

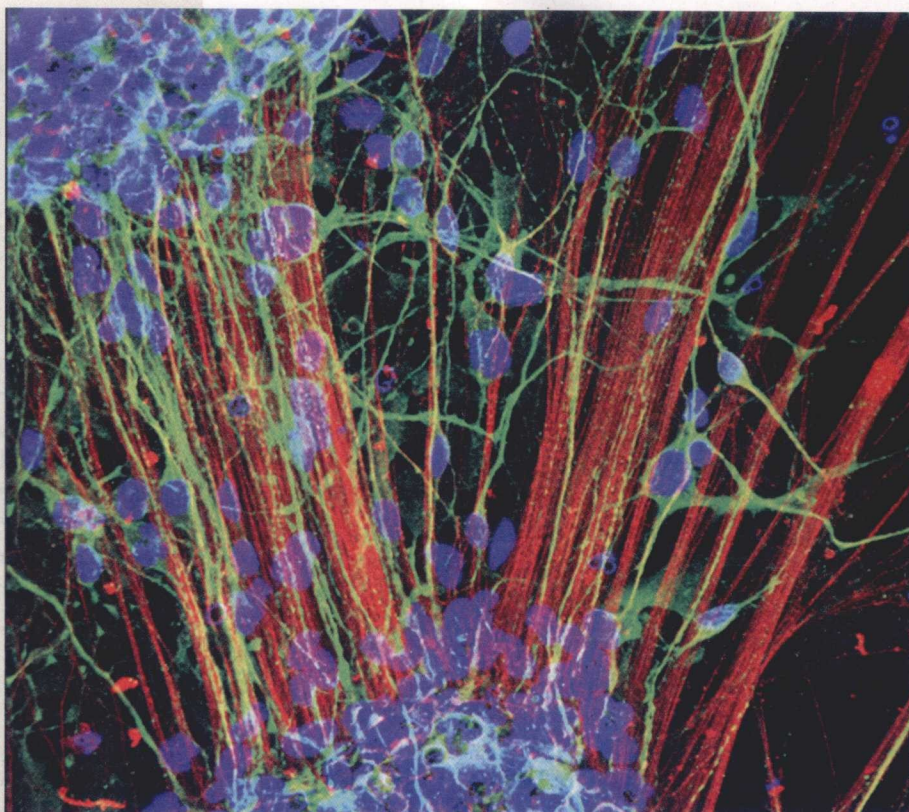
CELL AND MOLECULAR BIOLOGY

CONCEPTS AND EXPERIMENTS

Gerald Karp

7th Edition

7th Edition



Cell and Molecular Biology

Concepts and Experiments

常州大学图书馆
藏书章

Gerald Karp

Chapter 12 was revised in collaboration with

James G. Patton
DEPARTMENT OF BIOLOGICAL SCIENCES
VANDERBILT UNIVERSITY

WILEY

VICE PRESIDENT & PUBLISHER
ACQUISITIONS EDITOR
MARKETING MANAGER
ASSOCIATE DIRECTOR OF MARKETING
CONTENT MANAGER
ASSISTANT EDITOR
ASSOCIATE CONTENT EDITOR
SENIOR PRODUCT DESIGNER
PRODUCTION EDITOR
DESIGN DIRECTOR
SENIOR DESIGNER
PHOTO EDITOR
PRODUCTION MANAGEMENT SERVICES

Kaye Pace
Kevin Witt
Clay Stone
Amy Scholz
Juanita Thompson
Lauren Stauber
Lauren Morris
Bonnie Roth
Sandra Dumas
Harry Nolan
Madelyn Lesure
Jennifer Atkins
Furino Production

COVER PHOTO CREDIT: Courtesy Fred H. Gage and Kristen Brennand

Stethoscope icon repeated throughout text: ©Alan Crawford/istockphoto

This book was typeset in 10.5/12 Adobe Caslon at Aptara and printed and bound by QuadGraphics, Inc. The cover was printed by QuadGraphics, Inc.

Founded in 1807, John Wiley & Sons, Inc. has been a valued source of knowledge and understanding for more than 200 years, helping people around the world meet their needs and fulfill their aspirations. Our company is built on a foundation of principles that include responsibility to the communities we serve and where we live and work. In 2008, we launched a Corporate Citizenship Initiative, a global effort to address the environmental, social, economic, and ethical challenges we face in our business. Among the issues we are addressing are carbon impact, paper specifications and procurement, ethical conduct within our business and among our vendors, and community and charitable support. For more information, please visit our website: www.wiley.com/go/citizenship.

The paper in this book was manufactured by a mill whose forest management programs include sustained yield harvesting of its timberlands. Sustained yield harvesting principles ensure that the number of trees cut each year does not exceed the amount of new growth.

This book is printed on acid-free paper.

Copyright © 2013, 2010, 2008, 2005, 2002 John Wiley and Sons, Inc.. 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, scanning or otherwise, except as permitted under Sections 107 or 108 of the 1976 United States Copyright Act, without either the prior written permission of the Publisher or authorization through payment of the appropriate per-copy fee to the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, (978) 750-8400, fax (978) 646-8600. Requests to the Publisher for permission should be addressed to the Permissions Department, John Wiley & Sons, Inc., 111 River Street, Hoboken, NJ 07030-5774, (201) 748-6011, fax (201) 748-6008.

Evaluation copies are provided to qualified academics and professionals for review purposes only, for use in their courses during the next academic year. These copies are licensed and may not be sold or transferred to a third party. Upon completion of the review period, please return the evaluation copy to Wiley. Return instructions and a free of charge return shipping label are available at www.wiley.com/go/returnlabel. Outside of the United States, please contact your local representative.

ISBN 13 978-1118-20673-7
ISBN 13 978-1118-30179-1

Printed in the United States of America.
10 9 8 7 6 5

Nobel Prizes Awarded for Research in Cell and Molecular Biology Since 1958

<i>Year</i>	<i>Recipient*</i>	<i>Prize</i>	<i>Area of Research</i>	<i>Pages in Text</i>
2012	John B. Gurdon	M & P**	Animal cloning, nuclear reprogramming	513
	Shinya Yamanaka		Cell reprogramming	22, 519
	Brian K. Kobilka	Chemistry	G protein-coupled receptors	621
	Robert J. Lefkowitz			
2011	Bruce A. Beutler	M & P	Innate immunity	700
	Jules A. Hoffmann		Dendritic cells and Adaptive immunity	707
	Ralph M. Steinman			
2009	Venkatraman Ramakrishnan	Chemistry	Ribosome structure and function	479
	Thomas A. Steitz			
	Ada E. Yonath			
	Eliazbeth H. Blackburn	M & P	Telomeres and telomerase	505
2008	Carol W. Greider			
	Jack W. Szostak			
	Francoise Barré-Sinoussi	M & P	Discovery of HIV	24
	Luc Montagnier			
2007	Harald zur Hausen		Role of HPV in cancer	668
	Martin Chalfie	Chemistry	Discovery and development of GFP	273, 737
	Osamu Shimomura			
	Roger Tsien			
2006	Mario R. Capecchi	M & P	Development of techniques for knockout mice	778
	Martin J. Evans			
	Oliver Smithies			
2004	Andrew Z. Fire	M & P	RNA Interference	455, 780
	Craig C. Mello			
	Roger D. Kornberg	Chemistry	Transcription in eukaryotes	433, 494
2003	Richard Axel	M & P	Olfactory receptors	634
	Linda B. Buck			
	Aaron Ciechanover	Chemistry	Ubiquitin and proteasomes	541
	Avram Hershko			
2002	Irwin Rose			
	Peter Agre	Chemistry	Structure of membrane channels	150, 152
2001	Roderick MacKinnon			
	Sydney Brenner	M & P	Introduction of <i>C. elegans</i> as a model organism	18
	John Sulston			
	H. Robert Horvitz		Apoptosis in <i>C. elegans</i>	657
2000	John B. Fenn	Chemistry	Electrospray ionization in MS	758
	Koichi Tanaka		MALDI in MS	758
	Kurt Wüthrich		NMR analysis of proteins	57
	Leland H. Hartwell	M & P	Control of the cell cycle	576, 611
1999	Tim Hunt			
	Paul Nurse			
	Arvid Carlsson	M & P	Synaptic transmission and signal transduction	168
1998	Paul Greengard			617
	Eric Kandel			
	Günter Blobel	M & P	Protein trafficking	281
1997	Robert Furchgott	M & P	NO as intercellular messenger	655
	Louis Ignarro			
	Ferid Murad			

