

GLOBAL  
EDITION



# Concepts of Genetics

TWELFTH EDITION

Klug • Cummings • Spencer • Palladino • Killian



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CONCEPTS OF  
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TWELFTH EDITION  
GLOBAL EDITION

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# About the Authors



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He received his B.S. degree in Biology from The College of New Jersey and his Ph.D. in Anatomy and Cell Biology from the University of Virginia. For more than 15 years he directed a laboratory of undergraduate student researchers supported by external funding from the National Institutes of Health, biopharma companies, and other agencies. He and his undergraduates studied molecular mechanisms involved in innate immunity of mammalian male reproductive organs and genes involved in oxygen homeostasis and ischemic injury of the testis. He has taught a wide range of courses including genetics, biotechnology, endocrinology, and cell and molecular biology. He has received several awards for research and teaching, including the 2009 Young Andrologist Award of the American Society of Andrology, the 2005 Distinguished Teacher Award from Monmouth University, and the 2005 Caring Heart Award from the New Jersey Association for Biomedical Research. He is co-author of the undergraduate textbook *Introduction to Biotechnology*. He was Series Editor for the Benjamin Cummings *Special Topics in Biology* booklet series, and author of the first booklet in the series, *Understanding the Human Genome Project*. When away from the university or authoring textbooks, Dr. Palladino can often be found watching or playing soccer or attempting to catch most any species of fish in freshwater or saltwater.



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B.A. degree in Molecular Biology and Biochemistry from Wesleyan University in Middletown, Connecticut, prior to working as a Research Technician in Molecular Genetics at Rockefeller University in New York, New York. He earned his Ph.D. in Developmental Genetics from New York University in New York, New York, and received his post-doctoral training at the University of Colorado–Boulder in the Department of Molecular, Cellular, and Developmental Biology. Prior to joining Colorado College, he was an Assistant Professor of Biology at the College of New Jersey in Ewing, New Jersey. His research focuses on the genetic regulation of animal development, and he has received funding from the National Institutes of Health and the National Science Foundation. Currently, he and his undergraduate research assistants are investigating the molecular genetic regulation of nervous system development using *C. elegans* and *Drosophila* as model systems. He teaches undergraduate courses in genetics, molecular and cellular biology, stem cell biology, and developmental neurobiology. When away from the classroom and research lab, Dr. Killian can often be found on two wheels exploring trails in the Pike and San Isabel National Forests.

## Dedication

We dedicate this edition to our long-time colleague and friend Harry Nickla, who sadly passed away in 2017. With decades of experience teaching Genetics to students at Creighton University, Harry's contribution to our texts included authorship of the *Student Handbook and Solutions Manual* (for the US edition) and the test bank, as well as devising most of the Extra Spicy problems at the end of each chapter. He was also a source of advice during the planning session for each new edition, and during our many revisions. We always appreciated his professional insights, friendship, and conviviality. We were lucky to have him as part of our team, and we miss him greatly.

WSK, MRC, CAS, MAP, and DJK

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# Explore Cutting-Edge Topics

**Concepts of Genetics** emphasizes the fundamental ideas of genetics, while exploring modern techniques and applications of genetic analysis. This best-selling text continues to provide understandable explanations of complex, analytical topics and recognizes the importance of teaching students how to become effective problem solvers.

Six Special Topics in Modern Genetics mini-chapters concisely explore cutting-edge, engaging, and relevant topics.

- **NEW!** CRISPR-Cas and Genome Editing
- DNA Forensics
- Genomics and Precision Medicine
- Genetically Modified Foods
- Gene Therapy
- **NEW!** Advances in Neurogenetics: The Study of Huntington Disease

Special Topic chapters include Review and Discussion questions, which are also assignable in Mastering Genetics.

