生命科学名著

LEWIN'S ESSENTIAL SECOND EDITION

GENES

LEWIN基因精要

(第二版

JOCELYN E. KREBS ELLIOTT S. GOLDSTEIN STEPHEN T. KILPATRICK

AAAA

学 版 社 www.sorencep.com

AAAA

AAAA

Lewin's Essential GENES

Second Edition

Jocelyn E. Krebs

University of Alaska, Anchorage

Elliott S. Goldstein

Arizona State University

Stephen T. Kilpatrick

University of Pittsburgh at Johnstown



JONES AND BARTLETT PUBLISHERS

Sudbury, Massachusetts

BOSTON TORONTO LONDON SINGAPORE

World Headquarters

www.jbpub.com

Jones and Bartlett Publishers 40 Tall Pine Drive Sudbury, MA 01776 978-443-5000 info@jbpub.com

Jones and Bartlett Publishers Canada 6339 Ormindale Way Mississauga, Ontario L5V 1J2 Canada

Jones and Bartlett Publishers International Barb House, Barb Mews London W6 7PA United Kingdom

Jones and Bartlett's books and products are available through most bookstores and online booksellers. To contact Jones and Bartlett Publishers directly, call 800-832-0034, fax 978-443-8000, or visit our website, www.jbpub.com.

Substantial discounts on bulk quantities of Jones and Bartlett's publications are available to corporations, professional associations, and other qualified organizations. For details and specific discount information, contact the special sales department at Jones and Bartlett via the above contact information or send an email to specialsales@jbpub.com.

Copyright © 2010 by Jones and Bartlett Publishers, LLC

All rights reserved. No part of the material protected by this copyright may be reproduced or utilized in any form, electronic or mechanical, including photocopying, recording, or by any information storage and retrieval system, without written permission from the copyright owner.

Production Credits

Chief Executive Officer: Clayton Jones Chief Operating Officer: Don W. Jones, Jr. President, Higher Education and Professional Publishing: Robert W. Holland, Jr.

V.P., Sales: William J. Kane

V.P., Design and Production: Anne Spencer V.P., Manufacturing and Inventory Control:

Therese Connell

Publisher, Higher Education: Cathleen Sether

Acquisitions Editor: Molly Steinbach Associate Editor: Megan R. Turner Editorial Assistant: Caroline Perry

Production Manager: Louis C. Bruno, Jr.

Associate Production Editor: Leah Corrigan Senior Marketing Manager: Andrea DeFronzo

Text Design: Anne Spencer Cover Design: Kristin E. Parker

Illustrations: Imagineering Media Services, Inc.

and Shepherd, Inc.

Photo Research Manager and Photographer:

Kimberly Potvin

Freelance Photo Researcher: Asuka Ohsawa

Composition: Shepherd, Inc.

Printing and Binding: Courier Kendallville

Cover Printing: Courier Kendallville

Cover Image: © Carin L. Cain, The Art of Science:

Medical and Scientific Visualization

(www.carincain.com)

About the cover: In this picture, eukaryotic gene expression is depicted as a video game. mRNA (purple) is transcribed from chromosomes (blue), processed (scissors), and transported from the nucleus (green circle) where it is translated by ribosomes in the cytoplasm to polypeptides. Antisense RNAs (pink) aid in the regulation of mRNA stability.

Library of Congress Cataloging-in-Publication Data

Lewin's essential genes / by Jocelyn E. Krebs, Elliott S. Goldstein, and Stephen T. Kilpatrick. — 2nd ed.

p.; cm.

Rev. ed. of: Essential genes / Benjamin Lewin. c2006.

Condensed and updated ed. of: Genes IX / Benjamin Lewin. c2008.

Includes index.

ISBN 978-0-7637-5915-5 (alk. paper)

1. Genetics. 2. Genes. I. Krebs, Jocelyn E. II. Goldstein, Elliott S. III. Kilpatrick, Stephen T. IV. Lewin Benjamin. Essential genes. V. Lewin, Benjamin. Genes IX. VI. Title Essential genes.

[DNLM: 1. Genes. 2. DNA Replication. 3. Eukaryotic Cells—physiology. 4. Gene Expression. 5. Proteins—genetics. 6. Recombination, Genetic. QU 470 E78 2009]

QH430.L4 2009

576.5—dc22

2008047274

6048

Printed in the United States of America
13 12 11 10 09 10 9 8 7 6 5 4 3 2 1

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 less than 15 years ago. 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 in the subject. Compared to the full edition, there is a redirected focus on essential topics and (in some areas) more background and introductory material.

