LEWIN'S GENIES X

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

LONDO

SINGAPORE

Brief Table of Contents

Contents	viii
Preface	XX

Part 1. GENES AND CHROMOSOMES 1

Chapter 1. Genes Are DNA 2

Chapter 2. Genes Code for Proteins 26
Edited by Esther Siegfried, Pennsylvania State
University, Altoona

Chapter 3. Methods in Molecular Biology and Genetic Engineering 42

Edited by John Brunstein, University of British Columbia

Chapter 4. The Interrupted Gene 79

Edited by Donald Forsdyke, Queens University

Chapter 5. The Content of the Genome 98

Chapter 6. Genome Sequences and Gene Numbers 118

Chapter 7. Clusters and Repeats 139

Chapter 8. Genome Evolution 159

Chapter 9. Chromosomes 189

Edited by Hank W. Bass, Florida State University

Chapter 10. Chromatin 220

Part 2. DNA REPLICATION AND RECOMBINATION 262

Chapter 11. The Replicon 263

Edited by Stephen D. Bell, Oxford University

Chapter 12. Extrachromosomal Replicons 282

Edited by Søren Johannes Sørensen & Lars Hestbjerg Hansen, University of Copenhagen

Chapter 13. Bacterial Replication Is Connected to the Cell Cycle 299

Edited by Barbara Funnell, University of Toronto

Chapter 14. DNA Replication 320

Edited by Peter Burgers, Washington University Medical School

Chapter 15. Homologous and Site-Specific Recombination 348

Edited by Hannah L. Klein & Samantha Hoot, New York University Langone Medical Center

Chapter 16. Repair Systems 391

Chapter 17. Transposable Elements and Retroviruses 419

Edited by Damon Lisch, University of California, Berkeley

Chapter 18. Somatic Recombination and Hypermutation in the Immune System 458

Edited by Paolo Casali, Institute for Immunology, University of California, Irvine

Part 3. TRANSCRIPTION AND POSTTRANSCRIPTIONAL MECHANISMS 503

Chapter 19. Prokaryotic Transcription 504

Edited by Richard Gourse, University
of Wisconsin, Madison

Chapter 20. Eukaryotic Transcription 546

Chapter 21. RNA Splicing and Processing 573

Edited by Xiang-Dong Fu, University of California,
San Diego, School of Medicine

Chapter 22. mRNA Stability and Localization 618

Edited by Ellen Baker, University of Nevada, Reno

Chapter 23. Catalytic RNA 642

Edited by Douglas J. Briant, University of Victoria

Chapter 24. Translation 665

Edited by Cheryl Keller Capone, Pennsylvania State University Chapter 25. Using the Genetic Code 704

Edited by John Perona, University of California, Santa Barbara

Part 4. GENE REGULATION 734

Chapter 26. The Operon 735

Edited by Liskin Swint-Kruse, University of Kansas School of Medicine

Chapter 27. Phage Strategies 767

Chapter 28. Eukaryotic Transcription Regulation 795

Chapter 29. Epigenetic Effects Are Inherited 828

Edited by Trygve Tollefsbol, University of Alabama, Birmingham

Chapter 30. Regulatory RNA 861

Glossary 881 Index 905

Contents

Preface xx About the Authors xxiii	Chapter 2. Ge Edited by Esther Sie
DADT 4 CENEC AND	2.1 Introductio
PART 1. GENES AND	2.2 A Gene Cod
CHROMOSOMES 1 Chapter 1. Genes Are DNA 2	2.3 Mutations i Complemen
1.1 Introduction 3	2.4 Mutations A
1.2 DNA Is the Genetic Material of Bacteria and Viruses 5	Gain-of-Fur 2.5 A Locus Ma Alleles 31
1.3 DNA Is the Genetic Material of Eukaryotic Cells 6	2.6 A Locus Ma
Polynucleotide Chains Have Nitrogenous Bases Linked to a Sugar–Phosphate Backbone 7	Allele 31
1.5 Supercoiling Affects the Structure of DNA 8	2.7 Recombination of DNA 32
1.6 DNA Is a Double Helix 10	2.8 The Genetic
1.7 DNA Replication Is Semiconservative 12	2.9 Every Seque
1.8 Polymerases Act on Separated DNA Strands at the Replication Fork 13	Frames 36 2.10 Prokaryotic
1.9 Genetic Information Can Be Provided by DNA or RNA 14	Proteins 3 2.11 Several Pro
1.10 Nucleic Acids Hybridize by Base Pairing 16	Protein Pro
1.11 Mutations Change the Sequence of DNA 17	2.12 Proteins Ar acting 39
1.12 Mutations May Affect Single Base Pairs or Longer Sequences 18	2.13 Summary
1.13 The Effects of Mutations Can Be Reversed 20	References 41
1.14 Mutations Are Concentrated at Hotspots 20	Chapter 3. Me
1.15 Many Hotspots Result from Modified Bases 21	and Genetic Er
1.16 Some Hereditary Agents Are Extremely Small 23	Edited by John Brui
1.17 Summary 24	3.1 Introductio

