



PRINCIPLES OF GENETICS

SNUSTAD • SIMMONS • JENKINS

PRINCIPLES OF GENETICS

D. Peter Snustad

University of Minnesota

Michael J. Simmons

University of Minnesota

John B. Jenkins

Swarthmore College

Epilogue by James F. Crow



John Wiley & Sons, Inc.

New York • Chichester • Brisbane • Toronto • Singapore • Weinheim

ACQUISITIONS EDITOR David Harris
SENIOR DEVELOPMENTAL EDITOR Barbara Heaney
SENIOR MARKETING MANAGER Catherine Faduska
SENIOR PRODUCTION EDITOR Katharine Rubin
DESIGNER Harry Nolan
MANUFACTURING MANAGER Dorothy Sinclair
PHOTO EDITOR Lisa Passmore
PHOTO RESEARCHER Ramón Rivera Moret
ILLUSTRATION EDITOR Edward Starr
DEVELOPMENTAL PROGRAM ASSISTANT Pui Szeto

Cover Photos *Background:* Philippe Plailly/Science Photo Library/Photo Researchers *From left to right, top to bottom:* Oliver Meches/Photo Researchers; M. Wurtz/Biozentrum, University of Basel/Science Photo Library/Photo Researchers; Biophoto Associates/Photo Researchers; Marc Chamberlain/Tony Stone Images; Philippe Plailly/Eurelios/Science Photo Library/Photo Researchers; David Scharf/Peter Arnold, Inc.; Courtesy of Lisa Passmore; Courtesy of Jeffrey L. Carpenter, Carolyn D. Silflow, and D. Peter Snustad, Department of Genetics & Cell Biology, University of Minnesota, St. Paul; NIBSC/Science Photo Library/Photo Researchers.

This book was set in 10/12 Palatino by Ruttle, Shaw & Wetherill, and printed and bound by R.R. Donnelley/Willard. The cover was printed by Phoenix Color.

Recognizing the importance of preserving what has been written, it is a policy of John Wiley & Sons, Inc. to have books of enduring value published in the United States printed on acid-free paper, and we exert our best efforts to that end.

The paper in this book was manufactured by a mill whose forest management programs include sustained yield harvesting of its timberlands. Sustained yield harvesting principles ensure that the number of trees cut each year does not exceed the amount of new growth.

Copyright © 1997 by John Wiley & Sons, Inc.

All rights reserved. Published simultaneously in Canada.

Reproduction or translation of any part of this work beyond that permitted by Sections 107 and 108 of the 1976 United States Copyright Act without the permission of the copyright owner is unlawful. Requests for permission or further information should be addressed to the Permissions Department, John Wiley & Sons, Inc.

Library of Congress Cataloging in Publication Data:

Snustad, D. Peter.

Principles of genetics / D. Peter Snustad, Michael J. Simmons, John B. Jenkins.

p. cm.

Includes bibliographical references and index.

ISBN 0-471-31196-0 (alk. paper)

1. Genetics. I. Simmons, Michael J. II. Jenkins, John B.

III. Title.

QH430.S68 1997

576.6—dc21

96-39102

CIP

Printed in the United States of America

10 9 8 7 6 5 4 3 2 1

About the Authors

D. Peter Snustad is a Professor in the Department of Genetics and Cell Biology at the University of Minnesota, Twin Cities. He received his B.S. degree in science specialization from the University of Minnesota and his M.S. and Ph.D. degrees in genetics from the University of California, Davis. During his 31 years as a member of the faculty at Minnesota, he has taught courses at all levels from general biology to advanced biochemical genetics. For 20 years, his research focused on bacteriophage T4 morphogenesis and the interaction between T4 and its host, *Escherichia coli*. For the past 11 years, his research group has studied the genetic control of the cytoskeleton in *Arabidopsis thaliana* and the glutamine synthetase gene family in *Zea mays*. He has served on the National Institutes of Health Molecular Cytology Study Section and as Program Chairperson for the Annual Meeting of the Genetics Society of America. His honors include the Morse-Amoco and Stanley Dagley Memorial teaching awards. A lifelong love of the Canadian wilderness has kept him in nearby Minnesota.

Michael J. Simmons is a Professor in the Department of Genetics and Cell Biology at the University of Minnesota, Twin Cities. He received his B.A. degree in biology from St. Vincent College in Latrobe, Pennsylvania, and his M.S. and Ph.D. degrees in genetics from the University of Wisconsin, Madison. Dr. Simmons has taught courses in general biology, genetics, population biology, population genetics, and molecular biology. His research activities are focused on the genetic significance of transposable genetic elements, especially those present in the genome of *Drosophila melanogaster*. He has served on advisory committees at the National Institutes of Health and is currently a member of the Editorial Board of *Genetics*, published by the Genetics Society of America. In 1986, Dr. Simmons received the Morse-Amoco teaching award from the University of Minnesota in recognition of his contributions to undergraduate education. One of his favorite activities, figure skating, is especially compatible with the Minnesota climate.

John B. Jenkins is a Professor in the Department of Biology at Swarthmore College, where he teaches genetics, human genetics, and evolution. He received his B.S. and M.S. degrees from Utah State University, where he studied with Eldon J. Gardner, and his Ph.D. from the University of California, Los Angeles, where he studied chemical mutagenesis with Elof Axel Carlson. Dr. Jenkins's research interests are in the areas of mutation, behavior genetics, cytogenetics, and Huntington's disease. He has authored textbooks on genetics and human genetics and has co-authored a collection of classic papers in genetics. He is a member of the Genetics Society of America, the American Society of Human Genetics, and other scientific societies. He has served on numerous committees and panels of the Genetics Society of America, American Society of Human Genetics, and the National Science Foundation. He has served on the Editorial Board of the Education Section of the *American Journal of Human Genetics* and the Board of Reviewers for the *Journal of Medical Genetics*. His love of fishing frequently takes him to the streams of Pennsylvania and the lakes of New Hampshire.

Dedications

To my son Eric, my best friend Judy, and my campfire buddies Jason and Oak. Thanks for sharing those special times.

D.P.S.

To my family, especially to Benjamin John.

M.J.S.

With much love to my extraordinary wife Dotti and to my wonderful children, John, Soraya, Jessica, and Charlotte, all of whom bring so much joy to my life.

J.B.J.