## SPECIAL TOPICS IN MODERN GENETICS 1

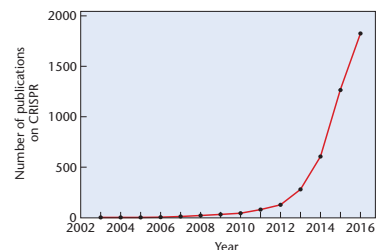
### CRISPR-Cas and Genome Editing

Genetic research is often a slow incremental process that may extend our understanding of a concept or improve the efficiency of a genetic technology. More rarely, discoveries advance the field in sudden and profound ways. For example, studies in the early 1980s led to the discovery of catalytic RNAs, which transformed how geneticists think about RNA. Around the same time, the development of the polymerase chain reaction (PCR) provided a revolutionary tool for geneticists and other scientists. Rapid and targeted DNA amplification is now indispensable to genetic research and medical science. Given this context, one can appreciate how rare and significant a discovery would be that both illuminates a novel genetic concept as well as yields a new technology for genetics research and application. CRISPR-Cas is exactly that.

For over a century, scientists have studied the biological warfare between bacteria and the viruses that infect them. However, in 2007, experiments confirmed that bacteria have a completely novel defense mechanism against viruses known as CRISPR-Cas. This discovery completely changed the scope of our understanding of how bacteria and viruses combat one another, and coevolve. Moreover, the CRISPR-Cas system has now been adapted as an incredibly powerful tool for genome editing.

The ability to specifically and efficiently edit a genome has broad implications for research, biotechnology, and medicine. For decades, geneticists have used various strategies for genome editing with many successes, but also with limited efficiency and a significant investment of time and resources. CRISPR-Cas has been developed into an efficient, cost-effective molecular tool that can introduce precise and specific edits to a genome. It is not without its limitations, but it represents a technological leap, which we have not seen, arguably, since the innovation of PCR.

The discovery of CRISPR-Cas has impacted genetics and other related fields at an unprecedented pace (Figure ST 1.1). CRISPR-Cas is the focus of numerous patent applications and disputes, has been approved for use in clinical trials to treat disease, has been used to edit the genome of human embryos as a proof of concept for future medical applications, has instigated international



**FIGURE ST 1.1** The number of publications returned in a search for “CRISPR” in PubMed by year.

discussions on its ethical use, and is most deserving of its own chapter in a genetics textbook.

#### ST 1.1 CRISPR-Cas Is an Adaptive Immune System in Prokaryotes

Bacteria and viruses (bacteriophages or phages) engage in constant biological warfare. Consequently, bacteria exhibit a diverse suite of defense mechanisms.

For example, bacteria express endonucleases (restriction enzymes), which cleave specific DNA sequences. Such restriction enzymes destroy foreign bacteriophage DNA, while the bacterium protects its own DNA by methylating it. As you know (from Chapter 20), restriction enzymes have been adopted by molecular biologists for use in recombinant DNA technology. Bacteria can also defend against phage attack by blocking phage adsorption, blocking phage DNA insertion, and inducing suicide in infected cells to prevent the spread

of infection to other cells. All of these defense mechanisms are considered **innate immunity** because they are not tailored to a specific pathogen.

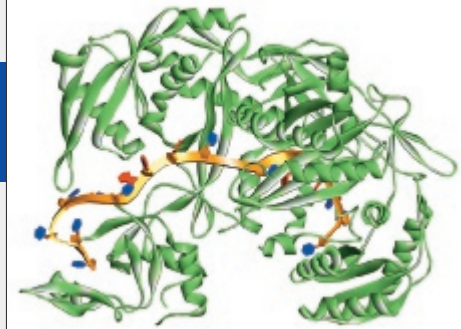
“CRISPR-Cas has been developed into an efficient, cost-effective molecular tool that can introduce precise and specific edits to a genome.”

# Explore the Latest Updates

The 12th edition has been heavily updated throughout, including a reorganization and expansion of coverage of gene regulation in eukaryotes. This expansion reflects our growing knowledge of the critical roles RNA and epigenetics play in regulating gene activity.

**NEW!** Gene regulation in eukaryotes has been expanded into three chapters: transcriptional regulation (Ch. 17), posttranscriptional regulation (Ch. 18), and epigenetic regulation (Ch. 19).

## 18



Crystal structure of human Argonaute2 protein interacting with "guide" RNA. Argonaute2 plays an important role in mediating a posttranscriptional RNA-induced silencing pathway.