<i>Year</i>	<i>Recipient*</i>	<i>Prize</i>	<i>Area of Research</i>	<i>Pages in Text</i>
1997	Jens C. Skou	Chemistry	Na ⁺ /K ⁺ -ATPase	157
	Paul Boyer		Mechanism of ATP synthesis	201
	John Walker			
	Stanley B. Prusiner	M & P	Protein nature of prions	66
1996	Rolf M. Zinkernagel	M & P	Recognition of virus-infected cells by the immune system	727
	Peter C. Doherty			
1995	Edward B. Lewis	M & P	Genetic control of embryonic development	EP12
	Christiane Nüsslein-Volhard			
	Eric Wieschaus			
1994	Alfred Gilman	M & P	Structure and function of GTP-binding (G) proteins	624
	Martin Rodbell			
1993	Kary Mullis	Chemistry	Polymerase chain reaction (PCR)	769
	Michael Smith		Site-directed mutagenesis (SDM)	778
	Richard J. Roberts	M & P	Intervening sequences	444
	Phillip A. Sharp			
1992	Edmond Fischer	M & P	Alteration of enzyme activity by phosphorylation/dephosphorylation	115, 627
	Edwin Krebs			
1991	Erwin Neher	M & P	Measurement of ion flux by patch-clamp recording	152
	Bert Sakmann			
1990	Joseph E. Murray	M & P	Organ and cell transplantation in human disease	716, 20
	E. Donnall Thomas			
1989	J. Michael Bishop	M & P	Cellular genes capable of causing malignant transformation	695
	Harold Varmus			
	Thomas R. Cech	Chemistry	Ability of RNA to catalyze reactions	477
	Sidney Altman			
1988	Johann Deisenhofer	Chemistry	Bacterial photosynthetic reaction center	218
	Robert Huber			
	Hartmut Michel			
1987	Susumu Tonegawa	M & P	DNA rearrangements responsible for antibody diversity	713
1986	Rita Levi-Montalcini	M & P	Factors that affect nerve outgrowth	379
	Stanley Cohen			
1985	Michael S. Brown	M & P	Regulation of cholesterol metabolism and endocytosis	319
	Joseph L. Goldstein			
1984	Georges Köhler	M & P	Monoclonal antibodies	782
	Cesar Milstein			
	Niels K. Jerne		Antibody formation	704
1983	Barbara McClintock	M & P	Mobile elements in the genome	408
1982	Aaron Klug	Chemistry	Structure of nucleic acid-protein complexes	79
1980	Paul Berg	Chemistry	Recombinant DNA technology	764
	Walter Gilbert		DNA sequencing technology	771
	Frederick Sanger			
	Baruj Bennacerraf	M & P	Major histocompatibility complex	716
	Jean Dausset			
	George D. Snell			
1978	Werner Arber	M & P	Restriction endonuclease technology	764
	Daniel Nathans			
	Hamilton O. Smith			
	Peter Mitchell	Chemistry	Chemiosmotic mechanism of oxidative phosphorylation	187
1976	D. Carleton Gajdusek	M & P	Prion-based diseases	66
1975	David Baltimore	M & P	Reverse transcriptase and tumor virus activity	694
	Renato Dulbecco			
	Howasrd M. Temin			

<i>Year</i>	<i>Recipient*</i>	<i>Prize</i>	<i>Area of Research</i>	<i>Pages in Text</i>
1974	Albert Claude Christian de Duve George E. Palade	M & P	Structure and function of internal components of cells	275
1972	Gerald Edelman Rodney R. Porter Christian B. Anfinsen	M & P Chemistry	Immunoglobulin structure Relationship between primary and tertiary structure of proteins	711 63
1971	Earl W. Sutherland	M & P	Mechanism of hormone action and cyclic AMP	627
1970	Bernard Katz Ulf von Euler Luis F. Leloir	M & P Chemistry	Nerve impulse propagation and transmission Role of sugar nucleotides in carbohydrate synthesis	165 285
1969	Max Delbrück Alfred D. Hershey Salvador E. Luria	M & P	Genetic structure of viruses	23, 422
1968	H. Gobind Khorana Marshall W. Nirenberg Robert W. Holley	M & P	Genetic code Transfer RNA structure	462 465
1966	Peyton Rous	M & P	Tumor viruses	694
1965	Francois Jacob Andre M. Lwoff Jacques L. Monod	M & P	Bacterial operons and messenger RNA	484, 428
1964	Dorothy C. Hodgkin	Chemistry	X-ray structure of complex biological molecules	758
1963	John C. Eccles Alan L. Hodgkin Andrew F. Huxley	M & P	Ionic basis of nerve membrane potentials	164
1962	Francis H. C. Crick James D. Watson Maurice H. F. Wilkins John C. Kendrew Max F. Perutz	M & P Chemistry	Three-dimensional structure of DNA Three-dimensional structure of globular proteins	393 58
1961	Melvin Calvin	Chemistry	Biochemistry of CO ₂ assimilation during photosynthesis	226
1960	F. MacFarlane Burnet Peter B. Medawar	M & P	Clonal selection theory of antibody formation	704
1959	Arthur Kornberg Severo Ochoa	M & P	Synthesis of DNA and RNA	550, 463
1958	George W. Beadle Joshua Lederberg Edward L. Tatum Frederick Sanger	M & P Chemistry	Gene expression Primary structure of proteins	427 55

*In a few cases, corecipients whose research was in an area outside of cell and molecular biology have been omitted from this list.

**Medicine and Physiology

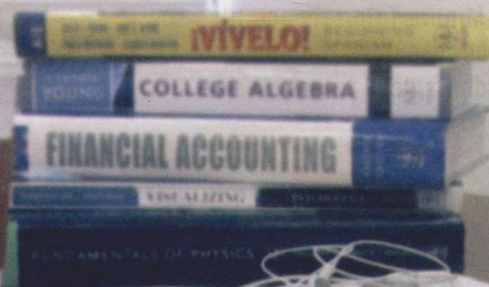
WileyPLUS

WileyPLUS is a research-based online environment for effective teaching and learning.

WileyPLUS builds students' confidence because it takes the guesswork out of studying by providing students with a clear roadmap:

- what to do
- how to do it
- if they did it right

It offers interactive resources along with a complete digital textbook that help students learn more. With *WileyPLUS*, students take more initiative so you'll have greater impact on their achievement in the classroom and beyond.



