科学版研究生教学丛书

遗传学

从基因到基因组

GENETICS

From Genes to Genomes

LELAND H. HARTWELL
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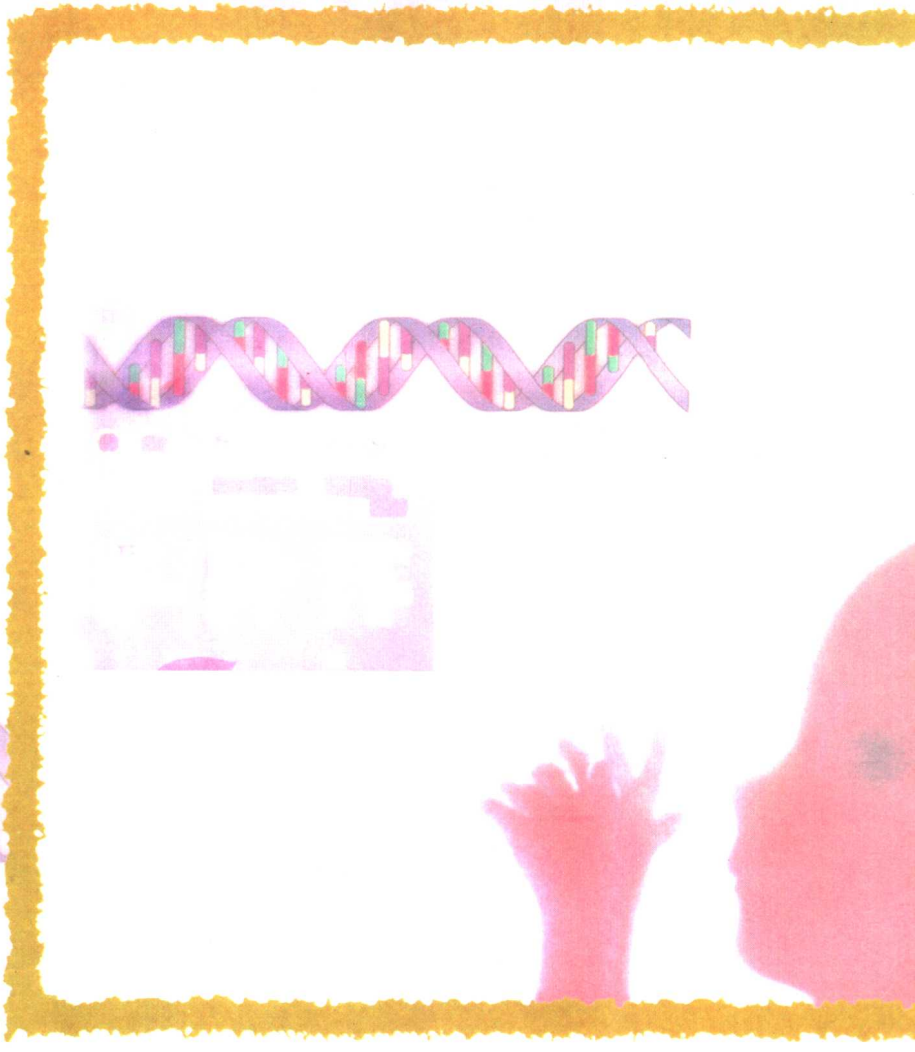
RUTH C. VERES



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影印版

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GENETICS

From Genes to Genomes

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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。

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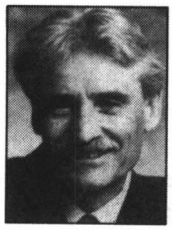
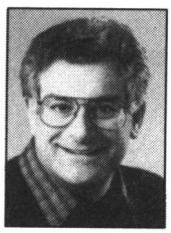


Dr. Leland Hartwell received his Ph.D. from the Massachusetts Institute of Technology. Dr. Hartwell held assistant and associate professorships at the University of California before joining the faculty of the University of Washington, where he continues as a full professor. In 1996, Dr. Hartwell joined 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 sequenator 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.

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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.

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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.

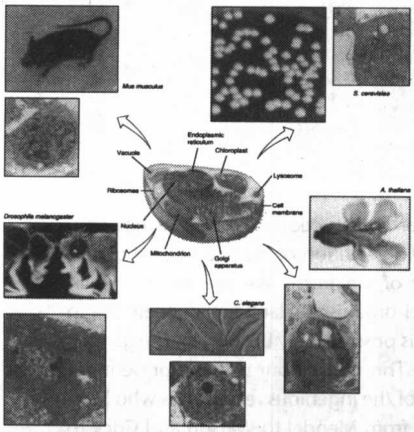
Part III (Chapters 8, 9, and 10) describes the ***Use of Genetic Engineering to Unravel the Information in Genomes*** and includes topics on mapping and analysis of genomes, detection of genotype, and the use of cloning, PCR, and hybridization in genetic analysis.

