FOURTH EDITION

Lewin's Essential GENES

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To Benjamin Lewin, for setting the bar high.

To my mother, Ellen Baker, for raising me with a love of science; to the memory of my stepfather, Barry Kiefer, for convincing me science would stay fun; and to my wife, Susannah, and my sons, Rhys and Frey—thanks for laughing at my biology jokes.

Jocelyn Krebs

To my family: my wife, Suzanne, whose patience, understanding, and confidence in me are amazing; my children, Andy, Hyla, and Gary, who have taught me so much about using the computer; and my grandchildren, Seth and Elena, whose smiles and giggles inspire me. And to the memory of my mentor and dear friend, Lee A. Snyder, whose professionalism, guidance, and insight demonstrated the skills necessary to be a scientist and teacher. I have tried to live up to his expectations. This is for you, Doc.

Elliott Goldstein

To my wife, Lori; my parents, David and Sandra; and my children, Jennifer, Andrew, and Sarah.

Stephen Kilpatrick

Brief Contents

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Preface

Of the diverse ways to study the living world, molecular biology has been most remarkable in the speed and breadth of its expansion. New data are acquired daily, and new insights into well-studied processes come on a scale measured in weeks or months rather than years. It's difficult to believe that the first complete organismal genome sequence was obtained only a couple decades ago, and today personalized medicine is a reality, and routine individual whole-genome sequencing is not far in the future. The structure and function of genes and genomes and their associated cellular processes are sometimes elegantly and deceptively simple but frequently amazingly complex, and no single book can do justice to the realities and diversities of natural genetic systems. The purpose of this book is to provide a clear and concise overview of the field for the undergraduate student; it may also be appropriate for some medical school courses on the subject. Compared to the full edition, there is a redirected focus on essential topics and (in some areas) more background and introductory material.

Much of the revision and reorganization of this edition follows that of *Lewin's GENES XII,* but there are many updates and features that are new to this book. The new and rapidly changing field of CRISPR/Cas9 genome editing is discussed in Chapter 2, *Methods in Molecular Biology and Genetic Engineering*, from the perspective of genome modification; the biology and detailed mechanism of CRISPR are discussed in the context of the ever-expanding understanding of noncoding regulatory RNAs—now covered in two chapters (Chapter 27, *Noncoding RNA*, and Chapter 28, *Regulatory RNA*). This edition is generally reorganized for a more logical flow of topics, and many chapters and sections within chapters have been renamed to better indicate their contents. Several topics have been more streamlined: the two introductory chapters in the last edition have been combined into one, and immune recombination has been moved into the chapter on recombination (Chapter 13) to focus more on the molecular mechanisms of somatic recombination, with reduced focus on the cell biology of the immune system. There are extensive updates throughout the book to reflect research advances in many fields in addition to those just mentioned, particularly in *Chromatin* (Chapter 8), *Eukaryotic Transcription Regulation* (Chapter 25), and *Epigenetics* (Chapter 26).

This book is organized into four parts. **Part I, Genes and Chromosomes**, comprises Chapters 1–8. Chapter 1 serves as an introduction to the structure and function of DNA and contains basic introductions to DNA replication and gene expression. Chapter 2 provides information on molecular laboratory techniques. Chapter 3 introduces the interrupted structures of eukaryotic genes, and Chapters 4–6 discuss genome structure and evolution. Chapter 7 discusses the structure of viral, prokaryotic, and eukaryotic chromosomes, while Chapter 8 focuses on the more detailed structure of eukaryotic chromatin.

Part II, DNA Replication and Recombination, comprises Chapters 9–15. Chapters 9–12 provide detailed discussions of DNA replication in plasmids, viruses, and prokaryotic and eukaryotic cells. Chapter 13 covers different classes of recombination, including roles in meiosis, DNA repair, and the human immune system. Chapter 14 discusses DNA repair pathways in detail, and Chapter 15 focuses on different types of transposable elements.

Part III, Gene Expression, includes Chapters 16–22. Chapters 16 and 17 provide more in-depth coverage of bacterial and eukaryotic transcription,

respectively. Chapters 18–20 are concerned with RNA, discussing messenger RNA, RNA stability and localization, RNA processing, and the catalytic roles of RNA. Chapters 21 and 22 discuss translation and the genetic code.

Part IV, Gene Regulation, comprises Chapters 23–28. In Chapter 23, the regulation of bacterial gene expression via operons is discussed. Chapter 24 covers the regulation of gene expression during phage development as they infect bacterial cells. Chapters 25 and 26 both focus on eukaryotic gene regulation, with extensive discussion of the epigenetic mechanism in Chapter 26. Finally, Chapters 27 and 28 cover RNA-based control of gene expression in prokaryotes and eukaryotes.

