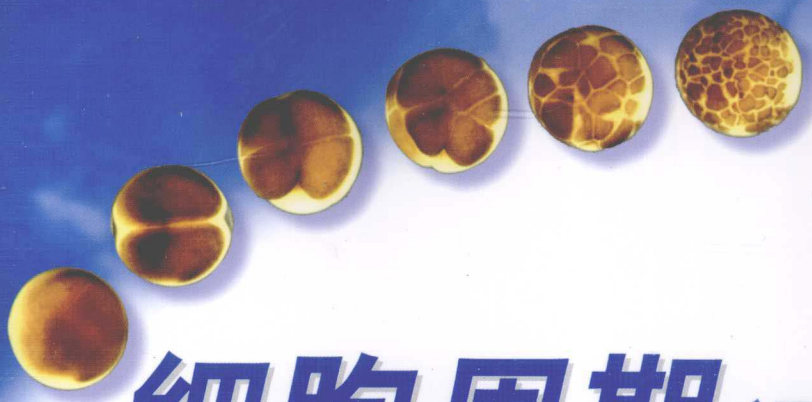
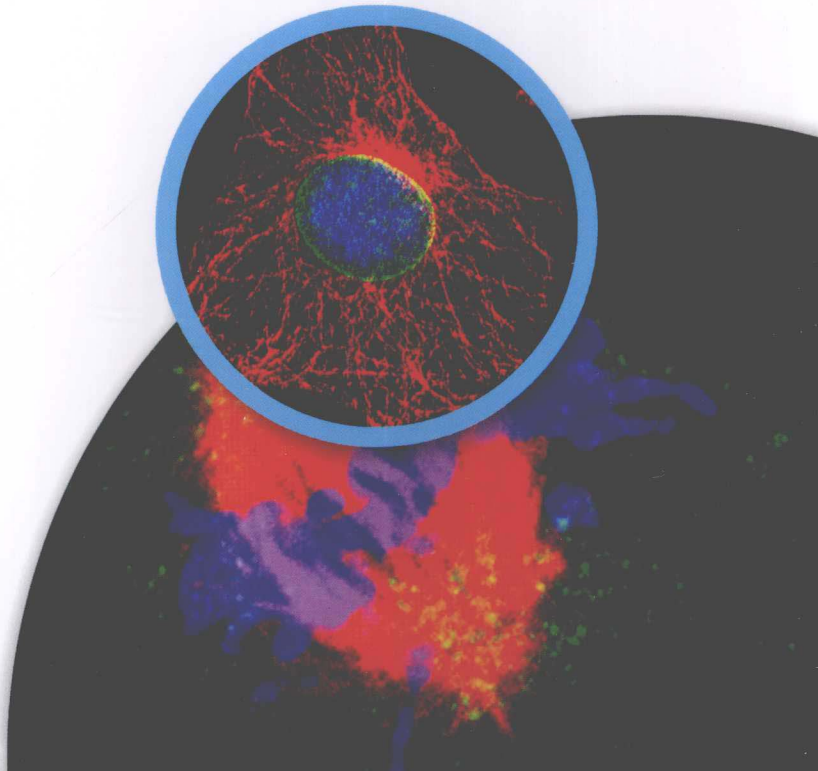
内附光盘



细胞周期调控原理

〔英〕 D.O.摩尔根 著
李朝军 潘飞燕 戴 谷 梁 娟 译

The Cell Cycle: Principles of Control



科学出版社
www.sciencep.com

细胞周期调控原理

[redacted]

The Cell Cycle: Principles of Control

细胞周期调控原理

The Cell Cycle: Principles of Control

〔英〕D. O. 摩尔根 著

李朝军 潘飞燕 戴 谷 梁 娟 译

科学出版社

北京

图字:01-2008-0360 号

内 容 简 介

本书是一本清楚简明的指导书,将大量的知识组织成一个连贯的框架,重点是强调细胞分裂的关键问题以及分子机制是如何进化解决这些问题的。全书共十二章,内容包括:细胞周期概述、模式生物、细胞周期调控系统、染色体复制、有丝分裂过程、胞质分裂、减数分裂、细胞增殖和生长的调控,以及 DNA 损伤反应和肿瘤的细胞周期。每一章节由多个小节组成,每个小节为两页,有限定的主题、正文、图例和定义,书后附有全书参考文献、词汇表以及索引。

本书利于从事细胞生物学研究和教学的教师以及研究人员参考使用,同时还可作为研究生和高年级本科生的学习用书。

本书正文中彩图请见随书所配光盘。

图书在版编目(CIP)数据

细胞周期调控原理/(英)摩尔根(Morgan, D. O.)著;李朝军,潘飞燕,戴谷,梁娟译. —北京:科学出版社,2010
ISBN 978-7-03-026962-1

Ⅰ.①细… Ⅱ.①摩…②李…③潘…④戴…⑤梁… Ⅲ.①细胞生物学 Ⅳ.①Q2

中国版本图书馆 CIP 数据核字(2010)第 040133 号

责任编辑:李 悦/责任校对:邹慧卿
责任印制:钱玉芬/封面设计:王 浩

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

铭浩彩色印装有限公司 印刷

科学出版社发行 各地新华书店经销

*

2010 年 4 月第 一 版 开本:890×1240 1/16
2010 年 4 月第一次印刷 印张:21
印数:1—3 000 字数:630 000

定价:75.00 元(含光盘)

