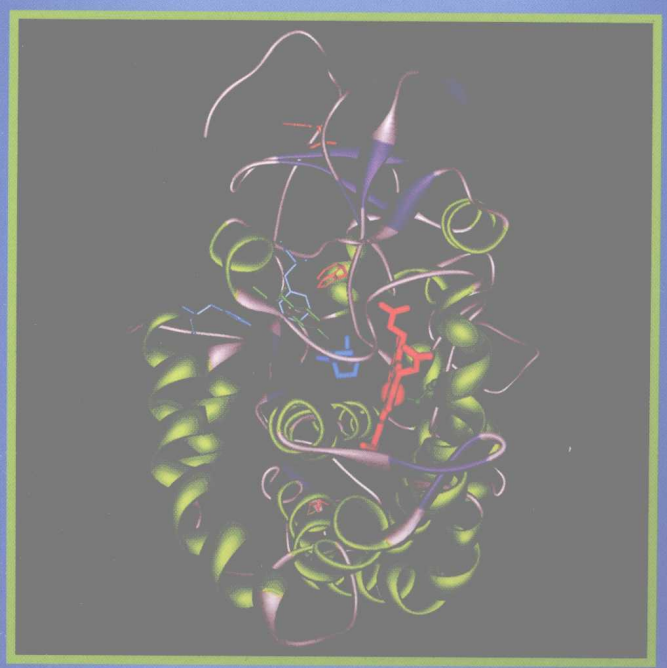
Robert F. Weaver／著　郑用链　张富春 等／编译

MOLECULAR BIOLOGY

分子生物学

（第三版）



科学出版社
www.sciencep.com

分子生物学
Molecular Biology

第三版
Third Edition

Robert F. Weaver 著
郑用琏 张富春 等 编译

科学出版社
北京

图字：01-2006-6125 号

内 容 简 介

分子生物学是生命科学发展过程中诞生的一门实验性极强的新兴学科。美国著名分子生物学家 Robert F. Weaver 遵循这一学科发展的特点，1999 年出版了 *Molecular Biology* 一书。全书以原始研究论文为基础，通过对实验的设计、对结果的分析而逐步展开对分子生物学理论的讲述，文字通俗流畅，叙述由浅入深。随着学科的迅速发展，几经修订再版的 *Molecular Biology* 第三版共有分子生物学方法，原核生物、真核生物转录，转录后加工，翻译，DNA 复制、重组和转座和基因组学等八部分二十四章，书后还写有术语表。每一章节都以提出科学问题、展开研究过程开始，以提供思考习题、推荐阅读文献结束，理论讲述逻辑严密，实验过程提炼清晰，特色鲜明、内容详尽，图文并茂易读易记。是研究生和生命科学相关专业的科研、教学人员不可多得的一本优秀参考书。

Robert F. Weaver
Molecular Biology, Third Edition
ISBN 0-07-284611-9

图书在版编目(CIP)数据

分子生物学＝Molecular Biology：第 3 版：英文/(美)韦弗(Weaver, R. F.)著；郑用琏等编译. —改编本. —北京：科学出版社，2008
(中国科学院研究生院教学丛书)
ISBN 978-7-03-020964-1

Ⅰ. 分… Ⅱ. ①韦…②郑… Ⅲ. 分子生物学-研究生-教材-英文 Ⅳ. Q7

中国版本图书馆 CIP 数据核字(2008)第 137681 号

责任编辑：周 辉/责任校对：陈玉凤
责任印制：张克忠/封面设计：耕者设计工作室

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

新 蕾 印 刷 厂 印刷

科学出版社发行 各地新华书店经销

*

2008 年 8 月第 三 版 开本：A4(890×1240)
2008 年 8 月第一次印刷 印张：56 1/2
印数：1—3 000 字数：1 880 000

定价：118.00 元(含光盘)

(如有印装质量问题，我社负责调换<新蕾>)