For instructors who prefer to order topics with the essentials of DNA replication and gene expression followed by more advanced topics, the following chapter sequence is suggested:

Introduction: Chapter 1
Gene Structure and Genome Structure: Chapters 3–6
DNA Replication: Chapters 9–12
Transcription: Chapters 16–19
Translation: Chapters 21–22
Regulation of Gene Expression: Chapters 7–8 and either 23–28 (prokaryotic and eukaryotic topics) or 25–28 (more focus on eukaryotes)

Other chapters can be covered at the instructor's discretion.

To the Instructor

This edition contains many pedagogical components to help the instructor engage students in the topic. Each chapter section concludes with Concept and Reasoning Checks: one or two questions for review, conceptual synthesis, hypothesizing, or application of the information. Each chapter includes a set of End-of-Chapter Questions with answers to half of the questions provided to the students; the other questions could be used as homework assignments or quizzes. Additional instructional tools are available on the accompanying website (see below).

To the Student

There are a number of features in the book to help you learn as you read. Each section is summarized with a bulleted list of Key Concepts. Key Terms are highlighted in boldface in the text and defined in the margin for easy reference and are compiled into the Glossary at the end of the book. Each chapter includes a set of End-of-Chapter Questions intended for self-assessment. Most chapters contain at least one feature box with additional background material or more in-depth details on an issue relevant to the chapter's focus. Boxes fall into one of four categories: Essential Ideas, Historical Perspectives, Methods and Techniques, and Medical Applications. In many cases these represent areas of ongoing research in the field. Finally, each chapter concludes with suggested Further Reading, a brief list of current reviews and pivotal papers to supplement and reinforce the chapter content.

Supplements

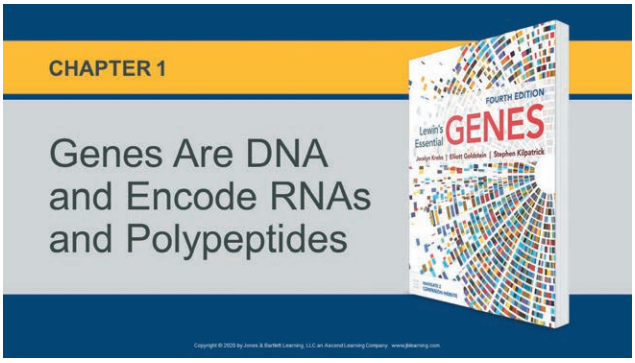
Jones & Bartlett Learning offers an impressive variety of traditional and interactive multimedia supplements to assist instructors and aid students in mastering molecular biology. Additional information and review copies of any of the following items are available through your Jones & Bartlett Learning sales representative or by going to http://www.jblearning.com

For the Student

- **Companion Website:** Jones & Bartlett Learning has developed an interactive companion website dedicated exclusively to this title. Students will find a variety of study aids and resources at go.jblearning.com/EssGenes4eCWS, all designed to explore the concepts of molecular biology in more depth and to help students master the material in the book. A variety of activities are available to help students review class material, such as an interactive summary, web-based learning exercises, study quizzes, a searchable glossary,

and links to animations, videos, and podcasts, all to help students master important terms and concepts.

For the Instructor



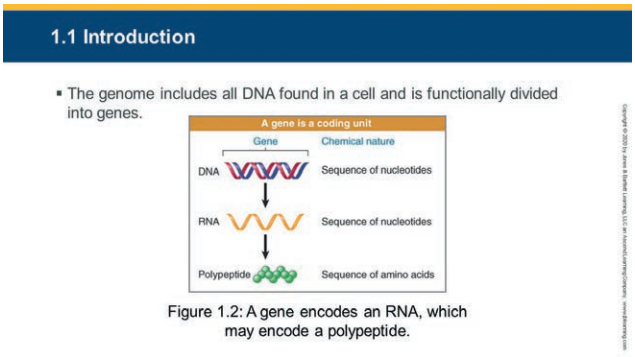


Figure 1.2: A gene encodes an RNA, which may encode a polypeptide.

- **PowerPoint Lecture Outline:** Created and revised by author Stephen T. Kilpatrick, slides in PowerPoint format provide the instructor with customizable lecture outlines, notes, and images for each chapter of *Lewin's Essential GENES, Fourth Edition*.
- **PowerPoint Image Bank:** The Image Bank provides the illustrations, photographs, and tables (to which Jones & Bartlett Learning holds the copyright or permission to reprint digitally) inserted into each slide. With the slides, you can quickly and easily copy individual image slides into your existing lecture slides.

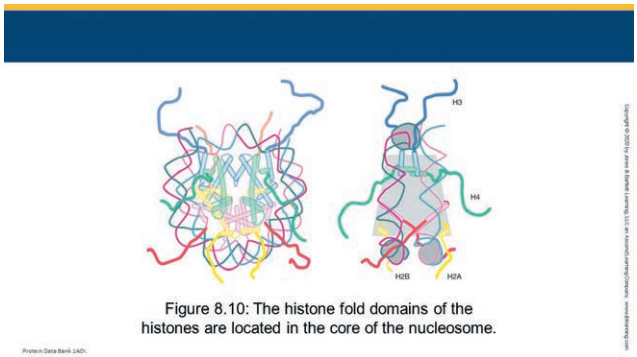


Figure 8.10: The histone fold domains of the histones are located in the core of the nucleosome.