Now available for



Blackboard

For more information, visit www.wileyplus.com

WileyPLUS

**ALL THE HELP, RESOURCES, AND PERSONAL
SUPPORT YOU AND YOUR STUDENTS NEED!**

www.wileyplus.com/resources

**1st DAY OF
CLASS**
... AND BEYOND!

2-Minute Tutorials and all
of the resources you and your
students need to get started

WileyPLUS

**Student
Partner
Program**

Student support from an
experienced student user

Wiley Faculty Network



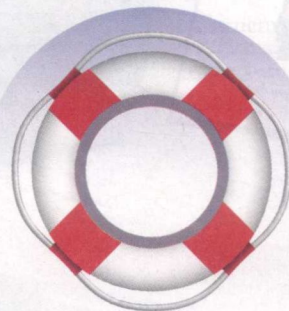
Collaborate with your colleagues,
find a mentor, attend virtual and live
events, and view resources

www.WhereFacultyConnect.com

WileyPLUS

**Quick
Start**

Pre-loaded, ready-to-use
assignments and presentations
created by subject matter experts



Technical Support 24/7
FAQs, online chat,
and phone support

www.wileyplus.com/support



© Courtney Keating/
iStockphoto

Your *WileyPLUS* Account Manager,
providing personal training
and support

To Patsy and Jenny

About the Author

Gerald C. Karp received a bachelor's degree from UCLA and a Ph.D. from the University of Washington. He conducted postdoctoral research at the University of Colorado Medical Center before joining the faculty at the University of Florida. Gerry is the author of numerous research articles on the cell and molecular biology of early development. His interests have included the synthesis of RNA in early embryos, the movement of mesenchyme cells during gastrulation, and

cell determination in slime molds. For 13 years, he taught courses in molecular, cellular, and developmental biology at the University of Florida. During this period, Gerry coauthored a text in developmental biology with N. John Berrill and authored a text in cell and molecular biology. Finding it impossible to carry on life as both full-time professor and author, Gerry gave up his faculty position to concentrate on the revision of this textbook every three years.

About the Cover

The micrograph on the cover of the book shows human nerve cells that have developed (differentiated) in a culture dish from undifferentiated stem cells. The stem cells used in this experiment were pluripotent cells, that is, they were capable of developing into any one of the many different types of cells that make up the human body. In this experiment, the stem cells were driven to differentiate specifically into nerve cells by adding a number of neuron-specific factors to the medium in which the stem cells were growing. Normally, human pluripotent stem cells are only found within the very early stages of a human embryo, but the stem cells used in this experiment were not derived from an embryo but instead were generated experimentally. They were induced from a type of connective tissue cell called a fibroblast by forcing the fibroblast to express a number of genes that it would not normally express. Forcing adult fibroblasts (or other types of adult cells) to express these

"stem cell genes" causes them to lose their differentiated properties, such as the production of collagen, and become what has been termed *induced pluripotent stem cells* (or *iPS cells*). As discussed on page 22, iPS cells may one day play a key role in replacing the cells of diseased tissues and organs. The fibroblasts used in this experiment were not derived from a healthy person but from a person who had been diagnosed with schizophrenia. We don't understand the molecular basis of schizophrenia, but it is hoped that studying the differentiation of nerve cells from persons with this disease will provide important insights into the underlying basis of the disease. Such cells may also serve as a useful tool to screen potential drugs for their effectiveness in treating the disease being studied. Because of these features, such iPS cells have been referred to as "patients in a Petri dish." (Courtesy Fred H. Gage and Kristen Brennand.)

Preface to the Seventh Edition

Before I began work on the *first* edition of this text, I drew up a number of basic guidelines regarding the type of book I planned to write.

- I wanted a text suited for an introductory course in cell and molecular biology that ran either a single semester or 1–2 quarters. I set out to draft a text of about 800 pages that would not overwhelm or discourage students at this level.
- I wanted a text that elaborated on fundamental concepts, such as the relationship between molecular structure and function, the dynamic character of cellular organelles, the use of chemical energy in running cellular activities and ensuring accurate macromolecular biosynthesis, the observed unity and diversity at the macromolecular and cellular levels, and the mechanisms that regulate cellular activities.
- I wanted a text that was grounded in the experimental approach. Cell and molecular biology is an experimental science and, like most instructors, I believe students should gain some knowledge of how we know what we know. With this in mind, I decided to approach the experimental nature of the subject in two ways. As I wrote each chapter, I included enough experimental evidence to justify many of the conclusions that were being made. Along the way, I described the salient features of key experimental approaches and research methodologies. Chapters 8 and 9, for example, contain introductory sections on techniques that have proven most important in the analysis of cytomembranes and the cytoskeleton, respectively. I included brief discussions of selected experiments of major importance in the body of the chapters to reinforce the experimental basis of our knowledge. I placed the more detailed aspects of methodologies in a final “techniques chapter” because (1) I did not want to interrupt the flow of discussion of a subject with a large tangential section on technology and (2) I realized that different instructors prefer to discuss a particular technology in connection with different subjects.

For students and instructors who wanted to explore the experimental approach in greater depth, I included an Experimental Pathways at the end of most chapters. Each of these narratives describes some of the key experimental findings that have led to our current understanding of a particular subject that is relevant to the chapter at hand. Because the scope of the narrative is limited, the design of the experiments can be considered in some detail. The figures and tables provided in these sections are often those that appeared in the original research article, which provides the reader an opportunity to examine original data and to realize that its analysis is not beyond their means. The Experimental Pathways also illustrate the stepwise nature of scientific discovery, showing how the result of one study raises questions that provide the basis for subsequent studies.

- I wanted a text that was interesting and readable. To make the text more relevant to undergraduate readers, particularly premedical students, I included The Human Perspective. These sections illustrate that virtually all human disorders can

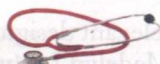
be traced to disruption of activities at the cellular and molecular level. Furthermore, they reveal the importance of basic research as the pathway to understanding and eventually treating most disorders. In Chapter 11, for example, The Human Perspective describes how small synthetic siRNAs may prove to be an important new tool in the treatment of cancer and viral diseases, including AIDS. In this same chapter, the reader will learn how the action of such RNAs were first revealed in studies on plants and nematodes. It becomes evident that one can never predict the practical importance of basic research in cell and molecular biology. I have also tried to include relevant information about human biology and clinical applications throughout the body of the text.

- I wanted a high-quality illustration program that helped students visualize complex cellular and molecular processes. To meet this goal, many of the illustrations have been “stepped-out” so that information can be more easily broken down into manageable parts. Events occurring at each step are described in the figure legend and/or in the corresponding text. I also sought to include a large number of micrographs to enable students to see actual representations of most subjects being discussed. Included among the images are many fluorescence micrographs that illustrate either the dynamic properties of cells or provide a means to localize a specific protein or nucleic acid sequence. Wherever possible, I have tried to pair line art drawings with micrographs to help students compare idealized and actual versions of a structure.

