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

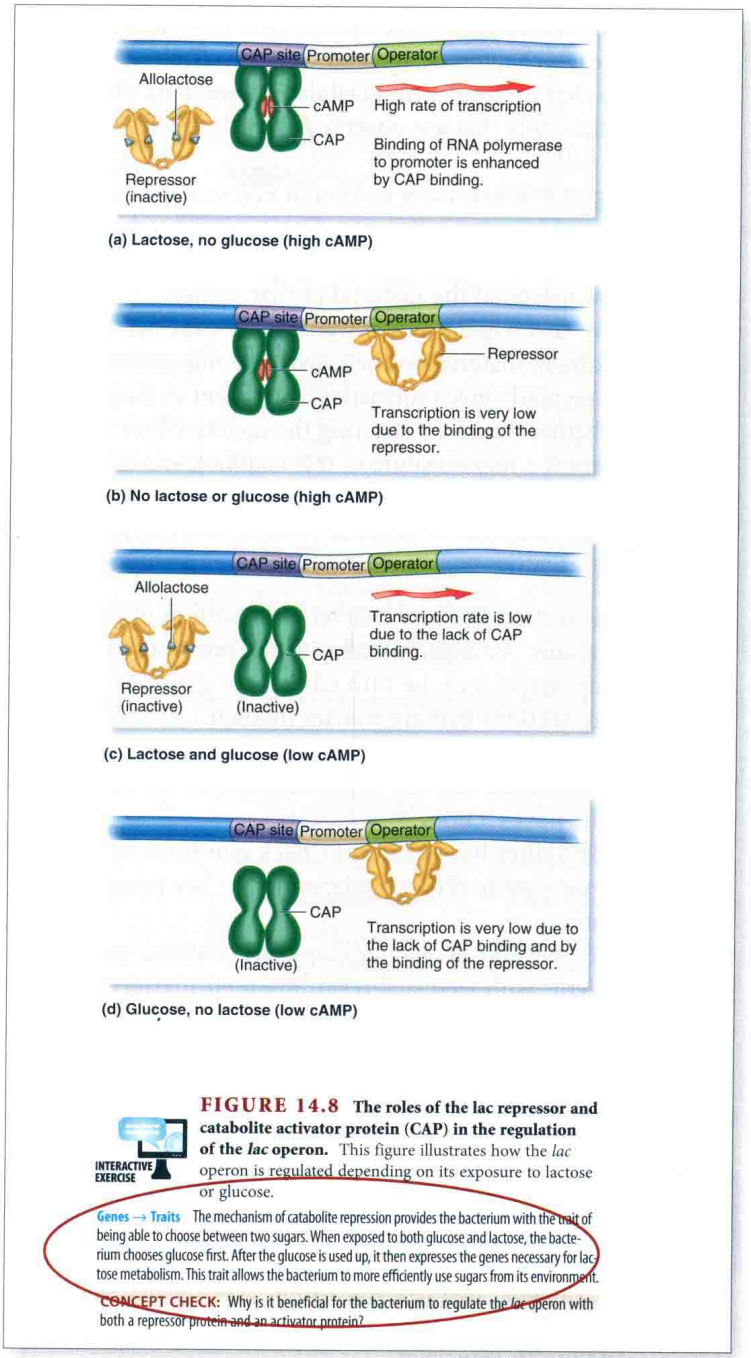


FIGURE 14.8 The roles of the lac repressor and catabolite activator protein (CAP) in the regulation of the *lac* operon. This figure illustrates how the *lac* operon is regulated depending on its exposure to lactose or glucose.

INTERACTIVE EXERCISE

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.

