

遗传学

从基因到基因组

GENETICS

From Genes to Genomes

LELAND H. HARTWELL

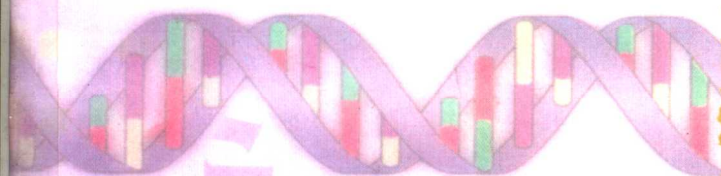
LEROY HOOD

MICHAEL L. GOLDBERG

ANN E. REYNOLDS

LEE M. SILVER

RUTH C. VERES



科学出版社

www.sciencep.com

影

印

版

科学版研究生教学丛书

遗传学

从基因到基因组

(影印版)

GENETICS

From Genes to Genomes

LELAND H. HARTWELL

Fred Hutchinson Cancer Research Center

LEROY HOOD

University of Washington

MICHAEL L. GOLDBERG

Cornell University

ANN E. REYNOLDS

University of Washington

LEE M. SILVER

Princeton University

RUTH C. VERES

科学出版社

北京

内 容 简 介

20 世纪大家见证了生物学核心领域遗传学的兴起。鉴定单个基因及其功能后, 遗传学研究者逐渐意识到, 没有基因是单独作用的, 各种生命事件是经由基因和蛋白质网络复杂分子的相互作用。

本书(见 www.mhhe.com/hartwell)试图集成当代遗传学知识和方法, 内容主要包括经典遗传学——基因传递规律; 分子遗传学——DNA 结构及其如何指导蛋白质合成; 基因组学——基因分离新技术和有机体完整基因组深入分析; 人类遗传学——基因如何调控健康和疾病状态; 生命形式的统一——来自不同有机体的信息合成为一个整体内核; 分子进化——物种如何进化和趋异。

本书适用于高等院校生命科学、医药卫生、农林渔牧等专业师生使用, 并可供相关专业研究人员阅读参考。

Leland H. Hartwell, Leroy Hood, Michael L. Goldberg, Ann E. Reynolds, Lee M. Silver, Ruth C. Veres.

Genetics: From Genes to Genomes

Copyright© 2000 by the McGraw-Hill Companies, Inc.

Authorized Reprinting by Science Press in China.

All rights reserved. For sale in the People's Republic of China only.

IE ISBN: 0-07-540923-2

本书英文影印版由科学出版社和美国麦格劳-希尔国际公司合作出版。未经出版者书面许可, 不得以任何方式复制或抄袭本书的任何部分。

版权所有, 翻印必究。

本书封面贴有 McGraw-Hill 公司防伪标签, 无标签者不得销售。

图书在版编目 (CIP) 数据

遗传学: 从基因到基因组 / (美) 哈特韦尔 (Hartwell, L. H.) 等著. —影印本. —北京: 科学出版社, 2003.4

(科学版研究生教学丛书)

书名原文: Genetics: From Genes to Genomes

ISBN 7-03-011098-6

I. 遗… II. 哈… III. 遗传学-教材-英文 IV. Q3

中国版本图书馆 CIP 数据核字 (2003) 第 022058 号

责任编辑: 谢灵玲 马学海 盖 宇
责任印制: 安春生/封面设计: 北新华文

科学出版社 出版

北京东黄城根北街16号

邮政编码: 100717

<http://www.sciencep.com>

双青印刷厂 印刷

科学出版社发行 各地新华书店经销

*

2003 年 4 月第 一 版 开本: 890×1240 1/16

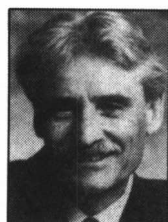
2003 年 4 月第一次印刷 印张: 55 3/4

印数: 1—3 000 字数: 1 866 000

定价: 78.00 元

(如有印装质量问题, 我社负责调换〈环伟〉)

ABOUT THE AUTHORS



Dr. Leland Hartwell received his Ph.D. from the Massachusetts Institute of Technology. Dr. Hartwell held assistant and associate professorships at the University of California before joining the faculty of the University of Washington, where he continues as a full professor. In 1996, Dr. Hartwell joined the Fred Hutchinson Cancer Research Center as a full member and senior advisor for scientific affairs, and was named president and director of the Center in July 1997.

Combining mutants and time-lapse photomicroscopy, Dr. Hartwell identified 32 genes in yeast that regulate the cell cycle with specific defects in spindle pole body duplication and segregation, DNA replication, mitosis, cytokinesis, and budding. He discovered a control point in the cell cycle, Start, where yeast cells exit the cell cycle to mate, arrest after nutritional starvation, and integrate growth with division. He used genetics to define many of the steps in the signal transduction pathway that feed into Start, including the cell-surface receptor for mating pheromone. The gene controlling Start, *CDC28*, was cloned in his lab and was the first CDK identified. He investigated the fidelity of chromosome transmission in the cell cycle, discovering that limitation or overexpression of many essential cell-cycle components lead to errors in chromosome transmission. Studies on how cells integrate the repair of DNA damage and cell division led to the discovery of cell-cycle checkpoints and the identification of six genes that control the DNA damage checkpoint.

Dr. Hartwell has received numerous awards and honors in the course of his career. Among them he received the Brandeis University Rosenteil Award in 1993 and the Sloan-Kettering Cancer Center Katherine Berkan Judd Award as well as the Genetics Society of America Medal in 1994. In 1995 he was awarded the MGH Warren Triennial Prize, and in 1996 he was awarded the Columbia University Horwitz Award and the Passano Award. Dr. Hartwell received the Albert Lasker Award for medical research in 1998.



Dr. Lee Hood received an M.D. from the Johns Hopkins Medical School and a Ph.D. in biochemistry from the California Institute of Technology. His research interests include immunology, development, and the development of biological instrumentation (e.g., the protein sequencer and the automated fluorescent DNA sequencer). His research played a key role in unraveling the mysteries of antibody diversity. Dr. Hood has taught molecular evolution, immunology, molecular biology, and biochemistry. He is currently the chairman (and founder) of

the cross-disciplinary Department of Molecular Biotechnology at the University of Washington. Dr. Hood has received a variety of awards including the Albert Lasker Award for Medical Research and the Dickson Prize in 1987, the Cefas Award for Biochemistry in 1989, and the Distinguished Service Award from the National Association of Teachers in 1998. He is deeply involved in K-12 science education. His hobbies include running, mountain climbing, and reading.