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 prokarytotic 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.



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.

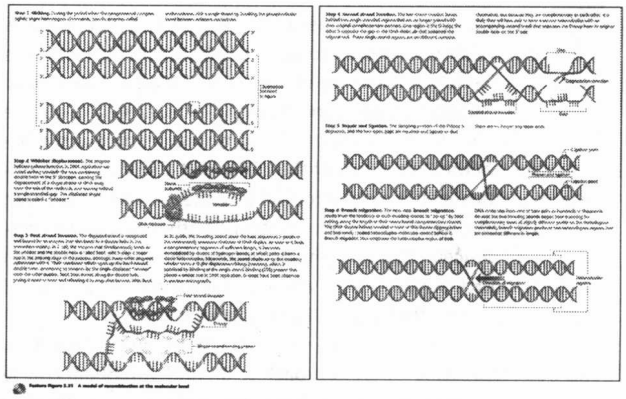
Part VII (Chapters 23 and 24) on ***How Genes Change*** explains the evolution of genes and genomes in populations and at the molecular level.

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

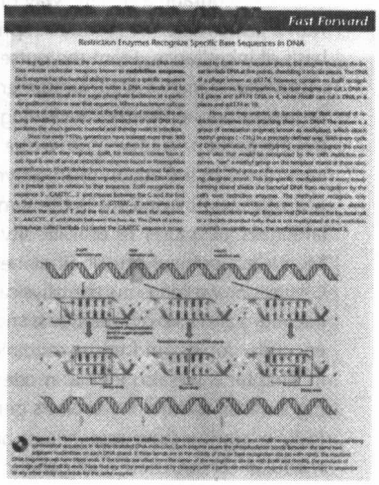
Introduction Each chapter begins with an engaging story related to the key ideas and principles of the chapter. This opening story is followed by a description of one or more overarching themes that unify the discussion, and then, in turn, by an advance organizer—a short, bulleted list of the chapter's 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.



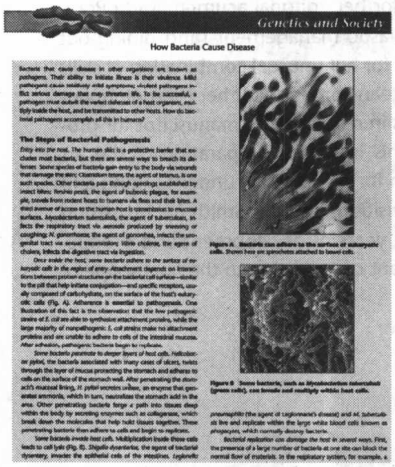
Comprehensive Examples These sections of the text are extensive case histories or research synopses that summarize the main points in the preceding section or chapter and show how they relate to each other. Very often these developed examples expand on the chapter's introductory story. In Chapter 6, *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



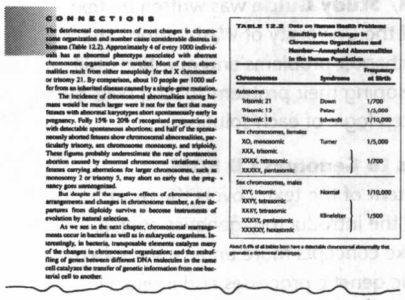
have a molecular basis. In Chapter 5, *DNA: How the Molecule of Heredity Carries, Replicates, and Recombines Information,* where we present in detail the structure of the DNA molecule, the Fast Forward essay explains how "Restriction Enzymes Recognize Specific Base Sequences in DNA." This simple introduction of restriction enzymes foreshadows a discussion in Chapter 8, *DNA at High Resolution: The Use of DNA Cloning, PCR, and Hybridization as Tools of Genetic Analysis,* about the use of restriction enzymes in DNA cloning. It thus relates the basic concept of DNA structure to the tools of biotechnology that depend on a knowledge of that structure.

