

Principles of
Molecular Virology
(Fifth Edition)

分子病毒学原理

(原著第五版)

Alan J. Cann



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Alan J. Cann

University of Leicester, UK

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Alan J. Cann.

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导 读

病毒虽然是最简单的生命形式,但却对人类的生存和社会发展有着重大的影响。纵观现代分子生物学的发展历程,病毒功不可没,对分子生物学的发展起到了巨大的推动作用。很多重大突破来自于对病毒的研究,如 T2 噬菌体感染大肠杆菌和烟草花叶病毒 TMV 重建实验证明了核酸而非蛋白质是遗传物质;病毒中逆转录的发现对中心法则的补充;由病毒产生的 T4 DNA 聚合酶、T4 DNA 连接酶、逆转录酶是全世界各地生物学、农业、动物、植物和微生物实验室的日常工具;基于病毒构建的表达载体也在基础研究、肿瘤基因治疗等领域发挥重要作用。随着科学技术的不断发展,病毒将会为现代生物学做出更大贡献,使一贯被人们视为恶魔的病毒为人类做出更大贡献。

病毒学不仅在生命科学的发展历程中曾发挥了举足轻重的作用,在新世纪也依然是万众瞩目的研究热点和科学前沿。不断出现的新病毒也对该研究领域提出新的挑战。其他学科的新技术、新方法为人们提供了更好的工具来研究病毒,认识病毒,控制病毒,利用病毒。分子病毒学是病毒学与分子生物学相互渗透融合而形成的一门学科,主要研究病毒基因组结构与功能,探寻病毒基因组复制、基因表达及其调控机制,提示病毒感染、致病的分子本质,为病毒基因工程疫苗和抗病毒药物的研制以及病毒病的诊断、预防和治疗提供理论基础及其依据。

《分子病毒学原理》这本书由英国莱斯特大学的资深教授 Alan J. Cann 博士主编。Alan J. Cann 博士在美国和英国都有工作经验,他教授本科生,研究生和博士生,主要研究分子病毒学和病毒发病机制。本书由 Elsevier 出版集团出版,该教材自 1992 年 10 月出版第一版以来,每隔几年再版一次,分别于 1996 年、2000 年和 2005 年出版了第二版、第三版和第四版,目前已至第五版。在第五版中作者以简明、清晰、图文并茂的风格论述现代分子病毒学。内容主要包括:病毒基础知识、病毒颗粒、病毒基因组、病毒复制、基因表达、病毒感染、病理机制、亚病毒介质等。书后附有词汇和缩写、亚病毒成员感染的分类、病毒学历史等。本书在国外的许多院校作为推荐教材,美国微生物学会称其“特色鲜明,比同类书中的任何一本都更适合大学生使用”。

病毒学的教学和科研在武汉大学有着悠久的历史。教学方面有针对非生物专业的全校通识课,对本科生的主干课,对研究生的选修课。其中对本科生的教学课程经历几代人的努力,从 1978 年至今未曾间断。多年的教学和科研经验让我选择了能综合介绍当今病毒学各个领域最新发展,并兼顾双语教学需要的本书作为教学用书。本书有三个特点:一是内容较为全面,从概论的角度介绍了病毒的生物学特征(颗粒,基因组,复制,表达,感染,病理机制以及亚病毒成员)。其中还介绍了近年来新出现的病毒病,并穿插了很多病毒学领域中分子生物学层面的最新研究进展。二是深入浅出,直观形象。该书虽是英文教科书,但其语言描述通俗易懂,并附有大量的插图,学生容易理解,对提高学生的专业英文水平也很有益处。三是该书含有国外重要病毒学学习网站的链接,更方便学生学习,特别是对那些学有余力的同学提供了很好的学习平台。可以说,全面、新颖和可读性强是该

教材的基本特点。

该书的编排方式科学,遵循从小到大,从简单到复杂,从细胞到个体的原则。具体而言第一章引言部分介绍了病毒的基本概念,病毒学的历史和常规研究病毒的方法,主要包括活体寄生系统方法,细胞培养方法,血清学/免疫学方法,超结构研究,分子生物学方法。

第二章介绍了病毒颗粒的功能和形成。讲解了病毒利用颗粒中包含的信息通过衣壳对称性构建复杂颗粒结构。主要以螺旋对称病毒、正 20 面体病毒和其他常见病毒类型为例阐述了蛋白质-核酸相互作用和基因组包装,病毒受体识别和结合,病毒衣壳与寄主细胞的其他相互作用。