编校人员名单

（按姓氏汉语拼音排序）

丁　冬 郑用琏　（第 8 章）
高友军 郑用琏　（第 23 章）
兰海燕 张富春 郑用琏　（第 11、12、13 章）
马　纪 张富春　（第 17、18、19 章）
唐忠辉 郑用琏　（第 7 章）
赵衍鑫 郑用琏　（第 16 章）
肖海林 郑用琏　（第 15 章）
徐启江 郑用琏　（第 6、9、10、14 章）
张富春 马　纪　（第 20、21 章）
张姿丽 郑用琏　（第 22 章）

编译版序

分子生物学是在分子水平上研究生物体的分子结构、分子间相互作用，分子与细胞、组织、器官及机体功能的科学，是生命科学发展过程中诞生的一门新兴学科，特别是克隆技术、分子标记技术、基因表达调控技术的日新月异，使分子生物学的理论得以迅速发展与不断完善。分子生物学作为一门实验性很强的学科，它的每一个结论，每一个概念都是源自研究者对大量科学实验结果的总结与提升。Dr. Robert F. Weaver 的 *Molecular Biology* 一书完全地遵循这一“认识论”的重要原则。正如作者在序言中开宗明义地表白了他的撰写初衷：“I really wanted a textbook that presented the concepts of molecular biology, along with the experiments that led to those concepts. 我希望这样的教科书，它能够清晰地陈述分子生物学的概述以及提出这些概念的实验。”也正是基于这一不同于其他分子生物学教材的特点，中国科学院推荐这一名著作为中国科学院研究生教学用书，科学出版社 2000 年以影印版的方式出版翻印发行了 *Molecular Biology* 一书。

在多年的分子生物学教学过程中，我们遵循语言通俗、表述流畅、内容翔实、科学性强、趣味性浓等原则，一直推崇该书作为教学的主要参考用书，而且尝试将该书作为双语教学使用的教材。*Molecular Biology* 一书从第一版到第三版的最大特色是，对每一分子生物学结论的介绍都是通过对实验的设计、对结果的分析而逐步展开的。全书以原始研究论文为基础，文字通俗流畅，叙述由浅入深，每一章节都以提出科学问题、展开研究过程开始，以提供思考习题、推荐阅读文献结束，很适合学生的阅读与理解，更利于知识的巩固与提高。凡是认真学过 *Molecular Biology* 英文教材的同学，普遍感到从中受益的不仅是准确地掌握了分子生物学的基本知识和清晰的基本概念，更为重要的是受到开展分子生物学理论研究的方法、思维、逻辑与分析的启迪和创新能力的提升。

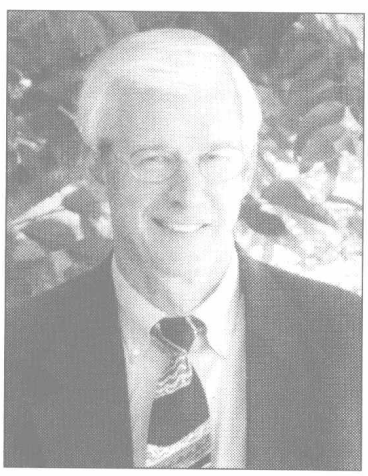
正因为 *Molecular Biology* 一书的理论讲述逻辑严密，实验过程提炼清晰，结论归纳严谨准确，编译者对全文翻译唯恐有失作者高超的写作功底，精彩的逻辑推理，巧妙的内容衔接……，在科学出版社编辑的倡导下，尝试着采用“编译版”、“导读版”的方式将这一世界名著推荐给学生，特别是研究生。显然“导读式的编译”科学名著，是一种形式上的创新，也是对编译者的挑战，我们在编译过程中，要求所有的编译者，在通读、精读原著的基础上，既要对章节内容进行高度的归纳，以帮助读者理解原文的科学内含，又要对文中图表进行准确的编译，以助益读者对实验的理解记忆，并努力保持 *Molecular Biology* 英文教材的特色。