(如有印装质量问题,我社负责调换)

译 者 序

从事细胞生物学的教学和科研近二十年，现在依然对细胞这个奇妙、精细、漂亮的结构兴致不减。各种大小分子构成了细胞，不同的细胞构成了人，众多的人组成了社会。从某种意义上来说，细胞、人、社会存在着共性，它们都是多维的集合体，对它们的研究可从时间和空间等多重尺度来考虑。经过细胞生物学家们近几十年的不懈努力，目前我们已经可以在时间这条轴线上对细胞有一个比较初步的了解。当然，这还仅仅只是一个开始，大量的空白依然需要后人来进行填补，更正或是挖掘，尤其是在空间尺度上。

细胞是生命活动的最小单位，和生命体一样，存在“生、老、病、死”的过程。其中的“生”——细胞分裂，是大家最喜欢研究和描述的话题。然而《细胞周期调控原理》这本书却有着自己鲜明的特性。每一章的每一节都可以说一个单独的课题，无论是用来教学还是科研参考都很有效。整本书聚焦于细胞周期调控系统，着重探讨调控系统对细胞周期各个事件的调控作用，以及影响调控系统本身的调控因素。特别是对一些细胞分裂、增殖的经典实验做了重点的说明。该书可作为生物学及医学专业研究生的参考用书，也适用于从事临床科学研究的工作人员。因此我们很乐意将摩尔根的这本外文原著翻译成中文介绍给大家。

译文的第一章到第六章由潘飞燕翻译，第七章到第十一章由李朝军翻译，第十二章由戴谷翻译，梁娟负责全文插图的翻译和改造，全文的统筹由李朝军负责。不过现在看来，我们答应科学出版社的约稿可能有些轻率。着手翻译的时候才发现，翻译一本书似乎比重新写一本书更难。不过在大家的共同努力下，最后终于完成。但鉴于我们自身水平有限，在对该书的理解以及中英文的表达上还存在很多的落差，译文中难免有不妥，甚至错误之处，敬请广大读者批评指正，我们将不胜感激！

李朝军

2010.2

前　言

细胞生物学的第一个世纪属于细胞学家，他们在显微镜前的辛苦观察结果揭示出所有的活体事物都由称为细胞的基本单位构成，所有的细胞都由先前存在的细胞分裂而来，每个子细胞含有与母细胞相同的一套染色体。在20世纪的转折期，细胞学和遗传学新兴领域的碰撞发现了染色体是遗传的物质决定者。随后出现了更为巨大的融合，完全隶属于不同领域的细胞学、遗传学和生物化学意识到所有的真核细胞利用相似的分子装置和调控机制来执行并指导染色体复制和细胞分裂的事件。我们现在可以自豪地回顾发现这些机制的令人惊奇的二十年，但是我们面临着一个新的问题：虽然有大量的信息存在，但这些信息如何整合成一个整体还没有清楚的认识。

本书致力于解决这一问题。我的目标是提供一本清楚简明的指导书，将大量的知识组织成一个连贯的框架，重点是强调细胞分裂的关键问题以及分子机制是如何进化解决这些问题的。尽管围绕关键法则来进行组织，但本书并不规避所谓的细节。相反，它涵盖了我们对细胞分裂了解的每一层面，如从细胞学家对主要事件的描述到生化学家在原子水平上对蛋白质结构的分析以及那些事件中的化学反应。所有这些层面都非常重要，也是十分迷人的。建筑师 Le Corbusier 在1935年描写现代航空器在形式和功能方面的惊人汇合时，说得更为有力："没有'细节'，一切都是整体的重要部分。本质上微观世界和宏观世界是一个整体。"

我衷心地感谢在撰写本书时很多同事提供了富有思想性和建设性的意见（见致谢），但我将对其中包含的信息负全部责任。大家都知道，教学原则有时要求夸大某些事实而忽略其他一些信息。对于那些过度强调或没有强调的科学发现，我向那些科学家表示歉意。

撰写本书初期，我并没有全身心地投入到其中，而是在瑞典乌普萨拉大学进行为期八个月的休假。在此之后的六年中，我每个暑假都回到乌普萨拉大学，在安静的生物化学中心图书馆进行写作，感谢这里的 Car-Hendrik Heldin 和他那些在 Ludwig 癌症研究所乌普萨拉分部的同事们，与他们在一起，我享受着撰写过程中无数次的讨论与午餐。

本书写成的每一步都受到 Miranda Robertson 和她在 New Science Press 的团队成员给予灵感性的指导。万分感谢 Eleanor Lawrence 卓越的编辑以及 Matthew McClements 精美的注解。也感谢 Karen Freeland，他和 Kerry Gardiner、Joanna Miles 一起给予了本项目热心熟练的指导。Lore Leighton 提供了极具价值的蛋白质结构图，Bruce Goatly 为印刷做了大量的工作。

最后，我要感谢我的家人，同时也向他们表示歉意，是他们一直陪伴在我身边，给予我理解和坚定不懈的支持。

David O Morgan

致　谢

The following individuals provided expert advice on entire chapters or parts of chapters:

Chapter 1 John Gerhart, University of California, Berkeley; Rebecca Heald, University of California, Berkeley; Andrew Murray, Harvard University; Kim Nasmyth, University of Oxford

