

GLOBAL
EDITION



Essentials of Genetics

TENTH EDITION

Klug • Cummings • Spencer • Palladino • Killian



EVOLVING CONCEPT OF THE GENE

The Evolving Concept of the Gene is a unique feature, integrated into key chapters, which highlights how scientists' understanding of the gene has changed over time. By underscoring how the conceptualization of the gene has evolved, our goal is to help students appreciate the process of discovery that has led to an ever more sophisticated understanding of hereditary information.

CHAPTER 3 pg. 66 Based on the pioneering work of Gregor Mendel, the gene was viewed as a heritable unit factor that determines the expression of an observable trait, or phenotype. ■

CHAPTER 4 pg. 82 Based on the work of many geneticists following the rediscovery of Mendel's work in the very early part of the twentieth century, the chromosome theory of inheritance was put forward, which hypothesized that chromosomes are the carriers of genes and that meiosis is the physical basis of Mendel's postulates. In the ensuing 40 years, the concept of a gene evolved to reflect the idea that this hereditary unit can exist in multiple forms, or alleles, each of which can have an impact on the phenotype in different ways, leading to incomplete dominance, codominance, and even lethality. It became clear that the process of mutation was the source of new alleles. ■

CHAPTER 7 pg. 160 Based on the gene-mapping studies in *Drosophila* and many other organisms from the 1920s through the mid-1950s, geneticists regarded genes as hereditary units organized in a specific sequence along chromosomes, between which recombination could occur. Genes were thus viewed as indivisible "beads on a string." ■

CHAPTER 9 pg. 199 Based on the model of DNA put forward by Watson and Crick in 1953, the gene was viewed for the first time in molecular terms as a sequence of nucleotides in a DNA helix that encodes genetic information. ■

CHAPTER 18 pg. 383 Based on the work of the ENCODE project, we now know that DNA sequences that have previously been thought of as "junk DNA," because they do not encode proteins, are nonetheless often transcribed into what we call noncoding RNA (ncRNA). Since the function of some of these RNAs is now being determined, we must consider whether the concept of the gene should be expanded to include DNA sequences that encode ncRNAs. At this writing, there is no consensus, but it is important for you to be aware of these current findings as you develop your final interpretation of a gene. ■

CHAPTER 15 pg. 319 The groundbreaking work of Jacob, Monod, and Lwoff in the early 1960s, which established the operon model for the regulation of gene expression in bacteria, expanded the concept of the gene to include noncoding regulatory sequences that are present upstream (5') from the coding region. In bacterial operons, the transcription of several contiguous structural genes whose products are involved in the same biochemical pathway is regulated in a coordinated fashion. ■

CHAPTER 13 pg. 278 In the 1940s, a time when the molecular nature of the gene had yet to be defined, groundbreaking work of Beadle and Tatum provided the first experimental evidence concerning the product of genes, their "one-gene:one-enzyme" hypothesis. This idea received further support and was later modified to indicate that one gene specifies one polypeptide chain. ■

CHAPTER 12 pg. 260 The elucidation of the genetic code in the 1960s supported the concept that the gene is composed of a linear series of triplet nucleotides encoding the amino acid sequence of a protein. While this is indeed the case in bacteria and viruses, in 1977, it became apparent that in eukaryotes, the gene is divided into coding sequences, called exons, which are interrupted by noncoding sequences, called introns (intervening sequences), which must be spliced out during production of the mature mRNA. ■



ESSENTIALS *of* GENETICS

Tenth Edition
Global Edition

William S. Klug

The College of New Jersey

Michael R. Cummings

Illinois Institute of Technology

Charlotte A. Spencer

University of Alberta

Michael A. Palladino

Monmouth University

Darrell J. Killian

Colorado College

Courseware Portfolio Manager: Michael Gillespie
Director of Portfolio Management: Beth Wilbur
Content Producer: Brett Coker
Managing Producer: Michael Early
Courseware Director, Content Development: Ginnie Simione Jutson
Courseware Editorial Assistant: Ashley Fallon
Acquisitions Editor, Global Edition: Moasenla Jamir
Associate Project Editor, Global Edition: Aurko Mitra
Senior Manufacturing Controller, Global Edition:
Caterina Pellegrino
Digital Producer: Wendy Romaniecki
Rich Media Content Producer: Robert Johnson
Media Production Manager, Global Edition: Vikram Kumar
Full-Service Vendor: Pearson CSC
Full-Service Project Management: Pearson CSC, Heidi Aguiar

Art Coordinators: Stephanie Marquez and Mark Mykytiuk,
Imagineeringart.com, Inc.
Design Manager: Maria Guglielmo Walsh
Interior Designer: Tamara Newnam
Cover Designer, Global Edition: SPi Global
Rights & Permissions Project Manager: Pearson CSC, Eric Schrader
Rights & Permissions Management: Ben Ferrini
Photo Researcher: Pearson CSC, Eric Schrader
Manufacturing Buyer: Stacey Weinberger, LSC Communications
Director of Field Marketing: Tim Galligan
Director of Product Marketing: Allison Rona
Executive Field Marketing Manager: Kelly Galli
Product Marketing Manger: Alysun Estes
Cover Photo: aida ricciardiello/Shutterstock

Attributions of third party content appear on page C-1, which constitutes an extension of this copyright page.

Pearson Education Limited

KAO Two
KAO Park
Hockham Way
Harlow
Essex
CM17 9SR
United Kingdom

and Associated Companies throughout the world

Visit us on the World Wide Web at: www.pearsonglobaleditions.com

© William S. Klug and Michael R. Cummings 2021

The rights of William S. Klug, Michael R. Cummings, Charlotte A. Spencer, Michael A. Palladino, and Darrell J. Killian to be identified as the authors of this work, have been asserted by them in accordance with the Copyright, Designs and Patents Act 1988.

Authorized adaptation from the United States edition, entitled *Essentials of Genetics*, 10th Edition, ISBN 978-0-13-489841-4 by William S. Klug, Michael R. Cummings, Charlotte A. Spencer, Michael A. Palladino, and Darrell J. Killian, published by Pearson Education ©2020.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without either the prior written permission of the publisher or a license permitting restricted copying in the United Kingdom issued by the Copyright Licensing Agency Ltd, Saffron House, 6–10 Kirby Street, London EC1N 8TS. This publication is protected by copyright, and permission should be obtained from the publisher prior to any prohibited reproduction, storage in a retrieval system, or transmission in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise. For information regarding permissions, request forms, and the appropriate contacts within the Pearson Education Global Rights and Permissions department, please visit www.pearsoned.com/permissions/.

All trademarks used herein are the property of their respective owners. The use of any trademark in this text does not vest in the author or publisher any trademark ownership rights in such trademarks, nor does the use of such trademarks imply any affiliation with or endorsement of this book by such owners.

This eBook is a standalone product and may or may not include all assets that were part of the print version. It also does not provide access to other Pearson digital products like MyLab and Mastering. The publisher reserves the right to remove any material in this eBook at any time.

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

ISBN 10: 1-292-35042-3

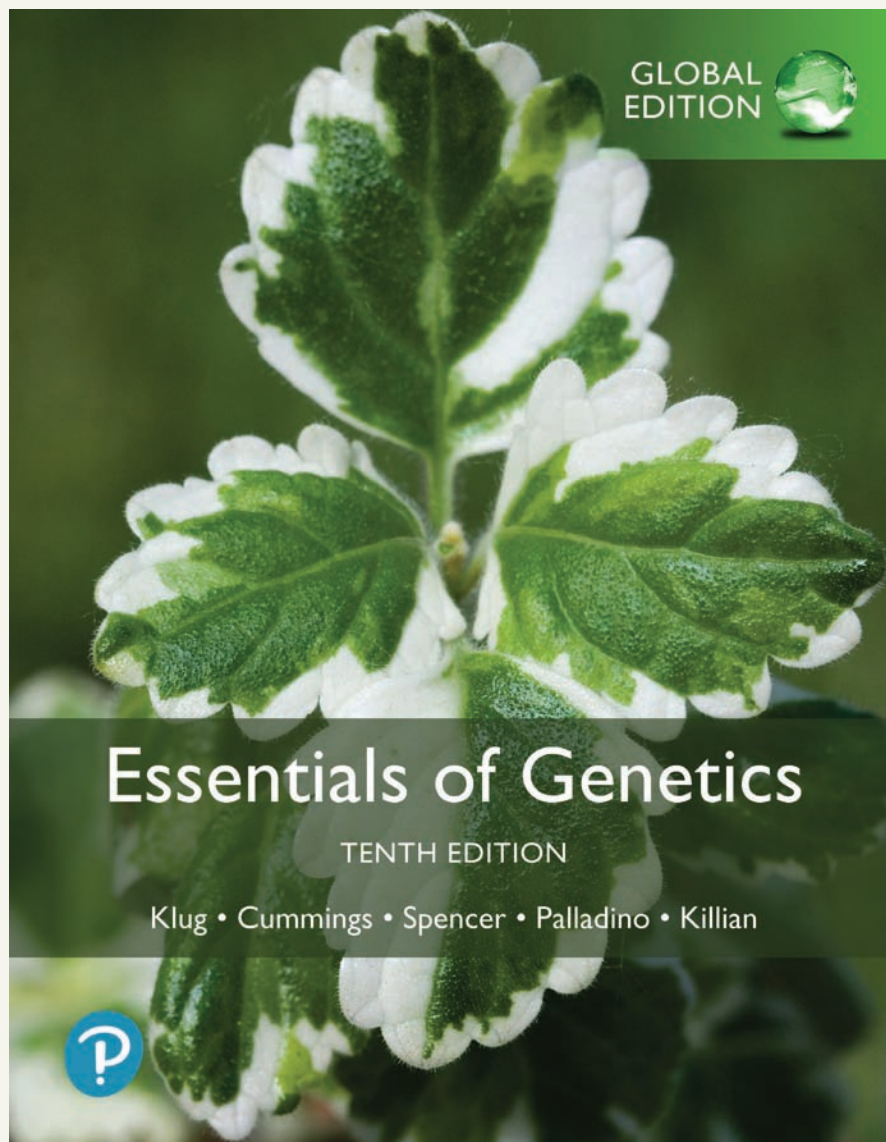
ISBN 13: 978-1-292-35042-4

eBook ISBN: 978-1-292-35054-7

Typeset by SPi Global

Focus on essential genetic topics and explore the latest breakthroughs

Known for its focus on conceptual understanding, problem solving, and practical applications, the bestselling *Essentials of Genetics* strengthens problem-solving skills and explores the essential genetics topics that today's students need to understand. The **10th Edition** has been extensively updated to provide comprehensive coverage of important, emerging topics such as CRISPR-Cas, epigenetics, and genetic testing and **Mastering Genetics** includes new tutorials on these topics, which prepare students for class and support the learning of key concepts.



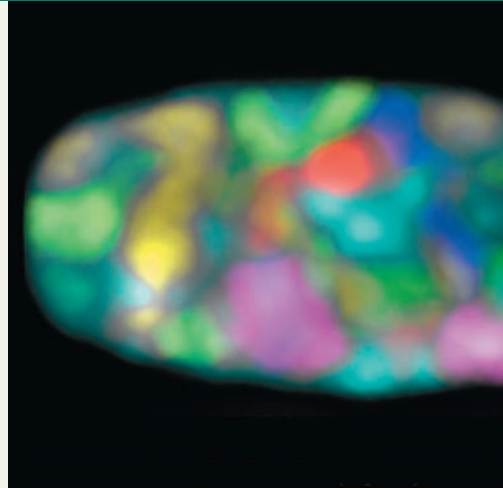
Make genetics relevant . . .

16

Regulation of Gene Expression in Eukaryotes

CHAPTER CONCEPTS

- While transcription and translation are tightly coupled in bacteria, in eukaryotes, these processes are spatially and temporally separated, and thus independently regulated.
- Chromatin remodeling, as well as modifications to DNA and histones, play important roles in regulating gene expression in eukaryotes.
- Eukaryotic transcription initiation requires the assembly of transcription regulatory proteins on DNA sites known as promoters, enhancers, and silencers.
- 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.
- RNA-binding proteins regulate mRNA stability, degradation, localization, and translation.
- Noncoding RNAs may regulate gene



Chromosome territories in a human fibroblast cell nucleus. Each chromosome is stained with a different-colored probe.