为了突出重点，压缩篇幅，编译版未对第 1、2、3、4、5、24 章和术语表进行编译。其他章节分别由华中农业大学生命科学技术学院、新疆大学生命科学院和东北林业大学生命科学院一直以 Robert F. Weaver 的 *Molecular Biology* 一书为教学参考书，长期从事分子生物学教学的教师以及部分博士研究生编译。由于编译者水平有限，时间仓促，不乏错误之处，恳望读者提出宝贵建设，以便对此书再版修订，更臻完善。

郑用琏　张富春

2007 年 11 月

ABOUT THE AUTHOR



(*Source* Ashvini C. Ganesh)

Rob Weaver was born in Topeka, Kansas, and grew up in Arlington, Virginia. He received his bachelor's degree in chemistry from the College of Wooster in Wooster, Ohio, in 1964. He earned his Ph. D. in biochemistry at Duke University in 1969, then spent two years doing postdoctoral research at the University of California, San Francisco, where he studied the structure of eukaryotic RNA polymerases with William J. Rutter.

He joined the faculty of the University of Kansas as an assistant professor of biochemistry in 1971, was promoted to associate professor, and then to full professor in 1981. In 1984, he became chair of the Department of Biochemistry, and served in that capacity until he was named Associate Dean of the College of Liberal Arts and Sciences in 1995.

Prof. Weaver is the divisional dean for the science and mathematic departments within the College, which includes supervising 14 different departments and programs. As a professor of molecular biosciences, he teaches courses in introductory molecular biology and the molecular biology of cancer. He directs a research laboratory in which undergraduates and graduate students participate in research on the molecular biology of a baculovirus that infects caterpillars.

Prof. Weaver is the author of many scientific papers resulting from research funded by the National Institutes of Health, the National Science Foundation, and the American Cancer Society. He has also co-authored two genetics textbooks and has written two articles on molecular biology in the *National Geographic Magazine*. He has spent two years performing research in European Laboratories as an American Cancer Society Research Scholar, one year in Zurich, Switzerland, and one year in Oxford, England.

PREFACE

This textbook is designed for an introductory course in molecular biology. But what is molecular biology? The definition of this elusive term depends on who is doing the defining. In this book, I consider molecular biology to be the study of genes and their activities at the molecular level.

When I was a student in college and graduate school I found that I became most excited about science, and learned best, when the instructor emphasized the experimental strategy and the data that led to the conclusions, rather than just the conclusions themselves. Thus, when I began teaching an introductory molecular biology course in 1972, I adopted that teaching strategy and have used it ever since. I have found that my students react as positively as I did.

One problem with this approach, however, was that no textbook placed as great an emphasis on experimental data as I would have liked. So I tried assigning reading from the literature in lieu of a textbook. Although this method was entirely appropriate for an advanced course, it was a relatively inefficient process and not practical for a first course in molecular biology. To streamline the process, I augmented the literature readings with handdrawn cartoons of the data I wanted to present. Later, when technology became available, I made transparencies of figures from the journal articles. But I really wanted a textbook that presented the concepts of molecular biology, along with experiments that led to those concepts. I wanted clear explanations that showed students the relationship between the experiments and the concepts. So, I finally decided that the best way to get such a book would be to write it myself. I had already coauthored a successful introductory genetics text in which I took an experimental approach-as much as possible with a book at that level. That gave me the courage to try writing an entire book by myself and to treat the subject as an adventure in discovery.

Organization

The book begins with a four-chapter sequence that should be a review for most students. Chapter 1 is a brief history of genetics. Chapter 2 discusses the structure and chemical properties of DNA. Chapter 3 is an overview of gene expression, and Chapter 4 deals with the nuts and bolts of gene cloning. All these are topics that the great majority of molecular biology students have already learned in an introductory genetics course. Still, students of molecular biology need to have a grasp of these concepts and may need to refresh their understanding of them. I do not deal specifically with these chapters in class; instead, I suggest students consult them if they need more work on these topics. These chapters are written at a more basic level than the rest of the book.