The most important changes in the seventh edition can be delineated as follows:

- Each of the illustrations has been carefully scrutinized and a large number of drawings have been modified with the goal of achieving greater consistency and quality. Particular attention has been paid to the continuity of color and rendering style for each structure and element, as they are represented within each figure, and throughout the book.
- The illustration program for the seventh edition includes a new feature called Figure in Focus. The premise of this feature is to highlight one of the chapter’s key topics in a visually interesting way. Focusing attention on these figures, through the use of line art, 3D molecular models, and micrographs, provides a clear visual explanation of one of the chapter’s core concepts.
- The body of information in cell and molecular biology is continually changing, which provides much of the excitement we all feel about our selected field. Even though only three years have passed since the publication of the sixth edition, nearly every discussion in the text has been modified to a greater or lesser degree. This has been done without allowing the chapters to increase significantly in length.
- Altogether, the seventh edition contains more than 100 new micrographs and computer-derived images, all of which were provided by the original source.

WileyPLUS



This online teaching and learning environment integrates the **entire digital textbook** with the most effective instructor and student resources to fit every learning style.

With *WileyPLUS*:

- Students achieve concept mastery in a rich, structured environment that's available 24/7
- Instructors personalize and manage their course more effectively with assessment, assignments, grade tracking, and more.

WileyPLUS can complement your current textbook or replace the printed text altogether.

For Students

Personalize the learning experience

Different learning styles, different levels of proficiency, different levels of preparation—each of your students is unique. *WileyPLUS* empowers them to take advantage of their individual strengths:

- Students receive timely access to resources that address their demonstrated needs, and get immediate feedback and remediation when needed.
- Integrated, multi-media resources include
 - Animations of key concepts based on the illustrations of the text.
 - Video library of clips from leading journals which can now be assigned with accompanying questions by Anne Hemsley, Antelope Valley Community College.
- *WileyPLUS* includes many opportunities for self-assessment linked to the relevant portions of the text. Students can take control of their own learning and practice until they master the material.

For Instructors

Personalize the teaching experience

WileyPLUS empowers you with the tools and resources you need to make your teaching even more effective:

- You can customize your classroom presentation with a wealth of resources and functionality from PowerPoint slides to a database of rich visuals. You can even add your own materials to your *WileyPLUS* course.

- With *WileyPLUS* you can identify those students who are falling behind and intervene accordingly, without having to wait for them to come to office hours.
- *WileyPLUS* simplifies and automates such tasks as student performance assessment, making assignments, scoring student work, keeping grades, and more.

- Pre and Post Lecture Assessment by Joel Piperberg, Millersville University.
- Test Bank, Instructor's Manual, and "Clicker" Questions by Joel Piperberg, Millersville University.
- **NEW** Lecture PowerPoint Presentations by Edmund B. Rucker, University of Kentucky.

Clinical and Experimental Focus!



- Clinical Case Studies and accompanying questions by Claire Walczak, Indiana University & Anthony Contento, SUNY Oswego.
- Clinical Connections Questions by Sarah VanVickle-Chavez, Washington University in St. Louis.
- Experimental Pathways Questions by Joel Piperberg, Millersville University.
- **NEW** Figure in Focus feature by Anthony Contento, SUNY Oswego, New podcasts & assessment questions accompany selected figures, highlighting important concepts & processes.

Book Companion Site (www.wiley.com/college/karp)

For the Student

- Quizzes for student self-testing.
- *Biology NewsFinder*; *Flash Cards*; and *Animations*.
- Answers to the end-of chapter Analytic Questions.
- Additional reading resources provide students with an extensive list of additional useful sources of information.
- Experimental Pathways for Chapters 5, 6, 7, 9, 12, 13, and 15.

For the Instructor

- Biology Visual Library; all images in jpg and PowerPoint formats.
- Instructor's Manual; Test Bank; Clicker Questions; Lecture PowerPoint Presentations.

Instructor Resources are password protected.

Acknowledgments

I am particularly grateful to James Patton of Vanderbilt University for providing a revised version of Chapter 12 on The Control of Gene Expression, which formed the basis of the current chapter in this text. There are many people at John Wiley & Sons who have made important contributions to this text. I continue to be grateful to Geraldine Osnato whose work and

support over two editions is not forgotten. Ably taking her place in this edition was Lauren Stauber, who served as the assistant editor on the project with the guidance of Kevin Witt. Thanks also go to Lauren Morris for directing the development of the diverse supplements that are offered with this text. I am particularly indebted to the Wiley production

staff, who are simply the best. Jeanine Furino, of Furino Production, served as the central nervous system, coordinating the information arriving from composers, copyeditors, proofreaders, illustrators, photo editors, designers, and dummies, as well as the constant barrage of text changes ordered by the author. Always calm, organized, and meticulous, she made sure everything was done correctly. Hilary Newman and Jennifer Atkins were responsible for obtaining all of the many new images that are found in this edition. Hilary and Jennifer are skillful and perseverant, and I have utmost confidence in their ability to obtain any image requested. The book has a complex illustration program and Kathy Naylor did a superb job in coordinating all of the many facets required

to guide it to completion. The elegant design of the book and cover is due to the efforts of Madelyn Lesure, whose talents are evident. A special thanks is owed Laura Ierardi who skillfully laid out the pages for each chapter.

I am especially thankful to the many biologists who have contributed micrographs for use in this book; more than any other element, these images bring the study of cell biology to life on the printed page. Finally, I would like to apologize in advance for any errors that may occur in the text, and express my heartfelt embarrassment. I am grateful for the constructive criticism and sound advice from the following reviewers of the most recent editions:

Seventh edition reviewers:

STEVE ALAS
*California State Polytechnic University,
Pomona*

RAVI ALLADA
Northwestern University

KARL J. AUFDERHEIDE
Texas A&M University

KENNETH J. BALAZOVICH
University of Michigan

ALLAN BLAKE
Seton Hall University

MARTIN BOOTMAN
Babraham Institute

DAVID BOURGAIZE
Whittier College

KENT D. CHAPMAN
University of North Texas

KATE COOPER
Loras College

LINDA DEVEAUX
Idaho State University

RICHARD E. DEARBORN
Albany College of Pharmacy

BENJAMIN GLICK
The University of Chicago

REGINALD HALABY
Montclair State University

MICHAEL HAMPSEY
*University of Medicine and Dentistry
of New Jersey*

MICHAEL HARRINGTON
University of Alberta

MARCIA HARRISON
Marshall University

R. SCOTT HAWLEY
American Cancer Society Research Professor

REBECCA HEALD
University of California, Berkeley

MARK HENS
University of North Carolina, Greensboro

JEN-CHIH HSIEH
State University of New York at Stony Brook

MICHAEL JONZ
University of Ottawa

ROLAND KAUNAS
Texas A&M University

TOM KELLER
Florida State University

REBECCA KELLUM
University of Kentucky

GREG M. KELLY
University of Western Ontario

KIM KIRBY
University of Guelph

CLAIRE M. LEONARD
William Paterson University

FAITH LIEBL
Southern Illinois University, Edwardsville

JON LOWRANCE
Lipscomb University

CHARLES MALLERY
University of Miami

MICHAEL A. MCALEAR
Wesleyan University

JOANN MEERSCHAERT
St. Cloud State University

JOHN MENNINGER
University of Iowa

KIRSTEN MONSEN
Montclair State University

ALAN NIGHORN
University of Arizona

ROBERT M. NISSEN
*California State University,
Los Angeles*

VERONICA C. NWOSU
North Carolina Central University

GREG ODORIZZI
University of Colorado, Boulder

JAMES G. PATTON
Vanderbilt University

CHARLES PUTNAM
University of Arizona

DAVID REISMAN
University of South Carolina

SHIVENDRA V. SAHI
Western Kentucky University

INDER M. SAXENA
University of Texas, Austin

TIM SCHUH
St. Cloud State University

ERIC SHELDEN
Washington State University

ROGER D. SLOBODA
Dartmouth College

ANN STURTEVANT
University of Michigan-Flint

WILLIAM TERZAGHI
Wilkes University

PAUL TWIGG
University of Nebraska-Kearney

CLAIRE E. WALCZAK
Indiana University

PAUL E. WANDA
Southern Illinois University, Edwardsville

ANDREW WOOD
Southern Illinois University

DANIELA ZARNESCU
University of Arizona

JIANZHI ZHANG
University of Michigan

Thanks are still owed to the following reviewers of the previous several editions:

LINDA AMOS
MRC Laboratory of Molecular Biology

GERALD T. BABCOCK
Michigan State University

WILLIAM E. BALCH
The Scripps Research Institute

JAMES BARBER
Imperial College of Science—Wolfson Laboratories

JOHN D. BELL
Brigham Young University

WENDY A. BICKMORE
Medical Research Council, United Kingdom

ASHOK BIDWAI
West Virginia University

- DANIEL BRANTON
Harvard University
- THOMAS R. BREEN
Southern Illinois University
- SHARON K. BULLOCK
Virginia Commonwealth University
- RODERICK A. CAPALDI
University of Oregon
- GORDON G. CARMICHAEL
University of Connecticut Health Center
- RATNA CHAKRABARTI
University of Central Florida
- K. H. ANDY CHOO
*Royal Children's Hospitals—
The Murdoch Institute*
- DENNIS O. CLEGG
University of California—Santa Barbara
- RONALD H. COOPER
University of California—Los Angeles
- PHILIPPA D. DARBRE
University of Reading
- ROGER W. DAVENPORT
University of Maryland
- SUSAN DESIMONE
Middlebury College
- BARRY J. DICKSON
Research Institute of Molecular Pathology
- DAVID DOE
Westfield State College
- ROBERT S. DOTSON
Tulane University
- JENNIFER A. DOUDNA
Yale University
- MICHAEL EDIDIN
Johns Hopkins University
- EVAN E. EICHLER
University of Washington
- ARRI EISEN
Emory University
- ROBERT FILLINGAME
University of Wisconsin Medical School
- ORNA COHEN-FIX
*National Institute of Health, Laboratory of
Molecular and Cellular Biology*
- JACEK GAERTIG
University of Georgia
- REGINALD HALABY
Montclair State University
- ROBERT HELLING
University of Michigan
- ARTHUR HORWICH
Yale University School of Medicine
- JOEL A. HUBERMAN
Roswell Park Cancer Institute
- GREGORY D. D. HURST
University College London
- KEN JACOBSON
University of North Carolina
- MARIE JANICKE
University at Buffalo—SUNY
- HAIG H. KAZAZIAN, JR.
University of Pennsylvania
- LAURA R. KELLER
Florida State University
- NEMAT O. KEYHANI
University of Florida
- NANCY KLECKNER
Harvard University
- WERNER KÜHLBRANDT
Max-Planck-Institut für Biophysik
- JAMES LAKE
University of California—Los Angeles
- ROBERT C. LIDDINGTON
Burnham Institute
- VISHWANATH R. LINGAPPA
University of California—San Francisco
- JEANNETTE M. LOUTSCH
Arkansas State University
- MARGARET LYNCH
Tufts University
- ARDYTHE A. MCCrackEN
University of Nevada—Reno
- THOMAS MCKNIGHT
Texas A&M University
- MICHELLE MORITZ
University of California—San Francisco
- ANDREW NEWMAN
Cambridge University
- JONATHAN NUGENT
University of London
- MIKE O'DONNELL
Rockefeller University
- JAMES PATTON
Vanderbilt University
- HUGH R. B. PELHAM
MRC Laboratory of Molecular Biology
- JONATHAN PINES
Wellcome/CRC Institute
- DEBRA PIRES
University of California—Los Angeles
- MITCH PRICE
Pennsylvania State University
- DONNA RITCH
University of Wisconsin—Green Bay
- JOEL L. ROSENBAUM
Yale University
- WOLFRAM SAENGER
Freie Universität Berlin
- RANDY SCHEKMAN
University of California—Berkeley
- SANDRA SCHMID
The Scripps Research Institute
- TRINA SCHROER
Johns Hopkins University
- DAVID SCHULTZ
University of Louisville
- ROD SCOTT
Wheaton College
- KATIE SHANNON
University of North Carolina—Chapel Hill
- JOEL B. SHEFFIELD
Temple University
- DENNIS SHEVLIN
College of New Jersey
- HARRIETT E. SMITH-SOMERVILLE
University of Alabama
- BRUCE STILLMAN
Cold Spring Harbor Laboratory
- ADRIANA STOICA
Georgetown University
- COLLEEN TALBOT
California State University, San Bernardino
- GISELLE THIBAUDEAU
Mississippi State University
- JEFFREY L. TRAVIS
University at Albany—SUNY
- NIGEL UNWIN
MRC Laboratory of Molecular Biology
- AJIT VARKI
University of California—San Diego
- JOSE VAZQUEZ
New York University
- JENNIFER WATERS
Harvard University
- CHRIS WATTERS
Middlebury College
- ANDREW WEBBER
Arizona State University
- BEVERLY WENDLAND
Johns Hopkins University
- GARY M. WESSEL
Brown University
- ERIC V. WONG
University of Louisville
- GARY YELLEN
Harvard Medical School
- MASASUKE YOSHIDA
Tokyo Institute of Technology
- ROBERT A. ZIMMERMAN
University of Massachusetts

To the Student

At the time I began college, biology would have been at the bottom of a list of potential majors. I enrolled in a physical anthropology course to fulfill the life science requirement by the easiest possible route. During that course, I learned for the first time about chromosomes, mitosis, and genetic recombination, and I became fascinated by the intricate activities that could take place in such a small volume of cellular space. The next semester, I took Introductory Biology and began to seriously consider becoming a cell biologist. I am burdening you with this personal trivia so you will understand why I wrote this book and to warn you of possible repercussions.

Even though many years have passed, I still find cell biology the most fascinating subject to explore, and I still love spending the day reading about the latest findings by colleagues in the field. Thus, for me, writing a text on cell biology provides a reason and an opportunity to keep abreast with what is going on throughout the field. My primary goal in writing this text is to help generate an appreciation in students for the activities in which the giant molecules and minuscule structures that inhabit the cellular world of life are engaged. Another goal is to provide the reader with an insight into the types of questions that cell and molecular biologists ask and the experimental approaches they use to seek answers. As you read the text, think like a researcher; consider the evidence that is presented, think of alternate explanations, plan experiments that could lead to new hypotheses.

You might begin this approach by looking at one of the many electron micrographs that fill the pages of this text. To take this photograph, you would be sitting in a small, pitch-black room in front of a large metallic instrument whose column rises several meters above your head. You are looking through a pair of binoculars at a vivid, bright green screen. The parts of the cell you are examining appear dark and colorless against the bright green background. They are dark because they've been stained with heavy metal atoms that deflect a fraction of the electrons within a beam that is being focused on the viewing screen by large electromagnetic lenses in the wall of the column. The electrons that strike the screen are accelerated through the evacuated space of the column by a force of tens of thousands of volts. One of your hands may be gripping a knob that controls the magnifying power of the lenses. A simple turn of this knob can switch the image in front of your eyes from that of a whole field of cells to a tiny part of a cell, such as a few ribosomes or a small portion of a single membrane. By turning other knobs, you can watch different parts of the specimen glide across the screen, giving you the sensation that you're driving around inside a cell.