### Posttranscriptional Regulation in Eukaryotes

#### CHAPTER CONCEPTS

- Following transcription, there are several mechanisms that regulate gene expression, referred to as posttranscriptional regulation.
- Alternative splicing allows for a single gene to encode different protein isoforms with different functions.
- The interaction between cis-acting mRNA sequence elements and trans-acting RNA-binding proteins regulates mRNA stability, degradation, localization, and translation.
- Noncoding RNAs may regulate gene expression by targeting mRNAs for destruction or translational inhibition.
- Posttranslational modification of proteins can alter their activity or promote their degradation.

and the synthesis of a 3' poly-A tail. Each of these steps can be regulated to control gene expression. After mature mRNAs are exported to the cytoplasm, they follow different paths: They may be localized to specific regions of the cell; they may be stabilized or degraded; or they may be translated robustly or stored for translation at a later time. Even after translation, protein activity, localization, and stability can be altered through covalent protein modifications. These and other eukaryotic posttranscriptional regulatory mechanisms are summarized in [Figure 18.1](#).

Whereas the regulation of transcription depends on transcription factors and DNA regulatory elements (see Chapter 17), many posttranscriptional mechanisms involve RNA-level regulation. Moreover, posttranscriptional regulation is not only centered on RNA, but, in some cases, is regulated by RNA. Noncoding RNAs play important roles in the regulation of eukaryotic gene expression.

In this chapter, we will explore several important mechanisms and themes of eukaryotic posttranscriptional regulation. As you read on, keep in mind that while scientists have learned a great deal about how genes are regulated at the posttranscriptional level, there are still many unanswered questions for the curious student to ponder.

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### Epigenetic Regulation of Gene Expression

In toadflax, the shape of individual flowers changes from bilateral symmetry (photo on the left) to radial symmetry (photo on the right) in a naturally occurring, heritable gene silencing epimutation associated with the methylation of a single gene. There is no alteration of the DNA sequence at this locus.

#### CHAPTER CONCEPTS

**NEW!** A new chapter focuses on epigenetics, updating and expanding coverage that used to be in a Special Topics chapter.

# and Ethical Considerations

With the rapid growth of our understanding of genetics and the ongoing introduction of powerful tools that can edit genes and genomes, it's important to encourage students to confront ethical issues and consider questions that arise in the study of genetics.



## GENETICS, ETHICS, AND SOCIETY

### Down Syndrome and Prenatal Testing—The New Eugenics?

**D**own syndrome is the most common chromosomal abnormality seen in newborn babies. Prenatal diagnostic tests for Down syndrome have been available for decades, especially to older pregnant women who have an increased risk of bearing a child with Down syndrome. Scientists estimate that there is an abortion rate of about 30 percent for fetuses that test positive for Down syndrome in the United States, and rates of up to 85 percent in other parts of the world, such as Taiwan and France.

Many people agree that it is morally acceptable to prevent the birth of a genetically abnormal fetus. However, many others argue that prenatal genetic testing, with the goal of eliminating congenital disorders, is unethical. In addition, some argue that prenatal genetic

testing followed by selective abortion is eugenic. How does eugenics apply, if at all, to screening for Down syndrome and other human genetic defects?

The term *eugenics* was first defined by Francis Galton in 1883 as “the science which deals with all influences that improve the inborn qualities of a race; also with those that develop them to the utmost advantage.” Galton believed that human traits such as intelligence and personality were hereditary and that humans could selectively mate with each other to create gifted groups of people—analogueous to the creation of purebred dogs with specific traits. Galton did not propose coercion but thought that people would voluntarily select mates in order to enhance particular genetic outcomes for their offspring.

In the early to mid-twentieth century, countries throughout the world adopted eugenic policies with the aim of enhancing desirable human traits (positive eugenics) and eliminating undesirable ones (negative eugenics). Many countries, including Britain, Canada, and the United States, enacted compulsory sterilization programs for the “feeble-minded,” mentally ill, and criminals. The eugenic policies of Nazi Germany were particularly infamous, resulting in forced human genetic experimentation and the slaughter of tens of thousands of disabled people. The eugenics movement was discredited after World War II, and the evils perpetuated in its name have tainted the term *eugenics* ever since.