Chapter 5 describes a number of common techniques used by molecular biologists. It would not have been possible to include all the techniques described in this book in one chapter, so I tried to include the most common or, in a few cases, valuable techniques that are not mentioned elsewhere in the book. When I teach this course, I do not present Chapter 5 as such. Instead, I refer students to it when we first encounter a technique in a later chapter. I do it that way to avoid boring my students with technique after technique. I also realize that the concepts behind some of these techniques are rather sophisticated, and the students' appreciation of them is much deeper after they've acquired more experience in molecular biology.

Chapters 6-9 describe transcription in prokaryotes. Chapter 6 introduces the basic transcription apparatus, including promoters, terminators, and RNA polymerase, and shows how transcripts are initiated, elongated, and terminated. Chapter 7 describes the control of transcription in three different operons, then Chapter 8 shows how bacteria and their phages control transcription of many genes at a time, often by providing alternative sigma factors. Chapter 9 discusses the interaction between prokaryotic DNA-binding proteins, mostly helix-turn-helix proteins, and their DNA targets.

Chapters 10-13 present control of transcription in eukaryotes. Chapter 10 deals with the three eukaryotic RNA polymerases and the promoters they recognize. Chapter 11 introduces the general transcription factors that collaborate with the three RNA polymerases and points out the unifying theme of the TATA-box-binding protein, which participates in transcription by all three polymerases. Chapter 12 explains the functions of genespecific transcription factors, or activators. This

chapter also illustrates the structures of several representative activators and shows how they interact with their DNA targets. Chapter 13 describes the structure of eukaryotic chromatin and shows how activators can interact with histones to activate or repress transcription.

Chapters 14-16 introduce some of the posttranscriptional events that occur in eukaryotes. Chapter 14 deals with RNA splicing. Chapter 15 describes capping and polyadenylation, and Chapter 16 introduces a collection of fascinating "other posttranscriptional events," including rRNA and tRNA processing, *trans*-splicing, and RNA editing. This chapter also discusses two kinds of posttranscriptional control of gene expression: (1) RNA interference; and (2) modulating mRNA stability (using the transferrin receptor gene as the prime example).

Chapters 17-19 describe the translation process in both prokaryotes and eukaryotes. Chapter 17 deals with initiation of translation, including the control of translation at the initiation step. Chapter 18 shows how polypeptides are elongated, with the emphasis on elongation in prokaryotes. Chapter 19 provides details on the structure and function of two of the key players in translation: ribosomes and tRNA.

Chapters 20-23 describe the mechanisms of DNA replication, recombination, and translocation. Chapter 20 introduces the basic mechanisms of DNA replication and repair, and some of the proteins (including the DNA polymerases) involved in replication. Chapter 21 provides details of the initiation, elongation, and termination steps in DNA replication in prokaryotes and eukaryotes. Chapters 22 and 23 describe DNA rearrangements that occur naturally in cells. Chapter 22 discusses homologous recombination and Chapter 23 deals with translocation.

Chapter 24 presents concepts of genomics and proteomics. The chapter begins with an old-fashioned positional cloning story involving the Huntington disease gene and contrasts this lengthy and heroic quest with the relative ease of performing positional cloning with the human genome (and other genomes) in hand.

New to the Third Edition

One of the most obvious changes has been the addition of Analytical Questions to each chapter (except Chapter 1). I have always intended the Review Questions to check students' retention of the material in each chapter, and the answers are readily available in the text and figures. But many users of the book have asked me for questions that require a bit more thought and extrapolation beyond the presented material. That is the purpose of the new Analytical Questions. I thank Marie Pizzorno for her contribution to this new set of questions and welcome further contributions to expand these questions in future editions.

Most of the chapters of this third edition have been updated and include new information. Here are a few highlights:

Chapter 6 : A considerable amount of new structural information has been added on prokaryotic RNA polymerase, including new x-ray crystal structures of the prokaryotic RNA polymerase holoenzyme and of the holoenzyme bound to DNA.

Chapter 7 : The x-ray crystal structure of the complex of *lac* DNA, CAP-cyclic AMP, and the α-CTD of RNA polymerase shows exactly what part of the CAP protein contacts the α-CTD.