This edition is generally updated and reorganized for a more logical flow of topics. In particular, discussion of chromatin organization and nucleosome structure now precedes the discussion of eukaryotic transcription, because chromosome organization is critical to all DNA transactions in the cell, and current research in the field of transcriptional regulation is heavily biased toward the study of the role of chromatin in this process. The discussion of transcriptional activation and chromatin remodeling has accordingly been combined into one chapter (Chapter 26). Two chapters on transposons and retrotransposons have been combined into one (Chapter 21). Chapter 30, "Genetic Engineering," has been expanded. Throughout the book, there is additional background material and some expanded coverage of evolutionary genetic concepts. Many new figures are included in this book, some reflecting new developments in the field.

This book is organized into five parts. **Part I** (**Genes**) comprises Chapters 1 through 6. Chapters 1 and 2 serve as an introduction to the structure and function of DNA and contain basic coverage of DNA

replication and gene expression. Chapter 3 introduces the interrupted structures of eukaryotic genes, and Chapters 4 through 6 discuss genome structure and evolution.

Part II (Proteins) comprises Chapters 7 through 10. Chapters 7 to 9 provide general introductions to gene expression: transcription, translation, and the genetic code. Chapter 10 covers the transport of proteins within cells.

Part III (Prokaryotic Gene Expression) includes Chapters 11 through 14. Chapter 11 provides more in-depth coverage of bacterial transcription. In Chapters 12 and 13, the regulation of bacterial gene expression via operons and regulatory RNAs, including RNAi, are discussed. Chapter 14 covers the regulation of expression of genes during phage development as they infect bacterial cells.

Part IV (DNA Replication and Recombination) comprises Chapters 15 through 23. Chapters 15 to 18 provide detailed discussions of DNA replication in plasmids, viruses, and prokaryotic and eukaryotic cells. Chapters 19 through 22 cover recombination and its roles in DNA repair and the human immune system, with Chapter 21 focusing on different types of transposable elements. Chapter 23 discusses the structure of eukaryotic chromosomes.

Part V (Eukaryotic Gene Expression) includes Chapters 24 through 30. In Chapter 24, the structure of nucleosomes and chromatin is discussed; chromatin remodeling and other chromosomal alterations are covered in Chapters 26 and 27. Chapters 25 and 26 describe eukaryotic transcription and its regulation, with Chapter 28 detailing posttranscriptional RNA processing. Chapter 29 provides a discussion of ribozymes. Chapter 30 introduces basic molecular techniques for the study of genes and gene expression.

Although the chapter on genetic engineering has been placed at the end of the book, instructors may choose to use the information from this chapter at any point appropriate for their courses, such as following the introductory chapters, 1 and 2.

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: Chapters 1-2

Gene and Genome Structure: Chapters 3-6

DNA Replication: Chapters 15–18

Transcription: Chapters 7, 11, 25, and 28

Translation: Chapters 8-9

Regulation of Gene Expression: Chapters 12-14,

22-23, and 26

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

To the Instructor

This edition contains many new pedagogical components to help the instructor engage students in the topic. The text has been revised to be more accessible for students at introductory levels. Each chapter section concludes with *Concept and Reasoning Checks*: one or two questions for review, conceptual synthesis, hypothesizing, or application of learning. 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. There are additional instructional tools available on the Instructor's ToolKit CD-ROM and accompanying Web site (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 as well as compiled into the Glossarv 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.

Ancillaries

Jones and Bartlett Publishers 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 and Bartlett sales representative or by going to http://www.jbpub.com/biology.

Online Student Study Guide

Jones and Bartlett Publishers and Brent Nielsen of Brigham Young University have developed an interactive, electronic study guide dedicated exclusively to this title. Students will find a variety of study aids and resources at http://biology.jbpub.com/lewin/essentialgenes, 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.

Instructor's ToolKit CD-ROM

The *Instructor's ToolKit CD-ROM* contains a suite of files to help professors teach their courses. The materials are cross-platform for Windows and Macintosh systems. All the files on the CD are ready for online courses using the **WebCT** or **Blackboard** formats.

- The **PowerPoint**® **Image Bank** provides the illustrations, photographs, and tables (to which Jones and Bartlett Publishers holds the copyright or has permission to reprint digitally) inserted into PowerPoint slides. With the Microsoft PowerPoint program, you can quickly and easily copy individual image slides into your existing lecture slides.
- The **PowerPoint Lecture Outline Slides** presentation package provides images and lecture notes, created by Hao Nguyen, of California State University, Sacramento, for each chapter of *Lewin's Essential Genes, Second Edition*. A PowerPoint viewer is provided on the CD. Instructors with the Microsoft PowerPoint software can customize the outlines, figures, and order of presentation.
- The **Test Bank**, also created by Hao Nguyen, is provided as a text file with over 700 questions in a variety of formats.

Acknowledgments

The authors would like to thank the following individuals for their assistance in the preparation of this book:

The editorial, production, marketing, and sales teams at Jones & Bartlett have been exemplary in

all aspects of this project. Cathy Sether, Molly Steinbach, and Lou Bruno deserve special mention. Cathy brought us together on this project and in doing so launched an efficient and amiable partnership. She has provided able leadership and has been an excellent resource as we ventured into new territories. Molly and Lou have handled the daily responsibilities of the writing and production phases with friendly professionalism, helpful guidance, and appropriate doses of humor.