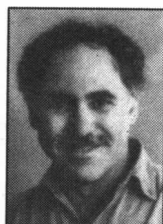
Dr. Michael L. Goldberg is a professor at Cornell University, where he teaches introductory genetics. He was an undergraduate at Yale University and received his Ph.D. in biochemistry from Stanford University. Dr. Goldberg performed postdoctoral research at the Biozentrum of the University of Basel in Switzerland and at Harvard University. He received an NIH

Fogarty Senior International Fellowship for study at Imperial College in England and at the University of Rome, Italy. His current research utilizes the tools of *Drosophila* genetics to investigate the mechanisms that ensure proper chromosome segregation during mitosis and meiosis.



Dr. Ann Reynolds is an educator and author who has been teaching genetics and biology since 1990. An affiliate faculty member of the Genetics Department at the University of Washington, her research has included studies of gene regulation in *E. coli*, chromosome structure and DNA replication in yeast, and chloroplast gene expression in marine algae.

She is a graduate of Mount Holyoke College and received her Ph.D. from Tufts University. Dr. Reynolds was a postdoctoral research fellow with the Harvard University Department of Molecular Biology. Dr. Reynolds was also an author and producer of the laser disc and CD ROM *Genetics: Fundamentals to Frontiers*.



Dr. Lee M. Silver is a professor at Princeton University in the Departments of Molecular Biology, Ecology, and Evolutionary Biology and in the Program in Neuroscience. Dr. Silver graduated from the University of Pennsylvania with B.A. and M.S. degrees in physics and from Harvard University with a Ph.D. in biophysics. He was a research fellow at the Sloan-Kettering Institute for Cancer Research and a senior scientist at Cold Spring Harbor Laboratory before coming to Princeton. He is the author of

Remaking Eden: Cloning and Beyond in a Brave New World. He is also the coeditor in chief of a new international journal entitled *Cloning: Science and Policy*, and coeditor in chief of *Mammalian Genome*, the official journal of the International Mammalian Genome Society. In 1993 Dr. Silver was elected a fellow of the American Association for the Advancement of Science (AAAS).

Dr. Silver's own research has made intensive use of the mouse as a model organism to study the genetics of reproduction, development, and evolution. His current research focuses on the genetic components of behavior. At Princeton, he has taught courses in genetics, mammalian genetics, biotechnology and society, and developmental biology in the Department of Molecular Biology and human genetics, reproduction, and public policy in Princeton's Woodrow Wilson School of Public and International Affairs.



Ruth C. Veres is a science writer and editor with 25 years of experience in textbook publishing. She obtained her B.A. from Swarthmore College and M.A. degrees from Columbia University in New York and Tufts University. In addition to developing and editing more than 30 texts in the fields of political science, economics, psychology, nutrition, chemistry, and biology, she has coauthored a book on the immune system and an introductory biology text. She has also taught writing and languages at the University of California at Berkeley. She lives in San Francisco with her husband.

CONTRIBUTORS

Genetics research tends to proceed down highly specialized paths. A number of experts in specific areas generously provided information in their areas of expertise. We thank them for their contributions to this text.

Eric E. Alani, *Cornell University*
 Charles F. Aquadro, *Cornell University*
 Anthony B. Bleecker, *University of Wisconsin*
 Deborah Brosnan, *University of Oregon*
 Ronald A. Butow, *University of Texas, Southwestern Medical Center, Dallas*
 Rita A. Calvo, *Cornell University*
 Michael Culbertson, *University of Wisconsin*
 Ian Duncan, *Washington University, St. Louis*
 Sarah Elgin, *Washington University, St. Louis*
 Thomas D. Fox, *Cornell University*
 Leonard P. Guarente, *Massachusetts Institute of Technology*
 Kenneth J. Kemphues, *Cornell University*
 Joel G. Kingsolver, *University of Washington*

John T. Lis, *Cornell University*
 Ross J. MacIntyre, *Cornell University*
 Patrick H. Masson, *University of Wisconsin*
 Jeffry B. Mitton, *University of Colorado*
 Martha A. Mutschelr, *Cornell University*
 June B. Nasrallah, *Cornell University*
 Debra Nero, *Cornell University*
 Richard D. Palmiter, *University of Washington*
 Philip S. Perleman, *University of Texas, Southwestern Medical Center, Dallas*
 Fabio Piano, *Cornell University*
 Harry T. Stinson, Jr., *Cornell University*
 William T. Sullivan, *University of California, Santa Cruz*
 Volker M. Vogt, *Cornell University*
 Douglas Wallace, *Emory University*
 Jonathan Widom, *Northwestern University*
 Mariana F. Woolfner, *Cornell University*
 William B. Wood, *University of Colorado*
 Andrew Wright, *Tufts University*
 Stanley A. Zahler, *Cornell University*

2AG92/01

PREFACE

The twentieth century witnessed the emergence of genetics as a central discipline in biology. In 1900 Gregor Mendel's laws of heredity were rediscovered; in the 1950s, James Watson and Francis Crick found that DNA, the molecule of heredity, is a double helix; and in the 1990s, the Human Genome Project progressed beyond expectations. For much of the century, the study of genetics focused on the identification of individual genes and their function. In the last decade of the century, however, another idea gained currency—the concept that no gene acts alone, instead it is through complex molecular interactions within and among vast networks of genes and proteins that organisms ultimately live and die.