NEW! Regulation of gene expression has been expanded and is now divided into coverage of bacteria in Chapter 15 and coverage of eukaryotes in Chapter 16.

Virtually all cells in a multicellular eukaryotic organism contain a complete genome; however, such organisms often possess different cell types with diverse morphologies and functions. This simple observation highlights the importance of the regulation of gene expression in eukaryotes. For example, skin cells and muscle cells differ in appearance and function because they express different genes. Skin cells express keratins, fibrous structural proteins that bestow the skin with protective properties. Muscle cells express high levels of myosin II, a protein that mediates muscle contraction. Skin cells do not express myosin II, and muscle cells do not express keratins.

In addition to gene expression that is cell-type specific, some genes are only expressed under certain conditions or at certain times. For example, when oxygen levels in the blood are low, such as at high altitude or after rigorous exercise, expression of the hormone erythropoietin is upregulated, which leads to an increase in red blood cell production and thus oxygen-carrying capacity.

P. 326

Coverage of CRISPR-Cas is expanded and integrated in multiple chapters – Chapters 1, 15, 17, and Special Topics Chapters ST3 and ST6.

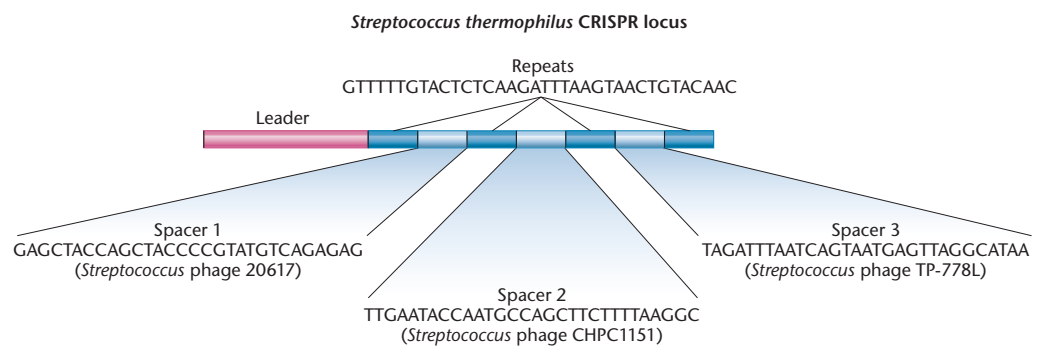


FIGURE 15.13 A CRISPR locus from the bacterium *Streptococcus thermophilus* (LMG18311). Spacer sequences are derived from portions of bacteriophage genomes and are flanked on either side by a repeat sequence. Only 3 of 33 total spacers in this CRISPR locus are shown.

P. 322

with current high interest topics

SPECIAL TOPICS IN MODERN GENETICS 2

Genetic Testing

Earlier in the text (see Chapters 17 and 18), we reviewed essential concepts of recombinant DNA technology and genomic analysis. Because of the Human Genome Project and related advances in genomics, researchers have been making rapid progress in identifying genes involved in both single-gene diseases and complex genetic traits. As a result, **genetic testing**—the ability to analyze DNA, and increasingly RNA, for the purposes of identifying specific genes or sequences associated with different genetic conditions—has advanced very rapidly.

Genetic testing, including genomic analysis by DNA sequencing, is transforming medical diagnostics. Technologies for genetic testing have had major impacts on the diagnosis of disease and are revolutionizing medical treatments based on the development of specific and effective pharmaceuticals. In this Special Topics chapter we provide an overview of applications that are effective for the genetic testing of children and adults and examine historical and modern methods. We consider the impact of different genetic technologies on the diagnosis of human diseases and dis-

dystrophy. Other tests have been developed for disorders that may involve multiple genes such as certain types of cancers.

Gene tests are used for prenatal, childhood, and adult prognosis and diagnosis of genetic diseases; to identify carriers; and to identify genetic diseases in embryos created by *in vitro* fertilization, among other applications. For genetic testing of adults, DNA from white blood cells is commonly used. Alternatively, many genetic tests can be carried out on cheek cells, collected by swabbing the inside of the mouth, or on hair cells. Some genetic testing can be carried out on gametes.

What does it mean when a genetic test is performed for *prognostic* purposes, and how does this differ from a *diagnostic* test? A prognostic test predicts a person's likelihood of developing a particular genetic disorder. A diagnostic test for a genetic condition

“Genetic testing, including genomic analysis by DNA sequencing, is transforming medical diagnostics. Technologies for genetic testing have had major

NEW! Special Topics chapter on Genetic Testing guides students through the many contexts in which genetic testing is becoming prominent and explores many questions and ethical concerns related to its use.

P. 474

SPECIAL TOPIC X

SPECIAL TOPICS IN MODERN GENETICS 4

Advances in Neurogenetics: The Study of Huntington Disease

As the result of groundbreaking advances in molecular genetics and genomics made since the 1970s, new fields in genetics and related disciplines have emerged. One new field is **neurogenetics**—the study of the genetic basis of normal and abnormal functioning of the nervous system, with emphasis on brain functions. Research in this field includes the genes associated with neurodegenerative disorders, with the ultimate goal of developing effective therapies to combat these devastating conditions. Of the many such diseases, including Alzheimer disease, Parkinson disease, and amyotrophic lateral sclerosis (ALS), **Huntington disease (HD)** stands out as a model for the genetic investigation of neurodegenerative disorders. Not only is it monogenic and 100 percent penetrant, but nearly all analytical approaches in molecular genetics have been successfully applied to the study of HD, validating its significance as a model for these diseases.

HD is an autosomal dominant disorder characterized by adult onset of defined and progressive behavioral changes, including uncontrolled movements (chorea), cognitive decline, and psychiatric disturbances, with death occurring within 10 to 15 years after symptoms appear. HD was one of the first examples of complete dominance in human inheritance, with no differences in phenotypes between homozygotes and heterozygotes. In the vast majority of cases, symptoms do not develop until about age 45. Overall, HD currently affects about 25,000 to 30,000 people in North America.

The disease is named after George Huntington, a nineteenth-century physician. He was not the first to describe the disorder,

know about the molecular and cellular mechanisms associated with the disorder, particularly those discovered during the study of transgenic model systems. Finally, we will consider how this information is being used to develop a range of therapies.

ST 4.1 The Search for the Huntington Gene

Mapping the gene for Huntington disease was one of the first attempts to employ a method from a landmark 1980 paper by Botstein, White, and Davis in which the authors proposed that DNA sequence variations in humans could be

detected as differences in the length of DNA fragments produced by cutting DNA with restriction enzymes. These differences, known as restriction fragment length polymorphisms (RFLPs), could be visualized using Southern blots (see Chapter 18 for a discussion of RFLPs, and Chapter 17 for a discussion of Southern blots). The authors estimated that a collection of about 150 RFLPs distributed across the genome could be used with pedigrees to detect linkage anywhere in the genome between an RFLP marker and a disease gene of interest. In practical terms, this meant that it would be possible to map a disease gene with no information about the gene, its gene product, or its function—an approach referred to as reverse genetics.

“Driving with my father through a wooded road leading from Easthampton to Amagansett, we suddenly came upon two women, mother and daughter, both bowing, twisting, grimacing. I stared in wonderment, almost in fear. What could it mean?”

NEW! Special Topics chapter on Advances in Neurogenetics: The Study of Huntington Disease, explores how genetic analysis has informed scientists about the disease's causes, symptoms, and future treatment. All Special Topics chapters include a series of questions that help students review key ideas or facilitate personal contemplations and group discussions, and are assignable in Mastering Genetics.

SPECIAL TOPIC 4

P. 506

Explore the latest ethical considerations



GENETICS, ETHICS, AND SOCIETY

Down Syndrome and Prenatal Testing—The New Eugenics?

Down 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.

Some people agree that it is morally acceptable to prevent the birth of a genetically abnormal fetus. However, 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 disorders?

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—analogs 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 people with disabilities. 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 *eugenics* when we speak about genetic testing for Down syndrome and other genetic disorders? Some people argue that it is not eugenic to select for healthy children because there is no coercion, the state is not involved, and the goal is the elimination of suffering. Others point out that such voluntary actions still constitute eugenics, since they involve a form of bioengineering for “better” human beings.

Now that we are entering an era of unprecedented knowledge about our genomes and our predisposition to genetic disorders, we must make decisions about whether our attempts to control or improve human genomes are ethical and what limits we should place on these efforts. The story of the eugenics

movement provides us with a powerful cautionary tale about the potential misuses of genetic information.

Your Turn

Take time, individually or in groups, to consider the following questions. Investigate the references and links to help you discuss some of the ethical issues surrounding genetic testing and eugenics.

1. Do you think that modern prenatal and preimplantation genetic testing followed by selective abortion is eugenic? Why or why not?

For background on these questions, see McCabe, L., and McCabe, E. (2011). Down syndrome: Coercion and eugenics. Genet. Med. 13:708–710. Another useful discussion can be found in Wilkinson, S., (2015). Prenatal screening, reproductive choice, and public health. Bioethics 29:26–35.

2. If genetic technologies were more advanced than today, and you could choose the traits of your children, would you take advantage of that option? Which traits would you choose—height, weight, intellectual abilities, athleticism, artistic talents? If so, would this be eugenic? Would it be ethical?

To read about similar questions answered by groups of Swiss law and medical students, read Elger, B., and Harding, T., (2003). Huntington’s disease: Do future physicians and lawyers think eugenically? Clin. Genet. 64:327–338.

P. 141

Genetics, Ethics, and Society essays

provide synopses of ethical issues related to current findings in genetics that impact directly on society today. They include a section called *Your Turn*, which directs students to related resources of short readings and websites to support deeper investigation and discussion of the main topic of each essay.

Case Studies at the end of each chapter

have been updated with new topics. Students can read and answer questions about a short scenario related to one of the chapter topics. Each Case Study links the coverage of formal genetic knowledge to everyday societal issues, and they include ethical considerations.

CASE STUDY To test or not to test

Thomas discovered a devastating piece of family history when he learned that his brother had been diagnosed with Huntington disease (HD) at age 49. This dominantly inherited autosomal condition usually begins around age 45 with progressive dementia, muscular rigidity, and seizures and ultimately leads to death when affected individuals are in their early 60s. There currently is no effective treatment or cure for this genetic disorder. Thomas, now 38, wonders what the chances are that he also has inherited the mutant allele for HD, leading him to discuss with his wife whether they should seek genetic counseling and whether he should undergo genetic testing. They have two teenage children, a boy and a girl.

1. If they seek genetic counseling, what issues would likely be discussed? Which of these pose grave ethical dilemmas?
2. If you were in Thomas’s position, would you want to be tested and possibly learn that you were almost certain to develop the disorder sometime in the next 5–10 years?
3. If Thomas tests positive for the HD allele, should his children be told about the situation, and if so, at what age? Who should make the decision about having the son and daughter tested?

Fulda, K., and Lykens, K. (2006). Ethical issues in predictive genetic testing: A public health perspective. *J. Med. Ethics* 32:143–147.

P. 74

Learn genetics concepts and problem solving in Mastering Genetics

CRISPR: The Discovery of Bacterial Adaptive Immunity

Part B - CRISPR-Cas9: Defense overview

Now that you are familiar with the bacterial DNA sequences encoding the CRISPR-Cas system, let's examine how the system functions when a bacterial cell is confronted with a phage infection. As noted above, the general mechanism shown here is of the type II CRISPR-Cas system.

Suppose a bacterium is infected by a phage it has not encountered before. Drag the blue labels to indicate the steps of the CRISPR-Cas immune response. Then drag the pink labels to demonstrate your understanding of the three main phases of the immune response.

Transcription of CRISPR locus, yielding pre-crRNA
Phage infects the bacterial cell with its DNA
Phage DNA incorporated as a new spacer into CRISPR array
crRNA BIOGENESIS
crRNA-Cas recognizes and complementary target DNA of invading phage
Pre-crRNA processed into mature crRNA
INTERFERENCE

SPACER ACQUISITION

Submit Request Answer

NEW! Tutorials have been added to the library on topics like CRISPR-Cas and epigenetics, to help students master important and challenging concepts.