Chapter 8 : This chapter shows a new insight into how transcription is controlled in bacterial cells infected with λ phage, including new evidence that shows how NusA facilitates transcription termination by facilitating the formation of a hairpin at the terminator, and how the λ N protein overrides termination by inhibiting hairpin formation. Also, we know how the heat shock σ-factor appears so rapidly after heat shock in *E. coli*: Elevated temperature melts inhibitory secondary structure in the mRNA, rendering it more accessible to ribosomes.

Chapter 10 : New structural information on RNA polymerase II and its mechanism is presented in Chapter 10. For example: The structure of yeast polymerase II at atomic resolution reveals a deep cleft that can accept a linear DNA template from one end to the other. The catalytic center, containing a Mg^{2+} ion, lies at the bottom of the cleft. A highly mobile clamp appears to swing open to allow the DNA template to enter the cleft.

Chapter 11 : Chapter 11 examines a new class II transcription elongation factor: Sometimes, phosphorylation on serine 2 of the RNA polymerase II CTD is also lost during elongation and that can cause pausing of the polymerase. For elongation to begin again, rephosphorylation of serine 2 of the CTD must occur.

Chapter 12 : This chapter presents new information on insulators and insulator regulation, and new insights into how transcription can be controlled by covalent modifications, including ubiquitination and sumoylation of transcription factors.

Chapter 13 : A new concept of a histone code is introducted in Chapter 13, with the interferon-β (INF-β) gene as an example. In principle, each particular combination of methylations, acetylations, phosphorylations, and ubiquitinations can send a different message to the cell about activation or repression of transcription.

Chapter 14 : A minor class of introns with 5′-splice sites and branchpoints can be spliced with the help of a variant class of snRNAs, including U11, U12, U4atac, and U6atac.

Chapter 15 : The CTD of the largest subunit of RNA polymerase II serves as a platform for assembly of factors that carry out capping, polyadenylation, and splicing. These factors come and go as needed, and the phosphorylation state of the CTD can change as transcription progresses. Also, new information on the coupling of polyadenylation and transcription termination is presented.

Chapter 16 : We introduce a more widespread form of RNA editing: Some adenosines in mRNAs of higher eukaryotes, including fruit flies and mammals, must be deaminated to inosine posttranscriptionally for the mRNAs to code for the proper proteins. Enzymes known as adenosine deaminases active on RNAs (ADARs) carry out this kind of RNA editing.

Chapter 17 : We introduce a new eukaryotic translation initiation factor: This factor, eIF5B, is homologous to the prokaryotic factor IF2. It resembles IF2 in binding GTP and stimulating association of the two ribosomal subunits.

Chapter 19 : We examine another role for IF1 in prokaryotic translation initiation: preventing aminoacyl tRNAs from binding to the ribosomal A site until the initiation phase is over.

Chapter 24 : This chapter has seen the greatest change, as befits such a rapidly evolving subdiscipline. The proteomics part of the chapter has been expanded, including new techniques to probe protein-protein interactions. To relfect this expansion, the chapter has been renamed Genomics and Proteomics. We have also designed a short tutorial on the use of the NCBI website including: querying the database for a sequence match; finding information on a gene of interest; and viewing the structure of a protein of interest in three dimensions by rotating the structure on the computer screen.

The genomics part of the chapter has also been extensively revised. For example, the positional cloning of the Huntington disease (HD) gene has been moved to the beginning of the chapter as an introduction to genomics to illustrate how laborious such searches were before the genomics era. We also present a hypothesis to explain why expansion of the polyglutamine tract in huntingtin leads to the deterioration of the central nervous system that characterizes HD.

We also show that is is possible to define the essential gene set of a simple organism by mutating one gene at a time to see which genes are required for life. In principle, it is also possible to define the minimal genome-the set of genes that is the minimum required for life.

Supplements

- A presentation CD-ROM contains digital files for all of the line art, tables, and photographs in the text in an easy-to-use format. This format is compatible with either PC or Macintosh.
- Text-Specific Website
  The following website, specific to this text, provides access to digital image files, updates, and web links for both students and instructors. Separate message boards for both instructor and student discussion are also available:
  www. mhhe. com/weaver3

ACKNOWLEDGMENTS

In writing this book, I have been aided immeasurably by the advice of many editors and reviewers. They have contributed greatly to the accuracy and readability of the book, but they cannot be held accountable for any remaining errors or ambiguities. For those, I take full responsibility. I would like to thank the following people for their help.