Genetics: From Genes to Genomes reflects this new perspective. This book represents a new approach to an undergraduate course in genetics. It represents the way we, the authors, currently view the molecular basis of life. We integrate formal genetics—the rules by which genes are transmitted; molecular genetics—the structure of DNA and how it directs the structure of proteins; genomics and information science—the new technologies that enable gene isolation and a comprehensive analysis of the entire gene set in an organism; human genetics—how genes control health and disease; the unity of life forms—synthesis of information from many different organisms into one coherent whole; and molecular evolution—how species have evolved and diverged. The strength of this integrated approach is that students who have completed the text will have a strong command of genetics as it is practiced today by university and corporate researchers who are rapidly changing our understanding of living organisms, including ourselves; increasing our ability to prevent, treat, and diagnose disease and to engineer new life forms for food and medical uses; and, ultimately, creating the ability to replace or correct detrimental genes.

To encourage a genetic way of thinking, we begin the book with a presentation of Mendelian principles and the chromosomal basis of inheritance. From the outset, however, the integration of Mendelian genetics with fundamental molecular mechanisms is central to our approach. The Prologue presents the foundation of this integration. In Chapter 1, we tie Mendel's studies of pea-shape inheritance to the action of an enzyme that determines whether a pea is round or wrinkled. In the same chapter, we point to the relatedness of patterns of heredity in all organisms by using Mendelian principles to look at heredity in humans. Starting in Chapter 5, we focus on the physical dimensions of DNA; the implications and uses of mutations; and how the double helix of DNA encodes, copies, and transmits biological information. Beginning in Chapter 8 we also look at modern genetic techniques, including such biotechnology tools as gene cloning, hybridization, and PCR, exploring how researchers have used them to reveal the modular construction and genetic relatedness of genomes. We

then show how the modular construction of genomes has contributed to the relatively rapid evolution of life and helped generate the enormous diversity of life forms we see around us. A detailed discussion of model organisms clarifies that their use in the study of human biology is possible only because of the genetic relatedness of all organisms. Throughout our text, we present the scientific reasoning of some of the ingenious researchers who have carried out genetic analysis, from Mendel to Watson and Crick to the collaborators on the Human Genome Project.

ORGANIZATION

The Prologue outlines the central themes of *Genetics: From Genes to Genomes*. We hope students will read this section carefully because it establishes the foundation for our integrated presentation of Mendelian and molecular genetics.

Part I (Chapters 1, 2, 3, and 4) on the *Basic Principles: How Traits Are Transmitted* presents a thorough discussion of Mendelian genetics; the chromosome theory of inheritance; and linkage, recombination, and mapping.

Part II (Chapters 5, 6, and 7) covers *What Genes Are and What They Do*, including the structure and function of DNA, the role of mutation in defining genes, and the details of gene expression.

Part III (Chapters 8, 9, and 10) describes the *Use of Genetic Engineering to Unravel the Information in Genomes* and includes topics on mapping and analysis of genomes, detection of genotype, and the use of cloning, PCR, and hybridization in genetic analysis.

Part IV (Chapters 11, 12, 13, and 14) on *How Genes Travel* presents the molecular mechanisms underlying the chromosomal transmission of genetic information in eukaryotes and prokaryotes.

Part V (Chapters 15, 16, and 17) on *How Genes Are Regulated* discusses prokaryotic and eukaryotic gene regulation as well as the regulation of the cell cycle.

Part VI (Chapters 18–22) presents *Gene Regulation and Development: Portraits of Model Eukaryotic Organisms*. This **Genetic Portraits** unit contains five chapters, each one profiling a different model organism whose study has greatly contributed to genetic research. Included are

Saccharomyces cerevisiae: Genetic Portrait of Yeast
Arabidopsis thaliana: Genetic Portrait of a Model Plant
Caenorhabditis elegans: Genetic Portrait of a Simple Metazoan
Drosophila melanogaster: Genetic Portrait of a Fruit Fly
Mus musculus: Genetic Portrait of a House Mouse.

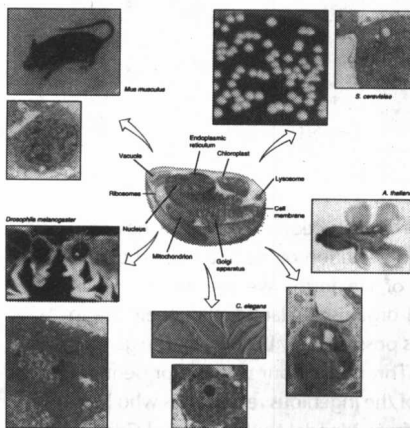


Figure 1.6. Eukaryotic cells have many features to examine. The similarity of cellular structure in our model organisms is visible in the micrograph accompanying the photo of each of the entire organisms above. As discussed in Chapter 11, each cell contains a variety of complex membrane organelles in the cytoplasmic matrix and has the majority of their genetic material contained within membrane-enclosed nuclei. Review Chapter 1.6 for the details of gene regulation in eukaryotes. Each model has characteristic variations, but the basic cellular plan is the same.

We anticipate that instructors will choose to cover one or two portrait chapters during the semester. Students may then use the specifics of the selected model organism to build an understanding of the principles and applications discussed in the text. The unique genetic manipulations and properties of each model make them important for addressing different biological questions using

genetic analysis. In the portraits, we explain how biologists learned that the evolutionary relatedness of all organisms enables the extrapolation from a model to the analysis of other living forms. The portraits should thus help students understand how insights from one model organism can suggest general principles applicable to other organisms, including humans.

Part VII (Chapters 23 and 24) on **How Genes Change** explains the evolution of genes and genomes in populations and at the molecular level.

The **Epilogue** discusses **Human Genetics and the Future of Biology**. The focus of this closing essay is on the changing role of genetics research as a way to decipher biological networks and systems. Biology is now a science based on three levels of molecular information: information encoded in DNA, and information in proteins, and information encompassed in interactions among cells and tissues. The potential impact on the field of preventive medicine intensifies the need to confront many social and ethical issues.

CHAPTER FEATURES

Introduction Each chapter begins with an engaging story related to the key ideas and principles of the chapter. This opening story is followed by a description of one or more overarching themes that unify the discussion, and then, in turn, by an advance organizer—a short, bulleted list of the chapter's topics in the order in which they appear in the text. The intent of the introduction is to create a narrative and conceptual framework that will help students organize and remember the vast amount of vocabulary and experimental data they encounter.

