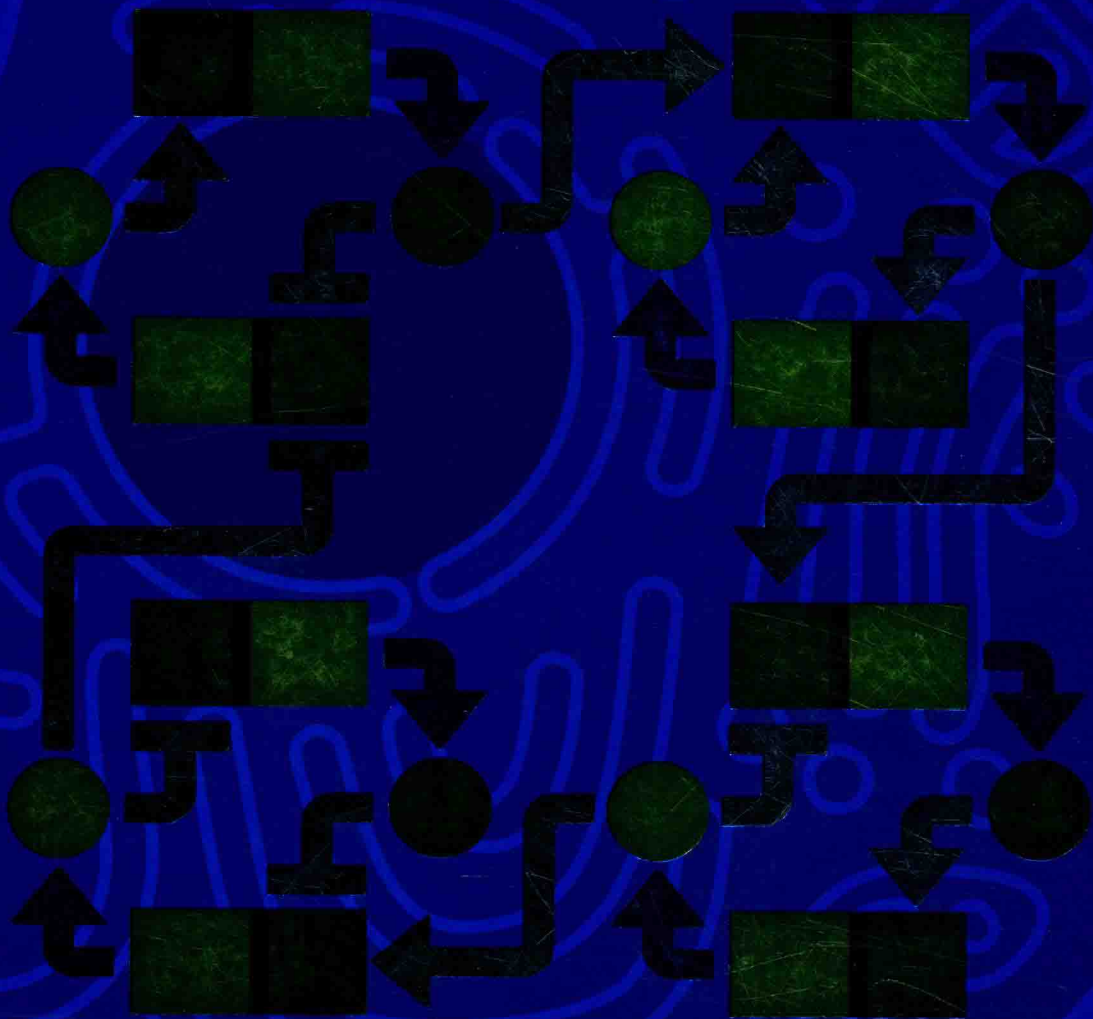


# Molecular Biology of THE CELL

Sixth Edition



ALBERTS   JOHNSON   LEWIS   MORGAN   RAFF   ROBERTS   WALTER

# Molecular Biology of **THE CELL**

Sixth Edition

Bruce Alberts  
Alexander Johnson  
Julian Lewis  
David Morgan  
Martin Raff  
Keith Roberts  
Peter Walter



With problems by  
John Wilson  
Tim Hunt

## Garland Science

Vice President: Denise Schanck  
Associate Editor: Allie Bochicchio  
Production Editor and Layout: EJ Publishing Services  
Senior Production Editor: Georgina Lucas  
Text Editors: Sherry Granum Lewis and Elizabeth Zayatz  
Illustrator: Nigel Orme  
Structures: Tiago Barros  
Designer: Matthew McClements, Blink Studio, Ltd.  
Copyeditor: Jo Clayton  
Proofreader: Sally Huish  
Indexer: Bill Johncocks  
Permissions Coordinator: Sheri Gilbert  
Back Cover Photograph: Photography, Christophe Carlinet;  
Design, Nigel Orme

*Molecular Biology of the Cell* Interactive Media:  
Artistic and Scientific Direction: Peter Walter  
Narration: Julie Theriot  
Director of Digital Publishing: Michael Morales  
Editorial Assistant: Leah Christians  
Production Editor: Natasha Wolfe

© 2015 by Bruce Alberts, Alexander Johnson, Julian Lewis,  
David Morgan, Martin Raff, Keith Roberts, and Peter Walter.

This book contains information obtained from authentic and highly regarded sources. Every effort has been made to trace copyright holders and to obtain their permission for the use of copyright material. Reprinted material is quoted with permission, and sources are indicated. A wide variety of references are listed. Reasonable efforts have been made to publish reliable data and information, but the author and the publisher cannot assume responsibility for the validity of all materials or for the consequences of their use.

All rights reserved. No part of this book covered by the copyright herein may be reproduced or used in any format in any form or by any means—graphic, electronic, or mechanical, including photocopying, recording, taping, or information storage and retrieval systems—without permission of the publisher.

## Library of Congress Cataloging-in-Publication Data

Alberts, Bruce, author.

Molecular biology of the cell / Bruce Alberts, Alexander Johnson, Julian Lewis, David Morgan, Martin Raff, Keith Roberts, Peter Walter ; with problems by John Wilson, Tim Hunt. -- Sixth edition.

p. ; cm.

Preceded by Molecular biology of the cell / Bruce Alberts ... [et al.]. 5th ed. c2008.

Includes bibliographical references and index.

ISBN 978-0-8153-4432-2 (hardcover) -- ISBN 978-0-8153-4464-3 (paperback)

I. Title.

[DNLM: 1. Cells. 2. Molecular Biology. QU 300]

QH581.2

572.8--dc23

2014031818

Published by Garland Science, Taylor & Francis Group, LLC, an informa business,  
711 Third Avenue, New York, NY 10017, US  
3 Park Square, Milton Park, Abingdon, OX14 4RN, UK

Printed in the United States of America

15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

 **Garland Science**  
Taylor & Francis Group

Visit our website at <http://www.garlandscience.com>

## About the Authors

**Bruce Alberts** received his PhD from Harvard University and is the Chancellor's Leadership Chair in Biochemistry and Biophysics for Science and Education, University of California, San Francisco. He was the editor-in-chief of *Science* magazine from 2008 until 2013, and for twelve years he served as President of the U.S. National Academy of Sciences (1993–2005). **Alexander Johnson** received his PhD from Harvard University and is Professor of Microbiology and Immunology at the University of California, San Francisco. **Julian Lewis** (1946–2014) received his DPhil from the University of Oxford and was an Emeritus Scientist at the London Research Institute of Cancer Research UK. **David Morgan** received his PhD from the University of California, San Francisco, and is Professor of the Department of Physiology there as well as the Director of the Biochemistry, Cell Biology, Genetics, and Developmental Biology Graduate Program. **Martin Raff** received his MD from McGill University and is Emeritus Professor of Biology at the Medical Research Council Laboratory for Molecular Cell Biology at University College London. **Keith Roberts** received his PhD from the University of Cambridge and was Deputy Director of the John Innes Centre, Norwich. He is Emeritus Professor at the University of East Anglia. **Peter Walter** received his PhD from the Rockefeller University in New York and is Professor of the Department of Biochemistry and Biophysics at the University of California, San Francisco, and an Investigator at the Howard Hughes Medical Institute. **John Wilson** received his PhD from the California Institute of Technology and pursued his postdoctoral work at Stanford University. He is Distinguished Service Professor of Biochemistry and Molecular Biology at Baylor College of Medicine in Houston. **Tim Hunt** received his PhD from the University of Cambridge where he taught biochemistry and cell biology for more than 20 years. He worked at Cancer Research UK until his retirement in 2010. He shared the 2001 Nobel Prize in Physiology or Medicine with Lee Hartwell and Paul Nurse.