Thanks for the creation of many of the End of Chapter Questions go to Brent Nielsen. We also thank the authors of the special topics boxes found throughout the text:

Loree Burns

Jamie Kass, New York Academy of Sciences Brent Nielsen, Brigham Young University Teri Shors, University of Wisconsin, Oshkosh Esther Siegfried, University of Pittsburgh at Johnstown

We thank Hao Nguyen of California State University, Sacramento, for writing the test bank and lecture outlines. Finally, we would like express our gratitude to the reviewers of this edition, whose feedback helped to shape the text in many ways:

Salem Al-Maloul, Hashemite University James Botsford, New Mexico State University David Bourgaize, Whittier College
John Boyle, University of Mississippi
Mary Connell, Appalachian State University
Robert Dotson, Tulane University
Julia Frugoli, Clemson University
Daniel Herman, University of Wisconsin,
Eau Claire

Stan Ivey, Delaware State University Christi Magrath, Troy University Mitch McVey, Tufts University Hao Nguyen, California State University, Sacramento

Stacy Darling Novak, University of La Verne Eva Sapi, University of New Haven Ben Stark, Illinois Institute of Technology Takashi Ueda, Florida Gulf Coast University Ramakrishna Wusirika, Michigan Technological University

Anastasia Zimmerman, College of Charleston

Jocelyn E. Krebs Elliott S. Goldstein Stephen T. Kilpatrick

Preface xix

About the Authors

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 author of *GENES* and *CELLS*.



Jocelyn E. Krebs received a B.A. in Biology from Bard College, Annandale-on-Hudson, NY, and a Ph.D. in Molecular and Cell Biology from the University of California, Berkeley. For her Ph.D. thesis, she studied the roles of DNA topology and insulator elements in transcriptional regulation. 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 an Associate Professor. She directs a 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. She teaches courses in molecular biology for undergraduates, graduate students, and first-year medical students. She also teaches a Molecular Biology of Cancer course and has taught Genetics and Introductory Biology. She lives in Eagle River, AK, with her partner and a house full of dogs and cats. Her non-work passions include hiking, camping, and snowshoeing.



Elliott S. Goldstein earned his B.S. in Biology from the University of Hartford (Connecticut) and his Ph.D. in Genetics from the University of Minnesota, Department of Genetics and Cell Biology. Following this, he was awarded an N.I.H. 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 is an Associate Professor in the Cellular, Molecular, and Biosciences program in the School of Life Sciences and in the Honors Disciplinary Program. His research interests are in the area of molecular and developmental genetics of early embryogenesis in Drosophila melanogaster. In recent years, he has focused on the *Drosophila* counterparts of the human proto-oncogenes jun and fos. His primary teaching responsibilities are 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 B.S. in Biology from Eastern College (now Eastern University) in St. Davids, PA, and a Ph.D. from the Program in Ecology and Evolutionary Biology at Brown University. His thesis research was an investigation of the population genetics of

interactions between the mitochondrial and nuclear genomes of *Drosophila melanogaster*. Since 1995, Dr. Kilpatrick has taught at the University of Pittsburgh at Johnstown (UPJ) in Johnstown, PA. His regular teaching duties include undergraduate courses in nonmajors biology, introductory majors biology, and advanced undergraduate courses in genetics, evolution, molecular genetics, and biostatistics. He has also supervised a number of undergraduate research projects in evolutionary genetics. Dr. Kilpatrick's major professional focus has been in biology edu-

cation. He has participated in the development and authoring of ancillary materials for several introductory biology, genetics, and molecular genetics texts as well as writing articles for educational reference publications. For his classes at UPJ, Dr. Kilpatrick has developed many active learning exercises in introductory biology, genetics, and evolution. Dr. Kilpatrick resides in Johnstown, PA, with his wife and three children. Outside of scientific interests, he enjoys music, literature, and theater and occasionally performs in local community theater groups.