Because the study of cell function requires the use of considerable instrumentation, such as the electron microscope just described, the investigator is physically removed from the subject being studied. To a large degree, cells are like tiny black boxes. We have developed many ways to probe the

boxes, but we are always groping in an area that cannot be fully illuminated. A discovery is made or a new technique is developed and a new thin beam of light penetrates the box. With further work, our understanding of the structure or process is broadened, but we are always left with additional questions. We generate more complete and sophisticated constructions, but we can never be sure how closely our views approach reality. In this regard, the study of cell and molecular biology can be compared to the study of an elephant as conducted by six blind men in an old Indian fable. The six travel to a nearby palace to learn about the nature of elephants. When they arrive, each approaches the elephant and begins to touch it. The first blind man touches the side of the elephant and concludes that an elephant is smooth like a wall. The second touches the trunk and decides that an elephant is round like a snake. The other members of the group touch the tusk, leg, ear, and tail of the elephant, and each forms his impression of the animal based on his own limited experiences. Cell biologists are limited in a similar manner as to what they can learn by using a particular technique or experimental approach. Although each new piece of information adds to the preexisting body of knowledge to provide a better concept of the activity being studied, the total picture remains uncertain.

Before closing these introductory comments, let me take the liberty of offering the reader some advice: Don't accept everything you read as being true. There are several reasons for urging such skepticism. Undoubtedly, there are errors in this text that reflect the author's ignorance or misinterpretation of some aspect of the scientific literature. But, more importantly, we should consider the nature of biological research. Biology is an empirical science; nothing is ever proved. We compile data concerning a particular cell organelle, metabolic reaction, intracellular movement, etc., and draw some type of conclusion. Some conclusions rest on more solid evidence than others. Even if there is a consensus of agreement concerning the "facts" regarding a particular phenomenon, there are often several possible interpretations of the data. Hypotheses are put forth and generally stimulate further research, thereby leading to a reevaluation of the original proposal. Most hypotheses that remain valid undergo a sort of evolution and, when presented in the text, should not be considered wholly correct or incorrect.

Cell biology is a rapidly moving field and some of the best hypotheses often generate considerable controversy. Even though this is a textbook where one expects to find material that is well tested, there are many places where new ideas are presented. These ideas are often described as models. I've included such models because they convey the current thinking in the field, even if they are speculative. Moreover, they reinforce the idea that cell biologists operate at the frontier of science, a boundary between the unknown and known (or thought to be known). Remain skeptical.

Topics of Human Interest

NOTE: An f after a page denotes a figure; t denotes a table; fn denotes a footnote; HP denotes a Human Perspective box; EP denotes an Experimental Pathway box.

Acquired immune deficiency syndrome.

See AIDS

Acute lymphoblastic leukemia (ALL),

Chapter 16, 685–686

Acute myeloid leukemia (AML), Chapter 16, 685–686

Adaptive (acquired) immune response,

Chapter 17, 703–724

Adenoviruses, Chapter 1, 24, Chapter 4, 163, Chapter 11, 444–446

Adrenoleukodystrophy (ALD), Chapter 5, 208HP

African populations, genomes of, Chapter 10, 402, 419HP

Agammaglobulinemia, Chapter 17, 703

Aging:

and Down syndrome (trisomy 21),

Chapter 14, 609HP

and free radicals, Chapter 2, 35HP

and insulin-like growth factors, Chapter 15, 646

and mitochondrial disorders, Chapter 5, 208HP

premature (progeria), Chapter 12, 490, 608, Chapter 13, 569HP

and telomeres, Chapter 12, 506–508

AIDS (acquired immune deficiency syndrome):

and helper T cells, Chapter 17, 709, 717

resistance, Chapter 15, 626HP,

Chapter 17, 717

resistance to drugs, Chapter 2, 74–75, Chapter 3, 106–108HP

therapies for, Chapter 11, 458HP

ALD (adrenoleukodystrophy),

Chapter 5, 208–209HP

Alzheimer's disease (AD), Chapter 2,

66–70HP, Chapter 10, 418HP,

Chapter 15, 667

Anesthetics, Chapter 4, 167–169

Aneuploidy, Chapter 14, 584, 608–609HP, Chapter 16, 666–667

Antacid medications, Chapter 4, 159–160

Antibiotics, Chapter 3, 106–108HP, Chapter 11, 474

Antidepressants, Chapter 4, 169

Anti-inflammatory drugs, and cancer, Chapter 16, 669

Antioxidants, Chapter 2, 35HP

Appetite, Chapter 3, 117

Arthritis, rheumatoid, Chapter 17, 724–726HP

Ataxia-telangiectasia, Chapter 14, 579–580

Atherosclerosis, Chapter 8, 307–308, 313–315EP, Chapter 10, 417–418HP

Autoimmune diseases, Chapter 7, 250, 257, Chapter 17, 706, 721, 724–726HP

Bacterial toxins, Chapter 8, 302, Chapter 15, 627

Bacteriophage therapy, Chapter 1, 26

Benign tumors, Chapter 16, 670

Biofilms, Chapter 1, 13, Chapter 4, 163

Biomarkers, Chapter 2, 72–73, Chapter 16, 693

Blistering diseases, Chapter 7, 250, 257, Chapter 9, 356

Blood-brain barrier, and tight junctions, Chapter 7, 262

Blood cell differentiation, Chapter 17, 703f

Blood clots, Chapter 2, 47, Chapter 7, 246–247

Blood glucose, Chapter 3, 117, Chapter 4, 157, Chapter 15, 631–632, 644–646

Blood group (blood type), Chapter 4, 129, 130f, Chapter 10, 416, Chapter 17, 716

Bone marrow, in immune system, Chapter 17, 699, 700f, 703, 721, 724HP

Bone marrow transplantation, Chapter 1, 20HP, Chapter 8, 307HP

Booster shots, Chapter 17, 707

Breast cancer:

BRCA mutations, Chapter 16, 678–679, 692

DNA microarray data, use of, Chapter 16, 686

immunotherapy, Chapter 16, 688

incidence, Chapter 16, 665f

risk factors, Chapter 16, 668–669, 678, 679, 693

Burkitt's lymphoma, Chapter 12, 521, Chapter 16, 668, 680

Calorie-restricted diet, and life span, Chapter 15, 647HP

Cancer, Chapter 16, 664–698

causes, Chapter 16, 667–669

and cell adhesion, Chapter 7, 257HP

and cell cycle regulation, Chapter 14, 579–580, 586–587, 596

and cell senescence, Chapter 16, 670, 678, 682f

and cell signaling, Chapter 16, 678–680

and chromosomal aberrations, Chapter 12, 504–505HP, Chapter 16, 666, 667f, 692

and DNA repair genes, Chapter 13, 569–570HP, Chapter 16, 681

epidemiology, Chapter 16, 668

gene expression analysis, Chapter 16, 685–687

genetics, Chapter 16, 668–687

genome, Chapter 16, 683–684

and growth factor receptors, Chapter 16, 678, 679, 688, 693

and inflammation, Chapter 16, 668

inherited syndromes, Chapter 16, 673t

metastatic spread, Chapter 7, 256HP, Chapter 16, 692–693

and mismatch repair, Chapter 16, 673t

normal vs. malignant cell properties, Chapter 16, 665–667

and oncogenes, Chapter 16, 671, 679–681, 691, 694–697EP

and *TP53* gene, Chapter 16, 678

and *RB* gene, Chapter 16, 672–674

risk factors, Chapter 16, 668

and telomeres, Chapter 12, 508

therapy, Chapter 10, 398, Chapter 11, 458HP, Chapter 16, 687–691

and tumor-suppressor genes, Chapter 16, 671–673

use of DNA microarray data in diagnosis and treatment of, Chapter 16, 685–687

and viruses, Chapter 16, 668–669, 694–697EP

Carcinogens, Chapter 8, 280, Chapter 16, 668, 676, 694EP

Cell-mediated immunity, Chapter 17, 703, 706–709, 716–723

Cell replacement therapy, Chapter 1, 20–23HP, Chapter 12, 518

Cervical cancer, Chapter 16, 668, 670, 693

Chemotherapy drugs, Chapter 4, 129f, Chapter 9, 341, Chapter 10, 398, 418HP, Chapter 16, 677f