Given the history of the eugenics movement, is it fair to use the term

### **NEW! Genetics, Ethics, and Society** essays

appear in many chapters. Each one provides a synopsis of an ethical issue, related to chapter content, that impacts society today. Each includes a section called **Your Turn**, directing students to resources to help them explore the issue and answer questions.

**NEW and REVISED! Case Studies** conclude each chapter, introducing a short vignette of an everyday genetics-related situation and posing several discussion questions, including one focusing on ethics.

### CASE STUDY Fish tales

**C**ontrolling the overgrowth of invasive aquatic vegetation is a significant problem in the waterways of most U.S. states. Originally, herbicides and dredging were used for control, but in 1963, diploid Asian carp were introduced in Alabama and Arkansas. Unfortunately, through escapes and illegal introductions, the carp spread rapidly and became serious threats to aquatic ecosystems in 45 states. Beginning in 1983, many states began using triploid, sterile grass carp as an alternative, because of their inability to reproduce, their longevity, and their voracious appetite. On the other hand, this genetically modified exotic species, if not used properly, can reduce or eliminate desirable plants and outcompete native fish, causing more damage than good. The use of one exotic species to control other exotic species has had a problematic history across the globe, generating controversy and criticism. Newer methods for genetic modification of organisms to achieve specific outcomes will certainly

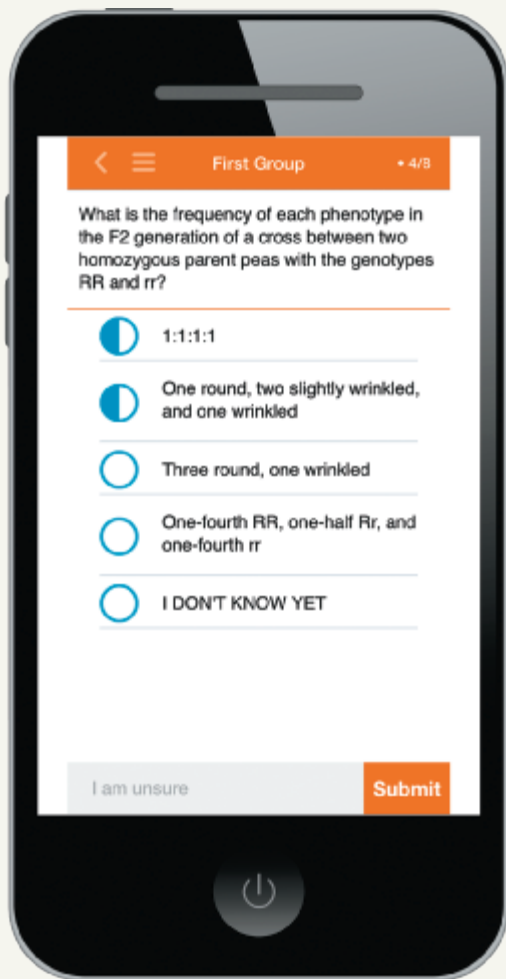
become more common in the future and raise several interesting questions.

1. Why would the creation and use of a tetraploid carp species be unacceptable in the above situation?
2. If you were a state official in charge of a particular waterway, what questions would you ask before approving the use of a laboratory-produced, triploid species in this waterway?
3. What ethical responsibilities accompany the ecological and economic risks and benefits of releasing exotic species into the environment? Who pays the costs if ecosystems and food supplies are damaged?

See Seastedt, T. R. (2015). Biological control of invasive plant species: A reassessment for the Anthropocene. *New Phytologist* 205:490–502.