Brief Table of Contents

Chapter 16. Extrachromosomal Replicons 385

PART I. GENES 1 Chapter 1. Genes Are DNA 2	Chapter 17. Bacterial Replication Is Connected to the Cell Cycle 402
Chapter 2. Genes Code for Proteins 29 Chapter 3. The Interrupted Gene 50 Chapter 4. The Content of the Genome 71	Chapter 18. DNA Replication 421 Chapter 19. Homologous and Site-Specific Recombination 446
Chapter 5. Genome Sequences and Gene Numbers 97 Chapter 6. Clusters and Repeats 121	 Chapter 20. Repair Systems 475 Chapter 21. Transposons, Retroviruses, and Retrotransposons 500 Chapter 22. Immune Diversity 534
PART II. PROTEINS 154	Chapter 23. Chromosomes 560
Chapter 7. Messenger RNA 155 Chapter 8. Translation 183 Chapter 9. Using the Genetic Code 217	PART V. EUKARYOTIC GENE EXPRESSION 582
Chapter 10. Protein Localization 242	Chapter 24. Chromatin 583 Chapter 25. Eukaryotic Transcription 612
PART III. PROKARYOTIC GENE EXPRESSION 263	Chapter 26. Eukaryotic Transcription Regulation 633
Chapter 11. Bacterial Transcription 264 Chapter 12. The Operon 294 Chapter 13. Regulatory RNA 320 Chapter 14. Phage Strategies 340	Chapter 27. Epigenetic Effects Are Inherited 668 Chapter 28. RNA Splicing and Processing 691 Chapter 29. Catalytic RNA 723 Chapter 30. Genetic Engineering 745
PART IV. DNA REPLICATION AND RECOMBINATION 368 Chapter 15. The Replicon 369	Glossary 767 Appendix: Answers to Even-Numbered Questions 790

Index 792

Contents

Preface xvii	Chapter 2. Genes Code for Proteins 29
About the Authors xx	2.1 Introduction 30
PART I. GENES 1	2.2 Most Genes Code for Polypeptides 31
Chapter 1. Genes Are DNA 2	Historical Perspectives: One Gene: One Enzyme— George W. Beadle and Edward L. Tatum, 1941
1.1 Introduction 3	2.3 Mutations in the Same Gene Cannot Complement 33
1.2 DNA Is the Genetic Material of Bacteria, Viruses, and Eukaryotic Cells 4	2.4 Mutations May Cause Loss-of-Function or Gain-of-
Historical Perspectives: Determining That DNA Is the Genetic	Function 34
Material 6	2.5 A Locus May Have Many Alleles 35
1.3 Polynucleotide Chains Have Nitrogenous Bases Linked to a Sugar-Phosphate Backbone 6	2.6 Recombination Occurs by Physical Exchange of DNA 37
1.4 DNA Is a Double Helix 8	2.7 The Genetic Code Is Triplet 39
1.5 Supercoiling Affects the Structure of DNA 11	2.8 Every Coding Sequence Has Three Possible Reading
1.6 DNA Replication Is Semiconservative 12	Frames 42
Polymerases Act on Separated DNA Strands at the Replication Fork 14	2.9 Bacterial Genes Are Colinear with Their Products 42
1.8 Genetic Information Can Be Provided by DNA or RNA 15	2.10 Several Processes Are Required to Express the Product of a Gene 43
1.9 Nucleic Acids Hybridize by Base Pairing 17	2.11 Proteins Are <i>trans</i> -Acting, but Sites on DNA Are <i>cis</i> -Acting 46
1.10 Mutations Change the Sequence of DNA 19	2.12 Summary 47
1.11 Mutations May Affect Single Base Pairs or Longer Sequences 20	Chapter 3. The Interrupted Gene 50
1.12 The Effects of Mutations Can Be Reversed 22	3.1 Introduction 51
1.13 Mutations Are Concentrated at Hotspots 23	3.2 An Interrupted Gene Consists
1.14 Some Hereditary Agents Are Extremely Small 25	of Exons and Introns 52
1.15 Summary 26	3.3 Organization of Interrupted Genes

Methods	and Techniques: The Discovery of Introns by DNA-RNA Hybridization 56	Chapte		Genome Sequences and Gene Numbers 97
3.4	Exon Sequences Are Conserved but Introns Vary 57	5 1		etion 98
3.5	Genes Show a Wide Distribution of Sizes Primarily Due to Intron Size and Number Variation 59	5.2		tic Gene Numbers Range Over an Order of
3.6	Some DNA Sequences Code for More Than One Polypeptide 61	5.3	Total Ge	ne Number Is Known for Several
3.7	How Did Interrupted Genes Evolve? 63	h.	-	tes 100
3.8	Some exons can be Equated with Protein	5.5	The Hum	ny Different Types of Genes Are There? 102
3.9	The Members of a Gene Family Have a Common Organization 66	5.6	Expected How Are	Genes and Other Sequences Distributed in ome? 106
		5.7		romosome Has Several Male-Specific
Спарт	er 4. The Content of the Genome 71	Methods (and Tech	niques: Tracing Human History through the
4.1	Introduction 72	5.8	Morphol	ogical Complexity Evolves by Adding New
4.2	Genomes Can Be Mapped at Several Levels of Resolution 73		Gene Fur	nctions 110
4.3	Individual Genomes Show Extensive Variation 74			ny Genes Are Essential? 112
	RFLPs and SNPs Can Be Used for Genetic Mapping 76			0,000 Genes Are Expressed at Widely Levels in a Eukaryotic Cell 115
4.5	Why Are Some Genomes So Large? 77		Expresse <i>Masse</i>	d Gene Number Can Be Measured <i>en</i> 116
		5.12	Summary	/ 118
4.7		Chapte	er 6.	Clusters and Repeats 121
		6.1	Introduc	tion 122
4.8	identity denes 83			plication Is a Major Force in Evolution 123
4.9	Some Organelles Have DNA 85			lusters Are Formed by Duplication and ce 124
Methods	and Techniques: Using mtDNA to Reconstruct Human Phylogenies 86	6.4	Sequence Clock 1	e Divergence Is the Basis for the Molecular
4.10	Organelle Genomes Are Circular DNAs That Code for Organelle Proteins 89	6.5	The Rate	of Neutral Substitution Can Be Measured ergence of Repeated Sequences 130
4.11	The Chloroplast Genome Codes for Many Proteins and RNAs 91	Methods (and Tech	niques: Detecting Selection via Sequence
4.12	Mitochondria and Chloroplasts Evolved by Endosymbiosis 92		Unequal Clusters	Crossing-over Rearranges Gene 132