Cholera, Chapter 4, 163, Chapter 15, 627

Cholesterol:

and familial hypercholesterolemia, Chapter 8, 319–320EP

and LDL, atherosclerosis, Chapter 8, 313–314, Chapter 10, 417HP, 418HP, Chapter 11, 458HP, Chapter 12, 535

Chromosome alterations and aberrations: and apoptosis, Chapter 16, 681

deletions, and retinoblastoma, Chapter 16, 673

duplications, Chapter 10, 407, 407f, 409–410, Chapter 12, 504–505HP

and *myc* oncogene, Chapter 16, 680, 682f

nondisjunction, Chapter 14, 608–609HP

and oncogene activation, Chapter 16, 657, 657f

Chronic myelogenous leukemia (CML), Chapter 2, 75–76, Chapter 16, 690

Ciliopathies, Chapter 9, 349–350HP

Clonal selection theory, Chapter 17, 704–706

Cloning, Chapter 12, 512–514

Cockayne syndrome, Chapter 13, 569–570HP

Collagen, diseases of, Chapter 7, 238–239

Colon cancer:

and anti-inflammatory drugs, Chapter 16, 668

gene mutations in, Chapter 16, 683f

hereditary nonpolyposis, Chapter 16, 683

and mismatch repair, Chapter 16, 683

and tumor-suppressor genes, Chapter 16, 678

Color blindness, Chapter 12, 499, Chapter 15, 626

Congenital Diseases of Glycosylation (CDGs), Chapter 8, 286–287

Topics of Human Interest (continued)

- Creutzfeldt-Jakob disease (CJD)**, Chapter 2, 66HP
- Cystic fibrosis**, Chapter 4, 162–163HP, Chapter 8, 282, Chapter 11, 475
- Deafness, and myosin mutations**, Chapter 9, 364
- Diabetes**, Chapter 10, 417–418HP
- Diabetes insipidus**, Chapter 4, 151, Chapter 15, 626HPt
- Diabetes, type 1**, Chapter 1, 20, Chapter 17, 724–726HP
- Diabetes, type 2**, Chapter 10, 418, Chapter 15, 646
- Diarrhea, and osmosis**, Chapter 4, 150, Chapter 15, 627
- Diet, and cancer**, Chapter 16, 668
- DNA fingerprinting**, Chapter 10, 402
- DNA repair**, Chapter 13, 564–568
- Down syndrome (trisomy 21)**, Chapter 12, 505HP, Chapter 14, 608–609HP
- Drug development**, Chapter 2, 75–76, Chapter 8, 301, Chapter 16, 689–691, Chapter 17, 725–726HP
- Dwarfism**, Chapter 7, 240
- Embryonic development:**
cell movements, Chapter 7, 243f, Chapter 9, 381
cilia, Chapter 9, 349HP
and epithelial-mesenchymal transitions, Chapter 7, 257
and genomic imprinting, Chapter 12, 532
and miRNAs, Chapter 12, 539–540
- Embryonic stem (ES) cells**, Chapter 1, 21–22, Chapter 18, 779–780
- Enzyme replacement therapy**, Chapter 8, 307HP
- Epstein-Barr virus**, Chapter 16, 682
- Exercise**, Chapter 5, 188HP
- Fabry disease**, Chapter 8, 306HPt
- Fragile X syndrome**, Chapter 10, 405HP
- Free radicals and aging**, Chapter 2, 35HP
- Gaucher's disease**, Chapter 8, 306HP
- Gene number**, Chapter 10, 411–412
- Gene therapy**, Chapter 1, 23–24, Chapter 4, 163
- Genomic analysis, human** Chapter 10, 411–420
- Gleevec**, Chapter 2, 75–76, Chapter 16, 691
- Glycolipids, diseases of**, Chapter 4, 126, Chapter 8, 306–307HP
- Graft rejection**, Chapter 17, 716–717
- Heart attacks, heart disease**, Chapter 4, 159, Chapter 7, 246–247, 255HP
and nitroglycerine, Chapter 15, 656
- Heart muscle:**
contraction, and gap junctions, Chapter 7, 263–264, Chapter 15, 649
and miRNAs, Chapter 12, 539–540
- Heartburn**, Chapter 4, 159, 159f
- Hemolytic anemias**, Chapter 4, 147
- Hemophilia, from “jumping” genetic elements**, Chapter 10, 409
- Herceptin**, Chapter 16, 688
- Herpes viruses**, Chapter 16, 669
- HIV (human immunodeficiency virus)**, Chapter 1, 24–25
and helper T cells, Chapter 17, 709
- Human Genome Project**, Chapter 10, 420HP
- Human papillomaviruses (HPV)**, Chapter 16, 669, 678
- Humoral immunity**, Chapter 17, 703, 710–716, 723–724
- Huntington's disease**, Chapter 10, 404–405HP, 417HP, Chapter 15, 657HP
- Hydrocephalus**, Chapter 7, 253
- Hypertension**, Chapter 3, 104, Chapter 15, 626
- I-cell disease**, Chapter 8, 306HP
- Immune response**, Chapter 17, 699–730
adaptive (acquired), Chapter 17, 703, 704, 707–710, 722–724
innate, Chapter 17, 700–703
overview, Chapter 17, 699–704
primary, Chapter 17, 711f
secondary, Chapter 17, 711f
against self, Chapter 17, 699, 706, 720, 721, 724–726HP
- Immune system**, Chapter 17, 699–730
- Immunization**, Chapter 17, 706–707
- Immunotherapy**, Chapter 2, 67, 68, Chapter 16, 688–689
- Inborn errors of metabolism**, Chapter 11, 427
- Induced pluripotent stem cells**, Chapter 1, 22–23, Chapter 12, 518–519
- Infections:**
bacterial, adaptive immune responses, Chapter 17, 703, 706–707
bacterial, as a cancer-causing agent, Chapter 16, 669
bacterial, innate immune responses, Chapter 17, 700–703
protective mechanisms, Chapter 17, 700–703
resistant bacterial, Chapter 3, 106–108HP
- Inflammation**, Chapter 7, 255HP, Chapter 17, 702, 710, 725–726HP
- Influenza**, Chapter 1, 25
- Innate immune responses**, Chapter 17, 700–703
- Insulin signaling**, Chapter 4, 157, Chapter 15, 644–645, Chapter 17, 724HP
- Interferons (IFNs)**, Chapter 17, 703, 707, 724, 725–726HP
- Interleukins (ILs)**, Chapter 17, 708, 709t, 723
- Kaposi's sarcoma**, Chapter 15, 626HP, Chapter 16, 669
- Kartagener syndrome**, Chapter 9, 349HP
- Karyotypes**, Chapter 12, 503f, Chapter 14, 609f, Chapter 16, 667f
- Kidneys:**
failure from diabetes, Chapter 7, 237
polycystic disease, Chapter 9, 349HP
tight junctions, Chapter 7, 262
- Lactose tolerance**, Chapter 10
- Leukemias:**
and chromosomal translocations, Chapter 11, 458HP, Chapter 12, 504–505HP, Chapter 16, 690–691
and gene-expression profiling, Chapter 16, 686–687
- Leukocyte adhesion deficiency (LAD)**, Chapter 7, 255–256HP
- Listeria**, Chapter 9, 374
- Longevity**, Chapter 2, 35HP, Chapter 5, 208–209, Chapter 15, 646
- Lysosomal storage disorders**, Chapter 8, 306–307HP
- Macular degeneration**, Chapter 10, 418HP, Chapter 11, 452HP
- Mad cow disease**, Chapter 2, 66HP
- Malaria**, Chapter 17, 717
- Marijuana**, Chapter 4, 170
- Marker chromosomes**, Chapter 12, 509
- Melanoma**, Chapter 13, 570, Chapter 16
- Metabolism, anaerobic and aerobic**, Chapter 5, 188HP
- Metastasis**, Chapter 7, 256HP, Chapter 16, 665f, 687, 693
- Microbiome, human**, Chapter 1, 15
- Mitochondrial diseases**, Chapter 5, 207–208HP
- Multiple sclerosis (MS)**, Chapter 4, 168, Chapter 17, 724–726HP
- Muscle fibers and contractility**, Chapter 5, 188HP, Chapter 9, 364–371
- Muscular dystrophies**, Chapter 4, 147, Chapter 11, 475, Chapter 12, 490
- Mutagenic agents**, Chapter 16, 667–668, 675
- Mutations:**
in cancer, Chapter 16, 669–687
and mitochondrial disorders, Chapter 5, 207–208HP
and radiation, Chapter 10, 392, Chapter 13, 567
in rearranged antibody DNA, Chapter 17, 715
and splicing, Chapter 11, 449
in tumor-suppressor genes vs. oncogenes, Chapter 16, 671
- Nerve cells, mitochondrial abnormalities**, Chapter 5, 207–208HP
- Nerve gas**, Chapter 3, 104, Chapter 4, 170
- Nervous system disorders**, Chapter 5, 207–208HP, Chapter 9, 356, Chapter 10, 404–405HP, Chapter 16, 673
- Neurofibrillary tangles (NFTs)**, Chapter 2, 70, Chapter 9, 331
- Nicotine addiction**, Chapter 4, 171EPfn
- Niemann-Pick type C disease**, Chapter 8, 306t, 318
- Non-Hodgkin's B-cell lymphoma**, Chapter 16, 688
- “Nonself,”** Chapter 17, 700
- Nonsteroidal anti-inflammatory drugs (NSAIDs)**, Chapter 16, 669
- Ovarian cancer**, Chapter 16, 665f, 678