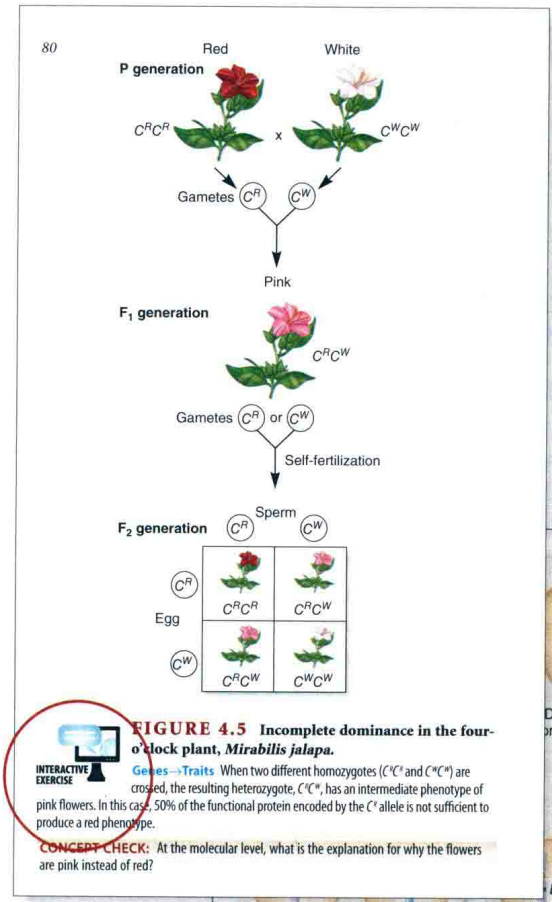
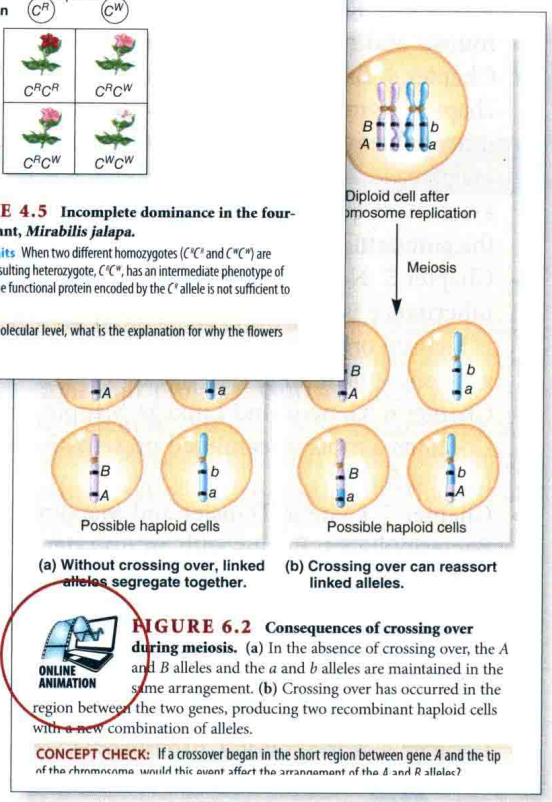


FIGURE 4.5 Incomplete dominance in the four-o'clock plant, *Mirabilis jalapa*.

INTERACTIVE EXERCISE

Genes→Traits When two different homozygotes (C^RC^R and C^WC^W) are crossed, the resulting heterozygote, C^RC^W, has an intermediate phenotype of pink flowers. In this case, 50% of the functional protein encoded by the C^R allele is not sufficient to produce a red phenotype.

CONCEPT CHECK: At the molecular level, what is the explanation for why the flowers are pink instead of red?



ONLINE ANIMATION

FIGURE 6.2 Consequences of crossing over during meiosis. **(a)** In the absence of crossing over, the *A* and *B* alleles and the *a* and *b* alleles are maintained in the same arrangement. **(b)** Crossing over has occurred in the region between the two genes, producing two recombinant haploid cells with a new combination of alleles.

CONCEPT CHECK: If a crossover began in the short region between gene *A* and the tip of the chromosome, would this event affect the arrangement of the *A* and *B* alleles?

