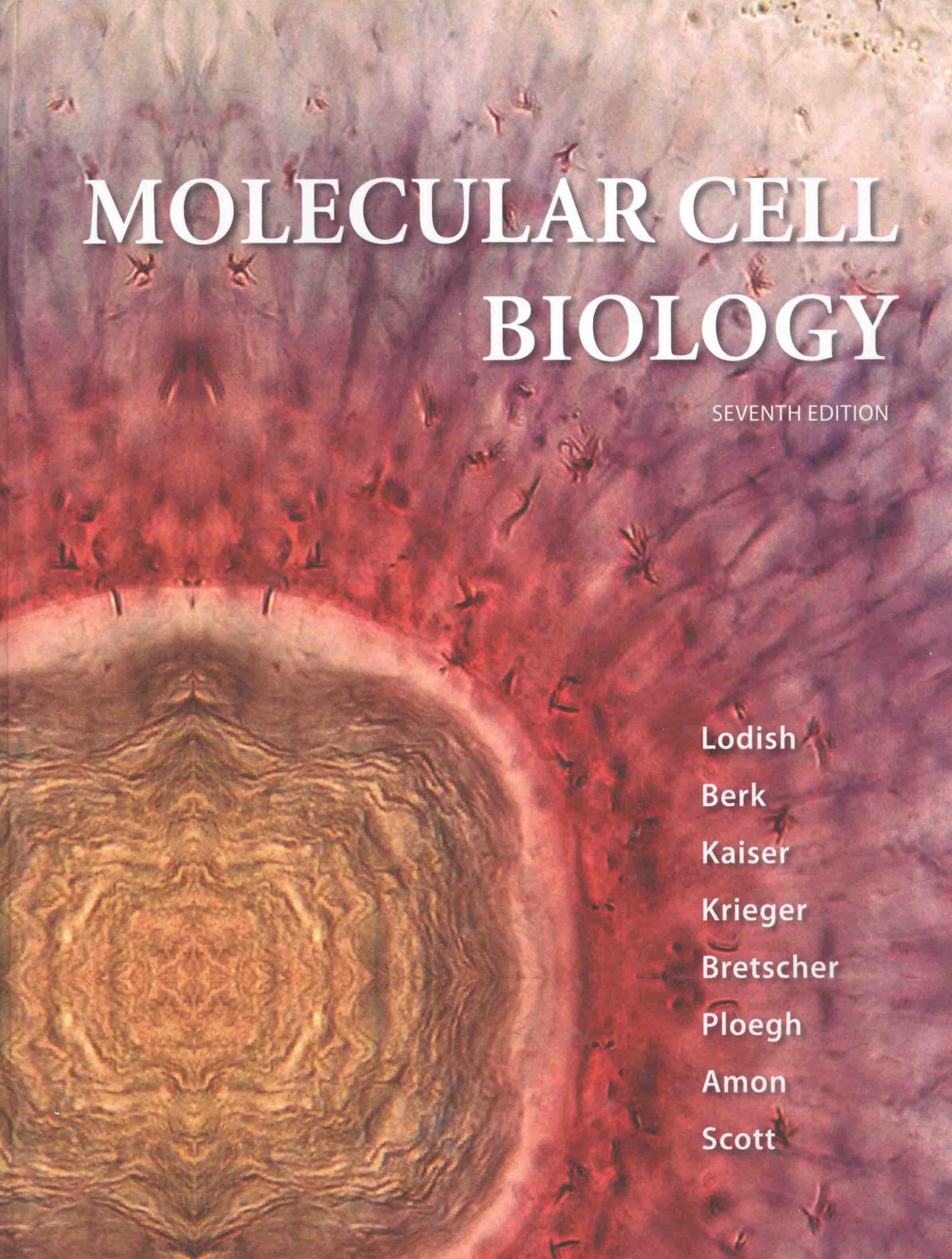
MOLECULAR CELL BIOLOGY

SEVENTH EDITION



Lodish
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MOLECULAR CELL BIOLOGY

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ANGELIKA AMON is Professor of Biology at the Massachusetts Institute of Technology, a member of the Koch Institute for Integrative Cancer Research, and Investigator at the Howard Hughes Medical Institute. She is also a member of the National Academy of Sciences. Her laboratory studies the molecular mechanisms that govern chromosome segregation during mitosis and meiosis and the consequences—aneuploidy—when these mechanisms fail during normal cell proliferation and cancer development. Dr. Amon teaches undergraduate and graduate courses in cell biology and genetics.