**Cover design:** Cell biology is not only about the structure and function of the myriad molecules that comprise a cell, but also about how this complex chemistry is controlled. Understanding the cell's elaborate regulatory feedback networks will require quantitative approaches.





**Julian Hart Lewis**

August 12, 1946—April 30, 2014

# Preface

Since the last edition of this book appeared, more than five million scientific papers have been published. There has been a parallel increase in the quantity of digital information: new data on genome sequences, protein interactions, molecular structures, and gene expression—all stored in vast databases. The challenge, for both scientists and textbook writers, is to convert this overwhelming amount of information into an accessible and up-to-date understanding of how cells work.

Help comes from a large increase in the number of review articles that attempt to make raw material easier to digest, although the vast majority of these reviews are still quite narrowly focused. Meanwhile, a rapidly growing collection of online resources tries to convince us that understanding is only a few mouse-clicks away. In some areas this change in the way we access knowledge has been highly successful—in discovering the latest information about our own medical problems, for example. But to understand something of the beauty and complexity of how living cells work, one needs more than just a wiki- this or wiki- that; it is enormously hard to identify the valuable and enduring gems from so much confusing landfill. Much more effective is a carefully wrought narrative that leads logically and progressively through the key ideas, components, and experiments in such a way that readers can build for themselves a memorable, conceptual framework for cell biology—a framework that will allow them to critically evaluate all of the new science and, more importantly, to understand it. That is what we have tried to do in *Molecular Biology of the Cell*.

In preparing this new edition, we have inevitably had to make some difficult decisions. In order to incorporate exciting new discoveries, while at the same time keeping the book portable, much has had to be excised. We have added new sections, such as those on new RNA functions, advances in stem cell biology, new methods for studying proteins and genes and for imaging cells, advances in the genetics and treatment of cancer, and timing, growth control, and morphogenesis in development.

The chemistry of cells is extremely complex, and any list of cell parts and their interactions—no matter how complete—will leave huge gaps in our understanding. We now realize that to produce convincing explanations of cell behavior will require quantitative information about cells that is coupled to sophisticated mathematical/computational approaches—some not yet invented. As a consequence, an emerging goal for cell biologists is to shift their studies more toward quantitative description and mathematical deduction. We highlight this approach and some of its methods in a new section at the end of Chapter 8.

Faced with the immensity of what we have learned about cell biology, it might be tempting for a student to imagine that there is little left to discover. In fact, the more we find out about cells, the more new questions emerge. To emphasize that our understanding of cell biology is incomplete, we have highlighted some of the major gaps in our knowledge by including *What We Don't Know* at the end of each chapter. These brief lists include only a tiny sample of the critical unanswered questions and challenges for the next generation of scientists. We derive great pleasure from the knowledge that some of our readers will provide future answers.

The more than 1500 illustrations have been designed to create a parallel narrative, closely interwoven with the text. We have increased their consistency between chapters, particularly in the use of color and of common icons; membrane pumps and channels are a good example. To avoid interruptions to the text, some material has been moved into new, readily accessible panels. Most of the important protein structures depicted have now been redrawn and consistently colored. In each



case, we now provide the corresponding Protein Data Bank (PDB) code for the protein, which can be used to access online tools that provide more information about it, such as those on the RCSB PDB website ([www.rcsb.org](http://www.rcsb.org)). These connections allow readers of the book to explore more fully the proteins that lie at the core of cell biology.

John Wilson and Tim Hunt have again contributed their distinctive and imaginative problems to help students gain a more active understanding of the text. The problems emphasize quantitative approaches and encourage critical thinking about published experiments; they are now present at the end of all chapters. The answers to these problems, plus more than 1800 additional problems and solutions, all appear in the companion volume that John and Tim have written, *Molecular Biology of the Cell, Sixth Edition: The Problems Book*.

We live in a world that presents us with many complex issues related to cell biology: biodiversity, climate change, food security, environmental degradation, resource depletion, and human disease. We hope that our textbook will help the reader better understand and possibly contribute to meeting these challenges. Knowledge and understanding bring the power to intervene.

We are indebted to a large number of scientists whose generous help we mention separately in the detailed acknowledgments. Here we must mention some particularly significant contributors. For Chapter 8, Hana El-Samad provided the core of the section on Mathematical Analysis of Cell Functions, and Karen Hopkin made valuable contributions to the section on Studying Gene Expression and Function. Werner Kuhlbrandt helped to reorganize and rewrite Chapter 14 (Energy Conversion: Mitochondria and Chloroplasts). Rebecca Heald did the same for Chapter 16 (The Cytoskeleton), as did Alexander Schier for Chapter 21 (Development of Multicellular Organisms), and Matt Welch for Chapter 23 (Pathogens and Infection). Lewis Lanier aided in the writing of Chapter 24 (The Innate and Adaptive Immune Systems). Hossein Amiri generated the enormous online instructor's question bank.

Before starting out on the revision cycle for this edition, we asked a number of scientists who had used the last edition to teach cell biology students to meet with us and suggest improvements. They gave us useful feedback that has helped inform the new edition. We also benefited from the valuable input of groups of students who read most of the chapters in page proofs.

Many people and much effort are needed to convert a long manuscript and a large pile of sketches into a finished textbook. The team at Garland Science that managed this conversion was outstanding. Denise Schanck, directing operations, displayed forbearance, insight, tact, and energy throughout the journey; she guided us all unerringly, ably assisted by Allie Boichichio and Janette Scobie. Nigel Orme oversaw our revamped illustration program, put all the artwork into its final form, and again enhanced the back cover with his graphics skills. Tiago Barros helped us refresh our presentation of protein structures. Matthew McClements designed the book and its front cover. Emma Jeffcock again laid out the final pages, managing endless rounds of proofs and last-minute changes with remarkable skill and patience; Georgina Lucas provided her with help. Michael Morales, assisted by Leah Christians, produced and assembled the complex web of videos, animations, and other materials that form the core of the online resources that accompany the book. Adam Sendroff provided us with the valuable feedback from book users around the world that informed our revision cycle. Casting expert eyes over the manuscript, Elizabeth Zayatz and Sherry Granum Lewis acted as development editors, Jo Clayton as copyeditor, and Sally Huish as proofreader. Bill Johncocks compiled the index. In London, Emily Preece fed us, while the Garland team's professional help, skills, and energy, together with their friendship, nourished us in every other way throughout the revision, making the whole process a pleasure. The authors are extremely fortunate to be supported so generously.

We thank our spouses, families, friends, and colleagues for their continuing support, which has once again made the writing of this book possible.

Just as we were completing this edition, Julian Lewis, our coauthor, friend, and colleague, finally succumbed to the cancer that he had fought so heroically for ten years. Starting in 1979, Julian made major contributions to all six editions, and, as our most elegant wordsmith, he elevated and enhanced both the style and tone of all the many chapters he touched. Noted for his careful scholarly approach, clarity and simplicity were at the core of his writing. Julian is irreplaceable, and we will all deeply miss his friendship and collaboration. We dedicate this Sixth Edition to his memory.

# Note to the Reader

## Structure of the Book

Although the chapters of this book can be read independently of one another, they are arranged in a logical sequence of five parts. The first three chapters of Part I cover elementary principles and basic biochemistry. They can serve either as an introduction for those who have not studied biochemistry or as a refresher course for those who have. Part II deals with the storage, expression, and transmission of genetic information. Part III presents the principles of the main experimental methods for investigating and analyzing cells; here, a new section entitled “Mathematical Analysis of Cell Functions” in Chapter 8 provides an extra dimension in our understanding of cell regulation and function. Part IV describes the internal organization of the cell. Part V follows the behavior of cells in multicellular systems, starting with development of multicellular organisms and concluding with chapters on pathogens and infection and on the innate and adaptive immune systems.

## End-of-Chapter Problems

A selection of problems, written by John Wilson and Tim Hunt, appears in the text at the end of each chapter. New to this edition are problems for the last four chapters on multicellular organisms. The complete solutions to all of these problems can be found in *Molecular Biology of the Cell, Sixth Edition: The Problems Book*.

## References

A concise list of selected references is included at the end of each chapter. These are arranged in alphabetical order under the main chapter section headings. These references sometimes include the original papers in which important discoveries were first reported.

## Glossary Terms

Throughout the book, boldface type has been used to highlight key terms at the point in a chapter where the main discussion occurs. Italic type is used to set off important terms with a lesser degree of emphasis. At the end of the book is an expanded glossary, covering technical terms that are part of the common currency of cell biology; it should be the first resort for a reader who encounters an unfamiliar term. The complete glossary as well as a set of flashcards is available on the Student Website.