Chapter 2 Bruce A. Edgar, Fred Hutchinson Cancer Research Center

Chapter 3 William G. Dunphy, California Institute of Technology; Bruce Futcher, Stony Brook University; J. Wade Harper, Harvard Medical School; Douglas Kellogg, Sinsheimer Laboratories, University of California, Santa Cruz; Charles Sherr, St. Jude Children's Research Hospital; Michael D. Tyers, Samuel Lunenfeld Research Institute, Mount Sinai Hospital

Chapter 4 John Diffley, Cancer Research UK; Paul Kaufman, University of Massachusetts Medical School; Matthew Michael, Harvard University; Johannes Walter, Harvard Medical School

Chapter 5 William G. Dunphy, California Institute of Technology; Tatsuya Hirano, Cold Spring Harbor Laboratory; Douglas Koshland, Carnegie Institution of Washington; Jonathon Pines, University of Cambridge

Chapter 6 Arshad Desai, University of California, San Diego; Rebecca Heald, University of California, Berkeley; Tarun Kapoor, Rockefeller University;

Chapter 7 Angelika Amon, Massachusetts Institute of Technology; Sue Biggins, University of Washington; Jonathon Pines, University of Cambridge; Frank Uhlmann, Cancer Research UK

Chapter 8 Bruce Bowerman, University of Oregon; Christine Field, Harvard Medical School; Michael Glotzer, The University of Chicago; Rong Li, Stowers Institute for Medical Research

Chapter 9 Angelika Amon, Massachusetts Institute of Technology; R. Scott Hawley, Stowers Institute for Medical Research; Neil Hunter, University of California, Davis; Nancy Kleckner, Harvard University

Chapter 10 Nicholas Dyson, Massachusetts General Hospital Cancer Center; Bruce A. Edgar, Fred Hutchinson Cancer Research Center; Martin Raff, University College London

Chapter 11 Karlene Cimprich, Stanford University School of Medicine; Stephen J. Elledge, Harvard Medical School; David Toczyski, University of California, San Francisco; Rodney Rothstein, Columbia University

Chapter 12 J. Michael Bishop, The George Williams Hooper Foundation, University of California, San Francisco; Paul Edwards, Hutchison/MRC Research Centre, University of Cambridge; Gerard Evan, University of California, San Francisco

We are grateful to the following for providing or permitting the use of illustrations:

Figure 1-4 Polytene chromosomes packed in the nucleus of a cell from the *Drosophila* salivary gland. Courtesy of John Sedat.

Figure 2-1 The budding yeast *Saccharomyces cerevisiae* and the fission yeast *Schizosaccharomyces pombe*. Panel (a) courtesy of Greg Tully; panel (b) courtesy of Kathleen Gould.

Figure 2-2 Early divisions in the frog *Xenopus laevis*. Courtesy of James C. Smith and Huw Williams.

Figure 2-3 Patterns of cell division in the early embryo of the fly *Drosophila melanogaster*. Courtesy of Tony Shermoen and Patrick O'Farrell.

Figure 2-4 Mammalian cells growing in culture. Courtesy of Susanne Steggerda.

Figure 2-7 Cell-cycle arrests in budding yeast *cdc* mutants. Courtesy of Greg Tully.

Figure 2-17 Analysis of cellular DNA content by flow cytometry. Courtesy of Liam Holt.

Figure 2-18 Synchronous progression through the cell cycle. Courtesy of Pei Jin.

Figure 4-6 Identification of a replicon cluster by radioactive labeling. Adapted from Huberman, J.A. and Tsai, A.: **Direction of DNA replication in mammalian cells.** *J. Mol. Biol.* 1973, 75:5–12.

Figure 4-7 Replication foci in nuclei of S-phase cells. Courtesy of Brian Kennedy.

Figure 4-8 Association of the ORC with replication origins in *Drosophila* follicle cells. Photographs kindly provided by Stephen P. Bell. From Austin, R.J., Orr-Weaver, T.L. and Bell, S.P.: ***Drosophila* ORC specifically binds to ACE3, an origin of DNA replication control element.** *Genes Dev.* 1999, 13:2639–2649. ©1999 Cold Spring Harbor Laboratory Press.

Figure 4-12 Rereplication in yeast cells with deregulated ORC, Mcm2–7 and Cdc6. Courtesy of Van Nguyen and Joachim Li.

Figure 4-25b Basic units of chromatin structure. From Bednar, J., Horowitz, R.A., Grigoryev, S.A., Carruthers, L.M., Hansen, J.C., Koster, A.J. and Woodcock, C.L.: **Nucleosomes, linker DNA, and linker histone form a**

unique structural motif that directs the higher-order folding and compaction of chromatin. *Proc. Natl Acad. Sci. USA* 1998, **95**:14173–14178. Copyright 1998 National Academy of Sciences, U.S.A.

Figure 5-16 Localization of Plk in mitotic cells. Kindly provided by Francis Barr and Ulrike Grunewald. From Barr, F.A., Sillje, H.H. and Nigg, E.A.: **Polo-like kinases and the orchestration of cell division.** *Nat. Rev. Mol. Cell Biol.* 2004, 5:429–440.

Figure 5-18 Localization of aurora kinases in mitotic cells. Courtesy of Toru Hirota.

Figure 5-21 Models of SMC and cohesin structure. Panels (a) and (b) reproduced from **The Journal of Cell Biology, 2002, 156, 419–424** by copyright permission of The Rockefeller University Press.