Genes for rRNA Form Tandem Repeats Including an Invariant Transcription Unit 137

4.13 Summary 94

6.8	Crossover Fixation Could Maintain Identical Repeats 139	Chapter 8. Translation 183
6.9	Satellite DNAs Often Lie in Heterochromatin 143	8.1 Introduction 184
	Arthropod Satellites Have Very Short Identical Repeats 144	8.2 Translation Occurs by Initiation, Elongation, and Termination 185
6.11	Mammalian Satellites Consist of Hierarchical	8.3 Special Mechanisms Control the Accuracy of Translation 187
6.12	Repeats 145 Minisatellites Are Useful for Genetic Mapping 148	8.4 Initiation in Bacteria Needs 30S Subunits and Accessory Factors 188
6.13	Summary 150	8.5 A Special Initiator tRNA Starts the Polypeptide Chain 190
	II. PROTEINS 154	8.6 mRNA Binds a 30S Subunit to Create the Binding Site for a Complex of IF-2 and fMet-tRNA _f 191
	er 7. Messenger RNA 155 Introduction 156	8.7 Small Eukaryotic Subunits Scan for Initiation Sites on mRNA 193
7.2	mRNA Is Produced by Transcription and Is Translated 157	8.8 Elongation Factor Tu Loads Aminoacyl-tRNA into the A Site 195
7.3	The Secondary Structure of Transfer RNA Is a Cloverleaf 158	8.9 The Polypeptide Chain Is Transferred to AminoacyltRNA 197
7.4	The Acceptor Arm and Anticodon Are at Opposite Ends of the tRNA Tertiary Structure 160	8.10 Translocation Moves the Ribosome 198
7.5	Messenger RNA Is Translated by Ribosomes 161	8.11 Elongation Factors Bind Alternately to the Ribosome 199
7.6	Many Ribosomes Can Bind to One mRNA 162	8.12 Uncharged tRNA Causes the Ribosome to Trigger the
Methods	and Techniques: Demonstrating That Ribosomal Subunits Are Recycled 164	Stringent Response 200
7.7	The Cycle of Bacterial Messenger RNA 165	8.13 Three Codons Terminate Translation and Are Recognized by Protein Factors 202
	Eukaryotic mRNA Is Modified During or After Its Transcription 167	Historical Perspectives: The Naming of the Amber, Ochre, and Opal Codons 204
7.9	The 5' End of Eukaryotic mRNA Is Capped 169	8.14 Ribosomal RNA Pervades Both Ribosomal Subunits 206
7.10	The 3' Terminus of Eukaryotic mRNA Is Polyadenylated 170	8.15 Ribosomes Have Several Active Centers 208
7.11	Bacterial mRNA Degradation Involves Multiple	8.16 Two rRNAs Play Active Roles in Translation 210
	Enzymes 171	8.17 Summary 212
7.12	Two Pathways Degrade Eukaroytic mRNA 172	Chantage O Union the Constituted 217
7.13	Nonsense Mutations Trigger a Surveillance System 174	Chapter 9. Using the Genetic Code 217 9.1 Introduction 218
7.14	Eukaryotic RNAs Are Transported 176	9.2 Related Codons Represent Related Amino
7.15	mRNA Can Be Localized Within a Cell 177	Acids 218
	Summary 178	9.3 Codon-Anticodon Recognition Involves

