Molecular Biology of THE CELL

Fifth Edition

ALBERTS JOHNSON LEWIS RAFF ROBERTS WALTER

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Preface

In many respects, we understand the structure of the universe better than the workings of living cells. Scientists can calculate the age of the Sun and predict when it will cease to shine, but we cannot explain how it is that a human being may live for eighty years but a mouse for only two. We know the complete genome sequences of these and many other species, but we still cannot predict how a cell will behave if we mutate a previously unstudied gene. Stars may be 10^{43} times bigger, but cells are more complex, more intricately structured, and more astonishing products of the laws of physics and chemistry. Through heredity and natural selection, operating from the beginnings of life on Earth to the present day—that is, for about 20% of the age of the universe—living cells have been progressively refining and extending their molecular machinery, and recording the results of their experiments in the genetic instructions they pass on to their progeny.

With each edition of this book, we marvel at the new information that cell biologists have gathered in just a few years. But we are even more amazed and daunted at the sophistication of the mechanisms that we encounter. The deeper we probe into the cell, the more we realize how much remains to be understood. In the days of our innocence, working on the first edition, we hailed the identification of a single protein—a signal receptor, say—as a great step forward. Now we appreciate that each protein is generally part of a complex with many others, working together as a system, regulating one another's activities in subtle ways, and held in specific positions by binding to scaffold proteins that give the chemical factory a definite spatial structure. Genome sequencing has given us virtually complete molecular parts-lists for many different organisms; genetics and biochemistry have told us a great deal about what those parts are capable of individually and which ones interact with which others; but we have only the most primitive grasp of the dynamics of these biochemical systems, with all their interlocking control loops. Therefore, although there are great achievements to report, cell biologists face even greater challenges for the future.

In this edition, we have included new material on many topics, ranging from epigenetics, histone modifications, small RNAs, and comparative genomics, to genetic noise, cytoskeletal dynamics, cell-cycle control, apoptosis, stem cells, and novel cancer therapies. As in previous editions, we have tried above all to give readers a conceptual framework for the mass of information that we now have about cells. This means going beyond the recitation of facts. The goal is to learn how to put the facts to use—to reason, to predict, and to control the behavior of living systems.

To help readers on the way to an active understanding, we have for the first time incorporated end-of-chapter problems, written by John Wilson and Tim Hunt. These emphasize a quantitative approach and the art of reasoning from experiments. A companion volume, *Molecular Biology of the Cell, Fifth Edition: The Problems Book* (ISBN 978-0-8153-4110-9), by the same authors, gives complete answers to these problems and also contains more than 1700 additional problems and solutions.

A further major adjunct to the main book is the attached Media DVD-ROM disc. This provides hundreds of movies and animations, including many that are new in this edition, showing cells and cellular processes in action and bringing the text to life; the disc also now includes all the figures and tables from the main

book, pre-loaded into PowerPoint® presentations. Other ancillaries available for the book include a bank of test questions and lecture outlines, available to qualified instructors, and a set of 200 full-color overhead transparencies.

Perhaps the biggest change is in the physical structure of the book. In an effort to make the standard Student Edition somewhat more portable, we are providing Chapters 21–25, covering multicellular systems, in electronic (PDF) form on the accompanying disc, while retaining in the printed volume Chapters 1–20, covering the core of the usual cell biology curriculum. But we should emphasize that the final chapters have been revised and updated as thoroughly as the rest of the book and we sincerely hope that they will be read! A Reference Edition (ISBN 978-0-8153-4111-6), containing the full set of chapters as printed pages, is also available for those who prefer it.

Full details of the conventions adopted in the book are given in the Note to the Reader that follows this Preface. As explained there, we have taken a drastic approach in confronting the different rules for the writing of gene names in different species: throughout this book, we use the same style, regardless of species, and often in defiance of the usual species-specific conventions.

As always, we are indebted to many people. Full acknowledgments for scientific help are given separately, but we must here single out some exceptionally important contributions: Julie Theriot is almost entirely responsible for Chapters 16 (Cytoskeleton) and 24 (Pathogens, Infection, and Innate Immunity), and David Morgan likewise for Chapter 17 (Cell Cycle). Wallace Marshall and Laura Attardi provided substantial help with Chapters 8 and 20, respectively, as did Maynard Olson for the genomics section of Chapter 4, Xiaodong Wang for Chapter 18, and Nicholas Harberd for the plant section of Chapter 15.

We also owe a huge debt to the staff of Garland Science and others who helped convert writers' efforts into a polished final product. Denise Schanck directed the whole enterprise and shepherded the wayward authors along the road with wisdom, skill, and kindness. Nigel Orme put the artwork into its final form and supervised the visual aspects of the book, including the back cover, with his usual flair. Matthew McClements designed the book and its front cover. Emma Jeffcock laid out its pages with extraordinary speed and unflappable efficiency, dealing impeccably with innumerable corrections. Michael Morales managed the transformation of a mass of animations, video clips, and other materials into a user-friendly DVD-ROM. Eleanor Lawrence and Sherry Granum updated and enlarged the glossary. Jackie Harbor and Sigrid Masson kept us organized. Adam Sendroff kept us aware of our readers and their needs and reactions. Marjorie Anderson, Bruce Goatly, and Sherry Granum combed the text for obscurities, infelicities, and errors. We thank them all, not only for their professional skill and dedication and for efficiency far surpassing our own, but also for their unfailing helpfulness and friendship: they have made it a pleasure to work on the book.

Lastly, and with no less gratitude, we thank our spouses, families, friends and colleagues. Without their patient, enduring support, we could not have produced any of the editions of this book.