## Nomenclature for Genes and Proteins

Each species has its own conventions for naming genes; the only common feature is that they are always set in italics. In some species (such as humans), gene names are spelled out all in capital letters; in other species (such as zebrafish), all in lowercase; in yet others (most mouse genes), with the first letter in uppercase and rest in lowercase; or (as in *Drosophila*) with different combinations of uppercase and lowercase, according to whether the first mutant allele to be discovered produced a dominant or recessive phenotype. Conventions for naming protein products are equally varied.

This typographical chaos drives everyone crazy. It is not just tiresome and absurd; it is also unsustainable. We cannot independently define a fresh convention for each of the next few million species whose genes we may wish to study.



Moreover, there are many occasions, especially in a book such as this, where we need to refer to a gene generically—without specifying the mouse version, the human version, the chick version, or the hippopotamus version—because they are all equivalent for the purposes of our discussion. What convention then should we use?

We have decided in this book to cast aside the different conventions that are used in individual species and follow a uniform rule: we write all gene names, like the names of people and places, with the first letter in uppercase and the rest in lowercase, but all in italics, thus: *Apc*, *Bazooka*, *Cdc2*, *Dishevelled*, *Egl1*. The corresponding protein, where it is named after the gene, will be written in the same way, but in roman rather than italic letters: *Apc*, *Bazooka*, *Cdc2*, *Dishevelled*, *Egl1*. When it is necessary to specify the organism, this can be done with a prefix to the gene name.

For completeness, we list a few further details of naming rules that we shall follow. In some instances, an added letter in the gene name is traditionally used to distinguish between genes that are related by function or evolution; for those genes, we put that letter in uppercase if it is usual to do so (*LacZ*, *RecA*, *HoxA4*). We use no hyphen to separate added letters or numbers from the rest of the name. Proteins are more of a problem. Many of them have names in their own right, assigned to them before the gene was named. Such protein names take many forms, although most of them traditionally begin with a lowercase letter (actin, hemoglobin, catalase), like the names of ordinary substances (cheese, nylon), unless they are acronyms (such as GFP, for Green Fluorescent Protein, or BMP4, for Bone Morphogenetic Protein #4). To force all such protein names into a uniform style would do too much violence to established usages, and we shall simply write them in the traditional way (actin, GFP, and so on). For the corresponding gene names in all these cases, we shall nevertheless follow our standard rule: *Actin*, *Hemoglobin*, *Catalase*, *Bmp4*, *Gfp*. Occasionally in our book we need to highlight a protein name by setting it in italics for emphasis; the intention will generally be clear from the context.

For those who wish to know them, the table below shows some of the official conventions for individual species—conventions that we shall mostly violate in this book, in the manner shown.

Organism	Species-Specific Convention		Unified Convention Used in This Book	
	Gene	Protein	Gene	Protein
Mouse	<i>Hoxa4</i>	Hoxa4	<i>HoxA4</i>	HoxA4
	<i>Bmp4</i>	BMP4	<i>Bmp4</i>	BMP4
	<i>integrin <math>\alpha</math>-1, Itga1</i>	integrin $\alpha$ 1	<i>Integrin <math>\alpha</math>1, Itga1</i>	integrin $\alpha$ 1
Human	<i>HOXA4</i>	HOXA4	<i>HoxA4</i>	HoxA4
Zebrafish	<i>cyclops, cyc</i>	Cyclops, Cyc	<i>Cyclops, Cyc</i>	Cyclops, Cyc
<i>Caenorhabditis</i>	<i>unc-6</i>	UNC-6	<i>Unc6</i>	Unc6
<i>Drosophila</i>	<i>sevenless, sev</i> (named after recessive phenotype)	Sevenless, SEV	<i>Sevenless, Sev</i>	Sevenless, Sev
	<i>Deformed, Dfd</i> (named after dominant mutant phenotype)	Deformed, DFD	<i>Deformed, Dfd</i>	Deformed, Dfd
Yeast				
<i>Saccharomyces cerevisiae</i> (budding yeast)	<i>CDC28</i>	Cdc28, Cdc28p	<i>Cdc28</i>	Cdc28
<i>Schizosaccharomyces pombe</i> (fission yeast)	<i>Cdc2</i>	Cdc2, Cdc2p	<i>Cdc2</i>	Cdc2
<i>Arabidopsis</i>	<i>GAI</i>	GAI	<i>Gai</i>	GAI
<i>E. coli</i>	<i>uvrA</i>	UvrA	<i>UvrA</i>	UvrA



***Molecular Biology of the Cell, Sixth Edition: The Problems Book***

by John Wilson and Tim Hunt (ISBN: 978-0-8153-4453-7)

*The Problems Book* is designed to help students appreciate the ways in which experiments and simple calculations can lead to an understanding of how cells work. It provides problems to accompany Chapters 1–20 of *Molecular Biology of the Cell*. Each chapter of problems is divided into sections that correspond to those of the main textbook and review key terms, test for understanding basic concepts, pose research-based problems, and now include MCAT-style questions which help students to prepare for standardized medical school admission tests. *Molecular Biology of the Cell, Sixth Edition: The Problems Book* should be useful for homework assignments and as a basis for class discussion. It could even provide ideas for exam questions. Solutions for all of the problems are provided in the book. Solutions for the end-of-chapter problems for Chapters 1–24 in the main textbook are also found in *The Problems Book*.

## RESOURCES FOR INSTRUCTORS AND STUDENTS

The teaching and learning resources for instructors and students are available online. The instructor's resources are password-protected and available only to adopting instructors. The student resources are available to everyone. We hope these resources will enhance student learning and make it easier for instructors to prepare dynamic lectures and activities for the classroom.

### **Instructor Resources**

Instructor Resources are available on the Garland Science Instructor's Resource Site, located at [www.garlandscience.com/instructors](http://www.garlandscience.com/instructors). The website provides access not only to the teaching resources for this book but also to all other Garland Science textbooks. Adopting instructors can obtain access to the site from their sales representative or by emailing [science@garland.com](mailto:science@garland.com).

#### *Art of Molecular Biology of the Cell, Sixth Edition*

The images from the book are available in two convenient formats: PowerPoint® and JPEG. They have been optimized for display on a computer. Figures are searchable by figure number, by figure name, or by keywords used in the figure legend from the book.

#### *Figure-Integrated Lecture Outlines*

The section headings, concept headings, and figures from the text have been integrated into PowerPoint presentations. These will be useful for instructors who would like a head start creating lectures for their course. Like all of our PowerPoint presentations, the lecture outlines can be customized. For example, the content of these presentations can be combined with videos and questions from the book or Question Bank, in order to create unique lectures that facilitate interactive learning.

#### *Animations and Videos*

The 174 animations and videos that are available to students are also available on the Instructor's Website in two formats. The WMV-formatted movies are created for instructors who wish to use the movies in PowerPoint presentations on Windows® computers; the QuickTime-formatted movies are for use in PowerPoint for Apple computers or Keynote® presentations. The movies can easily be downloaded using the "download" button on the movie preview page. The movies are correlated to each chapter and callouts are highlighted in color.

#### *Media Guide*

This document provides an overview to the multimedia available for students and instructors and contains the text of the voice-over narration for all of the movies.

#### *Question Bank*

Written by Hossein Amiri, University of California, Santa Cruz, this greatly expanded question bank includes a variety of question formats: multiple choice,

short answer, fill-in-the-blank, true-false, and matching. There are 35–60 questions per chapter, and a large number of the multiple-choice questions will be suitable for use with personal response systems (that is, clickers). The Question Bank was created with the philosophy that a good exam should do much more than simply test students' ability to memorize information; it should require them to reflect upon and integrate information as a part of a sound understanding. This resource provides a comprehensive sampling of questions that can be used either directly or as inspiration for instructors to write their own test questions.

#### *Diploma® Test Generator Software*

The questions from the Question Bank have been loaded into the Diploma Test Generator software. The software is easy to use and can scramble questions to create multiple tests. Questions are organized by chapter and type and can be additionally categorized by the instructor according to difficulty or subject. Existing questions can be edited and new ones added. The Test Generator is compatible with several course management systems, including Blackboard®.

#### *Medical Topics Guide*

This document highlights medically relevant topics covered throughout *Molecular Biology of the Cell* and *The Problems Book*. It will be particularly useful for instructors with a large number of premedical, health science, or nursing students.