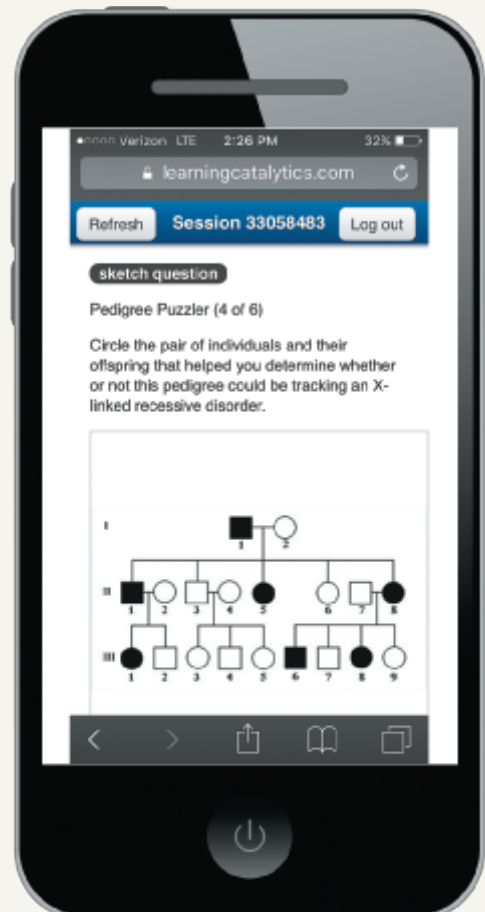
# Learn Genetics Concepts and Problem Solving

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# with Mastering Genetics

## Transcription and RNA Processing

During transcription, RNA polymerase synthesizes RNA from a DNA template with the help of accessory proteins. In this tutorial, you will review the steps of transcription in eukaryotes and bacteria and investigate splicing of mRNAs in eukaryotes.

### Part A - Transcription in bacteria

The diagram below shows a length of DNA containing a bacterial gene.

Drag the labels to their appropriate locations in the diagram to describe the function or characteristics of each part of the gene. Not all labels will be used.

• Hints

Submit My Answers Give Up

Incorrect; Try Again; 4 attempts remaining

You labeled 2 of 5 targets incorrectly. Keep in mind that the origin of replication is involved in the copying of DNA, which is a different process than the synthesis of RNA from a DNA template.

Tutorials and activities feature personalized wrong-answer feedback and hints that emulate the office-hour experience to guide student learning.

100 Practice Problems offer more opportunities to develop problem-solving skills. These questions appear only in Mastering Genetics and include targeted wrong-answer feedback to help students learn.

## Practice Problem 37

### Part A

Can you identify the bases that will be added to this parent strand during DNA replication?

Drag the labels to the appropriate targets to identify the sequence and orientation of the daughter strand. Blue labels can be used once, more than once, or not at all.

Submit My Answers Give Up

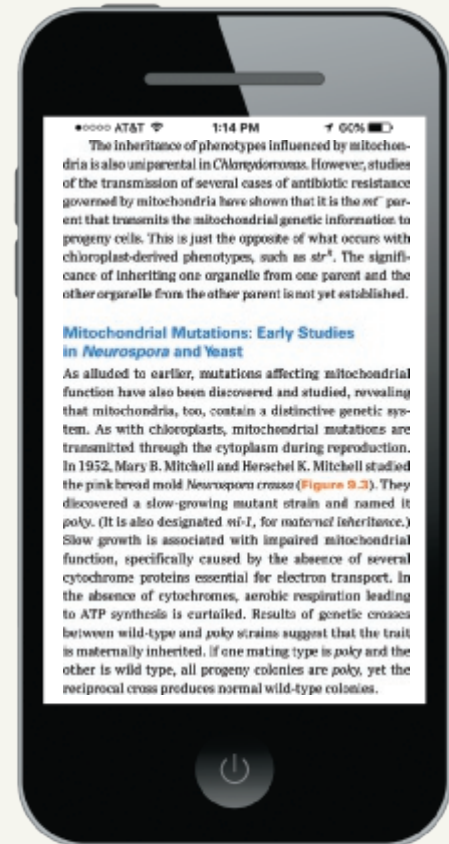
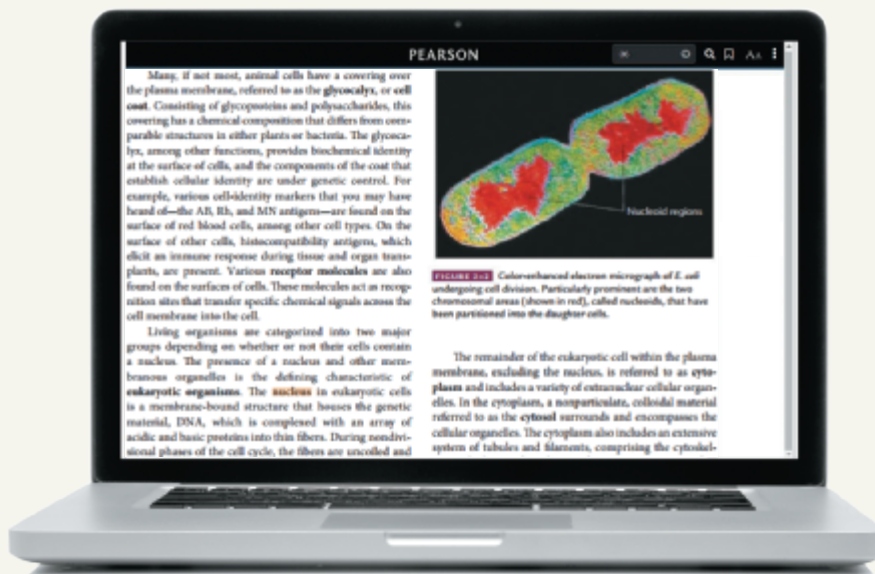
Incorrect; Try Again

