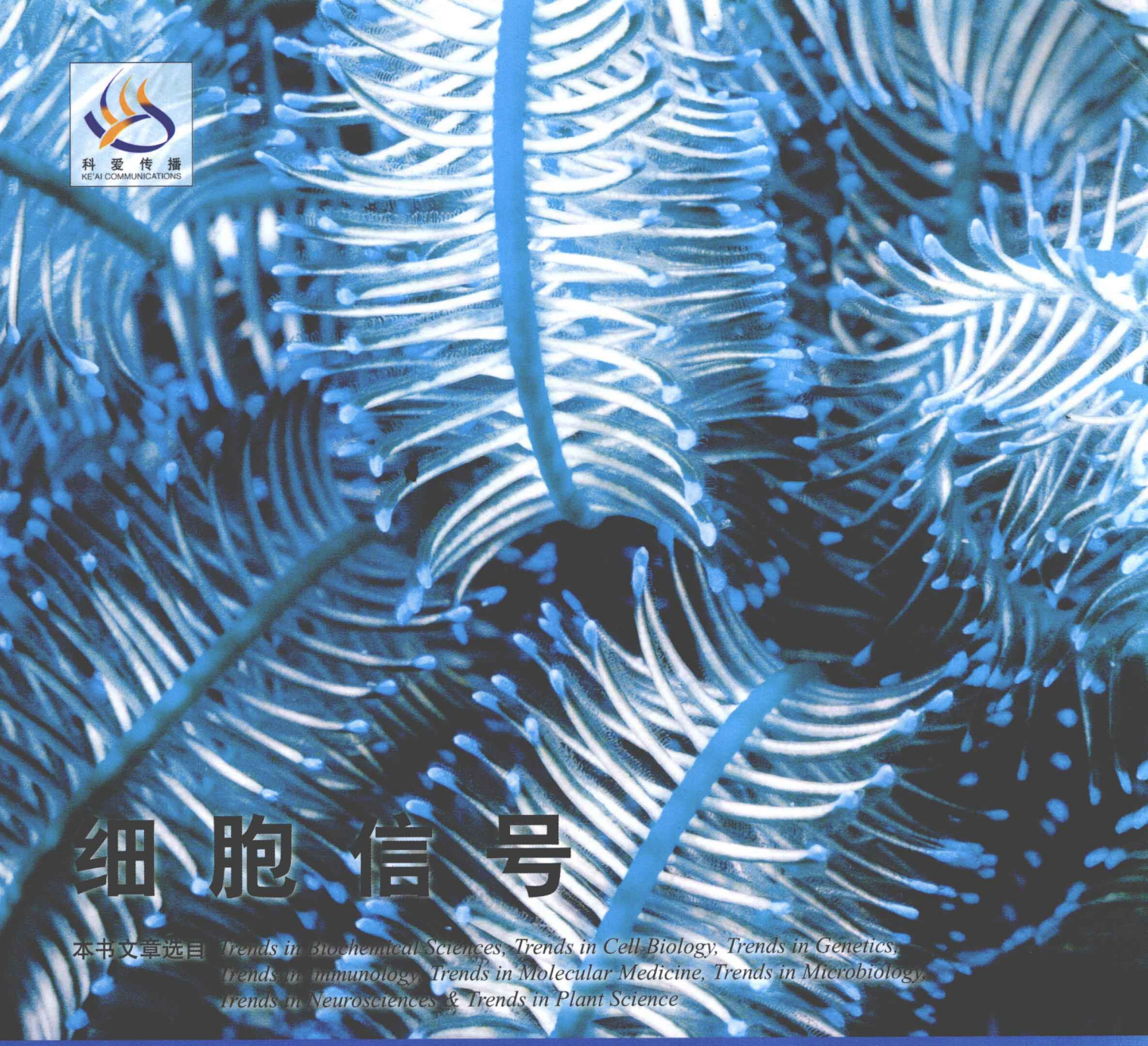

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细胞信号

本书文章选自 *Trends in Biochemical Sciences, Trends in Cell Biology, Trends in Genetics, Trends in Immunology, Trends in Molecular Medicine, Trends in Microbiology, Trends in Neurosciences & Trends in Plant Science*

NEW FOCUS in Life Sciences

生命科学新视野 3

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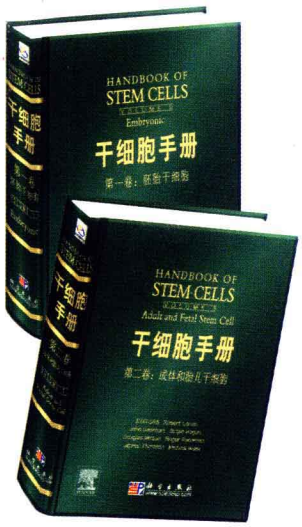

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Handbook of Stem Cells

《干细胞手册》（导读版）

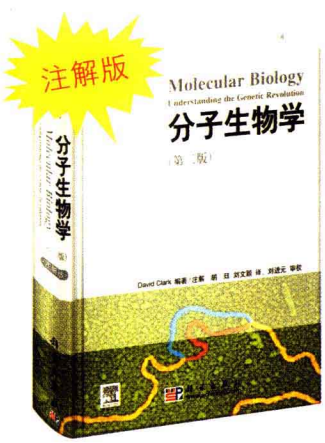
（第一卷：胚胎干细胞；第二卷：成体和胎儿干细胞）
原著：Robert Lanza 等
译注：裴雪涛　教授（军事医学科学院）等

干细胞领域的新发现对科研和社会的影响越来越深远，其最终将产生针对肿瘤、心脏病、糖尿病，以及影响人类健康的许多其他疾病的新的治疗手段。

《干细胞手册》这部书分为上下两册内容，整合了该领域必备的生物学知识、手段、方法、研究等，以及国际专家对于每一个特定的器官系统相关知识发展现状的介绍。干细胞领域的所有主题无一例外地被收录其中，包括基础生物学/机制、早期发育、外胚层、中胚层、内胚层、方法（例如如何分离和培养动物和人胚胎干细胞的具体描述）、针对特定人类疾病的干细胞的应用、法规与伦理，等等。它们凝集了 12 位编辑和超过 300 位学者和科学家的共同努力，正是他们开拓性的工作使得我们对干细胞有了精确的理解。

这两本书将成为学生和科研人员必备的全面的参考书。

美国国家科学院主席，一版再版、享誉世界的经典名著《细胞的分子生物学》（Molecular Biology of the Cell）的主编 Bruce Alberts 教授为本书作序。



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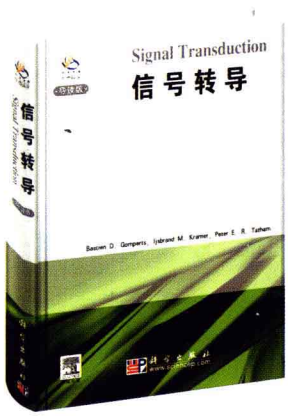
Molecular Biology: Understanding the Genetic Revolution

《分子生物学》第二版（注解版）

原著：[美]David Clark
中文注解翻译：刘进元等（清华大学）

本书分为 26 章，涉及数百个专题，基本上总括了分子生物学的基本理论、核心内容以及主要技术，并且涵盖了分子生物学领域的医学、农业和社会等方面的最新研究进展，是一本用来探索生物学问题的导向性教材。一位权威专家对本书的评价是这样的："本书内容覆盖之广，精辟独到的见解之多，让人不禁赞叹著者的工作是如此之出色。"。

* 满足读者两方面的需求：既要牢固掌握生物学专业的基本概念，又要对生物学的新发现和应用有所了解。
* 语言简洁，图文并茂，风格独特。
* 每页加中文注解和专业名词的中文解释。



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Signal Transduction

《信号转导》（导读版）

原著：Bastien D. Gomperts
导读：陈晔光（清华大学）

本书从基本概念开始，介绍了细胞怎样对外界刺激（激素、细胞因子、神经递质、黏附分子、细胞外基质等）作出反应，这些输入信号如何进行整合和协调。前半部分介绍基本概念，解释了第二信使（特别是环核苷酸和钙）的形成和作用，以及 GTP 结合蛋白介导的信号通路。其他章节涉及细胞因子和黏附分子介导的复杂信号级联的形成。本书的结尾在分子水平上描述了信号分子怎样与它们所处的环境相互作用，信号分子之间又是如何通过结构域相连的。

书中每个主题都由一篇历史性随笔引出，并大量引用参考文献，详细描述了关键实验，从而使读者了解最近和最前沿的研究工作。大量的概念性图片有助于对概念性内容的理解。

从始至终，作者面对争论，挑战教条，对模棱两可的论点进行了讨论，而页边的注释又添加了本书的趣味性。

本书是一本非常有价值的参考书，适用于生物化学与分子生物学、细胞生物学等相关专业的高年级大学生、研究生阅读，也可作为高校相关专业教师的教学和科研参考书，亦可供生物医学、药理学、免疫学及相关领域的研究人员参考。

New Focus in Life Sciences

细胞信号

3

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细胞信号

10 Centrosome control of the cell cycle

Trends in Cell Biology, Volume 15, Issue 6, June 2005 Pages 303-311

Stephen Doxsey, Wendy Zimmerman and Keith Mikule

中心粒控制着细胞周期

一个世纪以前，人们便发现了一个微小的、由辐射状排列的细胞质丝包围着的暗色结构。现在，我们已经知道那些丝状结构是微管，而那个暗色的细胞器是中心粒。不仅如此，中心粒的作用也比传统观念所认为的微管组织中心要重要得多。最新研究结果显示中心粒能够为许多调节蛋白的附着提供支撑骨架。细胞周期调控蛋白是其中一个调节蛋白。该蛋白与中心粒的结合是控制细胞周期所必需的。这些研究表明包括G1-S期、G2-有丝分裂期和中期到后期在内的数个分裂时期转换均需要中心粒的参与。本文讨论了一些最新的研究数据，这些数据都说明了中心粒和细胞周期循环的直接相关性。

19 Plant signalling: the inexorable rise of auxin

Trends in Cell Biology, Volume 16, Issue 8, August 2006 Pages 397-402

Andrew J. Fleming

植物信号转导——高涨的生长素

信号分子沿着细胞场运动形成了一种模式，该模式诱导不同细胞之间产生差异性反应，这是发育生物学的一个基本概念。最近，人们发现了一种新的调节植物生长因子（生长素）在组织中运动的系统，该系统通过控制生长素转运蛋白在亚细胞水平上的不对称分布来控制生长素的运动。对生长素极性运输的发育和生理学研究，揭示了一个控制器官发生、干细胞定位及植物对环境反应的基本机制。在这篇文章中，作者探讨了鉴定生长素转运蛋白以及这些蛋白参与生长素信号转导途径等方面的一些重要进展。

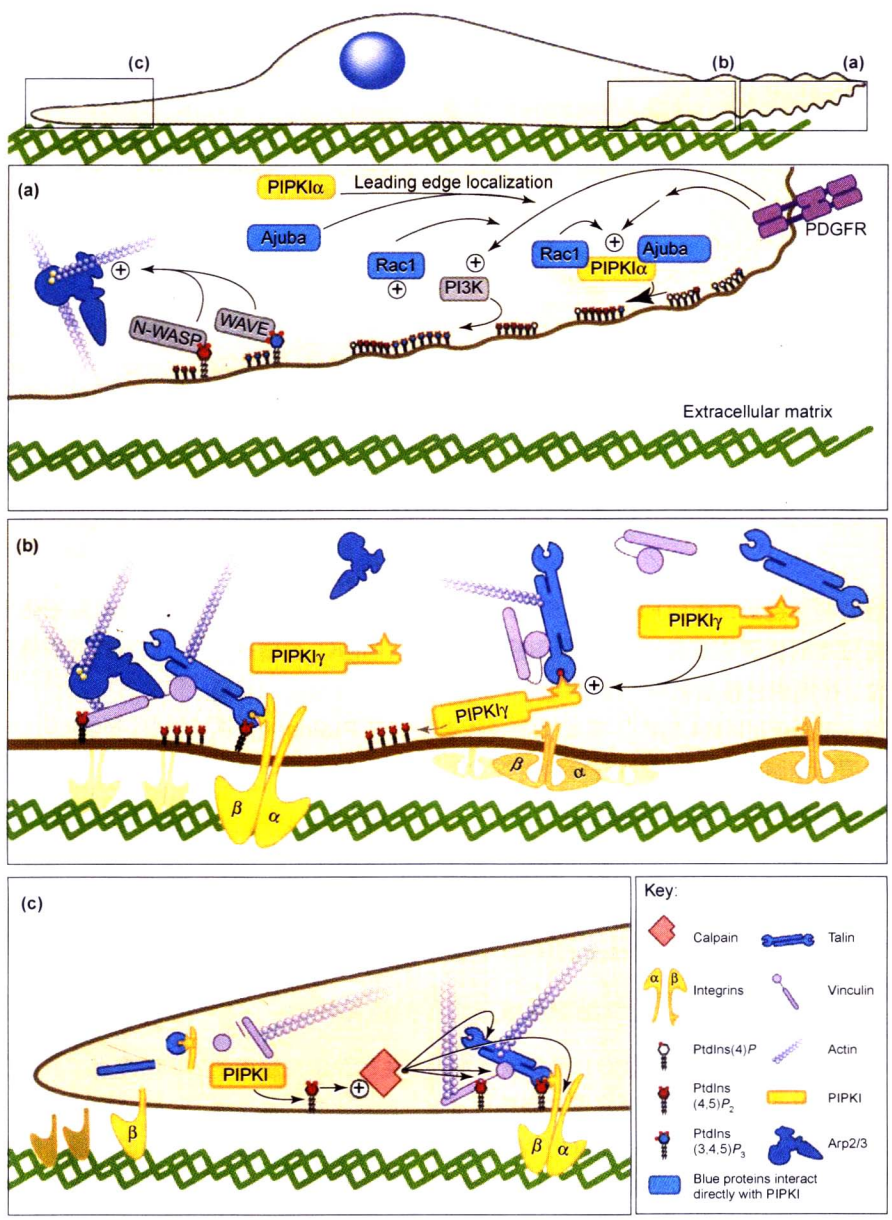
25 Movin' on up: the role of PtdIns(4,5)P_2 in cell migration

Trends in Cell Biology, Volume 16, Issue 6, June 2006 Pages 276-284

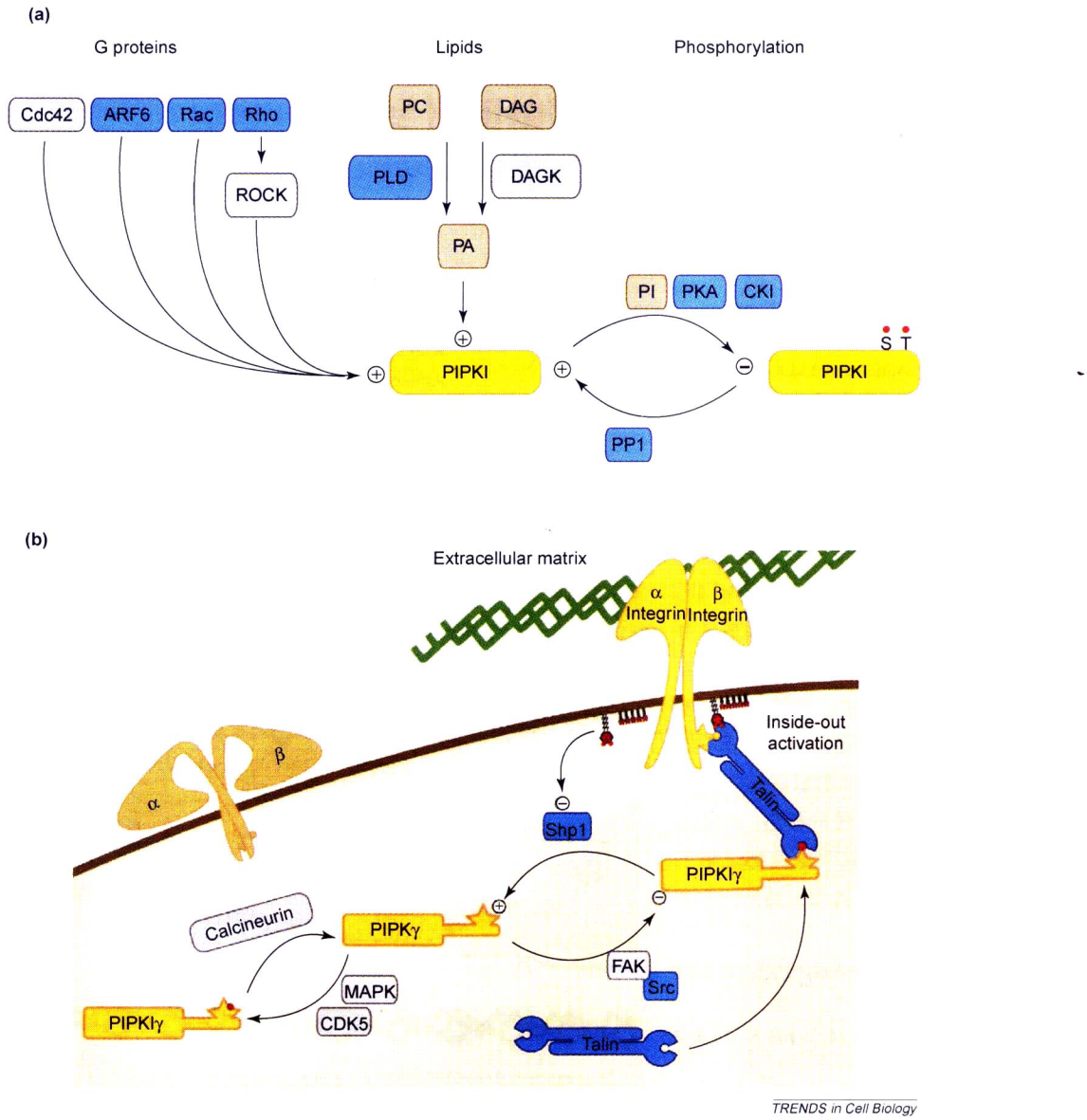
Kun Ling, Nicholas J. Schill, Matthew P. Wagoner, Yue Sun and Richard A. Anderson

4,5-二磷酸磷脂酰肌醇[PtdIns(4,5)P_2]在细胞迁移中的作用

细胞的迁移需要协调许多生物化学反应过程，包括细胞介质再分配和细胞骨架重建等。最新的研究结果显示4,5-二磷酸磷脂酰肌醇[PtdIns(4,5)P_2]参与这些过程的调控。许多参与迁移工具



TRENDS in Cell Biology



组装的关键蛋白受到PtdIns(4,5)P2的调节。PtdIns(4,5)P_2在这些位点的协调合成依赖于I型磷脂酰肌醇激酶（PIPK）的精确定位。在细胞迁移过程中，两个I型PIPK作用，并在膜皱折和粘着斑上形成PtdIns(4,5)P_2。在本文中，作者探讨了PtdIns(4,5)P_2在调节细胞对迁移刺激过程中的应答作用，以及迁移过程中的细胞是如何控制PtdIns(4,5)P_2作用的。

34 Turning cells red: signal transduction mediated by erythropoietin

Trends in Cell Biology, Volume 15, Issue 3, March 2005, Pages 146-155

Terri D. Richmond, Manprit Chohan and Dwayne L. Barber

使细胞变红：促红细胞生成素介导的信号转导

促红细胞生成素（EPO）是控制红细胞产生的关键细胞因子的调节因子。1985年发现了促红细胞生成素，四年之后，其同源受体也成功分离。此后，人们对了解这对配体-受体组合所特有的促进类血红细胞有丝分裂、生存以及分化的能力产生了浓厚兴趣。基因敲除小鼠帮助我们阐明了配体、受体以及下游参与者在鼠类动物血红细胞发生过程中的作用。该文章简要概括了促红细胞生成素介导的信号转导途径及其重要性。

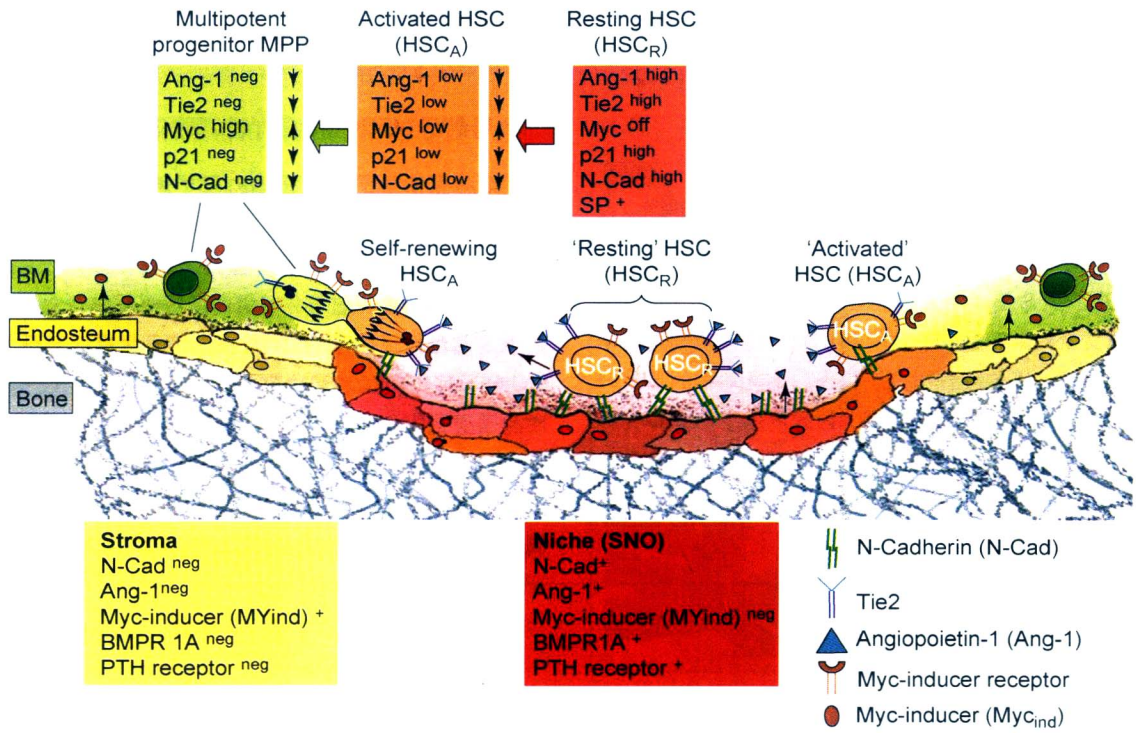
44 More than just proliferation: Myc function in stem cells

Trends in Cell Biology, Volume 15, Issue 3, March 2005, Pages 128-137

Mark J. Murphy, Anne Wilson and Andreas Trumpp

不仅仅是增殖：Myc对干细胞的作用

成熟个体中的干细胞对于维持可再生组织的再生能力是必不可少的，例如上皮细胞、肠胃粘膜以及造血系统等。最近，通过对小鼠的研究，人们发现了转录因子和肿瘤蛋白c-Myc的一些意料之外的功能。它不仅参与了干细胞的更新、干细胞和前体细胞的分化，而且还与干细胞与其周边微环境的相互作用密切相关。结合近来对Myc基因和造血干细胞的研究结果，我们提出了一个新的假设：休眠中的造血干细胞在干细胞内外微环境的相互作用下受到激发，并在其交界处实现自我更新和分化。



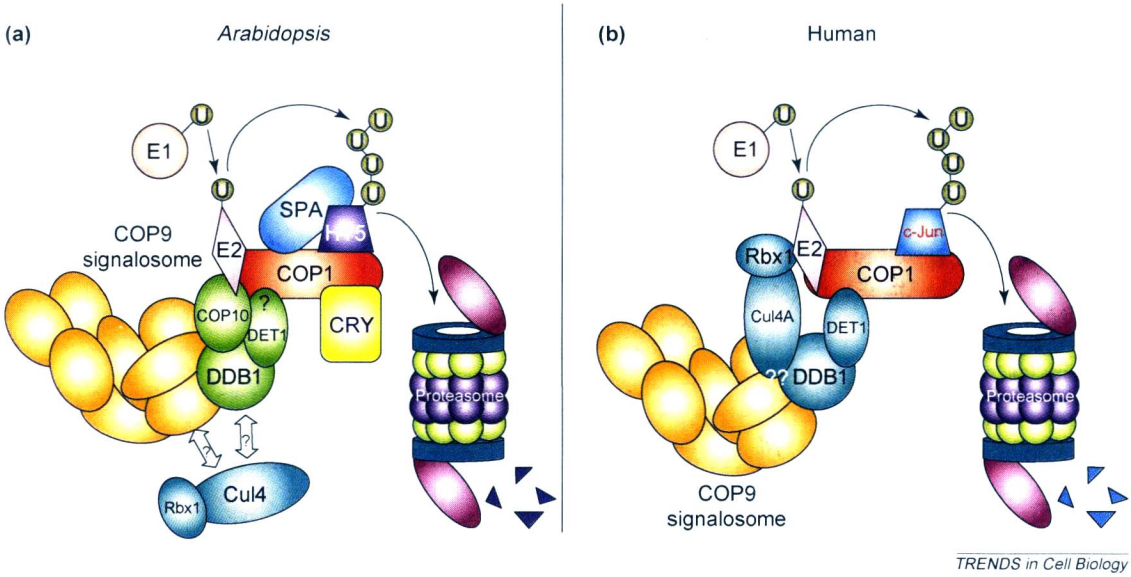
54 COP1-from plant photomorphogenesis to mammalian tumorigenesis

Trends in Cell Biology, Volume 15, Issue 11, November 2005 Pages 618-625

Chunling Yi and Xing Wang Deng

COP1：从植物的光形态发生到哺乳动物的肿瘤形成

组成型光形态发生蛋白（COP1）在高等植物和脊椎动物之间是保守的，它含有 RING 指区、卷曲螺旋和 WD40 区。在高等植物中，COP1 起着 E3 泛素连接酶的作用，通过特异地作用于光受体及其下游的转录因子，对他们进行泛素化和降解来抑制光信号的反应。植物细胞中的 COP1 活性与其在黑暗和光照条件下的细胞质和细胞核的定位密切相关。此外，人们还发现许多信号分子都可以同 COP1 相互作用，从而调节其活性。最近，科学家们开始探索哺乳动物 COP1 的功能和调控方式。初步的研究结果表明，哺乳动物的 COP1 有可能通过调节 p53 和 c-Jun 的活性，从而在肿瘤发生和逆境反应过程中起作用。



62 The interaction between FOXO and SIRT1: tipping the balance towards survival

Trends in Cell Biology, Volume 14, Issue 8, August 2004, Pages 408-412

Maria E. Giannakou and Linda Partridge

FOXO 和 SIRT1 的相互作用：死里逃生

当NAD依赖性蛋白——脱酰基化酶Sir2过量表达时，面包酵母（budding yeast）和线虫（*Caenorhabditis elegans*）的寿命均得以延长。线虫的生命延长需要FOXO家族的转录因子daf-16。最新发表的三篇文章对哺乳动物的Sir2和FOXO的同源物进行了系统研究，阐明了这一遗传互作的分子机理。哺乳动物的SIRT1能够去掉FOXO3或FOXO4蛋白的酰基，因此削弱了FOXO介导的细胞程序化死亡，缓解由FOXO诱发的细胞周期阻断。SIRT1可能是通过改变FOXO依赖性反应来实现细胞从死亡到生存的转变，由此延长了寿命。

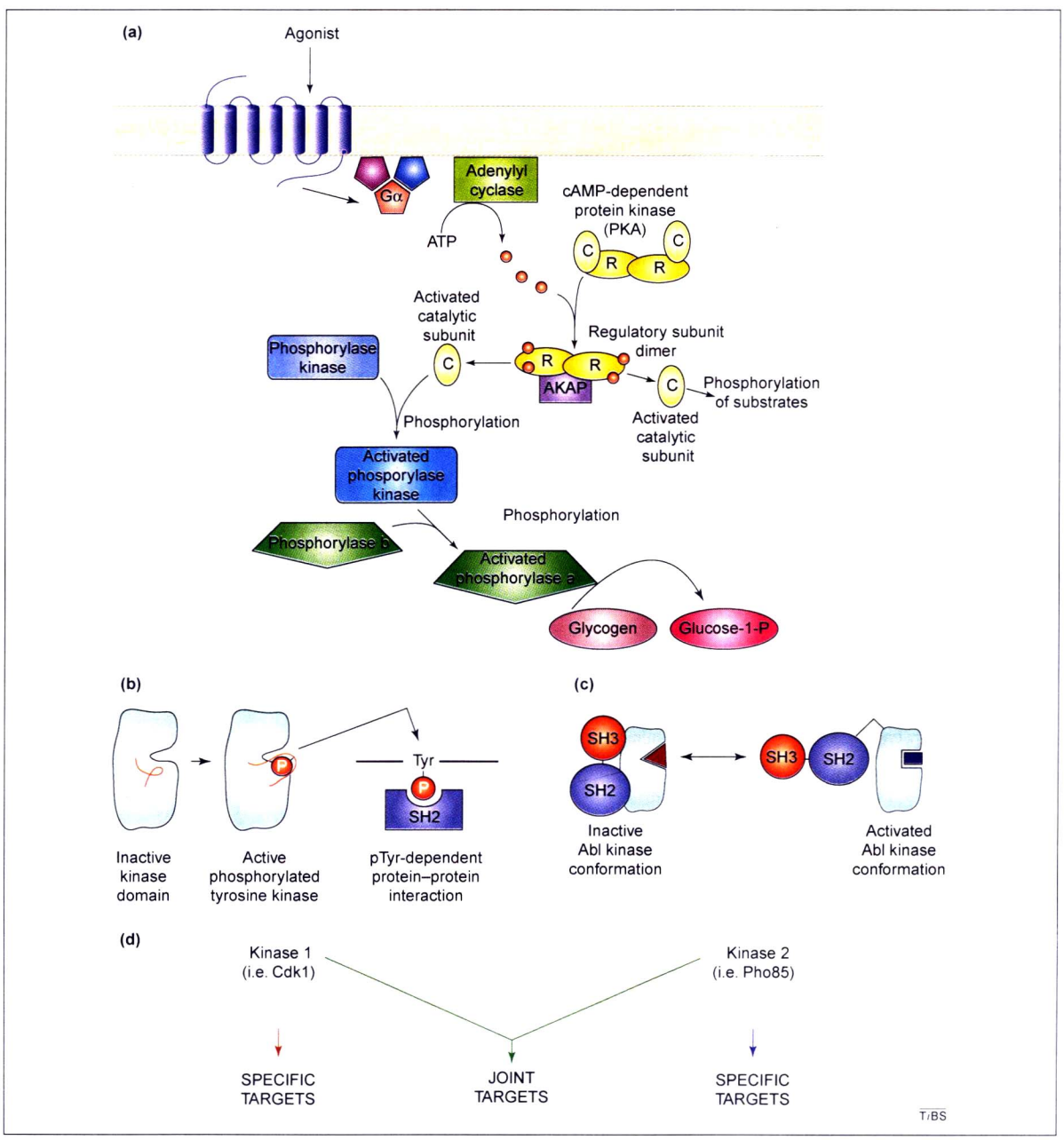
67 Protein phosphorylation in signaling - 50 years and counting

Trends in Biochemical Sciences, Volume 30, Issue 6, June 2005, Pages 286-290

Tony Pawson, and John D. Scott

信号转导过程中的蛋白质磷酸化：50 年的探索和未来

细胞生物学的基本驱动力是了解细胞组织和行为的动态特性。基因组序列告诉我们一个生物的编码潜力；而转录分析所揭示的是细胞中所表达的部分基因。然而，由此产生的蛋白质则处于不断的动态变化过程中。蛋白质在感受外来信号（如外来生长因子的刺激）或内源的DNA损伤信号之后，其活性、亚细胞定位、分子间作用关系和稳定性一直处于持续的改变中。研究蛋白质的磷酸化不仅为揭示正常细胞的调控提供了基础，同时也阐明了许多与人类疾病发生相关的信号转导途径。和许多科学的研究一样，这一领域的成就既归功于有洞察力的思索，也受益于很多偶然的发现。



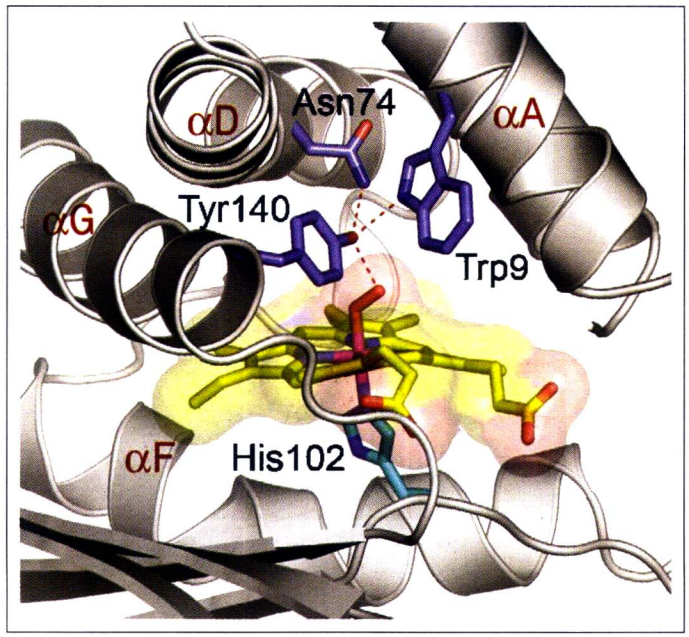
72 Nitric oxide signaling: no longer simply on or off

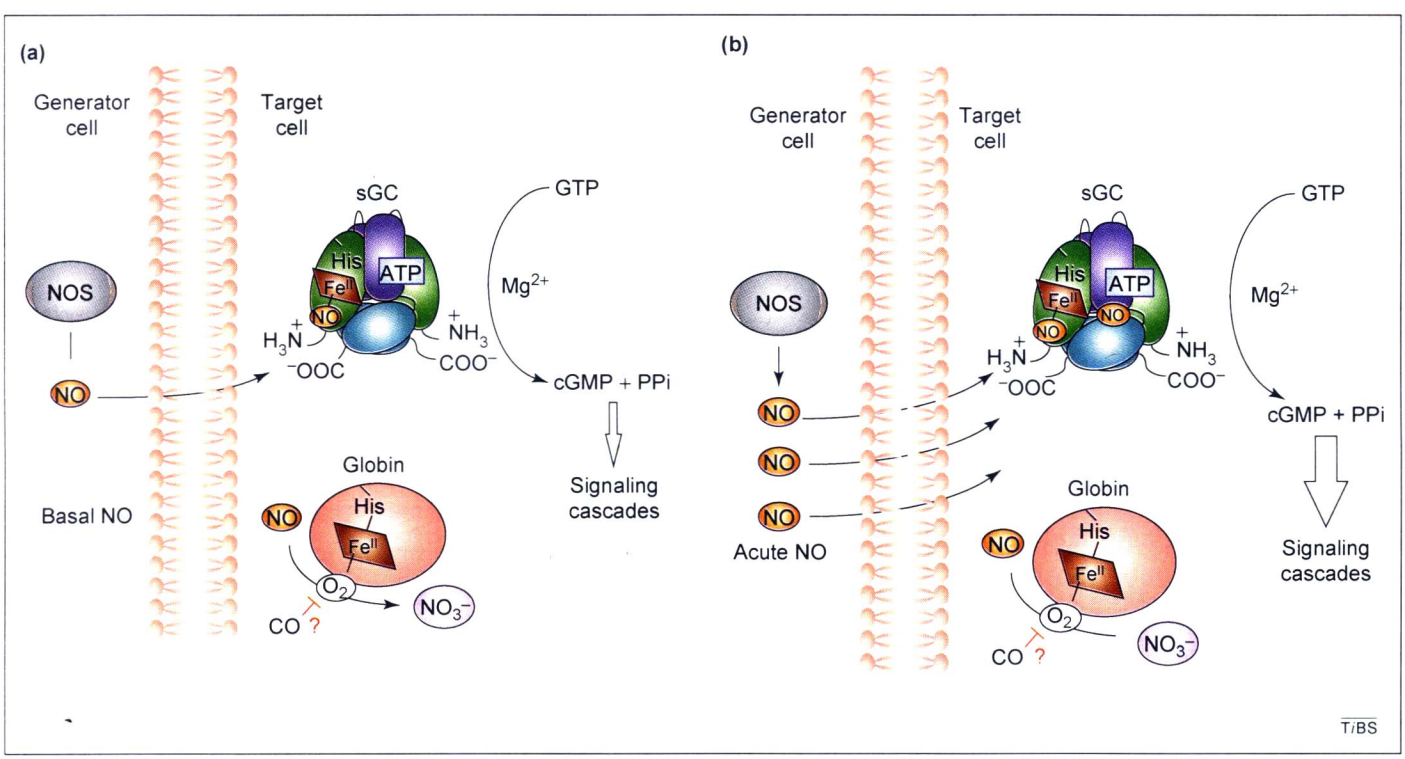
Trends in Biochemical Sciences, Volume 31, Issue 4, April 2006, Pages 231-239

Stephen P. L. Cary, Jonathan A. Winger, Emily R. Derbyshire and Michael A. Marletta

一氧化氮信号：不再是简单的开与关的问题

在许多组织中，一氧化氮（NO）能够通过结合或激活水溶性的胍基化环化酶来产生第二信使cGMP，引发不同的生理反应。在体内，本底的一氧化氮和cGMP信号维持目标细胞处于休息状态（如平滑肌的静止状态），但是，剧烈的NO/cGMP信号爆发则能够刺激快速反应（如平滑肌的舒张）。最近的研究显示sGC异源二聚体的每一个亚基至少包含四个模块区域，其中，N-端的血红素区是H-NOX蛋白家族所特有的一个结构域，能够结合O_2或NO。它在原核生物和高等真核生物中是保守的。对这些结构域的研究阐明了sGC分辨配体的分子基础。另外的研究发现了由NO所激发的两种不同的临时功能状态：稳定的单一NO-血红素复合体的形成产生本底活性状态，而增加一个NO则产生瞬时的全激活状态。核苷酸能够调整这一酶反应的时间长短与强度。总之，这些研究展现了体内两种绝然不同的NO/cGMP信号形式的生化基础。





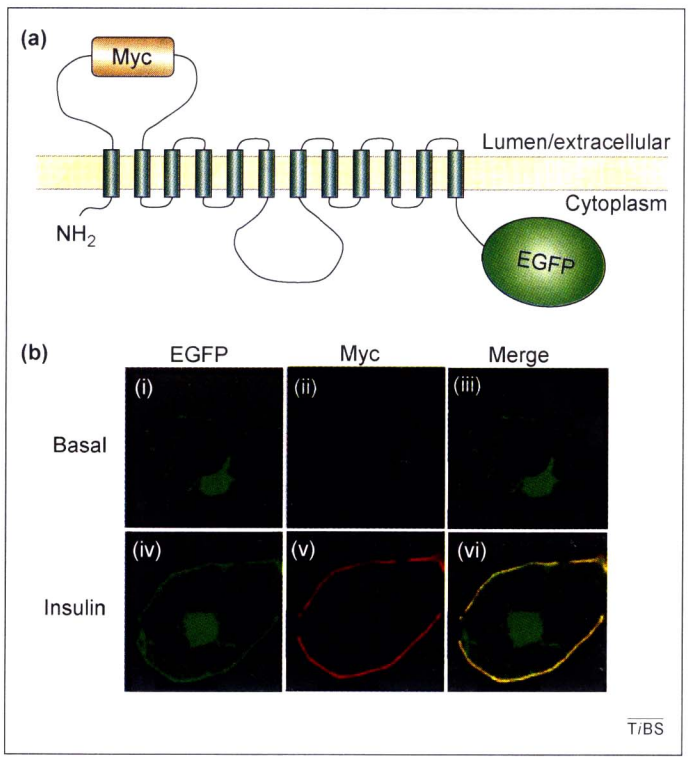
81 Bridging the GAP between insulin signaling and GLUT4 translocation

Trends in Biochemical Sciences, Volume 31, Issue 4, April 2006, Pages 215-222

Robert T. Watson and Jeffrey E. Pessin

搭起胰岛素信号和葡萄糖转移蛋白4转移之间的桥梁

胰岛素在结合和激活细胞表面的受体之后能够激发信号的级联反应，并由此调控许多细胞过程。胰岛素可以抑制肝脏的葡萄糖产生，提高葡萄糖向肌肉和脂肪组织的运输，从而维持体内的葡萄糖平衡。在细胞水平上，位于胞内储藏位置的葡萄糖转运蛋白4（GLUT4）受到胰岛素的刺激之后，移位到细胞表面的质膜上，引起葡萄糖的摄取。尽管人们对与胰岛素受体激发通路相关的上游分子已经有很多了解，但是对这个信号通路下游过程却一无所知，特别是该信号通路如何作用于GLUT4亚细胞储藏单元以及如何改变GLUT4的亚细胞定位。最近，包括AS160、PIKfyve和synip在内的数个候选信号分子的发现帮助我们在胰岛素的信号通路和GLUT4的亚细胞定位之间建立了功能联系。下一步的工作将集中剖析这些分子是如何调控GLUT4胞内转运步骤的。



89 Getting to know your neighbours; a new mechanism for cell intercalation

Trends in Genetics, 2004, Volume 21, Issue 2, Pages 70-73

Kelly K. Nikolaidou and Kathy Barrett

了解你的邻居：一种新的细胞迁入机制

当一个胚胎形成原肠和神经组织时，背腹轴长度缩短，而与之垂直的头尾轴长度增加，使整个胚胎的长度加倍。这一过程称之为汇集延伸，是一种非常有效的组织形态改变方式，并在发育过程中不断被运用。最新的果蝇和其它模式生物研究工作为阐述这一过程是如何发生的指明了新方向。

93 MAP kinase kinase kinases and innate immunity

Trends in Immunology, Volume 27, Issue 1, January 2006, Pages 40-48

Antony Symons, Soren Beinke and Steven C. Ley

MAP 激酶级联通路和天然免疫

Toll样受体应答于固定的一类微生物分子，如发炎早期细胞因子、肿瘤坏死因子受体和白细胞间介素-1等，在天然免疫应答中发挥着重要作用。这些受体能够激活丝裂素活化蛋白（MAP）激酶的每一种主要亚型：细胞外信号调节激酶、c-Jun 氨基末端激酶和 p38 MAP 激酶。而这些激酶对于细胞的生存和控制免疫介质的表达至关重要。因此可见，MAP 激酶级联通路将 MAP 激酶和参与天然免疫的受体联系在一起。本文对特异性MAP激酶级联通路（MAP3-激酶）研究的最新进展和上述受体调控MAP3-激酶活性的机制做了综合评述。

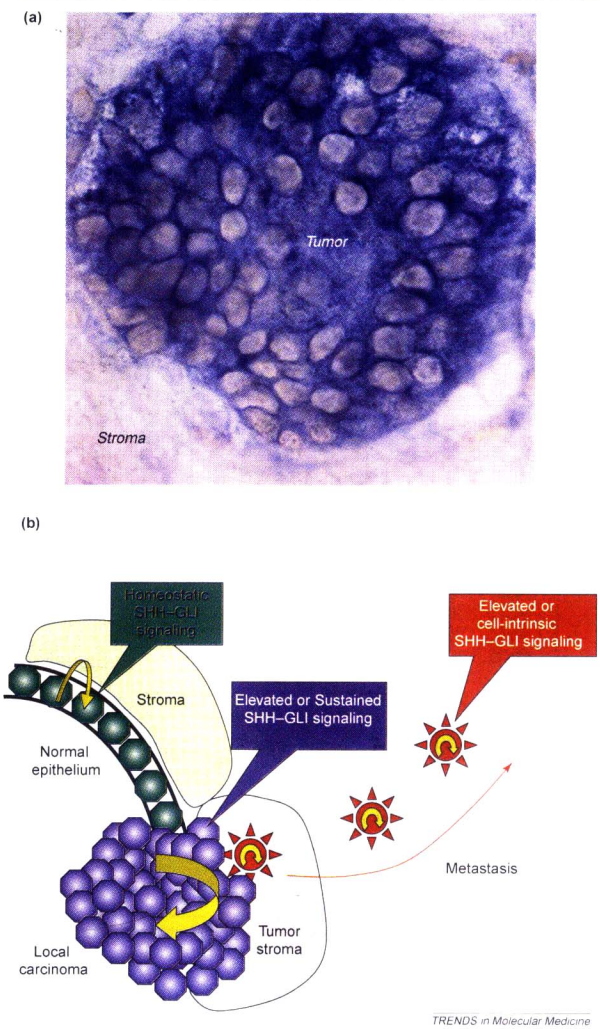
102 Interference with HH-GLI signalling inhibits prostate cancer

Trends in Molecular Medicine, Volume 11, Issue 5, May 2005, Pages 199-203

Barbara Stecca, Christophe Mas and Ariel Ruiz i Altaba

干扰 HH–GLI 信号通路可抑制前列腺癌

Hh-Gli信号通路控制着组织形成模式的许多方面：细胞增殖、分化和再生以及调节不同器官的细胞数目等。成人的Hh-Gli信号通路在许多干细胞和再生组织中仍然有活性。然而，已证明人类的很多癌症的发生与Hh-Gli信号通路的失控和不恰当的激活有关。近期的三篇文章表明该通路中的一些元件在人类前列腺肿瘤中表达，而且更重要的是前列腺肿瘤有赖于持续不断的Hh-Gli信号的存在。这些结果为治疗这种不治之症提供了新的机遇。



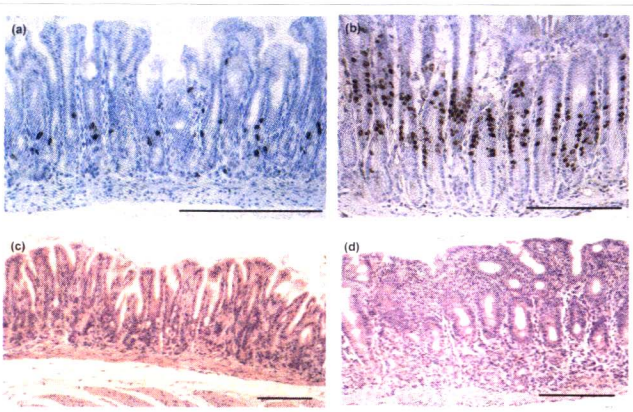
107 *Helicobacter pylori*-induced epithelial cell signalling in gastric carcinogenesis

Trends in Microbiology, Volume 12, Issue 1, January 2004, Pages 29-36

Michael Naumann and Jean E. Crabtree

胃癌发生过程中幽门螺杆菌所诱导的胃上皮细胞信号通路

幽门螺杆菌是一种危害人类健康的强势微生物病原体，世界上超过50%的人口的胃幽门部位受到这种细菌的感染。幽门螺杆



菌可引发胃炎。不仅如此，这种病菌感染以后还可以引起慢性胃炎和胃溃疡，在少数情况下还可以诱发胃癌。只有少数感染幽门螺杆菌的病人会发展为胃癌患者的原因可能与宿主易感性差异、环境因子的不同和机体的遗传多样性相关。该文章论述了胃病中幽门螺杆菌所诱导的胃上皮细胞信号转导的特征，同时还探讨了临床研究和模式动物研究的一些结果，提供了体内胃上皮细胞增殖与幽门螺杆菌菌株差异相关的证据。另外，本文还探讨了幽门螺杆菌诱发上皮细胞过度增殖过程和直接控制上皮细胞信号的机制，特别是在激活酪氨酸激酶受体、细胞与细胞之间的互作和细胞运动中的作用。

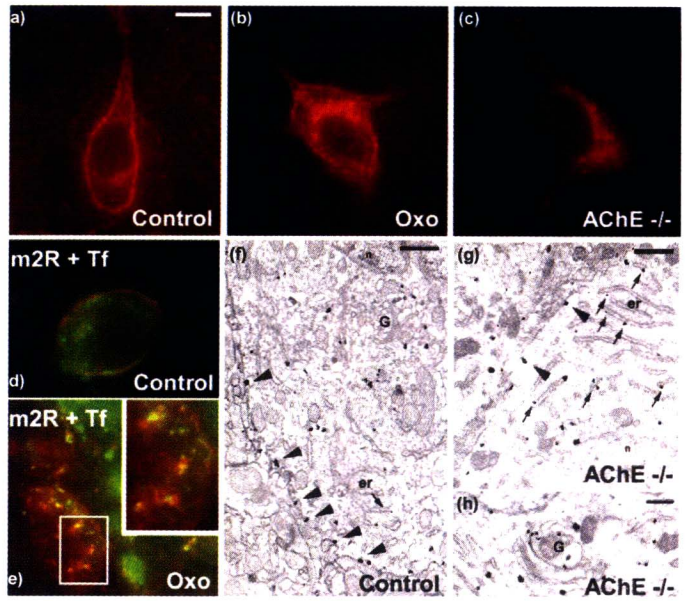
115 Intraneuronal trafficking of G-protein-coupled receptors *in vivo*

Trends in Neurosciences, Volume 29, Issue 3, March 2006, Pages 140-147

Véronique Bernard, Marion Décossas, Isabel Liste and Bertrand Bloch

体内 G- 蛋白偶联受体在神经元内的转运

大量的体外研究表明G-蛋白偶联受体（GPCRs）在细胞表面的丰度和存在与否受到神经元环境的调节，也是复杂的神经元内物质运输的结果。然而对于机体如何实现这一过程的调控却知之甚少。神经元功能的调控（如生理、病理或治疗条件下神经递质的释放或神经元的兴奋性）的关键是调节这些受体在神经元表面的有效性。本文探讨了神经元细胞的受体激活（急性对慢性）时间长短对GPCRs神经突触内物质运输的影响，他们还发现这一运输过程可能在不同亚细胞区域（如胞体、树突和轴突终末）是不一样的。



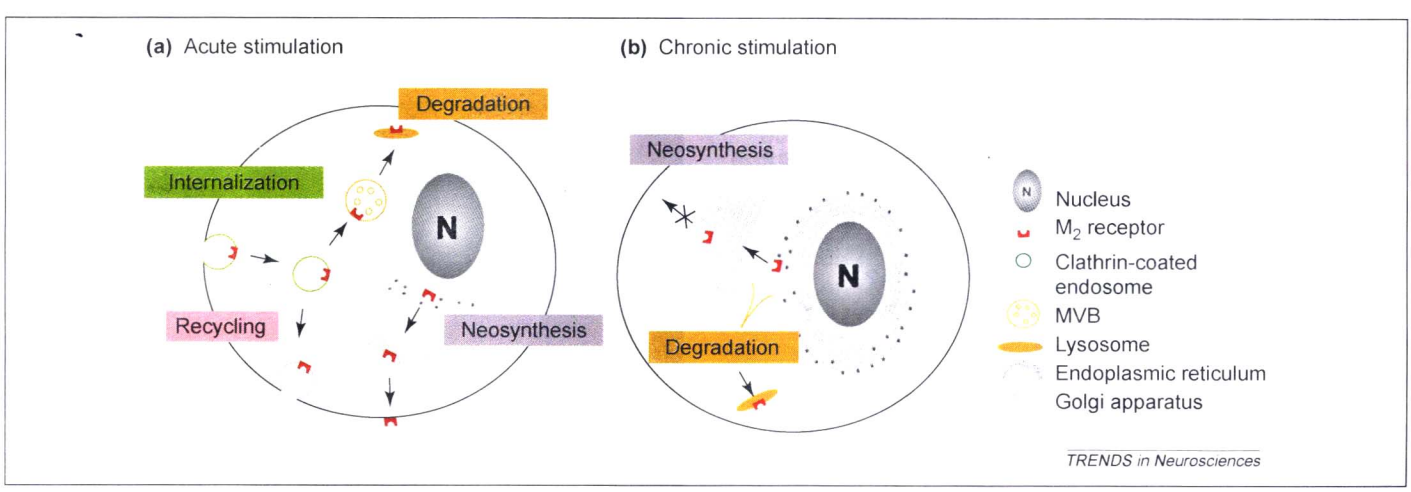
123 Free radicals and aging

Trends in Neurosciences, Volume 27, Issue 10, October 2004, Pages 595-600

Gustavo Barja

自由基与衰老

衰老的特征是极限功能的衰退和线粒体DNA突变的积累，这些特征在像大脑这类含有有丝分裂后细胞的器官中表现尤为显著。越来越多的证据表明氧自由基在这些衰老的变化中的部分作用。对衰老速度不同的几种动物对比研究表明，在高等脊椎动物中，线粒体氧自由基的产生速率与线粒体 DNA 的氧化损伤状态呈正相关，而与寿命长短呈负相关。组织中脂肪酸的不饱和度也与寿命呈负相关。这是已知的两个能够将氧化胁迫和衰老联系起来的性状。此外，控制卡路里的摄入也可以减缓衰老，并且以同等比例抑制线粒体中（尤其是复合体 I）中氧自由基的产生。本文综合评述了这些结果，并重点论述了对大脑的研究结果。



129 A novel role for abscisic acid emerges from underground

Trends in Plant Science, Volume 11, Issue 9, September 2006, Pages 434-439

Ive De Smet, Hanma Zhang, Dirk Inzé and Tom Beeckman

脱落酸的一种新作用

侧根的不断形成是根系发生的一个重要部分，这一机制赋予了植物发育的可塑性，使之能应对多变的土壤环境。以前我们已经知道脱落酸（ABA）参与了胁迫应答，最近，越来越多的证据表明它在侧根的形成中发挥着重要的作用。ABA 受体的突变体 fca-1 在侧根的形成过程中表现出异常的反应。有趣的是，ABA似乎在侧根发育的不同阶段均发挥着不同的作用。ABA在侧根发育中的新功能恰恰符合它作为一种胁迫相关激素的普遍功能特性，包括它在种子休眠中的作用。

135 Plant neurobiology: an integrated view of plant signalling

Trends in Plant Science, Volume 11, Issue 8, August 2006, Pages 413-419

Eric D. Brenner, Rainer Stahlberg, Stefano Mancuso, Jorge Vivanco, František Baluška and Elizabeth Van Volkenburgh

植物神经生物学：对植物信号的整体认识

植物神经生物学是一门新兴的关于植物生物学研究的学科，旨在阐明植物如何将它们从环境中获得的信息转变为最适当的发育、生长和繁殖信号。信号的产生、交流和应答机制的整合在整株水平上协调着植物的行为。这一系统包括长距离电信号、囊泡所介导的特定维管组织中的生长素的运输，以及等同于动物中神经元的化学物质的产生。植物神经生物学正在走向揭示整体植株水平、植物与植物之间及其植物与其周边环境之间的信号转导机制研究。本文对此进行了回顾。

142 Plant thioredoxins are key actors in the oxidative stress response

Trends in Plant Science, Volume 11, Issue 7, July 2006, Pages 329-334

Christina Vieira Dos Santos and Pascal Rey

植物的硫氧还蛋白在氧化胁迫应答中扮演着重要角色

硫氧还蛋白是一类广泛存在的二硫键还原酶，它调控目的蛋白的氧化还原状态。尽管植物中的硫氧还蛋白表现出其他生物体所没有的多样性，但是它们的很多生理功能尚未确定。根据近期对硫氧还蛋白的靶蛋白和相关遗传修饰后的植物研究结果显示，这一类蛋白似乎在植物对氧化胁迫的抗性方面发挥着基本作用。硫氧还蛋白能够通过为脂过氧化氢酶的还原酶提供还原力或修复被氧化的蛋白，帮助植物避免氧化损伤。此外，其它一些证据表明，在植物抗氧化剂的网络中，硫氧还蛋白是清洁机制的调控因子，也是信号通路中的作用元件。

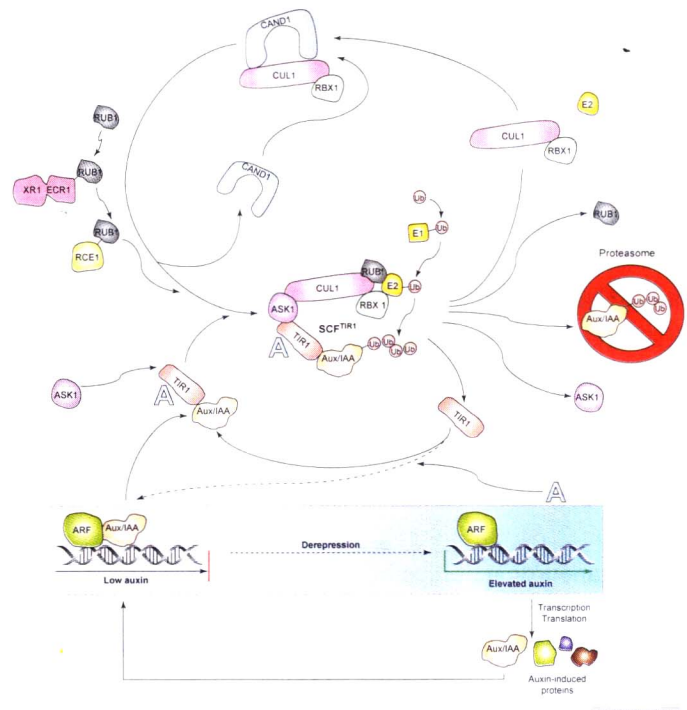
148 Receptors for auxin: will it all end in TIRs?

Trends in Plant Science, Volume 11, Issue 5, May 2006, Pages 217-223

George O. Badescu and Richard M. Napier

生长素受体：难道仅仅是 TIR 这类蛋白吗？

TIR1 蛋白在参与泛素化过程和调控Aux/IAA转录因子降解方面的作用已被揭示多年了。然而，近年来的研究结果表明TIR1本身也是生长素的结合位点。TIR1对生长素的亲和性和特异性都符合作为核生长素受体的特性，在此基础上我们将TIR1的特性与生长素结合蛋白ABP1的特性进行了比较。在探讨生长素通过TIR1发挥作用的机制以及TIR1家族其他蛋白参与其他生长素应答反应的可能性的基础上，我们认为TIR1受体系统很可能可以解释大部分生长素介导的反应，但并不是全部。



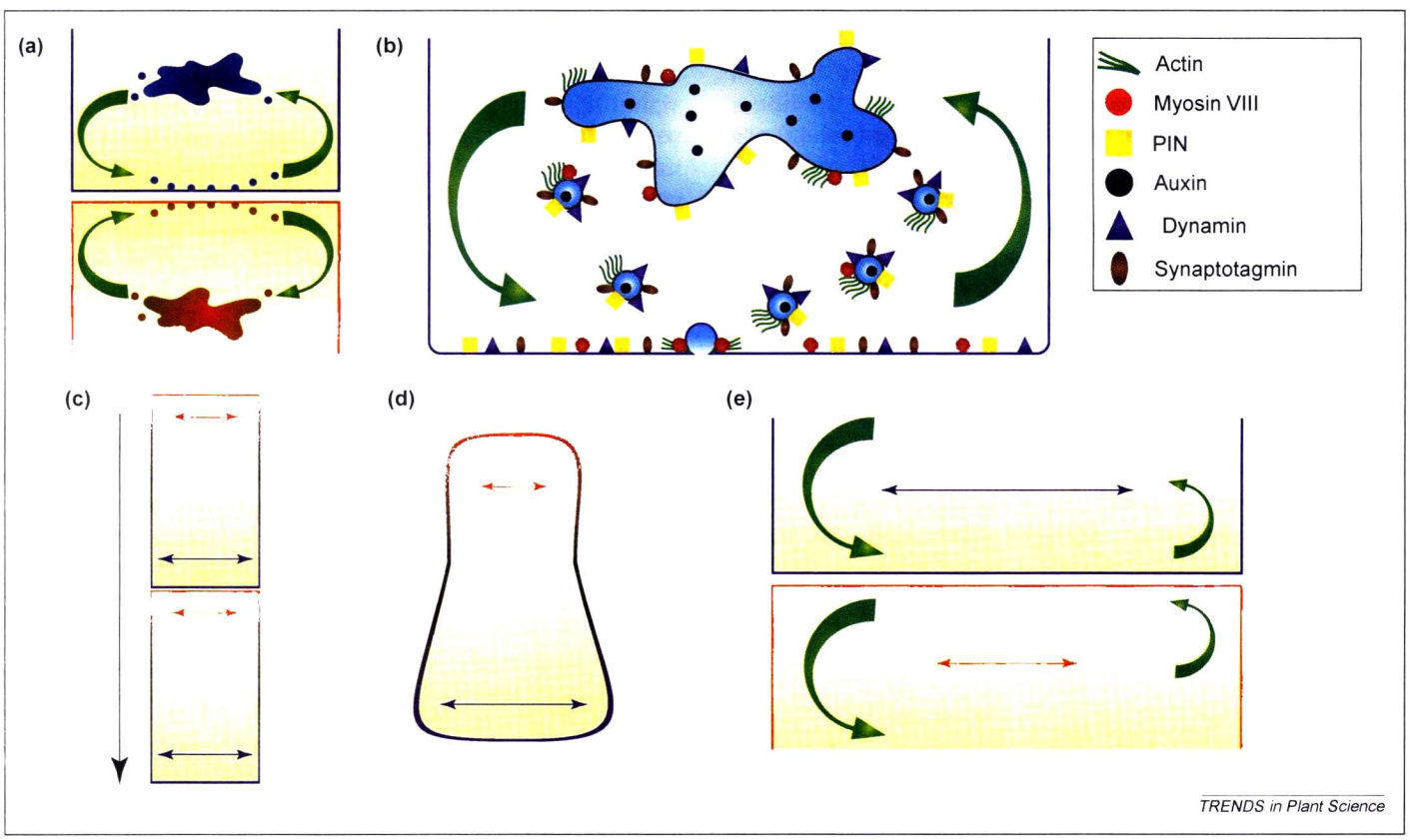
155 Plant synapses: actin-based domains for cell-to-cell communication

Trends in Plant Science, Volume 10, Issue 3, March 2005, Pages 106-111

František Baluška, Dieter Volkmann and Diedrik Menzel

植物神经突触：基于肌动蛋白的细胞与细胞之间信息交流

动作电位影响植物的多种生理过程，植物利用这种经典的动作电位进行快速、长距离的信号传导，对此人们已有多年的认识。另外，植物还合成多种神经信号分子，协助完成一些几乎可以认为是智能的行为。近来的生态生理学研究所得到的突破性进展表明，植物的根可以辨认“自己”与“异己”，而动物中类似的辨认能力依赖于神经突触的行为。本文提出植物细胞之间也能建立一种与神经突触相似的信息交换方式。另外，当受到病原菌、寄生虫和潜在的共生生物的胁迫时，植物还会通过构建黏附连接的方式协调不同植物细胞之间的信息交流。作者认为这些黏附连接与动物中的免疫神经突触非常类似。



161 New signalling molecules regulating root hair tip growth

Trends in Plant Science, Volume 9, Issue 5, May 2004, Pages 217-220

Jozef Šamaj, František Baluška and Diedrik Menzel

调控根毛顶端生长的新信号分子

根毛是由沿根长轴方向排列的生毛细胞（形成根毛的表皮细胞）的管状突起顶端生长的结果。到目前为止，关于根毛形成的信号传导过程还知之甚少。最近的两个研究结果表明NADPH氧化酶和磷脂酶D等与信号传导有关的酶在根毛的生长和发育过程中发挥着重要的作用。由NADPH氧化酶所产生的活性氧（ROS）可以激活位于根毛顶端的钙离子通道，而在这些钙离子通道的作用下形成聚集于顶端的钙离子梯度，这是根尖生长的遗传特征。

165 Reactive oxygen gene network of plants

Trends in Plant Science, Volume 9, Issue 10, October 2004, Pages 490-498

Ron Mittler, Sandy Vanderauwera, Martin Gollery and Frank Van Breusegem

植物的活性氧基因网络

活性氧（ROS）控制着植物的许多不同生理过程，但是作为一种有毒分子它们同样可以伤害细胞。植物是如何解决这个矛盾的？答案尚未知晓。然而已经明确的是，ROS在细胞中的稳态水平是受到严格调控的。在拟南芥中存在一个包含至少152个基因的网络，参与调控ROS的水平。这个网络非常活跃而且高度冗余，它负责编码ROS清除蛋白和ROS产生蛋白。尽管近期的研究已经揭示了该网络中的一些主要成员，但是许多关于它的调控模式，以及它对植物生长发育和胁迫应答的信号网络的保护和调控作用等问题仍然没有答案。

（齐兴云 刘春明 译）

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Chromosome Segregation and Aneuploidy series

Centrosome control of the cell cycle

Stephen Doxsey[1], Wendy Zimmerman[2] and Keith Mikule[1]

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Early observations of centrosomes, made a century ago, revealed a tiny dark structure surrounded by a radial array of cytoplasmic fibers. We now know that the fibers are microtubules and that the dark organelles are centrosomes that mediate functions far beyond the more conventional role of microtubule organization. More recent evidence demonstrates that the centrosome serves as a scaffold for anchoring an extensive number of regulatory proteins. Among these are cell-cycle regulators whose association with the centrosome is an essential step in cell-cycle control. Such studies show that the centrosome is required for several cell-cycle transitions, including G_1 to S-phase, G_2 to mitosis and metaphase to anaphase. In this review (which is part of the *Chromosome Segregation and Aneuploidy* series), we discuss recent data that provide the most direct links between centrosomes and cell-cycle progression.

Introduction

Chemical reactions in solution can be inefficient. In a multi-component biochemical reaction, the first component must locate, contact and modify its target before other steps can proceed. However, if all components of the reaction are physically linked together at a common site, the efficiency of the process can be enhanced. Perhaps the best example of such 'solid-state biochemistry' is the formation of signaling 'modules' in which multiple kinases are physically integrated in a way that facilitates a series of sequential binary interactions, thus creating a protein kinase cascade [1]. Mathematical modeling indicates that protein scaffolding can significantly increase the efficiency of kinase signaling pathways [2]. Physical linkage of molecules in a common pathway could increase the local concentration of components, limit nonspecific interactions and provide spatial control for regulatory pathways by positioning them at specific sites in proximity to cellular targets (e.g. other pathways, organelles, etc.) or to incoming signals from within or outside the cell. Scaffolding mechanisms could also provide temporal control of signaling events such as activation of cell-cycle transitions. In the process, the scaffold network could itself be monitored by its ability to ensure anchoring and functional outputs of regulatory pathways.

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A growing body of evidence indicates that centrosomes serve as multiplatform scaffolds for a multitude of signaling networks. The centrosome in animal cells is usually located at the cell center, where it serves to nucleate polarized microtubule arrays for organizing cytoplasmic organelles and primary cilia in interphase cells, and for mitotic spindle organization and cytokinesis during mitosis. The centrosome is ~1–2 μm in diameter and consists of two barrel-shaped centrioles arranged perpendicular to one another, surrounded by the pericentriolar material (PCM). Estimates suggest that the centrosome comprises hundreds of proteins, including many large (200–450 kDa) coiled-coil scaffold proteins that serve as docking sites for a growing number of regulatory and other activities (Table 1; see also Supplementary Table S1 online) [3]. The PCM is in part organized by centrioles [4] and contains γ-tubulin ring complexes (γTuRCs), which nucleate microtubules, although other proteins also appear to be involved in this process [5]. Microtubule anchoring (distinct from nucleation) can occur at the distal appendages of the older or 'mother' centriole at least during some cell-cycle stages [6].

Table 1. Proteins reported to localize to the centrosome[a]

Category	Number of proteins per category
Ubiquitination and protein degradation	23
Nuclear transport/spindle assembly	4
Cytoskeletal regulators	22
CDKs and cyclins	5
Mitotic regulators	8
Chaperonins	3
Apoptosis related	8
DNA damage checkpoint	4
MAPK pathway	8
Spindle checkpoint	6
Mitotic exit/MEN	9
Cytokinesis/SIN	11
Transcription regulators	4
mRNA/mRNA processing	6
G_1/S regulation	2
Wnt signaling	3
Membrane receptor signaling	13
Other kinases/phosphatases	7
Golgi regulation	2
Other enzymes	10
Structural/scaffold proteins	60
Microtubule associated proteins (MAPS)	31
Motor proteins	15
Calcium binding	5
Other proteins	30
Viral proteins and infectious agents	13

[a]For a complete, extensively referenced, tabulation of the individual proteins, see Supplementary Table S1 online.

As many regulatory molecules are found at centrosomes, it is tempting to speculate that centrosomes serve as solid-state signaling machines capable of regulating many cellular functions, although, in most cases, the function of the centrosome-anchored fraction of these molecules has not been determined.

The substantial number of regulatory molecules that localize to the mammalian centrosome suggests the presence of complex regulatory networks at this site. For example, scaffold proteins such as the budding/fission yeast Nud1p/Cdc11p anchor multiple signaling molecules at the spindle pole body (the yeast centrosome equivalent) to control mitotic exit and cytokinesis [7]. In addition, many coiled-coil centrosomal proteins that act as scaffolds for anchoring protein kinases have been identified (e.g. protein kinases A, B and C) [8]. More recent results demonstrate a requirement for centrosomal anchoring of regulatory pathways in the control of cell-cycle progression (see below and **Box 1**). These observations provide some of the first functional links between centrosomes and regulatory networks and are the focus of this review. We discuss recent studies, primarily in mammalian cells, that provide the most direct evidence for a link between centrosomes and cell-cycle progression from G_1 to S-phase (G_1–S), G_2 to M-phase (G_2–M) and metaphase to anaphase (M–A); centrosomal regulation of cytokinesis has been reviewed recently [9].

The centrosome in the G_1–S transition

Removal of core centrosome components

Studies designed to remove centrioles and associated PCM from cells by microsurgical cutting [10] or laser ablation [11] have provided direct evidence for centrosomes in cell-cycle progression (**Figure 1**a,b). Removal of core centrosome components resulted in the formation of acentriolar microtubule organizing centers (MTOCs) containing several PCM proteins [11,12], similar to those of higher plants and some meiotic systems [13,14]. The animal cells containing acentriolar MTOCs formed functional mitotic spindles, but about half failed to cleave into two daughter cells during cytokinesis. All cells with acentriolar MTOCs, whether they completed cytokinesis or failed (forming tetraploid cells), did not initiate DNA replication (BrdU-negative, **Figure 1**a). Moreover, ablation of one of two centrosomes in prometaphase cells produced a centrosome-containing daughter that continued to cycle (BrdU-positive) and a daughter cell with an acentriolar MTOC that did not enter S-phase (BrdU-negative, **Figure 1**b). By contrast, extra centrosomes (or nuclei) created by cell-fusions or by inhibition of cytokinesis using actin-perturbing drugs, did not inhibit cell-cycle progression [15,16]. In addition, cell-cycle progression did not appear to require centrosome-associated microtubules. Normal cycling diploid cells progressed through G_1 without microtubules (after nocodazole treatment), suggesting that they were not required for this cell-cycle transition.

Box 1. Coordinating cycles: cell, centrosome and DNA cycles

Accurate cell division requires the coordinated completion of three separate but interdependent cycles namely, the cell, centrosome and nuclear cycles [42–44] (**Figure I**). However, recent reports [24,29] have suggested that both the nuclear and cell cycles depend upon the centrosome or centrosome cycle for advancement.

The cell cycle

The cell, or cytoplasmic, cycle consists of the sequential activation and deactivation of cyclin-dependent kinases (CDKs). Control is provided through the availability of partner cyclins (cyc) and by phosphorylation/dephosphorylation events. CDK inhibitors (CKIs) provide a third level of CDK regulation by binding to and inactivating CDK–cyc complexes. p53 family members and other proteins transcriptionally regulate CKI levels. CKIs are upregulated in response to signaling pathways that monitor nutrient availability (i.e. serum), osmolarity/-salinity, temperature, DNA damage and other parameters and serve to arrest the cell cycle [45].

The centrosome cycle

Following cytokinesis, a normal diploid cell inherits one centrosome with two centrioles that replicates during S-phase, separates around G_2–M, and becomes part of the spindle poles during M phase. The molecular details of centrosome duplication are unclear. However, most researchers would agree that duplication is initiated at the G_1–S transition and is coincident with Cdk2-dependent phosphorylation of centrosome substrates and the subsequent moving apart or 'splitting' of the centriole pair (blue/red cylinder) [23,46]. Daughter centrioles then arise from the side of each centriole on or near the pericentriolar material (PCM) and become mature full-length structures by the end of G_2. By M-phase both centrosomes have acquired the maximal amount of PCM.

The nuclear cycle

During each cell-division cycle, the genome must be duplicated, condensed and precisely divided among daughter cells. Approximately at G_1–S, Cdk2 phosphorylation of the origin of replication (ORC)-bound pre-replication complex initiates DNA polymerase recruitment and firing of the origins [44], followed by complete genome replication in S-phase. In G_2, the nucleotide excision repair complex detects DNA mismatches or strand breaks and halts the cell cycle through checkpoint kinase activation, so that repairs can be completed before entry into mitosis. At the end of G_2, Cdk1 activation initiates nuclear envelope breakdown and chromosome condensation, two hallmarks of mitotic entry. Nuclear lamin phosphorylation, along with microtubule ingression are responsible for nuclear envelope breakdown [43], whereas chromosome condensation requires histone H3 phosphorylation [47]. Mitosis proceeds with chromosome alignment on the metaphase plate, separation of sister chromatids at anaphase and cytokinesis.

Linking cycles

The use of common regulatory complexes, such as CDKs, to coordinate the cell, centrosome and nuclear cycles is one way of coupling them. Another method of coordination is accomplished by localizing complexes to a given site. This occurs at the centrosome at both the G_1–S and G_2–M transitions (large red arrows; see also **Table 1**). At G_1–S, cycE recruitment to the centrosome is needed for DNA replication [24], whereas Cdk2 activity is required at the centrosome to start its cycle [23]. At G_2–M, centrosome-bound Cdk1 is activated first and initiates mitosis [29]. These strategies not only provide a template for cell-cycle activation at certain key stages but, in the process, could serve to monitor the integrity of the centrosome (at least the binding sites for cell-cycle regulatory molecules).

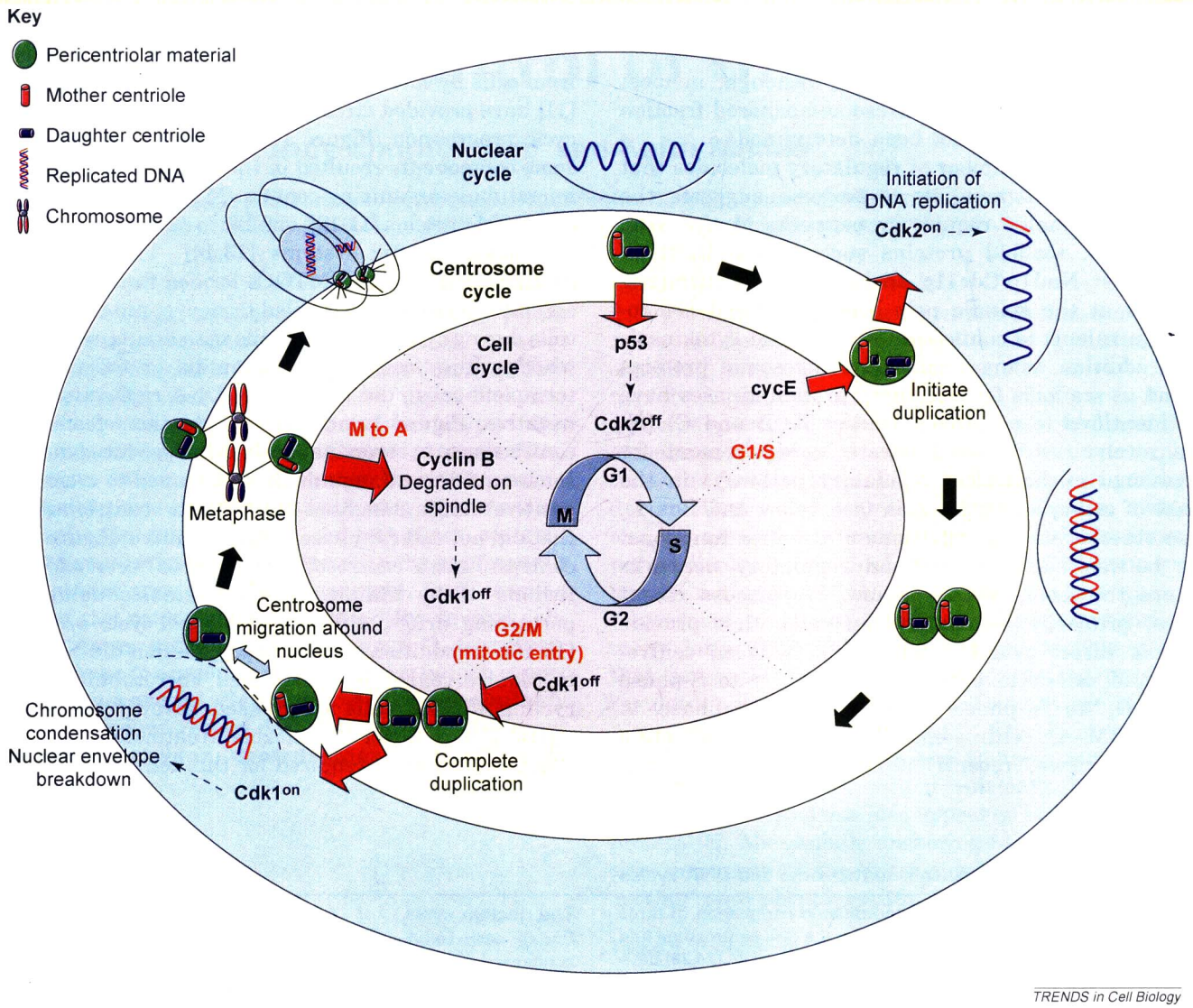

Figure I. Centrosome-associated steps during the cell cycle. Only the cell-cycle transitions that appear to require centrosomes are shown (red arrows).

By contrast, cells arrested within G_1 in the presence of taxol or in nocodazole after failed cytokinesis [17,18]. However, results from these experiments are difficult to interpret as stabilized microtubules in taxol-treated cells and the consequences of failed cytokinesis might influence cell-cycle progression.

Changes in centrosome protein expression levels or localization induce G_1 arrest

Molecular studies have also uncovered a role for individual centrosome components in cytokinesis and cell-cycle progression (**Figure 1**c,d). Centriolin is a component of the mother centriole that shares homology with Nud1p and Cdc11p [19], budding and fission yeast proteins involved in cytokinesis/mitotic exit, respectively [9]. Centriolin depletion or overexpression of the Nud1p/Cdc11p homology domain delayed cytokinesis for extended periods of time. Following the cytokinesis delay, cells did not progress into S-phase but remained in the G_1 peak when examined by flow cytometry (2N DNA content). AKAP450 is a protein of the PCM with a C-terminal domain that serves a centrosome targeting function [20,21]. Ectopic expression of the AKAP450 C-terminus mislocalized endogenous AKAP450 and protein kinase A (PKA) from centrosomes and induced cytokinesis defects and G_1 arrest. Thus, the results from both centrosome protein perturbation and centrosome/centriole removal studies suggest that G_1 arrest could be a consequence of prior cytokinesis defects.

Does mitotic dysfunction cause G_1 arrest?

The central role of centrosomes in mitotic spindle organization and cytokinesis suggests that mitotic dysfunction leads to G_1 arrest. However, recent studies indicate this might not be the case. Microinjection of antibodies against PCM-1 into early interphase mouse zygotes prevented cell-cycle progression into S-phase [22]. In another study, over 20 proteins found at five distinct regions of the centrosome (**Figure 1**c,d) were individually targeted for depletion by siRNAs. Many showed no