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

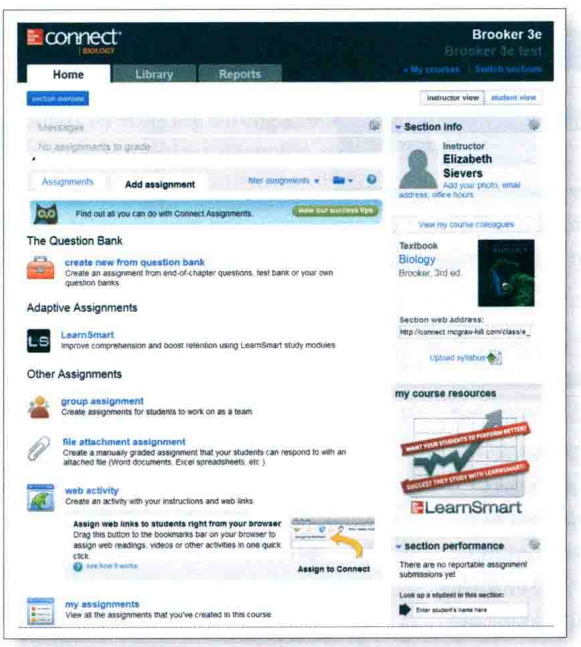
Digital resources can help you achieve your instructional goals—making your students more responsible for learning outside of class by meeting your students where they live: on the go and online. Use the text and digital tools to empower students to come to class more prepared and ready to engage!

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**.

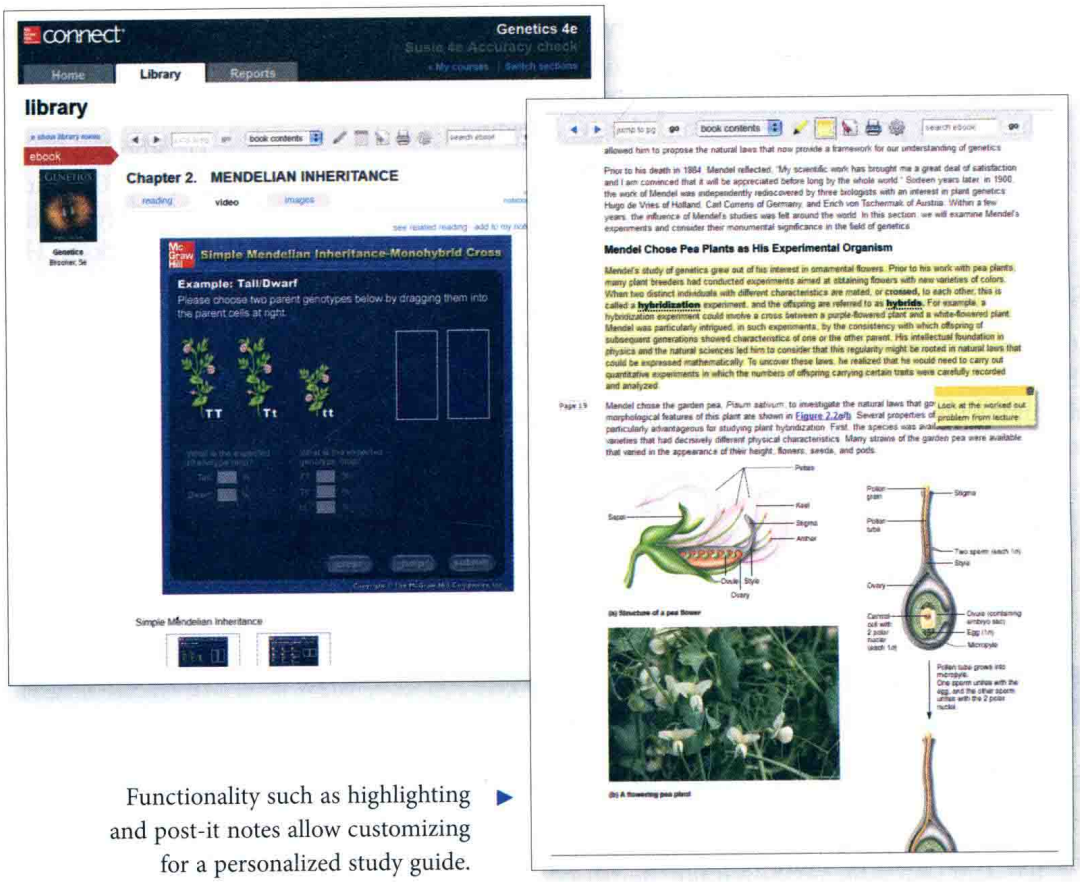
Help Your Students by Making Assignments—Reading, Homework, and LearnSmart