- Pap smear**, Chapter 16, 670, 670t, 693
Parkinson's disease, Chapter 5, 208HP, Chapter 15, 657
Periodontal disease, Chapter 7, 257HP
Peroxisomal diseases, Chapter 5, 208–209HP
Polycystic kidney disease, Chapter 9, 349HP
Prader-Willi syndrome, Chapter 12, 532
Precocious puberty, Chapter 15, 626HP
Pregnancy, IgG-based immunity, Chapter 17, 713
Prilosec, Chapter 4, 159, 159f
Prions, Chapter 2, 66–67HP
Prostate cancer, Chapter 2, 73, Chapter 15, 658
Prozac, Chapter 4, 170

Radiation, as a carcinogen, Chapter 10, 392, Chapter 13, 564–568, Chapter 14, 579–580
Retinoblastoma, Chapter 16, 673–675
Retinitis pigmentosum, Chapter 15, 625, 626t
Retroviruses (RNA tumor viruses), Chapter 16, 668, 671, 679, 694–697EP
Rheumatoid arthritis, Chapter 17, 724–726HP
RNA interference, clinical applications, Chapter 11, 458–459HP

Scurvy, Chapter 7, 238
“Self,” Chapter 17, 700, 721, 724–726HP, 730EP
 antibodies against, Chapter 17, 701f, 724–726HP
 distinguishing from nonself, Chapter 17, 721, 724, 726HP
 immunologic tolerance, Chapter 17, 706, 709f, 721

Sex chromosomes, abnormal number of, Chapter 14, 609HP
Sexual arousal, Chapter 15, 656
Sickle cell anemia, Chapter 2, 55, Chapter 11, 462
Skin:
 blistering diseases, Chapter 7, 250, 257, Chapter 9, 356
 cancers, Chapter 13, 569–570HP
 grafts, Chapter 17, 716
 histology, Chapter 9, 357f
 tight junctions, Chapter 7, 260–262
Smell (olfaction), Chapter 15, 634–635
Smoking, Chapter 4, 171EPfn, Chapter 16, 669
Snake venom, Chapter 3, 104, Chapter 4, 172EP
Speech and language disorders, Chapter 10, 414
Sphingolipid storage diseases, Chapter 8, 306HP
Spongiform encephalopathy, Chapter 2, 66HP
Statin drugs, Chapter 2, 69HP, Chapter 8, 314
Stem cells, Chapter 1, 20–23HP, Chapter 13, 564, Chapter 16, 670, 692–693
Stroke, Chapter 7, 246, 255HP
Systemic lupus erythematosus (SLE), Chapter 17, 725–726HP

Taste (gustation), Chapter 15, 634
Tay-Sachs disease, Chapter 8, 306–307HP
Testosterone, Chapter 2, 49, Chapter 15, 626HP, 658
Thymus gland, Chapter 17, 703, 721, 724HP
Tolerance, immunologic (towards “self”), Chapter 17, 706, 709f, 721
Trans fats, Chapter 2, 49
Transplant rejection, Chapter 17, 716, 721

Tuberculosis, Chapter 3, 106HP, Chapter 8, 309
Tumor necrosis factors (TNFs), Chapter 15, 658–659, Chapter 17, 708, 725HP

Ultraviolet light, DNA damage from, Chapter 13, 564–570, Chapter 16, 667

Vaccination, Chapter 17, 706–707
Viagra, Chapter 15, 656
Viruses, Chapter 1, 23–26, Chapter 16, 667–668
 acquired immune responses to, Chapter 17, 701f, 703
 and cancer, Chapter 16, 667–668, 694–697EP
 innate immune responses to, Chapter 17, 701f, 702–703
 interactions with T cells, Chapter 17, 707, 716–718, 727–728EP
 and oncogenes, Chapter 16, 694–697EP
 provirus, Chapter 1, 25–26, Chapter 16, 694EP
 resistance to, and interferon, Chapter 17, 701f, 703, 724
 treatment with RNAi, Chapter 11, 458HP
Vision, Chapter 15, 623, 624, 625–626HP, 634
Vitamin C deficiency, Chapter 7, 238

Weed killers, Chapter 6, 225
Whooping cough, Chapter 15, 627

X chromosome inactivation, Chapter 12, 499–500, 509
Xeroderma pigmentosum (XP), Chapter 13, 569–570HP

Zellweger syndrome (ZS), Chapter 5, 208HP