#### *Blackboard and Learning Management System (LMS) Integration*

The movies, book images, and student assessments that accompany the book can be integrated into Blackboard or other LMSs. These resources are bundled into a "Common Cartridge" or "Upload Package" that facilitates bulk uploading of textbook resources into Blackboard and other LMSs. The LMS Common Cartridge can be obtained on a DVD from your sales representative or by emailing [science@garland.com](mailto:science@garland.com).

### **Resources for Students**

The resources for students are available on the *Molecular Biology of the Cell* Student Website, located at [www.garlandscience.com/MBOC6-students](http://www.garlandscience.com/MBOC6-students).

#### *Animations and Videos*

There are 174 movies, covering a wide range of cell biology topics, which review key concepts in the book and illuminate subcellular processes. The movies are correlated to each chapter and callouts are highlighted in color.

#### *Cell Explorer Slides*

This application teaches cell morphology through interactive micrographs that highlight important cellular structures.

#### *Flashcards*

Each chapter contains a set of flashcards, built into the website, that allow students to review key terms from the text.

#### *Glossary*

The complete glossary from the book is available on the website and can be searched and browsed.



# Acknowledgments

In writing this book we have benefited greatly from the advice of many biologists and biochemists. We would like to thank the following for their suggestions in preparing this edition, as well as those who helped in preparing the first, second, third, fourth, and fifth editions. (Those who helped on this edition are listed first, those who helped with the first, second, third, fourth, and fifth editions follow.)

## General:

Steven Cook (Imperial College London), Jose A. Costoya (Universidade de Santiago de Compostela), Arshad Desai (University of California, San Diego), Susan K. Dutcher (Washington University, St. Louis), Michael Elowitz (California Institute of Technology), Benjamin S. Glick (University of Chicago), Gregory Hannon (Cold Spring Harbor Laboratories), Rebecca Heald (University of California, Berkeley), Stefan Kanzok (Loyola University Chicago), Doug Kellogg (University of California, Santa Cruz), David Kimelman (University of Washington, Seattle), Maria Krasilnikova (Pennsylvania State University), Werner Kühlbrandt (Max Planck Institute of Biophysics), Lewis Lanier (University of California, San Francisco), Annette Müller-Taubenberger (Ludwig Maximilians University), Sandra Schmid (University of Texas Southwestern), Ronald D. Vale (University of California, San Francisco), D. Eric Walters (Chicago Medical School), Karsten Weis (Swiss Federal Institute of Technology)

**Chapter 2:** H. Lill (VU University)

**Chapter 3:** David S. Eisenberg (University of California, Los Angeles), F. Ulrich Hartl (Max Planck Institute of Biochemistry), Louise Johnson (University of Oxford), H. Lill (VU University), Jonathan Weissman (University of California, San Francisco)

**Chapter 4:** Bradley E. Bernstein (Harvard Medical School), Wendy Bickmore (MRC Human Genetics Unit, Edinburgh), Jason Brickner (Northwestern University), Gary Felsenfeld (NIH), Susan M. Gasser (University of Basel), Shiv Grewal (National Cancer Institute), Gary Karpen (University of California, Berkeley), Eugene V. Koonin, (NCBI, NLM, NIH), Hiten Madhani (University of California, San Francisco), Tom Misteli (National Cancer Institute), Geeta Narlikar (University of California, San Francisco), Maynard Olson (University of Washington, Seattle), Stephen Scherer (University of Toronto), Rolf Sternglanz (Stony Brook University), Chris L. Woodcock (University of Massachusetts, Amherst), Johanna Wysocka and lab members (Stanford School of Medicine)

**Chapter 5:** Oscar Aparicio (University of Southern California), Julie P. Cooper (National Cancer Institute), Neil Hunter (Howard Hughes Medical Institute), Karim Labib (University of Manchester), Joachim Li (University of California, San Francisco), Stephen West (Cancer

Research UK), Richard D. Wood (University of Pittsburgh Cancer Institute)

**Chapter 6:** Briana Burton (Harvard University), Richard H. Ebright (Rutgers University), Daniel Finley (Harvard Medical School), Michael R. Green (University of Massachusetts Medical School), Christine Guthrie (University of California, San Francisco), Art Horwich (Yale School of Medicine), Harry Noller (University of California, Santa Cruz), David Tollervy (University of Edinburgh), Alexander J. Varshavsky (California Institute of Technology)

**Chapter 7:** Adrian Bird (The Wellcome Trust Centre, UK), Neil Brockdorff (University of Oxford), Christine Guthrie (University of California, San Francisco), Jeannie Lee (Harvard Medical School), Michael Levine (University of California, Berkeley), Hiten Madhani (University of California, San Francisco), Duncan Odom (Cancer Research UK), Kevin Struhl (Harvard Medical School), Jesper Svejstrup (Cancer Research UK)

**Chapter 8:** Hana El-Samad [major contribution] (University of California, San Francisco), Karen Hopkin [major contribution], Donita Brady (Duke University), David Kashatus (University of Virginia), Melanie McGill (University of Toronto), Alex Mogilner (University of California, Davis), Richard Morris (John Innes Centre, UK), Prasanth Potluri (The Children's Hospital of Philadelphia Research Institute), Danielle Vidaurre (University of Toronto), Carmen Warren (University of California, Los Angeles), Ian Woods (Ithaca College)

**Chapter 9:** Douglas J. Briant (University of Victoria), Werner Kühlbrandt (Max Planck Institute of Biophysics), Jeffrey Lichtman (Harvard University), Jennifer Lippincott-Schwartz (NIH), Albert Pan (Georgia Regents University), Peter Shaw (John Innes Centre, UK), Robert H. Singer (Albert Einstein School of Medicine), Kurt Thorn (University of California, San Francisco)

**Chapter 10:** Ari Helenius (Swiss Federal Institute of Technology), Werner Kühlbrandt (Max Planck Institute of Biophysics), H. Lill (VU University), Satyajit Mayor (National Centre for Biological Sciences, India), Kai Simons (Max Planck Institute of Molecular Cell Biology and Genetics), Gunnar von Heijne (Stockholm University), Tobias Walther (Harvard University)

**Chapter 11:** Graeme Davis (University of California, San Francisco), Robert Edwards (University of California, San



Francisco), Bertil Hille (University of Washington, Seattle), Lindsay Hinck (University of California, Santa Cruz), Werner Kühlbrandt (Max Planck Institute of Biophysics), H. Lill (VU University), Roger Nicoll (University of California, San Francisco), Poul Nissen (Aarhus University), Robert Stroud (University of California, San Francisco), Karel Svoboda (Howard Hughes Medical Institute), Robert Tampé (Goethe-University Frankfurt)

**Chapter 12:** John Aitchison (Institute for System Biology, Seattle), Amber English (University of Colorado at Boulder), Ralf Erdmann (Ruhr University of Bochum), Larry Gerace (The Scripps Research Institute, La Jolla), Ramanujan Hegde (MRC Laboratory of Molecular Biology, Cambridge, UK), Martin W. Hetzer (The Salk Institute), Lindsay Hinck (University of California, Santa Cruz), James A. McNew (Rice University), Nikolaus Pfanner (University of Freiburg), Peter Rehling (University of Göttingen), Michael Rout (The Rockefeller University), Danny J. Schnell (University of Massachusetts, Amherst), Sebastian Schuck (University of Heidelberg), Suresh Subramani (University of California, San Diego), Gia Voeltz (University of Colorado, Boulder), Susan R. Wentz (Vanderbilt University School of Medicine)

**Chapter 13:** Douglas J. Briant (University of Victoria, Canada), Scott D. Emr (Cornell University), Susan Ferro-Novick (University of California, San Diego), Benjamin S. Glick (University of Chicago), Ari Helenius (Swiss Federal Institute of Technology), Lindsay Hinck (University of California, Santa Cruz), Reinhard Jahn (Max Planck Institute for Biophysical Chemistry), Ira Mellman (Genentech), Peter Novick (University of California, San Diego), Hugh Pelham (MRC Laboratory of Molecular Biology, Cambridge, UK), Graham Warren (Max F. Perutz Laboratories, Vienna), Marino Zerial (Max Planck Institute of Molecular Cell Biology and Genetics)

**Chapter 14:** Werner Kühlbrandt [major contribution] (Max Planck Institute of Biophysics), Thomas D. Fox (Cornell University), Cynthia Kenyon (University of California, San Francisco), Nils-Göran Larsson (Max Planck Institute for Biology of Aging), Jodi Nunnari (University of California, Davis), Patrick O'Farrell (University of California, San Francisco), Alastair Stewart (The Victor Chang Cardiac Research Institute, Australia), Daniela Stock (The Victor Chang Cardiac Research Institute, Australia), Michael P. Yaffe (California Institute for Regenerative Medicine)