第三章介绍了病毒基因组的结构和复杂性。按照病毒基因组的分类讲解了“大”DNA 基因组病毒,“小”DNA 基因组病毒,正链 RNA 病毒,负链 RNA 病毒,片段化和多组分病毒基因组及每类病毒基因组中的主要代表。同时简要介绍了分子遗传学,病毒遗传学中病毒的突变、逆转录、转座、进化和现代流行病学。

第四、五、六章介绍了病毒的复制,遗传信息的表达和病毒的感染。重点以噬菌体为例讲解了病毒吸附、穿透、脱壳,基因的复制和表达、组装、成熟、释放。也包括其他原核生物基因表达的调控,真核生物基因表达的调控以及表达的转录调控和转录后调控。植物、动物对病毒感染的免疫应答,以及病毒如何逃避宿主的免疫应答机制。简要介绍了病毒感染的预防和基因治疗方法。

第七、八章介绍了病理机制及病毒相关的疾病如艾滋、癌症等,并简要介绍了新出现的病毒,亚病毒成员如无病毒基因组,无基因组病毒,伴随体和类病毒,并重点介绍了朊病毒。

因为本教材的内容十分丰富,可根据授课学时对课程教学内容做出选择。一方面,对非关键的内容,如教材中的第二章将病毒的颗粒中衣壳对称性和病毒构建的空间结构算法等内容进行简要介绍,将之作为阅读材料供学生课后阅读;对与其他课程有重复的内容,如病毒感染与凋亡的内容与细胞生物学内容重复,病毒感染与免疫应答中部分内容与免疫学内容重复,则可简要介绍,鼓励感兴趣的同学继续查阅最新的研究进展。另一方面,授课教师查阅大量资料,对教材内容作必要的补充。针对目前病毒学研究的重点方向是医学病毒,也可以介绍流感病毒、SARS 病毒、乙型肝炎病毒、艾滋病毒、甲型流感病毒,手足口病病毒等新出现的或引起严重流行趋势的病毒病等专题。同时,推荐人民卫生出版社 2002 年出版的中文版《分子病毒学》作为学生的学习参考教材,方便学生通过中文材料进一步巩固和强化病毒学相关基础知识。也建议理论和实际相联系,教学与科研相结合,配合相关的病毒学实验课程,最大限度地利用现有软硬件资源为提高我国的“分子病毒学”的教学水平做出重要的贡献。

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第五版前言

这本书我差点没写成。第四版出版以来,我本人发生了很多改变。因此开始讨论是否该出版新版本时,我有些犹豫。在我看来,最重要的改变之一就是 MicrobiologyBytes.com 网站的创办,以及相关的网页空间,例如 MicrobiologyBytes 在 Facebook 上的网页。用 Elvis Costello 的话说,“我每天都在写这本书”。那么为什么你还要阅读它呢? 尽管在很多方面互联网都远胜印刷书籍,但我们仍对这本书有着强烈的需求,因为有时能在同一个地方获得所有核心知识是很好的(例如准备考试复习时)。外加上一个版本的其他语言的译版(如中文版),以及亚马逊 Kindle 的版本,我将以这种方式使更广泛的读者受益。

我同意撰写新版本后,就一直想做到两件事。首先我想全面地更新技术知识,但与此同时我也需要根据过去几年在网上撰写文章的经验,完全地重著整本书,以使得这本书能够更易为读者接受。但愿我已经做到了这一点。

感谢 Elsevier 的全体成员,没有你们的辛勤工作和坚强的信念,这版书将无法问世。尽管我们并没有见过面,但是他们的邮件一直存在于我的收件箱内,时刻提醒着我该交稿了。

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2011 年 1 月

Preface to the Fifth Edition

This is the book I nearly didn't write. Quite a lot has changed for me since the fourth edition was published, and when discussions began as to whether to produce a new edition, I had my doubts. From my perspective, one of the main things that has changed is MicrobiologyBytes.com—there, and in related spaces such as the MicrobiologyBytes page on Facebook, in the words of Elvis Costello, "Every day I write the book." So why are you reading this? Although the Internet is far better than printed books for many things, there is clearly still a strong demand for this book because sometimes it's good to have a core of knowledge in one place (e.g., when it comes to revision for exams). Add to that the translations into other languages (including Chinese) that the last edition received, plus the Amazon Kindle version, and I can reach a wide and appreciative audience in this format.