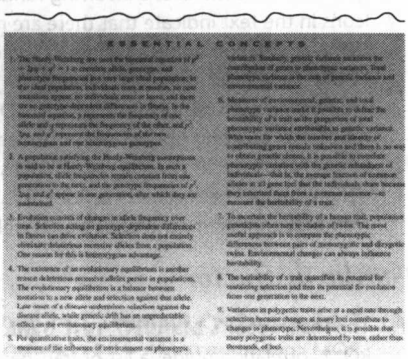
Genetics and Society Essays These essays explore the social and ethical issues created by the multiple applications of modern genetic research. They cover a wide variety of topics from the right to privacy to the question of who has the right to make reproductive decisions. In Chapter 9, the Genetics and Society essay asks "Does DNA Fingerprinting Serve the Interests of Justice?" In Chapter 10, the essay examines "The Patentability of DNA." In Chapter 13, it looks at "How Bacteria Can Cause Disease," presenting the mechanisms of bacterial pathogenesis step by step and describing the defense mechanisms that fight infection.


Genetics and Society

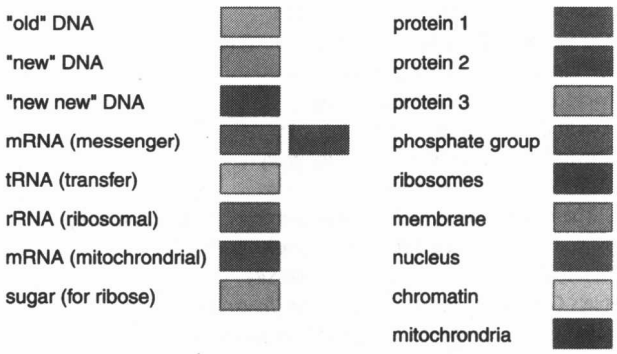
How Bacteria Cause Disease

Connections and Essential Concepts Each chapter closes with a **Connections** section that serves as a bridge between the topics in the just-completed chapter and those in the up-coming chapter or chapters. The Connections section is followed by an **Essential Concepts** section that helps students focus on the most critical information—the chapter's "take-home" messages. The end-of-chapter exercises include solved problems, **Social and Ethical Issues** discussion questions, and a diverse set of problems and questions for the student to solve.


CONNECTIONS


ESSENTIAL CONCEPTS

Outstanding Art Work The quality of the art is critical to the success of this text, and you will find that the photos, electron micrographs, and line art have been carefully selected and rendered to give students the best presentation possible. Color consistency has been used in rendering the line art to aid student comprehension. The following key is a guide to the use of color in our illustrations.



REFERENCE SECTION

In the back of the text, we provide a **Genetic Nomenclature Appendix.** Since the study of genetics is a relatively new science, a completely consistent nomenclature, similar to those found in more established sciences, does not exist. Instead, the details of gene notation differ from model organism to model organism. To assist students in understanding the use of gene symbols throughout the book, and particularly in the section on model organisms, this concise appendix details the minor differences in notation by organism.

Mastering the vocabulary of genetics is critical to understanding the science. To aid in that mastery, we provide a detailed **Glossary.**

The **Answer Appendix** contains answers to selected end-of-chapter problems. Students can build their problem-solving skills by working through the solved problems within each chapter and then, for the unsolved problems, checking the solutions they arrive at on their own against the answers in the Answer Appendix.

ACKNOWLEDGMENTS

The creation of a project of this scope is never solely the work of the authors. We are grateful to our colleagues around the world who took the time to review this manuscript and make suggestions for its improvement. Their willingness to share their experiences and expertise was a tremendous help to us.

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SUPPLEMENTS

For the Student

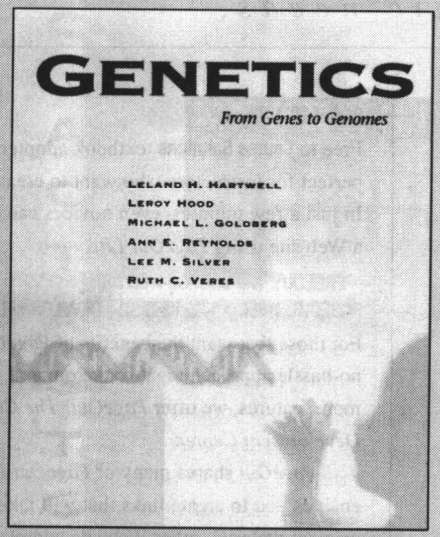
- The **Solutions Manual/ Study Guide** was written by text author Ann Reynolds, of the University of Washington. The solutions to the end-of-chapter problems and questions will aid the students in developing their problem-solving skills by providing the step-by-step logic of each solution.
- **Genetics: 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.



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CONTENTS