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. ▶

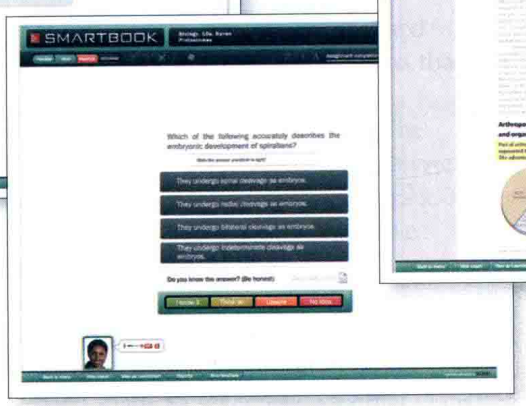


Functionality such as highlighting and post-it notes allow customizing for a personalized study guide. ▶

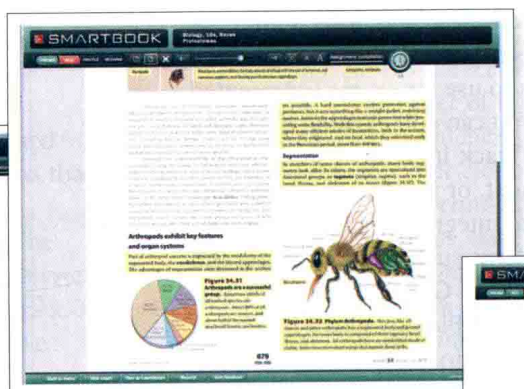
SMARTBOOK™

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.

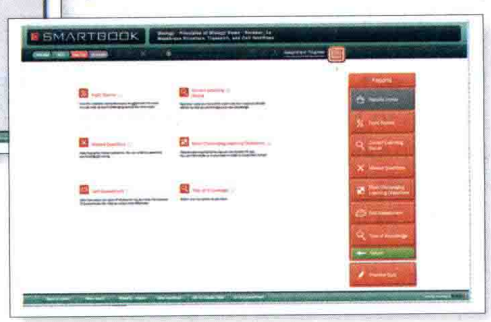
▲ The Smartbook experience starts by previewing key concepts from the chapter and ensuring that you understand the big ideas.



▲ 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.