You labeled 2 of 13 targets incorrectly. U represents uracil. Note that uracil is part of a ribonucleotide and is a component of RNA, not DNA.



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# Preface

It is essential that textbook authors step back and look with fresh eyes as each edition of their work is planned. In doing so, two main questions must be posed: (1) How has the body of information in their field—in this case, Genetics—grown and shifted since the last edition? (2) Which pedagogic innovations that are currently incorporated into the text should be maintained, modified, or deleted? The preparation of the 12th edition of *Concepts of Genetics*, a text well into its fourth decade of providing support for students studying in this field, has occasioned still another fresh look. And what we focused on in this new edition, in addition to the normal updating that is inevitably required, were three things:

## 1. The importance of continuing to provide comprehensive coverage of important, emerging topics.

In this regard, we continue to include a unique approach in genetics textbooks that offers readers a set of abbreviated, highly focused chapters that we label **Special Topics in Modern Genetics**. In this edition, these provide unique, cohesive coverage of six important topics: *CRISPR-Cas and Genomic Editing*, *DNA Forensics*, *Genomics and Precision Medicine*, *Genetically Modified Foods*, *Gene Therapy*, and *Advances in Neurogenetics: The Study of Huntington Disease*. The initial and final chapters in this series are both new to this edition.

## 2. The recognition of the vastly increased knowledge resulting from the study of gene regulation in eukaryotes.

To that end, the single chapter on this topic in previous editions has been expanded to three chapters: “Transcriptional Regulation in Eukaryotes” (Chapter 17), “Posttranscriptional Regulation in Eukaryotes” (Chapter 18), and “Epigenetic Regulation of Gene Expression” (Chapter 19). This extended coverage reflects many recent discoveries that reveal that RNA in many forms other than those that are essential to the process of transcription and translation (mRNA, tRNA, and rRNA) play critical roles in the regulation of eukaryotic gene activity. As well, it is now clear based on molecular studies related to epigenetics that this topic is best taught as an integral part of eukaryotic gene regulation. This new material provides the student exposure to modern coverage of a significant research topic.

## 3. The importance of providing an increased emphasis on ethical considerations that genetics is bringing into everyday life.

Regarding this point, we have converted the essay feature *Genetics, Technology, and Society* to one with added emphasis on ethics and renamed it *Genetics, Ethics, and Society*. Approximately half the chapters have new or revised essays. In addition, the feature called *Case Study*, which appears near the end of all chapters, has been recast with an increased focus on ethics. Both of these features increase the opportunities for active and cooperative learning.

## Goals

In the 12th edition of *Concepts of Genetics*, as in all past editions, we have five major overarching goals. Specifically, we have sought to:

- Emphasize the basic concepts of genetics.
- Write clearly and directly to students, providing understandable explanations of complex, analytical topics.
- Maintain our strong emphasis on and provide multiple approaches to problem solving.
- Propagate the rich history of genetics, which so beautifully illustrates how information is acquired during scientific investigation.
- Create inviting, engaging, and pedagogically useful full-color figures enhanced by equally helpful photographs to support concept development.