Third Edition Reviewers
David Asch
Youngstown State University
Gerard Barcak
University of Maryland School of Medicine
Bonnie Baxter
Hobart & William Smith Colleges
André Bédard
McMaster University
Felix Breden
Simon Fraser University
Laura Bull
UCSF Liver Center Laboratory
James Ellis
Developmental Biology Program, Hospital for Sick Children, Toronto, Ontario
Robert Helling
The University of Michigan
David Hinkle
University of Rochester
Robert Leamnson
University of Massachusetts at Dartmouth
David Mullin
Tulane University
Marie Pizzorno
Bucknell University
Michael Reagan
College of St. Benedict/St. John's University
Rodney Scott
Wheaton College

Second Edition Reviewers
Anne Britt
University of California, Davis
Mark Bolyard
Southern Illinois University
M. Suzanne Bradshaw
University of Cincinnati
Robert Brunner
University of California, Berkeley
Stephen J. D'Surney
University of Mississippi
Caroline J. Decker
Washington State University
Jeffery DeJong
University of Texas, Dallas
John S. Graham
Bowling Green State University
Ann Grens
Indiana University
Ulla M. Hansen
Boston University
Laszlo Hanzely
Northern Illinois University
Robert B. Helling
University of Michigan
Martinez J. Hewlett
University of Arizona
David C. Hinkle
University of Rochester
Barbara C. Hoopes
Colgate University
Richard B. Imberski
University of Maryland
Cheryl Ingram-Smith
Pennsylvania State University
Alan Kelly
University of Oregon
Robert N. Leamnson
University of Massachusetts, Dartmouth
Karen A. Malatesta
Princeton University
Robert P. Metzger
San Diego State University
David A. Mullin
Tulane University
Brian K. Murray
Brigham Young University
Michael A. Palladino
Monmouth University
James G. Patton
Vanderbilt University
Martha Peterson
University of Kentucky
Marie Pizzorno
Bucknell University
Florence Schmieg
University of Delaware
Zhaomin Yang
Auburn University

First Edition Reviewers
Rodney P. Anderson
Ohio Northern University
Kevin L. Anderson
Mississippi State University
Prakash H. Bhuta
Eastern Washington University
Dennis Bogyo
Valdosta State University
Richard Crawford
Trinity College
Christopher A. Cullis
Case Western Reserve University
Beth De Stasio
Lawrence University
R. Paul Evans
Brigham Young University
Edward R. Fliss
Missouri Baptist College
Michael A. Goldman
San Francisco State University
Robert Gregerson
Lyon College
Eileen Gregory
Rollins College
Barbara A. Hamkalo
University of California, Irvine
Mark L. Hammond
Campbell University
Terry L. Helser
State University of New York, Oneonta
Carolyn Herman
Southwestern College
Andrew S. Hopkins
Alverno College
Carolyn Jones
Vincennes University
Teh-Hui Kao
Pennsylvania State University
Mary Evelyn B. Kelley
Wayne State University
Harry van Keulen
Cleveland State University
Leo Kretzner
University of South Dakota
Charles J. Kunert
Concordia University
Robert N. Leamnson
University of Massachusetts, Dartmouth
James D. Liberatos
Louisiana Tech University
Cran Lucas
Louisiana State University
James J. McGivern
Gannon University
James E. Miller
Delaware Valley College
Robert V. Miller
Oklahoma State University
George S. Mourad
Indiana University Purdue University
David A. Mullin
Tulane University
James R. Pierce
Texas A&M University, Kingsville
Joel B. Piperberg
Millersville University
John E. Rebers
Northern Michigan University
Florence Schmieg
University of Delaware
Brian R. Shmaefsky
Kingwood College
Paul Keith Small
Eureka College
David J. Stanton
Saginaw Valley State University
Francis X. Steiner
Hillsdale College
Amy Cheng Vollmer
Swarthmore College
Dan Weeks
University of Iowa
David B. Wing
New Mexico Institute of Mining & Technology