Contents ix

9.4	tRNA Contains Modified Bases 221	PART II	I.	PROKARYOTIC GENE
9.5	Modified Bases Affect Anticodon–Codon Pairing 222			EXPRESSION 263
9.6	There Are Sporadic Alterations of the Universal Code 224	Chapter 1 11.1 Intro		Bacterial Transcription 264
9.7	Novel Amino Acids Can Be Inserted at Certain Stop Codons 225	11.2 Trans	cripti	on Occurs by Base Pairing in a "Bubble" ed DNA 266
9.8	tRNAs Are Charged with Amino Acids by Synthetases 226			ription Reaction Has Three Stages 267
9.9	Aminoacyl-tRNA Synthetases Fall into Two Groups 227	11.4 A Mo	del fo al Str	or Enzyme Movement Is Suggested by the ucture 269
9.10	Synthetases Use Proofreading to Improve Accuracy 229	11.5 Bacte	erial F me ar	RNA Polymerase Consists of the Core ad Sigma Factor 271
9.11	Suppressor tRNAs Have Mutated Anticodons That Read New Codons 230			RNA Polymerase Find Promoter ? 272
Medical i	Applications: Therapies for Nonsense Mutations 232	11.7 Sigma	a Fact	tor Controls Binding to Promoters 273
	Recoding Changes Codon Meanings 235			Recognition Depends on Consensus 276
9.13	Frameshifting Occurs at Slippery Sequences 236	11.9 Promo	oter I	Efficiencies Can Be Increased or Decreased
9.14	Bypassing Involves Ribosome Movement 238	by Mu		
	Summary 239			ng Is an Important Feature of on 279
Chapt	er 10. Protein Localization 242			on of Sigma Factors May Control
10.1	Introduction 243	Initia		
10.2	Protein Translocation May Be Posttranslational or			cors Directly Contact DNA 282
	Cotranslational 244	11.13 Bacte	erial T	ranscription Termination 283
	! Ideas: Conservation and Function of the Hsp Family of Chaperones 246			ermination Requires a Hairpin and a gion 284
10.3	The Signal Sequence Interacts with the SRP 248			Is a Site-Specific Terminator
10.4	The SRP Interacts with the SRP Receptor 250	Prote		
10.5	The Translocon Forms a Pore 252	11.16 Antito	ermin	ation May Be a Regulated Event 287
10.6	Posttranslational Membrane Insertion Depends on Signal Sequences 253	11.17 Summ		
10.7	Bacteria Use Both Cotranslational and			The Operon 294
	Posttranslational Translocation 258	12.1 Introd	ductio	on 295
10.8	Summary 260			Gene Clusters Are Coordinately 298

Historical Perspective	s: An	Unstab	ole	Intermedia	te Carrying
Information	n from	Genes	to	Ribosomes	for Protein
Synthesis	299				

- 12.3 The *lac* Operon Is Negative Inducible 300
- 12.4 lac Repressor Is Controlled by a Small-Molecule Inducer 301
- 12.5 cis-Acting Constitutive Mutations Identify the Operator 303
- 12.6 trans-Acting Mutations Identify the Regulator Gene 304
- 12.7 lac Repressor Is a Tetramer Made of Two
 Dimers 305
- 12.8 lac Repressor Binding to the Operator Is Regulated by an Allosteric Change in Conformation 307
- 12.9 lac Repressor Protein Binds to Three Operators and Interacts with RNA Polymerase 309
- 12.10 The Operator Competes with Low-Affinity Sites to Bind Repressor 310
- 12.11 The *lac* Operon Has a Second Layer of Control: Catabolite Repression 312
- 12.12 The *trp* Operon Is a Repressible Operon with Three Transcription Units 313
- 12.13 Translation Can Be Regulated 314
- 12.14 Summary 316

Chapter 13. Regulatory RNA 320

- 13.1 Introduction 321
- 13.2 Attenuation: Alternative RNA Secondary Structure Control 322
- 13.3 Termination of *Bacillus subtilis trp* Genes Is Controlled by Tryptophan and by tRNA^{Trp} 323
- 13.4 The *E. coli* Tryptophan Operon Is Controlled by Attenuation 324
- 13.5 Attenuation Can Be Controlled by Translation 327
- 13.6 A Riboswitch in the 5' UTR Region Can Control Translation of the mRNA 329
- 13.7 Bacteria Contain Regulator sRNAs 330

Medical Applications: Artificial Antisense Genes Can Be Used to Turn Off Viruses and Cancer Genes 332

- 13.8 Eukaryotes Contain Regulator RNAs 332
- Methods and Techniques: Microarrays and Tiling Experiments 336
- 13.9 Summary 337

Chapter 14. Phage Strategies 340

- 14.1 Introduction 341
- 14.2 Lytic Development Is Divided into Two Periods 341
- 14.3 Lytic Development Is Controlled by a Cascade 343
- 14.4 Two Types of Regulatory Events Control the Lytic Cascade 345
- 14.5 Lambda Immediate Early and Delayed Early Genes
 Are Needed for Both Lysogeny and the Lytic
 Cycle 346
- 14.6 The Lytic Cycle Depends on Antitermination by pN 347
- Lysogeny Is Maintained by the Lambda Repressor Protein 349
- 14.8 The Lambda Repressor and Its Operators Define the Immunity Region 350
- 14.9 The DNA-Binding Form of the Lambda Repressor Is a Dimer 351
- 14.10 Lambda Repressor Uses a Helix-Turn-Helix Motif to Bind DNA 352
- 14.11 Repressor Dimers Bind Cooperatively to the Operator 354
- 14.12 Lambda Repressor Maintains an Autoregulatory Circuit 356
- 14.13 Cooperative Interactions Increase the Sensitivity of Regulation 357
- 14.14 The *cII* and *cIII* Genes Are Needed to Establish Lysogeny 358
- 14.15 Lysogeny Requires Several Events 359
- 14.16 The Cro Repressor Is Needed for Lytic Infection 361