A library of over 100 Practice Problems offers more opportunities to assign high quality problems for student homework or practice. These questions appear only in Mastering Genetics and include targeted wrong-answer feedback to help students learn from their mistakes. They are similar to end-of-chapter questions in terms of topic coverage and difficulty.

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 Previous Answers Request Answer

✘ 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.

Give students anytime, anywhere access with Pearson eText

Pearson eText is a simple-to-use, mobile-optimized, personalized reading experience. It allows students to easily highlight, take notes, and review key vocabulary all in one place—even when offline. Seamlessly integrated videos engage students and give them access to the help they need, when they need it.

NEW! Pearson eText increases student engagement with embedded videos.

The image shows a tablet displaying a Pearson eText page. The page title is "2.4: Meiosis Creates Haploid Gametes And Spores And Enhances Ge...". The main content is "Figure 2.10" with the caption "The changes in chromosome structures during prophase I, which characterize each of the events of the process." Below the caption is a diagram showing five stages of chromosome structure: Chromosomes, Bivalent, Tetrad, Chiasma, and Terminalization. Below the diagram is a video player with the title "Watch BioFlix: Meiosis: Prophase I". The video player shows a 3D illustration of chromosomes with a play button in the center. To the right of the tablet, there are two circular callouts. The top callout shows a search bar, a bookmark icon, and a font size icon, with a "Show highlights" toggle switch below. The bottom callout shows three colored squares (yellow, green, pink) and a text box containing "Recall this informa exam on Friday" with a "Share" toggle switch below.

Instructor support you can rely on

Chapter 5: Chromosome Mapping in Eukaryotes

Download instructor resources from the links below.

PowerPoint Presentation Tools

Download Chapter 5 Lecture Presentation	zip, 228.1 MB	📄
Download Chapter 5 Clicker Questions	zip, 2.2 MB	📄
Download Chapter 5 Art and Photo PowerPoint Presentation Tools	zip, 9.6 MB	📄

JPEG Images

Download Chapter 5 JPEGs - Labeled	zip, 5.2 MB	📄
Labeled JPEG images from the chapter.		
Download Chapter 5 JPEGs - Unlabeled	zip, 2.9 MB	📄
Unlabeled JPEG images from the chapter.		

Essentials of Genetics

includes a full suite of instructor support materials in the Instructor Resources area in Mastering Genetics. Resources include lecture presentations, clicker questions, and art and photos in PowerPoint®; labeled and unlabeled JPEGs of images from the text; and a test bank.

learning | catalytics™

Allison Rona | Pearson | Log out

Courses Questions Classrooms Training and Support Help Feedback Student view

My Courses > Klug Concepts 12e > Klug Genetics > Question 51125

🔍 Search again + Add to module

📘 This question is provided by Pearson, © 2018.

Question

Sex Linkage (2 of 3)

You take a full family history and draw the following pedigree showing the pattern of inheritance of red-green color blindness in this family. Mark all individuals that must be heterozygous carriers of the X-linked recessive condition.

Instructors also have access to Learning Catalytics. With Learning Catalytics, you'll hear from every student when it matters most. You can pose a variety of questions in class that help students recall ideas, apply concepts, and develop critical-thinking skills. Your students respond using their own smartphones, tablets, or laptops. You can monitor responses with real-time analytics and find out what your students do—and don't—understand. Then, you can adjust your teaching accordingly and even facilitate peer-to-peer learning, helping students stay motivated and engaged. Write your own questions, pull from a shared library of community-generated questions, or use Pearson's content clusters, which pose 2-5 questions about a single data set or scenario.

About the Authors



William S. Klug is an Emeritus Professor of Biology at The College of New Jersey (formerly Trenton State College) in Ewing, New Jersey, where he served as Chair of the Biology Department for 17 years. He received his B.A. degree in Biology from Wabash College in Crawfordsville, Indiana,

and his Ph.D. from Northwestern University in Evanston, Illinois. Prior to coming to The College of New Jersey, he was on the faculty of Wabash College, where he first taught genetics, as well as general biology and electron microscopy. His research interests have involved ultrastructural and molecular genetic studies of development, utilizing oogenesis in *Drosophila* as a model system. He has taught the genetics course as well as the senior capstone seminar course in Human and Molecular Genetics to undergraduate biology majors for over four decades. He was the recipient in 2001 of the first annual teaching award given at The College of New Jersey, granted to the faculty member who “most challenges students to achieve high standards.” He also received the 2004 Outstanding Professor Award from Sigma Pi International, and in the same year, he was nominated as the Educator of the Year, an award given by the Research and Development Council of New Jersey. When not revising one of his textbooks, immersed in the literature of genetics, or trying to avoid double bogies, Dr. Klug can sometimes be found paddling in the Gulf of Mexico or in Maine’s Penobscot Bay.



Michael R. Cummings is a Research Professor in the Department of Biological, Chemical, and Physical Sciences at Illinois Institute of Technology, Chicago, Illinois. For more than 25 years,

he was a faculty member in the Department of Biological Sciences and in the Department of Molecular Genetics at the University of Illinois at Chicago. He has also served on the faculties of Northwestern University and Florida State University. He received his B.A. from St. Mary’s College in Winona, Minnesota, and his M.S. and Ph.D. from Northwestern University in Evanston, Illinois. In addition to this text, he has written textbooks in human genetics and general biology. His research interests center on the molecular organization and physical mapping of the heterochromatic regions of human acrocentric chromosomes. At the undergraduate level, he teaches courses in molecular genetics, human genetics, and general biology, and has received numerous

awards for teaching excellence given by university faculty, student organizations, and graduating seniors. When not teaching or writing, Dr. Cummings can often be found far offshore fishing for the one that got away.



Charlotte A. Spencer is a retired Associate Professor from the Department of Oncology at the University of Alberta in Edmonton, Alberta, Canada. She has also served as a faculty member in the Department of Biochemistry at the

University of Alberta. She received her B.Sc. in Microbiology from the University of British Columbia and her Ph.D. in Genetics from the University of Alberta, followed by post-doctoral training at the Fred Hutchinson Cancer Research Center in Seattle, Washington. Her research interests involve the regulation of RNA polymerase II transcription in cancer cells, cells infected with DNA viruses, and cells traversing the mitotic phase of the cell cycle. She has taught undergraduate and graduate courses in biochemistry, genetics, molecular biology, and oncology. She has also written booklets in the Prentice Hall Exploring Biology series. When not writing and editing contributions to genetics textbooks, Dr. Spencer works on her hazelnut farm and enjoys the peace and quiet of a remote Island off the west coast of British Columbia.



Michael A. Palladino is Vice Provost for Graduate Studies, former Dean of the School of Science, and Professor of Biology at Monmouth University in West Long Branch, New Jersey. 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.



Darrell J. Killian is an Associate Professor in the Department of Molecular Biology at Colorado College in Colorado Springs, Colorado. He received his 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 postdoctoral 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 and the test bank, as well as devising many of the data-based problems found near the end of each chapter. He was also a source of advice during the planning session for each new edition. 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.

Contents

1 Introduction to Genetics 25

- 1.1 Genetics Has an Interesting Early History 26
 - 1.2 Genetics Progressed from Mendel to DNA in Less Than a Century 27
 - 1.3 Discovery of the Double Helix Launched the Era of Molecular Genetics 28
 - 1.4 Development of Recombinant DNA Technology Began the Era of DNA Cloning 30
 - 1.5 The Impact of Biotechnology Is Continually Expanding 31
 - 1.6 Genomics, Proteomics, and Bioinformatics Are New and Expanding Fields 32
 - 1.7 Genetic Studies Rely on the Use of Model Organisms 32
 - 1.8 Genetics Has Had a Profound Impact on Society 34
- Problems and Discussion Questions 35

2 Mitosis and Meiosis 36

- 2.1 Cell Structure Is Closely Tied to Genetic Function 37
- 2.2 Chromosomes Exist in Homologous Pairs in Diploid Organisms 39
- 2.3 Mitosis Partitions Chromosomes into Dividing Cells 41
- 2.4 Meiosis Creates Haploid Gametes and Spores and Enhances Genetic Variation in Species 45
- 2.5 The Development of Gametes Varies in Spermatogenesis Compared to Oogenesis 48
- 2.6 Meiosis Is Critical to Sexual Reproduction in All Diploid Organisms 50
- 2.7 Electron Microscopy Has Revealed the Physical Structure of Mitotic and Meiotic Chromosomes 50

EXPLORING GENOMICS

PubMed: Exploring and Retrieving Biomedical Literature 51

CASE STUDY: Timing is everything 52

Insights and Solutions 52

Problems and Discussion Questions 53

3 Mendelian Genetics 55

- 3.1 Mendel Used a Model Experimental Approach to Study Patterns of Inheritance 56
- 3.2 The Monohybrid Cross Reveals How One Trait Is Transmitted from Generation to Generation 57
- 3.3 Mendel's Dihybrid Cross Generated a Unique F_2 Ratio 60
- 3.4 The Trihybrid Cross Demonstrates That Mendel's Principles Apply to Inheritance of Multiple Traits 63
- 3.5 Mendel's Work Was Rediscovered in the Early Twentieth Century 65

EVOLVING CONCEPT OF THE GENE 66

- 3.6 Independent Assortment Leads to Extensive Genetic Variation 66
- 3.7 Laws of Probability Help to Explain Genetic Events 66
- 3.8 Chi-Square Analysis Evaluates the Influence of Chance on Genetic Data 67
- 3.9 Pedigrees Reveal Patterns of Inheritance of Human Traits 70
- 3.10 Tay–Sachs Disease: The Molecular Basis of a Recessive Disorder in Humans 72

EXPLORING GENOMICS

Online Mendelian Inheritance in Man 73

CASE STUDY: To test or not to test 74

Insights and Solutions 74

Problems and Discussion Questions 75

4 Modification of Mendelian Ratios 77

- 4.1 Alleles Alter Phenotypes in Different Ways 78
 - 4.2 Geneticists Use a Variety of Symbols for Alleles 78
 - 4.3 Neither Allele Is Dominant in Incomplete, or Partial, Dominance 79
 - 4.4 In Codominance, the Influence of Both Alleles in a Heterozygote Is Clearly Evident 80
 - 4.5 Multiple Alleles of a Gene May Exist in a Population 80
 - 4.6 Lethal Alleles Represent Essential Genes 82
- ### EVOLVING CONCEPT OF THE GENE 82
- 4.7 Combinations of Two Gene Pairs with Two Modes of Inheritance Modify the 9:3:3:1 Ratio 83
 - 4.8 Phenotypes Are Often Affected by More Than One Gene 84
 - 4.9 Complementation Analysis Can Determine if Two Mutations Causing a Similar Phenotype Are Alleles of the Same Gene 88
 - 4.10 Expression of a Single Gene May Have Multiple Effects 90
 - 4.11 X-Linkage Describes Genes on the X Chromosome 90
 - 4.12 In Sex-Limited and Sex-Influenced Inheritance, an Individual's Gender Influences the Phenotype 92
 - 4.13 Genetic Background and the Environment Affect Phenotypic Expression 94
 - 4.14 Extranuclear Inheritance Modifies Mendelian Patterns 96

GENETICS, ETHICS, AND SOCIETY

Mitochondrial Replacement and Three-Parent Babies 100

CASE STUDY: Is it all in the genes? 101

Insights and Solutions 101

Problems and Discussion Questions 102

5 Sex Determination and Sex Chromosomes 107

- 5.1 X and Y Chromosomes Were First Linked to Sex Determination Early in the Twentieth Century 108
- 5.2 The Y Chromosome Determines Maleness in Humans 109
- 5.3 The Ratio of Males to Females in Humans Is Not 1.0 112
- 5.4 Dosage Compensation Prevents Excessive Expression of X-Linked Genes in Humans and Other Mammals 113
- 5.5 The Ratio of X Chromosomes to Sets of Autosomes Can Determine Sex 116
- 5.6 Temperature Variation Controls Sex Determination in Reptiles 118

