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国外优秀生命科学教学用书

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Genes to Proteins

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从基因到蛋白质 第3版 影印版

Burton E. Tropp

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序

在上个世纪，1953 年 DNA 双螺旋结构的解析和 1956 年中心法则的成形宣告着分子生物学时代的到来。分子生物学凭其影响力的自然渗透和许多科学家几十年的辛勤耕耘成为生命科学的基石学科。52 年后的今天，定义遗传物质流动方向的中心法则仍然是分子生物学的框架，即遗传物质通过 DNA 复制来实现传代，通过转录合成 RNA，再通过翻译从 mRNA 合成蛋白质。当然，现代的分子生物学教材都会加入基因表达的调控和分子生物学方法的相关内容。另外，有许多分子生物学教材会以介绍生物活性大分子蛋白质和核酸的结构为开胃菜，这两类大分子是所有分子生物学事件的主要执行者。

《分子生物学——从基因到蛋白质》前两版书名是《分子生物学》，分别在 1983 年和 1987 年出版，由先后在 Brandeis 大学和加州大学圣地亚哥分校教授生物化学和分子生物学课程的 David Freifelder 教授编写并修订的。《分子生物学——从基因到蛋白质》第 3 版是由纽约城市大学皇后学院的 Burton E. Tropp 教授编写的，具有以下 4 个主要特色：

1. 基础性强，翔实全面

该书共包括六部分 20 章。第一到第三部分共 7 章是引导性基础知识：包括蛋白质的结构和功能；核酸结构、核酸技术和染色体结构；遗传分析及病毒对分子生物学的贡献和地位。第四到第六部分共 12 章是分子生物学的核心内容：包括 DNA 代谢(DNA 复制,DNA 损伤和修复,DNA 重组和转座)，RNA 的合成和加工(细菌内的转录和基因表达调控,真核细胞内 mRNA 转录、调控和转录后加工,核糖体 RNA、转运 RNA 和细胞器 RNA 的合成)，以及蛋白质的合成(转运 RNA 和遗传密码,核糖体和翻译过程)。该书对所涉及内容的描述非常全面翔实，并具有一定的前沿性，非常适用于初学者。

2. 结构、思路清晰

譬如它将分子生物学技术的部分内容非常自然地融入到相应的蛋白质部分和核酸部分，逻辑性很好，易于学习和掌握。其他技术内容也被自然地整合到相关的知识部分。在描述 DNA 复制的内容时，基因表达与调控部分均分为细菌和真核进行介绍，线条清晰明了。本书所有内容的编排重点突出，前后呼应，目标明确，没有任何拖泥带水的部分。

3. 语言简练易懂，科学故事性强

该书行文流畅，语言简练易懂。而且注重发掘一些知识所涉及的科学问题是什么、怎样被发现的、由谁发现的等等。这对培养学生的科学思维非常重要。在这一点上它拥有 Robert Weaver 所编写的分子生物学教材的优点，而且比那本书所涉及的实验证明浅显，更加适用于本科生学习。

4. 插图设计精美、丰富

高质量且大量的插图为学生和老师提供了丰富的教辅材料，每一章都有主题大纲，附录有关键词索引。综合以上特色，本人认为该书是一本非常优秀的分子生物学入门教材，适用于没有多少生物学专业知识的学生和读者使用。在后基因组时代的今天，理解和欣赏基因表达和调控的奇妙应该成为大众文化一道亮丽的风景线。希望此书的引进能帮助更多的读者进入这样的科学欣赏境界。

张翼
武汉大学生命科学学院
2008 年 10 月 21 日

Dedication

To my wife Roslyn and to our family, Jonathan, Lauren, Matthew, Julie, Paul, Erica, Sarah, Rachel, Gabrielle, Katie and Gracie and to the memory of my parents Sol and Renee Tropp.