Chapter 2	. Genes	Code	for	Proteins	26
Edited by Est	her Siegfried	1			

- n 27
- des for a Single Polypeptide 28
- in the Same Gene Cannot
- May Cause Loss-of-Function or nction 30
- ay Have Many Different Mutant
- ay Have More Than One Wild-type
- tion Occurs by Physical Exchange
- c Code Is Triplet 34
- ence Has Three Possible Reading
- Genes Are Colinear with Their
- cesses Are Required to Express the duct of a Gene 38
- re trans-acting, but Sites on DNA Are cis-
- 41

ethods in Molecular Biology ngineering 42

nstein

- n 43
- 3.2 Nucleases 44

References 24

3.3	Cloning 46	Chapter 5. The Content of the Genome 98
3.4	Cloning Vectors Can Be Specialized for Different	5.1 Introduction 99
3.5	Purposes 49 Nucleic Acid Detection 52	5.2 Genomes Can Be Mapped at Several Levels of Resolution 100
3.6	DNA Separation Techniques 54	5.3 Individual Genomes Show Extensive Variation 101
	DNA Sequencing 57 PCR and RT-PCR 59	5.4 RFLPs and SNPs Can Be Used for Genetic Mapping 102
	Blotting Methods 65	5.5 Eukaryotic Genomes Contain Both Nonrepetitive and Repetitive DNA Sequences 104
	DNA Microarrays 68 Chromatin Immunoprecipitation 71	5.6 Eukaryotic Protein-Coding Genes Can Be Identified by the Conservation of Exons 105
	Gene Knockouts and Transgenics 73	5.7 The Conservation of Genome Organization Helps to Identify Genes 108
5.15	Summary 78	5.8 Some Organelles Have DNA 110
•	ter 4. The Interrupted Gene 79 The by Donald Forsdyke	5.9 Organelle Genomes Are Circular DNAs That Code for Organelle Proteins 112
	Introduction 80	5.10 The Chloroplast Genome Codes for Many Proteins and RNAs 114
	An Interrupted Gene Consists of Exons and Introns 81	5.11 Mitochondria and Chloroplasts Evolved by Endosymbiosis 114
	Exon and Intron Base Compositions Differ 82	5.12 Summary 116
4.4	Organization of Interrupted Genes May Be Conserved 82	References 116
4.5	Exon Sequences under Negative Selection Are Conserved but Introns Vary 84	Chapter 6. Genome Sequences and Gene Numbers 118
4.6	Exon Sequences under Positive Selection Vary but Introns Are Conserved 85	6.1 Introduction 119
4.7	Genes Show a Wide Distribution of Sizes 86	6.2 Prokaryotic Gene Numbers Range Over an Order
	Some DNA Sequences Code for More Than	of Magnitude 120
One Polypeptide 88	• • •	6.3 Total Gene Number Is Known for Several Eukaryotes 121
4.9	Some Exons Can Be Equated with Protein Functional Domains 90	6.4 How Many Different Types of Genes Are There? 123
4.10	Members of a Gene Family Have a Common Organization 91	6.5 The Human Genome Has Fewer Genes Than Originally Expected 125
4.11	Genetic Information Is Not Completely Contained	6.6 How Are Genes and Other Sequences Distributed