GENETICS, ETHICS, AND SOCIETY

A Question of Gender: Sex Selection in Humans 119

CASE STUDY: Is the baby a boy or a girl? 120

Insights and Solutions 121

Problems and Discussion Questions 121

6 Chromosome Mutations: Variation in Number and Arrangement 123

- 6.1 Variation in Chromosome Number: Terminology and Origin 124
- 6.2 Monosomy and Trisomy Result in a Variety of Phenotypic Effects 125
- 6.3 Polyploidy, in Which More Than Two Haploid Sets of Chromosomes Are Present, Is Prevalent in Plants 128
- 6.4 Variation Occurs in the Composition and Arrangement of Chromosomes 131
- 6.5 A Deletion Is a Missing Region of a Chromosome 132
- 6.6 A Duplication Is a Repeated Segment of a Chromosome 134
- 6.7 Inversions Rearrange the Linear Gene Sequence 136
- 6.8 Translocations Alter the Location of Chromosomal Segments in the Genome 137
- 6.9 Fragile Sites in Human Chromosomes Are Susceptible to Breakage 139

GENETICS, ETHICS, AND SOCIETY

Down Syndrome and Prenatal Testing—The New Eugenics? 141

CASE STUDY: Fish tales 142

Insights and Solutions 142

Problems and Discussion Questions 143

7 Linkage and Chromosome Mapping in Eukaryotes 145

- 7.1 Genes Linked on the Same Chromosome Segregate Together 146

- 7.2 Crossing Over Serves as the Basis of Determining the Distance between Genes during Mapping 147
- 7.3 Determining the Gene Sequence during Mapping Requires the Analysis of Multiple Crossovers 152
- 7.4 As the Distance between Two Genes Increases, Mapping Estimates Become More Inaccurate 159

EVOLVING CONCEPT OF THE GENE 160

- 7.5 Chromosome Mapping Is Now Possible Using DNA Markers and Annotated Computer Databases 161
- 7.6 Other Aspects of Genetic Exchange 161

EXPLORING GENOMICS

Human Chromosome Maps on the Internet 163

CASE STUDY: Links to autism 164

Insights and Solutions 164

Problems and Discussion Questions 165

8 Genetic Analysis and Mapping in Bacteria and Bacteriophages 168

- 8.1 Bacteria Mutate Spontaneously and Are Easily Cultured 169
- 8.2 Genetic Recombination Occurs in Bacteria 169
- 8.3 The F Factor Is an Example of a Plasmid 176
- 8.4 Transformation Is Another Process Leading to Genetic Recombination in Bacteria 177
- 8.5 Bacteriophages Are Bacterial Viruses 178
- 8.6 Transduction Is Virus-Mediated Bacterial DNA Transfer 181

GENETICS, ETHICS, AND SOCIETY

Multidrug-Resistant Bacteria: Fighting with Phage 182

CASE STUDY: To test or not to test 183

Insights and Solutions 183

Problems and Discussion Questions 184

9 DNA Structure and Analysis 185

- 9.1 The Genetic Material Must Exhibit Four Characteristics 186
 - 9.2 Until 1944, Observations Favored Protein as the Genetic Material 186
 - 9.3 Evidence Favoring DNA as the Genetic Material Was First Obtained during the Study of Bacteria and Bacteriophages 187
 - 9.4 Indirect and Direct Evidence Supports the Concept That DNA Is the Genetic Material in Eukaryotes 192
 - 9.5 RNA Serves as the Genetic Material in Some Viruses 193
 - 9.6 The Structure of DNA Holds the Key to Understanding Its Function 193
- **EVOLVING CONCEPT OF THE GENE 199**
- 9.7 Alternative Forms of DNA Exist 199

- 9.8** The Structure of RNA Is Chemically Similar to DNA, but Single Stranded **200**
- 9.9** Many Analytical Techniques Have Been Useful during the Investigation of DNA and RNA **201**

EXPLORING GENOMICS

Introduction to Bioinformatics: BLAST **202**

CASE STUDY: Credit where credit is due **203**

Insights and Solutions **204**

Problems and Discussion Questions **204**

10 DNA Replication 206

- 10.1** DNA Is Reproduced by Semiconservative Replication **207**
- 10.2** DNA Synthesis in Bacteria Involves Five Polymerases, as Well as Other Enzymes **211**
- 10.3** Many Complex Issues Must Be Resolved during DNA Replication **214**
- 10.4** A Coherent Model Summarizes DNA Replication **217**
- 10.5** Replication Is Controlled by a Variety of Genes **218**
- 10.6** Eukaryotic DNA Replication Is Similar to Replication in Bacteria, but Is More Complex **219**
- 10.7** Telomeres Solve Stability and Replication Problems at Eukaryotic Chromosome Ends **220**

GENETICS, ETHICS, AND SOCIETY

Telomeres: The Key to a Long Life? **223**

CASE STUDY: At loose ends **224**

Insights and Solutions **224**

Problems and Discussion Questions **225**

11 Chromosome Structure and DNA Sequence Organization 226

- 11.1** Viral and Bacterial Chromosomes Are Relatively Simple DNA Molecules **227**
- 11.2** Mitochondria and Chloroplasts Contain DNA Similar to Bacteria and Viruses **228**
- 11.3** Specialized Chromosomes Reveal Variations in the Organization of DNA **230**
- 11.4** DNA Is Organized into Chromatin in Eukaryotes **232**
- 11.5** Eukaryotic Genomes Demonstrate Complex Sequence Organization Characterized by Repetitive DNA **236**
- 11.6** The Vast Majority of a Eukaryotic Genome Does Not Encode Functional Genes **239**

EXPLORING GENOMICS

Database of Genomic Variants: Structural Variations in the Human Genome **239**

CASE STUDY: Helping or hurting? **240**

Insights and Solutions **240**

Problems and Discussion Questions **241**

12 The Genetic Code and Transcription 242

- 12.1** The Genetic Code Exhibits a Number of Characteristics **243**
- 12.2** Early Studies Established the Basic Operational Patterns of the Code **243**
- 12.3** Studies by Nirenberg, Matthaei, and Others Deciphered the Code **244**
- 12.4** The Coding Dictionary Reveals the Function of the 64 Triplets **249**
- 12.5** The Genetic Code Has Been Confirmed in Studies of Bacteriophage MS2 **250**
- 12.6** The Genetic Code Is Nearly Universal **251**
- 12.7** Different Initiation Points Create Overlapping Genes **251**
- 12.8** Transcription Synthesizes RNA on a DNA Template **252**
- 12.9** RNA Polymerase Directs RNA Synthesis **252**
- 12.10** Transcription in Eukaryotes Differs from Bacterial Transcription in Several Ways **255**
- 12.11** The Coding Regions of Eukaryotic Genes Are Interrupted by Intervening Sequences Called Introns **257**
- **EVOLVING CONCEPT OF THE GENE 260**
- 12.12** RNA Editing May Modify the Final Transcript **261**
- 12.13** Transcription Has Been Visualized by Electron Microscopy **261**

CASE STUDY: Treatment dilemmas **261**

GENETICS, ETHICS, AND SOCIETY

Treating Duchenne Muscular Dystrophy with Exon-Skipping Drugs **262**

Insights and Solutions **262**

Problems and Discussion Questions **263**

13 Translation and Proteins 265

- 13.1** Translation of mRNA Depends on Ribosomes and Transfer RNAs **265**
- 13.2** Translation of mRNA Can Be Divided into Three Steps **269**
- 13.3** High-Resolution Studies Have Revealed Many Details about the Functional Bacterial Ribosome **273**
- 13.4** Translation Is More Complex in Eukaryotes **274**
- 13.5** The Initial Insight That Proteins Are Important in Heredity Was Provided by the Study of Inborn Errors of Metabolism **275**
- 13.6** Studies of *Neurospora* Led to the One-Gene: One-Enzyme Hypothesis **275**
- 13.7** Studies of Human Hemoglobin Established That One Gene Encodes One Polypeptide **277**
- **EVOLVING CONCEPT OF THE GENE 278**
- 13.8** Variation in Protein Structure Is the Basis of Biological Diversity **278**
- 13.9** Proteins Function in Many Diverse Roles **281**

CASE STUDY: Crippled ribosomes **282**

Insights and Solutions **283**

Problems and Discussion Questions **283**

14 Gene Mutation, DNA Repair, and Transposition 285

14.1 Gene Mutations Are Classified in Various Ways **286**

14.2 Mutations Can Be Spontaneous or Induced **288**

14.3 Spontaneous Mutations Arise from Replication Errors and Base Modifications **289**

14.4 Induced Mutations Arise from DNA Damage Caused by Chemicals and Radiation **291**

14.5 Single-Gene Mutations Cause a Wide Range of Human Diseases **294**

14.6 Organisms Use DNA Repair Systems to Counteract Mutations **295**

14.7 The Ames Test Is Used to Assess the Mutagenicity of Compounds **300**

14.8 Transposable Elements Move within the Genome and May Create Mutations **301**

CASE STUDY: An unexpected diagnosis **305**

Insights and Solutions **306**

Problems and Discussion Questions **307**

15 Regulation of Gene Expression in Bacteria 309

15.1 Bacteria Regulate Gene Expression in Response to Environmental Conditions **310**

15.2 Lactose Metabolism in *E. coli* Is Regulated by an Inducible System **310**

15.3 The Catabolite-Activating Protein (CAP) Exerts Positive Control over the *lac* Operon **316**

15.4 The Tryptophan (*trp*) Operon in *E. coli* Is a Repressible Gene System **317**

■ **EVOLVING CONCEPT OF THE GENE 319**

15.5 RNA Plays Diverse Roles in Regulating Gene Expression in Bacteria **319**

15.6 CRISPR-Cas Is an Adaptive Immune System in Bacteria **321**

CASE STUDY: MRSA in the National Football League (NFL) **323**

Insights and Solutions **324**

Problems and Discussion Questions **324**

16 Regulation of Gene Expression in Eukaryotes 326

16.1 Organization of the Eukaryotic Cell Facilitates Gene Regulation at Several Levels **327**

16.2 Eukaryotic Gene Expression Is Influenced by Chromatin Modifications **328**

16.3 Eukaryotic Transcription Initiation Requires Specific *Cis*-Acting Sites **329**

16.4 Eukaryotic Transcription Initiation Is Regulated by Transcription Factors That Bind to *Cis*-Acting Sites **331**

16.5 Activators and Repressors Interact with General Transcription Factors and Affect Chromatin Structure **333**

16.6 Regulation of Alternative Splicing Determines Which RNA Spliceforms of a Gene Are Translated **334**

16.7 Gene Expression Is Regulated by mRNA Stability and Degradation **337**

16.8 Noncoding RNAs Play Diverse Roles in Posttranscriptional Regulation **339**

16.9 mRNA Localization and Translation Initiation Are Highly Regulated **341**

16.10 Posttranslational Modifications Regulate Protein Activity **342**

EXPLORING GENOMICS

Tissue-Specific Gene Expression **343**

CASE STUDY: A mysterious muscular dystrophy **344**

Insights and Solutions **344**

Problems and Discussion Questions **345**

17 Recombinant DNA Technology 347

17.1 Recombinant DNA Technology Began with Two Key Tools: Restriction Enzymes and Cloning Vectors **348**

17.2 DNA Libraries Are Collections of Cloned Sequences **353**

17.3 The Polymerase Chain Reaction Is a Powerful Technique for Copying DNA **355**

17.4 Molecular Techniques for Analyzing DNA and RNA **357**

17.5 DNA Sequencing Is the Ultimate Way to Characterize DNA at the Molecular Level **359**

17.6 Creating Knockout and Transgenic Organisms for Studying Gene Function **362**

17.7 Genome Editing with CRISPR-Cas **365**

EXPLORING GENOMICS

Manipulating Recombinant DNA: Restriction Mapping **368**

CASE STUDY: Ethical issues and genetic technology **368**

Insights and Solutions **369**

Problems and Discussion Questions **369**

18 Genomics, Bioinformatics, and Proteomics 371

18.1 Whole-Genome Sequencing Is Widely Used for Sequencing and Assembling Entire Genomes **372**

18.2 DNA Sequence Analysis Relies on Bioinformatics Applications and Genome Databases **373**

- 18.3** The Human Genome Project Revealed Many Important Aspects of Genome Organization in Humans **377**
- 18.4** The “Omics” Revolution Has Created a New Era of Biological Research **379**
- **EVOLVING CONCEPT OF THE GENE 383**
- 18.5** Comparative Genomics Provides Novel Information about the Human Genome and the Genomes of Model Organisms **384**
- 18.6** Metagenomics Applies Genomics Techniques to Environmental Samples **386**
- 18.7** Transcriptome Analysis Reveals Profiles of Expressed Genes in Cells and Tissues **388**
- 18.8** Proteomics Identifies and Analyzes the Protein Composition of Cells **390**
- 18.9** Synthetic Genomes and the Emergence of Synthetic Biology **394**