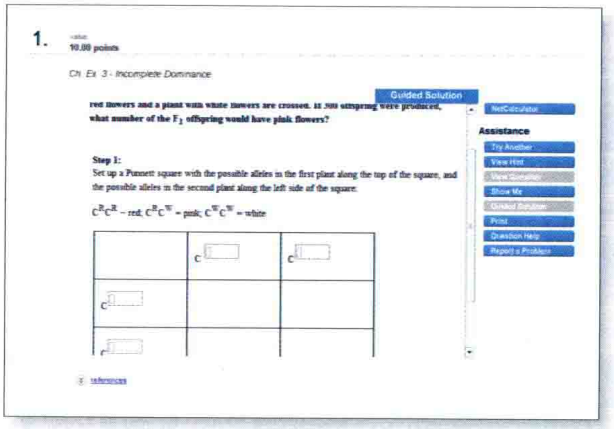


The reports in SmartBook help identify topics where you need more work. ▼



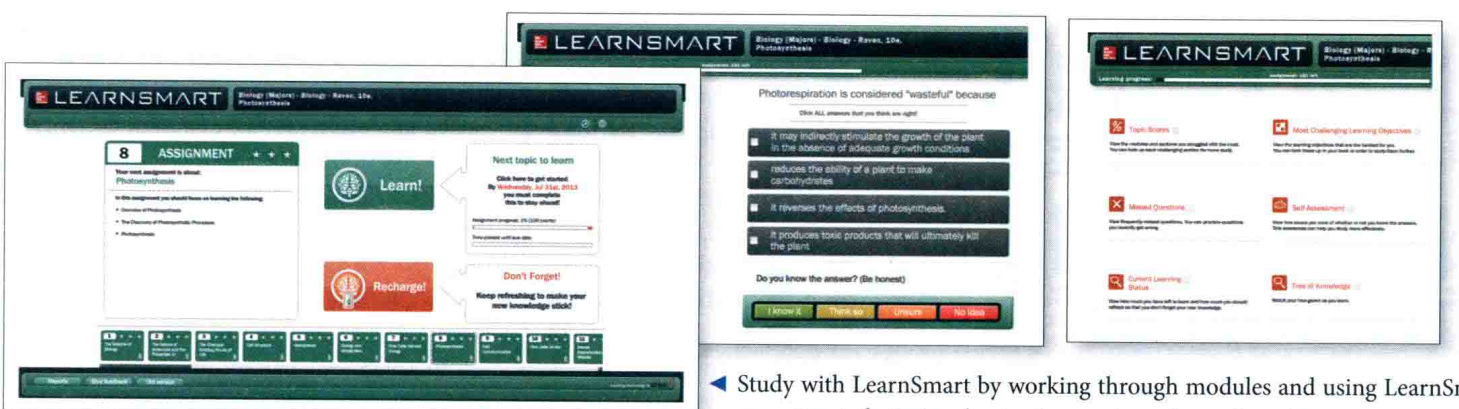
Help your students prepare for class and revisit content by assigning homework in Connect and LearnSmart.

▲ 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.

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

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

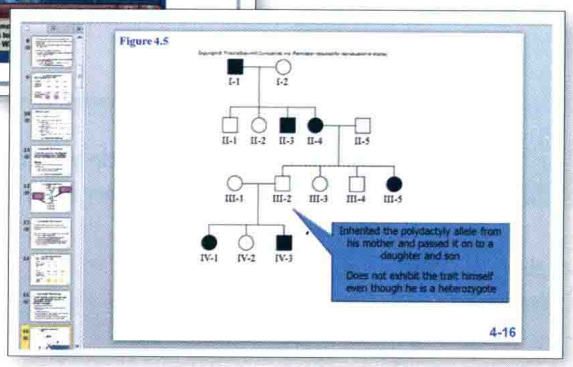
▲ Download the LearnSmart app from iTunes or Google Play and work on LearnSmart from anywhere!

◀ 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.

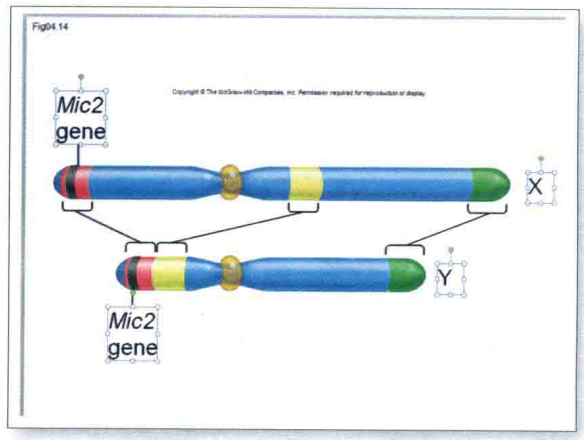
Presentation Tools

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

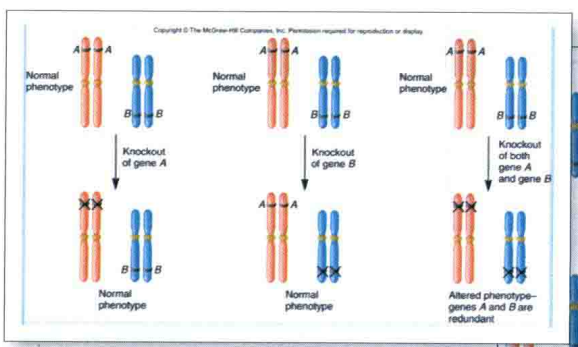
◀ Animation PowerPoints contain full-color animations illustrating important processes, which are fully embedded in PowerPoint slides for easy use in your presentations.