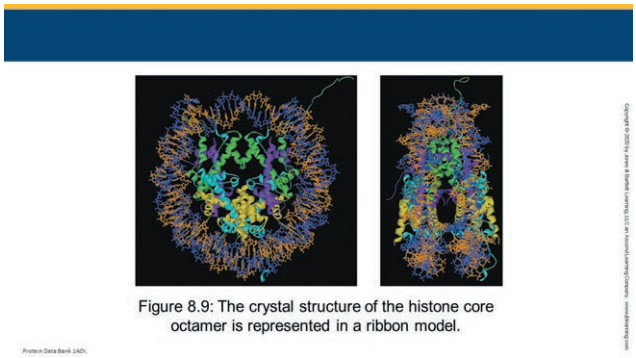


Figure 8.9: The crystal structure of the histone core octamer is represented in a ribbon model.

- **Answers to End-of-Chapter Questions:** Each chapter of *Lewin's Essential GENES, Fourth Edition* includes a set of End-of-Chapter Questions with answers to half of the questions provided to the students; the other questions may be used as homework assignments or quizzes. An answer guide for the second half of these questions is available as an instructor download.
- **Test Bank:** An electronic Test Bank is provided as a text file with over 700 questions in a variety of formats and is available as an instructor download.

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About the Author

Benjamin Lewin founded the journal *Cell* in 1974 and was editor until 1999. He founded the Cell Press journals *Neuron*, *Immunity*, and *Molecular Cell*. In 2000, he founded Virtual Text, which was acquired by Jones & Bartlett Publishers in 2005. He is also the original author of *GENES* and *CELLS*.

Jocelyn E. Krebs received a BA in biology from Bard College, Annandale-on-Hudson, NY, and a PhD in molecular and cell biology from the University of California, Berkeley. For her PhD dissertation, she studied the roles of DNA topology and insulator elements in transcriptional regulation in the laboratory of Dr. Marietta Dunaway. She performed her postdoctoral training as an American Cancer Society Fellow at the University of Massachusetts Medical School in the laboratory of Dr. Craig Peterson, where she focused on the roles of histone acetylation and chromatin remodeling in transcription. In 2000, Dr. Krebs joined the faculty in the Department of Biological Sciences at the University of Alaska Anchorage, where she is now a full professor. She has served as the Director of Alaska INBRE (IDeA Network of Biomedical Research Excellence) and is currently the Pilot Core Director for American Indian/Alaska Native Clinical Translational Research Program (AI/AN CTRP, an NIH-funded IDeA-CTR), which is an Alaska–Montana partnership supporting research that addresses health disparities in indigenous communities. She directed a long-standing research group studying chromatin structure and function in transcription and DNA repair in the yeast *Saccharomyces cerevisiae* and the role of chromatin remodeling in embryonic development in the frog *Xenopus,* with a particular focus on the role of a gene deleted in the human neurodevelopmental condition called Williams syndrome. She is now president of the Board of Trustees of the Williams Syndrome Association. She teaches undergraduates (majors and nonmajors), graduate students, and first-year medical students in the areas of introductory biology, human biology, genetics, molecular biology, epigenetics, and molecular biology of cancer. She lives in Portland, OR (teaching online and occasionally commuting back to Alaska) with her wife, their two sons, and a house full of cats. Her passions include hiking, camping, gardening, and art.

Elliott S. Goldstein earned his BS in biology from the University of Hartford (Connecticut) and his PhD in genetics from the University of Minnesota, Department of Genetics and Cell Biology. Following this, he was awarded an NIH Postdoctoral Fellowship to work with Dr. Sheldon Penman at the Massachusetts Institute of Technology. After leaving Boston, he joined the faculty at Arizona State University in Tempe, where he recently retired from the Cellular, Molecular, and Biosciences Program in the School of Life Sciences and in the Honors Disciplinary Program. His research interests have been in the area of molecular and developmental genetics of early embryogenesis in *Drosophila melanogaster*, including the *Drosophila* counterparts of the human proto-oncogenes *jun* and *fos*. His primary teaching responsibilities were in the undergraduate General Genetics course, as well as the graduate-level Molecular Genetics course. Dr. Goldstein lives in Tempe with his wife, his high school sweetheart. They have three children and two grandchildren. He is a bookworm who loves reading as well as underwater photography. His pictures can be found at http://www.public.asu.edu/~elliotg/

Stephen T. Kilpatrick received a BS in biology from Eastern College (now Eastern University) in St. Davids, PA, and a PhD from the Program in Ecology

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