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A 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 deals with the principles of the main experimental methods for investigating cells. It is not necessary to read these two chapters in order to understand the later chapters, but a reader will find it a useful reference.

Part IV discusses the internal organization of the cell.

Part V follows the behavior of cells in multicellular systems, starting with cell–cell junctions and extracellular matrix and concluding with two chapters on the immune system. Chapters 21–25 can be found on the Media DVD-ROM which is packaged with each book, providing increased portability for students.

End-of-Chapter Problems

A selection of problems, written by John Wilson and Tim Hunt, now appears in the text at the end of each chapter. The complete solutions to these problems can be found in *Molecular Biology of the Cell, Fifth 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 frequently include the original papers in which important discoveries were first reported. Chapter 8 includes several tables giving the dates of crucial developments along with the names of the scientists involved. Elsewhere in the book the policy has been to avoid naming individual scientists.

Media Codes

Media codes are integrated throughout the text to indicate when relevant videos and animations are available on the DVD-ROM. The four-letter codes are enclosed in brackets and highlighted in color, like this <ATCG>. The interface for the *Cell Biology Interactive* media player on the DVD-ROM contains a window where you enter the 4-letter code. When the code is typed into the interface, the corresponding media item will load into the media player.

Glossary Terms

Throughout the book, **boldface type** has been used to highlight key terms at the point in a chapter where the main discussion of them occurs. *Italic* is used to set off important terms with a lesser degree of emphasis. At the end of the book is the expanded **glossary**, covering technical terms that are part of the common currency of cell biology; it is intended as a first resort for a reader who encounters an unfamiliar term used without explanation.

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),

case and rest in lower case; or (as in *Drosophila*) with different combinations of upper and lower case, according to whether the first mutant allele to be discovered gave 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 the discussion. What convention then should we use?

We have decided in this book to cast aside the conventions for individual species and follow a uniform rule: we write all gene names, like the names of people and places, with the first letter in upper case and the rest in lower case, 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 upper case 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 lower-case 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, etc.). 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	*Hoxa4*	Hoxa4	*HoxA4*	HoxA4
	Bmp4	BMP4	*Bmp4*	BMP4
	integrin α-1, Itgα1	integrin α1	*Integrin α1, Itgα1*	integrin α1
Human	*HOXA4*	HOXA4	*HoxA4*	HoxA4
Zebrafish	*cyclops, cyc*	Cyclops, Cyc	*Cyclops, Cyc*	Cyclops, Cyc
Caenorhabditis	*unc-6*	UNC-6	*Unc6*	Unc6
Drosophila	*sevenless, sev* (named after recessive mutant phenotype)	Sevenless, SEV	*Sevenless, Sev*	Sevenless, Sev
	Deformed, Dfd (named after dominant mutant phenotype)	Deformed, DFD	*Deformed, Dfd*	Deformed, Dfd
Yeast				
Saccharomyces cerevisiae (budding yeast)	*CDC28*	Cdc28, Cdc28p	*Cdc28*	Cdc28
Schizosaccharomyces pombe (fission yeast)	*Cdc2*	Cdc2, Cdc2p	*Cdc2*	Cdc2
Arabidopsis	*GAI*	GAI	*Gai*	GAI
E. coli	*uvrA*	UvrA	*UvrA*	UvrA

Ancillaries

Molecular Biology of the Cell, Fifth Edition: The Problems Book
by John Wilson and Tim Hunt (ISBN: 978-0-8153-4110-9)
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, and pose research-based problems. *Molecular Biology of the Cell, Fifth 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 on the CD-ROM which accompanies the book. Solutions for the end-of-chapter problems in the main textbook are also found in *The Problems Book.*

***MBoC5* Media DVD-ROM**
The DVD included with every copy of the book contains the figures, tables, and micrographs from the book, pre-loaded into PowerPoint® presentations, one for each chapter. A separate folder contains individual versions of each figure, table, and micrograph in JPEG format. The panels are available in PDF format. There are also over 125 videos, animations, molecular structure tutorials, and high-resolution micrographs on the DVD. The authors have chosen to include material that not only reinforces basic concepts but also expands the content and scope of the book. The multimedia can be accessed either as individual files or through the *Cell Biology Interactive* media player. As discussed above, the media player has been programmed to work with the Media Codes integrated throughout the book. A complete table of contents and overview of all electronic resources is contained in the *MBoC5 Media Viewing Guide,* a PDF file located on the root level of the DVD-ROM and in the Appendix of the media player. The DVD-ROM also contains Chapters 21–25 which cover multicellular systems. The chapters are in PDF format and can be easily printed or searched using Adobe® Acrobat® Reader or other PDF software.

Teaching Supplements
Upon request, teaching supplements for *Molecular Biology of the Cell* are available to qualified instructors.

MBoC5 Transparency Set
Provides 200 full-color overhead acetate transparencies of the most important figures from the book.

MBoC5 Test Questions
A selection of test questions will be available. Written by Kirsten Benjamin (Amyris Biotechnologies, Emeryville, California) and Linda Huang (University of Massachusetts, Boston), these thought questions will test students' understanding of the chapter material.

MBoC5 Lecture Outlines
Lecture outlines created from the concept heads for the text are provided.

Garland Science Classwire™
All of the teaching supplements on the DVD-ROM (these include figures in PowerPoint and JPEG format; Chapters 21–25 in PDF format; 125 videos, animations, and movies) and the test questions and lecture outlines are available to qualified instructors online at the Garland Science Classwire™ Web site. Garland Science Classwire™ offers access to other instructional resources from all of the Garland Science textbooks, and provides free online course management tools. For additional information, please visit http://www.classwire.com/garlandscience or e-mail science@garland.com. (*Classwire* is a trademark of Chalkfree, Inc.)