Preface

Although the science of genetics is only 130 years old, it has grown at an explosive rate during the last half of the twentieth century and now impacts virtually all aspects of our lives. What began with the simple and elegant experiments of Gregor Mendel has blossomed into a mature science that is the focus of research throughout the world. When we started teaching 30 years ago, genetics was considered by many biologists to be just one of several specialized disciplines in biology. Today, it is viewed as the core of biology. Genetic approaches to the dissection of biological processes have proven invaluable. The powerful tools of molecular genetics are now routinely used to investigate phenomena as diverse as photosynthesis, the immune response, memory, and evolution. In addition, numerous practical applications of genetics have been documented in fields such as medicine, agriculture, pharmaceuticals, and forensics. Given the rapid growth of genetics during the last few decades, it follows that the teaching of genetics has also undergone major changes. *Principles of Genetics* is the culmination of our collective attempt to stay abreast of the exciting new developments in genetics without sacrificing rigor in the coverage of basic Mendelian genetics.

Our philosophy in teaching genetics—and in preparing this textbook—is that learning is best achieved by emphasizing basic principles, especially when these principles are introduced through the analysis of observations and experimental results. Not all genetics instructors will agree with all aspects of our approach to teaching genetics; however, we think that most of them will agree that an introductory course should not only convey concepts but also should demonstrate how genetics is done—how the results of genetic experiments lead to new knowledge.

Focus on the basic principles of genetics. Every week new and important discoveries in genetics are announced. Yet, all of these impressive accomplishments are rooted in basic principles that were elucidated by Mendel and his successors. This textbook strives to develop these principles carefully and thoroughly. We believe that an appreciation of current advances in genetics must be grounded on a foundation of basic principles. For example, the powerful tools of molecular genetics permit scientists to screen individuals for mutations that cause Huntington's disease (Chapter 20, Figure 20.11). However, only through an understanding of Mendelian genetics will students appreciate the 50 percent risk of Huntington's disease among the children of a parent with this disease (see *A Conversation with Nancy Wexler*).

Show how scientific concepts develop from observation and experimentation. No one should lose sight of the fact that genetics, like every science, is a human endeavor. What is known about genetics today is the result of considerable toil and effort. Thousands of geneticists have labored to discover the facts and develop the concepts that make up the science of genetics. Each discovery began with a rather tentative mix of ideas and observations. With careful scrutiny and experimental testing, these ideas and observations eventually gelled into something less tentative—a set of concepts supported by facts. Genetics is replete with examples of this process, many of which we present in this text to emphasize the central role of scientific experimentation in the evaluation of ideas and the importance of critical interpretation of experimental data in testing hypotheses. In addition, we have incorporated *Conversations* with eminent geneticists to emphasize the human component of the scientific process.

Incorporate human examples and show the relevance of genetics to societal issues. Experience has shown us that when we discuss human genetics, our students are more interested and pay closer attention. Because they are more attentive, students tend to comprehend complex concepts better when they are illustrated with human examples. For that reason, we have used human examples to illustrate genetic principles whenever possible. We have also included separate sections on the Human Genome Project, human gene mapping, human gene therapy, and human genetic disorders such as Huntington's disease, cystic fibrosis, and xeroderma pigmentosum. In addition, we have dedicated an entire chapter to behavior genetics (Chapter 26) in which we examine the effects of genes on traits such as intelligence, personality, and sexual orientation.

Genetics, perhaps more than any other science, has sparked numerous social, legal, and ethical debates, which is one reason why students find the subject so fascinating. Many of these controversial issues—genetic screening and its potential for misuse, DNA fingerprinting, genetic engineering, and gene therapy—are products of the Human Genome Project. Although some of these topics are controversial, we believe that it is important to involve students in an intelligent dialogue on these issues because society will increasingly be called upon to address such questions. Hopefully, this textbook will provide students with the background information needed to address these concerns in an informed manner.

Emphasize analytical thinking and problem solving. Genetics has always been a bit different from other disciplines in biology because of its heavy emphasis on analysis and problem solving. In this text, we have fleshed out the analytical nature of genetics in many ways—in the development of principles in classical genetics, in the discussion of experiments in molecular genetics, and in the presentation of calculations in population and quantitative genetics. We have provided special worked-out problems in the *Testing Your Knowledge* section at the end of each chapter to help students develop their analytical skills. For example, students usually master the concept of semiconservative DNA replication quite easily. However, when asked to properly package the parental and nascent DNA strands into chromatids and daughter chromosomes, they often are unable to do so. We have observed that when students work through *Testing Your Knowledge* problem 2 in Chapter 10, they develop an understanding of both semiconservative replication and the packaging of DNA into chromosomes.

AN ADAPTABLE ORGANIZATION

Our most difficult decisions in preparing this text related to organization and content. Should the text begin with Mendel and proceed roughly in chronological fashion? Should it begin with DNA and present classical transmission genetics afterward? Should population and quantitative genetics follow classical genetics, or should they be placed at the very end of the text? Should classical and molecular genetics be interwoven throughout the text? Obviously, there is no single “correct” way to teach the basic principles of genetics. Thus our goal was to create a text that covers all the core topics and has an adaptable organization. We believe that this text can be adapted to a variety of class formats. For example, if an instructor prefers to discuss molecular genetics prior to classical genetics, she or he can cover Chapters 9–14 and then return to Chapters 3–8. Another goal was to keep the length of the text reasonable. As genetics has grown, so has the length of genetics textbooks. Without doubt, the most challenging choices that we made during the preparation of this text involved the omission of some of our favorite experiments, topics, and historical events. Genetics is a rich and diverse discipline, and we hope that we have made sensible decisions regarding what to include and exclude in this book.

The organization of the text is a mixture of traditional and unique. The organization is unique in that we have recognized the important contributions of viruses (Chapter 15) and bacteria (Chapter 16) to the basic concepts of genetics by covering each in a separate chapter. The genetic basis of cancer is covered in Chap-

ter 22, which emphasizes the most important and recent research on this topic. It is also unique in dedicating an entire chapter (24) to immunogenetics, although this seems almost unavoidable given the impact of AIDS in our world. The organization is traditional in that we cover Mendelian genetics first (Chapters 3–8) and DNA, RNA, and proteins second (Chapters 9–14). The text contains 28 chapters and an epilogue. Chapters 1–2 provide an introduction to the science of genetics and the basic features of living organisms; Chapters 3–8 present the concepts of classical genetics; Chapters 9–14 present the core concepts of molecular genetics; Chapters 15–18 cover the genetics of viruses, bacteria, transposable elements and eukaryotic organelles; Chapters 19–24 contain more advanced topics in molecular genetics; and Chapters 25–28 contain topics on population, quantitative, evolutionary, and behavior genetics.

Finally, the epilogue, *Genetics: Yesterday, Today, and Tomorrow*, written by James F. Crow, an eminent geneticist and a leading contributor to genetics (and to the teaching of genetics), shares his personal views about the history and future prospects of this science. We do not believe that you can read his epilogue without feeling the excitement that has infected the people who have made genetics what it is. We thank Dr. Crow for providing a truly special ending to the text. His wit, charm, and wisdom are greatly appreciated; many thanks, Jim.