■ **GENETICS, ETHICS, AND SOCIETY**
Privacy and Anonymity in the Era of Genomic Big Data **396**

■ **EXPLORING GENOMICS**
Contigs, Shotgun Sequencing, and Comparative Genomics **396**

CASE STUDY: Your microbiome may be a risk factor for disease **397**

Insights and Solutions **397**

Problems and Discussion Questions **398**

19 The Genetics of Cancer 400

- 19.1** Cancer Is a Genetic Disease at the Level of Somatic Cells **401**
- 19.2** Cancer Cells Contain Genetic Defects Affecting Genomic Stability, DNA Repair, and Chromatin Modifications **403**
- 19.3** Cancer Cells Contain Genetic Defects Affecting Cell-Cycle Regulation **405**
- 19.4** Proto-oncogenes and Tumor-suppressor Genes Are Altered in Cancer Cells **407**
- 19.5** Cancer Cells Metastasize and Invade Other Tissues **409**
- 19.6** Predisposition to Some Cancers Can Be Inherited **409**
- 19.7** Environmental Agents Contribute to Human Cancers **410**

■ **GENETICS, ETHICS, AND SOCIETY**
Breast Cancer: The Ambiguities and Ethics of Genetic Testing **413**

CASE STUDY: Cancer-killing bacteria **413**

Insights and Solutions **414**

Problems and Discussion Questions **415**

20 Quantitative Genetics and Multifactorial Traits 416

- 20.1** Quantitative Traits Can Be Explained in Mendelian Terms **417**

- 20.2** The Study of Polygenic Traits Relies on Statistical Analysis **419**
- 20.3** Heritability Values Estimate the Genetic Contribution to Phenotypic Variability **422**
- 20.4** Twin Studies Allow an Estimation of Heritability in Humans **426**
- 20.5** Quantitative Trait Loci Are Useful in Studying Multifactorial Phenotypes **428**

CASE STUDY: A chance discovery **432**

■ **GENETICS, ETHICS, AND SOCIETY**
Rice, Genes, and the Second Green Revolution **432**

Insights and Solutions **433**

Problems and Discussion Questions **434**

21 Population and Evolutionary Genetics 436

- 21.1** Genetic Variation Is Present in Most Populations and Species **437**
- 21.2** The Hardy–Weinberg Law Describes Allele Frequencies and Genotype Frequencies in Population Gene Pools **439**
- 21.3** The Hardy–Weinberg Law Can Be Applied to Human Populations **441**
- 21.4** Natural Selection Is a Major Force Driving Allele Frequency Change **444**
- 21.5** Mutation Creates New Alleles in a Gene Pool **448**
- 21.6** Migration and Gene Flow Can Alter Allele Frequencies **449**
- 21.7** Genetic Drift Causes Random Changes in Allele Frequency in Small Populations **450**
- 21.8** Nonrandom Mating Changes Genotype Frequency but Not Allele Frequency **451**
- 21.9** Speciation Can Occur through Reproductive Isolation **452**
- 21.10** Phylogeny Can Be Used to Analyze Evolutionary History **455**

■ **GENETICS, ETHICS, AND SOCIETY**
Tracking Our Genetic Footprints out of Africa **458**

CASE STUDY: A tale of two Olivias **459**

Insights and Solutions **460**

Problems and Discussion Questions **460**

SPECIAL TOPICS IN MODERN GENETICS 1

Epigenetics 463

- ST 1.1** Molecular Alterations to the Genome Create an Epigenome **463**
- ST 1.2** Epigenetics and Monoallelic Gene Expression **466**
- ST 1.3** Epigenetics and Cancer **468**
- ST 1.4** Epigenetic Traits Are Heritable **470**
- ST 1.5** Epigenome Projects and Databases **472**

 SPECIAL TOPICS IN MODERN GENETICS 2

Genetic Testing 474

- ST 2.1** Testing for Prognostic or Diagnostic Purposes 474
- ST 2.2** Prenatal Genetic Testing to Screen for Conditions 474
- BOX 1** Recommended Uniform Screening Panel 475
- ST 2.3** Genetic Testing Using Allele-Specific Oligonucleotides 477
- ST 2.4** Microarrays for Genetic Testing 479
- ST 2.5** Genetic Analysis of Individual Genomes by DNA Sequencing 481
- BOX 2** Undiagnosed Diseases Network 482
- BOX 3** Genetic Analysis for Pathogen Identification During Infectious Disease Outbreaks 482
- ST 2.6** Genome-Wide Association Studies Identify Genome Variations That Contribute to Disease 485
- ST 2.7** Genetic Testing and Ethical, Social, and Legal Questions 487

 SPECIAL TOPICS IN MODERN GENETICS 3

Gene Therapy 492

- ST 3.1** What Genetic Conditions Are Candidates for Treatment by Gene Therapy? 492
- ST 3.2** How Are Therapeutic Genes Delivered? 493
- BOX 1** ClinicalTrials.gov 493
- ST 3.3** The First Successful Gene Therapy Trial 496
- ST 3.4** Gene Therapy Setbacks 496
- ST 3.5** Recent Successful Trials by Conventional Gene Therapy Approaches 497
- ST 3.6** Genome-Editing Approaches to Gene Therapy 499
- ST 3.7** Future Challenges and Ethical Issues 503
- BOX 2** Glybera: The First Commercial Gene Therapy to be Approved in the West Lasted Only Five Years 504
- BOX 3** Gene Doping for Athletic Performance? 505

 SPECIAL TOPICS IN MODERN GENETICS 4

Advances in Neurogenetics: The Study of Huntington Disease 506

- ST 4.1** The Search for the Huntington Gene 506
- BOX 1** George Huntington and His Namesake Disease 507
- ST 4.2** The *HTT* Gene and Its Protein Product 508
- ST 4.3** Molecular and Cellular Alterations in Huntington Disease 509
- ST 4.4** Transgenic Animal Models of Huntington Disease 511
- ST 4.5** Cellular and Molecular Approaches to Therapy 512

 SPECIAL TOPICS IN MODERN GENETICS 5

DNA Forensics 515

- ST 5.1** DNA Profiling Methods 515
- BOX 1** The Pitchfork Case: The First Criminal Conviction Using DNA Profiling 516
- ST 5.2** Interpreting DNA Profiles 520
- ST 5.3** Technical and Ethical Issues Surrounding DNA Profiling 521
- BOX 2** The Kennedy Brewer Case: Two Bite-Mark Errors and One Hit 522
- BOX 3** A Case of Transference: The Lukis Anderson Story 522

 SPECIAL TOPICS IN MODERN GENETICS 6

Genetically Modified Foods 524

- ST 6.1** What Are GM Foods? 524
- BOX 1** The Tale of GM Salmon—Downstream Effects? 526
- ST 6.2** Methods Used to Create GM Plants 527
- ST 6.3** GM Foods Controversies 530
- BOX 2** The New CRISPR Mushroom 530
- ST 6.4** The Future of GM Foods 532

 SPECIAL TOPICS IN MODERN GENETICS 7

Genomics and Precision Medicine 534

- ST 7.1** Pharmacogenomics 534
- BOX 1** Preemptive Pharmacogenomic Screening: The PGEN4Kids Program 536
- ST 7.2** Precision Oncology 537
- BOX 2** Precision Cancer Diagnostics and Treatments: The Lukas Wartman Story 538
- BOX 3** Cell Types in the Innate and Adaptive Immune Systems 539
- BOX 4** Steps in Cytotoxic T-cell Recognition, Activation, and Destruction of Cancer Cells 540
- ST 7.3** Precision Medicine and Disease Diagnostics 542
- ST 7.4** Technical, Social, and Ethical Challenges 542
- BOX 5** Beyond Genomics: Personal Omics Profiling 543

APPENDIX Solutions to Selected Problems and Discussion Questions **A-1**

GLOSSARY **G-1**

CREDITS **C-1**

INDEX **I-1**

Preface

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

Goals

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

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

- Emphasize concepts rather than excessive detail.
- Write clearly and directly to students in order to provide understandable explanations of complex analytical topics.
- Emphasize problem solving, thereby guiding students to think analytically and to apply and extend their knowledge of genetics.
- Provide the most modern and up-to-date coverage of this exciting field.
- Propagate the rich history of genetics that so beautifully elucidates how information is acquired as the discipline develops and grows.

- Create inviting, engaging, and pedagogically useful figures enhanced by meaningful photographs to support student understanding.
- Provide outstanding interactive media support to guide students in understanding important concepts through animations, tutorial exercises, and assessment tools.

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

New to This Edition

In addition to updating information with new findings in all chapters throughout the text, four chapters are new to this edition.

- **Two new chapters expand the coverage of the regulation of gene expression** The topic of genetic regulation was previously covered in a single chapter, but has now been split into two new chapters. The first (Chapter 15) involves regulation in bacteria, while the second (Chapter 16) focuses on eukaryotes. The bacterial coverage represents the pioneering work in this field and then concludes with an introduction to CRISPR-Cas. The eukaryotic coverage focuses on the regulation of gene expression first at the level of transcription, and then post-transcriptionally, where the expanded coverage focuses on mechanisms that regulate RNA. Research into posttranscriptional regulation in the past 15 years has highlighted the importance of topics such as alternative splicing, mRNA stability and decay, and regulatory noncoding RNAs. Collectively, the addition of these two new chapters provides students and instructors with a thorough, up-to-date presentation of these important aspects of genetics.
- **Two new Special Topics in Modern Genetics chapters** Special Topics chapters are focused and flexible, providing abbreviated, cohesive coverage of important topics in genetics. There are seven Special Topics chapters in this edition, two of which are new. Special Topics Chapter 2—*Genetic Testing* explores how genetic testing is becoming prominent in many contexts and how its use raises many questions and ethical concerns. Special Topics Chapter 4—*Advances in Neurogenetics: The Study of Huntington Disease* illustrates the many advances that have been made in the study of Huntington disease, a

monogenic human disorder that has been subjected to analysis using multiple approaches involving molecular genetics. As such, the chapter exemplifies the growing body of information that has accrued regarding the causes, symptoms, and future treatment of this disorder.

- **Expanded coverage of CRISPR-Cas** Since the previous edition was published, techniques for genome editing have vastly improved due to CRISPR-Cas technology. Thus, we have integrated information about CRISPR-Cas in several different locations within the text. The impact of genome editing with CRISPR-Cas is briefly introduced in Chapter 1. Then, in Chapter 15, students learn how CRISPR-Cas was originally discovered as a bacterial system that regulates the gene expression of bacterial viruses (bacteriophages), providing an immunity against infection. The mechanism and applications to biotechnology are subsequently covered in Chapter 17. Finally, the use of CRISPR-Cas genome editing for gene therapy and the production of genetically modified foods is discussed in Special Topics Chapter 3—*Gene Therapy* and Special Topics Chapter 6—*Genetically Modified Foods*.
- **Increased emphasis on ethics** We recognize in this edition 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 previously called *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 each case, a synopsis is presented of an ethical issue related to a current finding in genetics that impacts directly on society today. The feature then 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. In addition, another 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 as well.

New and Updated Coverage

Below is a chapter-by-chapter list of the most significant new and updated coverage present in this edition.

Ch. 1: Introduction to Genetics • New chapter introduction vignette emphasizing the significance of the discovery of CRISPR-Cas9, a powerful genome-editing system.