To our students and to our teachers,
from whom we continue to learn, and to our families,
for their support, encouragement, and love

PREFACE

In writing the seventh edition of *Molecular Cell Biology* we have incorporated many of the spectacular advances made over the past four years in biomedical science, driven in part by new experimental technologies that have revolutionized many fields. Fast techniques for sequencing DNA and RNA, for example, have uncovered many novel noncoding RNAs that regulate gene expression and identified hundreds of human genes that affect diseases such as diabetes, osteoporosis, and cancer. Genomics has also led to many novel insights into the evolution of life forms and the functions of individual members of multiprotein families. Exploring the most current developments in the field is always a priority in writing a new edition, but it is also important to us to communicate the basics of cell biology clearly. To this end, in addition to introducing new discoveries and technologies, we have streamlined and reorganized several chapters to clarify processes and concepts for students.

New Co-Author, Angelika Amon

The new edition of *MCB* introduces a new member to our author team, respected researcher and teacher Angelika Amon of the Massachusetts Institute of Technology. Her laboratory uses the budding yeast *S. cerevisiae* and mouse and cell culture models to gain a detailed molecular understanding of the regulatory circuits that control chromosome segregation and the effects of aneuploidy on cell physiology. Dr. Amon also teaches undergraduate and graduate courses in Cell Biology and Genetics.

Revised, Cutting Edge Content

The seventh edition of *Molecular Cell Biology* includes new and improved chapters:

- "Molecules, Cells and Evolution" (Chapter 1) now frames cell biology in the light of evolution: this perspective explains why scientists pick particular unicellular and multicellular "model" organisms to study specific genes and proteins that are important for cellular function.

- "Culturing, Visualizing, and Perturbing Cells" (Chapter 9) has been rewritten to include cutting edge methods including FRAP, FRET, siRNA, and chemical biology, making it a state-of-the-art methods chapter.

- "Signal Transduction and G Protein-Coupled Receptors" and "Signaling Pathways that Control Gene Expression" (Chapters 15 and 16) have been reorganized and illustrated with simplified overview figures, to help students navigate the complexity of signaling pathways.

- "The Eukaryotic Cell Cycle" (Chapter 19) now begins with the concepts of "START" (a cell's commitment to entering the cell cycle starting with DNA synthesis) and then progresses through the cycle stages. The chapter focuses on yeast and mammals and uses general names for cell cycle components when possible to improve student understanding.

- "Stem Cells, Cell Asymmetry, and Cell Death" (Chapter 21) now incorporates developmental topics, including new coverage of induced pluripotent stem (iPS) cells.

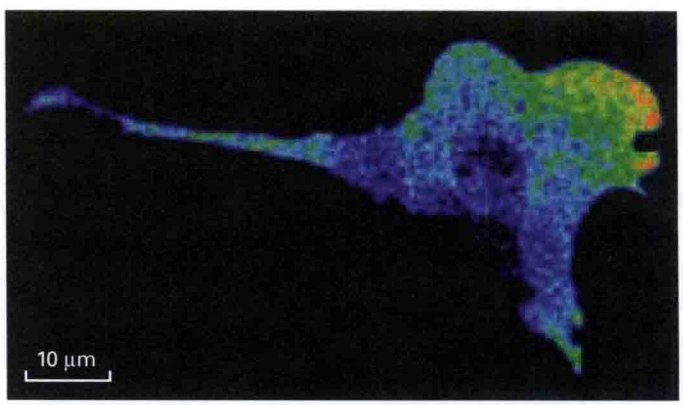


FIGURE 9-22 In this mouse fibroblast, FRET has been used to reveal that the interaction between an active regulatory protein (Rac) and its binding partner is localized to the front of the migrating cell.

Increased Clarity, Improved Pedagogy

As experienced teachers of both undergraduate and graduate students, we are always striving to improve student understanding. In this seventh edition, perennially confusing topics, such as cellular energetics, cell signaling, and immunology, have been streamlined and revised to improve student understanding. Each figure was reconsidered and, if possible, simplified to highlight key lessons. Heavily revised end-of-chapter materials include 30% new questions, including additional Analyze the Data problems to give students further practice at interpreting experimental evidence. The result is a balance of state-of-the-art currency and experimental focus with attention to clarity, organization, and pedagogy.