ART PROGRAM

Well-designed illustrations are an essential component of any science textbook. Stepped-out illustrations, showing each phase in a process, are an invaluable aid in communicating complex concepts. Thus we have worked very hard to make the illustrations in this text clear, attractive, and pedagogically effective. Approximately 700 figures and 200 photographs have been included to illustrate basic concepts, experimental procedures, and various genetic phenomena. Many complex figures are stepped-out and contain succinct labels to help students break down difficult processes into manageable parts. For example, in Chapter 12, the complex process of translation has been divided into chain initiation (Figure 12.15), chain elongation (Figure 12.17), and chain termination (Figure 12.19), with each component covered in a separate stepped-out illustration. In addition, in developing the illustrations, we have utilized the same color scheme throughout the text so that related items can be identified in different figures based on color.

CONVERSATIONS WITH GENETICISTS

During the writing of this book, one of our most enjoyable tasks was to have conversations with some truly

remarkable scientists. The book contains nine conversations with prominent geneticists. We are indebted to these people for sharing their insights about science and education, and we hope that you will find these conversations as fascinating as we have. We thank:

Thomas J. Bouchard, Jr.	University of Minnesota, Twin Cities
Deborah and Brian Charlesworth	University of Chicago
James F. Crow	University of Wisconsin, Madison
Margaret G. Kidwell	University of Arizona
Edward B. Lewis	California Institute of Technology
Johng K. Lim	University of Wisconsin, Eau Claire
James V. Neel	University of Michigan
Mary Lou Pardue	Massachusetts Institute of Technology
Nancy Wexler	Hereditary Disease Foundation, Santa Monica, California

We are grateful to each of these individuals for their willingness to contribute to this book.

PEDAGOGY

This text includes special features designed to emphasize the relevance of the topics discussed, to facilitate the comprehension of important concepts, and to assist students in evaluating their grasp of these concepts. However, we have tried to make sure that these features do not interfere with the flow of the scientific content of the text. The features include:

- **Sidelights (Technical, Historical, Human Genetics).** Throughout the text, special topics are presented in separate *Sidelight* sections: *Technical Sidelights* describe important experimental techniques; *Historical Sidelights* provide insights into the history of genetics; and *Human Genetics Sidelights* examine important aspects of human genetics.
- **Chapter-Opening Vignettes.** Each chapter opens with a vignette or brief story—usually related to human genetics or historical developments—that emphasizes the relevance of the topics discussed in the chapter.
- **Key points.** These learning aids are in-text summaries that appear at the end of each major section of the text. They are designed to help students review for exams and focus on the major concepts covered in each section.
- **Testing Your Knowledge.** At the end of each chapter, we have provided worked-out problems to help students hone their analytical and problem-solving

skills. The answers walk the students step by step through the solutions to the problems.

- **Questions and Problems.** Each chapter ends with 20 to 35 questions and problems. The range of questions will provide students with the opportunity to enhance their understanding of the concepts covered in the chapter and to further develop their analytical skills.

- **Answers.** Answers to the odd-numbered problems are given at the back of the text, and answers to all problems are included in the *Instructor's Manual and Test Questions* supplement prepared by Robert Ivarie of the University of Georgia.

SUPPLEMENTS

The Problems Workbook and Study Guide, by H. J. Price of Texas A & M University, is a hands-on workbook designed to improve problem solving skills and to reinforce terminology and concepts from the text. Features included are important concepts, terms, and names; additional problems for self-test; key figures from the text; thought challenging exercises, answers to problems, and approaches to problem solving.

Instructor's Resources on CD-ROM, designed as a lecture enhancer and database of instructor's materials, is highly functional and easy to use. This cross-platform CD-ROM contains the following components and is free to adopters of the text: (1) A database of all the illustrations from the text from which the instructor can create presentations, download to the desktop, and/or print to acetates (2) *Instructor's Manual and Test Questions*, written by Bob Ivarie of the University of Georgia, which contains sample syllabi, lecture outlines, key concepts, teaching strategies for difficult material, and approximately 40 test questions per chapter. The complete set of answers to problems in the text are included here as well. The material can be printed from the CD or exported to word-processing programs for creation of handouts or lecture notes. The *Instructor's Manual and Test Questions* will also be available in a print format. (3) The *Transparency Set* which contains full-color figures from the text. (4) *World Wide Web*. Materials relevant to *Principles of Genetics* which are available to faculty and students.

GenLink, a new electronic supplement that integrates the Table of Contents to the vast resources of the World Wide Web, provides relevant links to genetic sites for you and your students. Linked sites include the latest research findings, forums, and simulations. We invite you to make comments and suggestions at the GenLink homepage so that we can make this program an even more effective learning tool. Please visit GenLink at <http://www.wiley.com/genlink>.

Of Related Interest: Drlica, *Understanding DNA & Gene Cloning: A Guide For the Curious*, 3/e, 1997.

ACKNOWLEDGMENTS

This book has been greatly influenced by the genetics courses that we have taught over the last 30 years. We must, therefore, acknowledge the many contributions of our students at Swarthmore College and the University of Minnesota. We must also acknowledge the contributions of our teachers and of many colleagues who have contributed to our ongoing education. Their knowledge and wisdom are deeply appreciated.

Manuscript Reviewers

Our gratitude also goes out to a host of reviewers whose criticisms and comments helped to shape the content of this book. These generous critics gave their time and expertise to correct errors and suggest ways in which the book could be improved; we deeply appreciate all their efforts. Of course, any errors that remain are solely our own responsibility. In particular, we acknowledge the constructive comments of the following reviewers:

Faculty Reviewers

Robert Baker University of Southern California	Sandra D. Michael Binghamton University
Anna Berkovitz Purdue University	Gregory Phillips New Mexico State University
Rick Cavicchioli University of New South Wales	Ruth Phillips University of Wisconsin
Richard W. Cheney, Jr. Christopher Newport University	Jim Price Texas A & M University
James F. Crow University of Wisconsin— Madison	Susan Reimer James Madison University
Jerry Eberhart Biology Consultant	John Ringo University of Maine
Richard Gethman University of Maryland— Baltimore County	Dorothy Rosenthal Science Education Consultant
Ben Golden Kennesaw State College	Mark Sanders University of California— Davis
Charles Green Rowan College of New Jersey	John Schiefelbein University of Michigan
Keith Hartberg Bailey University	Millard Susman University of Wisconsin— Madison
Richard B. Imberski University of Maryland— College Park	
Bob Ivarie University of Georgia	
Clint Magill Texas A & M University	

Student Reviewers

Paul Bruinsma of Purdue University
Cameron Parry of New Mexico State University
Natalie Sanchez of New Mexico State University

Many people contributed to the development and production of this book. The project was initiated under the supervision of Sally Cheney, former biology editor at John Wiley & Sons. We are indebted to Sally for having confidence in our ability to produce a state-of-the-art genetics text. David Harris, current biology editor at John Wiley, guided the project to completion. David is responsible for many of the features that make this book unique, and we are especially grateful for his guidance and unbounded enthusiasm. We also thank Cathy Donovan, David's editorial program assistant, for her cheerful help throughout the project.