in DNA 93

4.12 Summary 95

References 96

in the Genome? 127

Genes 129

6.7 The Y Chromosome Has Several Male-Specific

6.8 How Many Genes Are Essential? 130

,	
6.9 About 10,000 Genes Are Expressed at Widely Differing Levels in a Eukaryotic Cell 133	8.10 Globin Clusters Arise by Duplication and Divergence 179
6.10 Expressed Gene Number Can Be Measured	8.11 Pseudogenes Are Nonfunctional Gene Copies 181
en masse 134 6.11 Summary 135	8.12 Genome Duplication Has Played a Role in Plant and Vertebrate Evolution 182
References 136	8.13 What Is The Role of Transposable Elements in Genome Evolution? 184
Chapter 7. Clusters and Repeats 139	8.14 There May Be Biases in Mutation, Gene Conversion,
7.1 Introduction 140	and Codon Usage 185
7.2 Unequal Crossing-over Rearranges Gene Clusters 142	8.15 Summary 186 References 187
7.3 Genes for rRNA Form Tandem Repeats Including an Invariant Transcription Unit 145	Chapter 9. Chromosomes 189
7.4 Crossover Fixation Could Maintain Identical Repeats 147	Edited by Hank W. Bass 9.1 Introduction 190
7.5 Satellite DNAs Often Lie in Heterochromatin 150	9.2 Viral Genomes Are Packaged into Their Coats 191
7.6 Arthropod Satellites Have Very Short Identical	9.3 The Bacterial Genome Is a Nucleoid 194
Repeats 152	9.4 The Bacterial Genome Is Supercoiled 195
7.7 Mammalian Satellites Consist of Hierarchical Repeats 152	9.5 Eukaryotic DNA Has Loops and Domains Attached to a Scaffold 197
7.8 Minisatellites Are Useful for Genetic Mapping 156	9.6 Specific Sequences Attach DNA to an Interphase
7.9 Summary 157	Matrix 198
References 158	9.7 Chromatin Is Divided into Euchromatin and Heterochromatin 199
Chapter 8. Genome Evolution 159	9.8 Chromosomes Have Banding Patterns 201
8.1 Introduction 160	9.9 Lampbrush Chromosomes Are Extended 202
8.2 DNA Sequences Evolve by Mutation and a Sorting Mechanism 161	9.10 Polytene Chromosomes Form Bands 203
8.3 Selection Can Be Detected by Measuring Sequence Variation 163	9.11 Polytene Chromosomes Expand at Sites of Gene Expression 204
8.4 A Constant Rate of Sequence Divergence Is a Molecular Clock 167	9.12 The Eukaryotic Chromosome Is a Segregation Device 205
8.5 The Rate of Neutral Substitution Can Be Measured from Divergence of Repeated Sequences 170	9.13 Regional Centromeres Contain a Centromeric HistonH3 Variant and Repetitive DNA 207
8.6 How Did Interrupted Genes Evolve? 172	9.14 Point Centromeres in <i>S. cerevisiae</i> Contain Short, Essential DNA Sequences 208
8.7 Why Are Some Genomes So Large? 175	9.15 The S. cerevisiae Centromere Binds a Protein
8.8 Morphological Complexity Evolves by Adding New	Complex 209
Gene Functions 176	9.16 Telomeres Have Simple Repeating Sequences 210
8.9 Gene Duplication Contributes to Genome Evolution 178	9.17 Telomeres Seal the Chromosome Ends and Function in Meiotic Chromosome Pairing 211

- **9.18** Telomeres Are Synthesized by a Ribonucleoprotein Enzyme 213
- 9.19 Telomeres Are Essential for Survival 214
- 9.20 Summary 215

References 216

Chapter 10. Chromatin 220

- 10.1 Introduction 222
- 10.2 DNA Is Organized in Arrays of Nucleosomes 222
- 10.3 The Nucleosome Is the Subunit of All Chromatin 225
- 10.4 Nucleosomes Are Covalently Modified 228
- 10.5 Histone Variants Produce Alternative
 Nucleosomes 231
- 10.6 DNA Structure Varies on the Nucleosomal Surface 234
- 10.7 The Path of Nucleosomes in the Chromatin Fiber 237
- 10.8 Replication of Chromatin Requires Assembly of Nucleosomes 239
- 10.9 Do Nucleosomes Lie at Specific Positions? 242
- 10.10 Nucleosomes Are Displaced and Reassembled During Transcription 245
- **10.11** DNase Sensitivity Detects Changes in Chromatin Structure 248
- 10.12 Insulators Define Transcriptionally Independent Domains 251
- 10.13 An LCR May Control a Domain 255
- **10.14** Summary 257

References 258

PART 2. DNA REPLICATION AND RECOMBINATION 262

Chapter 11. The Replicon 263

Edited by Stephen D. Bell

- 11.1 Introduction 264
- 11.2 Replicons Can Be Linear or Circular 265
- 11.3 Origins Can Be Mapped by Autoradiography and Electrophoresis 267

- 11.4 The Bacterial Genome Is (Usually) a Single Circular Replicon 268
- 11.5 Methylation of the Bacterial Origin Regulates
 Initiation 270
- 11.6 Origins May Be Sequestered After Replication 271
- 11.7 Archaeal Chromosomes Can Contain Multiple
 Replicons 272
- 11.8 Each Eukaryotic Chromosome Contains Many Replicons 272
- 11.9 Replication Origins Can Be Isolated in Yeast 274
- 11.10 Licensing Factor Controls Eukaryotic Rereplication 275
- 11.11 Licensing Factor Consists of MCM Proteins 277
- 11.12 D Loops Maintain Mitochondrial Origins 278
- **11.13** Summary 279