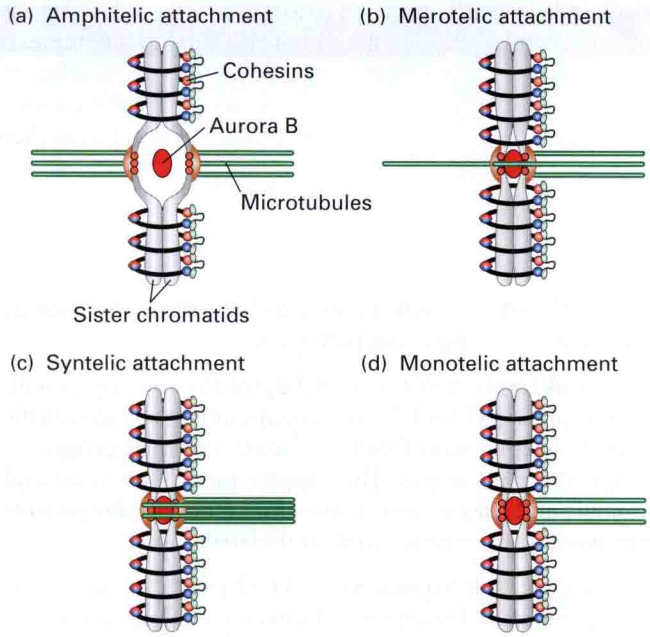
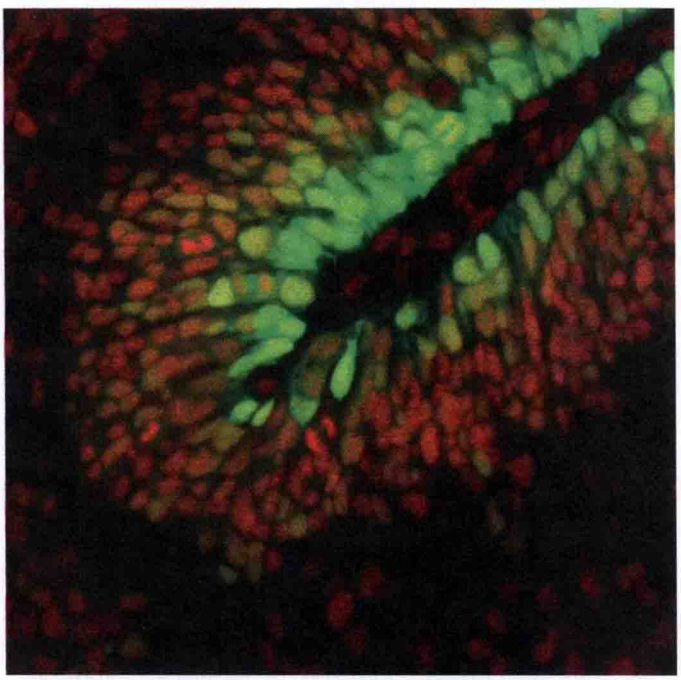


FIGURE 19-25 Stable and unstable chromosome attachments.