Many professionals at Wiley worked with us during the production of this text. Barbara Heaney, senior development editor, and Pui Szeto, developmental program assistant, kept the project on course. Their organizational skills and good judgment were indispensable for the completion of the project. We deeply appreciate their thoughtful input on a wide range of issues. Barbara Conover, developmental consultant, was responsible for editing our early drafts and for converting our ideas and crude diagrams into the stepped-out illustrations in the text. Barbara, thanks so much! The art program was designed and produced by Poole Visual Communication Group of Cincinnati, and we thank Anthony J. Poole, creative director, for his talent and patience. The art was polished by Wellington Studios. We also thank Edward Starr, Wiley art coordinator, who supervised the development of the art program. Lisa Passmore, photo editor, obtained all the photographs that we requested, and more; thank you, Lisa. We thank Harry Nolan, designer, for creating an eye-catching cover and for developing the text layout. Our gratitude also goes out to Katharine Rubin, production editor, and Betty Pessagno, copy editor, for correcting our mistakes and for putting all the pieces of this book into a common format. We thank Ethan Goodman, marketing manager, for his help in getting this textbook into the hands of prospective users; Bonnie Cabot, former supplements editor, for persuading Jim Price of Texas A & M University to develop a *Problems Workbook and Study Guide*, and Bob Ivarie of the University of Georgia to prepare the *Instructor's Manual and Test Questions*; great job, Bonnie. We also thank Jennifer Yee, current supplements editor, for guiding the supplements to completion.

Lastly, we would like to encourage everyone—students, teaching assistants, instructors, and other readers—to send any comments on the text, corrections, or suggestions for improvements to D. Peter Snustad at John Wiley & Sons, Inc., 605 Third Avenue, New York, NY, 10158-0012, or PSnustad@Wiley.Com.

BRIEF CONTENTS

1 An Introduction to the Science of Genetics

- Chapter 1 The Science of Genetics 3
- Chapter 2 Reproduction as the Basis of Heredity 14

2 Classical Genetic Analysis

- Chapter 3 Mendelism: The Basic Principles of Inheritance 40
- Chapter 4 Extensions of Mendelism 60
- Chapter 5 The Chromosomal Basis of Mendelism 78
- Chapter 6 Variations in Chromosome Number and Structure 99
- Chapter 7 Linkage, Crossing Over and Chromosome Mapping in Eukaryotes 128
- Chapter 8 Advanced Linkage Analysis 151

3 The Molecular Biology of Genes

- Chapter 9 DNA and the Molecular Structure of Chromosomes 180
- Chapter 10 Replication of DNA and Chromosomes 212
- Chapter 11 Transcription and RNA Processing 248
- Chapter 12 Translation and the Genetic Code 281
- Chapter 13 Mutation, DNA Repair, and Recombination 311
- Chapter 14 Definitions of the Gene 349

4 The Genetics of Viruses, Bacteria, Transposons, and Eukaryotic Organelles

- Chapter 15 The Genetics of Viruses 380
- Chapter 16 The Genetics of Bacteria 401
- Chapter 17 Transposable Genetic Elements 423
- Chapter 18 The Genetics of Mitochondria and Chloroplasts 443

5 Molecular Genetic Analysis

- Chapter 19 The Techniques of Molecular Genetics 462
- Chapter 20 Molecular Analysis of Genes and Gene Products 501

6 The Regulation of Gene Expression

- Chapter 21 Regulation of Gene Expression in Prokaryotes 540
- Chapter 22 Gene Regulation in Eukaryotes and the Genetic Basis of Cancer 572
- Chapter 23 The Genetic Control of Animal Development 605
- Chapter 24 The Genetic Control of the Vertebrate Immune System 637

7 The Genetic Analysis of Complex Traits

- Chapter 25 Complex Inheritance Patterns 667
- Chapter 26 The Genetic Control of Behavior 690

8 The Genetics of the Evolutionary Process

- Chapter 27 Population Genetics and Evolution 718
- Chapter 28 Genetics and Speciation 739