Feature Figures These special two-page spreads integrate line art and text to summarize important genetic processes in detail. For example, in Chapter 5 on *DNA: How the Molecule of Heredity Carries, Replicates, and Recombines Information*, the Feature Figure details a “Model of Recombination at the Molecular Level,” walking students through the basic steps of the process. In Chapter 17,

Cell-Cycle Regulation and the Genetics of Cancer, the Feature Figure details “Phenotypic Changes That Distinguish Tumor Cells from Normal Cells” outlines changes that produce uncontrolled cell growth, genomic and karyotypic instability, a potential for cellular immortality, and disruptions of local tissues that enable a tumor to invade distant tissues.

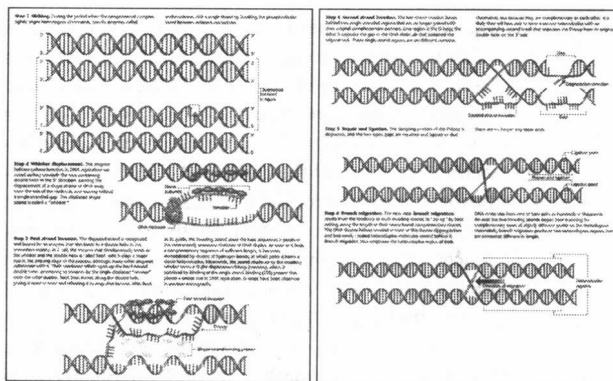
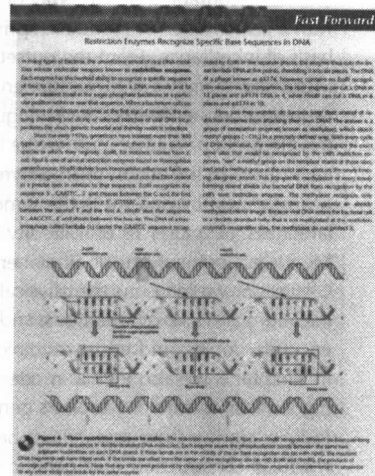


Figure 1.1. A model of recombination at the molecular level.

Comprehensive Examples These sections of the text are extensive case histories or research synopses that summarize the main points in the preceding section or chapter and show how they relate to each other. Very often these developed examples expand on the chapter's introductory story. In Chapter 6, *Anatomy and Function of a Gene: Dissection through Mutation*, for example, the opening story locates the rhodopsin gene on human chromosome 3 and explains that different mutations in the gene lead to night blindness or total blindness. The Comprehensive Example at the end of the chapter describes in detail “How Gene Mutations Affect Light-Receiving Proteins and Vision,” covering such topics as the cellular and molecular basis of vision; the evolution of the rhodopsin gene family; and many of the mutations, amino-acid substitutions, and unequal crossing over events that affect both black and white and color vision.

Fast Forward Essays

This feature prefigures detailed discussions of concepts and principles in later chapters, serving as a tool to integrate Mendelian and molecular genetics. Chapter 1, *Mendel's Breakthrough: Patterns, Particles, and Principles of Heredity*, contains two Fast Forward essays, one on the fact that “Genes Encode Proteins,” the other on techniques for “The Direct Analysis of Human Genotype.” These essays help students understand that Mendel's laws



Ken Belanger, *University of North Carolina, Chapel Hill*
 John Belote, *Syracuse University*
 Anna Berkovitz, *Purdue University*
 John Botsford, *New Mexico State University*
 Michael Breindl, *San Diego State University*
 Bruce Chase, *University of Nebraska, Omaha*
 Lee Chatfield, *University of Central Lancashire*
 Alan Christensen, *University of Nebraska*
 Bruce Cochrane, *University of South Florida*
 James Curran, *Wake Forest University*
 Rowland Davis, *University of California, Irvine*
 Paul Demchick, *Barton College*
 Stephen D'Surney, *University of Mississippi*
 Rick Duhrkopf, *Baylor University*
 Susan Dutcher, *University of Colorado*
 DuWayne Englert, *Southern Illinois University*
 Bentley Fane, *University of Arkansas*
 Victoria Finnerty, *Emory University*
 David Foltz, *Louisiana State University*
 David Futch, *San Diego State University*
 Ann Gerber, *University of North Dakota*
 Richard Gethmann, *University of Maryland, Baltimore County*
 Mike Goldman, *San Francisco State University*
 Elliott Goldstein, *Arizona State University*
 Nels Granholm, *South Dakota State University*
 Charles Green, *Rowan College of New Jersey*
 Poonam Gulati, *University of Houston*
 Stephen Hedman, *University of Minnesota*
 Ralph Hillman, *Temple University*
 Christine Holler-Dinsmore, *Fort Peck Community College*
 Martin Hollingsworth, *Tallahassee Community College*
 Nancy Hollingsworth, *State University of New York, Stony Brook*
 Andrew Hoyt, *Johns Hopkins University*
 Lynne Hunter, *University of Pittsburgh*
 Robert Ivarie, *University of Georgia*
 R. C. Jackson, *Texas Technological University*
 Duane Johnson, *Colorado State University*
 Chris Kaiser, *Massachusetts Institute of Technology*
 Kenneth J. Kempfues, *Cornell University*
 Susan Kracher, *Purdue University*
 Alan Koetz, *Illinois State University*
 Andrew Lambertsson, *University of Oslo*
 Don Lee, *University of Nebraska*
 John Locke, *University of Alberta*
 Larry Loeb, *University of Washington*
 Robertson McClung, *Dartmouth College*
 Peter Meacock, *University of Leicester*
 John Merriam, *University of California, Los Angeles*
 Beth Montelone, *Kansas State University*
 Patricia Moore, *Transylvania University*
 Gail Patt, *Boston University*
 Michael Perlin, *University of Louisville*
 Richard Richardson, *University of Texas, Austin*
 Mary Rykowski, *University of Arizona*
 Mark Sanders, *University of California, Davis*
 Randall Scholl, *Ohio State University*

David Sheppard, *University of Delaware*
 Anthea Stavroulakis, *Kingsborough Community College*
 John Sternick, *Mansfield University*
 David Sullivan, *Syracuse University*
 William Thwaites, *San Diego State University*
 Akfi Uzman, *University of Houston*
 Peter Webster, *University of Massachusetts*
 Dean Whited, *North Dakota State University*
 John Williamson, *Davidson College*
 John Zamora, *Middle Tennessee State University*
 Stephan Zweifel, *Carleton College*

Over the years a number of highly skilled publishing professionals helped us develop this book. We'd like to express our appreciation to Eirik Borge for his vision in launching the project, Laurel Smith for her refined and intelligent approach to art development, Marjorie Anderson for her editorial acumen, Kathi Prancan for her able and enthusiastic management (and dining-out extravaganzas), Kathy Naylor for her unusual combination of skills in art and text development; Jean Fornango for her top-notch, no-nonsense organizational skills in readying the manuscript for production; Richard Morel for his insightful preparation of the art manuscript; Ron Worthington for his scientific understanding and firm backing in a time of transition; and Jim Smith for his strong support throughout the final years of development and production. All have made a significant contribution to the final shape of this project.