Essential Ideas: The Mechanism of pQ Antitermination 363

- **14.17** What Determines the Balance Between Lysogeny and the Lytic Cycle? 363
- 14.18 Summary 374

Contents xi

PART IV. DNA REPLICATION AND RECOMBINATION 368

Chapter 15. The Replicon 369

- 15.1 Introduction 370
- 15.2 An Origin Usually Initiates Bidirectional Replication 371

Historical Perspectives: The Meselson-Stahl Experiment 372

- 15.3 The Bacterial Genome Is a Single Circular Replicon 373
- 15.4 Methylation of the Bacterial Origin Regulates
 Initiation 375
- 15.5 Each Eukaryotic Chromosome Contains Many Replicons 376
- 15.6 Replication Origins Bind the ORC 378
- 15.7 Licensing Factor Controls Eukaryotic Rereplication and Consists of MCM Proteins 379
- **15.8** Summary 382

Chapter 16. Extrachromosomal Replicons 385

- 16.1 Introduction 386
- 16.2 The Ends of Linear DNA Are a Problem for Replication 387
- 16.3 Terminal Proteins Enable Initiation at the Ends of Viral DNAs 388
- 16.4 Rolling Circles Produce Multimers of a Replicon 389
- **16.5** Rolling Circles Are Used to Replicate Phage Genomes 391
- 16.6 The F Plasmid Is Transferred by Conjugation between Bacteria 392
- 16.7 Conjugation Transfers Single-Stranded DNA 393
- 16.8 The Bacterial Ti Plasmid Transfers Genes into Plant Cells 395
- 16.9 Transfer of T-DNA Resembles Bacterial Conjugation 397
- **16.10** Summary 399

Chapter 17. Bacterial Replication Is Connected to the Cell Cycle 402

- 17.1 Introduction 403
- 17.2 Replication Is Connected to the Cell Cycle 403

Historical Perspectives: John Cairns and the Bacterial Chromosome 405

- 17.3 The Septum Divides a Bacterium into Progeny That Each Contain a Chromosome 405
- 17.4 Mutations in Division or Segregation Affect Cell Shape 407
- 17.5 FtsZ Is Necessary for Septum Formation 408
- 17.6 min Genes Regulate the Location of the Septum 409
- 17.7 Chromosomal Segregation May Require Site-Specific Recombination 410
- 17.8 Partitioning Separates the Chromosomes 412
- 17.9 Single-Copy Plasmids Have a Partitioning System 414
- 17.10 Plasmid Incompatibility Is Determined by the Replicon 415
- 17.11 How Do Mitochondria Replicate and Segregate? 416
- **17.12** Summary 417

Chapter 18. DNA Replication 421

- 18.1 Introduction 422
- 18.2 Initiation: Creating the Replication Forks at the Origin 422
- 18.3 DNA Polymerases Are the Enzymes That Make DNA 424
- 18.4 DNA Polymerases Control the Fidelity of Replication 426
- 18.5 DNA Polymerases Have a Common Structure 427
- 18.6 The Two New DNA Strands Have Different Modes of Synthesis 428
- 18.7 Replication Requires a Helicase and Single-Strand Binding Protein 429