**Chapter 15:** Henry R. Bourne (University of California, San Francisco), Dennis Bray (University of Cambridge), Douglas J. Briant (University of Victoria, Canada), James Briscoe (MRC National Institute for Medical Research, UK), James Ferrell (Stanford University), Matthew Freeman (MRC Laboratory of Molecular Biology, Cambridge, UK), Alan Hall (Memorial Sloan Kettering Cancer Center), Carl-Henrik Heldin (Uppsala University), James A. McNew (Rice University), Roel Nusse (Stanford University), Julie Pitcher (University College London)

**Chapter 16:** Rebecca Heald [major contribution] (University of California, Berkeley), Anna Akhmanova (Utrecht University), Arshad Desai (University of California, San Diego), Velia Fowler (The Scripps Research Institute, La Jolla), Vladimir Gelfand (Northwestern University), Robert Goldman (Northwestern University), Alan Rick Horwitz (University of Virginia), Wallace Marshall (University of California, San Francisco), J. Richard McIntosh

(University of Colorado, Boulder), Maxence Nachury (Stanford School of Medicine), Eva Nogales (University of California, Berkeley), Samara Reck-Peterson (Harvard Medical School), Ronald D. Vale (University of California, San Francisco), Richard B. Vallee (Columbia University), Michael Way (Cancer Research UK), Orion Weiner (University of California, San Francisco), Matthew Welch (University of California, Berkeley)

**Chapter 17:** Douglas J. Briant (University of Victoria, Canada), Lindsay Hinck (University of California, Santa Cruz), James A. McNew (Rice University)

**Chapter 18:** Emily D. Crawford (University of California, San Francisco), James A. McNew (Rice University), Shigekazu Nagata (Kyoto University), Jim Wells (University of California, San Francisco)

**Chapter 19:** Jeffrey Axelrod (Stanford University School of Medicine), John Couchman (University of Copenhagen), Johan de Rooij (The Hubrecht Institute, Utrecht), Benjamin Geiger (Weizmann Institute of Science, Israel), Andrew P. Gilmore (University of Manchester), Tony Harris (University of Toronto), Martin Humphries (University of Manchester), Andreas Prokop (University of Manchester), Charles Streuli (University of Manchester), Masatoshi Takeichi (RIKEN Center for Developmental Biology, Japan), Barry Thompson (Cancer Research UK), Kenneth M. Yamada (NIH), Alpha Yap (The University of Queensland, Australia)

**Chapter 20:** Anton Berns (Netherlands Cancer Institute), J. Michael Bishop (University of California, San Francisco), Trevor Bivona (University of California, San Francisco), Fred Bunz (Johns Hopkins University), Paul Edwards (University of Cambridge), Ira Mellman (Genentech), Caetano Reis e Sousa (Cancer Research UK), Marc Shuman (University of California, San Francisco), Mike Stratton (Wellcome Trust Sanger Institute, UK), Ian Tomlinson (Cancer Research UK)

**Chapter 21:** Alex Schier [major contribution] (Harvard University), Markus Affolter (University of Basel), Victor Ambros (University of Massachusetts, Worcester), James Briscoe (MRC National Institute for Medical Research, UK), Donald Brown (Carnegie Institution for Science, Baltimore), Steven Burden (New York University School of Medicine), Moses Chao (New York University School of Medicine), Caroline Dean (John Innes Centre, UK), Chris Doe (University of Oregon, Eugene), Uwe Drescher (King's College London), Gordon Fishell (New York University School of Medicine), Brigid Hogan (Duke University), Phil Ingham (Institute of Molecular and Cell Biology, Singapore), Laura Johnston (Columbia University), David Kingsley (Stanford University), Tom Kornberg (University of California, San Francisco), Richard Mann (Columbia University), Andy McMahon (University of Southern California), Marek Mlodzik (Mount Sinai Hospital, New York), Patrick O'Farrell (University of California, San Francisco), Duoia Pan (Johns Hopkins Medical School), Olivier Pourquie (Harvard Medical School), Erez Raz (University of Muenster), Chris Rushlow (New York University), Stephen Small (New York University), Marc Tessier-Lavigne (Rockefeller University)

**Chapter 22:** Simon Hughes (King's College London), Rudolf Jaenisch (Massachusetts Institute of Technology), Arnold Kriegstein (University of California, San Francisco), Doug Melton (Harvard University), Stuart Orkin (Harvard



University), Thomas A. Reh (University of Washington, Seattle), Amy Wagers (Harvard University), Fiona M. Watt (Wellcome Trust Centre for Stem Cell Research, UK), Douglas J. Winton (Cancer Research UK), Shinya Yamanaka (Kyoto University)

**Chapter 23:** Matthew Welch [major contribution] (University of California, Berkeley), Ari Helenius (Swiss Federal Institute of Technology), Dan Portnoy (University of California, Berkeley), David Sibley (Washington University, St. Louis), Michael Way (Cancer Research UK)

**Chapter 24:** Lewis Lanier (University of California, San Francisco).

**Readers:** Najla Arshad (Indian Institute of Science), Venice Chiueh (University of California, Berkeley), Quyen Huynh (University of Toronto), Rachel Kooistra (Loyola University, Chicago), Wes Lewis (University of Alabama), Eric Nam (University of Toronto), Vladimir Rvkin (Stony Brook University), Laasya Samhita (Indian Institute of Science), John Senderak (Jefferson Medical College), Phillipa Simons (Imperial College, UK), Anna Constance Vind (University of Copenhagen), Steve Wellard (Pennsylvania State University), Evan Whitehead (University of California, Berkeley), Carrie Wilczewski (Loyola University, Chicago), Anna Wing (Pennsylvania State University), John Wright (University of Alabama)

**First, second, third, fourth, and fifth editions:**

Jerry Adams (The Walter and Eliza Hall Institute of Medical Research, Australia), Ralf Adams (London Research Institute), David Agard (University of California, San Francisco), Julie Ahringer (The Gurdon Institute, UK), Michael Akam (University of Cambridge), David Allis (The Rockefeller University), Wolfhard Almers (Oregon Health and Science University), Fred Alt (CBR Institute for Biomedical Research, Boston), Linda Amos (MRC Laboratory of Molecular Biology, Cambridge), Raul Andino (University of California, San Francisco), Clay Armstrong (University of Pennsylvania), Martha Arnaud (University of California, San Francisco), Spyros Artavanis-Tsakonas (Harvard Medical School), Michael Ashburner (University of Cambridge), Jonathan Ashmore (University College London), Laura Attardi (Stanford University), Tayna Awabdy (University of California, San Francisco), Jeffrey Axelrod (Stanford University Medical Center), Peter Baker (deceased), David Baldwin (Stanford University), Michael Banda (University of California, San Francisco), Cornelia Bargmann (The Rockefeller University), Ben Barres (Stanford University), David Bartel (Massachusetts Institute of Technology), Konrad Basler (University of Zurich), Wolfgang Baumeister (Max Planck Institute of Biochemistry), Michael Bennett (Albert Einstein College of Medicine), Darwin Berg (University of California, San Diego), Anton Berns (Netherlands Cancer Institute), Merton Bernfield (Harvard Medical School), Michael Berridge (The Babraham Institute, Cambridge, UK), Walter Birchmeier (Max Delbrück Center for Molecular Medicine, Germany), Adrian Bird (Wellcome Trust Centre, UK), David Birk (UMDNJ—Robert Wood Johnson Medical School), Michael Bishop (University of California, San Francisco), Elizabeth Blackburn (University of California, San Francisco), Tim Bliss (National Institute for Medical Research, London), Hans Bode (University of California, Irvine), Piet Borst (Jan Swammerdam Institute, University