SUPPLEMENTS

For the Student

- The **Solutions Manual/ Study Guide** was written by text author Ann Reynolds, of the University of Washington. The solutions to the end-of-chapter problems and questions will aid the students in developing their problem-solving skills by providing the step-by-step logic of each solution.
- **Genetics: From Genes to Genomes CD ROM**, developed with the content of the text, covers the most challenging concepts in the introductory genetics course. The CD attempts to make concepts more understandable by using animations of basic genetic processes and interactive exercises and simulations involving fundamental principles. Icons in the text indicate that there are related topics on the CD. A correlation guide linking text topics marked by icons to the related CD material is included in the *Instructor's Manual*, on our web site, and on the CD ROM itself. Additional quizzing options allow students to self-test and identify those areas needing additional study. Glossary definitions can be reached via hot links. The CD also has links that connect to the book's own web site.

For the Instructor

- The **Instructor's Manual/ Test Bank** contains the CD ROM correlation guide, a list of transparencies, plus a test

bank containing approximately 2000 questions. The test bank is also available in computerized form compatible with either Windows or Macintosh machines.

- **Transparencies:** One hundred and fifty four-color illustrations from the text will be available to adopters.
- **Visual Resource Library:** A CD ROM product containing 200 key illustrations will be available in four-color digital files. The presentation software enables you to create custom slide shows and multimedia presentations. Images

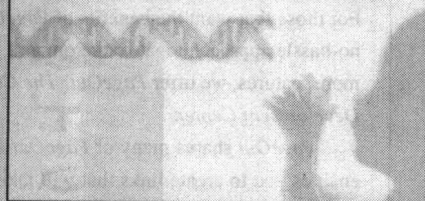
can also be exported for use in word-processing programs. Additional features enable the images to be sorted by name, type, locations, and user-defined keywords. Multiple images can be viewed at one time by using the Small Gallery View function. Jpeg files for all remaining line art is included, plus lecture outlines.

- **Web Site:** This text-specific web site can be reached at the URL www.mhhe.com/hartwell and provides additional materials for both students and instructors.

GENETICS

From Genes to Genomes

LELAND H. HARTWELL
LEROY HOOD
MICHAEL L. GOLDBERG
ANN E. REYNOLDS
LEE M. SILVER
RUTH C. VERES



MCGRAW-HILL IS PROUD TO OFFER AN EXCITING NEW SUITE OF MULTIMEDIA PRODUCTS AND SERVICES CALLED COURSE SOLUTIONS.

Designed specifically to help you with your individual course needs, **Course Solutions** will assist you in integrating your syllabus with our premier titles and state-of-the-art new media tools that support them.

AT THE HEART OF COURSE SOLUTIONS YOU'LL FIND:

- Fully integrated multimedia
- A full-scale Online Learning Center
- A Course Integration Guide

AS WELL AS THESE UNPARALLELED SERVICES:

- McGraw-Hill Learning Architecture
- McGraw-Hill Course Consultant Service
- Visual Resource Library (VRL) Image Licensing
- McGraw-Hill Student Tutorial Service
- McGraw-Hill Instructor Syllabus Service
- PageOut Lite
- PageOut: The Course Web Site Development Center
- Other Delivery Options

COURSE SOLUTIONS truly has the solutions to your every teaching need. Read on to learn how we can specifically help you with your classroom challenges.

SPECIAL ATTENTION

to your specific needs.

These "perks" are all part of the extra service delivered through McGraw-Hill's **Course Solutions**:

MCGRAW-HILL LEARNING ARCHITECTURE

Each McGraw-Hill *Online Learning Center* is ready to be ported into our *McGraw-Hill Learning Architecture*—a full course management software system for Local Area Networks and Distance Learning Classes. Developed in conjunction with Top Class software, *McGraw-Hill Learning Architecture* is a powerful course management system available upon special request.

MCGRAW-HILL COURSE CONSULTANT SERVICE

In addition to the *Course Integration Guide*, instructors using **Course Solutions** textbooks can access a special curriculum-based *Course Consultant Service* via a web-based threaded discussion list within each *Online Learning Center*. A **McGraw-Hill Course Solutions Consultant** will personally help you—as a text adopter—integrate this text and media into your course to fit your specific needs. This content-based service is offered in addition to our usual software support services.

VISUAL RESOURCE LIBRARY (VRL) IMAGE LICENSING

Most of our **Course Solutions** titles are accompanied by a *Visual Resource Library (VRL) CD-ROM*, which features text figures in electronic format. Previously, use of these images was restricted to in-class presentation only. Now, McGraw-Hill will license adopters the right to use appropriate VRL image files—**FREE OF CHARGE**—for placement on their local Web site! Some restrictions apply. Consult your McGraw-Hill sales representative for more details.

MCGRAW-HILL INSTRUCTOR SYLLABUS SERVICE

For new adopters of **Course Solutions** textbooks, McGraw-Hill will help correlate all text, supplement, and appropriate materials and services to your course syllabus. Simply call your McGraw-Hill sales representative for assistance.

PAGEOUT LITE

Free to **Course Solutions** textbook adopters, *PageOut Lite* is perfect for instructors who want to create their own Web site. In just a few minutes, even novices can turn their syllabus into a Web site using *PageOut Lite*.