New Discoveries, New Methodologies

- Covalent regulation of protein activity by ubiquitination/deubiquitination (Ch. 3)
- Molecular chaperones including the Hsp90 family of proteins (Ch. 3)
- Mammalian protein synthesis and the roles of polymerases delta (lagging strand) and epsilon (leading strand) in eukaryotic DNA synthesis (Ch. 4)
- Non-radioactive probes (for in-situ hybridization, for example) (Ch. 5)
- Quantitative PCR (and RT-PCR) and high-throughput DNA sequencing (Ch. 5)
- DNA fingerprinting using microsatellites and PCR (Ch. 6)
- Personal genome sequencing and the 1000 Genome Project (Ch. 6)
- Epigenetic mechanisms of transcriptional regulation (Ch. 7)
- Transcriptional regulation by non-coding RNAs (e.g., Xist in X-chromosome inactivation, siRNA-directed heterochromatin formation in fission yeast and DNA methylation in plants) (Ch. 7)
- Fluorescent mRNA labeling to follow mRNA localization in live cells (Ch. 8)
- Structure and function of the nuclear pore complex (Chs. 8 and 13)
- Additional coverage of FRAP, FRET, and siRNA techniques (Ch. 9)
- Lipid droplets and their formation (Ch. 10)
- Assembly of the multiprotein T-cell receptor complex (Ch. 10)
- Structure of the Na^+/K^+ ATPase (Ch. 11)
- Structure and mechanism of the multidrug transporter ABCB1 (MDR1) (Ch. 11)
- Structure and function of the cystic fibrosis transmembrane regulator (CFTR) (Ch. 11)
- The role of an anion antiporter in bone resorption (Ch. 11)
- Structures of complex I and II as well as the mechanism of electron flow and proton pumping in the electron transport chain (Ch. 12)
- Generation and inactivation of toxic reactive oxygen species (ROS) (Ch. 12)
- The mechanism of proton flow through the half-channels of ATP Synthase (Ch. 12)
- Tail-anchored membrane proteins (Ch. 13)
- How modifications of *N*-linked oligosaccharides are used to monitor protein folding and quality control (Ch. 13)
- The mechanism of formation of multivesicular endosomes involving ubiquitination and ESCRT (Ch. 14)
- Advances in our understanding of autophagy as a mechanism for recycling organelles and proteins (Ch. 14)
- Affinity purification techniques for studying signal transduction proteins (Ch. 15)
- Structure of the β-adrenergic receptor in the inactive and active states and with its associated trimeric G protein, $G_{\alpha s}$ (Ch. 15)
- Activation of EGF receptor by EGF via the formation of an asymmetric kinase domain dimer (Ch. 16)
- Hedgehog signaling in vertebrates involving primary cilia (Ch. 16)
- NF-κB signaling pathway and polyubiquitin scaffolds (Ch. 16)
- Integration of signals in fat cell differentiation via PPARγ (Ch. 16)
- Mechanism of Arp2/3 nucleation of actin filaments (Ch. 17)
- The dynamics of microfilaments during endocytosis and the role of endocytic membrane recycling during cell migration (Ch. 17)
- Intraflagellar transport and the function of primary cilia (Ch. 18)
- Plant mitosis and cytokinesis (Ch. 18)
- +TIPs as regulators of microtubule (+) end function (Ch. 18)
- Proteins involved in mitotic spindle formation and kinetochore attachment to microtubules (Ch. 19)
- Elastic fibers that permit many tissues to undergo repeated stretching and recoiling (Ch. 20)

- Extracellular matrix remodelling and degradation by matrix metalloproteinases (Ch. 20)
- Stem cells in the intestinal epithelium (Ch. 21)
- Regulation of gene expression in embryonic stem (ES) cells (Ch. 21)
- Generation of induced pluripotent stem (iPS) cells (Ch. 21)
- Advances in our understanding of regulated cell death (Ch. 21)
- Structure of the nicotinic acetylcholine receptor (Ch. 22)
- Molecular model of the MEC-4 touch receptor complex in *C. elegans* (Ch. 22)
- Synapse formation in neuromuscular junctions (Ch. 22)
- Toll-like receptors (TLRs) and the inflammasome (Ch. 23)
- Epigenetics and cancer (Ch. 24)



Cells being born in the developing cerebellum.

Medical Relevance

Many advances in basic cellular and molecular biology have led to new treatments for cancer and other significant human diseases. These medical examples are woven throughout the chapters where appropriate to give students an appreciation for the clinical applications of the basic science they are learning. Many of these applications hinge on a detailed understanding of multiprotein complexes in cells—complexes that catalyze cell movements; regulate DNA transcription, replication, and repair; coordinate metabolism; and connect cells to other cells and to proteins and carbohydrates in their extracellular environment.

The following is a list of new medical examples.

- Cholesterol transport and atherosclerosis as an illustration of the hydrophobic effect (Ch. 2)
- Use of genetically engineered corn with high lysine content to promote the growth of livestock as an illustration of importance of essential amino acids (Ch. 2)
- Poliovirus and HIV-1 as examples of viruses that infect only certain cell types due to tissue-specific cell surface receptors (Ch. 4)
- HPV vaccine and its ability to protect against common types of HPV, and the development of cervical cancer (Ch. 4)
- Huntington's disease as an example of a microsatellite expansion disease (Ch. 6)
- Potential treatment of cystic fibrosis using small molecules that would allow the mutant protein to traffic normally to the cell surface (Ch. 11)
- Role of genetic defects in ClC-7, a chloride ion channel, in the hereditary bone disease osteopetrosis (Ch. 11)
- Mitochondrial diseases such as Charcot-Marie-Tooth disease and Miller syndrome (Ch. 12)
- Use of ligand-binding domains of cell-surface receptors as therapeutic drugs, such as the extracellular domain of TNFα receptor to treat arthritis and other inflammatory conditions (Ch. 15)
- Role of Hedgehog (Hh) signaling in human cancers including medulloblastomas and rhabdomyosarcomas (Ch. 16)
- Role of B-Raf kinase in melanoma and use of selective inhibitors of B-Raf in cancer treatment (Ch. 16)
- Defects in a regulator of dynein as a cause of lissencephaly (Ch. 18)
- Elastic fiber protein fibrillin 1 and Marfan's Syndrome (Ch. 20)
- Use of iPS cells in uncovering the molecular basis of ALS (Ch. 21)
- Variations in human sense of smell (Ch. 22)
- Microarray analysis of breast cancer tumors as a way to distinguish gene expression patterns and individualize treatment (Ch. 24)