References 280

Chapter 12. Extrachromosomal

Replicons 282

Edited by Søren Johannes Sørensen & Lars Hestbjerg Hansen

- 12.1 Introduction 283
- 12.2 The Ends of Linear DNA Are a Problem for Replication 284
- 12.3 Terminal Proteins Enable Initiation at the Ends of Viral DNAs 285
- 12.4 Rolling Circles Produce Multimers of a Replicon 286
- 12.5 Rolling Circles Are Used to Replicate Phage Genomes 288
- 12.6 The F Plasmid Is Transferred by Conjugation between Bacteria 289
- 12.7 Conjugation Transfers Single-Stranded DNA 290
- 12.8 The Bacterial Ti Plasmid Causes Crown Gall Disease in Plants 292
- 12.9 T-DNA Carries Genes Required for Infection 293
- 12.10 Transfer of T-DNA Resembles Bacterial Conjugation 295
- 12.11 Summary 297

References 298

Chapter 13. Bacterial Replication Is Connected to the Cell Cycle 299

Edited by Barbara Funnell

- 13.1 Introduction 300
- 13.2 Replication Is Connected to the Cell Cycle 301
- 13.3 The Septum Divides a Bacterium into Progeny That Each Contain a Chromosome 302
- 13.4 Mutations in Division or Segregation Affect Cell Shape 304
- 13.5 FtsZ Is Necessary for Septum Formation 304
- **13.6** *min* and *noc/slm* Genes Regulate the Location of the Septum 306
- 13.7 Chromosomal Segregation May Require Site-Specific Recombination 307
- 13.8 Partition Involves Separation of the Chromosomes 308
- 13.9 Single-Copy Plasmids Have a Partitioning System 310
- **13.10** Plasmid Incompatibility Is Determined by the Replicon 312
- 13.11 The ColE1 Compatibility System Is Controlled by an RNA Regulator 313
- **13.12** How Do Mitochondria Replicate and Segregate? 315
- **13.13** Summary 316

References 317

Chapter 14. DNA Replication 320

Edited by Peter Burgers

- 14.1 Introduction 321
- 14.2 Initiation: Creating the Replication Forks at the Origin *oriC* 322
- 14.3 DNA Polymerases Are the Enzymes That Make DNA 324
- 14.4 DNA Polymerases Have Various Nuclease Activities 326
- 14.5 DNA Polymerases Control the Fidelity of Replication 326
- 14.6 DNA Polymerases Have a Common Structure 328

- 14.7 The Two New DNA Strands Have Different Modes of Synthesis 329
- 14.8 Replication Requires a Helicase and a Single-Strand Binding Protein 330
- 14.9 Priming Is Required to Start DNA Synthesis 331
- 14.10 Coordinating Synthesis of the Lagging and Leading Strands 332
- **14.11** DNA Polymerase Holoenzyme Consists of Subcomplexes 333
- 14.12 The Clamp Controls Association of Core Enzyme with DNA 334
- 14.13 Okazaki Fragments Are Linked by Ligase 337
- **14.14** Separate Eukaryotic DNA Polymerases Undertake Initiation and Elongation 338
- **14.15** Phage T4 Provides Its Own Replication Apparatus 340
- **14.16** Lesion Bypass Requires Polymerase Replacement 342
- **14.17** Summary 344

References 345

Chapter 15. Homologous and Site-Specific Recombination 348

Edited by Hannah L. Klein & Samantha Hoot

- **15.1** Introduction 350
- 15.2 Homologous Recombination Occurs between Synapsed Chromosomes in Meiosis 352
- **15.3** Double-Strand Breaks Initiate Recombination 353
- **15.4** Gene Conversion Accounts for Interallelic Recombination 355
- **15.5** The Synthesis-Dependent Strand-Annealing Model 357
- 15.6 Nonhomologous End-Joining Can Repair
 Double-Strand Breaks 358
- **15.7** The Single-Strand Annealing Mechanism Functions at Some Double-Strand Breaks 359
- **15.8** Break-Induced Replication Can Repair Double-Strand Breaks 359
- 15.9 Recombining Meiotic Chromosomes Are Connected by the Synaptonemal Complex 360