PAGEOUT: THE COURSE WEB SITE DEVELOPMENT CENTER

For those that want the benefits of *PageOut Lite*'s no-hassle approach to site development, but with even more features, we offer *PageOut: The Course Web Site Development Center*.

PageOut shares many of *PageOut Lite*'s features, but also enables you to create links that will take your students to your original material, other Web site addresses, and to *McGraw-Hill Online Learning Center* content. This means you can assign *Online Learning Center* content within your syllabus-based Web site. *PageOut*'s gradebook function will tell you when each student has taken a quiz or worked through an exercise, automatically recording their scores for you. *PageOut* also features a discussion board list where you and your students can exchange questions and post announcements, as well as an area for students to build personal Web pages.

OTHER DELIVERY OPTIONS

Online Learning Centers are also compatible with a number of full-service online course delivery systems or outside educational service providers. For a current list of compatible delivery systems, contact your McGraw-Hill sales representative.

And for your students...

MCGRAW-HILL STUDENT TUTORIAL SERVICE

Within each *Online Learning Center* resides a **FREE Student Tutorial Service**. This web-based "homework hotline"—available via a threaded discussion list—features guaranteed, 24-hour response time on weekdays.

www.mhhe.com/hartwell

BRIEF CONTENTS

ABOUT THE AUTHOR VI

PREFACE XIX

PROLOGUE 1

PART I

BASIC PRINCIPLES: HOW TRAITS ARE TRANSMITTED 8

CHAPTER 1

MENDEL'S BREAKTHROUGH: PATTERNS,
PARTICLES, AND PRINCIPLES OF
HEREDITY 10

CHAPTER 2

EXTENSIONS TO MENDEL: COMPLEXITIES IN
RELATING GENOTYPE TO PHENOTYPE 38

CHAPTER 3

THE CHROMOSOME THEORY OF
INHERITANCE 70

CHAPTER 4

LINKAGE, RECOMBINATION, AND THE
MAPPING OF GENES ON
CHROMOSOMES 105

PART II

WHAT GENES ARE AND WHAT THEY DO 142

CHAPTER 5

DNA: HOW THE MOLECULE OF HEREDITY
CARRIES, REPLICATES, AND
RECOMBINES 144

CHAPTER 6

ANATOMY AND FUNCTION OF A GENE:
DISSECTION THROUGH MUTATION 179

CHAPTER 7

GENE EXPRESSION: THE FLOW OF GENETIC
INFORMATION FROM DNA VIA RNA TO
PROTEIN 222

PART III

USING GENETIC ENGINEERING TO UNRAVEL THE INFORMATION IN GENOMES 260

CHAPTER 8

DNA AT HIGH RESOLUTION: USE OF DNA
CLONING, PCR, AND HYBRIDIZATION AS THE
TOOLS OF GENETIC ANALYSIS 262

CHAPTER 9

THE DIRECT DETECTION OF
GENOTYPE 308

CHAPTER 10

THE MAPPING AND ANALYSIS OF
GENOMES 341

PART IV

HOW GENES TRAVEL 388

CHAPTER 11

THE EUKARYOTIC CHROMOSOME: AN
ORGANELLE FOR PACKAGING AND
MANAGING DNA 390

CHAPTER 12

CHROMOSOMAL REARRANGEMENTS AND
CHANGES IN CHROMOSOME NUMBER
RESHAPE EUKARYOTIC GENOMES 419

CHAPTER 13

THE PROKARYOTIC CHROMOSOME: GENETIC
ANALYSIS IN BACTERIA 461

CHAPTER 14

THE CHROMOSOMES OF ORGANELLES
OUTSIDE THE NUCLEUS EXHIBITS NON-
MENDELIAN PATTERNS OF
INHERITANCE 501

PART V**How Genes Are Regulated 528****CHAPTER 15**

GENE REGULATION IN PROKARYOTES 530

CHAPTER 16

GENE REGULATION IN EUKARYOTES 558

CHAPTER 17CELL-CYCLE REGULATION AND THE
GENETICS OF CANCER 590**PART VI****GENE REGULATION
AND DEVELOPMENT:
PORTRAITS OF MODEL
EUKARYOTIC ORGANISMS 624****USING GENETICS TO STUDY
DEVELOPMENT**AN INTRODUCTION TO THE GENETIC
PORTRAITS 626**CHAPTER 18**SACCHAROMYCES CEREVISIAE: A GENETIC
PORTRAIT OF YEAST 638**CHAPTER 19**ARABIDOPSIS THALIANA: GENETIC PORTRAIT
OF A MODEL PLANT 655**CHAPTER 20**CAENORHABDITIS ELEGANS: GENETIC
PORTRAIT OF A SIMPLE MULTICELLULAR
ANIMAL 681**CHAPTER 21**DROSOPHILA MELANOGASTER: GENETIC
PORTRAIT OF THE FRUIT FLY 702**CHAPTER 22**MUS MUSCULUS: A GENETIC PORTRAIT OF
THE HOUSE MOUSE 731**PART VII****How Genes Change 752****CHAPTER 23**THE GENETIC ANALYSIS OF POPULATIONS
AND HOW THEY EVOLVE 754**CHAPTER 24**EVOLUTION AT THE MOLECULAR
LEVEL 783**EPILOGUE**HUMAN GENETICS AND THE FUTURE OF
BIOLOGY**APPENDIX A**GUIDELINES FOR GENE
NOMENCLATURE**APPENDIX B**