Subcomplexes 433	Medical Applications: Xeroderma Pigmentosum 482		
18.10 The Clamp Controls Association of Core Enzyme with DNA 434	20.4 Base Excision Repair Systems Require Glycosylases 485		
18.11 Coordinating Synthesis of the Lagging and Leading Strands 435	20.5 Error-Prone Repair 487		
	20.6 Controlling the Direction of Mismatch Repair 488		
18.12 Okazaki Fragments Are Linked by Ligase 438	20.7 Recombination-Repair Systems 491		
18.13 Separate Eukaryotic DNA Polymerases Undertake Initiation and Elongation 439	20.8 Nonhomologous End-Joining Also Repairs Double-Strand Breaks 493		
18.14 The Primosome Is Needed to Restart Replication 441	Medical Applications: p53 Is the "Guardian of the Genome" 494		
18.15 Summary 443	20.9 Summary 497		
Chapter 19. Homologous and Site-Specific Recombination 446	Chapter 21. Transposons, Retroviruses, and Retrotransposons 500		
19.1 Introduction 447	21.1 Introduction 501		
19.2 Homologous Recombination Occurs between Synapsed Chromosomes 448	21.2 Insertion Sequences Are Simple Transposition Modules 502		
19.3 Double-Strand Breaks Initiate Recombination 450	21.3 Transposition Occurs by Both Replicative and		
19.4 Recombining Chromosomes Are Connected by the	Nonreplicative Pathways 505		
Synaptonemal Complex 454	21.4 Mechanisms of Transposition 508		
19.5 Specialized Enzymes Catalyze 5' End Resection and Single-Strand Invasion 455	21.5 Controlling Elements Form Families of Transposons in Maize 512		
19.6 The Ruv System Resolves Holliday Junctions 458	Historical Perspectives: Barbara McClintock, 1950: The Origin		
19.7 Topoisomerases Relax or Introduce Supercoils in DNA 459	and Behavior of Mutable Loci in Maize 513		
Clinical Applications: Camptothecin and Topoisomerase I	21.6 Transposition of P Elements Causes Hybrid Dysgenesis 516		
Inhibition 462	21.7 The Retrovirus Life Cycle Involves Transposition-Like		
19.8 Site-Specific Recombination Resembles Topoisomerase Activity 463	Events 519		
19.9 Yeast Use a Specialized Recombination Mechanism	21.8 Retroviral RNA is Converted to DNA and Integrates into the Host Genome 521		
to Switch Mating Type 466	21.9 Retroviruses May Transduce Cellular Sequences 524		
Medical Applications: Trypanosomes Use Gene Switching to Evade the Host Immune System 468	21.10 Retroposons Fall into Three Classes 526		
19.10 Summary 471	21.11 Summary 529		
Chapter 20. Repair Systems 475	Chapter 22. Immune Diversity 534		
20.1 Introduction 476	22.1 Introduction 535		
20.2 Repair Systems Correct Damage to DNA 478	22.2 Immunoglobulin Genes Are Assembled from Their		

18.8 Priming Is Required to Start DNA Synthesis 430

18.9 DNA Polymerase Holoenzyme Consists of

Contents xiii

Parts in Lymphocytes 537

20.3 Nucleotide Excision Repair Systems Repair Several

Classes of Damage 480

22.3	Light Chains Are Assembled by a Single Recombination 539	PART V. EUKARYOTIC GENE
22.4	Heavy Chains Are Assembled by Two Successive Recombinations 541	EXPRESSION 582 Chapter 24. Chromatin 583
22.5	Immune Recombination Uses Two Types of Consensus Sequence 543	24.1 Introduction 584
22.6	The RAG Proteins Catalyze Breakage and Reunion 545	24.2 The Nucleosome Is the Subunit of All Chromatin 584
Medical .	Applications: ARTEMIS and SCID-A 548	24.3 Nucleosomes Have a Common Structure 586
	Class Switching Is Caused by DNA Recombination 548	24.4 Histone Variants Produce Alternative Nucleosomes 590
22.8	Somatic Mutation Is Induced by Cytidine Deaminase and Uracil Glycosylase 552	DNA Structure Varies on the Nucleosomal Surface 592
22.9	Avian Immunoglobulins Are Assembled from Pseudogenes 554	24.6 The Path of Nucleosomes in the Chromatin Fiber 594
22.10	T Cell Receptors Are Related to Immunoglobulins 555	Reproduction of Chromatin Requires Assembly of Nucleosomes 596
22.11	Summary 557	24.8 Do Nucleosomes Lie at Specific Positions? 598
	er 23. Chromosomes 560	DNase Hypersensitive Sites Reflect Changes in Chromatin Structure 601
	Introduction 561	24.10 An LCR May Control a Domain 602
23.2	Viral Genomes Are Packaged into Their Coats 562	24.11 Insulators Define Independent Domains 603
	The Bacterial Genome Is a Supercoiled Nucleoid 564	Methods and Techniques: Position Effect Variegation (PEV) and the Discovery of Insulators 606
23.4	Eukaryotic DNA Has Loops and Domains Attached to a Scaffold 566	24.12 What Constitutes a Regulatory Domain? 606 24.13 Summary 608
23.5	Chromatin Is Divided into Euchromatin and Heterochromatin 567	Chapter 25. Eukaryotic Transcription 612
23.6	Chromosomes Have Banding Patterns 569	25.1 Introduction 613
Methods	and Techniques: FISH, Chromosome Painting, and Spectral Karyotyping 570	Eukaryotic RNA Polymerases Consist of Many Subunits 615
23.7	Polytene Chromosomes Form Bands That Expand at Sites of Gene Expression 571	25.3 RNA Polymerase I Has a Bipartite Promoter 616
23.8	Centrosomes Often Contain Repetitive DNA 573	25.4 RNA Polymerase III Uses Both Downstream and Upstream Promoters 617
23.9	S. cerevisiae Centromeres Have Short Protein- Binding DNA Sequences 575	25.5 The Startpoint for RNA Polymerase II 619
23.10	Telomeres Have Simple Repeating Sequences 576	25.6 TBP Is a Universal Factor 621
	Summary 579	25.7 The Basal Apparatus Assembles at the Promoter 623