Ch. 2: Mitosis and Meiosis • New information on microtubules and microfilaments • Revised Figure 2.9 on Meiotic Prophase I • New Exploring Genomics (EG) entry: PubMed: Exploring and Retrieving Biomedical Literature • New Case Study (CS): Timing Is Everything

Ch. 3: Mendelian Genetics • New Table 3.2 on Dominant and Recessive Human Traits • New Now Solve This (NST) 3.5 on pedigree analysis

Ch. 4: Modification of Mendelian Ratios • New information in the “Mitochondria, Human Health, and Aging” section • New information on the *MERFF* mutation • New Genetics, Ethics, and Society (GES) entry: Mitochondrial Replacement and Three-Parent Babies

Ch. 5: Sex Determination and Sex Chromosomes • New information on Klinefelter syndrome • New GES: A Question of Gender: Sex Selection in Humans

Ch. 6: Chromosome Mutations: Variation in Number and Arrangement • Updated information on copy number variation • New GES: Down Syndrome and Prenatal Testing—The New Eugenics? • A new end of chapter problem involving mapping analysis in *Drosophila*.

Ch. 8: Genetic Analysis and Mapping in Bacteria and Bacteriophages • New GES: Multidrug-Resistant Bacteria: Fighting with Phage

Ch. 10: DNA Replication and Recombination • New details about DNA unwinding during replication • New section entitled “Telomeres in Disease, Aging, and Cancer” • Two new end of chapter problems involving telomeres and telomerase

Ch. 12: The Genetic Code and Transcription • Revised coverage of transcription and RNA processing in eukaryotes • New information on termination of transcription in bacteria • New section entitled “Why Do Introns Exist?” • New GES: Treating Duchene Muscular Dystrophy

Ch. 13: Translation and Proteins • Revised coverage of ribosome and tRNA structure • Revised coverage of translation in bacteria • Expanded coverage of translation in eukaryotes including new information on closed-loop translation, illustrated in a new figure (Fig. 13.10)

Ch. 14: Gene Mutation, DNA Repair, and Transposition • Reorganization of the section on mutation classification, including new table summaries • New and expanded coverage of human germ-line and somatic mutation rates • New, reorganized, and revised coverage of transposable elements, focusing on the major characteristics of retrotransposons and DNA transposons, as well as on how transposons create mutations • Three new figures and one new table

Ch. 15: Regulation of Gene Expression in Bacteria • New chapter that focuses specifically on gene regulation in bacteria • Expanded coverage on the roles of RNA in bacterial gene regulation • New coverage of CRISPR-Cas-mediated regulation of invading viral DNA sequences

Ch. 16: Regulation of Gene Expression in

Eukaryotes • New chapter that focuses specifically on gene regulation in eukaryotes • Revised and expanded coverage of alternative splicing, including a new figure, and its relevance to human disease • Expanded coverage on RNA stability and RNA decay including a new figure (Fig. 16.11) • Updated information on noncoding RNAs that regulate gene expression • Enriched coverage of ubiquitin-mediated protein degradation, including a new figure (Fig. 16.14)

Ch. 17: Recombinant DNA Technology • Updated content on modern sequencing technologies including a new figure (Fig. 17.12) on third-generation sequencing (single-strand DNA sequencing) • New section, “Genome Editing with CRISPR-Cas,” describes this system as a genome editing tool and includes a new figure (Fig. 17.16)

Ch. 18: Genomics, Bioinformatics, and

Proteomics • A new section, “DNA Sequence Analysis Relies on Bioinformatics Applications and Genome Databases,” integrating applications of bioinformatics, genome databases, and functional genomics for analyzing and understanding gene function by sequence analysis • Reorganized and revised content on the Human Genome Project, including a new end of chapter problem citing the PANTHER database as part of the Human Genome Project • Updated content on personal genome projects • New content on diploid genomes, mosaicism, and reference genomes and the pangenome to emphasize human genetic variations, including a new figure (Fig. 18.8) • Incorporated coverage of the Human Microbiome Project into a new section, “Metagenomics,” and expanded content to include a new Figure (Fig. 18.9) displaying microbiome results of patients with different human disease conditions • A new section titled “RNA Sequencing” • A new section, “Synthetic Genomes and the Emergence of Synthetic Biology,” including a new figure (Fig. 18.13) • New GES: Privacy and Anonymity in the Era of Genomic Big Data • Several new and revised end of chapter problems

Ch. 19: The Genetics of Cancer • Extended coverage of environmental agents that contribute to human cancers, including more information about both natural and human-made carcinogens • New subsection entitled “Tobacco Smoke and Cancer” explaining how a well-studied carcinogen induces a wide range of genetic effects that may lead to mutations and cancer

Ch. 20: Quantitative Genetics and Multifactorial Traits • Revised coverage of Expression QTLs (eQTLs) in the regulation of gene expression • New GES: Rice, Genes, and the Second Green Revolution • New CS: A Chance Discovery

Ch. 21: Population and Evolutionary Genetics • New figure (Fig. 21.7) on the relationship

between genotype and allele frequency • Important modifications to Figures 21.8 and 21.9 illustrating allele selection • New figure (Fig. 21.13) on the impact of selection types on the phenotypic mean and variance • Revised text and figure (Fig. 21.24) on molecular clocks • Updated information about the origins of the human genome • New figure (Fig. 21.26) on hominin contributions to the genome of modern humans

Special Topic 1: Epigenetics • Revised, updated, and expanded coverage of epigenetic topics, including histone modifications, noncoding RNAs, assisted reproductive technologies, and the heritability of stress-induced behaviors • Updated coverage of epigenetics and cancer • New section on “Epigenetics and Monoallelic Gene Expression” • New figures on DNA methylation, chemical modification of histones, genomic imprinting, random autosomal monoallelic gene expression, imprinting in germ cells, and maternal behavior and stress responses in rat pups

Special Topic 2: Genetic Testing • New Special Topics chapter emphasizing modern approaches to genetic testing including prenatal genetic testing, noninvasive procedures for testing fetal DNA, testing using allele-specific oligonucleotides, microarrays, and genetic analysis by DNA and RNA sequencing • Includes coverage of the recommended uniform screening panel, undiagnosed diseases network, and genetic analysis for pathogen identification during infectious disease outbreaks • Section on genome-wide association studies incorporates approaches for genomic analysis of disease conditions at the population level • A range of ethical, social, and legal considerations are discussed

Special Topic 3: Gene Therapy • Updated information on gene therapy trials that are under way • An expanded section “Genome Editing” highlighting the application of the CRISPR-Cas system and describing some of the most promising trials under way in humans and animals • New ethical considerations of CRISPR-Cas and germ-line and embryo editing • New section, “RNA-Based Therapeutics,” that includes coverage of antisense RNA; RNA interference; and updated trials for RNA-based therapeutics, including Spinraza as an antisense RNA modifying splicing for the treatment of spinal muscular atrophy • Updated content on roles of stem cells in gene therapy • New content on combining genome editing with immunotherapy

Special Topic 4: Advances in Neurogenetics: The Study of Huntington Disease • New Special Topics chapter that surveys the study of Huntington Disease (HD) from 1970 to the present • Coverage includes the genetic basis and progression of HD, the mapping and isolation of the gene responsible for the disorder, and information on the mutant gene product • Discussions

include information on the molecular and cellular alterations caused by the mutant protein, the use of transgenic animal models of HD, and the molecular and cellular approaches to therapy

Special Topic 5: DNA Forensics • New section entitled “DNA Phenotyping,” describing a controversial forensic method, including descriptions of how law-enforcement agencies currently use this new technology

Special Topic 6: Genetically Modified Foods • New section, entitled “Gene Editing and GM Foods,” describing how scientists are using the new techniques of gene editing (including ZFN, TALENS, and CRISPR-Cas) to create GM food plants and animals, and how these methods are changing the way in which GM foods are being regulated • A new box, “The New CRISPR Mushroom,” describing the development and regulatory approval of the first CRISPR-created GM food to be cleared for human consumption

Special Topic 7: Genomics and Precision Medicine • New section, entitled “Precision Oncology,” describing two targeted cancer immunotherapies: adoptive cell transfer and engineered T-cell therapy • Updated section, “Pharmacogenomics,” including a discussion of new trends in preemptive gene screening for pharmacogenomic variants • New box, “Preemptive Pharmacogenomic Screening: The pGEN-4Kids Program,” discussing preemptive gene screening that integrates DNA analysis into patient electronic health records

Emphasis on Concepts

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

To aid students in identifying the conceptual aspects of a major topic, each chapter begins with a section called **Chapter Concepts**, which identifies the most important ideas about to be presented. Then, throughout each chapter, **Essential Points** are provided that establish the key issues that have been discussed. And in the **How Do We Know?** question that starts each chapter’s problem set, students

are asked to identify the experimental basis of important genetic findings presented in the chapter. As an extension of the learning approach in biology called “Science as a Way of Knowing,” this feature enhances students’ understanding of many key concepts covered in each chapter. Finally, the second entry in each chapter’s problem set is labeled as a **Concepts Question**, which asks the student to review and comment on specific aspects of the Chapter Concepts found at the beginning of each chapter.

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

Emphasis on Problem Solving

Helping students develop effective problem-solving skills is one of the greatest challenges of a genetics course. The feature called **Now Solve This**, integrated throughout each chapter, asks students to link conceptual understanding in a more immediate way to problem solving. Each entry provides a problem for the student to solve that is closely related to the current text discussion. A pedagogic hint is then provided to aid in arriving at the correct solution. All chapters conclude with **Insights and Solutions**, a popular and highly useful section that provides sample problems and solutions that demonstrate approaches useful in genetic analysis. These help students develop analytical thinking and experimental reasoning skills. Digesting the information in *Insights and Solutions* primes students as they move on to the lengthier **Problems and Discussion Questions** section that concludes each chapter. Here, we present questions that review topics in the chapter and problems that ask students to think in an analytical and applied way about genetic concepts. The addition of Mastering Genetics extends our focus on problem solving online, and it allows students to get help and guidance while practicing how to solve problems.

Continuing Features

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

■ **Exploring Genomics** Appearing in numerous chapters, this feature illustrates the pervasiveness of genomics in the current study of genetics. Each entry asks students to access one or more genomics-related Web sites that collectively are among the best publicly available resources and databases. Students work through interactive exercises that ensure their familiarity with the type of

genomic or proteomic information available. Exercises instruct students on how to explore specific topics and how to access significant data. Questions guide student exploration and challenge them to further explore the sites on their own. Importantly, *Exploring Genomics* integrates genomics information throughout the text, as this emerging field is linked to chapter content. This feature provides the basis for individual or group assignments in or out of the classroom.

- **Case Studies** This feature, with an increased emphasis on ethical considerations, appears at the end of each chapter and provides the basis for enhanced classroom interactions. In each entry, a short scenario related to one of the chapter topics is presented, followed by several questions. These ask students to apply their newly acquired knowledge to real-life issues that may be explored in small-group discussions or serve as individual assignments.

For the Instructor

Mastering Genetics

<http://www.masteringgenetics.com>

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

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

Instructor Resources

The Instructor Resources, available for download in the Instructor area of Mastering Genetics, offer adopters of the text convenient access to a comprehensive and innovative set of lecture presentation and teaching tools. Developed to meet the needs of veteran and newer instructors alike, these resources include:

- The JPEG files of all text line drawings with labels individually enhanced for optimal projection results (as well as unlabeled versions) and all text tables.
- Most of the text photos, including all photos with pedagogical significance, as JPEG files.
- The JPEG files of line drawings, photos, and tables preloaded into comprehensive PowerPoint presentations for each chapter.
- A second set of PowerPoint presentations consisting of a thorough lecture outline for each chapter augmented by key text illustrations.
- An impressive series of concise instructor animations adding depth and visual clarity to the most important topics and dynamic processes described in the text.
- The instructor animations preloaded into PowerPoint presentation files for each chapter.
- PowerPoint presentations containing a comprehensive set of in-class Classroom Response System (CRS) questions for each chapter.
- In Word files, a complete set of the assessment materials and study questions and answers from the test bank, the text's in-chapter text questions, and the student media practice questions.