of Amsterdam), Henry Bourne (University of California, San Francisco), Alan Boyde (University College London), Martin Brand (University of Cambridge), Carl Branden (deceased), Andre Brandli (Swiss Federal Institute of Technology, Zurich), Dennis Bray (University of Cambridge), Mark Bretscher (MRC Laboratory of Molecular Biology, Cambridge), James Briscoe (National Institute for Medical Research, UK), Marianne Bronner-Fraser (California Institute of Technology), Robert Brooks (King's College London), Barry Brown (King's College London), Michael Brown (University of Oxford), Michael Bulger (University of Rochester Medical Center), Fred Bunz (Johns Hopkins University), Steve Burden (New York University of Medicine), Max Burger (University of Basel), Stephen Burley (SGX Pharmaceuticals), Keith Burridge (University of North Carolina, Chapel Hill), John Cairns (Radcliffe Infirmary, Oxford), Patricia Calarco (University of California, San Francisco), Zacheus Cande (University of California, Berkeley), Lewis Cantley (Harvard Medical School), Charles Cantor (Columbia University), Roderick Capaldi (University of Oregon), Mario Capecchi (University of Utah), Michael Carey (University of California, Los Angeles), Adelaide Carpenter (University of California, San Diego), John Carroll (University College London), Tom Cavalier-Smith (King's College London), Pierre Chambon (University of Strasbourg), Hans Clevers (Hubrecht Institute, The Netherlands), Enrico Coen (John Innes Institute, Norwich, UK), Philip Cohen (University of Dundee, Scotland), Robert Cohen (University of California, San Francisco), Stephen Cohen (EMBL Heidelberg, Germany), Roger Cooke (University of California, San Francisco), John Cooper (Washington University School of Medicine, St. Louis), Michael Cox (University of Wisconsin, Madison), Nancy Craig (Johns Hopkins University), James Crow (University of Wisconsin, Madison), Stuart Cull-Candy (University College London), Leslie Dale (University College London), Caroline Damsky (University of California, San Francisco), Johann De Bono (The Institute of Cancer Research, UK), Anthony DeFranco (University of California, San Francisco), Abby Dernburg (University of California, Berkeley), Arshad Desai (University of California, San Diego), Michael Dexter (The Wellcome Trust, UK), John Dick (University of Toronto, Canada), Christopher Dobson (University of Cambridge), Russell Doolittle (University of California, San Diego), W. Ford Doolittle (Dalhousie University, Canada), Julian Downward (Cancer Research UK), Keith Dudley (King's College London), Graham Dunn (MRC Cell Biophysics Unit, London), Jim Dunwell (John Innes Institute, Norwich, UK), Bruce Edgar (Fred Hutchinson Cancer Research Center, Seattle), Paul Edwards (University of Cambridge), Robert Edwards (University of California, San Francisco), David Eisenberg (University of California, Los Angeles), Sarah Elgin (Washington University, St. Louis), Ruth Ellman (Institute of Cancer Research, Sutton, UK), Beverly Emerson (The Salk Institute), Charles Emerson (University of Virginia), Scott D. Emr (Cornell University), Sharyn Endow (Duke University), Lynn Enquist (Princeton University), Tariq Enver (Institute of Cancer Research, London), David Epel (Stanford University), Gerard Evan (University of California, Comprehensive Cancer Center), Ray Evert (University of Wisconsin, Madison), Matthias Falk (Lehigh University), Stanley Falkow (Stanford



University), Douglas Fearon (University of Cambridge), Gary Felsenfeld (NIH), Stuart Ferguson (University of Oxford), James Ferrell (Stanford University), Christine Field (Harvard Medical School), Daniel Finley (Harvard University), Gary Firestone (University of California, Berkeley), Gerald Fischbach (Columbia University), Robert Fletterick (University of California, San Francisco), Harvey Florman (Tufts University), Judah Folkman (Harvard Medical School), Larry Fowke (University of Saskatchewan, Canada), Jennifer Frazier (Exploratorium®, San Francisco), Matthew Freeman (Laboratory of Molecular Biology, UK), Daniel Friend (University of California, San Francisco), Elaine Fuchs (University of Chicago), Joseph Gall (Carnegie Institution of Washington), Richard Gardner (University of Oxford), Anthony Gardner-Medwin (University College London), Peter Garland (Institute of Cancer Research, London), David Garrod (University of Manchester, UK), Susan M. Gasser (University of Basel), Walter Gehring (Biozentrum, University of Basel), Benny Geiger (Weizmann Institute of Science, Rehovot, Israel), Larry Gerace (The Scripps Research Institute), Holger Gerhardt (London Research Institute), John Gerhart (University of California, Berkeley), Günther Gerisch (Max Planck Institute of Biochemistry), Frank Gertler (Massachusetts Institute of Technology), Sankar Ghosh (Yale University School of Medicine), Alfred Gilman (The University of Texas Southwestern Medical Center), Reid Gilmore (University of Massachusetts, Amherst), Bernie Gilula (deceased), Charles Gilvarg (Princeton University), Benjamin S. Glick (University of Chicago), Michael Glotzer (University of Chicago), Larry Goldstein (University of California, San Diego), Bastien Gomperts (University College Hospital Medical School, London), Daniel Goodenough (Harvard Medical School), Jim Goodrich (University of Colorado, Boulder), Jeffrey Gordon (Washington University, St. Louis), Peter Gould (Middlesex Hospital Medical School, London), Alan Grafen (University of Oxford), Walter Gratzer (King's College London), Michael Gray (Dalhousie University), Douglas Green (St. Jude Children's Hospital), Howard Green (Harvard University), Michael Green (University of Massachusetts, Amherst), Leslie Grivell (University of Amsterdam), Carol Gross (University of California, San Francisco), Frank Grosveld (Erasmus Universiteit, The Netherlands), Michael Grunstein (University of California, Los Angeles), Barry Gumbiner (Memorial Sloan Kettering Cancer Center), Brian Gunning (Australian National University, Canberra), Christine Guthrie (University of California, San Francisco), James Haber (Brandeis University), Ernst Hafen (Universität Zurich), David Haig (Harvard University), Andrew Halestrap (University of Bristol, UK), Alan Hall (Memorial Sloan Kettering Cancer Center), Jeffrey Hall (Brandeis University), John Hall (University of Southampton, UK), Zach Hall (University of California, San Francisco), Douglas Hanahan (University of California, San Francisco), David Hanke (University of Cambridge), Nicholas Harberd (University of Oxford), Graham Hardie (University of Dundee, Scotland), Richard Harland (University of California, Berkeley), Adrian Harris (Cancer Research UK), John Harris (University of Otago, New Zealand), Stephen Harrison (Harvard University), Leland Hartwell (University of Washington, Seattle), Adrian Harwood (MRC Laboratory for Molecular Cell Biology and Cell Biology Unit, London),

Scott Hawley (Stowers Institute for Medical Research, Kansas City), Rebecca Heald (University of California, Berkeley), John Heath (University of Birmingham, UK), Ramanujan Hegde (NIH), Carl-Henrik Heldin (Uppsala University), Ari Helenius (Swiss Federal Institute of Technology), Richard Henderson (MRC Laboratory of Molecular Biology, Cambridge, UK), Glenn Herrick (University of Utah), Ira Herskowitz (deceased), Bertil Hille (University of Washington, Seattle), Alan Hinnebusch (NIH, Bethesda), Brigid Hogan (Duke University), Nancy Hollingsworth (State University of New York, Stony Brook), Frank Holstege (University Medical Center, The Netherlands), Leroy Hood (Institute for Systems Biology, Seattle), John Hopfield (Princeton University), Robert Horvitz (Massachusetts Institute of Technology), Art Horwich (Yale University School of Medicine), David Housman (Massachusetts Institute of Technology), Joe Howard (Max Planck Institute of Molecular Cell Biology and Genetics), Jonathan Howard (University of Washington, Seattle), James Hudspeth (The Rockefeller University), Simon Hughes (King's College London), Martin Humphries (University of Manchester, UK), Tim Hunt (Cancer Research UK), Neil Hunter (University of California, Davis), Laurence Hurst (University of Bath, UK), Jeremy Hyams (University College London), Tony Hyman (Max Planck Institute of Molecular Cell Biology and Genetics), Richard Hynes (Massachusetts Institute of Technology), Philip Ingham (University of Sheffield, UK), Kenneth Irvine (Rutgers University), Robin Irvine (University of Cambridge), Norman Iscove (Ontario Cancer Institute, Toronto), David Ish-Horowicz (Cancer Research UK), Lily Jan (University of California, San Francisco), Charles Janeway (deceased), Tom Jessell (Columbia University), Arthur Johnson (Texas A&M University), Louise Johnson (deceased), Andy Johnston (John Innes Institute, Norwich, UK), E.G. Jordan (Queen Elizabeth College, London), Ron Kaback (University of California, Los Angeles), Michael Karin (University of California, San Diego), Eric Karsenti (European Molecular Biology Laboratory, Germany), Ken Keegstra (Michigan State University), Ray Keller (University of California, Berkeley), Douglas Kellogg (University of California, Santa Cruz), Regis Kelly (University of California, San Francisco), John Kendrick-Jones (MRC Laboratory of Molecular Biology, Cambridge), Cynthia Kenyon (University of California, San Francisco), Roger Keynes (University of Cambridge), Judith Kimble (University of Wisconsin, Madison), Robert Kingston (Massachusetts General Hospital), Marc Kirschner (Harvard University), Richard Klausner (NIH), Nancy Kleckner (Harvard University), Mike Klymkowsky (University of Colorado, Boulder), Kelly Komachi (University of California, San Francisco), Eugene Koonin (NIH), Juan Korenbrot (University of California, San Francisco), Roger Kornberg (Stanford University), Tom Kornberg (University of California, San Francisco), Stuart Kornfeld (Washington University, St. Louis), Daniel Koshland (University of California, Berkeley), Douglas Koshland (Carnegie Institution of Washington, Baltimore), Marilyn Kozak (University of Pittsburgh), Mark Krasnow (Stanford University), Werner Kühlbrandt (Max Planck Institute for Biophysics), John Kuriyan (University of California, Berkeley), Robert Kypta (MRC Laboratory for Molecular Cell Biology, London), Peter Lachmann