9 Epilogue by James F. Crow 764

CONTENTS

An Introduction to the Science of Genetics

A Conversation with James Neel 1

CHAPTER 1 THE SCIENCE OF GENETICS 3

A Passion for Experimenting 3

Classical and Molecular Genetics 4

Genetics in the News 4

Genetics and Medicine 5

Genetics and Modern Agriculture 7

Genetics and Society 10

The Misuse of Genetics 11

The Principles of Genetics: An Overview 12

Historical Sidelight: The Lysenko Affair 12

CHAPTER 2 REPRODUCTION AS THE BASIS OF HEREDITY 11

An Accident in Cell Division 11

The Cell as the Basic Unit of Life 15

The Prokaryotic Cell 15

The Eukaryotic Cell 16

The Chromosome: An Overview 18

The Cell Cycle 20

Cell Division: Mitosis 20

Cell Division: Meiosis 24

Meiotic Abnormalities 27

The Evolutionary Significance of Meiosis 28

The Formation and Union of Gametes 28

Oogenesis: The Formation of the Egg 28

Spermatogenesis: The Formation of Sperm 29

Gamete Formation in Plants 31

The Life Cycles of Some Genetically Important

Organisms 31

Neurospora crassa: The Simple Bread Mold 31

Corn (Zea mays) 32

The Fruit Fly, Drosophila melanogaster 34

Humans 35

Technical Sidelight: Cell Cycle Checkpoints 21

Technical Sidelight: Giant Sperm 30

Classical Genetic Analysis

A Conversation with John K. Lim 38

CHAPTER 3 MENDELISM: THE BASIC PRINCIPLES OF INHERITANCE 10

The Birth of Genetics: A Scientific Revolution 10

Mendel's Study of Heredity 41

Mendel's Experimental Organism, the Garden Pea 41

Monohybrid Crosses: The Principles of Dominance and Segregation 42

Dihybrid Crosses: The Principle of Independent Assortment 44

Applications of Mendel's Principles 46

The Punnett Square Method 46

The Forked-Line Method 47

The Probability Method 47

Formulating and Testing Genetic Hypotheses 50

The Chi-Square Test 50

Mendelian Principles in Human Genetics 52

Pedigrees 52

Mendelian Segregation in Human Families 53

Genetic Counseling 54

Technical Sidelight: The Multiplicative and Additive

Rules of Probability 48

Technical Sidelight: Binomial Probabilities 55

CHAPTER 4 EXTENSIONS OF MENDELISM 60

Genetics Grows Beyond Mendel's Monastery Garden 60

Allelic Variation and Gene Function 61

Incomplete Dominance and Codominance 61

Multiple Alleles 62

Allelic Series 63

Testing Gene Mutations for Allelism 64

Variation Among the Effects of Mutations 65

Genes Function to Produce Polypeptides 65

Why Are Some Mutations Dominant and Others Recessive? 66

Gene Action: From Genotype to Phenotype 69

Interactions with the Environment 69

Environmental Effects on the Expression of Human Genes 69

Penetrance and Expressivity 70

Gene Interactions 72

Epistasis 72

Pleiotropy 74

The Genetic Basis of Continuous Phenotypic Variation 75

Historical Sidelight: Genetic Symbols: Evolution in a Dynamic Science 68

Human Genetics Sidelight: The Hapsburg Jaw: A Dominant Trait with Incomplete Penetrance and Variable Expressivity in the European Nobility 71

CHAPTER 5 THE CHROMOSOMAL BASIS OF MENDELISM 78

Sex, Chromosomes, and Genes 78

Chromosomes 79

Chromosome Number 79

Sex Chromosomes 79

The Chromosome Theory of Heredity 81

Experimental Evidence Linking the Inheritance of Genes to Chromosomes 81

Chromosomes as Arrays of Genes	82
Nondisjunction as Proof of the Chromosome Theory	83
The Chromosomal Basis of Mendel's Principles of Segregation and Independent Assortment	86
Sex-Linked Genes in Human Beings	88
Hemophilia, an X-linked Blood-Clotting Disorder	89
Color Blindness, an X-linked Vision Disorder	89
The Fragile X Syndrome and Mental Retardation	89
Genes on the Human Y Chromosome	90
Genes on Both the X and Y Chromosomes	90
Sex Chromosomes and Sex Determination	91
Sex Determination in Human Beings	91
Sex Determination in <i>Drosophila</i>	93
Sex Determination in Other Animals	93
Dosage Compensation of X-Linked Genes	94
Hyperactivation of X-linked Genes in Male <i>Drosophila</i>	95
Inactivation of X-linked Genes in Female Mammals	95
Historical Sidelight: <i>Drosophila</i>, T. H. Morgan, and "The Fly Room"	84
CHAPTER 6 VARIATION IN CHROMOSOME NUMBER AND STRUCTURE	99
Chromosomes, Agriculture, and Civilization	99
Cytological Techniques	100
Analysis of Mitotic Chromosomes	100
The Human Karyotype	102
Analysis of Meiotic Chromosomes	103
Cytogenetic Variation: An Overview	103
Polyploidy	103
Sterile Polyploids	103
Fertile Polyploids	106
Chromosome Doubling and the Origin of Polyploids	107
Experimental Production of Polyploids	107
Tissue-Specific Polyploidy and Polyteny	109
Aneuploidy	111
Trisomy in Human Beings	111
Monosomy	114
Deletions and Duplications of Chromosome Segments	114
Rearrangements of Chromosome Structure: An Overview	117
Inversions	118
Translocations	119
Compound Chromosomes and Robertsonian Translocations	121
Phenotypic Effects of Chromosome Rearrangements	123
Human Genetics Sidelight: Amniocentesis and	

Chorionic Biopsy: Procedures to Detect Aneuploidy in Human Fetuses	115
Technical Sidelight: <i>Oenothera</i>: Chromosome Rings and Other Things	122
CHAPTER 7 LINKAGE, CROSSING OVER, AND CHROMOSOME MAPPING IN EUKARYOTES	128
The World's First Chromosome Map	128
Linkage, Recombination, and Crossing Over	129
Exceptions to the Mendelian Principle of Independent Assortment	129
Frequency of Recombination as a Measure of Linkage Intensity	130
Crossing Over as the Physical Basis of Recombination	131
Evidence that Crossing Over Causes Recombination	133
Chiasmata and the Time of Crossing Over	134
Chromosome Mapping	135
Crossing Over as a Measure of Genetic Distance	135
Recombination Mapping with a Two-Point Testcross	136
Recombination Mapping with a Three-Point Testcross	137
Recombination Frequency and Genetic Map Distance	141
Chiasma Frequency and Genetic Map Distance	142
Genetic Distance and Physical Distance	143
Recombination and Evolution	144
Evolutionary Significance of Recombination	144
Suppression of Recombination by Inversions	144
Genetic Control of Recombination	145
Human Genetics Sidelight: Evidence for Linkage Between the Genes for Hemophilia and Color Blindness	138
CHAPTER 8 ADVANCED LINKAGE ANALYSIS	151
Huntington's Disease: A Challenge in Gene Mapping	151
Detection of Linkage in Experimental Organisms	152
Tetrad Analysis to Detect Linkage in Fungi	152
Balancer Chromosome Technique to Assign a Gene to a Chromosome in <i>Drosophila</i>	155
Specialized Mapping Techniques	157
Centromere Mapping with Ordered Tetrads in <i>Neurospora</i>	157
Cytogenetic Mapping with Deletions and Duplications in <i>Drosophila</i>	159
Linkage Analysis in Humans	163
Detection of Linked Loci by Pedigree Analysis	163

<i>Somatic Cell Genetics: An Alternative Approach to Gene Mapping</i>	166
<i>The Human Gene Map</i>	172
Technical Sidelight: The Relationship Between Genes and Bands in the Drosophila Polytene X Chromosome	162

The Molecular Biology of Genes

A Conversation with Mary Lou Pardue 178

CHAPTER 9 DNA AND THE MOLECULAR STRUCTURE OF CHROMOSOMES 180

<i>Discovery of "Nuclein"</i>	180
Functions of the Genetic Material	181
Proof That Genetic Information is Stored in DNA	181
<i>Discovery of Transformation in Bacteria</i>	182
<i>Proof That DNA Mediates Transformation</i>	183
<i>Proof That DNA Carries the Genetic Information in Bacteriophage T2</i>	184
<i>Proof That RNA Stores the Genetic Information in Some Viruses</i>	185
The Structures of DNA and RNA	186
<i>Nature of the Chemical Subunits in DNA and RNA</i>	186
<i>DNA Structure: The Double Helix</i>	186
<i>DNA Structure: Alternate Forms of the Double Helix</i>	191
<i>DNA Structure: Negative Supercoils In Vivo</i>	192
Chromosome Structure in Prokaryotes	194
Chromosome Structure in Eukaryotes	195
<i>Chemical Composition of Eukaryotic Chromosomes</i>	195
<i>One Large DNA Molecule per Chromosome</i>	196
<i>Three Levels of DNA Packaging in Eukaryotic Chromosomes</i>	199
<i>Centromeres and Telomeres</i>	202
Eukaryotic Genomes: Repeated DNA Sequences	205
<i>Detection of Repeated Sequences: DNA Renaturation Kinetics</i>	205
<i>Repeated Sequences in the Human Genome</i>	208
Technical Sidelight: DNA Renaturation Kinetics	207