15.10	The Synaptonemal Complex Forms after Double-Strand Breaks 362	16.9 Recombination Is an Important Mechanism to Recover from Replication Errors 406
15.11	Pairing and Synaptonemal Complex Formation Are Independent 364	16.10 Recombination-Repair of Double-Strand Breaks in Eukaryotes 407
15.12	The Bacterial RecBCD System Is Stimulated by <i>chi</i> Sequences 365	16.11 Nonhomologous End-Joining Also Repairs Double-Strand Breaks 409
15,13	Strand-Transfer Proteins Catalyze Single-Strand Assimilation 366	16.12 DNA Repair in Eukaryotes Occurs in the Context of Chromatin 410
15.14	Holliday Junctions Must Be Resolved 369	16.13 RecA Triggers the SOS System 413
15.15	Eukaryotic Genes Involved in Homologous Recombination 371	16.14 Summary 414 References 415
15.16	Specialized Recombination Involves Specific Sites 374	Chapter 17. Transposable Elements
15.17	Site-Specific Recombination Involves Breakage and Reunion 376	and Retroviruses 419 Edited by Damon Lisch
15.18	Site-Specific Recombination Resembles	17.1 Introduction 421
15.19	Topoisomerase Activity 376 Lambda Recombination Occurs in an Intasome 378	17.2 Insertion Sequences Are Simple Transposition Modules 423
	Yeast Can Switch Silent and Active Loci for Mating	
	Type 380	17.3 Transposition Occurs by Both Replicative and Nonreplicative Mechanisms 424
15.21	Unidirectional Gene Conversion Is Initiated by the Recipient MAT Locus 381	17.4 Transposons Cause Rearrangement of DNA 426
15.22	Antigenic Variation in Trypanosomes Uses Homologous Recombination 383	17.5 Replicative Transposition Proceeds Through a Cointegrate 427
15.23	Recombination Pathways Adapted for Experimental Systems 384	17.6 Nonreplicative Transposition Proceeds by Breakage and Reunion 428
15.24	Summary 386	17.7 Maize Transposons Can Cause Breakage and Rearrangements 430
Referen	ces 387	17.8 Transposons Form Families in Maize 432
Chap	ter 16. Repair Systems 391	17.9 The Role of Transposable Elements in Hybrid Dysgenesis 435
16.1	Introduction 392	17.10 P Elements Are Activated in the Germline 436
	Repair Systems Correct Damage to DNA 394	17.11 The Retrovirus Life Cycle Involves Transposition-Like
	Excision Repair Systems in <i>E. coli</i> 396	Events 438
16.4	Eukaryotic Nucleotide Excision Repair Pathways 397	17.12 Retroviral Genes Code for Polyproteins 439
16.5	Base Excision Repair Systems Require	17.13 Viral DNA Is Generated by Reverse Transcription 440
	Glycosylases 399	17.14 Viral DNA Integrates into the Chromosome 443
	Error-Prone Repair 402	17.15 Retroviruses May Transduce Cellular Sequences 444
16./	Controlling the Direction of Mismatch Repair 402	17.16 Yeast Ty Elements Resemble Retroviruses 445

16.8 Recombination-Repair Systems in *E. coli* 405

17.17	Many Kinds of Transposable Elements Reside in <i>Drosophila melanogaster</i> 447	18.16 Somatic Hypermutation (SHM) Generates Additional Diversity in Mice and Humans 483
17.18	Retroelements Fall into Three Classes 449	18.17 SHM Is Mediated by AID, Ung, Elements of the
17.19	The Alu Family Has Many Widely Dispersed Members 451	Mismatch DNA Repair (MMR) Machinery, and Translesion DNA Synthesis (TLS) Polymerases 484
17.20	LINEs Use an Endonuclease to Generate a Priming	18.18 Avian Igs Are Assembled from Pseudogenes 485
	End 451	18.19 B Cell Memory Allows for the Mounting of a Prompt and Strong Secondary Response 486
17.21	Summary 453	18.20 The TCR Is Related to the BCR 488
Referen	ces 455	
Chap ⁻	ter 18. Somatic Recombination	18.21 The TCR Functions in Conjunction with the MHC 490
	lypermutation in the Immune m 458	18.22 The Major Histocompatibility Locus Comprises a Cohort of Genes Involved in Immune
Edite	d by Paolo Casali	Recognition 492
18.1	The Immune System: Innate and Adaptive Immunity 460	18.23 Summary 494 References 496
18.2	The Innate Response Utilizes Conserved Recognition Molecules and Signaling Pathways 461	PART 3. TRANSCRIPTION
18.3	Adaptive Immunity 464	AND POSTTRANSCRIPTIONAL
18.4	Clonal Selection Amplifies Lymphocytes That Respond to Given Antigens 466	MECHANISMS 503
18.5	Ig Genes Are Assembled from Discrete DNA Segments in B Lymphocytes 468	Chapter 19. Prokaryotic Transcription 504
18.6	L Chains Are Assembled by a Single Recombination Event 469	Edited by Richard Gourse 19.1 Introduction 506
18.7	H Chains Are Assembled by Two Sequential Recombination Events 470	19.2 Transcription Occurs by Base Pairing in a "Bubble" of Unpaired DNA 507
18.8	Recombination Generates Extensive Diversity 472	19.3 The Transcription Reaction Has Three Stages 508
18.9	Immune Recombination Uses Two Types of Consensus Sequence 473	19.4 Bacterial RNA Polymerase Consists of Multiple Subunits 509
18.10	V(D)J DNA Recombination Occurs by Deletion or Inversion 474	19.5 RNA Polymerase Holoenzyme Consists of the Core Enzyme
18.11	Allelic Exclusion Is Triggered by Productive Rearrangements 474	and Sigma Factor 511 19.6 How Does RNA Polymerase Find Promoter
18.12	RAG1/RAG2 Catalyze Breakage and Religation of V(D)J Gene Segments 476	Sequences? 512 19.7 The Holoenzyme Goes through Transitions in the
18.13	Early IgH Chain Expression Is Modulated by RNA Processing 479	Process of Recognizing and Escaping from Promoters 512