BRIEF ANSWERS SECTION

GLOSSARY G-1**CREDITS C-1****INDEX I-1**

CONTENTS

ABOUT THE AUTHOR VI

PREFACE XIX

PROLOGUE 1

GENETICS: THE STUDY OF BIOLOGICAL INFORMATION 1

BIOLOGICAL INFORMATION IS ENCODED IN DNA MOLECULES 2

BIOLOGICAL FUNCTION EMERGES FROM PROTEIN MOLECULES 2

ALL LIVING THINGS ARE CLOSELY RELATED 3

THE MODULAR CONSTRUCTION OF GENOMES HAS ALLOWED THE RELATIVELY RAPID EVOLUTION OF COMPLEXITY 4

GENETIC TECHNIQUES PERMIT THE DISSECTION OF COMPLEXITY 6

OUR FOCUS IS ON HUMAN GENETICS 6

PART I

BASIC PRINCIPLES: HOW TRAITS ARE TRANSMITTED 8

CHAPTER 1

MENDEL'S BREAKTHROUGH: PATTERNS, PARTICLES, AND PRINCIPLES OF HEREDITY 10

BACKGROUND: THE HISTORICAL PUZZLE OF INHERITANCE 12

Artificial Selection Was the First Applied Genetic Practice 12

The Puzzle of Passing on Desirable Traits 12

A New Experimental Approach 14

GENETIC ANALYSIS ACCORDING TO MENDEL 16

Monohybrid Crosses Reveal Units of Inheritance and the Law of Segregation 16

Mendel's Results Reflect Basic Rules of Probability 18

Fast Forward 20

Genes Encode Proteins 20

Dihybrid Crosses Reveal the Law of Independent Assortment 21

Why Mendel's Work Was Unappreciated Before 1900 24

MENDELIAN INHERITANCE IN HUMANS:
A COMPREHENSIVE EXAMPLE 25

A Vertical Pattern of Inheritance Indicates a Rare Dominant Trait 26

A Horizontal Pattern of Inheritance Indicates a Rare Recessive Trait 27

Fast Forward 28

The Direct Analysis of Human Genotype 28

Genetics and Society 30

Developing Guidelines for Genetic Screening 30

CHAPTER 2

EXTENSIONS TO MENDEL: COMPLEXITIES IN RELATING GENOTYPE TO PHENOTYPE 38

EXTENSION TO MENDEL FOR SINGLE-GENE INHERITANCE 39

Dominance Is Not Always Complete 39

A Gene May Have More Than Two Alleles 42

One Gene May Contribute to Several Visible Characteristics 44

A Comprehensive Example: Sickle-Cell Syndrome Illustrates Many Extensions to Mendel's Analysis of Single-Gene Inheritance 47

EXTENSIONS TO MENDEL FOR MULTIFACTORIAL INHERITANCE 49

Two Genes Can Interact to Determine One Trait 49

Breeding Studies Help Decide How a Trait Is Inherited 55

The Same Genotype Does Not Always Produce the Same Phenotype 57

Genetics and Society 59

Disease Prevention versus the Right to Privacy 59

Even Continuous Variation Can Be Explained by Extensions to Mendelian Analysis 60

The Mouse's Coat and Tail: A Comprehensive Example of Multiple Alleles and Multifactorial Traits 62

CHAPTER 3

THE CHROMOSOME THEORY OF INHERITANCE 70

CHROMOSOMES CONTAIN THE GENETIC MATERIAL 71

Evidence That Genes Reside in the Nucleus 72

Evidence That Genes Reside in the Chromosomes 72

MITOSIS ENSURES THAT EVERY CELL IN AN ORGANISM CARRIES THE SAME CHROMOSOMES 76

During Interphase, Cells Grow and Replicate Their Chromosomes 76

During Mitosis (M Phase), Sister Chromatids Separate and Are Apportioned to Different Daughter Nuclei 77

Regulatory Checkpoints Ensure Correct Chromosome Separation During Mitosis 79

Fast Forward 80

How Gene Mutations Cause Errors in Mitosis 80

MEIOSIS PRODUCES HAPLOID GERM CELLS, OR GAMETES 82*Meiosis Consists of One Round of Chromosome Replication but Two Rounds of Nuclear Division 82**During Meiosis I, Homologous Chromosomes Pair, Exchange Parts, and Then Segregate from Each Other 83**During Meiosis II, Sister Chromatids Separate to Produce Haploid Gametes 87**A Summary of the Significant Events of Meiosis 87**Meiosis Contributes to Genetic Diversity 87**Meiosis and Mitosis: A Comparison 88***GAMETOGENESIS REQUIRES BOTH MITOTIC AND MEIOTIC DIVISIONS 90***Egg Formation in Humans: Asymmetrical Meiotic Divisions Produce One Large Ovum 90**Spermatogenesis in Humans: Symmetrical Meiotic Divisions Produce Four Sperm 91***VALIDATION OF THE CHROMOSOME THEORY 91***The Chromosome Theory Correlates Mendel's Laws with Chromosome Behavior during Meiosis 91**Specific Traits Are Transmitted with Specific Chromosomes 93**The Chromosome Theory Integrates Many Aspects of Gene Behavior 98***CHAPTER 4****LINKAGE, RECOMBINATION, AND THE MAPPING OF GENES ON CHROMOSOMES 105****GENE LINKAGE AND RECOMBINATION 106***Some Genes on the Same Chromosome Assort Together More Often than Not 106**Recombination Results When Crossing Over During Meiosis Separates Linked Genes 112***Genetics and Society 114***Mitotic Recombination and Cancer Formation 114**Linkage and Recombination: A Summary 118***MAPPING: LOCATING GENES ALONG A CHROMOSOME 118***Two-Point Crosses: Comparisons Help Establish Relative Gene Positions 119**Three-Point Crosses: A Faster, More Accurate Way to Map Genes 119**How Close Is the Correlation Between a Genetic Map and Physical Reality? 123***Fast Forward 124***Gene Mapping Leads to a Possible Cure for Cystic Fibrosis 124**Multiple Factor Crosses Help Establish Linkage Groups by Inference 124**Tetrad Analysis in Fungi: A Powerful Tool for Mapping and for Understanding the Mechanisms of Recombination 125***PART II****WHAT GENES ARE AND WHAT THEY DO 142****CHAPTER 5****DNA: HOW THE MOLECULE OF HEREDITY CARRIES, REPLICATES, AND RECOMBINES INFORMATION 144****EXPERIMENTS DESIGNATE DNA AS THE GENETIC MATERIAL 145***Chemical Characterization Localizes DNA in the Chromosomes 145**Bacterial Transformation Implicates DNA as the Substance of Genes 146**Convincing Evidence That Genes Are DNA: The Molecule Carries the Information Required for the Replication of Bacterial Viruses 149***THE WATSON-CRICK MODEL: DNA IS A DOUBLE HELIX 150***Nucleotides Are the Basic Building Blocks of DNA 150**The Double Helix Contains Two Antiparallel Chains That Associate by Complementary Base Pairing 152**The Double Helix May Assume Alternative Forms 153**DNA Structure Is the Foundation of Genetic Function 153***DNA STORES INFORMATION IN THE SEQUENCE OF ITS BASES 156***Much of DNA's Sequence-Specific Information Is Accessible Only When the Double Helix Is Unwound 156**Some Genetic Information Is Accessible Even in Intact, Double-Stranded DNA Molecules 156**A Few Viruses Use RNA as the Repository of Genetic Information 157***DNA REPLICATION: COPYING GENETIC INFORMATION FOR TRANSMISSION TO THE NEXT GENERATION 157***Complementary Base Pairing Produces Semiconservative Replication: An Overview 157**The Molecular Mechanism of Replication: Doubling the Double Helix 160**The Mechanics of DNA Replication at the Chromosomal Level 161**Cells Must Ensure the Accuracy of Their Genetic Information—Before, During, and After Replication 161***RECOMBINATION RESHUFFLES THE INFORMATION CONTENT OF DNA 164***During Recombination, DNA Molecules Break and Rejoin 165***Fast Forward 166***Restriction Enzymes Recognize Specific Base Sequences in DNA 166**A Molecular Model of Crossing Over 169*