(MRC Centre, Cambridge), Ulrich Laemmli (University of Geneva, Switzerland), Trevor Lamb (University of Cambridge), Hartmut Land (Cancer Research UK), David Lane (University of Dundee, Scotland), Jane Langdale (University of Oxford), Lewis Lanier (University of California, San Francisco), Jay Lash (University of Pennsylvania), Peter Lawrence (MRC Laboratory of Molecular Biology, Cambridge), Paul Lazarow (Mount Sinai School of Medicine), Robert J. Lefkowitz (Duke University), Michael Levine (University of California, Berkeley), Warren Levinson (University of California, San Francisco), Alex Levitzki (Hebrew University, Israel), Ottoline Leyser (University of York, UK), Joachim Li (University of California, San Francisco), Tomas Lindahl (Cancer Research UK), Vishu Lingappa (University of California, San Francisco), Jennifer Lippincott-Schwartz (NIH), Joseph Lipsick (Stanford University School of Medicine), Dan Littman (New York University School of Medicine), Clive Lloyd (John Innes Institute, Norwich, UK), Richard Locksley (University of California, San Francisco), Richard Losick (Harvard University), Daniel Louvard (Institut Curie, France), Robin Lovell-Badge (National Institute for Medical Research, London), Scott Lowe (Cold Spring Harbor Laboratory), Shirley Lowe (University of California, San Francisco), Reinhard Lührman (Max Planck Institute of Biophysical Chemistry), Michael Lynch (Indiana University), Laura Machesky (University of Birmingham, UK), Hiten Madhani (University of California, San Francisco), James Maller (University of Colorado Medical School), Tom Maniatis (Harvard University), Colin Manoil (Harvard Medical School), Elliott Margulies (NIH), Philippa Marrack (National Jewish Medical and Research Center, Denver), Mark Marsh (Institute of Cancer Research, London), Wallace Marshall (University of California, San Francisco), Gail Martin (University of California, San Francisco), Paul Martin (University College London), Joan Massagué (Memorial Sloan Kettering Cancer Center), Christopher Mathews (Oregon State University), Brian McCarthy (University of California, Irvine), Richard McCarty (Cornell University), William McGinnis (University of California, San Diego), Anne McLaren (Wellcome/Cancer Research Campaign Institute, Cambridge), Frank McNally (University of California, Davis), Freiderick Meins (Freiderich Miescher Institut, Basel), Stephanie Mel (University of California, San Diego), Ira Mellman (Genentech), Barbara Meyer (University of California, Berkeley), Elliot Meyerowitz (California Institute of Technology), Chris Miller (Brandeis University), Robert Mishell (University of Birmingham, UK), Avron Mitchison (University College London), N.A. Mitchison (University College London), Timothy Mitchison (Harvard Medical School), Quinn Mitrovich (University of California, San Francisco), Peter Mombaerts (The Rockefeller University), Mark Mooseker (Yale University), David Morgan (University of California, San Francisco), Michelle Moritz (University of California, San Francisco), Montrose Moses (Duke University), Keith Mostov (University of California, San Francisco), Anne Mudge (University College London), Hans Müller-Eberhard (Scripps Clinic and Research Institute), Alan Munro (University of Cambridge), J. Murdoch Mitchison (Harvard University), Richard Myers (Stanford University), Diana Myles (University of California, Davis), Andrew Murray (Harvard University), Shigekazu Nagata (Kyoto University, Japan), Geeta Narlikar (University of California, San Francisco), Kim Nasmyth (University of Oxford), Mark E. Nelson (University of Illinois, Urbana-Champaign), Michael Neuberger (deceased), Walter Neupert (University of Munich, Germany), David Nicholls (University of Dundee, Scotland), Roger Nicoll (University of California, San Francisco), Suzanne Noble (University of California, San Francisco), Harry Noller (University of California, Santa Cruz), Jodi Nunnari (University of California, Davis), Paul Nurse (Francis Crick Institute), Roel Nusse (Stanford University), Michael Nussenzweig (Rockefeller University), Duncan O'Dell (deceased), Patrick O'Farrell (University of California, San Francisco), Bjorn Olsen (Harvard Medical School), Maynard Olson (University of Washington, Seattle), Stuart Orkin (Harvard University), Terry Orr-Weaver (Massachusetts Institute of Technology), Erin O'Shea (Harvard University), Dieter Osterhelt (Max Planck Institute of Biochemistry), William Otto (Cancer Research UK), John Owen (University of Birmingham, UK), Dale Oxender (University of Michigan), George Palade (deceased), Barbara Panning (University of California, San Francisco), Roy Parker (University of Arizona, Tucson), William W. Parson (University of Washington, Seattle), Terence Partridge (MRC Clinical Sciences Centre, London), William E. Paul (NIH), Tony Pawson (deceased), Hugh Pelham (MRC, UK), Robert Perry (Institute of Cancer Research, Philadelphia), Gordon Peters (Cancer Research UK), Greg Petsko (Brandeis University), Nikolaus Pfanner (University of Freiburg, Germany), David Phillips (The Rockefeller University), Jeremy Pickett-Heaps (The University of Melbourne, Australia), Jonathan Pines (Gurdon Institute, Cambridge), Julie Pitcher (University College London), Jeffrey Pollard (Albert Einstein College of Medicine), Tom Pollard (Yale University), Bruce Ponder (University of Cambridge), Daniel Portnoy (University of California, Berkeley), James Priess (University of Washington, Seattle), Darwin Prockop (Tulane University), Mark Ptashne (Memorial Sloan Kettering Cancer Center), Dale Purves (Duke University), Efraim Racker (Cornell University), Jordan Raff (University of Oxford), Klaus Rajewsky (Max Delbrück Center for Molecular Medicine, Germany), George Ratcliffe (University of Oxford), Elio Raviola (Harvard Medical School), Martin Rechsteiner (University of Utah, Salt Lake City), David Rees (National Institute for Medical Research, London), Thomas A. Reh (University of Washington, Seattle), Louis Reichardt (University of California, San Francisco), Renee Reijo (University of California, San Francisco), Caetano Reis e Sousa (Cancer Research UK), Fred Richards (Yale University), Conly Rieder (Wadsworth Center, Albany), Phillips Robbins (Massachusetts Institute of Technology), Elizabeth Robertson (The Wellcome Trust Centre for Human Genetics, UK), Elaine Robson (University of Reading, UK), Robert Roeder (The Rockefeller University), Joel Rosenbaum (Yale University), Janet Rossant (Mount Sinai Hospital, Toronto), Jesse Roth (NIH), Jim Rothman (Memorial Sloan Kettering Cancer Center), Rodney Rothstein (Columbia University), Erkki Ruoslahti (La Jolla Cancer Research Foundation), Gary Ruvkun (Massachusetts General Hospital), David Sabatini (New York University), Alan Sachs (University of California, Berkeley), Edward Salmon (University of North Carolina,