19.8 Sigma Factor Controls Binding to DNA by

by Mutation 516

Recognizing Specific Sequences in Promoters 514

19.9 Promoter Efficiencies Can Bé Increased or Decreased

18.14 Class Switching Is Effected by DNA

18.15 CSR Involves Elements of the NHEJ Pathway 481

Recombination 480

19.10	Multiple Regions in RNA Polymerase Directly Contact Promoter DNA 517	20.9 Enhancers Contain Bidirectional Elements That Assist Initiation 563
19.11	Footprinting Is a High Resolution Method for Characterizing RNA Polymerase-Promoter and DNA-Protein Interactions in General 520	20.10 Enhancers Work by Increasing the Concentration of Activators Near the Promoter 564
19.12	Interactions between Sigma Factor and Core RNA Polymerase Change During Promoter Escape 522	20.11 Gene Expression Is Associated with Demethylation 565
19.13	A Model for Enzyme Movement Is Suggested by the Crystal Structure 523	20.12 CpG Islands Are Regulatory Targets 56720.13 Summary 569
19.14	A Stalled RNA Polymerase Can Restart 525	References 569
19.15	Bacterial RNA Polymerase Terminates at Discrete Sites 525	Chapter 21. RNA Splicing and Processing 573
19.16	How Does Rho Factor Work? 527	Edited by Xiang-Dong Fu
19.17	Supercoiling Is an Important Feature	21.1 Introduction 575
	of Transcription 530	21.2 The 5' End of Eukaryotic mRNA Is Capped 576
19.18	Phage T7 RNA Polymerase Is a Useful Model System 530	21.3 Nuclear Splice Junctions Are Short Sequences 578
19.19	Competition for Sigma Factors Can Regulate	21.4 Splice Junctions Are Read in Pairs 578
	Initiation 531	21.5 Pre-mRNA Splicing Proceeds through a Lariat 580
19.20	Sigma Factors May Be Organized into Cascades 533	21.6 snRNAs Are Required for Splicing 581
	Sporulation Is Controlled by Sigma Factors 534	21.7 Commitment of Pre-mRNA to the Splicing Pathway 583
	Antitermination Can Be a Regulatory Event 537	21.8 The Spliceosome Assembly Pathway 586
	The Cycle of Bacterial Messenger RNA 538	21.9 An Alternative Spliceosome Uses Different snRNPs
	Summary 541	to Process the Minor Class of Introns 589
	ces 542	21.10 Pre-mRNA Splicing Likely Shares the Mechanism with Group II Autocatalytic Introns 589
	ter 20. Eukaryotic Transcription 546	21.11 Splicing Is Temporally and Functionally Coupled wit
	Introduction 547	Multiple Steps in Gene Expression 591
20.2	Eukaryotic RNA Polymerases Consist of Many Subunits 549	21.12 Alternative Splicing Is a Rule, Rather Than an Exception, in Multicellular Eukaryotes 594
20.3	RNA Polymerase I Has a Bipartite Promoter 551	21.13 Splicing Can Be Regulated by Exonic and Intronic
20.4	RNA Polymerase III Uses Both Downstream and Upstream Promoters 552	Splicing Enhancers and Silencers 596
20.5	The Startpoint for RNA Polymerase II 554	21.14 trans-Splicing Reactions Use Small RNAs 598
	TBP Is a Universal Factor 555	21.15 The 3' Ends of mRNAs Are Generated by Cleavage and Polyadenylation 601
20.7	The Basal Apparatus Assembles at the Promoter 557	21.16 The 3' mRNA End Processing Is Critical for Transcriptional Termination 602
20.8	Initiation Is Followed by Promoter Clearance and Elongation 560	21.17 The 3' End Formation of Histone mRNA Requires U7 snRNA 604

21.18 tRNA Splicing Involves Cutting and Rejoining in Separate Reactions 605	23.5 Some Group I Introns Code for Endonucleases That Sponsor Mobility 651
21.19 The Unfolded Protein Response Is Related to tRNA Splicing 608	23.6 Group II Introns May Code for Multifunction Proteins 652
21.20 Production of rRNA Requires Cleavage Events	23.7 Some Autosplicing Introns Require Maturases 653
and Involves Small RNAs 609	23.8 The Catalytic Activity of RNase P Is Due to
21.21 Summary 612 References 613	RNA 653
References 013	23.9 Viroids Have Catalytic Activity 65423.10 RNA Editing Occurs at Individual Bases 656
Chapter 22. mRNA Stability	23.11 RNA Editing Can Be Directed by Guide RNAs 657
and Localization 618 Edited by Ellen Baker	23.12 Protein Splicing Is Autocatalytic 660
22.1 Introduction 619	23.13 Summary 661
22.2 Messenger RNAs Are Unstable Molecules 621	References 662
22.3 Eukaryotic mRNAs Exist in the Form of mRNPs from Their Birth to Their Death 622	Chapter 24. Translation 665 Edited by Cheryl Keller Capone
Prokaryotic mRNA Degradation Involves Multiple Enzymes 623	24.1 Introduction 667
22.5 Most Eukaryotic mRNA Is Degraded via Two Deadenylation-Dependent Pathways 625	24.2 Translation Occurs by Initiation, Elongation, and Termination 668
22.6 Other Degradation Pathways Target Specific mRNAs 628	24.3 Special Mechanisms Control the Accuracy of Translation 670
mRNA-Specific Half-Lives Are Controlled by Sequences or Structures within the mRNA 629	24.4 Initiation in Bacteria Needs 30S Subunits and Accessory Factors 671
22.8 Newly Synthesized RNAs Are Checked for Defects via a Nuclear Surveillance System 631	24.5 Initiation Involves Base Pairing between mRNA and rRNA 673
Quality Control of mRNA Translation Is Performed by Cytoplasmic Surveillance Systems 633	24.6 A Special Initiator tRNA Starts the Polypeptide Chain 674
22.10 Some Eukaryotic mRNAs Are Localized to Specific Regions of a Cell 636	24.7 Use of fMet-tRNA _f Is Controlled by IF-2 and the Ribosome 675
22.11 Summary 638	24.8 Small Subunits Scan for Initiation Sites on
References 639	Eukaryotic mRNA 677 24.9 Eukaryotes Use a Complex of Many Initiation
Chapter 23. Catalytic RNA 642	Factors 678
Edited by Douglas J. Briant	24.10 Elongation Factor Tu Loads Aminoacyl-tRNA
23.1 Introduction 643	into the A Site 681
23.2 Group I Introns Undertake Self-Splicing by Transesterification 644	24.11 The Polypeptide Chain Is Transferred to Aminoacyl- tRNA 683
23.3 Group I Introns Form a Characteristic Secondary	24.12 Translocation Moves the Ribosome 684
Structure 646	24.13 Flongation Factors Bind Alternately to the

23.4 Ribozymes Have Various Catalytic Activities 648

xvi

Contents

Ribosome 685

24.14	Three Codons Terminate Translation 686		The Ribosome Influences the Accuracy of Translation 726
24.15	Termination Codons Are Recognized by Protein Factors 687		Frameshifting Occurs at Slippery Sequences 728
24.16	Ribosomal RNA Pervades Both Ribosomal Subunits 689	25.17	Other Recoding Events: Translational Bypassing and the tmRNA Mechanism to Free Stalled
24.17	Ribosomes Have Several Active Centers 692		Ribosomes 730
24.18	16S rRNA Plays an Active Role in Translation 695		Summary 731
24.19	23S rRNA Has Peptidyl Transferase Activity 697	Reference	es /32
24.20	Ribosomal Structures Change When the Subunits Come Together 698	PART	4. GENE REGULATION 734
24.21	Summary 699	Chapte	er 26. The Operon 735
Referen	ces 700	•	by Liskin Swint-Kruse
Chant	ter 25. Using the Genetic Code 704	26.1	Introduction 737
Edited	d by John Perona		Structural Gene Clusters Are Coordinately Controlled 740
	Introduction 705	26.3	The <i>lac</i> Operon Is Negative Inducible 741
25.2	Related Codons Represent Chemically Similar Amino Acids 706		<i>lac</i> Repressor Is Controlled by a Small-Molecule Inducer 742
25.3	Codon-Anticodon Recognition Involves Wobbling 707		cis-Acting Constitutive Mutations Identify the Operator 744
25.4	tRNAs Are Processed from Longer Precursors 709		trans-Acting Mutations Identify the Regulator
25.5	tRNA Contains Modified Bases 710		Gene 744
25.6	Modified Bases Affect Anticodon–Codon Pairing 712		<i>lac</i> Repressor Is a Tetramer Made of Two Dimers 746
25.7	There Are Sporadic Alterations of the Universal Code 713		lac Repressor Binding to the Operator Is Regulated by an Allosteric Change in Conformation 748
25.8	Novel Amino Acids Can Be Inserted at Certain Stop Codons 715		lac Repressor Binds to Three Operators and Interact with RNA Polymerase 750
25.9	tRNAs Are Selectively Paired with Amino Acids by Aminoacyl-tRNA Synthetases 716		The Operator Competes with Low-Affinity Sites to Bind Repressor 751
25.10	Aminoacyl-tRNA Synthetases Fall into Two Families 718		The <i>lac</i> Operon Has a Second Layer of Control: Catabolite Repression 752
25.11	Synthetases Use Proofreading to Improve Accuracy 720		The <i>trp</i> Operon Is a Repressible Operon with Three Transcription Units 755
25.12	Suppressor tRNAs Have Mutated Anticodons That Read New Codons 722		The <i>trp</i> Operon Is Also Controlled by Attenuation 756
25.13	There Are Nonsense Suppressors for Each Termination Codon 723		Attenuation Can Be Controlled by Translation 757
25,14	Suppressors May Compete with Wild-Type Reading of the Code 724		Translation Can Be Regulated 760

27.18 The Cro Repressor Is Needed for Lytic **26.16** r-Protein Synthesis Is Controlled by Infection 789 Autoregulation 761 **26.17** Summary 763 **27.19** What Determines the Balance between Lysogeny and the Lytic Cycle? 790 References 764 **27.20** Summary 792 **Chapter 27.** Phage Strategies 767 References 793 **27.1** Introduction 769 **Chapter 28.** Eukaryotic Transcription 27.2 Lytic Development Is Divided into Two Periods 770 Regulation 795 **27.3** Lytic Development Is Controlled by a Cascade 771 **28.1** Introduction 796 **27.4** Two Types of Regulatory Events Control the Lytic 28.2 Mechanism of Action of Activators Cascade 772 and Repressors 798 27.5 The Phage T7 and T4 Genomes Show Functional 28.3 Independent Domains Bind DNA and Activate Clustering 773 Transcription 801 **27.6** Lambda Immediate Early and Delayed Early Genes 28.4 The Two-Hybrid Assay Detects Protein-Protein Are Needed for Both Lysogeny and the Lytic Interactions 802 Cycle 775 28.5 Activators Interact with the Basal Apparatus 803 27.7 The Lytic Cycle Depends on Antitermination by pN 776 **28.6** There Are Many Types of DNA-Binding Domains 805 27.8 Lysogeny Is Maintained by the Lambda Repressor 28.7 Chromatin Remodeling Is an Active Process 806 Protein 777 **28.8** Nucleosome Organization or Content May Be **27.9** The Lambda Repressor and Its Operators Define Changed at the Promoter 809 the Immunity Region 778 **28.9** Histone Acetylation Is Associated with Transcription **27.10** The DNA-Binding Form of the Lambda Repressor Activation 811 Is a Dimer 779 **28.10** Methylation of Histones and DNA Is 27.11 Lambda Repressor Uses a Helix-Turn-Helix Motif Connected 814 to Bind DNA 780 **28.11** Promoter Activation Involves Multiple Changes **27.12** Lambda Repressor Dimers Bind Cooperatively to Chromatin 815 to the Operator 782 **28.1** Histone Phosphorylation Affects Chromatin 27.13 Lambda Repressor Maintains an Autoregulatory Structure 816 Circuit 783 28.13 How Is a Gene Turned On? 818 **27.14** Cooperative Interactions Increase the Sensitivity **28.14** Yeast *GAL* Genes: A Model for Activation of Regulation 785

and Repression 819

28.15 Summary 821

References 823

27.15 The *cII* and *cIII* Genes Are Needed to Establish

27.16 A Poor Promoter Requires cII Protein 786

27.17 Lysogeny Requires Several Events 787

Lysogeny 785

Chapter 29. Epigenetic Effects Are Inherited 828

Edited by Trygve Tollefsbol

- 29.1 Introduction 829
- 29.2 Heterochromatin Propagates from a Nucleation Event 831
- 29.3 Heterochromatin Depends on Interactions with Histones 832
- 29.4 Polycomb and Trithorax Are Antagonistic Repressors and Activators 835
- 29.5 X Chromosomes Undergo Global Changes 837
- 29.6 Chromosome Condensation Is Caused by Condensins 840
- 29.7 CpG Islands Are Subject to Methylation 843
- 29.8 DNA Methylation Is Responsible for Imprinting 846
- 29.9 Oppositely Imprinted Genes Can Be Controlled by a Single Center 848
- 29.10 Epigenetic Effects Can Be Inherited 848
- 29.11 Yeast Prions Show Unusual Inheritance 851
- 29.12 Prions Cause Diseases in Mammals 853

29.13 Summary 855

References 855

Chapter 30. Regulatory RNA 861

- 30.1 Introduction 862
- **30.2** A Riboswitch Can Alter Its Structure According to Its Environment 863
- 30.3 Noncoding RNAs Can Be Used to Regulate Gene Expression 864
- 30.4 Bacteria Contain Regulator RNAs 866
- 30.5 MicroRNAs Are Widespread Regulators in Eukaryotes 869
- 30.6 How Does RNA Interference Work? 872
- 30.7 Heterochromatin Formation Requires
 MicroRNAs 875
- **30.8** Summary 877

References 877

Glossary 881

Index 905