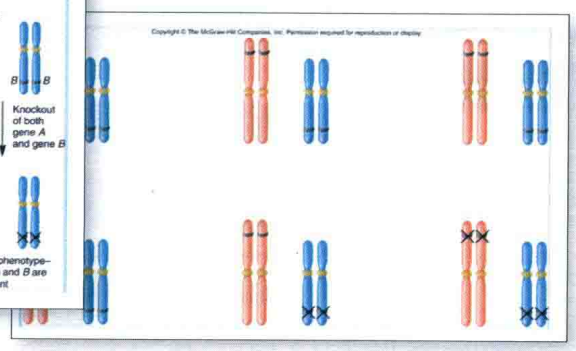


Lecture PowerPoints with animations fully embedded. ▶



▲ 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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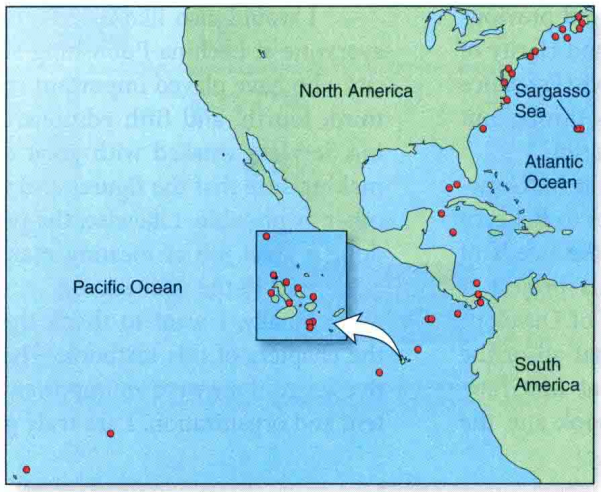
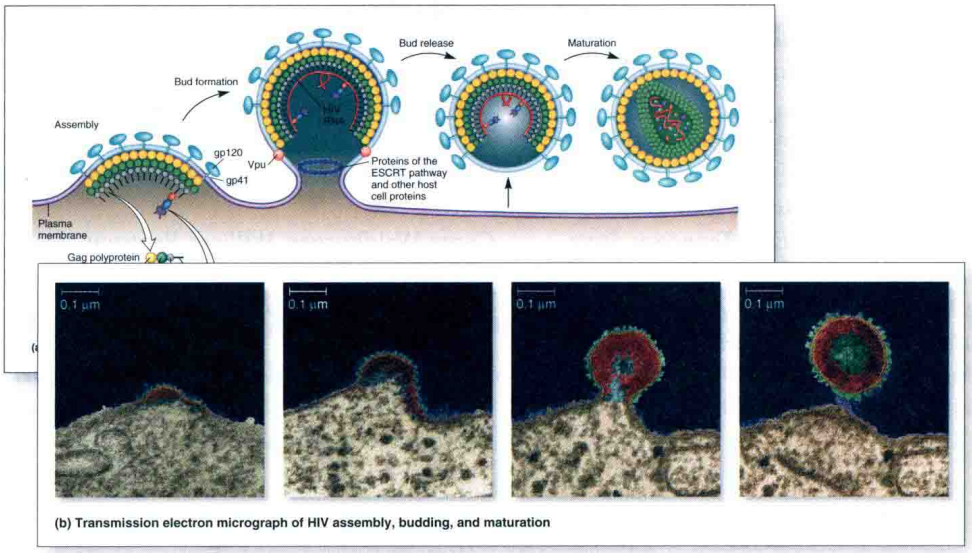
A Visual Guide to
GENETICS: ANALYSIS & PRINCIPLES

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.