Figure 5-22 Condensation and resolution of human sister chromatids in early mitosis. Kindly provided by Adrian T. Sumner. From Sumner, A.T.: **Scanning electron microscopy of mammalian chromosomes from prophase to telophase.** *Chromosoma* 1991, **100**:410–418. With kind permission of Springer Science and Business Media.

Figure 5-25 Structure of condensin. Panels (a) and (b) reproduced from **The Journal of Cell Biology, 2002, 156, 419–424** by copyright permission of The Rockefeller University Press.

Figure 5-26 Plk and aurora B are required for the removal of cohesin from chromosome arms in early mitosis. From Losada, A., Hirano, M. and Hirano, T.: **Cohesin release is required for sister chromatid resolution, but not for condensin-mediated compaction, at the onset of mitosis.** *Genes Dev.* 2002, **16**:3004–3016. ©2002 Cold Spring Harbor Laboratory Press.

Figure 6-1 Anatomy of the mitotic spindle. Panels (b) and (d) courtesy of Andrew Bajer.

Figure 6-6 Control of microtubule dynamics by associated proteins. Courtesy of Kazuhisa Kinoshita.

Figure 6-8 The mammalian centrosome Micrograph kindly provided by William R. Brinkley. Reprinted from *Ultrastruct. Res.*, Volume 57, McGill, M., Highfield, D.P., Monahan, T.M. and Brinkley, B.R.: **Effects of nucleic acid specific dyes on centrioles of mammalian cells**, Pages 43–53, ©1976, with permission from Elsevier.

Figure 6-10 The spindle pole body of budding yeast. Panel (a) kindly provided by Thomas H. Giddings and Mark Winey. Reprinted from *Curr. Opin. Cell Biol.*, Volume 14, Fisk, H.A., Mattison, C.P. and Winey, M.: **Centrosomes and tumour suppressors**, Pages 700–705, ©2002, with permission from Elsevier. Panel (c) kindly provided by Ian R. Adams. Reprinted from *Trends Cell. Biol.*, Volume 10, Adams, I.R. and Kilmartin, J.V.: **Spindle pole body duplication: a model for centrosome duplication?**, Pages 329–335, ©2000, with permission from Elsevier.

Figure 6-12 Reduplication of centrosomes in prolonged S-phase arrest. Courtesy of Edward H. Hinchcliffe.

Figure 6-13a Kinetochore structure. Courtesy of Jeremy Pickett-Heaps.

Figure 6-14a A possible mechanism for dynamic kinetochore–microtubule attachment. Photograph kindly provided by Stefan Westermann and Georjana Barnes. Reprinted from *Mol. Cell*, Volume 17, Westermann, S., Avila-Sakar, A., Wang, H.W., Niederstrasser, H., Wong, J., Drubin, D.G., Nogales, E. and Barnes, G.: **Formation of a dynamic kinetochore–microtubule interface through assembly of the Dam1 ring complex**, Pages 277–290, ©2005, with permission from Elsevier.

Figure 6-16 Recruitment of γ-tubulin to mitotic centrosomes. Images kindly provided by Alexey Khodjakov. Reproduced from **The Journal of Cell Biology, 1999, 146, 585–596** by copyright permission of The Rockefeller University Press.

Figure 6-18 Nuclear envelope breakdown in mitosis. Photographs kindly provided by Jan Ellenberg and Brian Burke. From Burke, B. and Ellenberg, J.: **Remodelling the walls of the nucleus.** *Nat. Rev. Mol. Cell Biol.* 2002, 3:487–497. Reprinted with copyright permission from Nature.

Figure 6-19 Fragmentation of the Golgi apparatus in mitosis. Photographs kindly provided by Joachim Seemann. Reprinted, with permission, from the *Annual Review of Cell and Developmental Biology*, Volume **18** ©2002 by Annual Reviews www.annualreviews.org

Figure 6-21b Stabilization of microtubules around chromosomes by Ran–GTP. Kindly provided by Rebecca Heald. Reprinted with permission from Kalab, P., Weis, K. and Heald, R.: **Visualization of a Ran-GTP gradient in interphase and mitotic *Xenopus* egg extracts.** *Science* 2002, **295**:2452–2456. Copyright 2002 AAAS.

Figure 6-23b Kinetochore-derived microtubule formation. Kindly provided by Helder Maiato and Alexey Khodjakov. Reproduced from **The Journal of Cell Biology, 2004, 167, 831–840** by copyright permission of The Rockefeller University Press.

Figure 6-25 Accumulation of syntelic attachments in the absence of aurora B kinase activity. Kindly provided by Michael A. Lampson and Tarun M. Kapoor. From Lampson, M.A., Renduchitala, K., Khodjakov, A. and Kapoor, T.M.: **Correcting improper chromosome-spindle attachments during cell division.** *Nat. Cell Biol.* 2004, 6:232–237. Reprinted with copyright permission from Nature.

Figure 6-27b Poleward force generation by the kinetochore. Kindly provided by Stefan Westermann and Georjana Barnes. Reprinted from *Mol. Cell*, Volume 17, Westermann, S., Avila-Sakar, A., Wang, H.W., Niederstrasser, H., Wong, J., Drubin, D.G., Nogales, E. and Barnes, G.: **Formation of a dynamic kinetochore–microtubule interface through assembly of the Dam1 ring complex**, Pages 277–290, ©2005, with permission from Elsevier.

Figure 7-6 Spindle checkpoint component Mad2 at unattached kinetochores. Kindly provided by Jennifer C. Waters. Reproduced from **The Journal of Cell Biology, 1998, 141, 1181–1191** by copyright permission of The Rockefeller University Press.

Figure 7-7 Alternative conformations of the Mad2 protein. Adapted from Curr. Biol., Volume **15**, De Antoni, A., Pearson, C.G., Cimini, D., Canman, J.C., Sala, V., Nezi, L., Mapelli, M., Sironi, L., Faretta, M., Salmon, E.D. and Musacchio, A.: **The Mad1/Mad2 complex as a template for Mad2 activation in the spindle assembly checkpoint**, Pages 214–225, ©2005, with permission from Elsevier. Original structure graphics kindly provided by Andrea Musacchio.

Figure 7-15 Anaphase defects in the presence of nondegradable cyclin mutants. Photographs kindly provided by Devin Parry and Patrick O'Farrell. Reprinted from *Curr. Biol.*, Volume **11**, Parry, D.H. and O'Farrell, P.H.: **The schedule of destruction of three mitotic cyclins can dictate the timing of events during exit from mitosis**, Pages 671–683, ©2001, with permission from Elsevier.

Figure 7-16 The APC helps promote spindle disassembly in budding yeast. Photographs kindly provided by David Pellman. Reprinted, with permission, from Juang, Y.-L., Huang, J., Peters, J.-M., McLaughlin, M.E., Tai, C.-Y. and Pellman, D.: **APC-mediated proteolysis of Ase1 and the morphogenesis of the mitotic spindle.** *Science* 1997, **275**:1311–1314. Copyright 1997 AAAS.

Figure 7-17 Nuclear envelope assembly in *Xenopus* embryo extracts. Photographs kindly provided by Martin Hetzer and Iain Mattaj. From Hetzer, M., Meyer, H.H., Walther, T.C., Bilbao-Cortes, D., Warren, G. and Mattaj, I.W.: **Distinct AAA-ATPase p97 complexes function in discrete steps of nuclear assembly.** *Nat. Cell Biol.* 2001, **3**:1086–1091. Reprinted with copyright permission from Nature.

Figure 8-7 Control of cytokinesis by the RhoGEF Pebble in the *Drosophila* embryo. Kindly provided by Sergei N. Prokopenko and Hugo J. Bellen. From Prokopenko, S.N., Brumby, A., O'Keefe, L., Prior, L., He, Y., Saint, R. and Bellen, H.J.: **A putative exchange factor for Rho1 GTPase is required for initiation of cytokinesis in *Drosophila*.** *Genes Dev.* 1999, 13:2301–2314. ©1999 Cold Spring Harbor Laboratory Press.

Figure 8-9a Microtubule behavior in the cleaving *Xenopus* embryo. Photograph kindly provided by Michael Danilchik and Kay Larkin. Reprinted from *Dev. Biol.*, Volume **194**, Danilchik, M.V., Funk, W.C., Brown, E.E. and Larkin, K.: **Requirement for microtubules in new membrane formation during cytokinesis of *Xenopus* embryos**, Pages 47–60, ©1998, with permission from Elsevier.

Figure 8-13 Positioning the contractile ring in *S. pombe*. Photographs kindly provided by Rafael R. Daga and Fred Chang. From Daga, R.R. and Chang, F.: **Dynamic positioning of the fission yeast cell division plane.** *Proc. Natl Acad. Sci. USA* 2005, **102**:8228–8232. Copyright 2005 National Academy of Sciences, U.S.A.

Figure 8-14 Positioning of cytokinesis by the mitotic spindle of embryonic cells. Kindly provided by Charles B. Shuster and David R. Burgess. Reproduced from **The Journal of Cell Biology, 1999, 146, 981–992** by copyright permission of The Rockefeller University Press.

Figure 8-16 Mitosis without cytokinesis in the *Drosophila* embryo. Courtesy of Barbara Fasulo and William Sullivan.

Figure 8-18 Membrane transport during cellularization. Kindly provided by John C. Sisson. From Papoulas, O., Hays, T.S. and Sisson, J.C.: **The golgin Lava lamp mediates dynein-based Golgi movements during *Drosophila* cellularization.** *Nat. Cell Biol.* 2005, 7:612–618. Reprinted with copyright permission from Nature.

Figure 8-20 Asymmetric division in a *Drosophila* neuroblast. Kindly provided by Silvia Bonaccorsi. From Giansanti, M.G., Gatti, M. and Bonaccorsi, S.: **The role of centrosomes and astral microtubules during asymmetric division of *Drosophila* neuroblasts.** *Development* 2001, **128**:1137–1145. Reprinted with permission from The Company of Biologists Ltd.

Figure 9-6 Early steps in homolog pairing. Photographs kindly provided by Denise Zickler. From Tessé, S., Storlazzi, A., Kleckner, N., Gargano, S. and Zickler, D.: **Localization and roles of Ski8p protein in *Sordaria* meiosis and delineation of three mechanistically distinct steps of meiotic homolog juxtaposition.** *Proc. Natl Acad. Sci. USA* 2003, **100**:12865–12870. Copyright 2005 National Academy of Sciences, U.S.A.

Figure 9-7 Homolog pairing defects in a *spo11* mutant. Photographs kindly provided by Denise Zickler. From Storlazzi, A., Tessé, S., Gargano, S., James, F., Kleckner, N. and Zickler, D.: **Meiotic double-strand breaks at the interface of chromosome movement, chromosome remodeling, and reductional division.** *Genes Dev.* 2003, 17:2675–2687. ©1999 Cold Spring Harbor Laboratory Press.

Figure 9-8 Electron microscopic analysis of chromosome structure in leptotene and early zygotene. Photographs kindly provided by Jim Henle and Nancy Kleckner. Panel (b) from Stack, S.M. and Anderson, L.K.: **Two-dimensional spreads of synaptonemal complexes from solanaceous plants. II. Synapsis in**

Lycopersicon esculentum (tomato). *Am. J. Bot.* 1986, 73:264–281. Panels (c) and (d) from Albini, S.M. and Jones, G.H.: **Synaptonemal complex spreading in *Allium cepa* and *A. fistulosum*. I. The initiation and sequence of pairing.** *Chromosoma* 1987, 95:324–338.

Figure 9-9 The synaptonemal complex. Photographs in panel (b) kindly provided by Karin Schmekel. Top photograph from Schmekel, K. and Daneholt, B.: **Evidence for close contact between recombination nodules and the central element of the synaptonemal complex.** *Chromosome Res.* 1998, 6:155–159; with kind permission from Springer Science and Business Media. Photographs in panel (c) kindly provided by Carole Rogers and Shirleen Roeder. Reproduced from **The Journal of Cell Biology, 2000, 148, 417–426** by copyright permission of The Rockefeller University Press.

Figure 9-10 Chiasmata. Reprinted from *Cell*, Volume 111, Blat, Y., Protacio, R., Hunter, N. and Kleckner, N.: **Physical and functional interactions among basic chromosome organizational features govern early steps of meiotic chiasma formation**, Pages 791–802, ©2002, with permission from Elsevier. Photograph taken from John, B.: *Meiosis* (Cambridge University Press, New York, 1990).

Figure 9-12 Microtubules of the first meiotic spindle in budding yeast. Courtesy of Mark Winey.

Figure 9-16 Securin destruction is required for meiotic anaphase I in mouse oocytes. Photographs kindly provided by Mary Herbert. From Herbert, M., Levasseur, M., Homer, H., Yallop, K., Murdoch, A. and McDougall, A.: **Homologue disjunction in mouse oocytes requires proteolysis of securin and cyclin B1.** *Nat. Cell Biol.* 2003, 5: 1023–1025. Reprinted with copyright permission from Nature.

Figure 9-18 Inhibition of Cdk1 triggers DNA synthesis after meiosis I. Photographs kindly provided by Keita Ohsumi. Reprinted by permission from Macmillan Publishers Ltd: *The EMBO Journal*, Iwabuchi, M., Ohsumi, K., Yamamoto, T.M., Sawada, W. and Kishimoto, T.: **Residual Cdc2 activity remaining at meiosis I exit is essential for meiotic M-M transition in *Xenopus* oocyte extracts.** *EMBO J.* 2000, 19:4513–4523, copyright 2000.

Figure 10-9 Antagonistic functions of the two E2F homologs in *Drosophila*. Photographs kindly provided by Maxim Frolov. From Frolov, M.V., Huen, D.S., Stevaux, O., Dimova, D., Balczarek-Strang, K., Elsdon, M. and Dyson, N.J.: **Functional antagonism between E2F family members.** *Genes Dev.* 2001, 15:2146–2160. ©2001 Cold Spring Harbor Laboratory Press.

Figure 10-20 Patterns of *cdc25 (string)* expression in the fly embryo. Photographs kindly provided by Bruce Edgar. From Edgar, B.A., Lehman, D.A. and O'Farrell, P.H.: **Transcriptional regulation of string (cdc25): a link between developmental programming and the cell cycle.** *Development* 1994, 120:3131–3143. Reprinted with permission from The Company of Biologists Ltd.

Figure 10-24 Analysis of growth control in the *Drosophila* eye. Kindly provided by Duojia Pan. Reprinted by permission from Macmillan Publishers Ltd: *Nature Cell Biology*, Gao, X., Zhang, Y., Arrazola, P., Hino, O., Kobayashi, T., Yeung, R.S., Ru, B. and Pan, D.: **Tsc tumour suppressor proteins antagonize amino-acid–TOR signalling.** *Nat. Cell Biol.* 2002, 4:699–704, copyright 2002.

Figure 11-7 RPA-dependent recruitment of ATR to sites of DNA damage. Kindly provided by Stephen J. Elledge. Reprinted with permission from Zou, L. and Elledge, S.J.: **Sensing DNA damage through ATRIP recognition of RPA-ssDNA complexes.** *Science* 2003, 300:1542–1548. Copyright 1997 AAAS.

Figure 11-8 Recruitment of the 9-1-1 complex to sites of DNA damage. Courtesy of Justine Melo and David Toczyski.

Figure 11-14 Abnormal DNA structures at stalled replication forks in yeast *chk2* mutants. Courtesy of Massimo Lopes and Marco Foiani.

Figure 11-18 Generation of a DNA damage response in senescent human cells. Photographs kindly provided by Fabrizio d'Adda di Fagagna. Reprinted by permission from Macmillan Publishers Ltd: *Nature*, d'Adda di Fagagna, F., Reaper, P.M., Clay-Farrace, L., Fiegler, H., Carr, P., Von Zglinicki, T., Saretzki, G., Carter, N.P. and Jackson, S.P.: **A DNA damage checkpoint response in telomere-initiated senescence.** *Nature* 2003, 426:194–198, copyright 2003.

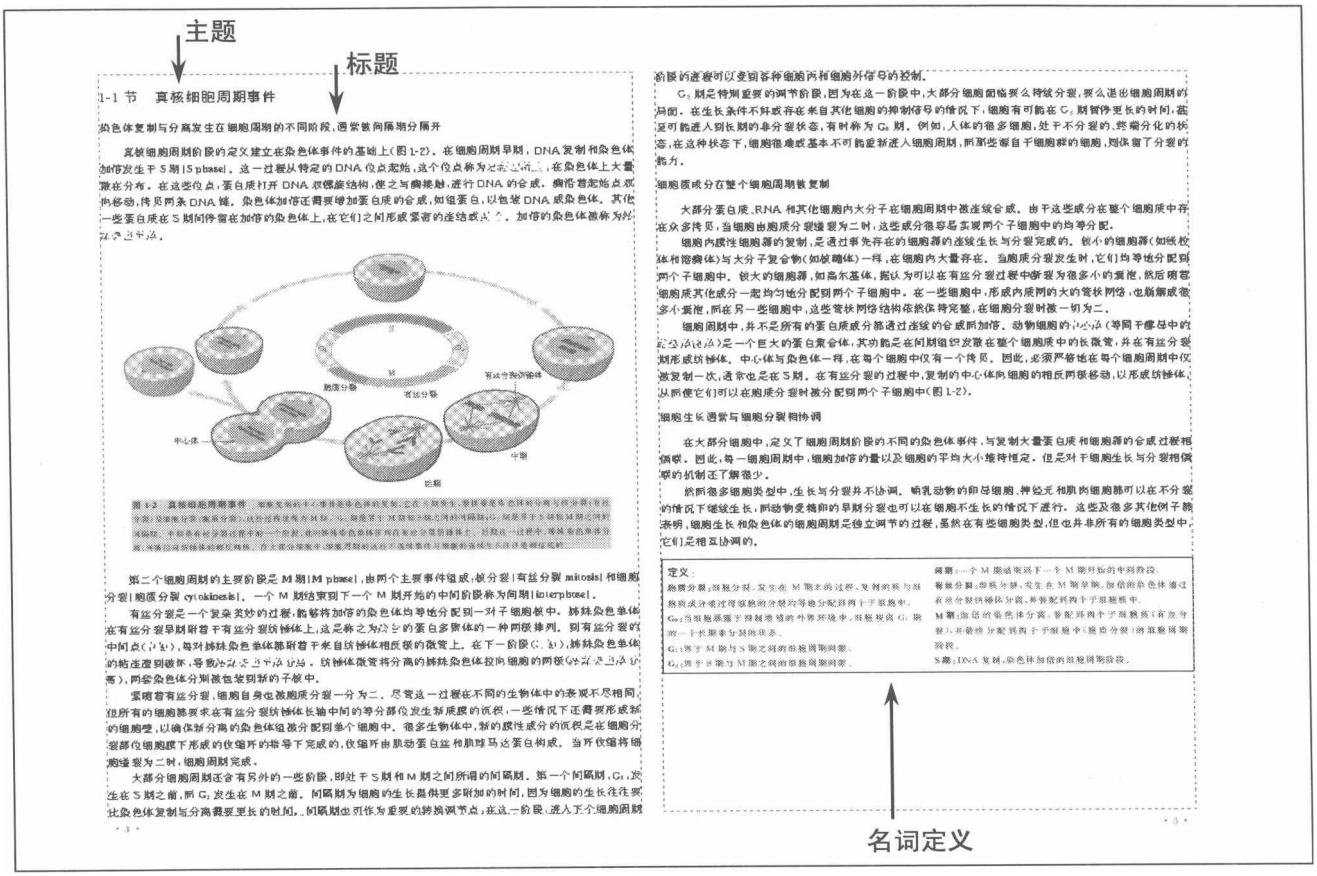
Figure 12-11 Chromosomal abnormalities in cancer cells. Courtesy of Kylie Gorringe, Mira Grigorova and Paul Edwards.

Figure 12-13 Telomere degeneration in the formation of carcinomas. Photograph kindly provided by Ronald A. DePinho. From Artandi, S.E., Chang, S., Lee, S.L., Alson, S., Gottlieb, G.J., Chin, L. and DePinho, R.A.: **Telomere dysfunction promotes non-reciprocal translocations and epithelial cancers in mice.** *Nature* 2000, 406:641–645. Reprinted with copyright permission from Nature.

Figure 12-15 Mitotic spindle defects arising from abnormal centrosome number. From Pihan, G.A., Wallace, J., Zhou, Y. and Doxsey, S.J.: **Centrosome abnormalities and chromosome instability occur together in pre-invasive carcinomas.** *Cancer Res.* 2003, 63:1398–1404.

Figure 12-18 Inhibition of the protein kinase Abl by imatinib. Reprinted from *Cancer Cell*, Volume 2, Shah, N. P., Nicoll, J.M., Nagar, B., Gorre, M.E., Paquette, R.L., Kuriyan, J. and Sawyers, C.L.: **Multiple BCR-ABL kinase domain mutations confer polyclonal resistance to the tyrosine kinase inhibitor imatinib (STI571) in chronic phase and blast crisis chronic myeloid leukemia**, Pages 117–125, ©2002, with permission from Elsevier.

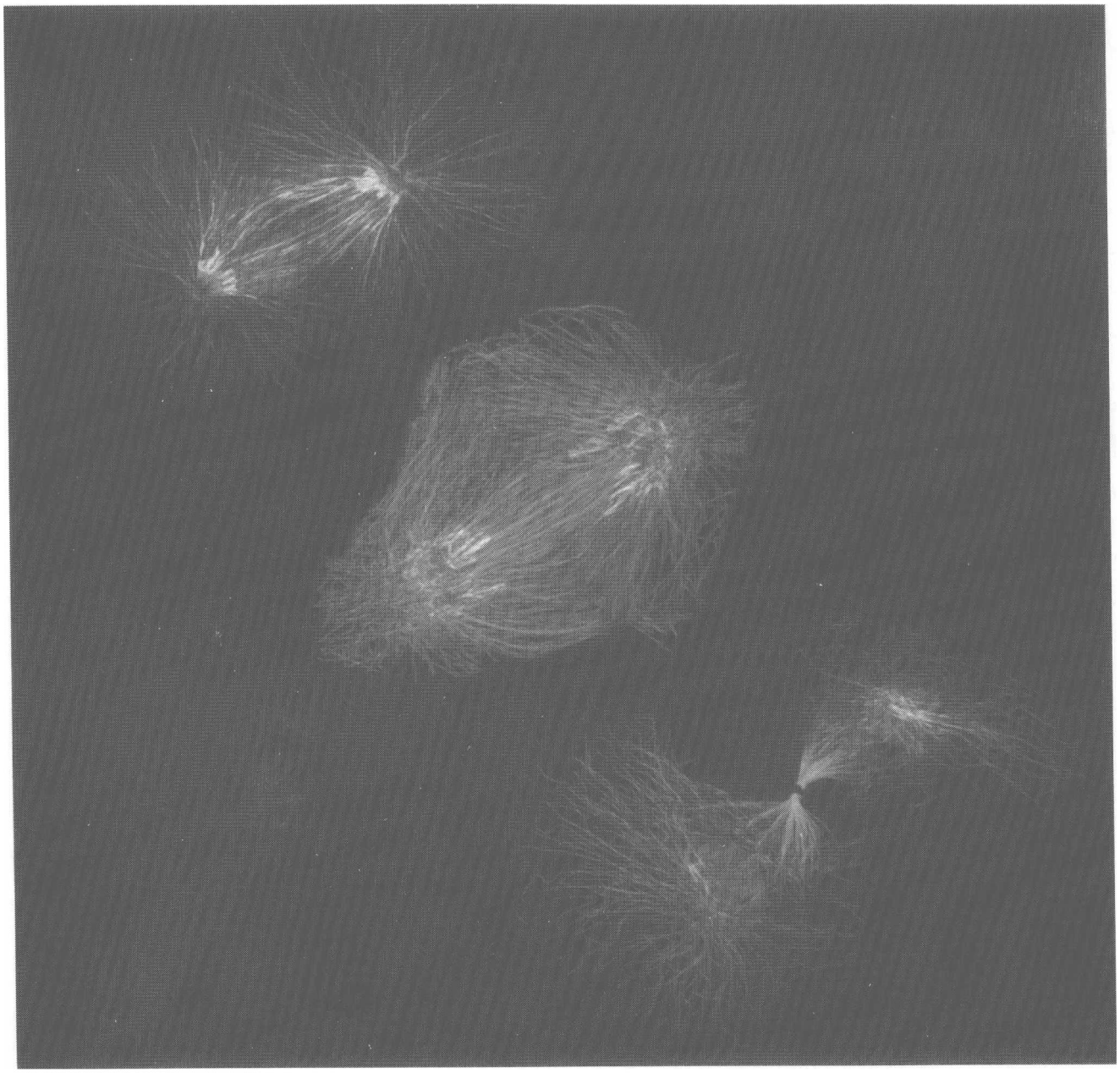
本书使用说明



《细胞周期调控原理》一书采用模块化原则编写，这样方便每个系列被用来教学，以及学习参考，同时也可使那些具有真正指导意义的重要内容进行整合。以上的示意图显示了这种模式化结构以及某些特殊的特征，即每一章节由多个小节组成，每个小节为两页，有限定的主题、正文、图例、定义等。每一小节中，全文被分成多个亚节，以一句话为标题，反映了行文的思路和章节整体的逻辑性。

全文通用的模式结构以及清晰的组织形式，利于教师们选择他们所要的素材，学生们也容易学习；对于工作在第一线的科研工作者，利用本书作为最新的参考文献，也可以寻找到他们所要进行的课题，或也可作为他们所需的任何一个课题的延续。

在本书最后部分，所有的定义和参考文献都被集中在一起，并明确标注了其所在的具体章节。词汇定义有时也包含了对文中定义的进一步阐述，参考文献包含了全部的作者而不仅仅是文中出现的简写名单。



细胞分裂的最后阶段，复制的染色体沿着由微管蛋白聚合物构成的轨道，被拉向母细胞的相反两端。
此图由 Julie Canman 惠供（见彩图光盘）。

目　录

第一章　细胞周期

细胞由称为细胞周期的一系列精细事件控制完成复制，在此过程中，染色体和其他成分被复制，然后分配到两个子细胞中。一个由调控蛋白构成的复杂网络控制了细胞周期阶段的进程。