总 目 录

CONTENTS

CHAPTER 1

A Brief History

The garden pea plant. This was the experimental subject of Gregor Mendel's genetic investigation. *Holt Studios International (Nigel Cattlin)/Photo Researchers, Inc.*

What is molecular biology? The term has more than one definition. Some define it very broadly as the attempt to understand biological phenomena in molecular terms. But this definition makes molecular biology difficult to distinguish from another well-known discipline, biochemistry. Another definition is more restrictive and therefore more useful: the study of gene structure and function at the molecular level. This attempt to explain genes and their activities in molecular terms is the subject matter of this book.

Molecular biology grew out of the disciplines of genetics and biochemistry. In this chapter we will review the major early developments in the history of this hybrid discipline, beginning with the earliest genetic experiments performed by Gregor Mendel in the mid-19th century. In Chapters 2 and 3 we will add more substance to this brief outline. By definition, the early work on genes cannot be considered molecular biology, or even molecular genetics, because early geneticists did not know the molecular nature

of genes. Instead, we call it transmission genetics because it deals with the transmission of traits from parental organisms to their offspring. In fact, the chemical composition of genes was not known until 1944. At that point, it became possible to study genes as molecules, and the discipline of molecular biology was born. ■

1.1 Transmission Genetics

In 1865, Gregor Mendel (Figure 1.1) published his findings on the inheritance of seven different traits in the garden pea. Before Mendel's research, scientists thought inheritance occurred through a blending of each trait of the parents in the offspring. Mendel concluded instead that inheritance is particulate. That is, each parent contributes particles, or genetic units, to the offspring. We now call these particles **genes**. Furthermore, by carefully counting the number of progeny plants having a given **phenotype**, or observable characteristic (e.g., yellow seeds, white flowers), Mendel was able to make some important generalizations. The word *phenotype*, by the way, comes from the same Greek root as *phenomenon*, meaning *appearance*. Thus, a tall pea plant exhibits the tall phenotype, or appearance. *Phenotype* can also refer to the whole set of observable characteristics of an organism.

Figure 1.1 Gregor Mendel. (*Source*: Courtesy of Dept. of Library Services/American Museum of Natural History, Neg. no. 219467.)

Mendel's Laws of Inheritance

Mendel saw that a gene can exist in different forms called **alleles**. For example, the pea can have either yellow or green seeds. One allele of the gene for seed color gives rise to yellow seeds, the other to green. Moreover, one allele can be **dominant** over the other, **recessive**, allele. Mendel demonstrated that the allele for yellow seeds was dominant when he mated a green-seeded pea with a yellowseeded pea. All of the progeny in the first filial generation (F_1) had yellow seeds. However, when these F_1 yellow peas were allowed to self-fertilize, some green-seeded peas reappeared. The ratio of yellow to green seeds in the second filial generation (F_2) was very close to 3 : 1.

The term *filial* comes from the Latin: *filius*, meaning son; *filia*, meaning daughter. Therefore, the first filial generation (F_1) contains the offspring (sons and daughters) of the original parents. The second filial generation (F_2) is the offspring of the F_1 individuals.

Mendel concluded that the allele for green seeds must have been preserved in the F_1 generation, even though it did not affect the seed color of those peas. His explanation was that each parent plant carried two copies of the gene; that is, the parents were **diploid**, at least for the characteristics he was studying. According to this concept, **homozygotes** have two copies of the same allele, either two alleles for yellow seeds or two alleles for green seeds. **Heterozygotes** have one copy of each allele. The two parents in the first mating were homozygotes; the resulting F_1 peas were all heterozygotes. Further, Mendel reasoned that sex cells contain only one copy of the gene; that is, they are **haploid**. Homozygotes can therefore produce sex cells, or **gametes**, that have only one allele, but heterozygotes can produce gametes having either allele.

This is what happened in the matings of yellow with green peas: The yellow parent contributed a gamete with a gene for yellow seeds; the green parent, a gamete with a gene for green seeds. Therefore, all the F_1 peas got one allele for yellow seeds and one allele for green seeds. They had not lost the allele for green seeds at all, but because yellow is dominant, all the seeds were yellow. However, when these heterozygous peas were self-fertilized, they produced gametes containing alleles for yellow and green color in equal numbers, and this allowed the green phenotype to reappear.

Here is how that happened. Assume that we have two sacks, each containing equal numbers of green and yellow marbles. If we take one marble at a time out of one sack and pair it with a marble from the other sack, we will wind up with the following results: one-quarter of the pairs will be

yellow/yellow; one-quarter will be green/green; and the remaining one-half will be yellow/green. The alleles for yellow and green peas work the same way. Recalling that yellow is dominant, you can see that only one-quarter of the progeny (the green/green ones) will be green. The other three-quarters will be *yellow* because they have at least one allele for yellow seeds. Hence, the ratio of yellow to green peas in the second (F_2) generation is 3 : 1.

Mendel also found that the genes for the seven different characteristics he chose to study operate independently of one another. Therefore, combinations of alleles of two different genes (e. g. yellow or green peas with round or wrinkled seeds, where yellow and round are dominant and green and wrinkled are recessive) gave ratios of 9 : 3 : 3 : 1 for yellow/round, yellow/wrinkled, green/round, and green/wrinkled, respectively. Inheritance that follows the simple laws that Mendel discovered can be called **Mendelian inheritance**.

SUMMARY Genes can exist in several different forms, or alleles. One allele can be dominant over another, so heterozygotes having two different alleles of one gene will generally exhibit the characteristic dictated by the dominant allele. The recessive allele is not lost; it can still exert its influence when paired with another recessive allele in a homozygote.

The Chromosome Theory of Inheritance

Other scientists either did not know about or uniformly ignored the implications of Mendel's work until 1900 when three botanists, who had arrived at similar conclusions independently, rediscovered it. After 1900, most geneticists accepted the particulate nature of genes, and the field of genetics began to blossom. One factor that made it easier for geneticists to accept Mendel's ideas was a growing understanding of the nature of chromosomes, which had begun in the latter half of the 19th century. Mendel had predicted that gametes would contain only one allele of each gene instead of two. If chromosomes carry the genes, their numbers should also be reduced by half in the gametes—and they are. Chromosomes therefore appeared to be the discrete physical entities that carry the genes.

This notion that chromosomes carry genes is the **chromosome theory of inheritance**. It was a crucial new step in genetic thinking. No longer were genes disembodied factors; now they were observable objects in the cell nucleus. (See Figure B1. 1 to review key structures in the cell.) Some geneticists, particularly Thomas Hunt Morgan (Figure 1. 2), remained skeptical of this idea. Ironically, in 1910 Morgan himself provided the first definitive evidence for the chromosome theory.

Figure 1. 2 Thomas Hunt Morgan. (*Source*: National Library of Medicine.)

Morgan worked with the fruit fly (*Drosophila melanogaster*), which was in many respects a much more convenient organism than the garden pea for genetic studies because of its small size, short generation time, and large number of offspring. When he mated red-eyed flies (dominant) with white-eyed flies (recessive), most, but not all, of the F_1 progeny were red-eyed. Furthermore, when Morgan mated the red-eyed males of the F_1 generation with their red-eyed sisters, they produced about onequarter white-eyed males, but no white-eyed females. In other words, the eye color phenotype was sex-linked. It was transmitted along with sex in these experiments. How could this be?

We now realize that sex and eye color are transmitted together because the genes governing these characteristics are located on the same chromosome—the X chromosome. (Most chromosomes, called **autosomes**, occur in pairs in a given individual, but the X chromosome is an example of a **sex chromosome**, of which the female fly has two copies and the male has one.) However, Morgan was reluctant to draw this conclusion until he observed the same sex linkage with two more phenotypes, miniature wing and yellow body, also in 1910. That was enough to convince him of the va-