Tribute to David Freifelder

David Freifelder taught biochemistry and molecular biology first at Brandeis University and later at the University of California, San Diego. His research interests and expertise were in a broad range of subjects. Therefore, he was qualified to write both general and specialized textbooks. He was a gifted writer and he devoted extensive time and energy to preparing a collection of textbooks and monographs. From his teaching and writing experiences he developed a remarkable understanding of the ways in which students learn. He organized his textbooks using a layering approach for coping with biological complexity. This acknowledgement is, therefore, offered as a tribute to David's memory.

Preface

The first two editions of *Molecular Biology*, written by David Freifelder, were published in 1983 and 1987. As stated in the preface to the second edition, Freifelder considered the book to be a multipurpose textbook "emphasizing basic molecular processes (such as the synthesis of DNA, RNA, and protein) and genetic phenomena in both prokaryotic and eukaryotic cells." This third edition retains these goals, a fact emphasized by the revised title, *Molecular Biology: Genes to Proteins*. The book is intended for undergraduate and first year graduate students, who have completed full year courses in college biology, general chemistry and organic chemistry. Since the second edition of this book, the human genome sequence was determined. Structures for many enzymes and macromolecular machines that participate in DNA replication, RNA synthesis, and protein synthesis have been solved. New pathways such as the RNA interference pathway have been elucidated. These and many other important advances in the field of molecular biology necessitated a complete revision of the book. Significant changes in the way that we teach college science courses also contributed to the need for a complete revision. In 1987, instructors usually used standard slides to show how a nucleic acid, protein, or macromolecular complex looks and works. Today we view these structures in three-dimensions and manipulate them on our computer screens. Furthermore, the Internet now serves as an incredibly rich source of molecular biology information and data. Finally, molecular biology is now such an integral part of introductory biology, genetics, microbiology, cell biology, developmental biology, evolutionary biology and biochemistry courses that all students have encountered various aspects of molecular biology before they actually enroll in a molecular biology course.

Whenever possible the book uses a discovery approach so students learn about the experimental evidence relevant to the concepts discussed. This pedagogical approach provides historical and experimental background information, permitting students to see how molecular biologists examine clues and develop the hypotheses that ultimately lead to new advances in molecular biology. When teaching molecular biology, I find this approach helps students become part of the discovery process. In this way they begin to understand the pleasure and sense of satisfaction investigators derive from solving a molecular biology problem. Of course, space does not allow every concept to be presented in this way. Therefore, when faced with a choice of simply presenting a concept or omitting it, I opted to present the concept. This book differs from the previous two editions in introducing the scientists into the discovery process. I chose to do this, not because it is important for the students to memorize the scientist's name, but rather because it is important for students to appreciate the human effort involved in the discovery process and to recognize that molecular biology is an evolving field. Thus, as additional experiments are performed we continue to obtain new information. Many of the students who enroll in a molecular biology course are interested in the medical sciences. In recognizing this interest, a major effort has been made to include interesting and important medical applications when they are relevant.

Chapter Organization

After an introduction to the field of molecular biology the book is divided into six sections: (1) protein structure and function, (2) nucleic acids and nucleoproteins, (3) genetics and virology, (4) DNA metabolism, (5) RNA synthesis and processing, and (6) protein synthesis. The material presented in the first two sections provides the basic information required to understand the chemical basis of molecular biology, while that provided in the third section provides information required to understand the biological basis of molecular biology. The order of the remaining chapters reflects the fact that genetic information in cells normally flows from DNA to RNA to protein. A major challenge in presenting new information in molecular biology, and indeed in most science courses, is that information presented in a later chapter is sometimes necessary to fully understand information in earlier chapters. This edition has tried to minimize this problem by introducing basic concepts and techniques that are required to understand molecular biology in the first three sections.