CHAPTER 10 REPLICATION OF DNA AND CHROMOSOMES 212

<i>Monozygotic Twins: Are They Identical?</i>	212
Basic Features of DNA Replication In Vivo	213
<i>Semiconservative Replication</i>	213
<i>Visualization of Replication Forks by Autoradiography</i>	218
<i>Unique Origins of Replication</i>	219
<i>Bidirectional Replication</i>	220

DNA Polymerases and DNA Synthesis In Vitro 223

<i>Discovery of DNA Polymerase I in Escherichia coli</i>	223
<i>Multiple DNA Polymerases</i>	225
<i>DNA Polymerase III: The Replicase in Escherichia coli</i>	226
<i>Proofreading Activities of DNA Polymerases</i>	226
The Complex Replication Apparatus	227
<i>Continuous Synthesis of One Strand; Discontinuous Synthesis of the Other Strand</i>	228
<i>Covalent Closure of Nicks in DNA by DNA Ligase</i>	229
<i>Initiation of DNA Chains with RNA Primers</i>	229
<i>Unwinding DNA With Helicases, DNA-Binding Proteins, and Topoisomerases</i>	231
<i>The Replication Apparatus: Prepriming Proteins, Primosomes, and Replisomes</i>	235
<i>Rolling-Circle Replication</i>	236
Unique Aspects of Eukaryotic Chromosome Replication	237
<i>The Cell Cycle</i>	238
<i>Multiple Replicons per Chromosome</i>	238
<i>Two DNA Polymerases at a Single Replication Fork</i>	240
<i>Duplication of Nucleosomes at Replication Forks</i>	240
<i>Telomerase: Replication of Chromosome Termini</i>	241
<i>Telomere Length and Aging in Humans</i>	242
Technical Sidelight: Cesium Chloride Equilibrium Density-Gradient Centrifugation and Sucrose Velocity Density-Gradient Centrifugation: Two Important and Distinct Tools	216

CHAPTER 11 TRANSCRIPTION AND RNA PROCESSING 248

<i>Storage and Transmission of Information with Simple Codes</i>	248
The Genetic Control of Metabolism: An Overview	249
Transfer of Genetic Information: The Central Dogma	250
<i>Transcription and Translation</i>	250
<i>Four Types of RNA Molecules</i>	251
The Process of Gene Expression	254
<i>An mRNA Intermediary</i>	254
<i>General Features of RNA Synthesis</i>	256
Transcription in Prokaryotes	258
<i>RNA Polymerase: A Complex Enzyme</i>	258
<i>Initiation of RNA Chains</i>	259
<i>Elongation of RNA Chains</i>	260
<i>Termination of RNA Chains</i>	260
<i>Concurrent Transcription, Translation, and mRNA Degradation</i>	260

Transcription and RNA Processing in Eukaryotes 262

- Three RNA Polymerases/Three Sets of Genes* 263
- Initiation of RNA Chains* 263
- RNA Chain Elongation and the Addition of 5' Methyl Guanosine Caps* 264
- Termination by Chain Cleavage and the Addition of 3' Poly(A) Tails* 266
- RNA Editing: Altering the Information Content of mRNA Molecules* 266

Interrupted Genes in Eukaryotes: Exons and Introns 268

- Early Evidence for Noncoding Sequences in Eukaryotic Genes* 269
- Some Very Large Eukaryotic Genes* 272
- Introns: Biological Significance?* 273

Removal of Intron Sequences by RNA Splicing 273

- tRNA Precursor Splicing: Unique Nuclease and Ligase Activities* 274
- Autocatalytic Splicing* 275
- Pre-mRNA Splicing: snRNAs, snRNPs, and the Spliceosome* 276

Technical Sidelight: An mRNA Intermediary: Evidence from Phage-Infected *E. coli* 255

CHAPTER 12 TRANSLATION AND THE GENETIC CODE 281

Sickle-Cell Anemia: Devastating Effects of a Single Base-Pair Change 281

Protein Structure 282

- Polypeptides: Twenty Different Amino Acid Subunits* 282
- Proteins: Complex Three-Dimensional Structures* 284

Protein Synthesis: Translation 286

- Overview of Protein Synthesis* 286
- Components Required for Protein Synthesis: Ribosomes and Transfer RNAs* 287
- Translation: The Synthesis of Polypeptides Using mRNA Templates* 292

The Genetic Code 297

- Properties of the Genetic Code: An Overview* 297
- Three Nucleotides per Codon* 298
- Deciphering the Code* 300
- Initiation and Termination Codons* 303
- A Degenerate and Ordered Code* 304
- A Nearly Universal Code* 305

Codon-tRNA Interactions 305

- Recognition of Codons by tRNAs: The Wobble Hypothesis* 305
- Suppressor Mutations That Produce tRNAs with Altered Codon Recognition* 306

In Vivo Evidence Confirms the Nature of the Genetic Code 308

Technical Sidelight: Cracking the Genetic Code: Synthetic mRNAs 302

CHAPTER 13 MUTATION, DNA REPAIR, AND RECOMBINATION 311

Xeroderma Pigmentosum: Defective Repair of Damaged DNA in Humans 311

Mutation: Source of the Genetic Variability Required for Evolution 312

Mutation: Basic Features of the Process 313

- Mutation: Somatic or Germinal* 313
- Mutation: Spontaneous or Induced* 314
- Mutation: Usually a Random, Nonadaptive Process* 314

Mutation: A Reversible Process 315

Mutation: Phenotypic Effects 316

- Mutations with Phenotypic Effects: Usually Deleterious and Recessive* 316
- Effects of Mutations in Human Globin Genes* 318
- Mutation in Humans: Blocks in Metabolic Pathways* 318
- Conditional Lethal Mutations: Powerful Tools for Genetic Studies* 322

Muller's Demonstration That X Rays Are Mutagenic 323

The Molecular Basis of Mutation 325

- Mutations Induced by Chemicals* 326
- Mutations Induced by Radiation* 331
- Mutations Induced by Transposable Genetic Elements* 333
- Expanding Trinucleotide Repeats and Inherited Human Diseases* 334

Screening Chemicals for Mutagenicity: The Ames Test 334

DNA Repair Mechanisms 336

- Light-Dependent Repair* 336
- Excision Repair* 337
- Mismatch Repair* 338
- Postreplication Repair* 339
- The Error-Prone Repair System* 340

Inherited Human Diseases with Defects in DNA Repair 340

DNA Recombination Mechanisms 341

- Recombination: Cleavage and Rejoining of DNA Molecules* 341
- Gene Conversion: DNA Repair Synthesis Associated with Recombination* 343

Human Genetics Sidelight: Tay-Sachs Disease, A Childhood Tragedy 320

CHAPTER 14 DEFINITIONS OF THE GENE 319

Sir Archibald Garrod and Human Inborn Errors of Metabolism 349

Evolution of the Concept of the Gene: Summary 350

Evolution of the Concept of the Gene: Function 353

- Mendel: Constant Factors Controlling Phenotypic Traits* 353

<i>Garrod: One Mutant Gene—One Metabolic Block</i>	353
<i>Early Evidence That Enzymes Are Controlled by Genes</i>	354
<i>Beadle and Tatum: One Gene—One Enzyme</i>	356
<i>One Gene—One Polypeptide</i>	358
Evolution of the Concept of the Gene: Structure	358
<i>The Pre-1940 Beads-on-a-String Concept</i>	358
<i>Discovery of Recombination Within the Gene</i>	358
<i>Recombination Between Adjacent Nucleotide Pairs</i>	359
<i>Colinearity Between the Coding Sequence of a Gene and Its Polypeptide Product</i>	361
A Genetic Definition of the Gene	362
<i>The Complementation Test as an Operational Definition of the Gene</i>	363
<i>Intragenic Complementation</i>	367
<i>Limitations on the Use of the Complementation Test</i>	370
Complex Gene-Protein Relationships	371
<i>Alternate Pathways of Transcript Splicing: Protein Isoforms</i>	371
<i>Assembly of Genes During Development: Human Antibody Chains</i>	372
<i>Human Genetics Sidelight: Human Inborn Errors of Metabolism</i>	351

The Genetics of Viruses, Bacteria, Transposons, and Eukaryotic Organelles

A Conversation with Margaret Kidwell 378

CHAPTER 15 THE GENETICS OF VIRUSES 380

<i>A Killer Unleashed</i>	380
The Discovery of Bacterial Viruses	381
The Structure and Life Cycle of a Bacterial Virus	382
Mapping the Bacteriophage Genome	385
<i>Phage Phenotypes</i>	385
<i>Genetic Recombination in Phage</i>	386
<i>Genetic Fine Structure</i>	386
T4: A Circular Genetic Map But a Linear Chromosome	390
Genes Within Genes: Bacteriophage ϕ X174	392
Phage Heterozygosity: A Clue to the Mechanism of Recombination	393
HIV: A Eukaryote Virus	394
<i>What Is AIDS?</i>	395
<i>The Structure of HIV</i>	395
<i>The HIV Life Cycle</i>	395
<i>The HIV Genome</i>	396
<i>The Course of HIV Infection</i>	397

The Origin of Viruses	398
<i>Human Genetics Sidelight: Genomic Fossils</i>	397

CHAPTER 16 THE GENETICS OF BACTERIA 401

<i>Drug Resistance and Sex in Bacteria</i>	401
Genetic Exchange in Bacteria: An Overview	402
Mutant Phenotypes in Bacteria	403
Basic Test for Transformation, Conjugation, and Transduction	404
Transformation	405
<i>The Process of Transformation</i>	405
<i>Transformation and Gene Mapping</i>	405
Conjugation	408
<i>The Discovery of Conjugation</i>	408
<i>F⁺ \times F⁻ Mating</i>	408
<i>Hfr Conjugation</i>	410
<i>F' Conjugation or Sexduction</i>	411
<i>Conjugation and Gene Mapping</i>	411
<i>Mapping Closely Linked Genes</i>	412
<i>On the Origin of Plasmids</i>	414
Transduction	414
<i>The Discovery of Transduction</i>	415
<i>Generalized Transduction</i>	415
<i>Specialized Transduction</i>	416
<i>Transduction and Gene Mapping</i>	419
The Evolutionary Significance of Sexuality in Bacteria	420

CHAPTER 17 TRANSPOSABLE GENETIC ELEMENTS 423

<i>Maize: From Colored Kernels to Transposable Elements</i>	423
Transposable Elements in Bacteria	424
<i>IS Elements</i>	424
<i>Composite Transposons</i>	426
<i>Tn3 Elements</i>	427
<i>The Medical Significance of Bacterial Transposons</i>	428
Transposable Elements in Eukaryotes	429
<i>Ac and Ds Elements in Maize</i>	429
<i>P Elements and Hybrid Dysgenesis in Drosophila</i>	431
<i>mariner, an Ancient and Widespread Transposon</i>	435
Retrotransposons	436
<i>Retrovirus-like Elements</i>	436
<i>Retroposons</i>	437
The Genetic and Evolutionary Significance of Transposable Elements	438
<i>Transposons and Genome Organization</i>	438
<i>Transposons and Mutation</i>	439
<i>Evolutionary Issues concerning Transposable Elements</i>	439
<i>Historical Sidelight: Barbara McClintock, The Discoverer of Transposable Elements</i>	425

Technical Sidelight: Genetic Transformation of Drosophila with P Elements 434

CHAPTER 18 THE GENETICS OF MITOCHONDRIA AND CHLOROPLASTS 443

Mitochondria, Chloroplasts, and the Biological Energy Wheel 443

- The Classical Genetics of Organelles 444
 - Leaf Variegation in Plants 444
 - Cytoplasmic Male Sterility in Maize 446
 - Antibiotic Resistance in Chlamydomonas 447
 - Metabolic Defects in Yeast 448

- The Molecular Genetics of Mitochondria 450
 - Mitochondrial DNA 450
 - Expression of Mitochondrial Genes 452
 - Interplay Between Mitochondrial and Nuclear Gene Products 453

Mitochondrial DNA and Human Disease 453

- The Molecular Genetics of Chloroplasts 454
 - Chloroplast DNA 454
 - Chloroplast Biogenesis 454

The Origin and Evolution of Mitochondria and Chloroplasts 456

- Eukaryotic Organelles as Endosymbionts* 456
- The Evolution of Mitochondria and Chloroplasts* 457

Molecular Genetic Analysis

A Conversation with Nancy Wexler 460

CHAPTER 19 THE TECHNIQUES OF MOLECULAR GENETICS 462

Treatment of Pituitary Dwarfism with Human Growth Hormone 462

- Basic Techniques Used to Clone Genes 463
 - The Discovery of Restriction Endonucleases 463
 - The Production of Recombinant DNA Molecules In Vitro 467
 - Amplification of Recombinant DNA Molecules in Cloning Vectors 467