MEDIA AND SUPPLEMENTS

For Students

NEW **BioPortal for *Molecular Cell Biology*** A robust teaching and learning tool with all of the study and quizzing resources available through the Companion Web Site (listed below) as well as a fully-interactive eBook. BioPortal also includes **NEW LearningCurve**, a self-paced adaptive quizzing tool for students. With questions tailored to their target difficulty level and an engaging scoring system, LearningCurve encourages students to incorporate content from the text into their study routine and provides them with a study plan upon completion.

Companion Web Site www.whfreeman.com/lodish7e

- **Podcasts** narrated by the authors give students a deeper understanding of key figures in the text and a sense of the thrill of discovery.
- More than 125 **animations and research videos** show the dynamic nature of key cellular processes and important experimental techniques.
- **Classic Experiment** essays focus on classic groundbreaking experiments and explore the investigative process.
- **Online Quizzing** is provided, including multiple-choice and short answer questions.

Student Solutions Manual (ISBN:1-4641-0230-9), written by Brian Storrie of the University of Arkansas for Medical Sciences, Eric A. Wong, Richard Walker, Glenda Gillaspy, and Jill Sible of Virginia Polytechnic Institute and State University and updated by Tom Huxford of San Diego State University, Stephanie Bingham of Barry University, Brian Sato of University of California-Irvine, Steve Amato of Johns Hopkins University, Greg Kelly of University of Western Ontario, Tom Keller of Florida State University, and Elizabeth Good of University of Illinois-Urbana-Champaign, contains complete worked-out solutions to all the end-of-chapter problems in the textbook.

eBook (ISBN: 1-4641-0229-5) This customizable eBook fully integrates the complete contents of the text and its interactive media in a format that features a variety of helpful study tools, including full-text searching, note-taking, bookmarking, highlighting, and more. Easily accessible on any Internet-connected computer via a standard Web browser, the eBook enables students to take an active approach to their learning in an intuitive, easy-to-use format. Visit **http://ebooks.bfwpub.com** to learn more.

For Instructors

NEW **BioPortal for *Molecular Cell Biology*** In addition to all student resources (including NEW LearningCurve quizzing tool) and a dynamic eBook, BioPortal also includes tools for instructors. Robust gradebook and assignment features allow instructors to assign any materials to their students and monitor their progress throughout the semester. Visit **http://courses.bfwpub.com** for more information.

Companion Web Site www.whfreeman.com/lodish7e

All the student resources, plus:

- All figures and tables from the book in **JPEG and PowerPoint** formats, which instructors can edit and project section by section, allowing students to follow underlying concepts. Optimized for lecture-hall presentation, including enhanced colors, enlarged labels, and boldface type.
- **Test Bank** in editable Microsoft Word format now featuring *new and revised questions* for every chapter. The test bank is written by Brian Storrie of the University of Arkansas for Medical Sciences and Eric A. Wong, Richard Walker, Glenda Gillaspy, and Jill Sible of Virginia Polytechnic Institute and State University and revised by Cindy Klevickis of James Madison University and Greg M. Kelly of the University of Ontario.
- Additional **Analyze the Data** problems are available in PDF format.
- Lecture-ready **Personal Response System "clicker" questions** are available as Microsoft Word files and Microsoft PowerPoint slides.

Instructor's Resource CD-ROM (ISBN: 1-4292-0126-6) includes all the instructor's resources from the Web site, including all the illustrations from the text, animations, videos, test bank files, clicker questions, and the solutions manual files.

Overhead Transparency Set (ISBN: 1-4292-0477-X) contains 250 key illustrations from the text, optimized for lecture-hall presentation.

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CONTENTS IN BRIEF

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