The book follows Freifelder's philosophy that "molecular biology must emphasize both molecules and biology, and that to be molecular, it must also be chemical and physical." With this philosophy in mind, the chapters' contents are as follows. **CHAPTER 1** provides a brief historical introduction to the field of molecular biology including the discovery of the double helix model, which provides a very clear example of structure-function relationships, a major theme in molecular biology and one that is emphasized throughout this book. **CHAPTER 2** introduces important information about the primary, secondary, tertiary, and quaternary structures of proteins and describes the structure of proteins and lipids in biological membranes. **CHAPTER 3** describes structure-function relationships in proteins. The chapter begins with an examination of specific proteins included specifically because they provide important insights into structure-function relationships encountered throughout the text. The second part of this chapter describes enzymes and enzyme kinetics, topics that are central to understanding the processes of DNA replication, repair, and recombination; RNA synthesis and processing; and protein synthesis. The third section of this chapter briefly describes the G-protein signal system. **CHAPTER 4** builds on the information provided in Chapter 1 about DNA structure, emphasizing conformational variations, helical stability, strand separation, helical reformation, circular DNA, and topoisomers. **CHAPTER 5** includes an examination of the physical techniques that are used to isolate and characterize nucleic acids and a discussion of techniques that use enzymes to manipulate DNA in the laboratory. **CHAPTER 6** describes the interactions between specific proteins and DNA to form nucleoprotein complexes. **CHAPTER 7** introduces concepts in genetic analysis that are essential for working in molecular biology, including a brief introduction to genetic recombination and descriptions of basic techniques used by molecular biologists to locate genes in bacteria, yeast, and higher organisms. **CHAPTER 8** provides some of the fundamental information that molecular biologists need to know about viruses. The information presented will help to place viral systems that are discussed in subsequent chapters in perspective. Some students and instructors may decide to skip this chapter but then refer back to appropriate sections when specific viruses are mentioned in subsequent chapters. **CHAPTER 9** presents both the general features of DNA replication and a detailed examination of the initiation, elongation, and termination stages of bacterial DNA replication. It also examines these stages in eukaryotes and the archaea. **CHAPTER 10** focuses on the different types of DNA damage that take place in cells and then explores the mechanisms that cells use to reverse DNA damage, excise and replace damaged elements, or tolerate the damage. **CHAPTER 11** explores homologous recombination models, based on

genetic and biochemical data. Individual steps of homologous recombination and the enzymes that carry out these reactions are described. **CHAPTER 12** examines transposons and other mobile elements with particular emphasis on the three types of reactions that can explain the movement of all mobile genetic elements. Some instructors may wish to assign the material covered in Chapter 11, Chapter 12, or both after completing Chapter 20. Chapters 11 and 12 are written in a way that makes this possible. **CHAPTER 13** examines bacterial RNA polymerase and its function in RNA synthesis. **CHAPTER 14** examines the mechanisms that bacteria use to regulate the synthesis of the different classes of RNA starting with the regulation of bacterial mRNA synthesis. **CHAPTER 15** examines the eukaryotic RNA polymerase II (the enzyme responsible for mRNA formation) and the general transcription factors that it requires for basal transcription. The chapter also describes how RNA polymerase II and the general transcription factors combine to form the basal transcription machinery. **CHAPTER 16** describes two types of transcriptional factors, transcription activators and Mediators, that interact with the basal transcription machinery to form the much more efficient transcription machine that is in fact responsible for eukaryotic mRNA synthesis. **CHAPTER 17** explores the various stages in cotranscriptional processing. It also describes RNA editing, messenger RNA export, and pathways for silencing messenger RNA. **CHAPTER 18** examines the role of RNA polymerase I and its accessory factors in synthesizing eukaryotic ribosomal RNA. It also describes the role of RNA polymerase III, and its accessory factors in synthesizing transfer RNA and other small RNA molecules, most notably the small nuclear RNA molecules (snRNAs) and the RNA polymerases present in mitochondria and chloroplasts. **CHAPTER 19** describes the structure and function of transfer RNA molecules and then examines how these molecules act along with mRNA and ribosomes to specify the amino acid sequences in proteins. **CHAPTER 20** examines ribosome structure and function so that students can learn how ribosomes are able to act as universal translators.

Supplements to the Text

Jones and Bartlett offers an array of ancillaries to assist instructors and students in teaching and mastering the concepts in this text. Additional information and review copies of any of the following items are available through your Jones and Bartlett sales representative, or by going to http://www.jbpub.com/biology/.