CHAPTER 6

ANATOMY AND FUNCTION OF A GENE: DISSECTION THROUGH MUTATION 179

MUTATIONS: PRIMARY TOOLS OF GENETIC ANALYSIS 180

Mutations Are Heritable Changes in Base Sequences That Modify the Information Content of DNA 180

Spontaneous Mutations Affecting Genes Occur at a Very Low Rate 181

Mutations Arise from Many Kinds of Random Events 182

Genetics and Society 188

A New Class of Human Mutation: Amplified Repeats with Medical Consequences 188

Impact: Mutations Have Consequences for the Evolution of Species and the Survival of Organisms 190

WHAT MUTATIONS TELL US ABOUT GENE STRUCTURE 191

Complementations Testing Reveals Whether Two Mutations Are in the Same or Different Genes 191

A Gene Is a Linear Sequence of Nucleotides That Can Mutate Independently and Recombine with Each Other 194

A Gene Is a Discrete Linear Set of Nucleotides 197

WHAT MUTATIONS TELL US ABOUT GENE FUNCTION 201

The One Gene, One Enzyme Hypothesis: A Gene Contains the Information for Producing a Specific Enzyme 201

Genes Direct the Synthesis of Proteins by Specifying the Identity and Order of Amino Acids in a Polypeptide Chain 203

HOW GENOTYPE CORRELATES WITH PHENOTYPE 207

Fast Forward 208

Using Mutagenesis to Look at Biological Processes 208

Dominance Relations Between Alleles Depend on the Relation Between Protein Function and Phenotype 208

HOW GENE MUTATIONS AFFECT LIGHT-RECEIVING PROTEINS AND VISION: A COMPREHENSIVE EXAMPLE 212

The Cellular and Molecular Basis of Vision 212

How Mutations in the Rhodopsin Family Influence the Way We See 213

CHAPTER 7

GENE EXPRESSION: THE FLOW OF GENETIC INFORMATION FROM DNA VIA RNA TO PROTEIN 222

THE GENETIC CODE: HOW PRECISE GROUPINGS OF THE 4 NUCLEOTIDES SPECIFY 20 AMINO ACIDS 224

In the Genetic Code, A Triplet Codon Represents Each Amino Acid 224

Mapping Studies Confirmed That a Gene's Nucleotide Sequence Is Colinear with a Polypeptide's Amino-Acid Sequence 225

Genetic Analysis Revealed That Nonoverlapping Codons Are Set in a Reading Frame 225

Cracking the Code: Biochemical Manipulations Revealed Which Codons Represent Which Amino Acids 228

The Genetic Code: A Summary 230

Using Genetics to Verify the Code 231

The Genetic Code Is Almost, But Not Quite, Universal 232

TRANSCRIPTION: RNA POLYMERASE SYNTHESIZES A SINGLE-STRANDED RNA COPY OF A GENE 232

Details of the Process 232

In Eukaryotes, RNA Processing after Transcription Produces a Mature Messenger RNA 232

TRANSLATION: BASE-PAIRING BETWEEN MRNA AND TRNAs DIRECTS ASSEMBLY OF A POLYPEPTIDE ON THE RIBOSOME 240

Transfer RNAs 240

Genetics and Society 242

HIV and Reverse Transcription: An Unusual DNA Polymerase Helps Give the AIDS Virus an Evolutionary Edge 242

Ribosomes Are the Sites of Polypeptide Synthesis 244

The Mechanism of Translation 244

Processing after Translation Can Change a Polypeptide's Structure 245

COMPREHENSIVE EXAMPLE: A COMPUTERIZED ANALYSIS OF GENE EXPRESSION IN *C. ELEGANS* 248

HOW MUTATIONS AFFECT GENE EXPRESSION 249

Mutations in a Gene's Coding Sequence Can Alter the Gene Product 249

Mutations in a Gene Outside the Coding Sequence Can Also Alter Gene Expression 249

Mutations in Genes Encoding the Molecules That Implement Expression May Affect Transcription, mRNA Splicing, or Translation 250

PART III

USING GENETIC ENGINEERING TO UNRAVEL THE INFORMATION IN GENOMES 260

CHAPTER 8

DNA AT HIGH RESOLUTION: USE OF DNA CLONING, PCR, AND HYBRIDIZATION AS THE TOOLS OF GENETIC ANALYSIS 262

CUTTING THE DNA: RESTRICTION ENZYMES SERVE AS MOLECULAR SCISSORS 264

Restriction Enzymes Fragment the Genome at Specific Sites 264

Different Restriction Enzymes Produce Fragments of Different Lengths 264

Genetics and Society 266

Serendipity in Science: The Discovery of Restriction Enzymes 266

Different Restriction Enzymes Produce Different Numbers of Fragments from the Same Genome 266

PURIFICATION AND AMPLIFICATION OF FRAGMENTS FOR STORAGE AND ANALYSIS 268