These goals collectively serve as the cornerstone of *Concepts of Genetics*. This pedagogic foundation allows the book to be used in courses with many different approaches and lecture formats.

Writing a textbook that achieves these goals and having the opportunity to continually improve on each new edition has been a labor of love for all of us. The creation of each of the twelve editions is a reflection not only of our passion for teaching genetics, but also of the constructive feedback and encouragement provided by adopters, reviewers, and our students over the past four decades.

## New to This Edition

New to this edition are four chapters. Two are Special Topics in Modern Genetics entries entitled “CRISPR-Cas and Genome Editing” and “Advances in Neurogenetics: The Study of Huntington Disease.” Both cover cutting-edge information and represent very recent breakthroughs in genetics. CRISPR, a genome-editing tool, is a straightforward technique that allows specific, highly accurate modification of DNA sequences within genes and is thus a powerful tool in the world of genetic research and gene therapy. In addition to this chapter, we call your attention to the introduction to Chapter 1 for an introduction to CRISPR and to also note that we have chosen this gene-editing system as the subject matter illustrated on the cover. Special Topics Chapter 6 illustrates the many of advances that have been made in the study of human neurogenetics. Huntington disease, a monogenic human disorder, has been subjected to analysis for over 40 years using every major approach and technique developed to study molecular genetics, and as such, exemplifies the growing body of information that has accrued regarding its causes, symptoms, and future treatment.

Additional new chapters arise from a major reorganization and expansion of our coverage of regulation of gene expression in eukaryotes, where we have split our previous coverage into three parts: transcriptional regulation (Chapter 17), posttranscriptional regulation (Chapter 18), and epigenetic regulation (Chapter 19). Chapter 18 includes much of the content previously contained in the Special Topics chapter *Emerging Roles of RNA* in the previous edition. Chapter 19, focused on epigenetics, is an expansion of the content previously contained in the *Epigenetics* Special Topics chapter from the previous edition.

Collectively, the addition of these four new chapters provides students and instructors with a much clearer, up-to-date presentation to these important aspects of genetics.

## Continuing Pedagogic Features

We continue to include features that are distinct from, and go beyond, the text coverage, which encourage active and cooperative learning between students and the instructor.

- **Modern Approaches to Understanding Gene Function** This feature highlights how advances in genetic technology have led to our modern understanding of gene function. Appearing in many chapters, this feature prompts students to apply their analytical thinking skills, linking the experimental technology to the findings that enhance our understanding of gene function.
- **Genetics, Ethics, and Society** This feature provides a synopsis of an ethical issue related to a current finding in genetics that impacts directly on society today. It includes a section called *Your Turn*, which directs students to related resources of short readings and Web sites to support deeper investigation and discussion of the main topic of each essay.
- **Case Study** This feature, at the end of each chapter, introduces a short vignette of an everyday genetics-related situation, followed by several discussion questions. Use of the Case Study should prompt students to relate their newly acquired information in genetics to ethical issues that they may encounter away from the course.
- **Evolving Concept of the Gene** This short feature, integrated in appropriate chapters, highlights how scientists’ understanding of the gene has changed over time. Since we cannot see genes, we must infer just what this unit of heredity is, based on experimental findings. By highlighting how scientists’ conceptualization of the gene has advanced over time, we aim to help students appreciate the process of discovery that has led to an ever more sophisticated understanding of hereditary information.
- **How Do We Know Question** Found as the initial question in the *Problems and Discussion Questions* at the end of each chapter, this feature emphasizes the pedagogic value of studying how information is acquired in science. Students are asked to review numerous findings discussed in the chapter and to summarize the process of discovery that was involved.
- **Concept Question** This feature, found as the second question in the *Problems and Discussion Questions* at the end of each chapter, asks the student to review and comment on common aspects of the Chapter Concepts, listed at the beginning of each chapter. This feature places added emphasis on our pedagogic approach of conceptual learning.
- **Mastering Genetics** This robust online homework and assessment program guides students through complex topics in genetics, using in-depth tutorials that coach students to correct answers with hints and feedback specific to their misconceptions. New content for the 12th edition of *Concepts of Genetics* includes Dynamic Study Modules and interactive flash cards that help students master basic content so they can be more prepared for class and for solving genetics problems.