TestGen EQ Computerized Testing Software

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

Mastering Genetics

<http://www.masteringgenetics.com>

Used by over a million science students, the Mastering platform is the most effective and widely used online tutorial, homework, and assessment system for the sciences. Perform better on exams with Mastering Genetics. As an instructor-assigned homework system, Mastering Genetics is designed to provide students with a variety of assessments to help them understand key topics and concepts and to build problem-solving skills. Mastering Genetics tutorials guide students through the toughest topics in genetics with self-paced tutorials that provide individualized coaching with hints and feedback specific to a student's individual misconceptions. Students can also explore Mastering Genetics' Study Area, which includes animations, the eText, *Exploring Genomics* exercises, and other study aids. The interactive eText 2.0 allows students to access their text on mobile devices, highlight text, add study notes, review instructor's notes, and search throughout the text, 24/7.

Acknowledgments

Contributors

We begin with special acknowledgments to those who have made direct contributions to this text. We thank Christy Fillman of the University of Colorado—Boulder, Jutta Heller of the University of Washington—Tacoma, Christopher Halweg of North Carolina State University, Pamela Osenkowski of Loyola University—Chicago, Matthew Marcello of Pace University, Susan Wesmiller of University of Pittsburgh School of Nursing, Mandy Schmella of University of Pittsburgh School of Nursing, and Fiona Rawle of the University of Toronto—Mississauga for their work on the media program. Virginia McDonough of Hope College and Cindy Malone of California State University—Northridge contributed greatly to the instructor resources. We thank the following instructors for their work on the test bank: Mark Haefele of Community College of Denver, Scott Harrison of Georgia Southern University, David Kass of Eastern Michigan University, and Stephen Page of Community College of Baltimore County. We also express special thanks to eagle-eyed Michelle Gaudette, recently retired from Tufts University. In her role as author of the *Student Handbook and Solutions Manual* and the test bank, she has reviewed and edited the end of chapter problems and their corresponding solutions in the manual and in the Answers Appendix.

We are grateful to all of these contributors not only for sharing their genetic expertise, but for their dedication to this project as well as the pleasant interactions they provided.

Proofreaders and Accuracy Checking

Reading the detailed manuscript of a textbook deserves more thanks than words can offer. Our utmost appreciation is extended to Michelle Gaudette, Tufts University, and Ann Blakey, Ball State University, who provided accuracy checking of many chapters, and to Kerri Tomasso, who proofread the entire manuscript. They confronted this task with patience and diligence, contributing greatly to the quality of this text.

Reviewers

All comprehensive texts are dependent on the valuable input provided by many reviewers. While we take full responsibility for any errors in this book, we gratefully acknowledge the help provided by those individuals who reviewed the content and pedagogy of this edition:

Jessica Cottrell, Seton Hall University
Tamara Davis, Bryn Mawr College
Christy Fillman, University of Colorado—Boulder
Christy Fleet, Emory and Henry College
Donna-Marie Gardner, Middlesex County College
Christopher Harendza, Montgomery County Community College
Alfredo Leon, Miami Dade College
Tamara Mans, North Hennepin Community College
Holly Morris, Lehigh Carbon Community College
Isaiah G. Schauer, Brazosport College

Brenna Traver, Penn State Schuylkill
Susan Wesmiller, University of Pittsburgh School of Nursing
Michelle Wien, Bryn Mawr College

Special thanks go to Mike Guidry of LightCone Interactive and Karen Hughes of the University of Tennessee for their original contributions to the media program.

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

Editorial and Production Input

At Pearson, we express appreciation and high praise for the editorial guidance of Michael Gillespie, whose ideas and efforts have helped to shape and refine the features of this edition of the text. Brett Coker, our Content Producer, has worked tirelessly to keep the project on schedule and to maintain our standards of high quality. In addition, our editorial team—Ginnie Simone Jutson, Executive Director of Development, Robert Johnson, Rich Media Content Producer, and Sarah Jensen, Director of Editorial Content for Mastering Genetics—have provided valuable input into the current edition. They have worked creatively to ensure that the pedagogy and design of the book and media package are at the cutting edge of a rapidly changing discipline. Brett Coker and Heidi Aguiar supervised all of the production intricacies with great attention to detail and perseverance. Outstanding copyediting was performed by Lucy Mullins, for which we are most grateful. Allison Rona, Alysun Estes, and Kelly Galli have professionally and enthusiastically managed the marketing of the text. Finally, the beauty and consistent presentation of the art work are the product of Imagineering of Toronto. Without the work ethic and dedication of the above individuals, the text would never have come to fruition.

Acknowledgments for the Global Edition

Pearson would like to acknowledge and thank the following for their work on the Global Edition.

Contributor

Juan Pablo Labrador, Trinity College Dublin

Reviewers

Ayse Elif Erson Bengan, Middle East Technical University
Adriaan Engelbrecht, University of the Western Cape
Chris Finlay, University of Glasgow
Francisco Ramos Morales, Universidad de Sevilla
Preeti Srivastava, Indian Institute of Technology Delhi

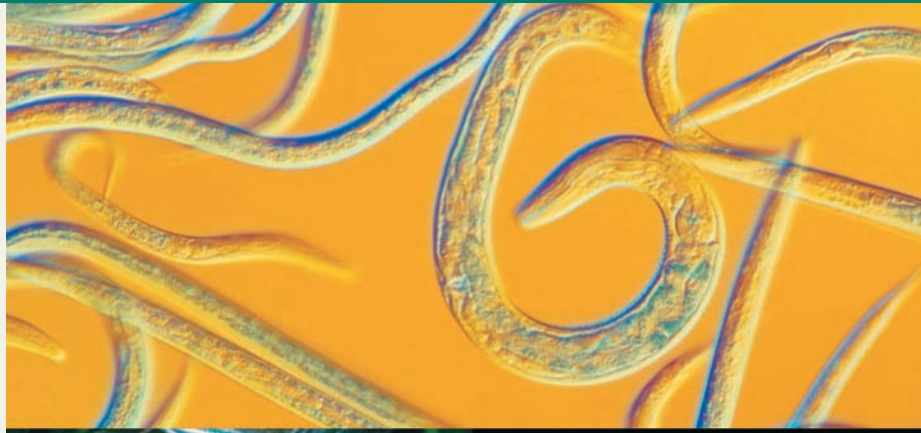
This page intentionally left blank

1

Introduction to Genetics

CHAPTER CONCEPTS

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



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

One of the small pleasures of writing a genetics textbook is being able to occasionally introduce in the very first paragraph of the initial chapter a truly significant breakthrough in the discipline that has started to have a major, diverse impact on human lives. In this edition, we are fortunate to be able to discuss the discovery of **CRISPR-Cas**, a molecular mechanism found in bacteria that has the potential to revolutionize our ability to rewrite the DNA sequence of genes from any organism. As such, it represents the ultimate tool in genetic technology, whereby the genome of organisms, including humans, may be precisely edited. Such gene modification represents the ultimate application of the many advances in biotechnology made in the last 35 years, including the sequencing of the human genome.

Although gene editing was first made possible with other methods, the CRISPR-Cas system is now the method of choice for gene modification because it is more accurate, more efficient, more versatile, and easier to use. CRISPR-Cas was initially discovered as a “seek and destroy” mechanism that bacteria use to fight off viral infection. CRISPR (clustered regularly interspersed short palindromic repeats) refers to part of the bacterial genome that produces RNA molecules, and Cas (CRISPR-associated) refers to a nuclease, or DNA-cutting enzyme. The CRISPR RNA binds to a matching sequence in the viral DNA (seek) and recruits the Cas nuclease to cut it (destroy). Researchers have harnessed this technology by synthesizing CRISPR RNAs that direct Cas nucleases to any chosen DNA sequence. In laboratory experiments, CRISPR-Cas has already been used to repair mutations in cells derived from individuals with genetic disorders, such as cystic fibrosis, Huntington disease,

sickle-cell disease, and muscular dystrophy. In the United States a clinical trial using CRISPR-Cas for genome editing in cancer therapy is recruiting participants, while proposals for treating a genetic form of blindness and genetic blood disorders are in preparation. In China, at least 86 patients have already started receiving treatments in CRISPR-Cas clinical trials for cancer.

The application of this remarkable system goes far beyond developing treatments for human genetic disorders. In organisms of all kinds, wherever genetic modification may benefit human existence and our planet, the use of CRISPR-Cas will find many targets. For example, one research group edited a gene in mosquitoes, which prevents them from carrying the parasite that causes malaria in humans. Other researchers have edited the genome of algae to double their output for biofuel production. The method has also been used to create disease-resistant strains of wheat and rice.

The power of this system, like any major technological advance, has already raised ethical concerns. For example, genetic modification of human embryos would change the genetic information carried by future generations. These modifications may have unintended and significant negative consequences for our species. In 2017, an international panel of experts discussed the science, ethics, and governance of human genome editing. The panel recommended caution, but not a ban, stating that human embryo modification should “only be permitted for compelling reasons and under strict oversight.”

CRISPR-Cas may turn out to be one of the most exciting genetic advances in decades. We will return later in the text to discuss its discovery in bacteria (Chapter 15), its development as a gene-editing tool (Chapter 17), its potential for gene therapy (Special Topic Chapter 3 Gene Therapy), and its uses in genetically edited foods (Special Topic Chapter 6 Genetically Modified Foods).

For now, we hope that this short introduction has stimulated your curiosity, interest, and enthusiasm for the study of genetics. The remainder of this chapter provides an overview of many important concepts of genetics and a survey of the major turning points in the history of the discipline.

1.1 Genetics Has an Interesting Early History

While as early as 350 B.C., Aristotle proposed that active “humors” served as bearers of hereditary traits, it was not until the 1600s that initial strides were made to understand the biological basis of life. In that century, the physician and anatomist William Harvey proposed the theory of **epigenesis**, which states that an organism develops from the fertilized egg

by a succession of developmental events that eventually transform the egg into an adult. The theory of epigenesis directly conflicted with the theory of **preformationism**, which stated that the fertilized egg contains a complete miniature adult, called a **homunculus** (Figure 1.1). Around 1830, Matthias Schleiden and Theodor Schwann proposed the **cell theory**, stating that all organisms are composed of basic structural units called cells, which are derived from preexisting cells. The idea of **spontaneous generation**, the creation of living organisms from nonliving components, was disproved by Louis Pasteur later in the century, and living organisms were then considered to be derived from preexisting organisms and to consist of cells.

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

Darwin and Mendel

In 1859, Darwin published *On the Origin of Species*, describing his ideas about evolution. Darwin’s geological, geographical, and biological observations convinced him that existing species arose by descent with modification from ancestral species. Greatly influenced by his voyage on the HMS *Beagle* (1831–1836), Darwin’s thinking led him to formulate the theory of **natural selection**, which presented an explanation of the mechanism of evolutionary change. Formulated and proposed independently by Alfred Russel Wallace, natural selection is based on the observation



FIGURE 1.1 Depiction of the *homunculus*, a sperm containing a miniature adult, perfect in proportion and fully formed.

that populations tend to produce more offspring than the environment can support, leading to a struggle for survival among individuals. Those individuals with heritable traits that allow them to adapt to their environment are better able to survive and reproduce than those with less adaptive traits. Over time, advantageous variations, even very slight ones, will accumulate. If a population carrying these inherited variations becomes reproductively isolated, a new species may result.

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

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

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

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

Mendel's Work on Transmission of Traits

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

The Chromosome Theory of Inheritance: Uniting Mendel and Meiosis

Mendel did his experiments before the structure and role of chromosomes were known. About 20 years after his work was published, advances in microscopy allowed researchers to identify chromosomes and establish that, in most eukaryotes, members of each species have a characteristic number of chromosomes called the **diploid number** ($2n$) in most of their cells. For example, humans have a diploid number of 46 (**Figure 1.2**). Chromosomes in diploid cells exist in pairs, called **homologous chromosomes**.

