

# Molecular Biology of THE CELL

Sixth Edition



ALBERTS   JOHNSON   LEWIS   MORGAN   RAFF   ROBERTS   WALTER

**Molecular Biology of**  
**THE CELL**  
Sixth Edition



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## 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



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**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 Bochicchio 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.)

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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)

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**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 Tollervey (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 Freiberg), 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. Wente (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)

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