- Construction and Screening of DNA Libraries 471
 - Construction of Genomic Libraries 472
 - Construction of cDNA Libraries 474
 - Screening DNA Libraries for Genes of Interest 474
 - Biological and Physical Containment of Recombinant DNA Molecules 476

The Manipulation of Cloned DNA Sequences In Vitro 477

- Phagemids: The Biological Purification of DNA Single Strands* 477
- Transcription Vectors: The Synthesis of RNA Transcripts In Vitro* 480

Joining DNAs with Linker and Adapter Molecules 482

In Vitro Site-Specific Mutagenesis 483

The Molecular Analysis of DNA, RNA, and Protein 484

- Analysis of DNAs by Southern Blot Hybridizations* 484
- Analysis of RNAs by Northern Blot Hybridizations* 486
- Analysis of Proteins by Western Blot Techniques* 488

The Molecular Analysis of Genes and Chromosomes 489

- Amplification of DNA by the Polymerase Chain Reaction (PCR)* 490
- Physical Maps of DNA Molecules Based on Restriction Enzyme Cleavage Sites* 490
- Nucleotide Sequences: The Ultimate Fine Structure Maps* 493

Human Genetics Sidelight: Treatment of Diabetes Mellitus with Human Insulin Produced in Bacteria 464

Technical Sidelight: Detection of a Mutant Gene Causing Cystic Fibrosis by Southern Blot Analysis 487

CHAPTER 20 MOLECULAR ANALYSIS OF GENES AND GENE PRODUCTS 501

Detection of the Tay-Sachs Mutation in Eight-Cell Pre-Embryos 501

- Map Position-Based Cloning of Genes 502
 - Restriction Fragment-Length Polymorphism Maps 503
 - Chromosome Walks and Jumps 506
 - Physical Maps and Clone Banks 508

Use of Recombinant DNA Technology to Identify Human Genes 509

- Huntington's Disease* 510
- Cystic Fibrosis* 513
- Duchenne Muscular Dystrophy* 516

Molecular Diagnosis of Human Diseases 517

The Human Genome Project 518

Human Gene Therapy 519

DNA Fingerprints 522

Paternity Tests 523

Forensic Applications 525

Production of Eukaryotic Proteins in Bacteria 526

Human Growth Hormone 526

Proteins with Industrial Applications 527

Transgenic Plants and Animals 528

Transgenic Animals: Microinjection of DNA into Fertilized Eggs 528

Transgenic Plants: The Ti Plasmid of Agrobacterium tumefaciens 530

Herbicide-Resistant Plants 532

- Use of Antisense RNAs to Block Gene Expression* 533
Technical Sidelight: DNA Tests and the Mystery of the Duchess Anastasia 524

The Regulation of Gene Expression

A Conversation with Edward B. Lewis 538

CHAPTER 21 REGULATION OF GENE EXPRESSION IN PROKARYOTES 540

D'Hérelle's Dream of Treating Dysentery in Humans by Phage Therapy 540

Constitutive, Inducible, and Repressible Gene Expression 543

Operons: Coordinately Regulated Units of Gene Expression 545

The Lactose Operon in *E. coli*: Induction and Catabolite Repression 547

Induction 548

Catabolite Repression 550

The Tryptophan Operon in *E. coli*: Repression and Attenuation 551

Repression 551

Attenuation 551

The Arabinose Operon in *E. coli*: Positive and Negative Controls 555

Bacteriophage Lambda: Lysogeny or Lysis 558

Repression of Lambda Lytic Pathway Genes During Lysogeny 559

The Lambda Lytic Regulatory Cascade 559

The Lambda Switch: Lytic Development or Lysogeny 562

Temporal Sequences of Gene Expression During Phage Infection 564

Translational Control of Gene Expression 566

Post-Translational Regulatory Mechanisms 567

Technical Sidelight: Proviruses as Vectors for Human Gene Therapy 542

CHAPTER 22 GENE REGULATION IN EUKARYOTES AND THE GENETIC BASIS OF CANCER 572

Cancer: Evidence for the Importance of Regulated Gene Expression 572

Spatial and Temporal Regulation of Eukaryotic Genes 573

Spatial Regulation of Tubulin Genes in Plants 573

Temporary Regulation of Globin Genes in Animals 574

Ways of Regulating Eukaryotic Gene Expression 574

Controlled Transcription of DNA 575

Alternate Splicing of RNA 575

Cytoplasmic Control of Messenger RNA Stability 576

Induction of Transcriptional Activity by Environmental and Biological Factors 577

Temperature: The Heat-Shock Genes 577

Light: The Ribulose 1,5-bisphosphate Carboxylase Genes in Plants 578

Signal Molecules: Genes That Respond to Hormones 579

Molecular Control of Transcription in Eukaryotes 581

DNA Sequences Involved in the Control of

Transcription: Enhancers and Silencers 581

Proteins Involved in the Control of Transcription: Transcription Factors 583

Gene Expression and Chromosome Organization 586

Transcription in Lampbrush Chromosome Loops 586

Transcription in Polytene Chromosome Puffs 587

The Molecular Organization of Transcriptionally Active DNA 588

Euchromatin and Heterochromatin 588

Gene Amplification 589

Activation and Inactivation of Whole Chromosomes 591

Inactivation of X Chromosomes in Mammals 591

Hyperactivation of X Chromosomes in Drosophila 592

Hypoactivation of X Chromosomes in Caenorhabditis 592

Gene Expression and Cancer 592

Tumor-inducing Retroviruses and Viral Oncogenes 593

Cellular Homologs of Viral Oncogenes: the Proto-oncogenes 595

Genetic Basis of Human Cancers 597

Mutant Cellular Oncogenes and Cancer 597

Chromosome Rearrangements and Cancer 599

Tumor-Suppressor Genes and Cancer 599

Is Cancer an Inherited Disease? 600

Technical Sidelight: GAL24, a Transcription Factor That Regulates the Genes Involved in Galactose Metabolism in Yeast 584

Human Genetics Sidelight: BRCA1, a Gene That Predisposes Women to Develop Breast Cancer 601

CHAPTER 23 THE GENETIC CONTROL OF ANIMAL DEVELOPMENT 605

Insect Wings: Evidence for the Genetic Control of Development 605

The Process of Development in Animals 606

Oogenesis and Fertilization 606

The Embryonic Cleavage Divisions and Blastula Formation 608

Gastrulation and Morphogenesis 608

Genetic Analysis of Development in Model Organisms 608