Chapel Hill), Aziz Sancar (University of North Carolina, Chapel Hill), Joshua Sanes (Harvard University), Peter Sarnow (Stanford University), Lisa Satterwhite (Duke University Medical School), Robert Sauer (Massachusetts Institute of Technology), Ken Sawin (The Wellcome Trust Centre for Cell Biology, UK), Howard Schachman (University of California, Berkeley), Gerald Schatten (Pittsburgh Development Center), Gottfried Schatz (Biozentrum, University of Basel), Randy Schekman (University of California, Berkeley), Richard Scheller (Stanford University), Giampietro Schiavo (Cancer Research UK), Ueli Schibler (University of Geneva, Switzerland), Joseph Schlessinger (New York University Medical Center), Danny J. Schnell (University of Massachusetts, Amherst), Michael Schramm (Hebrew University, Israel), Robert Schreiber (Washington University School of Medicine), James Schwartz (Columbia University), Ronald Schwartz (NIH), François Schweisguth (Institut Pasteur, France), John Scott (University of Manchester, UK), John Sedat (University of California, San Francisco), Peter Selby (Cancer Research UK), Zvi Sellinger (Hebrew University, Israel), Gregg Semenza (Johns Hopkins University), Philippe Sengel (University of Grenoble, France), Peter Shaw (John Innes Institute, Norwich, UK), Michael Sheetz (Columbia University), Morgan Sheng (Massachusetts Institute of Technology), Charles Sherr (St. Jude Children's Hospital), David Shima (Cancer Research UK), Samuel Silverstein (Columbia University), Melvin I. Simon (California Institute of Technology), Kai Simons (Max Planck Institute of Molecular Cell Biology and Genetics), Jonathan Slack (Cancer Research UK), Alison Smith (John Innes Institute, Norfolk, UK), Austin Smith (University of Edinburgh, UK), Jim Smith (The Gurdon Institute, UK), John Maynard Smith (University of Sussex, UK), Mitchell Sogin (Woods Hole Institute), Frank Solomon (Massachusetts Institute of Technology), Michael Solursh (University of Iowa), Bruce Spiegelman (Harvard Medical School), Timothy Springer (Harvard Medical School), Mathias Sprinzl (University of Bayreuth, Germany), Scott Stachel (University of California, Berkeley), Andrew Staehelin (University of Colorado, Boulder), David Standring (University of California, San Francisco), Margaret Stanley (University of Cambridge), Martha Stark (University of California, San Francisco), Wilfred Stein (Hebrew University, Israel), Malcolm Steinberg (Princeton University), Ralph Steinman (deceased), Len Stephens (The Babraham Institute, UK), Paul Sternberg (California Institute of Technology), Chuck Stevens (The Salk Institute), Murray Stewart (MRC Laboratory of Molecular Biology, Cambridge), Bruce Stillman (Cold Spring Harbor Laboratory), Charles Streuli (University of Manchester, UK), Monroe Strickberger (University of Missouri, St. Louis), Robert Stroud (University of California, San Francisco), Michael Stryker (University of California, San Francisco), William Sullivan (University of California, Santa Cruz), Azim Surani (The Gurdon Institute, University of Cambridge), Daniel Szollosi (Institut National de la Recherche Agronomique, France), Jack Szostak (Harvard Medical School), Clifford Tabin (Harvard Medical School), Masatoshi Takeichi (RIKEN Center for Developmental Biology, Japan), Nicolas Tapon (London Research Institute), Diethard Tautz (University of Cologne, Germany), Julie Theriot (Stanford University),

Roger Thomas (University of Bristol, UK), Craig Thompson (Memorial Sloan Kettering Cancer Center), Janet Thornton (European Bioinformatics Institute, UK), Vernon Thornton (King's College London), Cheryll Tickle (University of Dundee, Scotland), Jim Till (Ontario Cancer Institute, Toronto), Lewis Tilney (University of Pennsylvania), David Tollervey (University of Edinburgh, UK), Ian Tomlinson (Cancer Research UK), Nick Tonks (Cold Spring Harbor Laboratory), Alain Townsend (Institute of Molecular Medicine, John Radcliffe Hospital, Oxford), Paul Travers (Scottish Institute for Regeneration Medicine), Robert Trelstad (UMDNJ—Robert Wood Johnson Medical School), Anthony Trewavas (Edinburgh University, Scotland), Nigel Unwin (MRC Laboratory of Molecular Biology, Cambridge), Victor Vacquier (University of California, San Diego), Ronald D. Vale (University of California, San Francisco), Tom Vanaman (University of Kentucky), Harry van der Westen (Wageningen, The Netherlands), Harold Varmus (National Cancer Institute, United States), Alexander J. Varshavsky (California Institute of Technology), Donald Voet (University of Pennsylvania), Harald von Boehmer (Harvard Medical School), Madhu Wahi (University of California, San Francisco), Virginia Walbot (Stanford University), Frank Walsh (GlaxoSmithKline, UK), Trevor Wang (John Innes Institute, Norwich, UK), Xiaodong Wang (The University of Texas Southwestern Medical School), Yu-Lie Wang (Worcester Foundation for Biomedical Research, MA), Gary Ward (University of Vermont), Anne Warner (University College London), Graham Warren (Yale University School of Medicine), Paul Wassarman (Mount Sinai School of Medicine), Clare Waterman-Storer (The Scripps Research Institute), Fiona Watt (Cancer Research UK), John Watts (John Innes Institute, Norwich, UK), Klaus Weber (Max Planck Institute for Biophysical Chemistry), Martin Weigert (Institute of Cancer Research, Philadelphia), Robert Weinberg (Massachusetts Institute of Technology), Harold Weintraub (deceased), Karsten Weis (Swiss Federal Institute of Technology), Irving Weissman (Stanford University), Jonathan Weissman (University of California, San Francisco), Susan R. Wentz (Vanderbilt University School of Medicine), Norman Wessells (University of Oregon, Eugene), Stephen West (Cancer Research UK), Judy White (University of Virginia), William Wickner (Dartmouth College), Michael Wilcox (deceased), Lewis T. Williams (Chiron Corporation), Patrick Williamson (University of Massachusetts, Amherst), Keith Willison (Chester Beatty Laboratories, London), John Wilson (Baylor University), Alan Wolffe (deceased), Richard Wolfenden (University of North Carolina, Chapel Hill), Sandra Wolin (Yale University School of Medicine), Lewis Wolpert (University College London), Richard D. Wood (University of Pittsburgh Cancer Institute), Abraham Worcel (University of Rochester), Nick Wright (Cancer Research UK), John Wyke (Beatson Institute for Cancer Research, Glasgow), Michael P. Yaffe (California Institute for Regenerative Medicine), Kenneth M. Yamada (NIH), Keith Yamamoto (University of California, San Francisco), Charles Yocum (University of Michigan, Ann Arbor), Peter Yurchenco (UMDNJ—Robert Wood Johnson Medical School), Rosalind Zalin (University College London), Patricia Zambryski (University of California, Berkeley), Marino Zerial (Max Planck Institute of Molecular Cell Biology and Genetics).



# Contents

<b>PART I</b>	<b>INTRODUCTION TO THE CELL</b>	<b>1</b>
Chapter 1	Cells and Genomes	1
Chapter 2	Cell Chemistry and Bioenergetics	43
Chapter 3	Proteins	109
<b>PART II</b>	<b>BASIC GENETIC MECHANISMS</b>	<b>175</b>
Chapter 4	DNA, Chromosomes, and Genomes	175
Chapter 5	DNA Replication, Repair, and Recombination	237
Chapter 6	How Cells Read the Genome: From DNA to Protein	299
Chapter 7	Control of Gene Expression	369
<b>PART III</b>	<b>WAYS OF WORKING WITH CELLS</b>	<b>439</b>
Chapter 8	Analyzing Cells, Molecules, and Systems	439
Chapter 9	Visualizing Cells	529
<b>PART IV</b>	<b>INTERNAL ORGANIZATION OF THE CELL</b>	<b>565</b>
Chapter 10	Membrane Structure	565
Chapter 11	Membrane Transport of Small Molecules and the Electrical Properties of Membranes	597
Chapter 12	Intracellular Compartments and Protein Sorting	641
Chapter 13	Intracellular Membrane Traffic	695
Chapter 14	Energy Conversion: Mitochondria and Chloroplasts	753
Chapter 15	Cell Signaling	813
Chapter 16	The Cytoskeleton	889
Chapter 17	The Cell Cycle	963
Chapter 18	Cell Death	1021
Chapter 19	Cell Junctions and the Extracellular Matrix	1035
<b>PART V</b>	<b>CELLS IN THEIR SOCIAL CONTEXT</b>	<b>1035</b>
Chapter 20	Cancer	1091
Chapter 21	Development of Multicellular Organisms	1145
Chapter 22	Stem Cells and Tissue Renewal	1217
Chapter 23	Pathogens and Infection	1263
Chapter 24	The Innate and Adaptive Immune Systems	1297
Glossary		G: 1
Index		I: 1
Tables	The Genetic Code, Amino Acids	T: 1