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

Early in the twentieth century, Walter Sutton and Theodor Boveri independently noted that the behavior of chromosomes during meiosis is identical to the behavior of genes

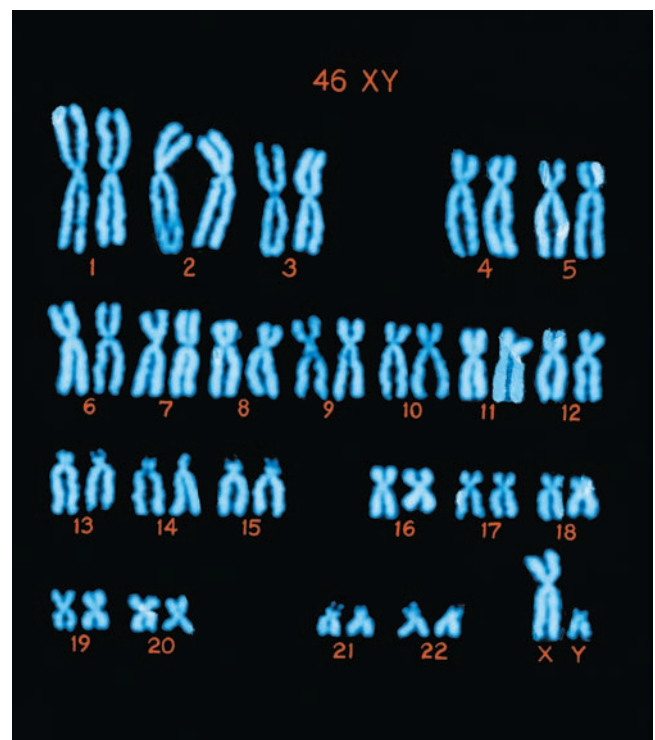


FIGURE 1.2 A colored image of a replicated set of human male chromosomes. Arranged in this way, the set is called a karyotype.

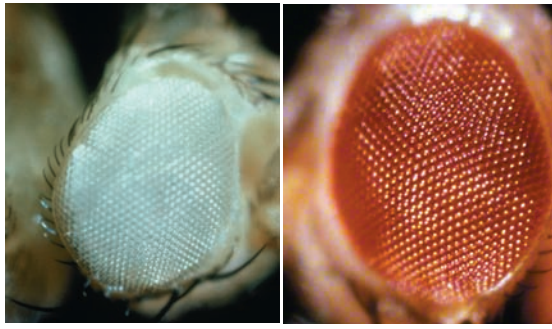


FIGURE 1.3 The white-eyed mutation in *D. melanogaster* (left) and the normal red eye color (right).

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

ESSENTIAL POINT

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

Genetic Variation

About the same time that the chromosome theory of inheritance was proposed, scientists began studying the inheritance of traits in the fruit fly, *Drosophila melanogaster*. Early in this work, a white-eyed fly (Figure 1.3) was discovered among normal (wild-type) red-eyed flies. This variation was produced by a **mutation** in one of the genes controlling eye color. Mutations are defined as any heritable change in the DNA sequence and are the source of all genetic variation.

The white-eye variant discovered in *Drosophila* is an **allele** of a gene controlling eye color. Alleles are defined as alternative forms of a gene. Different alleles may produce differences in the observable features, or **phenotype**, of an organism. The set of alleles for a given trait carried by an organism is called the **genotype**. Using mutant genes as markers, geneticists can map the location of genes on chromosomes (Figure 1.5).

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

Work on white-eyed *Drosophila* showed that the mutant trait could be traced to a single chromosome, confirming the idea that genes are carried on chromosomes. Once this relationship

was established, investigators turned their attention to identifying which chemical component of chromosomes carries genetic information. By the 1920s, scientists knew that proteins and DNA were the major chemical components of chromosomes. There are a large number of different proteins, present in both the nucleus and cytoplasm, and many researchers thought proteins carried genetic information.

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

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

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

The Structure of DNA and RNA

One of the great discoveries of the twentieth century was made in 1953 by James Watson and Francis Crick, who described the structure of DNA. DNA is a long, ladder-like macromolecule that twists to form a double helix (Figure 1.4). Each linear strand of the helix is made up of subunits called **nucleotides**. In DNA, there are four different nucleotides, each of which contains a nitrogenous base, abbreviated A (adenine), G (guanine), T (thymine),

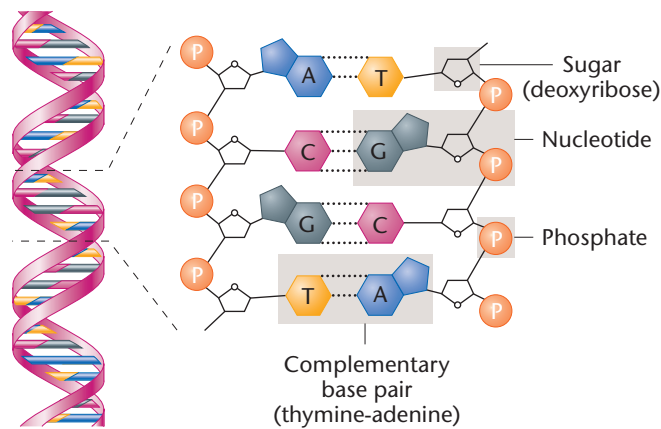


FIGURE 1.4 The structure of DNA showing the arrangement of the double helix (on the left) and the chemical components making up each strand (on the right). The dotted lines on the right represent weak chemical bonds, called hydrogen bonds, which hold together the two strands of the DNA helix.

or C (cytosine). These four bases, in various sequence combinations, ultimately encode genetic information. The two strands of DNA are exact complements of one another, so that the rungs of the ladder in the double helix always consist of A=T and G=C base pairs. Along with Maurice Wilkins, Watson and Crick were awarded a Nobel Prize in 1962 for their work on the structure of DNA. We will discuss the structure of DNA later in the text (see Chapter 9).

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

Gene Expression: From DNA to Phenotype

The genetic information encoded in the order of nucleotides in DNA is expressed in a series of steps that results in the formation of a functional gene product. In the majority of cases, this product is a protein. In eukaryotic cells, the process leading to protein production begins in the nucleus with **transcription**, in which the nucleotide sequence in one strand of DNA is used to construct a complementary RNA sequence (top part of **Figure 1.5**). Once an RNA molecule is produced, it moves to the cytoplasm, where the RNA—called **messenger RNA**, or **mRNA** for short—binds to a **ribosome**. The synthesis of proteins under the direction of mRNA is called **translation** (center part of **Figure 1.5**). The information encoded in mRNA (called the **genetic code**) consists of a linear series of nucleotide triplets. Each triplet, called a **codon**, is complementary to the information stored in DNA and specifies the insertion of a specific amino acid into a protein. Proteins (lower part of **Figure 1.5**) are polymers made up of amino acid monomers. There are 20 different amino acids commonly found in proteins.

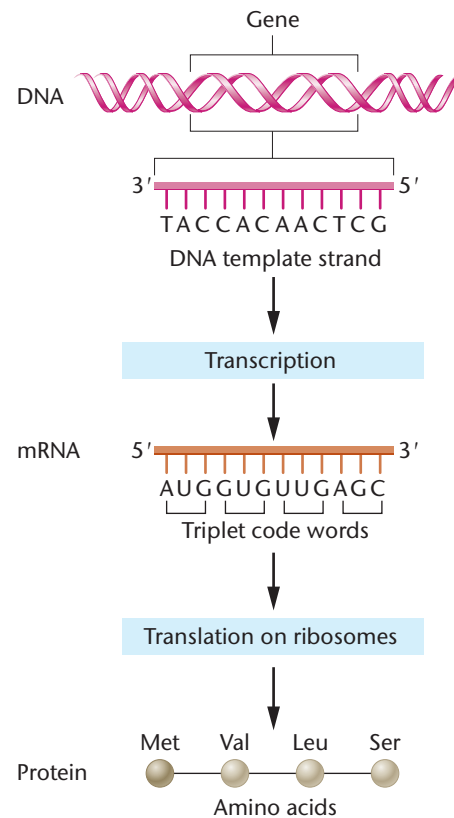


FIGURE 1.5 Gene expression consists of transcription of DNA into mRNA (top) and the translation (center) of mRNA (with the help of a ribosome) into a protein (bottom).

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

We now know that gene expression can be more complex than outlined here. Some of these complexities will be discussed later in the text (see Chapters 15 and 16).

Proteins and Biological Function

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

$$20^{100}$$

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

Enzymes form the largest category of proteins. These molecules serve as biological catalysts, lowering the energy

of activation in reactions and allowing cellular metabolism to proceed at body temperature.

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

Linking Genotype to Phenotype: Sickle-Cell Anemia

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

Sickle-cell anemia is caused by a mutant form of hemoglobin, the protein that transports oxygen from the lungs to cells in the body. Hemoglobin is a composite molecule made up of two different proteins, α -globin and β -globin, each encoded by a different gene. In sickle-cell anemia, a mutation in the gene encoding β -globin causes an amino acid substitution in 1 of the 146 amino acids in the protein.

Figure 1.6 shows the DNA sequence, the corresponding mRNA codons, and the amino acids occupying positions 4–7 for the normal and mutant forms of β -globin. Notice that the mutation in sickle-cell anemia consists of a change in one DNA nucleotide, which leads to a change in codon 6 in mRNA from GAG to GUG, which in turn changes amino acid number 6 in β -globin from glutamic acid to valine. The other 145 amino acids in the protein are not changed by this mutation.

NORMAL β -GLOBIN				
DNA.....	TGA	GGA	CTC	CTC.....
mRNA.....	ACU	CCU	GAG	GAG.....
Amino acid.....	Thr	Pro	Glu	Glu.....
	4	5	6	7
MUTANT β -GLOBIN				
DNA.....	TGA	GGA	CAC	CTC.....
mRNA.....	ACU	CCU	GUG	GAG.....
Amino acid.....	Thr	Pro	Val	Glu.....
	4	5	6	7

FIGURE 1.6 A single-nucleotide change in the DNA encoding β -globin (CTC \rightarrow CAC) leads to an altered mRNA codon (GAG \rightarrow GUG) and the insertion of a different amino acid (Glu \rightarrow Val), producing the altered version of the β -globin protein that is responsible for sickle-cell anemia.

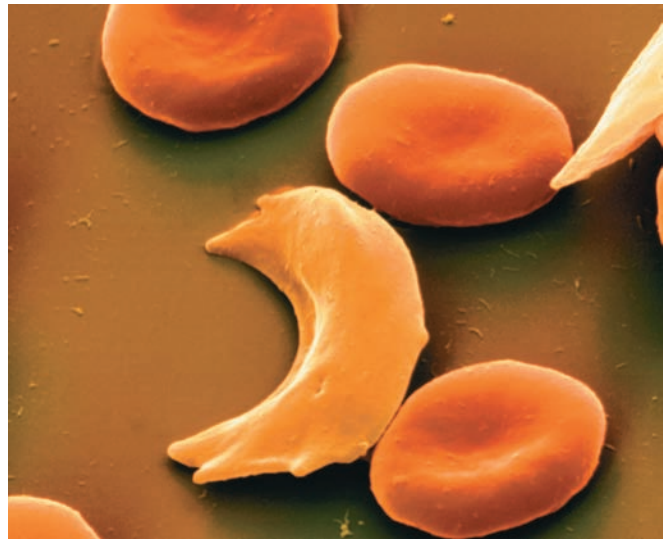


FIGURE 1.7 Normal red blood cells (round) and sickled red blood cells. The sickled cells block capillaries and small blood vessels.

ESSENTIAL POINT

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

Individuals with two mutant copies of the β -globin gene have sickle-cell anemia. Their mutant β -globin proteins cause hemoglobin molecules in red blood cells to polymerize when the blood's oxygen concentration is low, forming long chains of hemoglobin that distort the shape of red blood cells (**Figure 1.7**). Deformed cells are fragile and break easily, reducing the number of circulating red blood cells (anemia is an insufficiency of red blood cells). Sickle-shaped cells block blood flow in capillaries and small blood vessels, causing severe pain and damage to the heart, brain, muscles, and kidneys. All the symptoms of this disorder are caused by a change in a single nucleotide in a gene that changes one amino acid out of 146 in the β -globin molecule, demonstrating the close relationship between genotype and phenotype.

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

The era of recombinant DNA began in the early 1970s, when researchers discovered that **restriction enzymes**, used by bacteria to cut and inactivate the DNA of invading viruses, could be used to cut any organism's DNA at