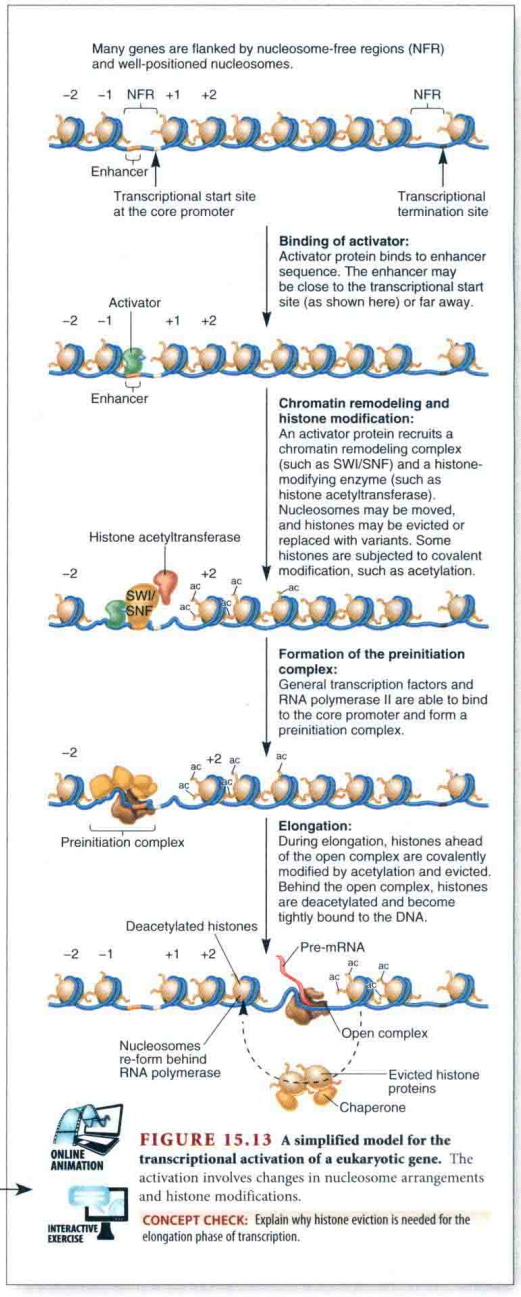


FIGURE 15.13 A simplified model for the transcriptional activation of a eukaryotic gene. The activation involves changes in nucleosome arrangements and histone modifications.

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

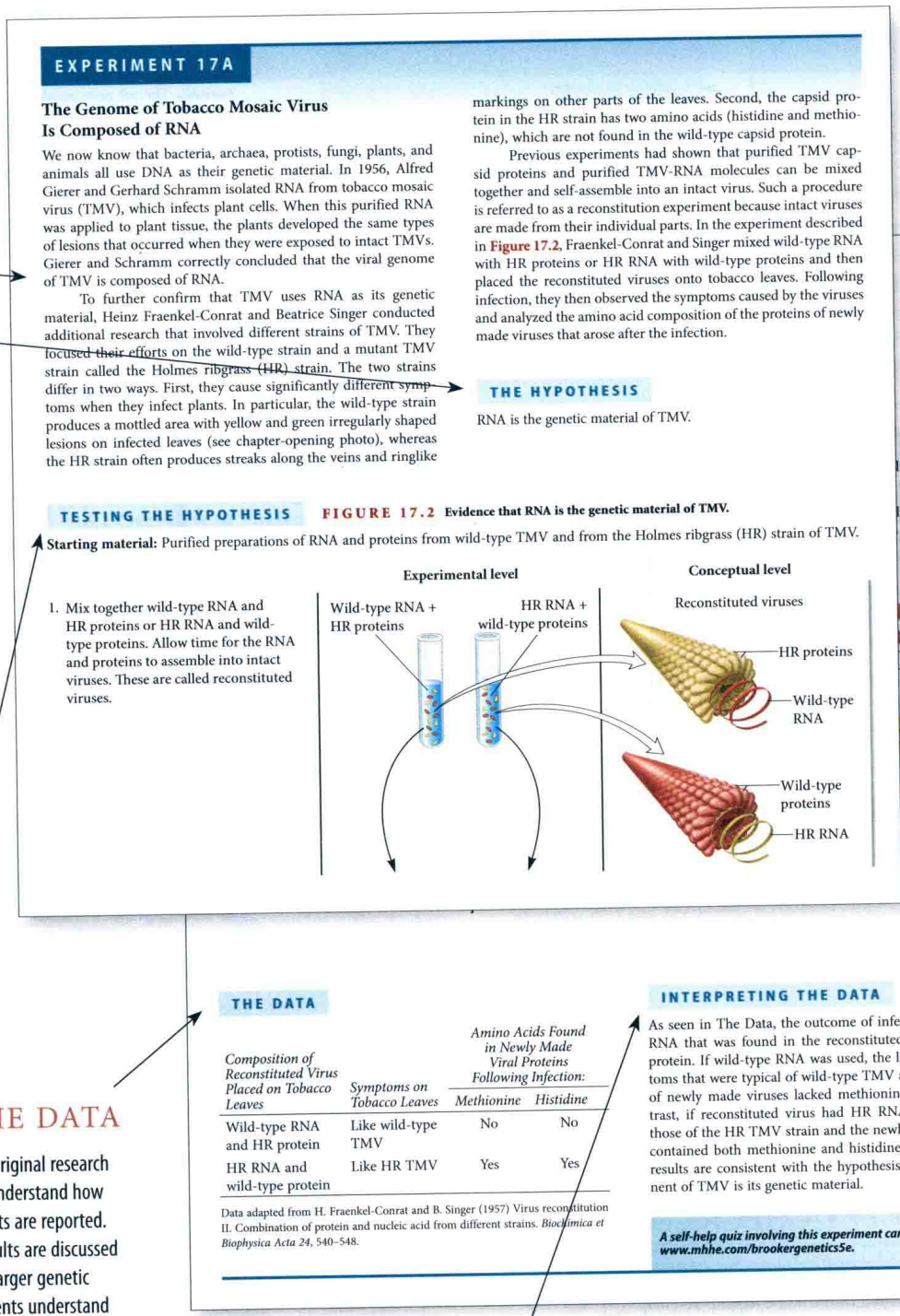
This section illustrates the experimental process, including the actual steps followed by scientists to test their hypothesis. Science comes alive for students with this detailed look at experimentation.

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.

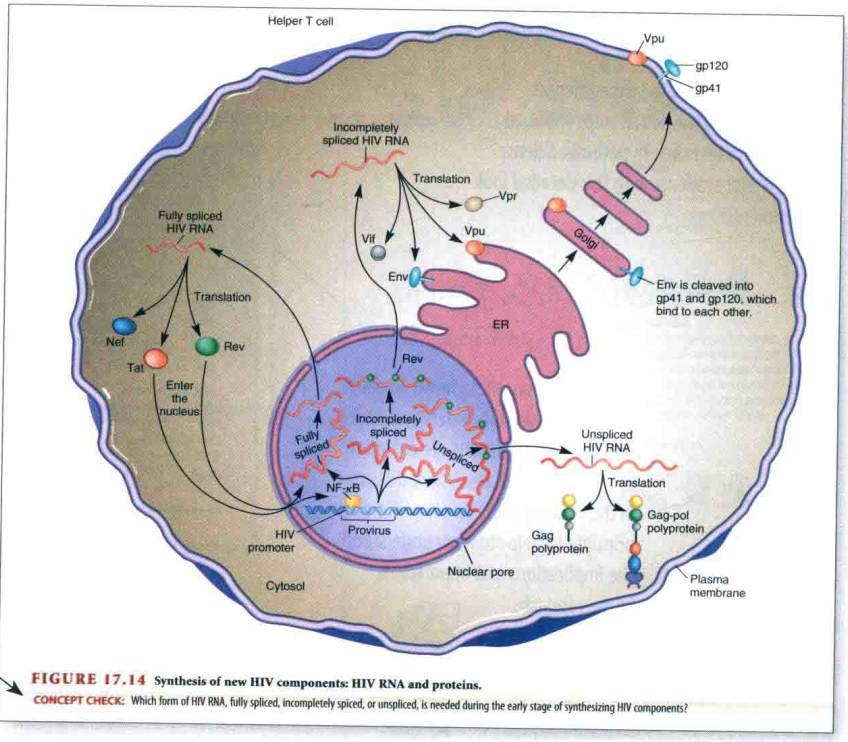


FIGURE 17.14 Synthesis of new HIV components: HIV RNA and proteins.

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.

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.

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.

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.