For the Student

Developed exclusively for the third edition of *Molecular Biology: Genes to Proteins*, the companion Web site offers a variety of resources to enhance understanding of molecular biology. The site contains a free on-line study guide with chapter outlines, quizzes to test comprehension and retention, and an interactive glossary. This Web site will also have links to relevant material such as animations, structural programs, and tutorials that are available on the Internet. This information will be organized in the same way as the chapters of this book. The URL for the Web site is http://biology.jbpub.com/molecular.

Laboratory Investigations in Molecular Biology presents well-tested protocols in molecular biology. The experiments are designed to guide students through realistic research projects and to provide students with instruction in methods and approaches that can be immediately translated into research projects conducted in modern research laboratories.

For the Instructor

Compatible with Windows and Macintosh platforms, the Instructor's ToolKit CD-ROM,

authored by Cheryl Ingram-Smith of Clemson University, provides instructors with the following traditional ancillaries:

- The **Instructor's Manual**, provided as a text file, includes chapter overviews, complete lecture outlines, and key terms from each chapter.
- The **PowerPoint® Image Bank** provides the illustrations, photographs, and tables (to which Jones and Bartlett holds the copyright or has permission to reproduce digitally) inserted into PowerPoint slides. You can quickly and easily copy individual images or tables into you existing lecture slides.
- The **PowerPoint Lecture Outline Slides** presentation package provides lecture notes and images for each chapter of *Molecular Biology: Genes to Proteins*. Instructors with the Microsoft PowerPoint software can customize the outlines, art, and order of presentation.

A Test Bank will be available to instructors through the Jones and Bartlett website. Visit www.jbpub.com/biology for more details.

A Note from the Author

I would like to tell a brief story that indicates just how far molecular biology has advanced in the past four decades. When I started out as a graduate student in the early 1960s we were all very excited about the rapid advances that were being made in molecular biology, especially the discovery of the genetic code. We viewed molecular biology as a discipline that soared above the other scientific disciplines that our classmates were studying. However, several of us were brought back down to earth one day when a young medical doctor, who was working as a postdoctoral fellow, challenged us to provide a single example of how molecular biology had actually benefited anybody in a clinical setting. After much consideration, we were only able to come up with one example. Molecular biology explained the cause of sickle cell anemia. However, the young doctor correctly pointed out that this knowledge did not really provide any benefit to individuals suffering from sickle cell anemia. As I wrote this book I thought about that challenge so many years ago. Molecular biology remains an exciting and rapidly developing discipline, but it also is a discipline that has a direct impact on our lives in so many different ways. There are so many examples of how molecular biology has contributed to our medical well being that it would take several books to describe them all. Therefore, a few examples will have to suffice. Techniques developed by molecular biologists help to detect bacterial and viral infections, produce new drugs and hormones, study the effectiveness of a chemotherapeutic agent used to treat a malignant disease, determine whether an individual has an inborn error of metabolism, and design drugs to treat diseases such AIDS. Although initial attempts to cure inborn errors of metabolism by genetic engineering have been unsuccessful, and indeed some have proved dangerous to the subject, it seems likely that the next generation of molecular biologists will solve this problem as well as a host of other health-related problems.

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I would like to acknowledge the assistance of the many people who helped to prepare the third edition of this molecular biology text. First and foremost, I wish to acknowledge the contributions made by two gifted molecular biologists: Hannah Klein (Departments of Biochemistry and Medicine, NYU Medical Center) and Joseph E. Peters (Department of Microbiology, Cornell University), the authors of Chapter 11 (Recombination) and Chapter 12 (Transposons and Other Mobile Elements), respectively. I also wish to thank the following talented scholars for reviewing one or more chapters and, in the process of doing so, correcting errors and making valuable suggestions to improve the book:

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Finally, I wish to thank my wife Roslyn for her support, concern, and understanding through the years during which this book was in preparation.

Brief Contents

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