Once I had agreed to write a new edition, I wanted to do two things. I wanted to update the technical knowledge throughout, but I also needed to completely rewrite the whole book to make it far more accessible, based on the experience I have gained writing online over the past few years. Hopefully I have achieved that.

I would like to thank all the staff of Elsevier, without whose hard work and persuasion this edition would never have appeared. Although we have never met face to face, they reside in my inbox, constantly reminding me that chapters are overdue.

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January 2011

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Introduction

WHAT'S IN THIS CHAPTER?

- ☛ We start by asking what a virus is, and we look at how viruses are different from all other organisms. Are viruses alive? It doesn't matter to a virus, but it is a frequently asked question, so we will consider possible answers.
- ☛ Then we spend a short time looking at the history of virology, because the way our present knowledge was acquired explains how we currently think about viruses.
- ☛ We finish by describing some techniques used to study viruses, ending right up to date with the most recent methods, which would have sounded like science fiction when the first edition of this book was published.

This book is about “molecular virology,” that is, virology at a molecular level. It looks at protein-protein, protein-nucleic acid, and protein-lipid interactions, which control the structure of virus particles; the ways viruses infect cells; and how viruses manage to replicate themselves. Later we will also examine the consequences of virus infection for host organisms, but it is important to consider the basic nature of viruses first. Before going into detail, it is useful to know a little about the history of virology, and in particular, how our present knowledge of viruses was achieved. Understanding this helps to explain how we think about viruses and what the current and future concerns of virologists are. That is the reason for this chapter.

There is more biological diversity between viruses than in all the rest of the bacterial, plant, and animal kingdoms put together. This is the result of the success of viruses in parasitizing all known groups of living organisms; understanding this diversity is the key to comprehending the interactions of viruses with their hosts. The principles behind some of the experimental techniques mentioned in this chapter may not be well known to all readers, so it may be helpful to explore the further reading at the end of this chapter to

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become more familiar with these methods or you will not be able to understand the current research literature. In this and subsequent chapters, terms in the text in bold red print are defined in the glossary found in Appendix 1. **WEB** (the WEB icon) tells you that you can find an interactive learning resource on the web site.

BOX 1.1. DON'T SAY VIRAL TO ME

If you read about viruses, you'll probably come across the word "viral" quite quickly. Most virologists use it these days, but I hate it. That's because the word virus is a noun, but "viral" is an adjective describing something relating to, or caused by a virus. As far as I'm concerned, using nouns as adjectives is wrong, but most people don't seem to mind this one. If you wanted to describe chicken soup, would you say it was chickenal flavored? If you want to use the word viral, good luck to you, just don't say it to me unless you use it properly, for example, "antiviral drug."

WHAT ARE VIRUSES?

Viruses are submicroscopic, obligate intracellular parasites. They are too small to be seen by optical microscopes, and they have no choice but to replicate inside host cells. This simple but useful definition goes a long way toward describing viruses and differentiating them from all other types of organisms. However, this short definition is not completely adequate. It is not a problem to differentiate viruses from multicellular organisms such as plants and animals. Even within the broad scope of microbiology covering prokaryotic organisms as well as microscopic eukaryotes such as algae, protozoa, and fungi, in most cases this simple definition is enough. However, a few groups of prokaryotic organisms also have specialized intracellular parasitic life cycles and overlap with this description. These are the *Rickettsiae* and *Chlamydiae*—obligate intracellular parasitic bacteria that have evolved to be so cell-associated that they can exist outside the cells of their hosts for only a short period of time before losing viability. A common mistake is to say that viruses are smaller than bacteria. Though this is true in most cases, size alone does not distinguish them. The largest virus known (Mimivirus) is 400 nm in diameter, while the smallest bacteria (e.g., *Mycoplasma*) are only 200 to 300 nm long. Nor does genetic complexity separate viruses from other organisms. The largest virus genome (Mimivirus, 1.2 Mbp (million base pairs)) is twice as big as the smallest bacterial genome (*Mycoplasma genitalium*, 0.58 Mbp), although it is still shorter than the smallest eukaryotic genome (the parasitic protozoan *Encephalitozoon*, 2.3 Mbp). For these reasons, it is necessary to go further to produce a definition of how viruses are unique: